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Focused Clinical Practice Update

Canadian Cardiovascular Society Clinical Practice Update on the Assessment and Management of Syncope

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ABSTRACT

Syncope is a symptom that occurs in multiple settings and has a variety of underlying causes, ranging from benign to life threatening. Determining the underlying diagnosis and prognosis can be challenging and often results in an unstructured approach to evaluation, which is ineffective and costly. In this first ever document, the Canadian Cardiovascular Society (CCS) provides a clinical practice update on the assessment and management of syncope. It highlights similarities and differences between the 2017 American College of Cardiology/American Heart Association/Heart Rhythm Society and the

Syncope is a common cardiovascular presentation, and syncope research has been expanding, resulting in guideline documents appearing since 2015 from the Heart Rhythm Society (HRS),¹ European Heart Rhythm Association,²

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RÉSUMÉ

La syncope qui est un symptôme survenant dans nombreux contextes et présentant un grand nombre de causes sous-jacentes va de la syncope bénigne à la syncope mettant en danger la vie. La détermination du diagnostic sous-jacent et du pronostic peut être difficile et aboutit souvent à une approche d'évaluation non structurée, qui s'avère inefficace et coûteuse. Dans ce tout premier document, la Société canadienne de cardiologie (SCC) fournit l'actualisation des recommandations de pratique clinique pour l'évaluation et la prise en charge de la syncope. Il présente les similarités et les différences entre

American College of Cardiology (ACC)/American Heart Association (AHA)/HRS,³ and European Society of Cardiology (ESC).⁴ The documents provide useful insights for what might be most useful for practicing physicians. Many items are similar, and we emphasize these as an international consensus. There also remain important differences, including the role of syncope units, whose implementation might pose challenges for some health care systems and for which evidence of utility, at least in a hospital setting, is not strong. In light of the importance of syncope we drew on the recent guideline documents on the diagnosis and management of

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2018 European Society of Cardiology guidelines, draws on new data following a thorough review of medical literature, and takes the best available evidence and clinical experience to provide clinical practice tips. Where appropriate, a focus on a Canadian perspective is emphasized in order to illuminate larger international issues. This document represents the consensus of a Canadian panel comprised of multidisciplinary experts on this topic with a mandate to formulate disease-specific advice. The primary writing panel wrote the document, followed by peer review from the secondary writing panel. The CCS Guidelines Committee reviewed and approved the statement. The practice tips represent the consensus opinion of the primary writing panel authors, endorsed by the CCS. The CCS clinical practice update on the assessment and management of syncope focuses on epidemiology, the initial evaluation including risk stratification and disposition from the emergency department, initial diagnostic work-up, management of vasovagal syncope and orthostatic hypotension, and syncope and driving.

syncope from the ACC/AHA/HRS³ and ESC⁴ professional organizations, we highlight similarities and differences among the guideline recommendations, draw on new data, and provide clinical practice tips. Where appropriate we focus on a Canadian perspective, to illuminate larger international issues.

Methods

This document was developed after a thorough consideration of medical literature and the best available evidence and clinical experience. It represents the consensus of a Canadian panel comprised of multidisciplinary experts on this topic with a mandate to formulate disease-specific advice. Expert representatives from the Canadian Cardiovascular Society (CCS; P.K.) and Canadian HRS Association (R.K.S., R.S.S., S.R.R., C.A.M., A.D.K.), the Canadian Society of Internal Medicine (J.C.G.) and the Canadian Association of Emergency Physicians (V.T.) comprised the primary writing panel, with additional representation from the patient sector, health care administration, primary practice, and neurology in the secondary writing panel (see the Acknowledgements section). The members of the primary writing panel provided the overall structure of this clinical practice update. The primary writing panel wrote the document, followed by peer review from the secondary writing panel with combined expertise to address our recommendations in the Canadian context. The CCS Guidelines Committee reviewed and approved the statement. The practice tips represent the consensus opinion of the primary writing panel authors, endorsed by the CCS.

Epidemiology

Syncope is a symptom that occurs in multiple settings and has multiple underlying causes. Lifetime syncope incidence is underestimated in the literature. Accurate assessment is difficult because available data are reflective of specific populations les recommandations de 2017 de l'American College of Cardiology, de l'American Heart Association et de la Heart Rhythm Society, et les recommandations de 2018 de la Société européenne de cardiologie, s'inspire des nouvelles données après un examen approfondi de la littérature médicale et puise dans les meilleures données scientifiques disponibles et l'expérience clinique pour donner des conseils de pratique clinique. Lorsque cela s'avère approprié, la perspective canadienne est mise en évidence dans le but d'éclairer les plus grands enjeux internationaux. Ce document représente le consensus d'un comité multidisciplinaire canadien composé d'experts sur ce sujet qui ont pour mandat de formuler des conseils propres à cette maladie. Le principal comité d'experts a écrit le document, et la revue par les pairs a été effectuée par le comité d'auteurs secondaire. Le comité des lignes directrices de la SCC a examiné et approuvé l'énoncé. Les conseils de pratique représentent le consensus des auteurs du comité principal et sont approuvés par la SCC. La mise à jour des recommandations de pratique clinique de la SCC pour l'évaluation et la prise en charge de la syncope est axée sur l'épidémiologie, l'évaluation initiale, notamment la stratification du risque et la disposition du service des urgences, le bilan diagnostique initial, la prise en charge de la syncope vasovagale et de l'hypotension orthostatique, ainsi que la syncope et la conduite automobile.

being evaluated, uncertainty exists regarding consistency of data collection and definitions, and there is an assumption of a proper diagnosis. With this in mind, the lifetime incidence of syncope in Canada and the Netherlands is estimated to be 32%-35% in the general population.^{5,6} A contemporary estimate of 19% was reported for the prevalence of syncope among randomly selected residents of Olmsted County (Minnesota) 45 years old or older over a 2-year period.⁷ Most studies on syncope epidemiology consistently report higher rates of incidence and prevalence in women compared with men, and with increasing age.⁸

With respect to acute care settings in Canada, syncope accounts for approximately 1% of all emergency department (ED) presentations and among syncope presentations, 12%-15% of patients are admitted to the hospital.⁹⁻¹¹ This is far fewer than reported international metrics, which range from 32% to 83%.^{1,12,13} Between 2004 and 2014, there were 98,730 hospitalizations with a primary diagnosis of syncope in Canada (excluding Quebec) for an age- and sex-standardized hospitalization rate of 0.54 per 1000 population.⁹ Over this time period, there was a modest 14% decrease in the rate of hospitalizations for syncope; however, presentations to the ED appear to be increasing.¹¹ Hospitalization rates differed significantly across the provinces, with higher rates in New Brunswick (0.9 per 1000 population) and Saskatchewan (0.7 per 1000 population) and lower rates in Alberta and Manitoba (0.3 per 1000 population).¹⁴ In-hospital mortality overall is 0.7%⁹ with an interprovincial range of 0.4%-1.1%.¹⁴ The economic burden of syncope, including costs of hospitalizations, outpatient visits, and physician and drug costs, was estimated to be over CAD\$90 million per year among patients who presented to the ED with a primary diagnosis of syncope between 2009 and 2014 in Alberta.¹¹ These estimates are lower than reported in other countries¹⁵ because most syncope-related costs are related to hospitalizations, and admission rates in Canada are much lower than in other countries.

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Initial Evaluation

Syncope is the common final presentation for a variety of conditions ranging from benign to life-threatening. Identifying the underlying cause might be challenging. The causes of syncope can generally be classified into categories of noncardiac syncope such as reflex syncope (vasovagal, situational, carotid sinus syndrome), orthostatic intolerance (dehydration, medication, neurogenic, postural orthostatic tachycardia, initial orthostatic hypotension [OH]), or cardiac syncope (arrhythmic, structural, cardiopulmonary).⁴ An initial evaluation consisting of a detailed history, physical exam (including standardized orthostatic vitals defined as blood pressure (BP) and heart rate changes in lying and sitting positions, on immediate standing, and after 3 minutes of upright posture) and 12-lead electrocardiogram (ECG) should be performed to determine whether an underlying cause of syncope can be identified as noncardiac, cardiac, or other, and to help determine prognosis (Fig. 1).^{3,4} This basic assessment is emphasized in both guideline documents with the distinction that the 2017 ACC/AHA/HRS guidelines³ provide a class I recommendation for this initial approach whereas the ESC⁴ document gives no class recommendation.

Practice Tip: Approach to patients who present with transient loss of consciousness

The initial ED syncope evaluation should consist of a careful and thorough history, physical exam (including standardized orthostatic vitals), and 12-lead ECG.

Risk Stratification

The role of risk stratification is to: (1) estimate prognosis; (2) influence decision to hospitalize; (3) establish urgency for specialist involvement and advanced investigations; and (4) ensure an appropriate discussion with the patient regarding their specific wishes and values. The final ED diagnosis is a good predictor of short-term prognosis: excellent for vasovagal, not as good for cardiac, and intermediate for those with an unknown cause or OH.¹⁶ If no serious underlying conditions are detected at the end of an ED evaluation, even in

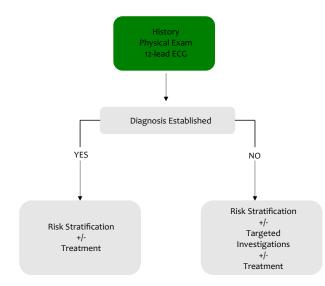


Figure 1. Initial evaluation of syncope. ECG, electrocardiogram.

patients with the likely etiology identified, risk stratification can assist triage decisions.^{3,4} Several ED syncope risk stratification tools have been developed to aid physician decisionmaking with the goals to reduce unnecessary hospitalizations and decrease health care costs. From these studies, certain predictors (older age; heart disease; abnormal ECG; abnormal lab values—hemoglobin/hematocrit, troponin, or natriuretic peptides; presumed etiology; or abnormal vital signs) have been consistently associated with poor prognosis.¹⁷⁻²¹ However, the prediction tools have not been widely adopted into clinical practice because of important methodological limitations and there is absent evidence they perform better than unstructured physician judgement.²² The use of prediction tools is given a class IIb recommendation in both guidelines.

Both syncope guidelines report lists of predictors on the basis of the initial evaluation to help identify low- and high-risk features for risk stratification (Table 1). Details for high-risk features on an ECG are shown in Table 2.^{3,4,19,20,23-27}

Beyond a short-term risk assessment, only the ACC/AHA/ HRS guidelines³ recommend physicians consider a long-term risk assessment at initial presentation, which is largely on the basis of comorbidity burden. Since the publication of these guidelines, a prediction tool, the Canadian Syncope Risk Score, addressing many of the limitations of prior risk scores was developed and validated.⁴¹ The Canadian Syncope Risk Score is comprised of 9 factors that capture clinical factors, abnormal ECG features, and elevated troponin (> 99th percentile of normal population), and presumed initial diagnosis in the ED to then stratify patients anywhere from "very low" to "very high" for a 30-day adverse event (Fig. 2). Although implementation studies are still lacking, it is suggested that if no serious underlying conditions are identified after an index ED evaluation, low-risk patients (score of -3 to 0) can be discharged home with no further follow-up,

| Table 1. | Low- and | high-risk | predictors | for ris | k stratification |
|----------|----------|-----------|------------|---------|------------------|
|----------|----------|-----------|------------|---------|------------------|

| | Low-risk features | High-risk features |
|---|--|--|
| History ^{17-21,28-35} | Prodrome typical of reflex syncope Triggers/specific situations typical of reflex syncope Positional syncope Absence of cardiovascular disease | Symptoms suggestive of cardiac disease Syncope during exertion or supine or without prodrome History of cardiovascular disease (ischemia, arrhythmic, obstructive, valvular |
| | | Concomitant trauma Family history of sudden cardiac death (age younger than 50 years) |
| Physical examination ^{17,30,36} | Normal | Abnormal vital signs Abnormal cardiac exam |
| 12-Lead ECG ^{17,21,29,36} | Normal | Any bradyarrhythmia, tachyarrhythmia, or conduction disease |
| Laboratory values ³⁷⁻⁴⁰ | Normal | Elevated cardiac biomarkers or other relevant abnormal blood tests with a suspected related diagnosis |

ECG, electrocardiogram.

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| Feature | Description | | |
|-------------------------|---|--|--|
| Bradyarrhythmia | | | |
| Sinus node dysfunction | Asymptomatic inappropriate sinus rate < 50 bpm or slow AF (40-50 bpm), sinus block, sinus pause > 3 seconds in the absence of negatively chronotropic medications | | |
| Conduction disease | Bifascicular block | | |
| | Intraventricular conduction delay (QRS 120 ms) | | |
| | Second-degree AV block type 1 with prolonged PR interval | | |
| | Second-degree AV block type 2 | | |
| | Third-degree AV block | | |
| Tachyarrhythmia | Ũ | | |
| Supraventricular | Ventricular pre-excitation | | |
| • | Supraventricular tachycardia or AF | | |
| Ventricular tachycardia | Nonsustained ventricular tachycardia Evidence of acute ischemia or previous myocardial infarction Long (> 460 ms) QT on repetitive ECG: or short (< 340 ms) QT interval Type 1 Brugada | | |
| | Brugada pattern (RBBB with ST elevation V1-V3) | | |
| | Arrhythmogenic right ventricular cardiomyopathy features (negative T waves in right precordial leads, epsilon wave, ventricular late potentials) Ventricular hypertrophy | | |

Table 2. High-risk electrocardiogram features

AF, atrial fibrillation; AV, atrioventricular; bpm, beats per minute; ECG, electrocardiogram; RBBB, right bundle branch block.

medium-risk patients (score of 1-3) can be discharged with follow-up on the basis of the type of serious condition suspected, and high-risk patients (score ≥ 4) might benefit from brief hospitalization.

| Category | Points |
|--|--------|
| Clinical evaluation | |
| Predisposition to vasovagal symptoms* | -1 |
| History of heart diseaset | 1 |
| Any systolic pressure reading < 90 or > 180 mm Hg‡ | 2 |
| Investigations | |
| Elevated troponin level (> 99th percentile of normal population) | 2 |
| Abnormal QRS axis (< –30° or > 100°) | 1 |
| QRS duration > 130 ms | 1 |
| Corrected QT interval > 480 ms | 2 |
| Diagnosis in emergency department | |
| Vasovagal syncope | -2 |
| Cardiac syncope | 2 |
| Total score (–3 to 11) | |

*Triggered by being in a warm crowded place, prolonged standing, fear, emotion or pain

[†]Includes coronary or valvular heart disease, cardiomyopathy, congestive heart failure and non-sinus rhythm (electrocardiogram evidence during index visit or documented history of ventricular or atrial arrhythmias, or device implantation) *Includes blood pressure values from triage until disposition from the emergency department

Figure 2. Canadian Syncope Risk Score.

Practice Tip: Risk stratification Identification of low-risk (benign condition) and high-

risk (serious condition) features on the basis of history, physical exam, and 12-lead ECG can aid physicians in predicting short-term and long-term prognosis.

Disposition from the ED

The decision for hospitalization is largely on the basis of the seriousness of the identified/presumed diagnosis in the ACC/AHA/HRS³ guidelines, whereas the ESC recommends a decision on the basis of high-risk features identified during the initial evaluation.⁴ We suggest an approach that incorporates both (Fig. 3). There is consensus among guidelines that in patients without a serious condition (eg, with possible reflex syncope or low-risk features), hospitalization is unlikely to improve short- and long-term outcomes and these patients should be managed in an outpatient setting. In patients with a serious medical condition or high-risk features, hospitalization might help to expedite treatment or further diagnostic workup.

The major difference between the guidelines is in the disposition of patients who are deemed "intermediate" risk. The ACC/AHA/HRS guidelines suggest use of a structured ED observation protocol (time-limited observation; ie, 6 to <48 hours and expedited access to cardiac testing/consultation) can be an effective strategy (class IIa recommendation), however, this is also on the basis of sparse data from randomized clinical studies.^{42,43}

The ESC guidelines⁴ provide a strong recommendation (class I) for an ED or outpatient syncope unit evaluation instead of admission to the hospital for this subgroup. A syncope unit is a facility featuring a standardized, fairly

| Total score | Estimated risk of serious adverse event,§ % | Risk category |
|----------------|--|------------------|
| -3 | 0.4 | Very Low |
| -2 | 0.7 | Very Low |
| -1 | 1.2 | Low |
| 0 | 1.9 | Low |
| 1 | 3.1 | Medium |
| 2 | 5.1 | Medium |
| 3 | 8.1 | Medium |
| 4 | 12.9 | High |
| 5 | 19.7 | High |
| 6 | 28.9 | Very High |
| 7 | 40.3 | Very High |
| 8 | 52.8 | Very High |
| 9 | 65.0 | Very High |
| 10 | 75.5 | Very High |
| 11 | 83.6 | Very High |

[§] Shrinkage-adjusted expected risk

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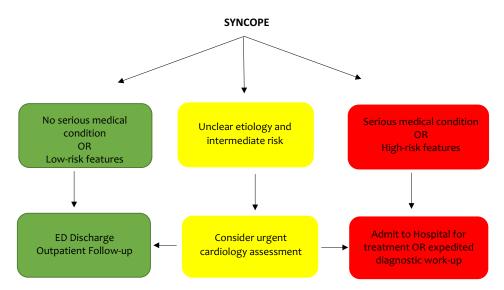


Figure 3. Approach to disposition decision from the Emergency Department (ED).

algorithmic approach to the diagnosis and management of syncope, with dedicated staff led by a syncope expert and expedited access to appropriate diagnostic tools, specialists, and therapies. The data suggesting syncope units improve diagnostic accuracy, reduce unnecessary testing, and decrease costs are limited.² Several preliminary quality indicators from the ESC^{2,4} have been suggested to assess the added value of syncope units including: (1) absolute rate of undiagnosed transient loss of consciousness should be reduced by 20%; (2) less than 20% of low-/intermediate-risk transient loss of consciousness should be admitted from the ED; and (3) syncope units should have a 20% reduction in costs compared with usual care and improve outcomes (ie, < 5% readmission for syncope and < 20% of paced patients with recurrence at 1 year).^{2,4} Overall, among hospitalized Canadians, the 30-day readmission rate for syncope is 1.1% with an interprovincial range of 1.1%-1.6%, 9,14 and 1-year readmission rate for syncope is 4% lower than international targets.^{2,4}

Some of the recommendations reflect local medical, cultural, or political contexts. This is particularly notable in the approach to syncope units. These are widespread in Europe and the United Kingdom, with significant resource investments, despite limited evidence that they improve outcomes. The ACC/AHA/HRS writers, and the CCS writers sometime before them, weighed the data against the barriers to establishing them in the fractured US system, and the implications of the decisions. Canadian reluctance was on the basis of our overall excellent metrics on syncope evaluation, which already exceed ESC standards.

Practice Tips: Disposition from the ED

- 1. Low-risk patients should be managed in an outpatient setting with reliable and timely access to community-based systems.
- 2. Inpatient evaluation is recommended for syncope patients with an identified serious condition (to facilitate

immediate treatment), or an unclear etiology and highrisk features.

3. An urgent cardiology assessment should be considered for patients deemed as intermediate-risk to help inform disposition from ED. This could be done in the community as long as there is reliable and timely access to cardiology care.

Values and preferences. In jurisdictions like Canada, caution about syncope units is driven by admission rates and readmission rates for syncope that are already below proposed international targets; substantial costs to a cost-contained publicly funded health care system that would be incurred; and weak evidence for benefit.

Initial Diagnostic Workup

Diagnostic testing is driven by the initial investigations including history, physical examination, and 12-lead ECG. A working hypothesis and differential diagnosis are crucial to determine the merits of individual tests and the extent and context of testing.

Practice Tips: Approach to additional investigations

- 1. The use of broad-based investigations in the workup of syncope is ineffective and costly.
- 2. Cardiac imaging (ie, echocardiogram or stress testing) should be on the basis of clinical suspicion of ischemic, structural, or valvular heart disease.
- 3. Advanced cardiac imaging (ie, computed tomography or magnetic resonance imaging) should be performed in select patients for whom determination of structural heart disease is inconclusive using standard imaging (ie, inflammatory, or infiltrative disease; congenital heart disease).
- 4. Regular stress testing should be performed in patients who present with syncope that occurs before, during, or after exertion.

Blood work has limited value unless a specific suspicion drives decision-making, such as suspected myocardial infarction, pulmonary embolism, or heart failure or any other condition for which the laboratory value might be helpful in obtaining a diagnosis. Current guidelines assign language of "might be useful" to cardiac imaging, largely to establish or eliminate the substrate for a mechanical explanation for syncope, or predisposition to ventricular arrhythmias related to underlying heart disease. Additional testing, particularly neurologic testing is discouraged, unless specifically suspected. Of importance, the ACC/AHA/HRS guideline³ aligns with previous "Choosing Wisely" language discouraging neurologic testing in patients with syncope as a routine test.^{44,45}

Practice Tips: Use of advanced brain imaging and carotid ultrasound

- 1. Brain imaging should be performed only for patients for whom intracranial disease is highly suspected as a possible contributing cause to syncope, or if there has been a suspicion of head trauma as result of syncope.
- 2. Carotid artery imaging in the absence of focal neurological findings should not be performed.

Cardiac monitoring is typically used in all patients during acute presentation with high yield. A recent multicenter report suggests that a 15-day monitoring immediately after an acute syncope episode identified 92% of arrhythmic outcomes among medium- and high-risk patients, including all ventricular arrhythmias.⁴⁶ However, the subsequent nature and extent of monitoring depend on the frequency, severity of syncope, and suspicion for an arrhythmic etiology (Fig. 4). Both guidelines emphasize that monitoring beyond the very acute phase should be tailored according to the frequency of symptoms. Conventional Holter monitoring for 24-72 hours has a limited role unless symptoms are very frequent; patch or external loop recorders are warranted if symptoms are likely to recur within a month.

The ACC/AHA/HRS guideline³ simply recommends that the recording method suit the situation, whereas the ESC guideline⁴ provides specific recommendations. There are 2 specific areas to highlight. First, the ESC suggests only considering noninvasive intermediate-term monitors such as external loop recorders, continuous Holter monitors, or patch monitors in patients who are likely to have recurrent syncope within 4 weeks. The differences are fairly stylistic.

Second, the ESC guideline recommends early use of implantable cardiac monitors in patients with at least 2 syncope events. This means that patients with infrequently recurrent syncope of suspected arrhythmic etiology should undergo early implantable cardiac monitor implantation, foregoing intermediate-term monitoring because of its low yield. Application of this in any health care setting is influenced by the access to and nature of intermediate-term monitors, which are highly variable across Canada.

Tilt-table testing has seen immense attrition in the past 20 years, but retains slightly different roles in both recent guidelines. The ESC guideline⁴ remains more liberal,

advocating tilt testing be considered in patients with suspected reflex syncope, OH, postural orthostatic tachycardia syndrome, or psychogenic syncope. The ACC/AHA/HRS guideline³ in large part supports the use of tilt-table testing when there is diagnostic uncertainty after an initial history and physical examination, and provides a class III recommendation against using tilt testing to determine drug treatment choice or treatment efficacy.

Practice Tip: Tilt-table testing

A tilt-table test should be considered only when there is diagnostic uncertainty. Usually this includes atypical presentations, older patients with few clues in the history, distinguishing convulsive syncope from epilepsy, and nonhemodynamic collapses.

Minor differences in wording between the documents can make differences in content seem large. For example, the ACC/AHA/HRS guideline³ does not recommend an electrophysiology study (EPS) in patients with a normal ECG and cardiac structure and function, unless an arrhythmic etiology is strongly suspected because of a low diagnostic yield. In contrast, the ESC guideline⁴ provides a class I recommendation for EPS in patients with syncope and a history of myocardial infarction and a class II recommendation in patients with syncope and bifascicular block. Both statements seem functionally equivalent upon close inspection. The role of EPS in patients with structurally normal hearts and bifascicular block is prominently endorsed by the ESC, although the data for this are sparse.⁴⁷⁻⁵¹

Practice Tip: EPS

The use of invasive EPS is very limited to those with suspected arrhythmic cause and abnormal ECG or structural heart disease, after noninvasive testing.

Values and Preferences: There is very weak evidence for the role of EPS other than in patients with structural heart disease. Measurements of sinus node dysfunction (such as sinus node recovery time) and conduction delay (such as HV interval) have poor test characteristics and have not been shown to improve outcomes.

A final notable difference between the 2 documents is the use of video monitoring to record syncope. The ESC guidelines formally support, with a class IIa recommendation, the use of video monitoring whether during tilt testing, spontaneous syncope in the community captured using smart phones or surveillance equipment, or formal hospital-based units. The most important diagnostic dilemmas include convulsive syncope vs epilepsy, and nonhemodynamic collapses because of conversion syndromes. Although potentially useful, the almost incomplete lack of data^{52,53} on these tools prevented the ACC/AHA/HRS from providing a similar recommendation.

Tailoring Cardiac Monitor Selection to Symptom Frequency

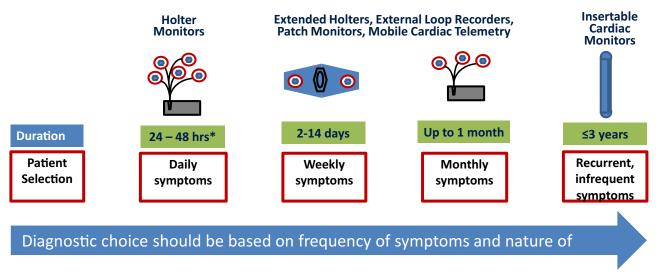


Figure 4. Selection of cardiac monitors for evaluation of suspected arrhythmic syncope.

Management of Syncope

As in any investigative and treatment model, a true application of "shared decision-making" between the care provider(s) and the patient must be considered to ensure respecting the patient's values, needs, and expectations (Fig. 5).

Management of vasovagal syncope

Vasovagal syncope (VVS) usually has a benign course; however, recurrent VVS can significantly reduce quality of life⁵⁴ and treatment might be required. Guidelines on who might benefit from treatment primarily depend on patient and physician preference. Management is on the basis of nonpharmacologic interventions comprised of education, lifestyle modifications, and reassurance. Most of these interventions have little evidence of efficacy but are simple to implement, not likely to cause harm, and should be recommended to all patients with VVS. The main difference between the ESC⁴ and ACC/AHA/HRS guidelines³ is an age recommendation, detailed later.

Nonpharmacological therapies. Education and reassurance of the benign nature of VVS significantly reduces recurrence of syncope in most patients. Avoidance of triggers and situations (ie, coughing, micturition, defecation, laughing, dehydration, crowded environments), as well as education on early identification of prodromes is essential to prevent many syncope/presyncope episodes. Increased water and salt intake are strongly recommended but are on the basis of very limited evidence. Lying down quickly with the onset of presyncope should be recommended to all patients, when feasible. Counter-pressure manoeuvres have been validated in a single randomized trial and 3 observational studies. Leg-crossing, limb/abdominal contractions, and squatting might all be useful in patients with a clear and sustained prodrome (> 1 minute). These manoeuvres are not recommended in older subjects because of evidence of ineffectiveness.

Pharmacologic therapy. Recurrent VVS refractory to nonpharmacological measures have been reported in 15%-20% of patients.⁴ Despite numerous randomized controlled trials, no single therapy has been proven to be highly effective. The ESC and ACC/AHA/HRS guidelines^{3,4} provide excellent treatment algorithms with some important practical differences. The ESC guideline⁴ proposes treatment on the basis of age: a "younger" population defined as those younger than 40 years and an "older" population, defined as older than 60 years, with an overlap for those between 40 and 60 years. Additionally, treatment in the ESC guideline⁴ is on the basis of a low BP phenotype defined as systolic BP \leq 110 mm Hg. These distinctions, which have almost no data to substantiate them, are not recommended in the ACC/AHA/HRS guidelines.

The ESC guideline⁴ proposes first-line therapy with either fludrocortisone or midodrine (class IIb) in patients with recurrent VVS and the low BP phenotype. In contrast, the ACC/AHA/HRS guideline³ suggests midodrine as first-line therapy (class IIa); fludrocortisone is recommended as a second-line therapy (class IIb). Another important difference is that the ACC/AHA/HRS guideline³ includes β -blockers in patients older than 42 years and selective serotonin reuptake inhibitors as second-line therapy, both class IIb recommendations. β -Blockers (class III) and serotonin reuptake inhibitors are not recommended in the ESC guidelines. The transatlantic differences are because of minor differences in the interpretation and weighing of the data.

Practice Tips: Pharmacotherapy in recurrent, refractory VVS

- 1. Fludrocortisone (0.2 mg/d once a day) or midodrine (5-15 mg every 4 hours, 3 times a day) are acceptable first-line options after nonpharmacological interventions.
- 2. β -Blockers may be used in patients older than 42 years as a second-line option, particularly in patients with other indications for β -blockade therapy.
- 3. Combination therapy is occasionally needed for patients with refractory VVS.

Cardiac pacing. Indications for cardiac pacing and whether any particular pacing algorithm is superior in selected patients with VVS remains controversial. The ACC/AHA/HRS guideline commissioned a specific systematic review on pacing as treatment for reflex-mediated (vasovagal, situational, or carotid sinus hypersensitivity) syncope.⁵⁵ An ACC/AHA/HRS class IIb recommendation is provided for dual-chamber pacing in a select population of patients 40 years of age or older with recurrent VVS and prolonged spontaneous pauses.³ In contrast, the ESC guideline provides a class IIa recommendation for patients with recurrent reflex syncope with spontaneous asystolic pauses due to "extrinsic (functional) causes (ie, vagally-mediated or adenosine-sensitive)" syncope. The ESC guideline⁴ further suggests that patients with reflex syncope and tilt-induced asystolic pauses might have an indication for dual-chamber pacing (class IIb). There is considerable and important uncertainty about whether specific sensors and pacing algorithms are necessary, and indeed whether responders to some pacing systems actually have VVS.

Practice Tip: Pacing indication for VVS

Patients 40 years of age or older with highly symptomatic recurrent VVS might benefit from dual-chamber pacing if they have either:

- 1. Documented symptomatic asystole > 3 seconds or asymptomatic asystole > 6 seconds; or
- 2. Tilt-induced: asystole > 3 seconds or heart rate < 40 beats per minute for > 10 seconds.

The patient should be seen urgently (within 2 weeks) by a cardiologist/electrophysiologist depending on the local practice to review results, decision regarding management, and arrange next steps for implantation, if needed.

Values and preferences. The possible benefits of pacing should be weighed against the uncertainty in the field, and the potential risks of chronic pacemaker therapy. It should be considered only in highly symptomatic patients and after other options are exhausted.

Management of orthostatic hypotension

Syncope due to OH is a frequent cause in older patients.⁵⁶ Neurogenic OH and drug-induced OH are the most common causes. In the presence of a postural decrease in BP $\geq 20/10$ mm Hg, OH should be considered as a potential cause of syncope. Multiple causes of syncope are not infrequent in this population. OH syncope might be an initial manifestation of other systemic disorders such as Parkinson disease, and related conditions, diabetes, or pure autonomic failure.

Nonpharmacological therapies. The ACC/AHA/HRS and ESC guidelines^{3,4} provide a class I recommendation for education, lifestyle measures, and adequate salt and water intake as first-line therapy for OH. Stopping or adjusting the doses of vasoactive agents such as angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, thiazides or other diuretics, calcium channel blockers, and β -blockers is routinely recommended (class IIa). In patients with persistent symptoms despite counter-pressure manoeuvres, compression garments (ESC recommended.

Practice Tips: Nonpharmacological management of OH

- 1. Education and reassurance.
- 2. Salt and water intake, if there are no contraindications.
- 3. Removal of any offending medications as long as there are no clear indications for their use or there is no suitable replacement.
- 4. Counter-pressure manoeuvres, compression garments, and head-up tilt sleeping.

Pharmacologic therapy. The ACC/AHA/HRS and ESC documents^{3,4} suggest that midodrine and fludrocortisone (class IIa) might be needed to prevent recurrence of syncope. In patients with refractory OH, the ACC/AHA/HRS guide-line recommends the use of droxidopa (class IIa), although this is not available in Canada. Other pharmacologic interventions are on the basis of low-level evidence and include octreotide in postprandial hypotension, and pyridostigmine.

Practice Tip: Pharmacotherapy in patients with OH Midodrine, fludrocortisone, or droxidopa (short-term use—not available in Canada) are acceptable first-line options after nonpharmacological interventions.

Syncope and Driving

Driving means independence and freedom for many people, and the loss of driving privileges can pose a severe hardship that can affect employment and quality of life. Conversely, there is societal concern and disapproval when someone becomes medically incapacitated while driving and causes death or injury to others. The challenge is how to balance these considerations.

More than 25 years ago, the CCS developed a formula to assess fitness to drive (risk of harm = fractional time spent

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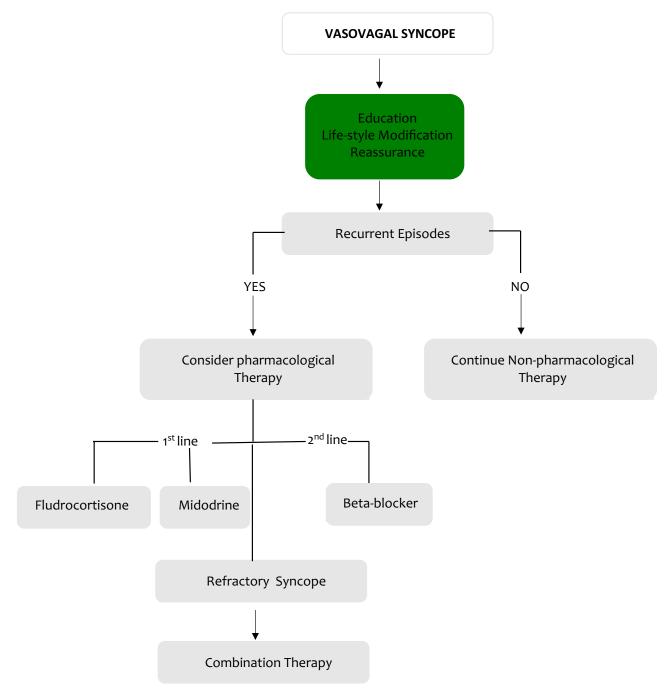


Figure 5. Management of vasovagal syncope.

driving \times type of vehicle \times risk of sudden incapacitation (< 1% accepted by general population \times probability of an event [syncope] resulting in a fatality or injury-producing accident [assumed 2% for all drivers]).⁵⁷ The formula provides a useful framework, but despite international interest has had modest regulatory effect because of lack of data. No other method to assess fitness to drive exists.

The ACC/AHA/HRS guideline³ makes a single recommendation regarding driving in patients with syncope (class IIa): health care providers should know the laws and restrictions in their individual jurisdictions, as these vary greatly. In the absence of data the writing committee provided only suggestions, and declined the opportunity to provide recommendations. The suggestions are almost solely on the basis of expert opinion and only for private drivers. In the European guidelines (as part of the practical instructions to 2018 document), advice is also extended to commercial drivers. A single Canadian report did document the low risk posed by patients with VVS, compared with the much higher risk of specific demographic groups. Indeed, the risks of many demographic groups exceed the tolerance proposed by the CCS formula.

Practice Tips: Driving and syncope

- 1. Risk of syncope while driving in patients with VVS is < 1% per year.
- 2. No driving restrictions for patients with a single VVS event unless high-risk features are present (eg, syncope while driving, lack of prodrome).
- 3. For patients with unexplained syncope or frequent VVS, or limited prodrome, a driving restriction for 1 month might be reasonable.

Values and preferences. Physicians and society need to balance societal safety and individual needs. Driving regulations vary greatly across jurisdictions. Physicians are strongly advised to understand the local regulations when offering their driving recommendations.

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