# Syncope Evaluation in the Emergency Department Study (SEEDS)

# A Multidisciplinary Approach to Syncope Management

Win K. Shen, MD; Wyatt W. Decker, MD; Peter A. Smars, MD; Deepi G. Goyal, MD;
Ann E. Walker, MS; David O. Hodge, MS; Jane M. Trusty, RN; Karen M. Brekke, SC;
Arshad Jahangir, MD; Peter A. Brady, MD; Thomas M. Munger, MD;
Bernard J. Gersh, MB, ChB, DPhil; Stephen C. Hammill, MD; Robert L. Frye, MD

- **Background**—The primary aim and central hypothesis of the study are that a designated syncope unit in the emergency department improves diagnostic yield and reduces hospital admission for patients with syncope who are at intermediate risk for an adverse cardiovascular outcome.
- *Methods and Results*—In this prospective, randomized, single-center study, patients were randomly allocated to 2 treatment arms: syncope unit evaluation and standard care. The 2 groups were compared with  $\chi^2$  test for independence of categorical variables. Wilcoxon rank sum test was used for continuous variables. Survival was estimated with the Kaplan-Meier method. One hundred three consecutive patients (53 women; mean age  $64\pm17$  years) entered the study. Fifty-one patients were randomized to the syncope unit. For the syncope unit and standard care patients, the presumptive diagnosis was established in 34 (67%) and 5 (10%) patients (P < 0.001), respectively, hospital admission was required for 22 (43%) and 51 (98%) patients (P < 0.001), and total patient-hospital days were reduced from 140 to 64. Actuarial survival was 97% and 90% (P=0.30), and survival free from recurrent syncope was 88% and 89% (P=0.72) at 2 years for the syncope unit and standard care groups, respectively.
- *Conclusions*—The novel syncope unit designed for this study significantly improved diagnostic yield in the emergency department and reduced hospital admission and total length of hospital stay without affecting recurrent syncope and all-cause mortality among intermediate-risk patients. Observations from the present study provide benchmark data for improving patient care and effectively utilizing healthcare resources. (*Circulation.* 2004;110:3636-3645.)

Key Words: syncope ■ diagnosis ■ prognosis

**S** yncope is a common clinical problem. The estimated incidence of self-reported syncope is 6.2 per 1000 person-years in the Framingham study<sup>1</sup>; the cumulative incidence is approximately 3% to 6% over 10 years. In selected patient populations, the lifetime prevalence of syncope could reach almost 50%.<sup>2,3</sup> In the United States, 1 to 2 million patients are evaluated for syncope annually, 3% to 5% of emergency department visits are for syncope evaluation, and 1% to 6% of urgent hospital admissions are for syncope.<sup>3–7</sup>

# See p 3621

Medical resource utilization and expenses associated with syncope management are enormous.<sup>5,8–13</sup> These facts have led to the development of several diagnostic and triaging pathways<sup>12–16</sup> and clinical guidelines.<sup>2,17–19</sup> Despite these efforts, extensive broad-based evaluations are performed and hospital admissions are frequent for patients presenting to an emergency department for syncope evaluation.<sup>4,11,12,14,16,19–23</sup>

In the clinical policy statement from the American College of Emergency Physicians,<sup>19</sup> the general recommendations for admission after a syncopal event in patients without an established cause of syncope (diagnosis) were based primarily on prognostic predictors of mortality and morbidity at 6 to 12 months after the index event.<sup>17,22,24–27</sup> The rationale for admitting patients with syncope is that the physician's assessment has indicated a cardiac cause is likely and that in-hospital evaluation would positively affect outcome. Although a noncardiac cause of syncope is not uncommon in patients with a history of heart disease,<sup>17,22,28</sup> difficulty establishing the cause of syncope in the emergency department and concern about arrhythmias have led to a "liberal" policy toward hospital admission for syncope evaluation.<sup>19</sup> It is not known whether such a policy positively affects patient outcome.

The genesis of the present study was based on the central question whether an area designated for syncope evaluation

Reprint requests to Dr Win Shen, Mayo Clinic, 200 First St SW, Rochester, MN 55905. E-mail wshen@mayo.edu © 2004 American Heart Association, Inc.

Received October 7, 2004; revision received October 22, 2004; accepted October 22, 2004.

From the Division of Cardiovascular Diseases (W.K.S., J.M.T., K.M.B., A.J., P.A.B., T.M.M., B.J.G., S.C.H., R.L.F.), the Department of Emergency Medicine (W.W.D., P.A.S., D.G.G., A.E.W.), and the Division of Biostatistics (D.O.H.), Mayo Clinic, Rochester, Minn.

Presented in part at the 77th Scientific Sessions of the American Heart Association, New Orleans, La, November 7-10, 2004.

| High-Risk Group  | Intermediate-Risk Group  | Low-Risk Group  |  |  |
|--|--|---|--|--|
| Chest pain compatible with acute coronary syndrome<br>Signs of congestive heart failure<br>Moderate/severe valvular disease<br>History of ventricular arrhythmias<br>ECG/cardiac monitor findings of ischemia<br>Prolonged QTc (>500 ms)<br>Trifascicular block or pauses between 2 and 3<br>seconds | Age $\geq$ 50 y<br>With previous history of:<br>Coronary artery disease<br>Myocardial infarction<br>Congestive heart failure<br>Cardiomyopathy without active symptoms or signs on<br>cardiac medications<br>Bundle-branch block or Q wave without acute<br>changes on ECG | Age <50 y<br>With no previous history of:<br>Cardiovascular disease<br>Symptoms consistent with reflex-mediated or<br>vasovagal syncope<br>Normal cardiovascular examination<br>Normal ECG findings |  |  |
| Persistent sinus bradycardia between 40 and 60 bpm   | Family history of premature ( $<$ 50 y), unexplained sudden death  |   |  |  |
| Atrial fibrillation and nonsustained ventricular tachycardia without symptoms  | Symptoms not consistent with a reflex-mediated or vasovagal cause  |   |  |  |
| Cardiac devices (pacemaker or defibrillator) with dysfunction  | Cardiac devices without evidence of dysfunction<br>Physician's judgment that suspicion of cardiac<br>syncope is reasonable   |   |  |  |

TABLE 1. Emergency Department Risk Stratification of Patients With Syncope of Unknown Cause

in the emergency department observational unit ("syncope unit") could affect diagnostic yield and the rate of hospital admission for syncope patients with intermediate-risk profiles for a poor prognosis. We hypothesized that a syncope unit equipped with diagnostic resources that target common causes of syncope would improve the diagnostic yield and reduce the hospital admission rate compared with standard care (controls) at the conclusion of the emergency department evaluation. The reduction in hospital admission would not negatively affect patient outcome.

# Methods

# Definitions

### Syncope

A clinical manifestation of a temporary interruption of global cerebral perfusion is defined as a sudden and transient loss of consciousness and postural tone with spontaneous recovery without therapeutic intervention.

## **Risk Stratification**

Risks of cardiovascular morbidity and mortality in patients with unexplained syncope evaluated in the emergency department were classified as high, intermediate, and low. Risk factors were extrapolated from studies conducted in the emergency department<sup>4,20–22</sup> and from the position papers of the American College of Physicians<sup>17,18</sup> and subsequently updated from the policy statements of the American College of Emergency Physicians.<sup>19</sup>

At the initial emergency department evaluation, patients were stratified into 3 risk categories, as summarized in Table 1, depending on their symptoms, signs, and laboratory results and the clinical judgment of the emergency department physician. High-risk patients met the general guidelines<sup>19</sup> for recommendation of hospital admission (level B recommendation: moderate clinical certainty with class II strength of clinical evidence). Intermediate-risk patients met the general guidelines for "consideration" of hospital admission (level C recommendation: preliminary, inconclusive, or conflicting evidence, or, in the absence of any published data, based on panel consensus). Low-risk patients met the general guidelines that hospital admission is not required.

### Causes of Syncope

Difficulty with establishing the cause of syncope and the "presumptive" nature of the diagnosis have been well discussed.<sup>29,30</sup> The 10 most clinically relevant diagnostic categories, as previously defined,<sup>31</sup> were used in the present study. The 10 diagnostic categories were organized on the basis of pathophysiological mechanisms and therapeutic targets. These 10 diagnostic categories are as follows: (1) bradyarrhythmias, (2) ventricular tachyarrhythmias, (3) supraventricular tachyarrhythmias, (4) structural cardiac or cardiopulmonary disease, (5) neurocardiogenic or situational syncope, (6) carotid sinus hypersensitivity, (7) cerebrovascular disease, (8) orthostatic intolerance (including orthostatic hypotension, drug-induced syncope, or dehydration), (9) others (syncope-like conditions such as psychogenic syncope or hyperventilation), and (10) unknown. If a cause was uncertain, the final diagnosis was reached by the consensus of 2 physicians of the executive committee.

# Patient Selection and Inclusion and Exclusion Criteria

Residents (18 years or older) of Olmsted County, Minnesota, and the 14 surrounding counties who had syncope and presented to the emergency department at Saint Mary's Hospital, Rochester, between January 2000 and April 2004 and met the inclusion criteria were eligible for the study.

### Inclusion Criteria

The study included patients who presented with syncope of undetermined cause and who had intermediate risk for an adverse cardiovascular outcome. All patients met the general guidelines for consideration of hospital admission.<sup>19</sup>

### Exclusion Criteria

The following patients were excluded from the study: (1) patients with an identified cause of syncope during initial evaluation in the emergency department; (2) patients with any condition that would require hospital admission, including sustained bradycardia (40 bpm), pauses >3 seconds, type 2 second-degree or complete heart block, sustained supraventricular or ventricular tachycardia, confirmed acute coronary syndrome, stroke, severe hemorrhage, hemoglobin <10 g/dL, major trauma, or motor vehicle accident; and (3) patients with nonsyncope syndromes, including light-headedness, dizziness, vertigo, presyncope, coma, shock, spells, fall, metabolic syndrome, typical seizure presentation or recurrence of known seizure or other state of altered mentation, or cardiac arrest.

### Study Design, Randomization, and Follow-Up

The present study was a prospectively designed, single-center study conducted in a tertiary-care teaching hospital. A pilot study to assess feasibility was conducted in 1999. The randomized trial was commenced in 2000. During the study period, a total of 320 698 patients were seen in the medical unit of the emergency department; 3502 (1.1%) were evaluated for syncope, loss of consciousness, or



### **Figure 1.** Study design and randomization scheme. Numbers in parentheses are number of patients. ED indicates emergency department.

fainting. Screening of every patient, risk stratification, and attainment of informed consent were conducted by an emergency department staff physician (well informed of the study protocol and current practice guidelines) assisted by a trained nursing study coordinator. The average postresidency professional experience of the 21 emergency department physicians exceeded 10 years. After screening, 795 patients met the inclusion criteria, and 262 of them consented to the study. Of these 262 patients, 70 were stratified to the high-risk group, 103 to the intermediate-risk group, and 90 to the low-risk group. Patients in high-risk and low-risk groups were followed up in the study registry. The intermediate-risk group, 103 patients, underwent randomization and entered the study. The study protocol was divided into 3 phases, according to the time sequences discussed below (Figure 1).

#### Phase 1

Phase 1 occurred from the time of arrival in the emergency department to dismissal from the emergency department. Patients arriving at the emergency department with a complaint of syncope were placed on a cardiac monitor, given nasal oxygen, and administered intravenous support. A complete history was taken, a physical examination was performed, and an ECG was obtained according to practice guidelines.<sup>19</sup> Eligible patients who provided written informed consent were randomly assigned in a 1-to-1 ratio to undergo evaluation according to standard care or to be admitted to the syncope unit. This study followed the guidelines for informed consent of the Institutional Review Board of the Mayo Foundation.

After a patient was randomly assigned to standard care (standard care group), the emergency department physician was responsible for making the decision whether further evaluation was required and the setting in which the evaluation should occur. Because of a patient's risk profile and limited additional diagnostic and therapeutic resources in the emergency department, most patients in this group were admitted to the hospital for further management. Additional emergency department diagnostic testing was performed at the discretion of the emergency department physician on the basis of the patient's initial emergency department history, physical examination, and laboratory findings.

Patients randomly assigned to evaluation in the syncope unit (syncope unit group) received continuous cardiac monitoring in a designated area in the observational unit for up to 6 hours. An emergency department physician and a registered nurse staffed the syncope unit. Vital signs and orthostatic blood pressure were checked hourly by the nursing staff. Echocardiography was performed in the syncope unit in patients with abnormal cardiovascular examination findings or an abnormal ECG (Table 1). Tilt-table testing was recommended for patients who had a history of cardiac disease or an abnormal ECG who presented with symptoms atypical for cardiogenic syncope or for patients without known or confirmed cardiac disease presented with symptoms atypical for neurocardiogenic syncope or orthostatic intolerance. The table was tilted to 70° for up to 45 minutes.<sup>2,32</sup> Patients were restricted from oral intake for 6 hours before the test. All patients received intravenous fluid on arrival in the emergency department. Tilt-table testing was performed in the electrophysiological laboratory near the syncope unit. Carotid sinus massage was performed with patients both supine and upright in conjunction with tilt-table testing. Beat-to-beat heart rate and blood pressure were monitored continuously with a multichannel surface ECG (Pruka Engineering) and volume clamp photoplethysmography.<sup>33</sup>

An electrophysiological consultation was obtained while the patient was in the syncope unit when interpretation of the tilt-table test result or triaging recommendations were needed. If these tests and consultations could not be performed while the patient was in the syncope unit, arrangements for an outpatient consultation at the Heart Rhythm Center, tilt-table testing, or echocardiography could be made within 72 hours after dismissal from the syncope unit. An educational booklet on syncope (Medical Education and Research, Mayo Press, MC 2945) was given to each patient at the time of dismissal from the syncope unit. The collaborative effort of physician and nursing staff from the emergency department, cardiovascular diseases, and electrophysiology constituted the multidisciplinary approach in the syncope unit.

#### Phase 2

Phase 2 was the period from the time of dismissal from the emergency department to the conclusion of the evaluation of the index event, defined as either the time of hospital dismissal (for patients admitted for inpatient evaluation) or the time of dismissal from the outpatient Heart Rhythm Center (for patients dismissed from the emergency department and for whom an outpatient evaluation was recommended). For patients who did not require or who declined a Heart Rhythm Center evaluation or follow-up, the index event concluded with dismissal from the emergency department.

### Phase 3

Phase 3 was the period from the time of conclusion of the evaluation of the index event to follow-up. Follow-up was conducted by mail or telephone with a prospectively designed survey. The survey consisted of 15 questions pertaining to the patient's response to the

|                                      | All Patients | Syncope Unit | Standard Care |      |
|--------------------------------------|--------------|--------------|---------------|------|
| Characteristic                       | (n=103)      | (n=51)       | (n=52)        | Р    |
| Age, y, mean±SD                      | 64±17        | 64±17        | 65±17         | 0.61 |
| Gender, n (%)                        |              |              |               | 0.92 |
| Men                                  | 50 (49)      | 25 (49)      | 25 (48)       |      |
| Women                                | 53 (51)      | 26 (51)      | 27 (52)       |      |
| Past medical history, n (%)          |              |              |               |      |
| Previous syncope                     | 58 (56)      | 24 (47)      | 34 (65)       | 0.06 |
| Coronary artery disease              | 44 (43)      | 20 (39)      | 24 (46)       | 0.48 |
| Structural heart disease*            | 9 (9)        | 2 (4)        | 7 (14)        | 0.09 |
| Stroke                               | 5 (5)        | 2 (4)        | 3 (6)         | 0.51 |
| Hypertension                         | 52 (50)      | 27 (53)      | 25 (48)       | 0.62 |
| Diabetes mellitus                    | 15 (15)      | 7 (14)       | 8 (15)        | 0.81 |
| Comorbidity (CA, COPD, CRF)          | 68 (66)      | 33 (65)      | 35 (67)       | 0.78 |
| Index syncope history, n (%)         |              |              |               |      |
| Witnessed position and circumstances | 70 (68)      | 31 (61)      | 39 (75)       | 0.12 |
| Supine                               | 2 (2)        | 1 (2)        | 1 (2)         | 0.99 |
| Sitting                              | 51 (50)      | 24 (47)      | 27 (52)       | 0.62 |
| Exercise or exertion                 | 6 (6)        | 5 (10)       | 1 (2)         | 0.09 |
| Driving                              | 3 (3)        | 1 (2)        | 2 (4)         | 0.57 |
| Prodromal symptoms, n (%)            | 89 (86)      | 42 (82)      | 47 (90)       | 0.23 |
| Recovery, n (%)                      |              |              |               |      |
| Confusion                            | 30 (29)      | 14 (27)      | 16 (31)       | 0.71 |
| Incontinence                         | 8 (8)        | 3 (6)        | 5 (10)        | 0.48 |
| Injury                               | 34 (33)      | 17 (33)      | 17 (33)       | 0.94 |
| Abnormal ECG at presentation, n (%)  | 59 (57)      | 29 (57)      | 30 (58)       | 0.93 |
| Hemoglobin <11 g/dL, n (%)           | 17 (17)      | 7 (14)       | 10 (19)       | 0.45 |

TABLE 2. Demographic and Clinical Characteristics

CA indicates cancer; COPD, chronic obstructive pulmonary disease; and CRF, chronic renal failure (creatinine >2 mg/dL).

\*Structural heart disease included valvular heart disease, hypertrophic cardiomyopathy, nonischemic cardiomyopathy, and noncoronary cardiac surgery.

evaluation of the index event, subsequent recurrence of syncope or major medical event, and additional evaluation.

# **Study End Points and Data Management**

The primary objective of the trial was to assess the effectiveness of the syncope unit in the management of syncope of undermined cause in patients with an intermediate risk of an adverse outcome. This objective was accomplished by determining 2 primary end points, diagnostic yield and hospital admission rate, at the completion of the emergency department evaluation (phase 1) and comparing them between the 2 randomized arms of the study. Secondary aims, complementary to the primary objective of the study and critically relevant to clinical care, included (1) net diagnostic yield and length of hospital stay at the completion of the evaluation of the index event (phase 2) and (2) all-cause mortality and recurrent syncope during follow-up (phase 3).

The patient's clinical history, presenting symptoms, physical examination findings, laboratory test results, and subsequent follow-up data related to the index event were collected according to a prospectively designed database.<sup>31</sup> The database contains more than 200 fields, with 1000 elements categorized as demographics, history, diagnostic and therapeutic intervention, laboratory data, and follow-up.

### **Power Estimate and Statistics**

Although the diagnostic yield and admission rates from the syncope unit are unknown, we estimated that the cause of syncope in at least 60% of this population was noncardiac<sup>23,28</sup>; most (80% to 90%) noncardiac causes of syncope could be determined by additional risk stratification and noninvasive testing provided in the syncope unit,31,34,35 and most (>80%) patients with a noncardiac cause of syncope would not require hospital admission. On the basis of these estimates, we assumed diagnosis and admission rates of 50% at the conclusion of evaluation of the syncope unit group. With 100 patients in each group, we would detect a difference of 19.4% with 80% power or a difference of 22.3% with 90% power. After patients had been enrolled in the study for 4 years, poor recruitment resulted in a decision by the executive committee to stop the study. Given that rate of recruitment, it would have taken an additional 4 years to reach the goal of 100 patients per group. It was decided that although the study would not be powered to detect the original difference between the groups, it would still provide useful information to illustrate the benefit of the syncope unit. After review of the data, it was obvious that the difference in the 2 primary end points for the study was very large. The power to detect a significant difference in the diagnosis rates given the interim result was 0.99. The conditional power to detect a significant difference in hospitalization was equally large at 0.99. The syncope unit and standard care groups were compared with the Fisher exact test for categorical variables. A Wilcoxon rank sum test was used to compare continuous variables. Survival was estimated with the Kaplan-Meier method. A log-rank test was used to compare survival between the groups.

# Results

# Study Population

The demographic features of the study population are summarized in Table 2. No significant differences existed between the 2 study groups in past medical history variables or

|                                | Phas    | Phase 1 |        | Phase 2 |         | Accumulative |  |
|--------------------------------|---------|---------|--------|---------|---------|--------------|--|
| Diagnosis                      | SU      | SC      | SU     | SC      | SU      | SC           |  |
| Bradycardia                    | 1       | 0       | 0      | 2       | 1       | 2            |  |
| Ventricular tachycardia        | 1       | 0       | 0      | 3       | 1       | 3            |  |
| Supraventricular tachycardia   | 0       | 0       | 0      | 0       | 0       | 0            |  |
| Cardiopulmonary syncope        | 0       | 0       | 1*     | 1†      | 1       | 1            |  |
| Neurocardiogenic syncope       | 21      | 2       | 6 (2)  | 14      | 27      | 16           |  |
| Carotid sinus hypersensitivity | 6       | 0       | 0      | 1       | 6       | 1            |  |
| Orthostatic syncope/drugs      | 4       | 3       | 1 (1)  | 16      | 5       | 19           |  |
| Others                         | 1‡      | 0       | 0      | 0       | 1       | 0            |  |
| Undetermined syncope           | 17      | 47      | 9 (1)  | 10      | 9       | 10           |  |
| Total patients§                | 51      | 52      | 17 (4) | 47      | 51      | 52           |  |
| Diagnostic yield (%)           | 34 (67) | 5 (10)  |        |         | 42 (82) | 42 (81)      |  |
| Р                              | <0.001  |         |        |         | 0.84    |              |  |

 
 TABLE 3.
 Diagnosis During Phase 1 and Phase 2 Evaluation and Accumulative Diagnosis

SC indicates standard care group; SU, syncope unit group.

Values are number of patients. Values in parentheses along SU column under Phase 2 are number of evaluations completed in the outpatient Heart Rhythm Center.

\*One patient with pulmonary embolism.

†One patient with severe aortic stenosis.

‡One patient with psychogenic syncope.

§No. patients undergoing diagnostic evaluation.

any of the clinical features associated with syncope at the index event. For the 103 study patients, the mean age was  $64\pm17$  years; 51% were women. Of the total study group, 44 patients (43%) had a previous history of coronary artery disease, 9 (9%) had structural heart disease, and 59 (57%) had an abnormal ECG. Recurrent syncope was present in



Figure 2. A, Triaging outcomes for patients randomized to syncope unit. n indicates number of patients; HRC, Heart Rhythm Center. B, Triaging outcomes of patients randomized to standard care.

58 patients (56%); syncope occurred in the supine position in 2 patients (2%) and in the sitting position in 51 (50%); 14 patients (14%) had no prodromal event; and 34 (33%) suffered minor injuries. The mean follow-up was  $18\pm10$ months.

### **Primary End Points**

At the time of dismissal from the emergency department (completion of phase 1 of the study), the presumptive cause of syncope had been established for 34 patients (67%) in the syncope unit group and 5 (10%) in the standard care group (P<0.001). The diagnostic outcomes are summarized in Table 3. For the syncope unit group, neurocardiogenic syncope was the most frequent diagnosis (21 patients [41%]). Of the 2 patients with an arrhythmogenic cause, 1 had ventricular tachycardia and 1 had transient bradycardia. In the standard care group, 5 patients (10%) had the presumptive diagnosis established in the emergency department (2 had presumed vasovagal syncope, and 3 had dehydration). All 5 patients had recurrent symptoms while receiving standard care in the emergency department.

The triaging outcomes and the relation of hospital admission or outpatient evaluation with respect to the diagnosis are shown in Figures 2A and 2B. Hospital admissions were recommended for 22 patients (43%) in the syncope unit group and for 51 patients (98%) in the standard care group (P<0.001). In the standard care group, hospital admission was recommended for the 1 patient with presumed neurocardiogenic syncope and for 3 patients with presumed orthostatic intolerance related to medications or dehydration, because of an atypical clinical presentation (no warning or syncope in the sitting position), a history of coronary artery disease, or previous myocardial infarction.



**Figure 3.** Long-term clinical outcomes. A, Survival free from death; B, survival free from recurrence syncope; C, survival free from combined death and recurrent syncope. Continuous line represents syncope unit group; dotted line represents standard care group.

# **Secondary End Points: Phase 2**

Because of the study design and the risk profiles of the study patients, all admitted patients were under the care of a cardiology service at Saint Mary's Hospital.

### **Diagnostic Yield**

Of the 22 patients admitted to the hospital after evaluation in the syncope unit, 14 were admitted for further treatment after a diagnosis had been established in the syncope unit and 8 for further diagnostic evaluation when a cause could not be determined in the syncope unit (Figure 2A). Of the 14 patients with a presumptive diagnosis, 6 had neurocardiogenic syncope, 2 had orthostatic intolerance, 4 had carotid sinus hypersensitivity, 1 had bradycardia, and 1 had ventric-

### TABLE 4. Major Tests and Consultations

|                                | Phase 1 |     | Phase 2 |    | Accumulative |    |
|--------------------------------|---------|-----|---------|----|--------------|----|
| Resource Used                  | SU      | SC  | SU      | SC | SU           | SC |
| Tilt-table testing             | 33      |     | 4       | 13 | 37           | 13 |
| Echocardiography               | 32      | 9   | 8       | 25 | 40*          | 34 |
| Catheterization                | •••     | ••• | 2       | 2  | 2            | 2  |
| Electrophysiology study        | •••     | ••• | 3       | 4  | 3            | 4  |
| Electrophysiology consultation | 17      |     | 16†     | 16 | 33           | 16 |
| Neurological consultation      | 2       | 0   | 1       | 3  | 3            | 3  |
| Loop recorder                  |         |     | 2‡      | 4§ | 2            | 4  |

SC indicates standard care group; SU, syncope unit group.

Values are number of patients.

\*Five patients had echocardiography during phases 1 and 2.

†Of the 16 consultations, 14 were performed at the outpatient Heart Rhythm Center.

‡Implantable loop recorder.

§External loop recorder.

ular tachycardia. Of the 8 patients who were admitted without a diagnosis, 5 had a diagnosis established during hospital evaluation. Among the 29 patients dismissed after evaluation in the syncope unit, the diagnosis was established for 20 in the syncope unit. For the 9 patients without a diagnosis, outpatient management was thought to be appropriate. Of these 9 patients, 5 declined further outpatient evaluation, and 4 had follow-up at the Heart Rhythm Center; the diagnosis was established for 3 of these 4 patients. At the completion of phase 2, 42 patients (82%) in the syncope unit group had a presumptive diagnosis established. The specific diagnoses established during phase 1 and phase 2 and the accumulative diagnoses established at the conclusion of phase 2 are summarized in Table 3.

The triaging outcomes in the standard care group are shown in Figure 2B. The specific diagnoses established during phase 2 and the accumulative diagnoses are also summarized in Table 3. Accumulative diagnoses were established for 42 patients (81%) in the standard care group. At the conclusion of phase 2, the diagnosis was established for 82% of the syncope unit group and 81% of the standard care group (P=0.84).

| TABLE 5. | Primary | Therapeutic | Intervention |
|----------|---------|-------------|--------------|
|          |         |             |              |

|                 | Pha | Phase 1 |     | Phase 2 |    | Accumulative* |  |
|-----------------|-----|---------|-----|---------|----|---------------|--|
| Primary Therapy | SU  | SC      | SU  | SC      | SU | SC            |  |
| Medical         | 11  | 1       | 32† | 44      | 43 | 45            |  |
| Pacemaker       |     | •••     | 5   | 3       | 5  | 3             |  |
| Defibrillator   |     | •••     | 1   | 3       | 1  | 3             |  |
| Surgery/PTCA    |     | •••     | 2   | 1       | 2  | 1             |  |
| Total           | 11  | 1       | 31  | 51      | 51 | 52            |  |

SC indicates standard care group; SU, syncope unit group.

Values are number of patients.

\*Accumulative primary therapies were not significantly different between the 2 study groups.

†0f the 32 patients, 1 declined pacemaker for carotid sinus hypersensitivity, and 2 had an implantable loop recorder to further investigate the cause of syncope.

# Length of Hospital Stay

Among the 22 patients admitted to the hospital after evaluation in the syncope unit, the mean hospital stay was  $2.9\pm2.3$ days (range 1 to 10 days; median 2.0 days), and the total number of patient-hospital days was 64. Of the 22 patients who were admitted, 13 were dismissed within 48 hours. Among the 51 patients in the standard care group admitted to the hospital, the mean hospital stay was  $2.7\pm3.6$  days (range 0 to 22 days; median 2.0 days), and the total number of patient-hospital days was 140. Of these 51 patients, 38 were dismissed within 48 hours. Although the total number of patient-hospital days that resulted from the higher rate of admission was larger for the standard care group, the mean length of hospital stay was not significantly different between the 2 groups (P=0.18).

# **Secondary End Points: Phase 3**

The actuarial occurrence of all-cause mortality, recurrent syncope, and a combined total mortality and recurrent syncope are shown in Figure 3. Of the total study cohort, 5 died during follow-up: 2 in the syncope unit group (1 of stroke, 1 of pneumonia) and 3 in the standard care group (1 of stroke, 2 of cancer). The probability of survival at 2 years was 97% for the syncope unit group and 90% for the standard care group (P=0.30). Recurrent syncope was reported in 9 patients (4 in the syncope unit group). The probability of being free of a syncopal event at 2 years was 88% for the syncope unit group and 89% for the standard care group (P=0.72).

# **Other Outcome Variables**

Major diagnostic tests and consultations during phases 1 and 2 of the study are summarized in Table 4. Echocardiography was performed in 32 patients in the syncope unit group, and 3 of these patients were admitted to the hospital after it was determined their ejection fraction was <0.40. During phase 2, 14 of the 16 electrophysiological consultations for the syncope unit group were conducted in an outpatient setting at the Heart Rhythm Center.

Primary therapeutic interventions are summarized in Table 5. Primary therapy was defined as the treatment recommended to target the presumed cause of syncope. Medical therapy included conservative measures such as education for prevention of recurrent syncope, liberal fluid intake, salt intake, or any adjustment or initiation of drug therapy. For patients without an established diagnosis, a medical approach was usually taken for prevention of recurrence. A pacemaker was implanted in 5 patients in the syncope unit group: 1 for intermittent high-degree heart block and 4 for carotid sinus hypersensitivity. Three patients in the standard care group received pacemaker therapy: 2 for sinus node dysfunction with documented pauses and 1 for carotid sinus hypersensitivity. A defibrillator was implanted in 1 patient in the syncope unit group for spontaneous and inducible ventricular tachycardia and in 3 patients in the standard care group who had inducible ventricular tachyarrhythmias. Two patients in the syncope unit group were found to have severe coronary artery disease and possible transient ventricular arrhythmias causing syncope; 1 underwent coronary artery bypass surgery, and 1 had multivessel angioplasty and stent placement. One patient in the standard care group had severe aortic stenosis and underwent aortic valve replacement.

### **Adverse Events**

No adverse events were noted as a result of the study in any of the patients. No complications occurred related to random allocation to the 2 groups or to the testing modalities in the syncope unit.

# Discussion

# Major Findings

In this prospectively designed, single-center, randomized study, the effectiveness of a designated syncope unit in the emergency department was examined for patients who presented with unexplained syncope with intermediate risk of increased cardiovascular mortality and morbidity. The main findings are as follows: (1) There was a significantly higher diagnostic yield and a decreased hospital admission rate for patients in the syncope unit group compared with those in the standard care group. (2) At the conclusion of the evaluation of the index event, the net diagnostic yield was similar for the 2 randomized groups. The total length of patient-hospital days was reduced by >50% for patients in the syncope unit group. (3) The reduced total length of hospital stay was related directly to the decreased hospital admission rate, whereas the mean length of stay was similar for the 2 study groups. (4) Follow-up outcomes for all-cause mortality and recurrent syncope were also similar for the 2 groups. These observations suggest that a syncope unit in the emergency department, with a multidisciplinary effort and appropriate resources, provides effective and efficient care for selected patients. The information from the present single-center study could provide benchmark data to assess whether this approach could be adopted in a more broad-based community hospital setting.

## Syncope Unit Design

The high incidence, multiple causes, and sporadic nature of syncope in a highly heterogeneous population make the diagnosis of syncope difficult. Several diagnostic protocols, pathways, and guidelines have been proposed to streamline the evaluation of syncope in both inpatient and outpatient settings.<sup>2,12-14,16-18,36-38</sup> Despite these efforts, there is no uniform strategy. Clinical evidence for effective triage of patients in the emergency department who have syncope is limited.<sup>19</sup> Although the diagnostic tools for evaluating syncope continue to evolve and improve,<sup>35</sup> it is not known whether any of these diagnostic modalities could be used in the emergency department and how clinical outcomes may be influenced.

The design of the syncope unit in the present study was based on the common causes of syncope and the available diagnostic tools suitable for emergency department practice. Multidisciplinary collaboration is not only useful but needed for the evaluation in the emergency department of patients with syncope, as evidenced by the numerous causes of syncope that require the attention of emergency department physicians, cardiologists, and electrophysiologists who share expertise in triage, diagnosis, therapy, and education. A neurological evaluation was not required in the present study because neurological conditions such as seizure and stroke, which are differentiated from syncope mainly by clinical presentation,<sup>2</sup> were excluded by the study design.

Continuous cardiac monitoring for up to 6 hours in the syncope unit may allow transient arrhythmias to be documented. During evaluation in the syncope unit, an arrhythmogenic cause was documented in 2 patients (4%). Although the diagnostic yield was seemingly low, and an inpatient evaluation would likely have documented an arrhythmogenic cause, earlier diagnosis could result in expedited inpatient management of this small segment of the population.

The 12% prevalence of carotid sinus hypersensitivity among the patients in the syncope unit group is important. Although the prevalence of carotid sinus hypersensitivity has not been determined precisely and is expected to be population dependent,<sup>39–41</sup> physicians should be aware that this condition is not uncommon among the elderly population. Results of the present study demonstrate that the diagnosis can be made in the emergency department when carotid sinus massage is performed in conjunction with continuous beatto-beat heart rate and blood pressure monitoring in patients both supine and upright, as required in this study.

Results from tilt-table testing highlighted that for patients with an intermediate-risk profile for a poor cardiovascular prognosis, the most common cause of syncope is neurocardiogenic. This observation is similar to findings from a previous study in patients with suspected or confirmed heart disease.28 Echocardiography provided quantitative information about cardiac function and demonstrated an ejection fraction <0.40 in 3 patients who then were admitted to the hospital. The information on normal cardiac structure and function was reassuring because most of the patients were triaged to outpatient evaluation. Electrophysiology consultation provided expertise in the interpretation of test results and contributed to the overall management of patients. Although the differential value of each component in the syncope unit could not be determined precisely, the combination of these resources increased diagnostic yield from 10% for patients in the standard care group to 67% for those in the syncope unit group. Our observations provide compelling evidence that when additional time and appropriate resources are provided in a syncope unit, the diagnostic yield increases, and the hospital admission rate decreases significantly.

# Syncope Unit Outcome

The effect of the syncope unit was assessed by clinical outcomes from 3 phases of this study: emergency department (phase 1), hospital or outpatient clinic (phase 2), and follow-up (phase 3). Despite efforts to develop a risk score,<sup>16</sup> diagnostic pathways,<sup>12,13,36,38</sup> and practice guidelines,<sup>19</sup> the hospital admission rate (for all patients presenting to an emergency department with a wide range of risk profiles and not limited to intermediate-risk patients) is high, ranging from 26% to 60%.<sup>4,14,20,23,38,42</sup> The high hospital admission rate for patients in the standard care group clearly reflects the difficulty in ascertaining which patients with syncope are at risk for an adverse event. The high diagnostic yield among patients in the syncope unit group clearly led to evidence-

based triaging and a reduced hospital admission rate. In the present study, the emergency department physicians and staff had direct access to the Heart Rhythm Center to arrange outpatient follow-up evaluation when indicated, because we recognized the presumptive feature of the diagnosis of syn-cope<sup>29,30</sup> and the possibility of a cardiac cause despite a positive response to tilt-table testing and carotid sinus massage.<sup>31,43</sup> This continuity of care between the emergency department and Heart Rhythm Center likely contributed to the lower admission rate and optimized care of patients.

All patients in the present study who required admission were admitted to a cardiology service because of the patients' risk profiles with an increased propensity for an adverse cardiac outcome. The accumulative diagnostic yield at the conclusion of phase 2 evaluation was comparable for the 2 study groups. Of the 42 patients in the syncope group who eventually had a diagnosis, the diagnosis was made in the syncope unit in 34 (81%). In the present study, the accumulative diagnoses of neurocardiogenic syncope and carotid sinus hypersensitivity were higher and orthostatic intolerance. drug-related syncope, and dehydration were lower for the syncope unit group than for the standard care group. Potentially, these differences could be explained by our practice patterns, readily available tilt-table testing, carotid sinus massage, electrophysiological consultation in the syncope unit, and the routine care of control patients by the cardiology service after admission. The in-hospital cardiology care of the standard care group could have reduced the need for further electrophysiological consultation and testing after risk profiles had been reviewed. The frequent diagnosis of orthostatic intolerance and the high frequency of a short hospital stay (<48 hours) for the standard care group provide further evidence that inpatient evaluation may not be necessary in a large portion of patients with syncope who are at intermediate risk for an adverse cardiovascular outcome.

The mean number of hospital days was similar for the 2 groups. For the syncope unit group, the longer hospital evaluation anticipated for patients without a diagnosis may have been offset by a more expedited therapeutic intervention for those with the diagnosis established in the syncope unit. For the standard care group, the anticipated longer evaluation and treatment may have been offset by the large number of patients with orthostatic intolerance and a short hospital stay who did not require in-hospital management. The overall decrease in total patient-hospital days for the syncope unit group, primarily the result of reduced admission, may have important ramifications for healthcare utilization and expenditures.

The effect of in-hospital care on clinical outcomes after syncope has been evaluated in the emergency department is not known.<sup>19</sup> Follow-up outcomes of all-cause mortality and recurrent syncope were not significantly different for the 2 groups. Although the present study was underpowered to address these secondary end points adequately, the comparable event rates for patients in the syncope unit group who received outpatient care and for patients in the standard care group, most of whom were admitted to the hospital, were reassuring. The decreased hospital admission rate and the total length of patient-hospital days did not adversely affect patient outcome during follow-up.

# **Study Limitations**

One of the potential limitations of this study could be the unblinded study design. Confounding factors such as the patient's preference for inpatient or outpatient evaluation and the physician's effort to make the diagnosis in the emergency department could be influenced by the randomization. We believe that such influences were minimal, because the improved diagnostic rates clearly were attributed to the resources available in the syncope unit, and admission was recommended according to current guidelines. Relevant clinical outcomes such as mortality and recurrent syncope were not likely affected by the unblinded design of the study. To minimize potential patient selection bias at a tertiary-care medical center, study cohorts were limited to patients from Olmsted County and the 14 surrounding counties. Why a large number of patients declined to participate in the present study could not be determined precisely; however, the complex interactions between conventional practice and medical economics likely affected the recruitment rate. Some patients were reluctant to enter the randomization because of concern about delays for in-hospital evaluation and a larger insurance deductible if hospital admission was not required after evaluation in the emergency department. These reasons for refusing to participate in the study were not risk dependent, and the possibility of their affecting an accurate representation of the intermediate-risk population could not be excluded. The absence of cost-benefit analysis is a major limitation. It is possible that a syncope unit may not be useful for most hospitals depending on costs of staffing, training, and prolonged patient stay in the emergency department. We appreciate that the resources available in our syncope unit are likely suitable for large referral centers, but the model can easily be adapted to any emergency department that has space for an observational unit, has the necessary equipment, and has cardiology consultation available. With tilt-table testing and electrophysiological support widely available, these resources conceivably could be available in most community hospitals.

The present study was not powered to assess the secondary end points. Because of the low event rates, a larger sample size will be needed to assess mortality and recurrent syncope. The differential impact of the various resources on the primary end points of the study could not be assessed. Future studies should consider protocols to establish the most effective syncope observational unit.

# **Clinical Significance and Potential Impact**

This study provides the first evidence of the effectiveness of a designated syncope unit in an emergency department for the evaluation of patients with intermediate-risk profiles. Similarly equipped observation units are widely used nationwide because they have been shown to be safe and cost-effective in the management of patients with intermediate-risk for unstable angina.<sup>44</sup> Our protocol had a similar design, with a period of cardiac monitoring followed by a diagnostic or prognostic test. Of the present intermediate-risk patient population, 39% arrived at the emergency department with unexplained syn-

cope (Figure 1). Multidisciplinary collaboration in the syncope unit provided efficient and effective evaluation and triage of the patients. With growing awareness of rapidly rising healthcare expenditures, the significant decrease in total patient-hospital days after evaluation in the syncope unit warrants a detailed cost analysis to optimize the costeffectiveness of this novel model for clinical practice in an emergency department.

### Acknowledgments

This study was supported by the Mayo Foundation and an investigator-initiated research grant from Medtronic Incorporated (Dr Shen). Dr Shen receives support from the National Institutes of Health (P50NS 32352 and R01HL 70302), and Dr Jahangir receives support from the National Institute on Aging (AG21201), the American Heart Association (0230133N), and the Mayo Foundation (CR75). We gratefully acknowledge the assistance of Kathy Budensiek and Kate Stai in the preparation of the manuscript.

### References

- Soteriades ES, Evans JC, Larson MG, Chen MH, Chen L, Benjamin EJ, Levy D. Incidence and prognosis of syncope. *N Engl J Med.* 2002;347: 878–885.
- Brignole M, Alboni P, Benditt D, Bergfeldt L, Blanc JJ, Bloch Thomsen PE, van Dijk JG, Fitzpatrick A, Hohnloser S, Janousek J, Kapoor W, Kenny RA, Kulakowski P, Moya A, Raviele A, Sutton R, Theodorakis G, Wieling W, Task Force on Syncope, European Society of Cardiology. Guidelines on management (diagnosis and treatment) of syncope. *Eur Heart J.* 2001;22:1256–1306.
- Kapoor WN. Evaluation and outcome of patients with syncope. *Med* (*Balt*). 1990;69:160–175.
- Day SC, Cook EF, Funkenstein H, Goldman L. Evaluation and outcome of emergency room patients with transient loss of consciousness. *Am J Med.* 1982;73:15–23.
- Kapoor WN, Karpf M, Wieand S, Peterson JR, Levey GS. A prospective evaluation and follow-up of patients with syncope. *N Engl J Med.* 1983; 309:197–204.
- Manolis AS, Linzer M, Salem D, Estes NA III. Syncope: current diagnostic evaluation and management. Ann Intern Med. 1990;112:850–863.
- 7. Manolis AS. The clinical spectrum and diagnosis of syncope. *Herz*. 1993;18:143–154.
- Calkins H, Byrne M, el-Atassi R, Kalbfleisch S, Langberg JJ, Morady F. The economic burden of unrecognized vasodepressor syncope. *Am J Med.* 1993;95:473–479.
- Olshansky B. Syncope: overview and approach to management. In: Grubb BP, Olshansky B, eds. Syncope: Mechanisms and Management. Armonk, NY: Futura Publishing; 1998:15–71.
- Krahn AD, Klein GJ, Yee R, Manda V. The high cost of syncope: cost implications of a new insertable loop recorder in the investigation of recurrent syncope. *Am Heart J.* 1999;137:870–877.
- Pires LA, Ganji JR, Jarandila R, Steele R. Diagnostic patterns and temporal trends in the evaluation of adult patients hospitalized with syncope. Arch Intern Med. 2001;161:1889–1895.
- Del Greco M, Cozzio S, Scillieri M, Caprari F, Scivales A, Disertori M, The ECSIT study (Epidemiology and Costs of Syncope in Trento). Diagnostic pathway of syncope and analysis of the impact of guidelines in a district general hospital. *Ital Heart J*. 2003;4:99–106.
- Farwell DJ, Sulke AN. Does the use of a syncope diagnostic protocol improve the investigation and management of syncope? *Heart*. 2004;90: 52–58.
- Ammirati F, Colivicchi F, Santini M, the OESIL 2 study (Osservatorio Epidemiologico della Sincope nel Lazio). Diagnosing syncope in clinical practice: implementation of a simplified diagnostic algorithm in a multicentre prospective trial. *Eur Heart J*. 2000;21:935–940.
- Cunningham R, Mikhail MG. Management of patients with syncope and cardiac arrhythmias in an emergency department observation unit. *Emerg Med Clin North Am.* 2001;19:105–121.
- Colivicchi F, Ammirati F, Melina D, Guido V, Imperoli G, Santini M, OESIL (Osservatorio Epidemiologico sulla Sincope nel Lazio) Study Investigators. Development and prospective validation of a risk stratifi-

cation system for patients with syncope in the emergency department: the OESIL risk score. *Eur Heart J.* 2003;24:811–819.

- Linzer M, Yang EH, Estes NA III, Wang P, Vorperian VR, Kapoor WN, Clinical Efficacy Assessment Project of the American College of Physicians. Diagnosing syncope, part 1: value of history, physical examination, and electrocardiography. *Ann Intern Med.* 1997;126:989–996.
- Linzer M, Yang EH, Estes NA III, Wang P, Vorperian VR, Kapoor WN, Clinical Efficacy Assessment Project of the American College of Physicians. Diagnosing syncope, part 2: unexplained syncope. *Ann Intern Med.* 1997;127:76–86.
- American College of Emergency Physicians. Clinical policy: critical issues in the evaluation and management of patients presenting with syncope. *Ann Emerg Med.* 2001;37:771–776.
- Eagle KA, Black HR. The impact of diagnostic tests in evaluating patients with syncope. *Yale J Biol Med.* 1983;56:1–8.
- Lee RT, Cook EF, Day SC, Goldman L. Long-term survival after transient loss of consciousness. J Gen Intern Med. 1988;3:337–343.
- Martin TP, Hanusa BH, Kapoor WN. Risk stratification of patients with syncope. Ann Emerg Med. 1997;29:459–466.
- 23. Elesber AA, Decker WW, Smars PA, Hodge DO, Shen WK. Impact of the application of the American College of Emergency Physicians recommendations for the admission of syncopal patients on a retrospectively studied population presenting to the emergency department. *Am Heart J*. In press.
- Kapoor WN, Hanusa BH. Is syncope a risk factor for poor outcomes? Comparison of patients with and without syncope. *Am J Med.* 1996;100: 646–655.
- Middlekauff HR, Stevenson WG, Stevenson LW, Saxon LA. Syncope in advanced heart failure: high risk of sudden death regardless of origin of syncope. J Am Coll Cardiol. 1993;21:110–116.
- Getchell WS, Larsen GC, Morris CD, McAnulty JH. Epidemiology of syncope in hospitalized patients. J Gen Intern Med. 1999;14:677–687.
- 27. Crane SD. Risk stratification of patients with syncope in an accident and emergency department. *Emerg Med J.* 2002;19:23–27.
- Alboni P, Brignole M, Menozzi C, Raviele A, Del Rosso A, Dinelli M, Solano A, Bottoni N. Diagnostic value of history in patients with syncope with or without heart disease. J Am Coll Cardiol. 2001;37:1921–1928.
- Klein GJ, Gersh BJ, Yee R. Electrophysiological testing: the final court of appeal for diagnosis of syncope? *Circulation*. 1995;92:1332–1335.
- Shen WK. Role of invasive electrophysiologic testing in the evaluation and management of syncope. *Card Electrophysiol Rev.* 1997;4:478–485.
- Chen LY, Gersh BJ, Hodge DO, Wieling W, Hammill SC, Shen WK. Prevalence and clinical outcomes of patients with multiple potential causes of syncope. *Mayo Clin Proc.* 2003;78:414–420.

- Fenton AM, Hammill SC, Rea RF, Low PA, Shen WK. Vasovagal syncope. Ann Intern Med. 2000;133:714–725.
- 33. Shen WK, Low PA, Rea RF, Lohse CM, Hodge DO, Hammill SC. Distinct hemodynamic profiles in patients with vasovagal syncope: a heterogeneous population. J Am Coll Cardiol. 2000;35:1470–1477.
- Calkins H, Shyr Y, Frumin H, Schork A, Morady F. The value of the clinical history in the differentiation of syncope due to ventricular tachycardia, atrioventricular block, and neurocardiogenic syncope. *Am J Med.* 1995;98:365–373.
- Kapoor WN. Current evaluation and management of syncope. *Circulation*. 2002;106:1606–1609.
- Croci F, Brignole M, Alboni P, Menozzi C, Raviele A, Del Rosso A, Dinelli M, Solano A, Bottoni N, Donateo P. The application of a standardized strategy of evaluation in patients with syncope referred to three syncope units. *Europace*. 2002;4:351–355.
- 37. Disertori M, Brignole M, Menozzi C, Raviele A, Rizzon P, Santini M, Proclemer A, Tomasi C, Rossillo A, Taddei F, Scivales A, Migliorini R, De Santo T, Evaluation of Guidelines in Syncope Study Group. Management of patients with syncope referred urgently to general hospitals. *Europace*. 2003;5:283–291.
- 38. Brignole M, Disertori M, Menozzi C, Raviele A, Alboni P, Pitzalis MV, Delise P, Puggioni E, Del Greco M, Malavasi V, Lunati M, Pepe M, Fabrizi D, Evaluation of Guidelines in Syncope Study Group. Management of syncope referred urgently to general hospitals with and without syncope units. *Europace*. 2003;5:293–298.
- Brignole M, Menozzi C, Lolli G, Bottoni N, Gaggioli G. Long-term outcome of paced and nonpaced patients with severe carotid sinus syndrome. *Am J Cardiol.* 1992;69:1039–1043.
- Richardson DA, Bexton RS, Shaw FE, Kenny RA. Prevalence of cardioinhibitory carotid sinus hypersensitivity in patients 50 years or over presenting to the accident and emergency department with "unexplained" or "recurrent" falls. *Pacing Clin Electrophysiol*. 1997;20(pt 2):820–823.
- Kenny RA. Syncope in the elderly: diagnosis, evaluation, and treatment. J Cardiovasc Electrophysiol. 2003;14(suppl):S74–S77.
- Schillinger M, Domanovits H, Mullner M, Herkner H, Laggner AN. Admission for syncope: evaluation, cost and prognosis. *Wien Klin Wochenschr.* 2000;112:835–841.
- Benditt DG, Ferguson DW, Grubb BP, Kapoor WN, Kugler J, Lerman BB, Maloney JD, Raviele A, Ross B, Sutton R, Wolk MJ, Wood DL, American College of Cardiology. Tilt table testing for assessing syncope. J Am Coll Cardiol. 1996;28:263–275.
- 44. Farkouh ME, Smars PA, Reeder GS, Zinsmeister AR, Evans RW, Meloy TD, Kopecky SL, Allen M, Allison TG, Gibbons RJ, Gabriel SE, Chest Pain Evaluation in the Emergency Room (CHEER) Investigators. A clinical trial of a chest-pain observation unit for patients with unstable angina. N Engl J Med. 1998;339:1882–1888.