Outcomes in Presyncope Patients: A Prospective Cohort Study

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Study objective: Presyncope is the sudden onset of a sense of impending loss of consciousness without losing consciousness (which differentiates it from syncope). Our goals are to determine the frequency of emergency department (ED) presyncope visits, management, 30-day outcomes, and emergency physicians' outcome prediction.

Methods: Our prospective study at 2 academic EDs included adults with presyncope and excluded patients with syncope, mental status changes, seizure, and significant trauma. We collected patient characteristics, ED management, cause (vasovagal, orthostatic, cardiac, or unknown) at the end of the ED visit, and 30-day outcomes. Serious outcomes included death, arrhythmia, myocardial infarction, structural heart disease, pulmonary embolism, and hemorrhage. We also collected physicians' confidence in assigning the cause and their prediction probability for 30-day serious outcomes.

Results: Presyncope constituted 0.5% of ED visits. We enrolled 881 patients: mean age 55.5 years, 55.9% women, and 4.7% hospitalized. Among 780 patients with 30-day follow-up, 40 (5.1%) experienced serious outcomes: death 0.3%, cardiovascular 3.1%, and noncardiac 1.8%. Of the 840 patients discharged home, 740 had follow-up data and 14 patients (1.9%) experienced serious outcomes after ED disposition. The area under the receiver operating characteristic curve for physician prediction probability was 0.58 (95% confidence interval 0.38 to 0.78). The incidence of serious outcomes was similar, whereas physician diagnostic confidence and prediction probability varied among the 4 causal groups.

Conclusion: Presyncope can be caused by serious underlying conditions. Emergency physicians had difficulty predicting patients at risk for serious outcomes after ED discharge. Future studies are needed to identify risk factors for serious outcomes after ED disposition. [Ann Emerg Med. 2015;65:268-276.]

Please see page 269 for the Editor's Capsule Summary of this article.

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INTRODUCTION

Background

Presyncope is the sudden onset of a sense of impending loss of consciousness. Unlike syncope, which is defined as a sudden transient loss of consciousness followed by spontaneous complete recovery, in presyncope there is no loss of consciousness.[1-3] During presyncope, the patient experiences 1 or more of the prodromal symptoms of syncope, such as lightheadedness or dizziness, nausea, sweating, weakness, or the visual symptoms for a short duration (a few seconds to a few minutes) but recovers before losing consciousness. It is the constellation of the above symptoms with the feeling of impending loss of consciousness that differentiates presyncope from other isolated nonspecific symptoms of dizziness or weakness. The use of the term *presyncope* is not uniform with some studies using the terminology *near-syncope* instead for the same condition.[2,3]

Importance

Presyncope as a condition is poorly studied. However, previous studies report that presyncope can be caused by serious underlying conditions such as arrhythmias that can lead to death and morbidity.[2,4,5] These serious underlying conditions, and the morbidity and mortality associated with them, constitute serious outcomes among presyncope patients. The majority of published studies combine the 2 conditions, syncope and presyncope, and report results.[6-11] Many experts and researchers, including the members of the European Society of Cardiology, are uncertain about the pathophysiology of presyncope and have concluded that literature evidence for syncope cannot necessarily be applied to presyncope patients.[1] None of the previous studies had prognosis of presyncope patients as their primary objective. Instead, they reported results of either subgroup analysis or presyncope among patients who had experienced syncope previously, or presyncope among patients with structural heart disease.[4,5,8,12,13] The conclusions of these studies are conflicting in regard to the prognosis of presyncope. With the exception of a small pilot study on

Editor's Capsule Summary

What is already known on this topic

The cause of presyncope and prognosis of emergency department (ED) presyncope patients is poorly defined.

What question this study addressed

This prospective observational study of 881 ED presyncope patients at 2 associated urban hospitals identifies serious outcomes diagnosed in the ED and within 30 days after discharge.

What this study adds to our knowledge

Five percent of presyncope patients had serious outcomes, two thirds of which were identified in the ED. The majority of the remaining patients can be safely discharged; however, it is difficult to identify the 1% to 2% of patients who will experience serious outcomes.

How this is relevant to clinical practice

Presyncope is not necessarily benign. Most presyncope patients can be discharged after evaluation, but care should be taken to ensure adequate follow-up because some patients will have late complications.

30-day outcomes, there are no previous studies on the burden caused by presyncope, the management and outcomes among presyncope patients.[2] Hence, we undertook this study on emergency department (ED) presyncope patients.

Goals of This Investigation

The goal of this study is to improve our understanding of presyncope by determining the frequency of ED visits because of presyncope, ED management of these patients, their 30-day outcomes, and emergency physicians' accuracy in predicting serious outcomes after ED disposition.

MATERIALS AND METHODS

Study Design and Setting

This was a prospective cohort study of adult presyncope patients presenting to the 2 academic EDs of The Ottawa Hospital, a large tertiary care center in Ottawa, Ontario, Canada, with more than 130,000 ED visits annually. We recruited patients during 23 months, from October 2010 to August 2012, during their ED visit.

Selection of Participants

We included consecutive adult patients (≥16 years) who experienced presyncope (as defined above) and presented to the ED within 24 hours of the event. We excluded patients who were previously enrolled in the study and those with the following exclusion criteria: loss of consciousness, change in their mental status from baseline after the event, obvious witnessed seizure, significant trauma requiring admission, presyncope after head trauma and those who could not provide proper history because of alcohol or illicit drug abuse or language barrier. We excluded patients with mental status changes because confirmation of presyncope would not be possible and because they were more likely to have experienced a cerebrovascular event than presyncope. We excluded patients who experienced significant trauma because if a serious outcome were to occur, it could be related to the trauma. Patients with head trauma can experience severe dizziness in the context of concussion, which could be mistaken for presyncope. Hence, we excluded patients who experienced head trauma preceding the symptoms. But we did include patients who experienced presyncope and then head injury. Because the study was observational, the Ottawa Health Science Network Research Ethics Board approved the protocol with the requirement of only verbal consent. We included patients regardless of whether they were admitted to the hospital or discharged home.

Methods of Measurement

On-duty emergency staff, including emergency physicians, screened consecutive patients presenting with syncope, presyncope, fainting, blackout, loss of consciousness, fall, collapse, seizure, dizziness, or light-headedness. Emergency physicians and emergency medicine residents under staff physician supervision applied the abovementioned inclusion and exclusion criteria to confirm eligibility and obtained verbal consent from eligible patients before inclusion in the study. We clearly specified that, for inclusion in the study, patients should have felt prodromal symptoms with a feeling of impending loss of consciousness and should not have lost consciousness. We collected patient demographics, event characteristics, medical history, investigations performed in the ED and their results, presumed cause of presyncope at the end of the ED visit, and patients' disposition. During the ED visit, the following variables were collected by the treating emergency physician: confirmation of the presyncope, application of inclusion and exclusion criteria, event details, medical history (atrial fibrillation/flutter or congestive heart failure), and physical examination details. Among patients with no serious outcome measures identified in the ED, we asked the treating physicians to provide their suspected cause and confidence in assigning the cause for the presyncope on an 11-point scale (0%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or 100%) from 0% to 100% (0%=least confidence and 100%=highest confidence) and their prediction probability for 30-day serious outcome occurrence on an 13-point scale (0%, 1%, 2%, 3%, 4%, 5%, 10%, 20%, 30%, 40%, 50%, 75%, or 100%), representing probabilities from 0% to 100%. ED investigations, disposition, and further outpatient testing were left to the treating physician's discretion. Chart review was

Serious outcome is defined as identification or occurrence of any of the following conditions related to presyncope within 30 days of the index visit.

a) Death: Because of presyncope or unknown causes.
b) Arrhythmias: Sustained (>30 seconds) or polymorphic ventricular tachycardia, sinus bradycardia less than 40 beats/min; sick sinus with alternating sinus bradycardia and tachycardia; sinus pause greater than 3 seconds; Mobitz type II atrioventricular heart block; complete heart block or junctional/idioventricular rhythm; alternating left and right bundle branch block, symptomatic (light-headedness/dizziness, hypotension—systolic BP <90 mm Hg) supraventricular tachycardia with rate greater than 100 beats/min; symptomatic atrial flutter or fibrillation with fast (>100 beats/min) or slow (RR interval greater than 3 seconds) ventricular rate; pacemaker or implantable cardioverter-defibrillator (ICD) malfunction with cardiac pauses, or an abnormal electrophysiologic study result (corrected sinus node recovery time >550 ms; His-ventricular intervals >100 ms; inducible ventricular tachycardia for greater than 30 seconds; polymorphic ventricular tachycardia/ventricular fibrillation in patients with Brugada or ventricular dysplasia or previous cardiac arrest; symptomatic supraventricular tachycardia, or Infra-Hisian block).
c) Myocardial infarction: Defined as a clinically important elevation in troponin or ECG change and must have been confirmed by the emergency physician or cardiologist or the most responsible physician.
d) Serious structural heart disease: (1) Aortic stenosis with valve area less than or equal to 1 cm^2; (2) hypertrophic cardiomyopathy with outflow tract obstruction; (3) left atrial myxoma or thrombus with outflow tract obstruction; or (4) pericardial effusion with ventricular wall motion abnormalities or pericardial; tamponade.
e) Aortic dissection: Confirmed by CT of the chest, transesophageal echocardiogram, MRI, or angiography.
f) Pulmonary embolism: Confirmed by ventilation-perfusion scan, CT scan of the chest, or angiography.
g) Severe pulmonary artery hypertension: Detected by cardiac catheterization or echocardiography, with a mean pulmonary arterial pressure greater than 30 mm Hg and was responsible for the presyncope.
h) Subarachnoid hemorrhage: Confirmed by CT/MRI of the brain with or without spinal fluid analysis by lumbar puncture.
i) Significant hemorrhage: Defined as presyncope associated with detected source of bleeding such as gastrointestinal bleeding, ruptured abdominal aortic aneurysm, or ectopic pregnancy that is clinically significant to cause presyncope in the opinion of the treating physician or that required transfusion.
j) Any other serious condition: Included conditions such as ectopic pregnancy, pneumothorax, and sepsis that will require treatment and will cause the patient to return to the ED if not detected.
k) Procedural interventions: Any interventions used to treat a cause of presyncope. The procedural interventions include pacemaker or defibrillator insertion, cardioversion for arrhythmias, surgery for valvular heart disease, dialysis for electrolyte abnormalities causing arrhythmia, chest tube/pigtail catheter insertion for pneumothorax or pleural effusion, or surgery for abdominal aortic aneurysm or ruptured spleen.

Figure 1. Definitions for serious outcomes.

used for abstraction of the following variables by the research nurses and coinvestigators (A.V., M.M.): demographics, arrival by ambulance, the reminder of the medical history, and results of ED investigations. We planned to have a second emergency physician conduct a blinded second assessment in a convenience sample of 10% of the study patients for interrater reliability.

We entered the data in SAS-based data entry screens (SAS Institute, Inc., Cary, NC). We improved the accuracy and completeness of data entry by using built-in range and logic checks, and by regular frequency reports.

Outcome Measures

We defined serious outcomes as identification or occurrence of any one of the following underlying conditions related to presyncope within 30 days of the index visit (Figure 1): myocardial infarction, arrhythmia, serious structural heart disease, pulmonary embolism, severe pulmonary hypertension, significant hemorrhage, subarachnoid hemorrhage, any other serious condition that required treatment, or death (because of presyncope or an unknown cause). A few researchers believe that presyncope is closely related to syncope.[2,5] Hence, our list of serious outcomes included all the conditions reported in previous syncope literature, with their standard definitions.[14] We avoided including soft outcomes such as nonsymptomatic sinus bradycardia. In addition, to capture any other serious conditions not identified in the syncope literature, we include a category "other serious conditions."

We assessed for serious outcome occurrence by reviewing the electronic medical records at the study hospital and conducting

a 30-day telephone follow-up. We specifically reviewed the following documents: ED records for the initial and return visits, hospital health records for inpatient and follow-up clinic notes, results of investigations performed both in the ED and on an outpatient basis, and death records. We conducted a 30-day telephone follow-up for enrolled patients to assess for serious outcome, with verbal consent obtained again at telephone contact. Final determination of serious outcome occurrence was confirmed by an adjudication committee of 2 blinded emergency physicians, with the third physician adjudicating in cases of disagreement.

Primary Data Analysis

We described continuous variables, using means with standard deviation (SD) and range; ordinal variables, using median with first and third quartiles; and categorical or dichotomous variables, using frequency and percentage. We constructed 95% confidence intervals (CIs) around proportions for our main outcomes, using large-sample or exact methods as appropriate. We conducted a sensitivity analysis for the incidence of serious outcomes among the study patients, with the assumptions that the patients lost to follow-up either experienced or did not experience serious outcomes within 30 days. We measured emergency physicians' ability to predict 30-day serious outcome by constructing a receiver operating characteristic curve and calculating the area under the curve. We used SAS (version 9.2) for data analysis.

The sample size was determined to estimate the primary outcome (proportion with serious outcomes within 30 days) with acceptable precision. We anticipated that between 3% and 7% of presyncope patients would experience serious outcomes within 30 days. Using a 2-sided CI for proportions, we calculated that a total of 850 patients would be adequate to limit the total width of the 95% CI to 2% to 4%.[15]

RESULTS

Characteristics of Study Subjects

There were a total of 263,218 ED visits at the study hospitals during the 23-month study period, of which 1,270 (0.5%) were due to presyncope. The flow of study patients is shown in Figure 2. After exclusion of double enrollments and refusals, 1,199 patients were eligible to be enrolled. Eight-hundred eighty-one presyncope patients (73.5% recruitment rate) were included in the study by 64 emergency physicians at the 2 study sites, with each physician recruiting a median of 13 patients (range 1 to 38). The characteristics of missed patients were similar to that of those who were enrolled in the study (mean age 58.5 years; 56% women). A second emergency physician blinded to the findings of the first physician assessed 62 patients (7%) for confirmation of the event as presyncope and eligibility to be included in the study. These interrater assessments were performed uniformly during the 23 months, and the κ between the 2 emergency physicians for confirmation of presyncope and inclusion in the study was 0.88 (95% CI 0.75 to 1.00).

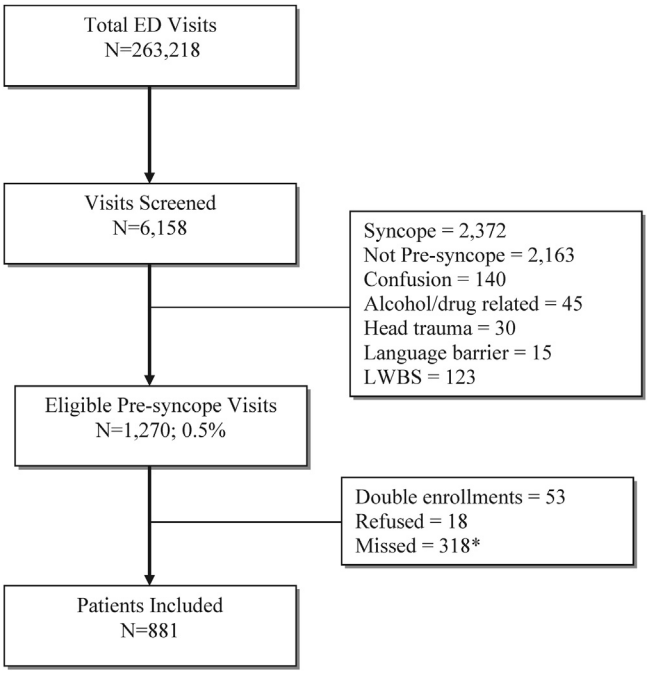

Figure 2. Patient flow. *The mean age of the missed patients was 58.5 years (SD=21.2 years; range 16 to 98 years) and 56% were women. The characteristics of missed patients were similar to that of those who were enrolled in the study. *LWBS*, Left without being seen.

The demographic and clinical characteristics of study patients are detailed in Table 1. Among 26 patients, a serious underlying condition causing the presyncope was evident in the ED. The treating emergency physician categorized the cause of presyncope for the remaining 855 patients, and 851 patients were assigned one of the 4 major causal categories: unknown, vasovagal, orthostatic hypotension, and cardiac. In the remaining 4 patients (0.5%), the physician was not able to differentiate the event between presyncope and seizure.

Main Results

The ED management and outcomes among the study patients are shown in Table 2. Ninety-two patients (10.4%; 95% CI 8.4% to 12.5%) were referred to consultants in the ED, and 41 patients (4.7%; 95% CI 3.3% to 6.0%) were admitted. Follow-up data for 30-day outcomes were available for 780 (88.5%) enrolled patients. Forty patients (5.1%; 95% CI 3.6% to 6.7%) experienced serious outcomes within 30 days of the index visit, and description of these patients is given in Appendix E1 (available online at http://www.annemergmed.com). The types of serious outcomes and their location of occurrence are shown in Table 3. There were 2 deaths (0.2%), both of which occurred outside the hospital and were due to unknown causes. Among the patients who experienced serious outcomes, 26 (3.3%; 95% CI 2.1% to 4.6%) experienced them in the ED, 1 patient experienced the outcome while hospitalized, and 13 patients (1.7%; 95% CI 0.6% to 2.8%) experienced them

Table 1. Demographic and clinical characteristics of enrolled ED presyncope patients.

Characteristics	Frequency (%) (N = 881)
Demographics	
Age, mean, SD, y	55.5 (21.2)
Range	16–103
Female patients	492 (55.9)
Arrival by ambulance	487 (55.3)
Witnessed presyncope	570 (64.7)
Medical history	
Hypertension	311 (35.3)
Diabetes	107 (12.2)
Coronary artery disease	114 (12.9)
Atrial fibrillation/flutter	78 (8.9)
Congestive heart failure	23 (2.61)
Valvular heart disease	25 (2.8)
Syncope	44 (5.0)
Classification of cause*	
Vasovagal	341 (40.1)
Orthostatic hypotension	105 (12.3)
Cardiac	59 (6.9)
Unknown	346 (40.7)

*Twenty-six patients had serious underlying conditions causing presyncope evident in the ED, and among 4 patients, the physician was unable to distinguish whether the patient experienced presyncope or seizure. The cause of presyncope for the remainder of the 851 patients is detailed above.

Table 2. Management and outcomes among 881 ED presyncope patients.

ED Management	Frequency (%) (N = 881)
ECG performed	806 (91.5)
Blood tests performed	730 (82.9)
Chest radiograph performed	220 (25.0)
CT of head performed	112 (12.7)
Specialist consultation in the ED	92 (10.4)
Admitted to the hospital	41 (4.7)
Outcomes*	**Frequency (%) (N = 780)**
Serious outcomes	40 (5.1)
Death	2 (0.3)†
Cardiovascular serious outcomes	24 (3.1)
Arrhythmias	18 (2.3)
Serious outcomes evident in the ED	26 (3.3)
Serious outcomes outside the hospital	13 (1.7)‡
Arrhythmias outside the hospital	9 (1.2)

CT, Computed tomography.
*Among the 881 enrolled patients, follow-up was achieved for 780 patients.
†Both deaths occurred outside the hospital. A description of 40 patients who experienced serious outcomes is detailed in Appendix E1 (available online at http://www.annemergmed.com).
‡A total of 40 patients experienced serious outcomes within 30 days of the index visit; 26 patients had these serious conditions detected during ED evaluation, 1 patient had the serious condition (cerebellar stroke) detected while admitted in the hospital, and the remaining 13 patients experienced the serious outcomes outside the hospital.

outside the hospital. We conducted a sensitivity analysis for the incidence of serious outcomes among the study patients, with the assumptions that all 101 patients lost to follow-up either experienced or did not experience serious outcomes within 30 days. We estimate that the incidence of serious outcomes under these 2 assumptions would be 16.0% (95% CI 13.6% to 18.4%) and 4.5% (95% CI 3.2% to 5.9%), respectively. At 30-day follow-up among the 4 patients with possible seizure, 1 received a diagnosis of complex partial seizure and the remaining 3 were confirmed as not having had a seizure. None of the 4 patients experienced serious outcomes.

Table 4 presents the demographic characteristics, management, and serious outcomes among 851 presyncope patients assigned to the 4 causal groups at the end of the ED visit by the emergency physician. The incidence of serious outcomes among patients in the 4 groups was as follows: 5 were in the vasovagal group (2 died from unknown cause, 2 patients experienced complete heart block, and 1 experienced myocardial infarction), 1 patient in the orthostatic hypotension group was found to have brain metastasis causing presyncopal symptoms, and 1 patient in the cardiac group experienced complete heart block. The incidence of serious outcomes was highest among patients with unknown cause (7 patients; 2.3%): 1 patient received a diagnosis of cerebellar stroke while admitted in the hospital, and 6 patients (2.0%) experienced serious outcomes outside the hospital. The serious outcomes among these 6 patients were as follows: 1 patient with orthostatic hypotension who needed inpatient treatment, 1 patient with pulmonary embolism, and 4 patients with arrhythmias (polymorphic ventricular tachycardia, sinus pause, complete heart block, and new-onset atrial fibrillation with high ventricular rate). Table 4 also presents the level of certainty for the physician attributing the cause to the episode of presyncope, as well as the physician-predicted likelihood that the patient would experience a serious outcome in the next 30 days. A graphic depiction of the physician scores for confidence in diagnosis of presyncope and prediction probability for 30-day serious outcomes is given in Appendices E2 and E3 (available online at http://www.annemergmed.com).

The time of serious outcomes occurrence among 13 of the 14 patients who experienced them after ED disposition is shown in Appendix E4 (available online at http://www.annemergmed.com). We were not able to ascertain the time for 1 study patient, who died within 30 days. Five of the 13 patients (38.5%), including 3 patients with arrhythmias, experienced serious outcome within the first 4 days, with the remainder evenly distributed throughout the next 26 days. Arrhythmia occurrence was also evenly distributed during the 30 days.

Figure 3 shows the receiver operating characteristic curve for emergency physicians' prediction probability for 30-day serious outcomes versus actual occurrence of serious outcomes among study patients. The area under the curve is 0.58 (95% CI 0.38 to 0.78).

LIMITATIONS

Our study does have some limitations. We recruited patients from 2 hospitals within the same city, and hence the results may not be generalizable.

Table 3. Frequency and location of occurrence of short-term serious adverse outcomes among 881 ED presyncope patients.

Serious Outcomes	Total, N=40	In ED, N=26	After ED Disposition, N=14*
Death	2	0	2
Cardiac presyncope	24	15	9
Supraventricular tachycardia	2	1	1
New/uncontrolled atrial fibrillation	6	6	0
Sinus node dysfunction	5	4	1
Complete atrioventricular block	4	0	4
Myocardial infarction	2	1	1
Ventricular arrhythmia	1	0	1
ICD malfunction	1	1	0
Pulmonary embolism	2	1	1
Serious structural heart disease	1	1	0
Other serious outcomes	14	11	3
Anemia†/significant hemorrhage	5	5	0
Sepsis	2	2	0
Others‡	7	4	3

ICD, Implantable Cardioverter Defibrillator.

*A total of 40 patients experienced serious outcomes within 30 days of the index visit; 26 patients had these serious conditions detected during ED evaluation, 1 patient had the serious condition (cerebellar stroke) detected while admitted in the hospital, and the remaining 13 patients experienced the serious outcomes outside the hospital.

†Requiring transfusions.

‡Other outcomes in ED included 1 patient with brain tumor, 1 with orthostatic hypotension who was admitted to the hospital, and 2 patients with acute abdominal conditions (appendicitis and iliopsoas abscess). Other outcomes after ED disposition included 1 patient with each of the following: cerebellar stroke, brain metastasis, and orthostatic hypotension.

Overall, 26.5% of eligible patients were not enrolled primarily because the physicians were overwhelmed with clinical duties and did not complete the physician data collection form. Though our recruitment rate of 73.5% is acceptable for a prospective study, it is possible that missed eligible patients were different from those who were recruited into the study. However, there were no systematic reasons for eligible patients being missed and not enrolled in the study. Therefore, we believe that our estimates are unlikely to be biased.

One of our objectives in the study was to perform interobserver assessment on 10% of study patients. We fell short of this objective and were able to achieve reliability assessment in only 7% of the study patients.

It is possible that the patients lost to follow-up experienced serious outcomes. It is unlikely that a significantly higher proportion of those lost to follow-up experienced serious outcomes to significantly change the results of our study. The majority of patients were discharged from the ED with no follow-up, and hence further confirmation of the cause of presyncope by a consultant is unavailable.

DISCUSSION

Our study is the largest prospective study conducted to date on presyncope, to our knowledge. Presyncope constitutes 0.5% of the ED visits at the study sites, and an important number of patients experience serious outcomes within 30 days. The majority of ED presyncope patients undergo testing in the ED. The prognosis of patients was the same regardless of the presumed cause of presyncope at the end of the ED visit. The incidence of serious outcomes was slightly higher in the first 4 days, after which it was evenly distributed. Emergency physicians had difficulty predicting serious outcomes that were not evident in the ED. We report the study results as per the Strengthening the Reporting of Observational Studies in Epidemiology guidelines for reporting observational studies.[16]

Table 4. Comparison of demographic characteristics, management, and outcomes for 851 presyncope patients classified into the 4 causal groups at the end of the ED visit.*

Characteristics	Vasovagal (N=341)	Orthostatic Hypotension (N=105)	Cardiac (N=59)	Unknown (N=346)
Age (SD), y	49.0 (20.8)	63.5 (21.6)	61.8 (17.9)	57.6 (20.4)
Range	16–103	19–94	19–89	18–97
ED management				
ECG performed	288 (84.5)	95 (90.5)	54 (91.5)	293 (84.7)
Blood tests performed	247 (72.4)	97 (92.4)	54 (91.5)	303 (87.6)
Chest radiograph performed	49 (14.4)	29 (27.6)	24 (40.7)	95 (27.5)
CT of head performed	24 (7.0)	15 (14.3)	4 (6.8)	61 (17.6)
Specialist consultation in the ED	7 (2.1)	10 (9.5)	19 (32.2)	35 (10.1)
Admitted to the hospital	3 (0.9)	6 (5.7)	4 (6.8)	11 (3.2)
Outcomes				
Successful follow-up	292 (85.6)	96 (91.4)	57 (96.6)	305 (88.1)
Serious outcomes after ED disposition	5 (1.7)	1 (1.0)	1 (1.7)	7 (2.3)
Physician certainty of cause of presyncope				
Median (Q1–Q3)	90 (70–90)	80 (70–90)	60 (50–80)	70 (40–90)
Physician prediction probability for 30-day serious outcome occurrence				
Median (Q1–Q3)	1 (1–2)	3 (1–5)	3 (2–10)	2 (1–5)

*Data are frequency (%) unless otherwise indicated. Twenty-six patients had serious underlying conditions causing presyncope evident in the ED, and among 4 patients, the physician was unable to distinguish whether the patient experienced presyncope or seizure. The 4 causal categories are the cause of presyncope at the end of the ED visit assigned by emergency physicians for the remainder of the 851 patients.

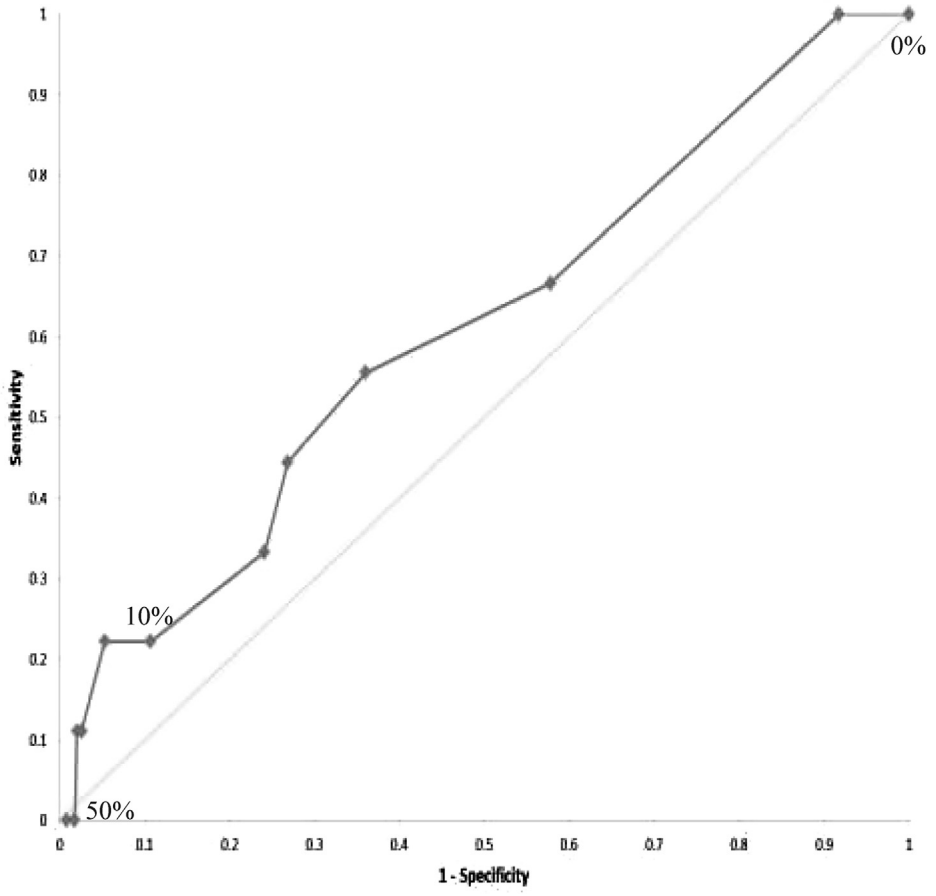

Figure 3. Receiver operating characteristic curves for emergency physicians' short-term serious outcome prediction among 840 presyncope patients discharged home from the ED. Area under the curve=0.58 (95% CI 0.38 to 0.78). The points along the receiver operating characteristic curve represent the prediction probability thresholds for 30-day serious outcomes: 0%, 1%, 2%, 3%, 4%, 5%, 10%, 20%, 30%, 40%, 50%, 75%, and 100%. There are 12 points on the receiver operating characteristic curve representing prediction probability thresholds of 0% to 75% because no patients in the study were assigned the 100% category.

Our study shows very good agreement among emergency physicians in ascertaining presyncope among patients.[17] Previously, studies have avoided examining presyncope because of concerns about proper patient identification.[18] In this study, we have shown that by clearly defining presyncope, it is feasible to achieve proper identification of presyncope patients. Our study of 5 patients with suspected cardiac presyncope had no ECG data. It is possible that the ECGs are missing or the physician was satisfied with reviewing the cardiac monitor or paramedic ECG strips.

Our study shows that presyncope, similar to syncope, can be caused by serious underlying conditions that can be life threatening in an important number of patients. The majority of the serious outcomes were cardiovascular, with arrhythmias being the most common. The results of the previously published studies are widely varied and confusing. At one extreme were studies reporting that presyncope can be dangerous, with one study reporting that any type of dizziness, including presyncope, can have a cardiovascular cause[12]; the second reporting that presyncope can be associated with arrhythmias[4]; and the third reporting that prognosis of presyncope is the same as syncope among patients with structural heart disease.[5] On the other extreme were 2 studies indicating that presyncope is a nonspecific symptom that is frequently associated with sinus rhythm[13] and presyncope is a low-risk predictor for serious outcome in older patients.[8] In all the above studies, the study population was not primarily presyncope patients. Because our study prospectively evaluated outcomes among presyncope patients, we can confirm that some patients do experience serious outcomes, including deaths and arrhythmias.

The incidence of serious outcomes in our study is lower than previously reported in a pilot study.[2] In this study, Grossman et al[2] reported that 20% of presyncope patients experienced serious outcomes. The authors of this study included conditions such as cortical stroke, carotid stenosis, and endarterectomy in the serious outcomes list. The serious outcomes "bradydysrhythmia treatment" and "alteration in dysrhythmics" were not clearly explained, and the study also reported a high proportion of patients with "sepsis" as serious outcome. With a large sample size, by including only relevant and clearly defined

conditions as serious outcomes, we believe that our results are more robust.

Among patients who experienced serious outcomes after ED disposition, all but 1 experienced it outside the hospital. This patient was admitted to the hospital because of mobility issues and later received a diagnosis by the neurology team of having experienced cerebellar stroke by magnetic resonance imaging (MRI) of the brain. Although we did not explore the reasons for admission among the study patients who were admitted to the hospital from the ED, our results clearly show that patients at risk for serious outcomes were not identified in the ED. The results are in stark contrast to those of the pilot study by Grossman et al,[2] which reported that none of their study patients experienced serious outcomes outside the hospital because all of them were admitted. This is most likely due to a huge difference in admission rates between the studies, with Grossman et al[2] reporting an admission rate of 49%, whereas the admission rate at our study hospitals was 4.7%. We previously reported a very low admission rate for ED syncope at one of the study hospitals.[19] The variations in admission rates are possibly related to the differences in the health care systems and the medicolegal implications in the 2 countries, with physicians in both countries defaulting to hospitalization or discharge home according to local preference. Although admitting a higher proportion of patients might not be the best use of health care dollars, our study clearly highlights the inability of physicians to identify those at risk for serious outcome.

The cause of presyncope was not identified in a substantial proportion of ED patients in our study. The patients who were assigned the cause of presyncope as vasovagal were younger; with lower proportions investigated or referred to consultants in the ED and admitted to the hospital from the ED. A higher proportion of patients in the cardiac group were referred for consultation in the ED. Serious outcomes occurred outside the hospital equally in all 4 groups and also occurred equally during the 30 days after the ED visit.

Our study shows that although the proportion of patients hospitalized is low, emergency physicians have difficulty in risk stratification of ED presyncope patients, as evidenced by a modest area under the curve. Future studies should identify risk factors for serious outcomes to aid the ED management and disposition decision.

In conclusion, our study found that presyncope is associated with serious underlying conditions in an important number of patients. Future studies should explore strategies for improved identification of patients at risk for serious outcomes.

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(continued from p. 255)

DIAGNOSIS:

Burkitt's lymphoma of the jaws. Diagnosis was established on histopathology. No other sites were involved by the tumor (Figure 3). The tumor regressed completely after initiation of a multiagent chemotherapy regimen.

Burkitt's lymphoma is a rapidly growing (doubling time 25.6 hours) malignant tumor caused by monoclonal proliferation of B-lymphocytes.[1] It can be classified as endemic (African type), sporadic, or AIDS related.[2] It is most commonly observed in children and young adults, with male predilection (male:female=2:1).[2] It accounts for 40% of lymphomas in children in western Europe and the United States.[3] The endemic type is highly associated with Epstein-Barr virus infection and predominantly affects craniofacial bones and kidneys.[2] The sporadic type more commonly presents with intra-abdominal involvement (bowel and intra-abdominal lymph nodes) but may manifest in the jaws.[3] Bone marrow and central nervous system involvement can occur. Because it can involve multiple sites, it is staged with the Ann Arbor or, more often, St Jude/Murphy system. Short-duration, high-intensity chemotherapy, combined with central nervous system prophylaxis, yields good survival in children and adults.[2-4]

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APPENDIX E1

Description of patients with short-term serious outcomes in the prospective ED presyncope study

No.	Age/Sex	Comments	Serious Outcome	Where Detected/ Occurred	Disposition
Short-term serious outcomes before ED disposition					
1	76 M	Previous ICD insertion, ventricular tachycardia detected on ED monitor. ICD not firing. Transferred to device clinic, adjustments were made.	Ventricular tachycardia as a result of ICD malfunction	ED	Home
2	46 F	Arthroscopic knee surgery 1 wk ago. Presented with shortness of breath, presyncope, and calf swelling. Pulmonary embolism was suspected, treated with LMWH and outpatient thrombosis follow-up arranged.	Pulmonary embolism confirmed by V/Q scan	ED	Home
3	63 M	Presyncope with new atrial flutter, increased ventricular rate, and hypotension. Treated in ED and prescribed Coumadin.	Arrhythmia (rapid atrial flutter)	ED	Home
4	86 M	Patient had loop monitor inserted before the index ED visit. Was interrogated; diagnosis of sinus pauses.	Arrhythmia (sinus pause)	ED	Admitted
5	54 F	Previous multiple abdominal surgeries for Crohn's disease, presented with fever. Diagnosis of sepsis.	Sepsis	ED	Admitted
6	87 M	Presyncope, generalized weakness and H/O colon cancer. CT abdomen showed right iliopsoas abscess.	Iliopsoas abscess	ED	Admitted
7	68 M	Palpitations, presyncope, and received diagnosis of SVT by EMS, resolved spontaneously.	Arrhythmia (SVT)	ED	Home
8	64 M	Patient had upper GI bleeding 2 days before the index visit and endoscopy showed ulcerated gastric mass. Returned with presyncope and ongoing upper GI bleeding. Received transfusion.	Significant hemorrhage	ED	Admitted
9	74 M	Patient with multiple medical conditions, with sudden-onset shortness of breath and presyncope. Received diagnosis of rapid atrial fibrillation; treated with intravenous metoprolol in ED.	Arrhythmia (rapid atrial fibrillation)	ED	Admitted
10	41 F	Presented with presyncope and shortness of breath, and found to be in profound bradycardia, with ECG showing intermittent junctional rhythm. Cardiology consulted, who discharged patient with outpatient echocardiogram and Holter.	Arrhythmia (sinus node dysfunction)	ED	Home
11	72 F	H/O cardiomyopathy, giant cell aortitis, and aortic valve replacement presented with profound bradycardia. Cardiology was consulted, who discharged the patient home with outpatient Holter. Holter showed sinus pauses with junctional escape rhythm.	Arrhythmia (sinus node dysfunction, junctional escape rhythm)	ED	Home
12	32 M	Presented with melena stools and received diagnosis of NSAID-induced GI bleed. Endoscopy showed esophageal and gastric varices with gastritis and duodenitis.	Significant hemorrhage	ED	Home
13	62 F	Presented with chest pain and presyncope. Received diagnosis of non–ST-segment elevation myocardial infarction.	Myocardial infarction	ED	Admitted
14	76 M	H/O myelodysplasia, in ED noted to have severe anemia and required transfusion.	Anemia requiring transfusion	ED	Home
15	34 M	Presented with chest pain and presyncope and was found to have new atrial fibrillation with rapid ventricular rate on ED monitor. Spontaneous reduction in ventricular rate, discharged with cardiology follow-up.	Arrhythmia (rapid atrial fibrillation)	ED	Home
16	79 M	Presented with fall. CT head performed in ED showed pituitary tumor. Admitted to neurosurgery for further management.	Pituitary tumor	ED	Admitted
17	80 F	H/O coronary artery disease with recent surgical valve repair. Found to be in rapid atrial fibrillation in ED and admitted for management of arrhythmia.	Arrhythmia (rapid atrial fibrillation)	ED	Admitted

Continued.

No.	Age/Sex	Comments	Serious Outcome	Where Detected/ Occurred	Disposition
18	55 M	Presyncope as a result of severe abdominal pain and received diagnosis of appendicitis. Admitted for surgical management.	Appendicitis	ED	Admitted
19	50 M	No cardiac history; presyncope while driving. Found to have symptomatic sinus pauses in ED monitor.	Arrhythmia (sinus pause)	ED	Admitted
20	54 F	No cardiac history. New-onset rapid atrial fibrillation identified through ED monitor. Treated with intravenous metoprolol, and cardiology follow-up organized.	Arrhythmia (rapid atrial fibrillation)	ED	Home
21	83 M	H/O coronary artery disease; arrived in ED with second episode of exertion presyncope on same day. Cardiology consulted, with diagnosis of aortic stenosis.	Structural heart disease (severe aortic stenosis)	ED	Admitted
22	91 F	No cardiac history; received diagnosis of orthostatic hypotension.	Orthostatic hypotension	ED	Admitted
23	93 F	Received diagnosis of anemia that required transfusion in the ED.	Anemia requiring transfusion	ED	Home
24	75 F	Received diagnosis of anemia that required transfusion in the ED.	Anemia requiring transfusion	ED	Admitted
25	77 M	Presented with presyncope and hypotension. Received diagnosis of sepsis in ED.	Sepsis	ED	Admitted
26	74 M	Multiple medical problems and presyncope; arrived to the ED by ambulance. Was observed to be in new-onset atrial fibrillation, with intermittent rapid ventricular rate on EMS monitor.	Arrhythmia (rapid atrial fibrillation)	ED	Admitted

Short-term serious outcomes after ED disposition

				Outpatient/Referral	Days After Index Visit
27	67 M	Presented with vertigo, not able to ambulate, and was referred to internal medicine for admission. Otorhinolaryngology and later neurology were consulted, who eventually made the final diagnosis.	Cerebellar stroke	Not applicable (patient was hospitalized)	1 day
28	76 M	Known Parkinson's disease. Presented with presyncope and fall. Discharged home with neurology follow-up. Returned with orthostatic hypotension and was admitted.	Orthostatic hypotension	Neurology*	1 day
29	75 M	Patient was discharged with outpatient cardiology follow-up and Holter, but returned within 3 days with complete heart block.	Arrhythmia (complete heart block)	Cardiology/Holter*	3 days
30	84 M	Known history of atrial fibrillation. Returned to ED with similar symptoms and received diagnosis of SVT with aberrancy.	Arrhythmia (SVT)	No referral	3 days
31	74 F	Was discharged home with cardiology follow-up. Returned 3 days later to ED with shortness of breath and received diagnosis of pulmonary embolism.	Pulmonary embolism	Cardiology†	3 days
32	88 M	Advised follow-up with PCP. Returned after 4 days with complete heart block.	Arrhythmia (complete heart block)	PCP*†	4 days
33	55 F	Presyncope was thought to be medication related; advised PCP follow-up. Returned to ED with complete heart block.	Arrhythmia (complete heart block)	PCP*†	11 days
34	85 M	Patient was discharged home with outpatient cardiology follow-up. Eleven days later returned to ED with syncope, admitted and monitored. Complete heart block and sinus pauses detected as inpatient on 13th day.	Arrhythmia (complete heart block)	Cardiology/Holter*	13 days
35	63 M	Urinary retention. Received diagnosis of vasovagal presyncope. Returned to ED with myocardial infarction	Myocardial infarction	Urology*†	17 days
37	57 F	Patient was discharged home at the index visit and advised to have PCP follow-up. Returned to ED with progressive symptoms of dizziness and ataxia and received diagnosis of cerebral metastasis.	Metastatic cancer	PCP*	18 days
38	59 F	History of breast cancer, not terminal. Died outside hospital, and cause not known.	Death	PCP	20 days
39	66 M	Discharged home with outpatient cardiology follow-up. On stress testing was found to have atrial fibrillation with pauses.	Arrhythmia (sinus pause)	Cardiology/Holter	27 days

Continued.

Short-term serious outcomes after ED disposition

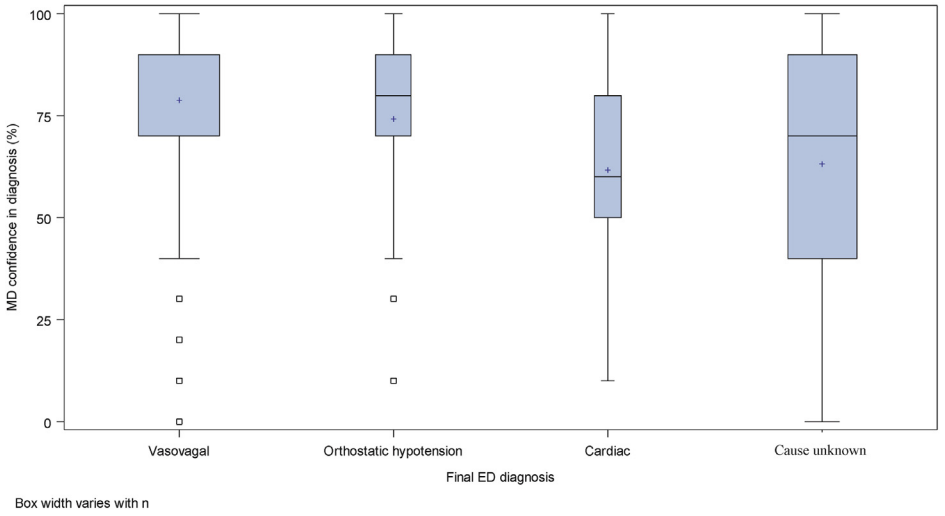
				Outpatient/Referral	Days After Index Visit
28	49 M	Was discharged with outpatient cardiology follow-up. Patient had several ED visits for syncope, and on the 30th day ventricular tachycardia was captured. Had ICD insertion shortly after.	Arrhythmia (sustained ventricular tachycardia)	Cardiology*	30 days
38	91 M	Patient from nursing home with dementia, stroke, but no terminal illness. Follow-up telephone call to the nursing home confirmed that patient died within 30 days. Correct date not known.	Death	No referral	Not available

ICD, Implantable cardioverter-defibrillator; *LMWH*, low molecular weight haparin; *V/Q*, ventilation perfusion scan; *H/O*, history of; *SVT*, supraventricular tachycardia; *GI*, gastrointestinal; *EMS*, emergency medical services; *NSAID*, nonsteroidal anti-inflammatory drug; *PCP*, primary care physician.
*Serious outcome occurred before follow-up.
†Not appropriate referral for the type of serious outcome.

APPENDIX E2

Physician confidence in final ED cause of presyncope

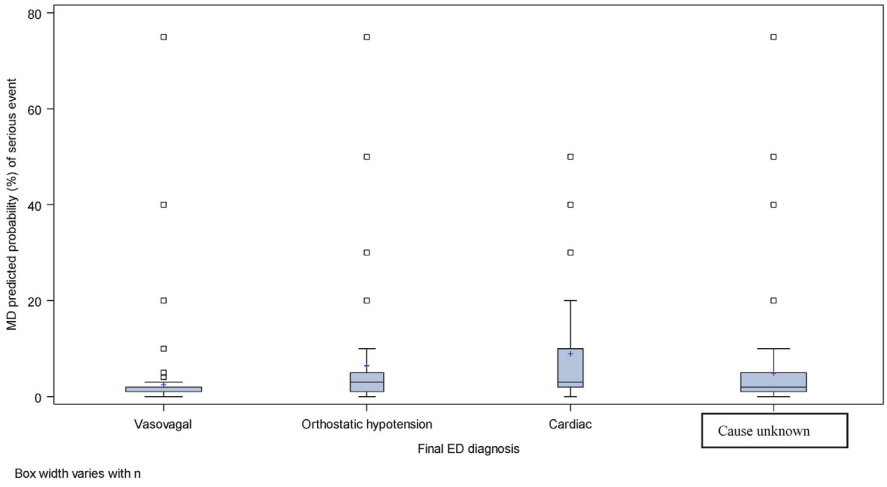
Twenty-six patients had serious underlying conditions causing presyncope evident in the ED, and among 4 patients, the physician was unable to distinguish whether the patient experienced presyncope or seizure. The 4 causal categories are the cause of the presyncope at the end of the ED visit assigned by emergency physicians for the remainder of the 851 patients. The mean is represented by the + sign within the box. The lower and upper limits of each box represent the first and third quartiles, respectively; the middle line represents the median. For vasovagal, the median is equal to the third (upper) quartile. Hence, the upper limit of the box for vasovagal presyncope represents the median.



APPENDIX E3

Physician prediction probability for 30-day serious outcome occurrence among the 4 causal categories

Twenty-six patients had serious underlying conditions causing presyncope evident in the ED, and among 4 patients, the physician was unable to distinguish whether the patient experienced presyncope or seizure. The 4 causal categories are the cause of the presyncope at the end of the ED visit assigned by emergency physicians for the remainder of the 851 patients.



APPENDIX E4

Timing of occurrence of short-term serious outcomes among presyncope patients after ED disposition

A total of 40 patients experienced serious outcomes within 30 days of the index visit; 26 patients had these serious conditions detected during ED evaluation; the time of occurrence of serious outcomes for the remaining 14 patients who experienced serious outcomes after ED disposition decision is show above (1 patient with cerebellar stroke detected while admitted in the hospital and 13 patients with serious outcomes outside the hospital).