The Appropriateness of an Ischemia Evaluation for Syncope

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Syncope, a transient loss of consciousness, is a common symptom that occurs in ≈20% to 40% of adults at least once in their lifetime. Although this presentation is often associated with a benign course or perhaps minor injury, major morbidity may also occur. An abundance of literature has examined the various causes of syncope, but up to 40% of patients may have no identifiable etiology for syncope. Vasovagal (vasodepressor) syncope and orthostatic hypotension are usually reported as the common causes, with ischemic heart disease accounting for a very low percentage of these presentations.

Starting with the pioneering work by Kapoor et al, it was recognized that the presence of heart disease portends a worse prognosis for patients with syncope compared with those with no structural heart disease. Therefore, a young adult with syncope of unknown origin and no structural or electric heart disease has a better outlook than a similar patient with newly diagnosed cardiomyopathy. Multiple algorithms for syncope evaluation make this important differentiation in terms of diagnosis and should also provide risk assessment and the planning of appropriate therapy.

The evaluation of syncope begins with a detailed history and physical examination, including blood pressures in supine and upright position. An ECG is reasonable for almost all patients with syncope of unexplained origin. This initial assessment can identify or be suggestive of the cause of syncope in ≈20% to 40% of patients. After this initial evaluation, patients with suspected or confirmed diagnost tests can undergo confirmatory tests and therapy. For the remainder of undiagnosed patients, additional testing is usually required to determine the presence or absence of structural heart disease.

A transthoracic echocardiogram is a logical early step in the clinical evaluation of syncope and is supported by clinical practice guidelines and appropriate use criteria. Even in the absence of signs or symptoms of cardiovascular disease, a resting echocardiogram would still be considered appropriate for patients who present with syncope, as multiple etiologies of syncope related to underlying structural heart disease can be uncovered, such as a variety of cardiomyopathies, valvular disorders, and cardiac tumors. Ischemia evaluation, including stress myocardial perfusion imaging (MPI) may then be considered in the context of newly discovered cardiomyopathies or other structural heart disease.

Perhaps the most clinically worrisome cause for syncope is myocardial ischemia, which may present with clues to this potential etiology, such as a preceding history of coronary artery disease (CAD) or ischemic ECG abnormalities. Severe ischemia rarely produces the depressed cardiac output and hypotension required to result in syncope. More likely, however, ischemia may cause syncope indirectly through the production of arrhythmias or activation of certain reflexes. Inferior wall myocardial ischemia may trigger the Bezold–Jarisch reflex, resulting in hypotension and bradycardia, which could precipitate syncope. However, such a high-grade right coronary artery occlusion would be rare in the absence of typical ischemic symptoms. Another plausible pathophysiological link between ischemia and syncope may be related to ischemia-triggered ventricular arrhythmias or atrioventricular block. For ventricular tachycardia to produce syncope, the duration needs to exceed 6 seconds with a ventricular rate sufficiently rapid to cause significant hypotension. Similarly, for transient atrioventricular block to cause syncope, there has to be an asystole or very slow ventricular escape rate lasting for at least 6 seconds. The diagnosis of these arrhythmias likely requires telemetry monitoring or long-term monitoring, potentially with an implantable loop recorder. Once these arrhythmias are identified, ischemia evaluation may be considered if clinically indicated; however, an initial ischemia evaluation would not uncover the arrhythmic pathogenesis of the syncope. There has been little evidence in the literature to guide the use of stress testing, including MPI as part of the syncope workup.

In an effort to bridge the gap between clinical knowledge and practice recommendations, in this issue of Circulation: Cardiovascular Imaging, Alfaroudi et al report their findings in 700 patients with syncope who underwent stress MPI as part of the evaluation. The stress MPI identified 53 patients (7.6%) with abnormal ejection fraction (<50%) and 41 patients (5.9%) with abnormal or equivocal MPI. Coronary angiography was infrequently performed in this trial, thus definitive information regarding the true incidence of CAD is not available. However, CAD and myocardial ischemia seem to be an infrequent explanation for syncope. The incidence of an abnormal perfusion study was low in all groups stratified for the likelihood of CAD by their Framingham Risk Score, ranging from 3.8 to 9.0%.

The current work fails to provide support for a strategy that incorporates MPI for the diagnosis and risk assessment of patients with syncope. The overall frequency of an abnormal MPI result was low and there was no correlation of the MPI findings with the Framingham Risk Score. Moreover, the prognostic use of an abnormal MPI was negligible in this
population, as compared with the ability to predict all-cause mortality based on the Framingham Risk Score.

On the basis of this study and given the lack of any evidence-based studies to the contrary, it seems that the use of stress imaging procedures, including MPI as part of the diagnostic workup for syncope, should be questioned. The most recent appropriate use criteria (AUC) state that, for low-risk syncope patients, the use of both stress echocardiography and stress MPI is inappropriate. However, stress imaging is felt to be appropriate for these patients at intermediate or high risk for coronary heart disease.\(^\text{10}\) It is interesting that the uncertain category was not used, as minimal data were previously available. The AUC have recently undergone a substantial change in terminology, which may clarify how tests and procedures may be used.\(^\text{12}\) With the new designations of maybe appropriate and rarely appropriate replacing the previous terms of uncertain and inappropriate, MPI now seems to be well-suited to the rarely appropriate category, irrespective of the clinical risk for ischemic heart disease.

The European Society of Cardiology guidelines for evaluation and management of syncope also provide recommendations for stress testing. Exercise testing is not routinely recommended and should be performed only if patients have syncope during or shortly after exercise.\(^\text{3}\) For young patients who have syncope post exertion, the diagnosis is generally because of reflex mechanisms or vasovagal syncope. When syncope has occurred during exercise, a stress test may uncover exercise-induced tachyarrhythmias or atrioventricular block. More often, however, is that syncope during exercise may be a marker of structural heart disease that limits cardiac output during exercise, such as aortic stenosis, hypertrophic cardiomyopathy, or pulmonary embolus.

An exercise ECG stress test (nonimaging) may suffice to identify and confirm arrhythmias or atrioventricular block responsible for syncope. MPI stress testing may not be required, although an assessment of underlying structural heart disease may be useful. If left ventricular systolic dysfunction is subsequently discovered, then further ischemia evaluation may be indicated and MPI should be considered as part of the evaluation.

The findings and implications of this report by AlJaroudi et al\(^\text{1}\) are important in terms of the context of the cost-effective evaluation of syncope. The costs involved in the diagnostic tests and hospitalizations of patients with syncope can be substantial.\(^\text{13}\) Therefore, given the demands for more cost-efficient health care delivery, it is incumbent on clinicians to use healthcare resources effectively and efficiently. This study fills in an important literature gap for the evaluation of patients with syncope. The demonstration of the limited prognostic value of routine MPI in patients of all coronary heart disease risk categories suggests the need to reassign these tests to the rarely appropriate category for patients with syncope but without a prior diagnosis of ischemic heart disease.

Disclosures
Dr Mitrani has served as a consultant for Medtronic Inc., St. Jude Medical, and Lifewatch Inc. The other authors have nothing to disclose.

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