

# Prognosis of Presyncope in Patients With Structural Heart Disease

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**Introduction and objectives.** Few data are available on the prognosis of presyncope in patients with structural heart disease. The aim of this study was to compare the clinical characteristics and long-term prognosis of patients with structural heart disease admitted for presyncope or syncope in the cardiology department of a tertiary hospital.

**Methods.** We reviewed the medical records of 449 patients (65% men, mean age 66.8 [13.1] years) with structural heart disease admitted because of syncope (n = 272) or presyncope (n = 177) during the period from 1992 to 1998. Clinical and demographic variables were analyzed and the final diagnosis was classified according to European Society of Cardiology criteria. The follow-up (available in 97.1% of patients) consisted of a personal interview with the patient or a review of the medical records and an interview with the relatives of the patients who had died.

**Results.** Both groups had similar demographic and clinical characteristics, except for the presence of atrial fibrillation on admission, which was more common in the presyncope group. Previous syncopal episodes were more frequent in patients admitted for syncope. The mechanism of the episode was considered arrhythmic in 25.7% of the patients with syncope and 22.0% of those in the presyncope group ( $P=.37$ ). After a mean follow-up of 57.4 [30.5 months] the survival curves were similar for both groups and no significant differences were found regarding the causes of death or the rate of sudden death.

**Conclusions.** The clinical characteristics and the long-term prognosis in patients with structural heart disease admitted to a cardiology department for presyncope are similar to those of patients admitted for syncope. This suggests that the approach to diagnosis and risk stratification should be similar in both groups of patients.

**Key words:** Syncope. Heart disease. Prognosis. Presyncope.

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## Pronóstico del presíncope en pacientes con cardiopatía estructural

**Introducción y objetivos.** Hay pocos datos sobre el pronóstico del presíncope en pacientes con cardiopatía. El objetivo del estudio es comparar las características clínicas y el pronóstico de los pacientes con cardiopatía estructural ingresados por síncope y por presíncope en un servicio de cardiología.

**Métodos.** Se ha revisado las historias clínicas de 449 pacientes (el 65%, varones; edad,  $66,8 \pm 13,1$  años) con cardiopatía estructural ingresados por síncope (n = 272) o presíncope (n = 177) entre 1992 y 1998, y se ha clasificado el diagnóstico final según los criterios de la Sociedad Europea de Cardiología. El seguimiento (completo en el 97,1%) se efectuó por conversación con el paciente, revisión de informes clínicos y entrevista con los familiares en caso de fallecimiento.

**Resultados.** No hubo diferencias significativas en las variables clínicas entre ambos grupos, excepto la fibrilación auricular al ingreso y el antecedente de síncope previo, más frecuentes en el grupo de presíncope y síncope, respectivamente. El episodio se consideró arritmico en el 25,7% de los pacientes con síncope y en el 22,0% con presíncope ( $p = 0,37$ ). Tras un seguimiento medio de  $57,4 \pm 30,5$  meses, las curvas de supervivencia fueron similares en ambos grupos, sin que hubiera diferencias significativas en las causas de muerte ni en la tasa de muerte súbita.

**Conclusiones.** Las características clínicas de los pacientes con cardiopatía estructural ingresados por presíncope son similares a las de los pacientes con síncope. El pronóstico tampoco difiere significativamente, por lo que la aproximación diagnóstica y la estratificación de riesgo deben ser similares en ambos grupos.

**Palabras clave:** Síncope. Cardiopatía. Pronóstico. Presíncope.

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## INTRODUCTION

In patients with structural heart disease, syncope can be a result of potentially lethal conditions such as ischemia, ventricular or supraventricular arrhythmias, extreme bradycardia, or the obstruction of ventricular emptying. Its diagnosis requires a complete cardiological examination, often involving invasive procedures such as coronary angiography or an electrophysiological study. Effective treatment, however, can prevent the recurrence of the problem and improve the prognosis of the patient.<sup>1-3</sup> Presyncope is often defined as a temporary light-headed or dizzy feeling or a transitory reduction—but not loss—of consciousness.<sup>4</sup> Its prevalence is high, although normally it is considered to be a rather non-specific symptom. However, in some cases its causes may be the same as those of syncope, of which it may be premonitory.<sup>5-7</sup> In high risk patients such as those with heart disease, it can often pose diagnostic and risk stratification problems that are little discussed in the literature. The aim of this work was to analyze the clinical characteristics and long-term prognosis of patients with structural heart disease admitted with presyncope to a hospital cardiology department, and to compare them with those of similar patients admitted with syncope during the same period.

## METHODS

The discharge forms of all patients admitted to the cardiology department of a tertiary hospital between January 1992 and December 1998 were reviewed in order to select those with structural heart disease who presented with either syncope or presyncope. Syncope was defined as a transitory complete loss of consciousness with spontaneous recovery after a few seconds or minutes. Presyncope was defined as a transitory feeling of an imminent loss of consciousness, often described by patients as dizziness, light-headedness or incomplete fainting. For a positive diagnosis, symptoms had to be transitory or short-lived: patients with symptoms of vertigo were excluded, as were those who reported a sensation of instability or who presented with vague symptoms that were difficult to classify and often of long duration. The medical histories of all included patients were reviewed; structural heart disease was diagnosed on the basis of medical background and the results of diagnostic examinations performed during hospitalization. Diagnoses of ischemic heart disease without infarction were based on patients' clinical histories plus at least one positive test result for ischemia, the revelation of significant lesions by coronary angiography, or all the aforementioned. Patients with stenosis or mild valve insufficiency were not included in the study, nor were those with hypertrophic cardiomyopathy (with a wall thickness <15 mm), doubtful changes in contractility or within the limits of normality, or isolated diastolic dysfunctions. Patients also excluded

were those with arrhythmias or primary conduction problems with no evidence of associated structural heart disease, and those admitted because of syncope within the context of acute myocardial infarction. Independent of any diagnosis made during a patient's stay in hospital, the final diagnosis of the cause of syncope or presyncope was established by examining the corresponding clinical history (using the criteria of the European Society of Cardiology).<sup>3</sup> When no solid diagnostic evidence was provided by the available clinical information or by test results, the episode of syncope or presyncope was considered to be of unknown cause. Follow-up procedures included either direct or telephone conversations with patients. For deceased patients, attempts were made to establish the cause of death by reviewing the available clinical reports (if death occurred in the hospital) or by interviewing family members or witnesses (if death occurred outside). Sudden death was defined as death within 1 hour of the onset of symptoms, or unexpected death during sleep or when the patient was alone. In the absence of reliable information on the circumstances surrounding death, the cause was considered to be unknown.

Normally distributed variables are expressed as means  $\pm$  standard deviation (SD). The Student *t* test was used to compare the means of normally distributed variables; the  $\chi^2$  or Fishers exact test was used to establish the relationship between categorical variables. To determine the variables with the greatest independent predictive power for mortality, the survival of the study population, and of each group, was examined by Cox regression analysis. The variables used in this analysis were age, sex, the presence of high blood pressure, diabetes or structural heart disease, syncope, or presyncope as the index episode, left bundle branch block at admission, atrial fibrillation at admission, and the cardiac or non-cardiac cause of the episode that led to admission. Kaplan-Meier survival curves were produced using SPSS v 7.5 software.

## RESULTS

### Characteristics of the Study Population

The study included 449 patients, 177 (39.4%) of whom were admitted for presyncope and 272 (60.6%) for syncope. Table 1 shows their demographic and clinical characteristics. The most common heart problems were ischemia with or without previous myocardial infarction (n=156 [34.7%] and n=103 [22.9%] respectively). No significant differences were seen between the 2 groups of patients other than in the frequency of atrial fibrillation, which was more common in the presyncope patients (n=50 [28.2%] compared to n=51 [18.8%] in the syncope group; *P*<.05), and the history of syncope prior to admission, which was more common in the syncope group.

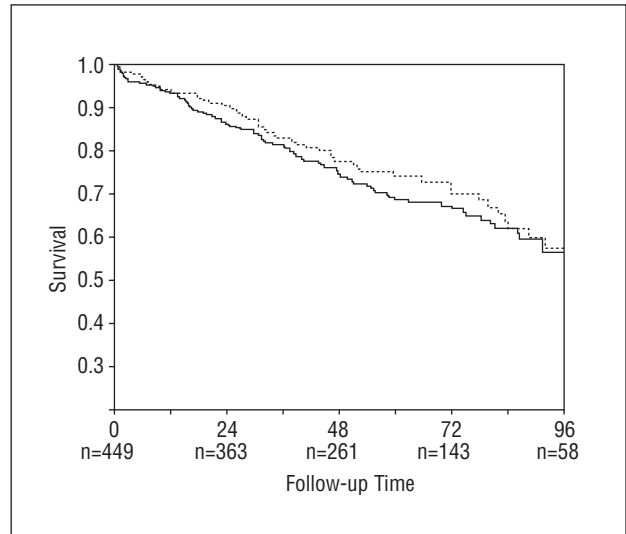
During hospitalization, 191 patients (70.2%) in the

**TABLE 1. Demographic and Clinical Characteristics of the Study Population\***

	Presyncope (n=177)	Syncope (n=272)	P
Age, years	67.2±11.7	66.5±14.0	.56
Sex, men/women	110/67	184/88	.23
High blood pressure	80 (45.2%)	122 (44.9%)	.94
Diabetes	41 (23.2%)	69 (25.4%)	.59
Previous syncope	18 (10.2%)	88 (32.4%)	<.001
Heart disease			.83
Ischemia with MI	66 (37.3%)	90 (33.1%)	
Ischemia without MI	38 (21.5%)	65 (23.9%)	
Valve disease	32 (18.1%)	51 (18.8%)	
Dilated cardiomyopathy	16 (9.0%)	30 (11.0%)	
Hypertrophic cardiomyopathy	8 (4.5%)	16 (5.9%)	
Others	17 (9.6%)	20 (7.3%)	
Atrial fibrillation	50 (28.2%)	51 (18.8%)	.02
LBBB	14 (7.9%)	17 (6.3%)	.50
LVEF≤0.4	63/120 (52.5%)	98/216 (45.4%)	.21
Follow-up, months	56.9±30.6	57.8±30.5	.76

\*LBBB indicates left bundle branch block; LVEF, left ventricular ejection fraction; MI, myocardial infarction.

syncope group underwent Holter monitoring whereas only 64 (36.2%;  $P<.001$ ) were so monitored in the presyncope group. An electrophysiological study was performed on 13 (4.8%) syncope and 7 presyncope (4%) patients; 14 (5.1%) syncope patients and 1 presyncope patient (0.6%;  $P<.05$ ) underwent a tilt-table test. Some 75.3% and 11% of the total population underwent echocardiographic examination and catheterization respectively, with no significant differences between the syncope and presyncope groups. The mechanism behind the episode leading to admission was classified as arrhythmic in 70 (25.7%) patients admitted with syncope and in 39 (22.0%) of those admitted with presyncope (no significant difference). The diagnosis of arrhythmic syncope was arrived at by standard electrocardiography in 53 patients (48.6%), by Holter monitoring in 50 (45.9%), and by the results of an electrophysiological examination in 6 (5.5%). In the syncope group, arrhythmia was associated with sinus dysfunction in 24 patients (34.3% of the patients with arrhythmic syncope), atrioventricular block in 31 (44.3%), supraventricular tachycardia in 1 (1.4%), and ventricular tachyarrhythmia in 14 (20%); among those admitted for presyncope, sinus dysfunction was diagnosed in 11 (28.2%), atrioventricular block in 19 (48.7%), supraventricular tachycardia in 2 (5.1%) and ventricular tachycardia in 7 (17.9%) (no significant difference between groups). A non-arrhythmic cause was determined in 16 patients belonging to the syncope group (5.9%) and in 15 (8.5%) in the presyncope group ( $P=.29$ ). Specific diagnoses in this etiological sub-



**Fig. 1.** Survival curves of patients admitted with syncope (continuous line) and presyncope (dashed line). No significant differences were seen between the 2 groups. n indicates number of patients remaining.

group were aortic stenosis (7 syncope patients and 5 presyncope patients) and pulmonary hypertension (2 syncope patients and 1 presyncope patient). A vasovagal etiology was determined in 37 syncope patients (13.6%) and in 15 presyncope patients (8.5%); this was established from anamnesis records in all cases except 1, in which the conclusion was drawn from a positive tilt-table test result. The number of episodes of unknown cause was 126 (46.3%) in the syncope group and 82 (46.3%) in the presyncope group ( $P=1$ ). Thirty eight patients with syncope (14%) and 19 (10.7%) with presyncope received a pacemaker as treatment for the episode that led to admission ( $P=.55$ ). An implantable defibrillator was indicated in 5 syncope patients and 1 presyncope patient.

### Mortality During Follow-up

The mean follow-up period was  $57.4\pm30.5$  months (median, 54.9 months). Thirteen patients were lost (2.9%) (no significant differences between syncope and presyncope groups). Syncope during follow-up was more common among the patients admitted with syncope ( $n=49$  [18.4%]) compared to  $n=23$  [13.3%] with presyncope), although the difference was not significant ( $P=.15$ ). In total, 145 patients died during follow-up (32.2%). No significant differences were seen in mortality among the patients admitted with presyncope (51/173; 29.5%) or syncope (94/263; 35.7%;  $P=.18$ ). Figure 1 shows the survival curves for both groups (no significant differences). In multivariate analysis, age and syncope of cardiac origin were predictors of mortality in the patients admitted with syncope. Diabetes was an independent predictor of morta-

lity among those admitted with presyncope. Patients admitted with presyncope attributed to a cardiac cause showed greater mortality (21/51; 41.2%) than those with a non-cardiac (9/40; 22.5%) or undetermined (21/82; 25.6%;  $P < .05$ ) cause.

### Cause of Death

The cause of death was obtained from hospital records for 75 patients (51.57%) and by interview with family members or witnesses for 49 patients (33.8%). For 15 patients of the syncope group (16% of those who died in this group) and 6 in the presyncope group (12%), no reliable information on the cause of death was available. No significant differences were seen between the 2 groups with respect to cause of death. In total, 33 (35.1%) cardiovascular deaths occurred among the syncope patients and 23 (45.1%) among the presyncope patients ( $P = .78$ ). Death was sudden in 15 (16.0%) and 7 (13.7%) patients respectively ( $P = .45$ ). In an analysis of different subgroups, significant differences were found in mortality with respect to type of structural heart disease. Among those with ischemic heart disease, mortality was 44/152 (28.9%) in the syncope group and 29/104 (27.9%) in the presyncope group ( $P = .85$ ). In patients with valve disease, these figures were 25/47 (53.2%) and 14/32 (43.8%;  $P = .41$ ), and among those with dilated cardiomyopathy they were 14/30 (46.7%) and 4/13 (30.8%) respectively ( $P = .50$ ).

### DISCUSSION

The results indicate that the clinical characteristics of patients with structural heart disease admitted with presyncope are similar to those of patients admitted with syncope. The mid-term prognosis for these groups is not significantly different either. This suggests that the diagnostic approach and the risk stratification procedures to be used in patients with presyncope and syncope should be similar. Presyncope is considered a rather non-specific symptom that is often very difficult to define. Accordingly, it frequently goes unmentioned in reviews or editorials on syncope.<sup>8</sup> Nonetheless, the prevalence of presyncope in the general population is high<sup>4,9</sup> and the number of patients who undergo cardiac examination because of this symptom is not inappreciable. A number of observational studies suggest that the prognosis associated with the complaint is benign,<sup>10,11</sup> but the majority do not differentiate between the episodic and acute character of presyncope and other symptoms such as dizziness or light-headedness of longer duration. It is therefore likely that presyncope associated with potentially dangerous conditions, such as arrhythmias, is inadequately represented in these studies. In patients with heart disease who suffer an episode of syncope, potentially

lethal arrhythmias need to be ruled out as a possible cause. Presyncope in this population can have similar causes;<sup>5-7</sup> in many patients it is preceded by syncope or is associated with prior episodes.<sup>6,12</sup> Its specificity and prognostic significance could be greater for patients with heart disease than for the general population. However, few data have been published in this respect. In 1 group of patients with ischemic heart disease studied because of their suffering syncope ( $n = 59$ ) or presyncope ( $n = 9$ ), the form of presentation was not predictive of total mortality, bradycardia or ventricular arrhythmias during follow-up.<sup>12</sup> In patients who had already suffered syncope (generally on a number of occasions) and who underwent prolonged electrocardiographic monitoring (with event recording), it was found that the percentage of arrhythmic events was lower in episodes of presyncope than syncope.<sup>7,13-15</sup> Similarly, in a heterogeneous group of patients, 62% of which suffered structural heart disease, arrhythmia was seen in 24% of recurrences in the form of presyncope and in 70% when in the form of syncope. In addition, three out of 6 patients with sinus rhythm during an episode of presyncope were later documented as experiencing arrhythmia during an episode of full syncope.<sup>15</sup> Similarly, in a study of 35 patients with syncope, structural heart disease and negative electrophysiological results, significant arrhythmia was seen in 3 out of 8 patients during a later episode of presyncope compared to 5 out of 6 patients who suffered a later episode of full syncope.<sup>7</sup> The lower percentage of significant arrhythmias registered during episodes of presyncope in these patients suggests that, in most cases, a vasovagal mechanism is in operation; the prognosis for patients with presyncope might also be better than that for patients with syncope. Our population differs from those of the above studies, however, in that it is formed of patients who had come to the hospital because of their symptoms and who had been admitted after an initial examination. These patients therefore probably suffered more severe episodes or had more serious underlying disease.

It has been suggested that the prognosis of patients with heart disease who suffer syncope depends mainly on the severity of the underlying heart disease, and not on the appearance of syncope.<sup>16</sup> Our results cannot discredit this hypothesis, which implies the absence of any prognostic value of syncope or presyncope. In other studies, however, syncope has been reported to be an independent predictor of mortality in cardiac patients.<sup>17</sup> In addition, in selected groups of patients with syncope and structural heart disease and who carried an implanted defibrillator, a high incidence of ventricular arrhythmias was observed that required treatment with the latter device. This suggests that an arrhythmic mechanism was responsible for inducing syncope in most cases.<sup>18-21</sup>

## Clinical Implications

Patients with syncope and severe structural heart disease are at an increased risk of sudden death,<sup>12,22-24</sup> in the majority of cases thought to be due to arrhythmia. A complete diagnostic examination is therefore recommended for such patients—in particular to rule out that the episode suffered should have its origin in arrhythmia. This frequently requires an invasive electrophysiological study. Fortunately, treatments now exist to prevent the recurrence of both bradyarrhythmias and rapid supraventricular or ventricular arrhythmias, thus preventing death.<sup>1-3</sup> The literature contains no data that indicate whether the same procedures should be followed in patients admitted with presyncope. However, in the absence of any large prospective studies, the present results suggest it is reasonable to follow a similar strategy.

## Limitations

Firstly, this is a retrospective study, with all the limitations of this type of design. The admission of the patients depended on the criterion of the attending physician rather than on any systematic protocol. Though the majority of patients with structural heart disease and episodes suggestive of presyncope were admitted routinely during the study period, a selection bias cannot be ruled out, i.e., those admitted may have had more severe heart disease, presyncope episodes with a greater risk profile, or both. This should be remembered when attempts are made to extrapolate the results. Secondly, a diagnosis of presyncope is often difficult to make; presyncope can quite easily be confused with other conditions. In particular, if the loss of consciousness is fleeting the patient might not recognize it as an episode of presyncope; this could lead to some episodes of full syncope being considered as presyncope. Furthermore, a differential diagnosis between dizziness, vertigo or even a short-lived anxiety crisis can also be difficult to make. Some of the study patients may therefore have been misdiagnosed with presyncope. This is, however, an inevitable limitation of clinical practice since the diagnosis of presyncope is based entirely on information provided by the patient and any available witnesses. Finally, the use of specific techniques for diagnosing arrhythmic syncope, such as programmed ventricular stimulation, was rare during the study period and tilt-table tests were not routinely performed. However, this limitation affects both study groups equally; it is therefore unlikely that the overall results would have been different had such procedures been used more often.

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