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Historical Criteria That Distinguish Syncope From Seizures

Robert Sheldon, MD, PHD,* Sarah Rose, PHD,* Debbie Ritchie, MN,* Stuart J. Connolly, MD,† Mary-Lou Koshman, RN,* Mary Anne Lee, MD,‡ Michael Frenneaux, MD,§ Michael Fisher, BSC,* William Murphy, MD‡

Calgary, Alberta; Hamilton, Ontario; and Cardiff, Wales

OBJECTIVES We prospectively sought evidence-based criteria that distinguished between seizures and syncope.

BACKGROUND Loss of consciousness is usually due to either seizures or syncope. There are no evidence-based historical diagnostic criteria that distinguish them.

METHODS A total of 671 patients with loss of consciousness completed a 118-item historical questionnaire. Data sets were complete for all subjects. The data set was randomly divided into two equal groups. The contributions of symptoms to diagnoses in one group were estimated with logistic regression and point scores were developed. The accuracy of the decision rule was then assessed using split-half analysis. Analyses were performed with and without inclusion of measures of symptom burden, which were the number of losses of consciousness and the duration of the history. The scores were tested using receiver-operator characteristic analysis.

RESULTS The causes of loss of consciousness were known satisfactorily in 539 patients and included seizures (n = 102; complex partial epilepsy [50 patients] and primary generalized epilepsy [52 patients]) and syncope (n = 437; tilt-positive vasovagal syncope [267 patients], ventricular tachycardia [90 patients] and other diagnoses such as complete heart block and supraventricular tachycardias [80 patients]). The point score based on symptoms alone correctly classified 94% of patients, diagnosing seizures with 94% sensitivity and 94% specificity. Including symptom burden did not significantly improve accuracy, indicating that the symptoms surrounding the loss of consciousness accurately discriminate between seizures and syncope.

CONCLUSIONS A simple point score of historical features distinguishes syncope from seizures with very high sensitivity and specificity. (J Am Coll Cardiol 2002;40:142–8) © 2002 by the American College of Cardiology Foundation

The diagnosis of the cause of transient loss of consciousness is a common clinical problem. Although symptoms such as seizure-like activity, tongue-biting and physical trauma are often used to diagnose a seizure disorder, this practice has been based upon anecdotal accretion rather than evidence. The recognition of convulsive syncope has added to the difficulties of diagnosis. The reliability of the diagnosis of the first loss of consciousness is surprisingly low (1), but this can be improved with preset simple diagnostic criteria (2). Previous attempts at defining diagnostic criteria have been limited by lack of quantitative data (3), lack of gold standard diagnostic groups (4,5), lack of populations with both seizures and syncope (3,4,6–8), retrospective analyses (3,5) and lack of translation of results into easily applied criteria (1–7). This frequently leads to laboratory investigations that may be expensive, invasive and inefficient (9–17).

We hypothesized that evidence-based diagnostic criteria could distinguish between syncope and seizures as causes of transient loss of consciousness. To test this we performed the Syncope Symptom Study. In this prospective study we administered a uniform questionnaire to 671 patients who were referred to three academic centers in Canada and Wales for assessment of transient loss of consciousness. We first studied patients with securely defined diagnoses based upon conventionally accepted objective tests. We compared their responses to identify the historic features that most accurately correlated with their diagnoses. Here we report simple historic features that distinguish seizures from syncope with high accuracy.

METHODS

Patient selection. The research ethics committees in all participating centers approved this study. Patients were eligible if they have had ≥1 loss of consciousness and consented to participate. They were recruited from university and private practice neurology and cardiology clinics;

From the *Cardiovascular Research Group, University of Calgary, Calgary, Alberta, Canada; †McMaster University, Hamilton, Ontario, Canada; ‡Department of Clinical Neurosciences, University of Calgary, Calgary, Alberta, Canada; and the §Wales Heart Research Institute, Cardiff, Wales, United Kingdom. Supported with unrestricted grants from Medtronic Inc, Minneapolis, Minnesota, and the Calgary General Hospital Volunteer Association, Calgary, Alberta, Canada. This paper is dedicated to the memory of our friend and colleague Dr Mary Anne Lee, who died on May 16, 2001.

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Abbreviations and Acronyms

ECG = electrocardiogram/electrocardiograph
EEG = electroencephalogram
IQR = interquartile range
ROC = receiver-operating characteristic
VT = ventricular tachycardia

pacemaker, arrhythmia and syncope clinics; and hospital cardiology wards. They were included in the main study if they had a diagnosis established according to preset criteria and if there was no reasonable diagnostic confusion. All patients had lost consciousness and at that time had also lost control of posture. Patients were excluded if they had more than one plausible cause of syncope. For example, a patient with lifelong vasovagal syncope and syncope due to ventricular tachycardia (VT) was excluded.

Gold standard diagnostic criteria. Patients had vasovagal syncope if they had a positive tilt test performed according to one of several methods (18–22). Patients had a diagnosis of VT as the cause of syncope if sustained VT was documented at the time of syncope, or if hemodynamically unstable, sustained monomorphic VT was induced during a subsequent electrophysiologic study (23). Patients had torsade de pointes VT if it was documented electrocardiographically at the time of syncope or shortly afterwards. Patients had complete heart block if complete heart block with a wide QRS escape rhythm was documented at the time of syncope or shortly afterwards. Patients had one of several supraventricular tachyarrhythmias if they had an established diagnosis of the relevant arrhythmia, and had their typical symptoms of palpitations immediately preceding a syncopal spell or awoke from syncope with those symptoms. Orthostatic hypotension was a cause if patients had a documented autonomic neuropathy with significant orthostatic hypotension and progressive presyncope during tilt table testing (24). Complex partial epilepsy or primary generalized epilepsy was diagnosed if patients had diagnostically positive electroencephalograms (EEGs).

Undiagnosed patients. All patients without an otherwise proven cause of syncope had an electrocardiogram (ECG) and a tilt table test. Patients with bifascicular block had a His bundle conduction study. Patients $\geq$60 years usually underwent ambulatory ECG.

Syncope symptom questionnaire. All patients completed a structured questionnaire with 118 items developed from Calkins et al. (6). The questions assessed symptom burden, provocative situations, perisyncopal symptoms, symptoms thought to be diagnostic of seizures, signs observed by bystanders and relevant medical history. Several versions were tested for clarity and comprehensiveness before the final version was selected. Completed questionnaires were checked for completion by study coordinators, and incomplete questionnaires were returned for revision. Cross-checking for incompatible entries assessed the accuracy of questionnaire completion.

Statistical analysis. We first randomly divided the sample of 538 patients with secure diagnoses into two halves for the separate development and testing of the clinical decision rule. In the development sample (n = 270), we compared the prevalence of each variable in the seizure and syncope groups using a chi-square test, and calculated the likelihood ratio for predicting the diagnosis of seizure versus syncope. The likelihood ratio of each variable is its prevalence in the seizure group divided by its prevalence in the syncope group. (The prevalence of a variable in a diagnostic group is equivalent to its sensitivity for that group. The sensitivity for seizures is the specificity for syncope and vice versa.) A variable with a likelihood ratio >1 is predictive of seizure and a variable with a ratio <1 is predictive of syncope.

We then developed a logistic regression model that predicted seizures on the basis of the development sample. Variables were retained in the model if $p < 0.05$ for the Wald statistic, and a practical diagnostic decision rule was derived from the regression coefficients (25). A point score was developed by assigning ±1, ±2, or ±3 points to each of the factors based on the relative magnitude of the estimated regression coefficient. Each coefficient was divided by the smallest absolute value of the coefficient retained in the model, then rounded to the nearest integer. The points were then summed and a diagnostic threshold chosen using receiver-operating characteristic (ROC) analysis (26). Because this process is equivalent to rounding the estimated logistic regression coefficients to the nearest integer, there is a small loss of accuracy. Using the diagnostic threshold, the apparent sensitivity, specificity and overall accuracy in this test sample were estimated.

We then tested the decision rule on the test sample of 268 patients. Using the diagnostic threshold established in the development sample, sensitivity and specificity for seizures were calculated.

Syncope and seizures often are chronic disorders, and their symptom burden may be a source of selection bias. This presents problems if the number of events, or duration of the history of the disorder, are used as diagnostic criteria. Therefore, we derived classification rules both with and without the inclusion of these variables. Finally, it might be that syncope patients who go on to have a known cause of syncope have different historic diagnostic features than do those who do not. Accordingly, we applied the decision rule to the 132 patients with syncope of unknown cause to assess the robustness of the classification schemes.

RESULTS

Patient population. There were 102 seizure patients and 569 syncope patients; the latter included 437 with an established cause. These included vasovagal syncope (267 patients); VT (90 patients); complete heart block (40 patients); supraventricular tachycardias (22 patients); sick sinus syndrome and hypersensitive carotid sinus syndrome (4 patients each); aortic stenosis (3 patients); cough syncope,

Table 1. Comparison of the Most Significant Historic Features in Patients With Seizures and Established Diagnoses of Syncope

	Sensitivity	Specificity	Likelihood Ratio	p Value (Chi-Square)
	Factors Most Strongly Predictive of Seizures			
Cut tongue	0.451	0.973	16.460	< 0.001
Head turning	0.431	0.968	13.481	< 0.001
Unusual posturing	0.353	0.973	12.880	< 0.001
Bedwetting	0.235	0.964	6.447	< 0.001
Blue color observed by bystanders	0.326	0.944	5.813	< 0.001
Limb jerking noted by others	0.686	0.877	5.566	< 0.001
Prodromal trembling	0.294	0.941	4.951	< 0.001
Prodromal preoccupation	0.078	0.982	4.284	0.002
Prodromal hallucinations	0.078	0.982	4.284	0.002
Behaviors not recalled	0.529	0.868	3.998	< 0.001
Loss of consciousness associated with stress	0.569	0.849	3.773	< 0.001
Muscle pain	0.157	0.954	3.433	0.004
Prodromal deja vu	0.137	0.959	3.341	0.009
Observed unresponsiveness	0.765	0.749	3.045	< 0.001
Postictal confusion	0.941	0.690	3.031	< 0.001
Postictal headaches	0.490	0.836	2.982	< 0.001
Prodromal mood changes	0.235	0.918	2.863	0.002
Abnormal behaviors* noted by bystanders	0.922	0.671	2.803	< 0.001
	Factors Most Strongly Predictive Against Seizures			
Presyncopal spells before loss of consciousness	0.275	0.274	0.378	< 0.001
Self-reported high blood pressure	0.098	0.690	0.316	0.002
Presyncope with hot/warm environments	0.078	0.731	0.291	0.004
Presyncope with needle	0.039	0.863	0.286	0.052
Prodromal vertigo	0.059	0.785	0.274	0.010
Any presyncope	0.235	0.137	0.273	< 0.001
Presynope after exercise	0.078	0.712	0.273	0.002
Hypertension (physician reported)	0.078	0.708	0.268	0.002
Warmth before a spell	0.078	0.662	0.232	< 0.001
Any chest pain	0.098	0.543	0.215	< 0.001
Nausea before a spell	0.059	0.722	0.211	0.001
Remembered loss of consciousness	0.118	0.425	0.204	< 0.001
Presyncope with prolonged sitting/standing	0.059	0.676	0.181	< 0.001
Diaphoresis before a spell	0.059	0.653	0.169	< 0.001
Chest pain before a spell	0.020	0.872	0.153	0.025
Palpitations before loss of consciousness	0.039	0.662	0.116	< 0.001
Dyspnea before loss of consciousness	0.020	0.763	0.083	< 0.001
Coronary heart disease	0.020	0.749	0.078	< 0.001
Loss of consciousness with prolonged sitting/standing	0.020	0.603	0.049	< 0.001

The univariate diagnostic behavior of each of the variables is expressed as its sensitivity, specificity and likelihood ratio for seizures. The likelihood ratio is the probability of a seizure patient experiencing the symptom divided by the probability of a syncope patient experiencing the symptom. *One or more of witnessed amnesia for abnormal behavior, witnessed unresponsiveness, unusual posturing or limb jerking. The p value is for the chi-square test for the 2×2 table formed by cross-tabulating the presence or absence of the factor with the variable indicating syncope/seizure.

pulmonary embolus and autonomic neuropathy (2 patients each) and hyperventilation (1 patient). Of the syncope patients, 421 had no evidence of structural heart disease and 146 had structural heart disease. There were 52 patients with primary generalized epilepsy and 50 patients with complex partial epilepsy. The seizure patients were younger (35 ± 12 years vs. 53 ± 20 years, $p < 0.001$), but there were no significant gender differences (44% of the seizure patients were men, compared with 55% of the syncope patients, $p = 0.062$). Seizure patients had more episodes of loss of consciousness (median 168 spells; interquartile range [IQR] 20 to 450) than syncope patients (median 3 spells; IQR 2 to 8; $p < 0.001$). Seizure patients also had a longer history (median 186 months; IQR 67 to 352) than syncope patients (median 24 months; IQR 0.33 to 169; $p < 0.001$).

Classifications based on symptoms alone. Table 1 lists the most important univariate diagnostic features. These features have a likelihood ratio >2.0 (predictive of seizure) or <0.5 (predictive of syncope) and had $p < 0.05$. Seizure patients were more likely to have had a cut tongue, bedwetting, prodromal deja vu, preoccupation, mood changes, hallucinations or trembling before loss of consciousness, postictal confusion, muscle pain, headaches, observed convulsive movements, head turning, unresponsiveness during loss of consciousness and blue skin observed by bystander. Patients with syncope were more likely to also experience

Table 2. Point Scores for the Diagnosis of Seizures, in the Absence of Knowledge of the Numbers and Historic Duration of Losses of Consciousness and Lightheaded Spells

Criteria	Regression Coefficient (SE)	p Value	Points
Waking with cut tongue	6.85 (2.03)	0.001	2
Abnormal behavior noted*	3.82 (1.37)	0.005	1
Loss of consciousness with emotional stress	3.97 (1.30)	0.002	1
Postictal confusion	3.52 (1.33)	0.008	1
Head turning to one side during loss of consciousness	3.67 (1.43)	0.010	1
Prodromal deja vu or jamais vu	2.75 (1.43)	0.055	1
Any presyncope	−4.70 (1.34)	< 0.001	−2
Loss of consciousness with prolonged standing or sitting	−5.37 (1.71)	0.002	−2
Diaphoresis before a spell	−5.73 (1.80)	0.001	−2

*Defined in Table 1; classified as seizure for points ≥1. The reported p value is for the Wald statistic.
SE = standard error.

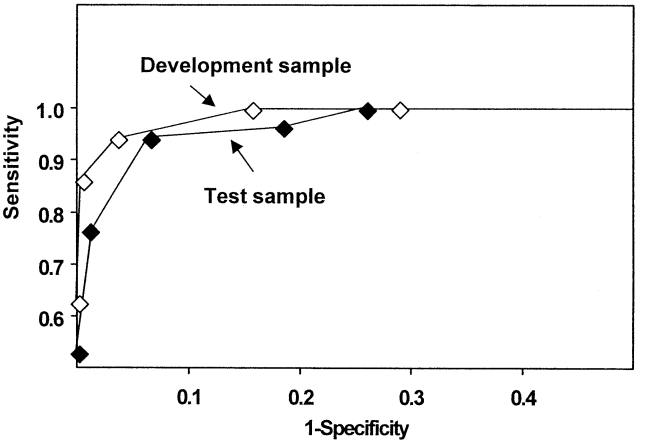

Figure 2. Receiver-operating characteristic analysis of the diagnostic score in the development and test samples of patients with seizures and patients with syncope of known causes.

presyncope, have loss of consciousness with prolonged sitting/standing, or have presyncope with needles, prolonged sitting/standing, warm/hot environments and exercise. They were more likely to experience symptoms such as diaphoresis, dyspnea, chest pain, palpitations, warmth, nausea, vertigo and presyncope before a spell. They were also more likely to have hypertension, chest pain and coronary artery disease.

A diagnostic point score was derived from the relative weighting of the regression coefficients without inclusion of estimates of symptom burden (Table 2). The diagnostic behavior of this point score is illustrated in Figure 1. A score of 1 provides a sharp demarcation between the diagnoses of syncope and seizures. Patients were classified as having seizures if their point score was ≥1. Figure 2 compares the ROC analysis of the diagnostic point score in the development sample and test sample. The diagnostic decision rule, when applied to patients in the development sample, resulted in an overall accuracy of 96%, with 94% sensitivity for seizures and 96.3% specificity. In the test sample, the overall accuracy observed was 94%, with a sensitivity of 94% for seizures and specificity of 94%.

Classifications based on symptoms and symptom burden. The regression coefficients and derived diagnostic point scores are listed in Table 3 for the model, including measures of symptom burden. Features that predicted seizures included a high number of losses of consciousness, head turning to one side during loss of consciousness, loss of consciousness with stress and unresponsiveness during loss of consciousness. Factors that predicted syncope notably included loss of consciousness after prolonged sitting or standing, diaphoresis before a spell and presyncope. Using a cutoff score of ≥0 to classify patients in the development sample resulted in an overall accuracy of 86.3%, sensitivity for seizures of 96% and specificity of 84%. In the test sample, the overall accuracy observed was 84.7% with a sensitivity for seizures of 92.1% and specificity of 83%.

The diagnostic behaviors of the two schemes (developed in the absence and presence of knowledge of symptom

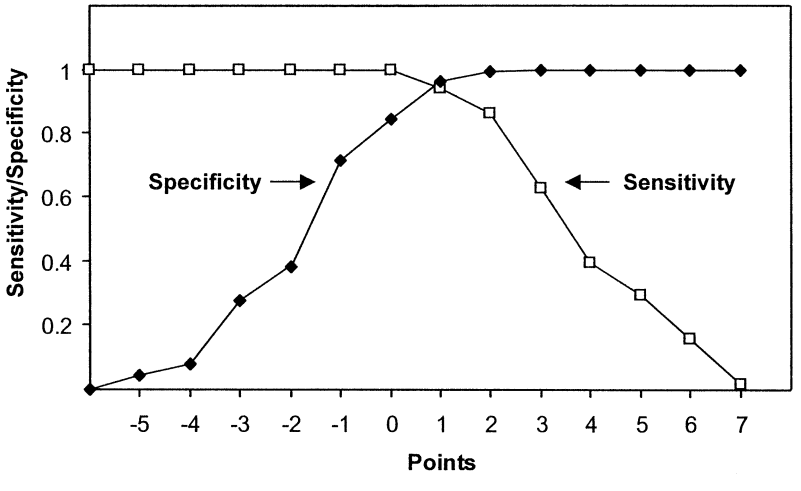

Figure 1. Sensitivity and specificity for the diagnosis of seizures using point score reported in Table 2. The population is the development sample of patients with seizures and patients with syncope of known causes.

Table 3. Point Scores for the Diagnosis of Seizures With Knowledge of the Numbers of Spells and the Length of the History of Losses of Consciousness and Lightheaded Spells

Criteria	Regression Coefficient (SE)	p Value	Points
Loss of consciousness with stress	4.73 (1.43)	0.001	2
Head turning to one side during loss of consciousness	4.56 (1.84)	0.013	2
Number of spells >30	3.60 (1.02)	< 0.001	1
Unresponsiveness during loss of consciousness	3.89 (1.09)	< 0.001	1
Diaphoresis before loss of consciousness	−2.72 (1.25)	0.029	−1
Any presyncope	−4.90 (1.30)	< 0.001	−2
Loss of consciousness with prolonged standing or sitting	−7.36 (2.11)	< 0.001	−3

Classify as seizure for point scores ≥0. The reported p value is for the Wald statistic. SE = standard error.

burden) were compared with ROC analysis (Fig. 3). The area under the curve for the classification scheme that did not account for symptom burden was 0.980, whereas the area under the curve for the scheme that accounted for symptom burden was 0.967. Therefore, knowledge of symptom burden did not improve the accuracy of the diagnostic scheme.

Syncope of unknown cause. Do the risk scores distinguish patients with seizures from patients with any syncope, whether or not the cause of the latter is known? We compared the sensitivity for syncope of the risk scores in these populations (Fig. 4). The classification scheme diagnosed 86% of the 132 patients apparently having syncope of undiagnosed cause as indeed having syncope. As well, the scheme behaved almost identically in 437 patients with syncope of known cause and 132 patients with syncope of unknown cause as for the 437 gold standard patients alone.

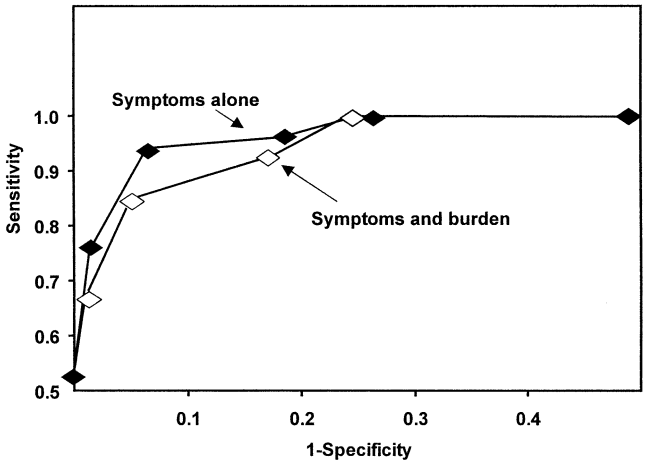

Figure 3. Receiver-operating characteristic analysis of the diagnostic score developed in the absence and presence of knowledge of symptom burden. The population is the development sample of patients with seizures and patients with syncope of known causes.

DISCUSSION

This study presents a simple point score of diagnostic criteria that distinguishes syncope from seizures with high accuracy. This is a common diagnostic problem for which no evidence-based classification schemes are available. The features that clinicians have used to diagnose seizures have featured symptoms characteristic of specific causes of these syndromes. For example, diagnostic features of seizures include myoclonic jerks, tongue biting, tonic spasm, staring, lip smacking and repetitive facial jerks or grimacing, prodromes of olfactory sensations, head turning or stiffening and a rising sensation in the abdomen. Criteria for syncope similarly have been related to specific causes; examples include nausea, fatigue and specific causal factors for vasovagal syncope. We used a large patient population drawn from both neurology and cardiology clinics and inpatient services to establish criteria that would cover a range of syndromes.

The classification schemes are simple. They provide evidence for the validity of previous anecdotal approaches and also illustrate the need for negative criteria. The classic seizure symptoms and signs of deja vu, cut tongue, limb jerking and postictal confusion all contributed to the diagnosis of seizures. Symptoms of syncope such as prodromal diaphoresis and palpitations, or provocation by prolonged sitting or standing, often have needed to be absent to diagnose a seizure. We had anticipated that the relatively common occurrence of convulsive syncope might confound the analysis (12). Indeed, 15% of our patients with syncope had abnormal limb jerking noted by others. That this was not a major problem may be because the classification scheme addresses it directly: to be diagnosed with epileptic seizures, patients generally have evidence of seizures and lack evidence of symptoms seen in patients with syncope.

We present sample diagnostic questions and the points awarded for an affirmative answer in Table 4. Points are awarded for each answer, and the sum of the points determines the diagnosis. The patient has seizures if the point score is ≥1 and syncope if the point score is <1. We omitted questions about the severity and duration of the history of losses of consciousness, because they did not greatly improve diagnostic accuracy. They might also reflect referral patterns and the refractory nature of diseases often seen in tertiary referral clinics, rather than the diagnosis itself. It is not necessary to know severity or duration to distinguish between syncope and seizures. Written classification schemes may improve diagnostic reliability; in patients with a transient loss of consciousness there was substantial diagnostic disagreement among physicians (1,2), and written diagnostic criteria improved inter-rater agreement.

The diagnostic instrument diagnosed 86% of patients with apparent syncope of undiagnosed etiology as having syncope. This slightly lower apparent sensitivity may be due

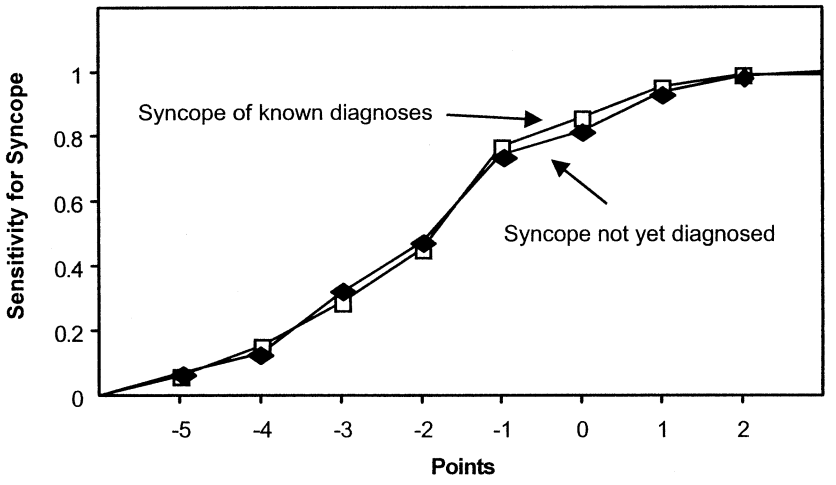

Figure 4. A comparison of the use of the diagnostic score for populations of syncope patients in the absence or presence of a known cause of syncope. The diagnostic score does not include symptom burden.

to different kinds of syncope in this group, or to patients with true and atypical seizures.

We anticipate that these questions might help with diagnostic determinations. Although we do not suggest that they supplant appropriate and targeted investigations in difficult cases, they may streamline initial patient assessment. This might be useful in a range of clinical and academic settings, and by preventing some unnecessary investigations these questions might reduce patient anxiety and morbidity as well as health costs. Similar analyses are underway to derive classification schemes for the various causes of syncope.

Study limitations. There are several factors that might limit the conclusions. We included only those seizure patients who had a diagnostic EEG, recognizing that many patients with seizures have normal interictal EEGs. The seizure patients were those with loss of consciousness and postural tone, having either primary generalized seizures or partial complex seizures. Although there are numerous other causes of seizures, these are the two most likely to be confused with convulsive syncope. There might be an accrual bias in that the patients were identified in tertiary care clinics and acute care facilities, and a recall bias in patients' memories. Similarly, the diagnostic criteria reflect the numeric balance of patients seen in our study. It might be that the syncope symptoms are more likely to be associated with vasovagal syncope rather than with less common syndromes such as VT. We had few patients with uncommon causes of syncope, nor did we include patients with pseudoseizures and patients with more than one diagnosis. However, the classification schemes do reflect the prevalence of syndromes and symptoms in tertiary care referral centers. We did not have a standardized investigational approach, and it is possible that more diagnoses of syncope would have been established if all patients, for example, underwent invasive electrophysiologic studies. However, these studies have a low yield in patients without manifest electrical or structural heart disease, and would serve only to determine the cause of syncope, not whether the diagnosis was syncope or seizure. Although we validated each classification scheme through independent confirmation using split-half analysis, this scheme should be validated externally in patients who present for the first time with loss of consciousness (2).

Table 4. Diagnostic Questions to Determine Whether Loss of Consciousness Is Due to Seizures or Syncope

Question	Points *(If Yes)*
At times do you wake with a cut tongue after your spells?	2
At times do you have a sense of deja vu or jamais vu before your spells?	1
At times is emotional stress associated with losing consciousness?	1
Has anyone ever noted your head turning during a spell?	1
Has anyone ever noted that you are unresponsive, have unusual posturing or have jerking limbs during your spells or have no memory of your spells afterwards? *(Score as yes for any positive response)*	1
Has anyone ever noted that you are confused after a spell?	1
Have you ever had lightheaded spells?	−2
At times do you sweat before your spells?	−2
Is prolonged sitting or standing associated with your spells?	−2

The patient has seizures if the point score is ≥1, and syncope if the point score is <1.

Reprint requests and correspondence: Dr. Robert Sheldon, Cardiovascular Research Group, University of Calgary, 3330 Hospital Drive NW, Calgary, Alberta T2N 4N1, Canada. E-mail: sheldon@ucalgary.ca.

REFERENCES

1. Hoefnagels WAJ, Padberg GW, Overweg J, Roos RAC. Syncope or seizure? A matter of opinion. Clin Neurol Neurosurg 1992;94:153–6.
2. Van Donselaar CA, Geerts AT, Meulstee J, Habbema JDF, Staal A. Reliability of the diagnosis of a first seizure. Neurology 1989;39:267–71.
3. Wayne HH. Syncope. Physiological considerations and an analysis of the clinical characteristics in 510 patients. Am J Med 1961;30:418–38.

4. Martin GJ, Adams SL, Martin HG, et al. Prospective evaluation of syncope. Ann Emerg Med 1984;13:499–504.
5. 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.
6. 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 loss of consciousness, and neurocardiogenic syncope. Am J Med 1995;98:365–73.
7. Hopkins A, Garman A, Clarke C. The first seizure in adult life. Value of clinical features, electroencephalography, and computerised tomographic scanning in prediction of seizure recurrence. Lancet 1988;1: 721–6.
8. Commission on Classification and Terminology of the International League Against Epilepsy. Proposal for revised clinical and electroencephalographic classification of epileptic seizures. Epilepsia 1981;22: 489–501.
9. Davis TL, Freemon FR. Electroencephalography should not be routine in the evaluation of syncope in adults. Arch Intern Med 1990;150:2027–9.
10. Calkins H, Byrne M, El-Tassi R, Kalbfleisch S, Langberg JJ, Morady F. The economic burden of unrecognized vasodepressor syncope. Am J Med 1993;95:473–9.
11. Klein GJ, Gersh BJ, Yee R. Electrophysiological testing. The court of final appeal for the diagnosis of syncope? Circulation 1995;92:1332–5.
12. Grubb BP, Gerard G, Roush K, et al. Differentiation of convulsive syncope and epilepsy with head-up tilt testing. Ann Intern Med 1991;115:871–6.
13. Krahn AD, Klein GJ, Norris C, Yee R. The etiology of syncope in patients with negative tilt table and electrophysiological testing. Circulation 1995;92:1819–24.
14. Sutton R, Petersen M. The economics of treating vasovagal syncope. Pacing Clin Electrophysiol 1997;20:849–50.
15. Gibson TC, Heitzman MR. Diagnostic efficacy of 24 hour electrocardiographic monitoring for syncope. Am J Cardiol 1984;53:1013–7.
16. Linzer M, Yang EH, Estes MA III, Wang P, Vorperian VR, Kapoor W. Diagnosing syncope. Part I. Value of history, physical examination, and electrocardiography. Ann Intern Med 1997;126:989–96.
17. Linzer M, Yang EH, Estes MA III, Wang P, Vorperian VR, Kapoor W. Diagnosing syncope. Part II. Unexplained syncope. Ann Intern Med 1997;127:76–87.
18. Sheldon R. Evaluation of a single-stage isoproterenol-tilt table test in patients with syncope. J Am Coll Cardiol 1993;22:114–8.
19. Morillo CA, Klein GJ, Zandri S, Yee R. Diagnostic accuracy of a low-dose isoproterenol head-up tilt protocol. Am Heart J 1995;129: 901–6.
20. Benditt DG, Ferguson DW, Grubb BP, et al. Tilt table testing for assessing syncope. J Am Coll Cardiol 1996;28:263–75.
21. Fitzpatrick AP, Theodorakis G, Vardas P, et al. Methodology of head-up tilt testing in patients with unexplained syncope. J Am Coll Cardiol 1991;17:125–30.
22. Sheldon R, Killam S. Methodology of isoproterenol-tilt table testing in patients with syncope. J Am Coll Cardiol 1992;19:773–9.
23. Sheldon RS, Rose S, Koshman ML. Isoproterenol tilt table testing in patients with syncope and structural heart disease. Am J Cardiol 1996;78:700–3.
24. Grubb BP, Karas B. Clinical disorders of the autonomic nervous system associated with orthostatic intolerance. An overview of classification, clinical evaluation, and management. Pacing Clin Electrophysiol 1999;22:798–810.
25. Bloch DA, Moses LE, Michel BA. Statistical approaches to classification. Methods for developing classification and other criteria rules. Arthritis Rheum 1990;33:1137–44.
26. Metz CE. Basic principles of ROC analysis. Semin Nucl Med 1978;8:283–98.