



## Syncope: Diagnostic Challenge and Economic Burden

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**Key words:** syncope, electrocardiogram, hospitalization rates, diagnostic yield

*IMAJ 2008;10:149–151*

Syncope is a common health problem that may have multiple possible causes, ranging from benign conditions to life-threatening diseases. These features make syncope a major health challenge to the treating physician attempting to diagnose the etiology of the event and differentiate the benign cases from those requiring quick interventions. Due to its potentially life-threatening etiology, patients often undergo a long and costly evaluation in order to reach a diagnosis. This turns syncope into both a clinical challenge and a financial burden on health care systems.

In their article in this issue of *IMAJ*, Shiyovich et al. [1] demonstrate that what is already known throughout the world is not different in Israel in terms of etiology, use of diagnostic tests and outcome. The authors describe the overuse of low yield expensive tests and the under-use of high yield tests like the tilt-table examination, resulting in high overall health expenditures for these patients. They also show that despite this high cost of evaluation, nearly half of the patients are discharged without an identified cause, as reported in other studies as well [2].

In order to make syncope evaluation simpler and less expensive, several guidelines have been compiled. According to the guidelines on syncope of the European Society of Cardiology [3] and a similar statement of the American Heart Association [4], the initial evaluation of patients with syncope is based on a thorough history and physical examination, supine and upright blood pressure measurement, and standard electrocardiogram. Subsequently, three questions should be addressed: a) Is it a true syncope (loss of consciousness attributable to cerebral hypoperfusion)? b) Does the initial evaluation lead to certain diagnosis, suspected diagnosis or unexplained diagnosis? c) Is heart disease present?

A certain diagnosis for syncope etiology, with the exception of multifactorial syncope, may be made for vasovagal syncope when precipitating events and typical prodromal symptoms are demonstrated, for situational syncope when it occurs immediately or during the specific situation, for orthostatic syncope when a decrease in systolic blood pressure  $\geq 20$  mmHg is associated with syncope, and for myocardial ischemia or

arrhythmia-related syncope when syncope occurs with ECG evidence of acute ischemia or specific arrhythmias. The absence of signs of overt heart disease can almost rule out cardiac related syncope, with the exception of syncope accompanied by palpitations that could be due to paroxysmal tachycardia. When the initial evaluation does not lead to a suspected diagnosis (unexplained syncope) and it is a single or very rare event, there is no need for further evaluation. However, when the initial evaluation leads to a suspected diagnosis or if the patient has experienced frequent or severe unexplained syncope events, further tests should be taken to rule out or confirm the suspected diagnosis. The most useful tests include carotid sinus massage and tilt-testing for reflex-mediated syncope; echocardiogram, Holter ECG, loop recording, electrophysiological study, or exercise stress testing for cardiac causes. Less useful tests, which are indicated only in selected cases, include electroencephalography, brain computed tomography, magnetic resonance imaging and carotid Doppler for epilepsy and transient ischemic attack; and coronary angiography, cardiac or pulmonary CT for cardiac causes [5].

To illustrate the problematic aspects of syncope evaluation and the need to establish and implement guidelines, apart from the high rates of unexplained etiology for syncope, also demonstrated in the article by Shiyovich and co-workers [1], several studies have also shown the low diagnostic yield and high costs of such investigations. Steinberg and Knilans [6] have shown in a pediatric population with syncope that only about 4% of the tests performed were diagnostic and that the average costs per diagnosis reached almost 7000 U.S. dollars. Another study followed patients hospitalized with syncope that was suspected to be of vasovagal etiology. These patients still underwent considerable diagnostic evaluation, which, of course, was found to have a very low yield [7].

Apart from the official guidelines of the European Society of Cardiology and the American Heart Association, many local position papers and task forces have issued guidelines for the evaluation of syncope. Owing to the wide range of possible etiologies and the numerous guidelines published, these comprehensive

diagnostic strategies are often difficult to implement and their effect on physician behavior, diagnostic yield and evaluation costs is still largely unknown. Simpson et al. [8] attempted to evaluate the potential of such diagnostic models and retrospectively applied them to a cohort of 100 patients. Their experience demonstrates that using standardized protocols can improve diagnostic yield without increasing cost per diagnosis. In a similar trial, the researchers found that retrospectively applying the American College of Emergency Physicians policy can significantly reduce hospitalization and increase the accuracy of diagnosis [9].

In a recent larger trial, Brignole and collaborators [10] performed a prospective systematic guideline-based evaluation, using the updated ESC guidelines, on patients referred to the emergency department of 11 general hospitals. With a high compliance rate of 86% to the guidelines, the authors found that in 98% of patients a definite diagnosis was established, hospitalization was appropriate in 25% of the patients, and the median in-hospital stay was 5.5 days. This study provided a frame of reference for the evaluation of syncope, based on the ESC guidelines.

Several interventional studies have tried to tackle the diagnostic yield and cost issues, but with somewhat conflicting conclusions. The EGSYS-2 group established a standardized-care pathway for syncope patients according to the guidelines of the ESC and compared their data to syncope patients who were not managed according to this pathway [11]. Overall, the standardized-care group had a lower hospitalization rate, shorter in-hospital stay, and fewer tests performed per patient than the usual-care group. More standardized-care patients had a diagnosis of neurally mediated and orthostatic syncope, whereas fewer had a diagnosis of unexplained syncope. The mean cost per patient and the mean cost per diagnosis were 19% and 29% lower in the standardized-care group, respectively. Ammirati et al. [12], in the OESIL 2 study, conclude that the use of specific simplified diagnostic guidelines resulted in an improvement of overall clinical performance. But they did not measure and compare the use of specific diagnostic tools or total costs per diagnosis. Similar results were also reported in a recent study [13], which again addressed only the diagnostic yield without looking into costs.

However, in another interventional trial, the ECSIT study, the introduction of guidelines led to reduced hospitalization rates with lower rates of unexplained syncope, but at the price of longer hospital stay, more diagnostic tests performed and higher total costs [14]. Farwell and Sulke [15], who also used a diagnostic protocol for patients presenting with syncope, found that more patients received an ultimate diagnosis and that the use of tests with high diagnostic effectiveness, such as tilt tests, increased. But, similar to the ECSIT study, the introduction of the protocol led to an increase in the costs of diagnosing syncope. The authors speculate that this may have been due to a significant lack of adherence to some aspects of the protocol and to the fact that there was no reduction in hospitalization rates.

The diagnostic problems and the enormous medical resource

utilization and expenses associated with syncope management have led to the establishment of designated syncope units or centers, which could be a walk-in clinic or part of the emergency department. This relatively new concept has prompted researchers to try and estimate their ability to improve diagnostic yield and reduce expenses. In the SEEDS trial, a syncope unit operating in the emergency department was evaluated as patients were randomly allocated to either syncope unit evaluation or standard care [16]. The syncope unit was found to have a higher diagnostic yield, which led to a lower hospitalization rate and shorter total length of hospital stay, without affecting patients' outcome. Brignole and co-researchers [17] evaluated syncope units established inside the cardiology department in six hospitals as compared to six matched hospitals without such units. Although only 11% of the overall syncope patients in the study hospitals were referred to the syncope units, the investigators found that using syncope units significantly lowers the hospitalization rate and lowers the number of diagnostic tests needed per diagnosis (with more high yield tests performed and less low yield tests). While other studies have also shown the higher diagnostic yield of syncope units [18,19], no clear evidence on the presumed reduction in costs is yet available.

In conclusion, syncope is a common condition among patients admitted to emergency care and poses a diagnostic challenge to the clinician and an economic burden to health systems. In this editorial we have shown several strategies aimed at improving diagnostic yield and reducing health costs. As most of the initiatives have attempted to implement standardized evaluation protocols that were shown to improve diagnostic yield, data are not conclusive as to whether this would lead to reduced costs as well. The novel syncope unit approach could be the answer to this challenge, but further evaluations, specifically of the economic issues, are warranted.

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