Diagnosis and Characteristics of Syncope in Older Patients Referred to Geriatric Departments

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OBJECTIVES: To test the applicability and safety of a standardized diagnostic algorithm in geriatric departments and to define the prevalence of different causes of syncope in older patients.

DESIGN: Multicenter cross-sectional observational study.

SETTING: In-hospital geriatric acute care departments and outpatient clinics.

PARTICIPANTS: Two hundred forty-two patients (aged ≥65, mean ± standard deviation = 79 ± 7, range 65–98) consecutively referred for evaluation of transient loss of consciousness to any of six clinical centers participating in the study. Of these, 11 had a syncope-like condition (5 transient ischemic attack; 6 seizures), and 231 had syncope (aged 65–74, n = 71; aged ≥75, n = 160).

MEASUREMENTS: Protocol designed to define etiology and clinical characteristics of syncope derived from European Society of Cardiology Guidelines on syncope.

RESULTS: No major complication occurred with use of the protocol. Neuurally mediated was the more prevalent form of syncope in this population (66.6%). Cardiac causes accounted for 14.7% of all cases. The neuroreflex form of syncope (vasovagal, situational, and carotid sinus syndrome) was more common in younger than in older patients (62.3% vs 36.2%; P = .001), whereas orthostatic syncope was more frequent in the older than in the younger group (30.5% vs 4.2%; P < .001). In only 10.4% of cases, syncope remained of unexplained origin. After initial evaluation, a definite diagnosis was possible in 40.1% of the cases, and a suspected diagnosis was obtained in 57.9%. Syncope of suspected cardiac origin after initial evaluation was confirmed in 43.7% of cases, and neuromediated causes were confirmed in 83.5% of the cases.

CONCLUSION: The protocol is applicable even beyond the age of 90 in geriatric departments. The standardized protocol is associated with a reduction in the frequency of unexplained syncope to about 10%.

Key words: syncope; elderly; geriatric department; cardiovascular disease; diagnostic protocol

W ith an incidence of at least 6% per year, a prevalence of 10% (23% in institutionalized elderly population), and a 30% 2-year recurrence rate, 1–4 syncope is recognized as an important clinical challenge in older patients. Despite the exponentially increasing incidence of syncope in people aged 70 and older, 4 data gathered in this population are limited. In particular, little is known about the relative frequency of causes of loss of consciousness in older persons, essentially because a standardized diagnostic protocol is infrequently used at older ages. The few studies that have included older patients with syncope were conducted before the introduction of routine neuroautonomic evaluation in diagnostic protocols. 5 Moreover, the majority of older patients referred to emergency departments after suspected syncope are transferred to geriatric or internal medicine units, where incomplete and nonstandardized diagnostic protocols are frequently in use. 6 Previous studies have analyzed the clinical characteristics of syncope in patients referred to emergency departments 6–8 or have discussed the application of standardized diagnostic protocols in this setting 8, 9 but not in geriatric departments. The Italian Group for the study of Syncope in the elderly (GIS) has designed a standardized algorithm derived from European Society of Cardiology guidelines published in 2001. 10 The present study, which was conducted out in older patients referred to geriatric departments after a transient loss of consciousness,
was aimed at defining the applicability of the GIS diagnostic algorithm, the relative prevalence of different causes of syncope, and the clinical characteristics of syncope.

METHODS

Patients
The study was conducted in patients aged 65 and older who, between June 2002 and March 2004, were consecutively referred to any of six participating centers for evaluation of a transient loss of consciousness. Exclusion criteria were symptoms limited to presyncope (a condition in which patients feel as though syncope is imminent), severe cognitive impairment (Mini-Mental State Examination score <14), active (<5 years) malignancies, and disability in more than four activities of daily living (ADLs). Written informed consent to participate in the study was obtained in all cases.

Diagnostic Protocol
Patients were evaluated following the GIS diagnostic algorithm (Figure 1). Initial evaluation included a structured clinical history, complete physical examination with blood pressure measurements in supine and standing position (1, 3, 5, and 10 min), 12-lead electrocardiogram (ECG), assessment of comorbidity using the Cumulative Illness Rating Scale (CIRS) and of depressive symptoms using the Geriatric Depression Scale, and functional evaluation using the activity of daily living and instrumental activity of daily living scales. When cardiac causes of syncope were suspected, standardized cardiovascular evaluation (Figure 1) was performed as the next step. Neurological evaluation (possibly including electroencephalography, computed tomography scan or carotid Doppler ultrasonography, based on type of presentation) for detecting seizures or cerebrovascular diseases (transient ischemic attack (TIA), drop attack, dizziness) was performed only in the presence of focal neurological symptoms reported after the episode of loss of consciousness. Formal psychiatric evaluation was required only when the loss of consciousness was associated with severe depressive symptoms or somatic complaints suggestive of psychiatric disorders.

Definitions
Syncope is defined as a transient, self-limited loss of consciousness usually leading to falling, in which the underlying mechanism is a transient global cerebral hypoperfusion. Syncope-like condition is a nonsyncopal loss of consciousness commonly misdiagnosed as syncope that may result from metabolic disorders (hypoglycemia, hypoxia, hyperventilation), epilepsy, intoxication, TIA, cataplexy, drop attack, or psychogenic syncope (somatization disorders).

Based on a review of literature that was conducted before the initiation of patient enrollment, causes of syncope were classified as reported in Table 1. Vasovagal, situational, and carotid sinus syndrome syncope usually are pooled together as neuroreflex syncope. This, together with orthostatic syncope, can be further pooled into a group called neuromediated syncope.

Figure 1. Diagnostic protocol of the Italian Group for the study of Syncope in the elderly study. *In selected cases only. ECG = electrocardiogram; ABPM = ambulatory blood pressure measurement; CSM = carotid sinus massage; EEG = electroencephalogram; CT = computed tomography.
Table 1. Etiology of Syncope

<table>
<thead>
<tr>
<th>Type of Syncope</th>
<th>Definition</th>
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| **Neuroreflex**  | a) Vasovagal: when precipitating events such as pain, emotional distress, or prolonged standing were associated with typical prodromic symptoms or when the loss of consciousness was induced during the tilt test  
  b) Situational: when syncope occurred during, or immediately after, micturition, defecation, cough, or swallowing  
  c) Carotid sinus syndrome: when carotid sinus massage in supine or upright position induced syncope with bradycardia or hypotension  
| **Orthostatic**  | When syncope or presyncope was associated with a drop in systolic blood pressure of > 20 mmHg within 5 minutes of standing up  
| **Cardiac**      | a) Mechanical when acute myocardial ischemia or severe intracardiac flow obstructions (e.g., aortic stenosis, left atrial myxoma or thrombus) could be detected  
  b) Arrhythmic, in cases of sinus bradycardia < 40 beats/min or recurrent sinoatrial block with pause > 3 sec, or second- (Mobitz II) or third-degree atrioventricular block, alternating left and right bundle branch block, paroxysmal supraventricular or ventricular tachycardia, pacemaker malfunction with cardiac pauses  
| **Multifactorial** | When multiple causes of syncope could be identified  
| **Drug-induced** | When a direct relationship could be established between drug consumption and syncope  

Cardiac Evaluation

Twenty-four-hour Holter ECG was performed only when arrhythmic causes were suspected and was considered diagnostic when advanced second-degree atrioventricular (AV) block, third-degree atrioventricular block, or sustained ventricular tachyarrhythmias were detected in association with syncope or presyncope. Mono- and two-dimensional echocardiography was performed in all cases of syncope of suspected cardiac cause, whereas exercise testing was performed in patients with syncope during exercise after ruling out severe aortic stenosis. Exercise testing was considered diagnostic if syncope associated with sustained ventricular tachyarrhythmias or, even in the absence of syncope, advanced AV block occurred during exercise.

Electrophysiological study was done when noninvasive assessment was inconclusive in the presence of syncope possibly due to cardiac arrhythmia. The electrophysiologic study was considered diagnostic in cases with sinus node recovery time of longer than 3 seconds, baseline His-ventricular interval greater than 100 ms, infrahisian second- or third-degree AV block occurring during atrial pacing or after ajmaline, or inducible syncopal or hypotensive supraventricular or ventricular tachyarrhythmias. Intermittent loop recorder was implanted in cases with unexplained recurrent or malignant (e.g., with severe trauma) syncope. Coronary angiography was limited to cases in which myocardial ischemia was strongly suspected to be the cause of syncope.

Neuroautonomic Evaluation

Tilt test was performed using the Italian protocol, previously validated in older patients under continuous ECG and systemic blood pressure (Finapres Ohmeda, Columbia, MD) monitoring. Briefly, the test consists of 20-minute passive orthostatism at an angle of 60° potentiated, if syncope does not occur, using sublingual nitroglycerin (400 μg) with further 15-minute observation at the same angle. The test was considered positive if hypotension, bradycardia, or both accompanied syncopal symptoms reproducing those reported by the patient. Carotid sinus massage (CSM) was performed according to the symptoms method. TIA or stroke in the preceding 3 months, or critical stenosis using Doppler ultrasonography elicited by carotid bruits, were contraindications to CSM.

Statistical Analysis

Statistical analysis was performed using StatSoft 6.0 (Tulsa, OK). Continuous variables, which were all normally distributed, were compared between groups using Student unpaired t test. Chi-square or Fisher exact tests were used when appropriate to compare dichotomous variables. P < .05 was considered significant. Data are reported as mean ± standard deviation or as percentages.

RESULTS

Of 28 geriatric departments initially invited to participate in GIS study, 12 refused immediately after examining the protocol, and 10 abandoned later because the protocol was felt to be too complicated or potentially harmful. Therefore, six departments (Appendix 1) finally agreed upon participation.

Characteristics of Study Population

Of 242 patients initially screened for suspected syncope, 11 (4.5%) who were diagnosed with a syncope-like condition (5 TIA, 6 seizures) after initial evaluation (Figure 2) were excluded from further analysis. The age of the remaining 231 patients (98 men and 133 women) was 79 ± 8 (range 60–98). One hundred eight patients were aged 80 and older. For the purpose of analysis, patients were divided into two age groups (65–75, n = 71; > 75, n = 160).

The main demographic and clinical characteristics of the two age groups are reported in Table 2. Sex distribution was similar in the two groups. Older patients were taking more drugs and had a higher index of chronic comorbidity and a worse functional and cognitive profile than younger individuals. The numbers of depressive symptoms, lifelong
episodes of syncope, falls, and syncope-related fractures were similar in the two groups.

Syncope Presentation
In 71% of cases, syncope occurred in the standing position, more frequently in older than in younger patients (Table 3). Syncope associated with postprandial hypotension was slightly but not significantly more frequent in the older group \((P = .06)\), whereas situational syncope prevailed in the younger one. In 5.7% of cases, syncope occurred in the supine position, with a similar frequency in both age groups. Immediately preceding, or “prodromic,” symptoms (neurovegetative symptoms such as dizziness, diaphoresis, nausea, abdominal discomfort or other symptoms such as dyspnea, palpitations, and chest pain)\(^1\) were frequent. In particular, 72.9% of patients reported at least one prodromic symptom, with a similar prevalence in the two age groups. In the whole series, prodromic symptoms were present in 58.8% of cardiac and 76.3% of neuromediated syncope \((P = .03)\).

Causes of Syncope
Results deriving from use of the diagnostic algorithm are presented in Figure 2. A definitive, explanatory cause of the loss of consciousness could be identified after the initial evaluation in 40.1% of cases, including 11 syncope-like episodes. At the same, initial evaluation, a suspected diagnosis could be made in 57.9% of cases. Loss of consciousness was evaluated to be of cardiac (22.8%), neuromediated (73.6%), or neurological (3.6%) origin. In only 2.0% of cases could no diagnosis be made at the first assessment. At second-level evaluation, cardiac and neuromediated syncope were confirmed in 43.7% and 83.5% of cases, respectively, whereas no neurological causes were confirmed. In patients with a normal ECG and no structural heart disease at initial evaluation, a cardiac cause of

Table 2. Main Demographic and Clinical Characteristics in the Whole Series and by Age Group

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All (N = 231)</th>
<th>65–74 (n = 71)</th>
<th>≥75 (n = 160)</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean ± SD</td>
<td>79 ± 7</td>
<td>71 ± 3</td>
<td>82 ± 5</td>
<td>.33</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>133 (57.6)</td>
<td>41 (57.7)</td>
<td>92 (57.5)</td>
<td>.005</td>
</tr>
<tr>
<td>Body mass index, kg/m², mean ± SD</td>
<td>25 ± 3</td>
<td>26 ± 4</td>
<td>24 ± 3</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Drugs, mean ± SD</td>
<td>3.4 ± 2.3</td>
<td>2.6 ± 2.0</td>
<td>3.8 ± 2.2</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Cumulative Illness Rating Scale score, mean ± SD</td>
<td>7.2 ± 3.5</td>
<td>6.2 ± 3.3</td>
<td>7.6 ± 3.4</td>
<td>.003</td>
</tr>
<tr>
<td>Activities of daily living, mean ± SD</td>
<td>0.7 ± 1.2</td>
<td>0.4 ± 0.8</td>
<td>0.8 ± 1.3</td>
<td>.03</td>
</tr>
<tr>
<td>Instrumental activities of daily living, mean ± SD</td>
<td>1.9 ± 3.0</td>
<td>0.8 ± 2.1</td>
<td>2.4 ± 3.3</td>
<td>.001</td>
</tr>
<tr>
<td>Mini-Mental State Examination score, mean ± SD</td>
<td>26.7 ± 4.0</td>
<td>28.3 ± 2.8</td>
<td>26.0 ± 4.3</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Geriatric Depression Scale score, mean ± SD</td>
<td>3.9 ± 3.7</td>
<td>3.8 ± 4.1</td>
<td>3.9 ± 3.5</td>
<td>.45</td>
</tr>
<tr>
<td>Syncope, mean ± SD</td>
<td>5.6 ± 8.4</td>
<td>5.3 ± 6.1</td>
<td>5.8 ± 9.3</td>
<td>.24</td>
</tr>
<tr>
<td>Falls, n (%)</td>
<td>147 (64)</td>
<td>55 (77)</td>
<td>92 (56)</td>
<td>.10</td>
</tr>
<tr>
<td>Fractures, n (%)</td>
<td>26 (11.2)</td>
<td>9 (12.6)</td>
<td>17 (10.6)</td>
<td>.35</td>
</tr>
</tbody>
</table>

*P-value for aged <75 versus ≥75; t test for all variables except chi-square for sex, falls, and fractures.
SD = standard deviation.
syncope emerged at the end of the diagnostic protocol in only one of 113 patients (0.9%).

As illustrated in Table 4, neuromediated syncope (the pooling of neuroreflex and orthostatic syncope) accounted for 66.6% of cases in the whole series, being the most common form of syncope. Cardiac causes were the second most frequent cause in the whole series (14.7% of cases). Syncope remained unexplained in 10.4% of cases. Cardiac and orthostatic causes of syncope were, respectively, borderline and significantly more frequent in older patients, whereas neuroreflex causes were more prevalent in younger patients. However, the pooled group of neuromediated syncope was the leading cause of syncope in patients aged 75 and older. The proportion of unexplained syncope was similar in the two groups.

**DISCUSSION**

To the authors’ knowledge, this is the first study reporting the use of a standardized diagnostic protocol for syncope in older patients admitted to geriatric departments. For this purpose, a diagnostic protocol was designed that followed the ongoing European Society of Cardiology guidelines on syncope, and 28 geriatric departments in Italy were invited to participate in the study. However, only six centers recruited patients, whereas 22 centers withdrew because of organizational barriers or of fear of performing the tilt test and CSM in older patients. This experience suggests that such a fear is poorly justified, because no adverse effect occurred in 223 tilt tests and with 151 CSMs, diagnostic tests that previous studies have proven to be valid and safe in older and younger patients.

The neurally mediated syncope, which had previously been reported to occur infrequently in older people, was the most frequent type of syncope in this population. However, in a previous study, the tilt test and CSM were not performed in older patients, and in this group, syncope remained unexplained in as many as 45.3% of cases, compared with only 10.4% of cases in the current study. The demonstration of the high prevalence of neurally mediated syncope in this older population was due to the systematic use of tilt test and CSM.

In contrast with previous reports, prodromic symptoms were remarkably frequent in this older population but proved to be poorly specific and, hence, of limited utility in orienting the diagnosis toward neurally mediated syncope. Indeed, it was found that prodromic symptoms—in most cases, neurovegetative symptoms—were highly prevalent in neuromediated (76.3%) and, although slightly less so, in cardiac (58.8%) syncope. For these reasons, further investigations, which in the diagnostic protocol are indicated as second-level tests (Figure 1), are mandatory to complete a differential diagnosis.

In this study, many patients reported only one or two, and often mild, neurovegetative prodromic symptoms, for example pallor or dizziness, which patients find difficult to recognize as harmful symptoms. If physicians would teach their patients how to rapidly recognize the neurovegetative prodromic symptoms, it might help in preventing the potentially most catastrophic consequences of the loss of consciousness, such as falls. Prevention of recurrent episodes of syncope is of particular relevance in older patients, in whom repeated syncope and falls may cause disability, depression, and mortality. A precise recognition of the causes of

### Table 3. Presentation of Syncope in the Whole Series and by Age Group

<table>
<thead>
<tr>
<th>Condition</th>
<th>All (N = 231)</th>
<th>65–74 (n = 71)</th>
<th>≥75 (n = 160)</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Supine position</td>
<td>5.7</td>
<td>7.1</td>
<td>5.0</td>
<td>.13</td>
</tr>
<tr>
<td>Standing position</td>
<td>71.2</td>
<td>63.4</td>
<td>74.7</td>
<td>.03</td>
</tr>
<tr>
<td>Postprandial</td>
<td>5.7</td>
<td>1.4</td>
<td>8.9</td>
<td>.06</td>
</tr>
<tr>
<td>Situational</td>
<td>12.6</td>
<td>21.2</td>
<td>7.6</td>
<td>.01</td>
</tr>
<tr>
<td>Other</td>
<td>5.8</td>
<td>6.9</td>
<td>3.8</td>
<td>.09</td>
</tr>
</tbody>
</table>

* P-value for difference between age groups, chi-square.

### Table 4. Causes of Syncope in the Whole Series and by Age Group

<table>
<thead>
<tr>
<th>Etiology of Syncope</th>
<th>All (N = 231)</th>
<th>65–74 (n = 71)</th>
<th>≥75 (n = 160)</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac</td>
<td>34 (14.7)</td>
<td>8 (11.3)</td>
<td>26 (16.3)</td>
<td>.06</td>
</tr>
<tr>
<td>Neuroreflex</td>
<td>102 (44.1)</td>
<td>44 (62)</td>
<td>58 (36.3)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Orthostatic</td>
<td>52 (22.5)</td>
<td>3 (4.2)</td>
<td>49 (30.5)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Drug-induced</td>
<td>11 (4.8)</td>
<td>3 (4.2)</td>
<td>8 (5)</td>
<td>.33</td>
</tr>
<tr>
<td>Multifactorial</td>
<td>8 (3.5)</td>
<td>3 (4.2)</td>
<td>5 (3.1)</td>
<td>.21</td>
</tr>
<tr>
<td>Unexplained</td>
<td>24 (10.4)</td>
<td>10 (14.1)</td>
<td>14 (8.8)</td>
<td>.10</td>
</tr>
</tbody>
</table>

* P-value for difference between age groups, chi-square.
syncope is valuable for reducing recurrent episodes, because it may help to identify specific treatments and behavioral strategies. Particularly in the older population, the high prevalence of vasodepressive syncope requires a careful re-assessment of drug therapy, with full consideration of possible nonpharmacological interventions.26

In the current series, 70% of syncopal episodes were witnessed. Witnesses may prove of crucial importance for the diagnosis, particularly in older patients who frequently are confused or affected by retrograde amnesia after a syncope or fall.

Finally, in this population, including very old patients referred to geriatric departments, initial evaluation could precisely identify all cardiac causes of syncope with the exception of one “false negative” case. This result was similar to that obtained previously in a general population of syncope patients.27 These observations support the conclusion that in older and younger patients with syncope, cardiac evaluation is recommended only when initial assessment suggests cardiac disease and not simply because they are older.

Limitations

The diagnostic criteria adopted in the present study are the most commonly accepted ones. Nevertheless, they could not exclude another possible diagnosis, because in syncope, no diagnostic criterion standard has been determined. This study does not answer the question of whether a standardized diagnostic approach may increase the efficacy of therapeutic interventions and may hence reduce recurrent syncope. To answer this question, specific randomized, controlled trials are needed.

CONCLUSION

In conclusion, this study demonstrated that a standardized protocol for the diagnosis of syncope may usefully be used in geriatric departments and that this diagnostic protocol is associated with a reduction in the frequency of unexplained syncope to about 10%. The prevalence of neuromediated syncope is high in older patients, in whom neuroauteomic evaluation is well tolerated and useful for more precisely identifying the mechanism of syncope. As previously reported in younger populations, cardiac syncope may be clearly identified or strongly suspected from the initial evaluation in older patients as well.

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