

Is the Prognostic Significance of Presyncope the Same as for Syncope?

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Syncope is defined as a transient loss of consciousness associated with a loss of postural tone, in which the patient recovers spontaneously without the need for electrical or pharmacological cardioversion.^{1,2} This symptom may have one of several causes, some of them completely benign and self-limiting, others potentially fatal. Diagnosis is primarily made on the basis of the medical history, physical examination and electrocardiogram. In addition to facilitating the diagnosis in a significant number of patients, these tools are also useful for establishing a risk profile and providing a more individualized idea of the need for more costly examinations such as the tilt-table test, electrophysiological study, or implantable loop recorder. This selective use significantly improves the diagnostic yield and cost-benefit ratio of these tests. The effectiveness of the various diagnostic tools, as well as risk stratification and the efficacy of the various therapeutic resources in patients with syncope have been the subject of numerous studies.^{1,2}

In contrast, presyncope is poorly covered in the literature. There is little information on the definition or prognostic significance of this symptom, or on the diagnostic and therapeutic approach that should be taken when it presents. Among other reasons, this is due to a complex, often confusing or nonexistent definition in the methodology of some articles and frequent difficulty to differentiate it from other symptoms such as dizziness or even syncope. Furthermore, many studies of patients with syncope do

not include patients with presyncope or simply combine patients with syncope and/or presyncope, without separate analysis of the endpoints according to this symptom. Hence, there are currently many questions about presyncope: How should it be defined? What are its main causes? Is its prognostic significance equivalent to that of syncope? Does it relate to the patient's underlying heart disease? Should the diagnostic and therapeutic approach be similar to that of patients with syncope? At this time many of these questions have no evidence-based answer. The García Reverte et al article published in this issue of the REVISTA ESPAÑOLA DE CARDIOLOGÍA discusses the prognostic significance of presyncope in patients with structural heart disease and provides useful information on the symptom.³

DEFINITION OF PRESYNCOPE

Although presyncope occurs more frequently than syncope and is more prevalent in the general population, it is difficult to delineate. Some authors define it as a transient alteration of consciousness, without complete loss,⁴ but this is a rather vague definition. The main differentiating characteristic of presyncope is that patients have the feeling that they are just about to lose consciousness. The symptoms associated with presyncope are relatively nonspecific, always self-limiting and are consistent with those appearing in the prodromal phase of syncope (increasing dizziness, dizzy spells, bewilderment, weakness, blurred vision, sweating, nausea).

The differentiation with syncope is relatively simple if a good medical history can be obtained or if there are eyewitnesses because, unlike syncope, presyncope does not cause full loss of consciousness or postural tone. However, particularly in older individuals, the patient may not be sure whether he or she fully lost consciousness. The differentiating factor between dizziness and presyncope is that patients feel they are about to lose consciousness, but the symptom is transient and lasts only a short time. Nonetheless, in

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clinical practice, this distinction may not be easy to ascertain through questioning.

CAUSES

A wide variety of conditions can lead to syncope, but the main causes are neurally mediated reflexes, arrhythmias and orthostatic hypotension. The frequency of each cause varies according to the population studied (hospitalized patients, emergency room patients or general population), the tests performed and the diagnostic criteria used. Whereas studies conducted in the 1980s indicated that the cause was unknown in 40% of the patients with syncope, the selective use of additional examinations has brought this percentage to around 15% at the present time.^{1,2}

The predominant mechanism of syncope is a transient drop in blood pressure that leads to cerebral hypoperfusion. Less severe or shorter-lasting hypotension due to the same cause would logically lead to presyncope instead of syncope. Presyncope may not have the same mechanism as syncope, however.

Although there is little information in the literature, among the general population (particularly patients without heart disease), presyncope is a less specific symptom than syncope, and the cause is often not determined. In many cases presyncope is caused by neurally mediated reflex mechanisms or by an upright position and less often by arrhythmias. This explains why some observational studies suggest a benign prognosis.

Several studies in patients who have already presented syncope of unknown origin and undergone prolonged electrocardiogram (ECG) recording with an implantable loop recorder have investigated the incidence and type of arrhythmias recorded during presyncope and syncope episodes.⁴⁻⁸ These studies indicate that the finding of heart rate alterations is less frequent in episodes manifesting as presyncope versus syncope. This fact is more evident in studies including only patients without heart disease.^{6,7} Additionally, this indicates that presyncope can occur among the population with heart disease or bundle-branch block for reasons similar to syncope and, in some patients, is associated with recurrent syncope; therefore its specificity in this group could be higher than among the general population or among patients without heart disease. The fact that many patients assessed for syncope also have presyncope episodes during follow-up (and vice versa) supports the possibility that syncope and presyncope may be manifestations of varying degrees of severity of the same mechanism, at least among these patients.

The research done by García Reverte et al found no differences in the proportion of syncope and

presyncope episodes with an arrhythmic cause (25.7% vs 22%). Among the events caused by arrhythmia, there were no differences between the 2 groups in the percentage of sinus node dysfunction, atrioventricular block, supraventricular tachycardia or ventricular tachycardia.³ A possible explanation for the differences observed between the various studies is that the patient groups differed in the presence and degree of severity of structural heart disease and that the studies analyzed (except for the one conducted by García Reverte et al) included patients with syncope of unrelated origin after a complete diagnostic assessment, which meant the population was highly selective.

DIAGNOSIS

In the case of syncope, a thorough medical history plus information obtained from a physical examination and ECG produces an etiological diagnosis in a high percentage of patients.¹ In the remaining cases, these measures might suggest the diagnosis and assist in the selection of additional examinations. In patients with unexplained syncope who have structural heart disease or an abnormal ECG, arrhythmias are the main cause of syncope. In these cases, the most useful diagnostic tests are electrophysiological study and loop recorders. The latter, whether external or implantable models, are the instrument of choice when bradyarrhythmia is suspected because electrophysiological study is not as sensitive for detection. In patients without structural heart disease and with a normal ECG, syncope is usually neurally mediated. In these cases, the tilt-table test is the most useful diagnostic tool. Schemes for the selective use of highly effective, diagnostically reliable additional examinations have recently been proposed.²

As in syncope, the selection of diagnostic tests based on the patient's clinical characteristics and the use of additional noninvasive, less costly examinations should be equally applicable in patients with presyncope. However, the literature contains no specific study on this aspect. In fact, neither the individual diagnostic effectiveness of the main additional examinations used in patients with syncope, nor that of the algorithms of selective and combined use of these examinations have been separately evaluated in patients with presyncope. Studies often include only patients with syncope or, to a lesser extent, patients with both symptoms, but make no separate analysis of diagnostic value according to the form of presentation.

PROGNOSIS AND RISK STRATIFICATION

The main determining factor of prognosis in patients with syncope is the presence of structural heart disease. Various studies conducted in the 1980s

showed that patients with syncope of cardiac origin had higher mortality than patients with syncope of non-cardiac or unknown origin. Nevertheless, later studies show that this higher mortality was not related to the cause of syncope and mainly due to the underlying heart disease. Middlekauff et al found ventricular dysfunction to be the main factor associated with a high risk of sudden death.⁹ In a later study comparing the survival of patients with or without syncope who had similar profiles in terms of underlying heart disease and other clinical variables, Kapoor et al¹⁰ found that syncope of cardiac origin was not an independent predictor of overall or cardiac mortality after one year of follow-up. The most important predictors of mortality were the type and severity of the underlying structural heart disease, particularly the presence of congestive heart failure.¹⁰ Consequently, structural heart disease in patients with syncope predicts a greater probability of arrhythmic origin and a poorer prognosis, indicating that an attempt should be made to detect, define and treat the underlying structural heart disease in order to decrease the probability of overall death as well as the probability of sudden death.

It would seem logical that if, in a "more severe" symptom such as syncope, the symptom itself is not the main determining factor of prognosis but instead the presence, type and severity of the underlying structural heart disease, then the same would be applicable to patients with presyncope. However, there is little discussion of this hypothesis in the literature.

The study done by García Reverte et al analyzes and compares the clinical characteristics and long-term prognosis of patients with structural heart disease admitted for a presyncope event to a cardiology unit with those of patients with heart disease admitted for a syncope episode. The authors compiled retrospective information on the medical histories of 449 patients and classified the final diagnosis according to the criteria of the European Society of Cardiology. The clinical characteristics of both patient groups were similar, except that patients with syncope were more likely to have a history of prior syncope episodes and patients with presyncope had a greater incidence of atrial fibrillation at the time of admission. Arrhythmia was the cause in a similar percentage of patients with syncope or presyncope (25.7% vs 22%, respectively), with no significant differences in overall mortality or sudden death after a mean follow-up of almost 5 years. In the multivariate analysis, age and cardiac origin were independent predictors of mortality in the group admitted for syncope, and both factors (along with diabetes) were predictors of mortality in the group admitted for presyncope.³

The study has obvious clinical importance because of its prognostic, diagnostic and therapeutic implications. As the authors suggest, since the

prognosis for patients with structural heart disease and presyncope is similar to that of patients with heart disease and syncope, the diagnostic approach and risk stratification used should be analogous in both groups of patients. In any case, the results of this study should be viewed in the light of certain important limitations, some of them resulting from its retrospective design.

The authors defined presyncope as an imminent, transient feeling of the loss of consciousness, frequently described in the medical history as dizziness, dizzy spells or incomplete syncope. Retrospective study of the patient's symptoms suggests that it may not have been easy to determine precisely whether the patient had presyncope, syncope or dizziness; some episodes of syncope might even have been included as presyncope or vice versa, and some cases of dizziness of short duration might have been included as presyncope, since the dividing line is sometimes difficult to establish, even prospectively. As was described, follow-up was done by direct or telephone contact with the patient. When death occurred in the hospital, an attempt was made to establish the cause from clinical reports, and when it occurred out of the hospital from interviews with relatives or close contacts; thus the precise cause of death may not have been determined in some cases.

In addition, selection bias may have been another limitation, since it is likely that the patients included had more severe heart disease or presyncope episodes and a higher probability of being admitted to the hospital. Consequently, it is more likely that a higher-risk population was selected, and the results of this study should only be applied to this type of patient. In fact, about half the patients in the series had a left ventricular ejection fraction below 40%.

Another important limitation is the high number of patients in whom the cause is never determined: 46.3% in both the syncope and presyncope groups. This was mainly due to the infrequent use of some additional tests of considerable diagnostic value in these patients, particularly the electrophysiological study (done only in 4.8% and 4% of the patients, respectively) and the tilt-table study (5.1% and 0.6%). This limitation may have affected the fact that the cardiac cause of syncope was a predictor of mortality in this study, and is consistent with results from studies conducted in the 1980s, where the percentage of patients with syncope of unknown origin was nearly 40% and contrary to studies done in the 1990s, where more selective use of new diagnostic tests lowered this percentage significantly. Naturally, the design of this study-in which all the patients had structural heart disease-does not elucidate the role of heart disease as a predictor of mortality, although the role of severity of ventricular dysfunction as a possible predictor of mortality could have been analyzed. Unfortunately, this variable was not included in the multivariate

analysis.

In conclusion, little information is found in the literature on the prognostic significance of presyncope among various groups of patients. The scientific evidence in patients with syncope and heart disease highlight the importance of the role of the latter as a key prognostic factor. The results published by García Reverte et al provide evidence for the prognostic role of presyncope (particularly when caused by arrhythmia) among patients with structural heart disease. In patients without heart disease, presyncope is associated less often with heart rate disorders than syncope and is less specific for the diagnostic study of these patients. Nevertheless, the paucity of studies in both patient groups (with and without heart disease) is a strong indication of the need to design and conduct studies that prospectively analyze the true prognostic value of presyncope in these patients. In the interim, the available information suggests that the diagnostic approach and risk stratification should be undertaken among patients with presyncope and heart disease in the same way as patients with syncope.

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