

# Analysis of Head-Up Tilt Test Responses in Patients Suffering From Syncope and High Blood Pressure

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We studied the difference in head-up tilt test responses between patients suffering from syncope who had hypertension and those who did not. A total of 338 consecutive patients with syncope underwent head-up tilt testing in our department from January 2003 to October 2004. Of these, 243 did not have hypertension (group A), whereas 95 did (group B). There were significant differences between the groups in age ( $P=.0001$ ), sex ( $P=.048$ ), timing of syncope development ( $P=.0001$ ), and prevalence of diabetes mellitus ( $P=.0001$ ). The head-up tilt test gave positive results in 168 patients (69.1%) in group A and in 63 (66.3%) in group B ( $P=.6$ ; NS). There was no significant difference between the groups in the proportion of positive responses that occurred in either the baseline or nitroglycerin-enhanced phase of the test ( $P=.673$ ; NS), nor in the time to onset of syncope in either phase ( $P=.69$ ; NS, and  $P=.28$ ; NS, respectively). However, there was a significant difference in the type of response (vasodepressor response, 33% in group A vs 49% in group B,  $P=.01$ ). In the multivariate analysis, no independent variable was found to be associated with the result of the head-up tilt test.

**Key words:** Syncope. Arterial hypertension. Tilt test.

## Análisis de la respuesta al test de tabla basculante de los pacientes con síncope que presentan hipertensión arterial

Para analizar las diferencias en la respuesta al test de tabla basculante (TTB) entre sujetos sin y con hipertensión arterial (HTA) hemos estudiado consecutivamente a los 338 pacientes con síncope que realizaron el TTB en nuestro servicio entre enero de 2003 y octubre de 2004. En 243 pacientes no se apreció hipertensión (grupo A), mientras que en 95 sí la había (grupo B). Encontramos diferencias entre ambos grupos en la edad ( $p = 0,0001$ ), el sexo ( $p = 0,048$ ), el tiempo de evolución de los síncope ( $p = 0,0001$ ) y el porcentaje de diabetes mellitus ( $p = 0,0001$ ). El TTB fue positivo en 168 pacientes (69,1%) del grupo A y 63 (66,3%) del grupo B ( $p = 0,6$ ; NS). No encontramos diferencias entre ambos grupos en el porcentaje de positividad al TTB durante la fase basal y durante la fase de nitroglicerina ( $p = 0,673$ ; NS), ni en el tiempo de aparición del síncope en ambas fases ( $p = 0,69$ ; NS, y  $p = 0,28$ ; NS), aunque sí en el tipo de respuesta (respuesta vasodepresora del 33% en el grupo A frente al 49% en el grupo B;  $p = 0,01$ ). En el análisis multivariable no se encontró ninguna variable independiente asociada con el resultado del TTB.

**Palabras clave:** Síncope. Hipertensión arterial. Test.

## INTRODUCTION

Many patients with syncope also have other diseases, such as high blood pressure or hypertension. In a recent population study on syncope,<sup>1</sup> the only study of this kind

carried out so far, hypertension was present in 59.8% of the patients with syncope, and in 53.9% of those patients whose cause of syncope was vasovagal. From the database of the Framingham heart study, we also know that the presence of hypertension is an independent predictor for syncope (odds ratio [OR] =1.46; 95% confidence interval [CI], 1.14-1.88).<sup>2</sup>

The most common identified cause of syncope is in fact vasovagal, and the head-up tilt test is a provocation test that is recommended in the diagnosis of syncope.<sup>3,4</sup> In previous studies by our group we examined the influence of different parameters, such as age and sex, on the results of the tilt test.<sup>5,6</sup> However, no studies have yet looked at the possible

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influence of other coexisting diseases in these patients. Furthermore, we have noticed that some patients who were not taking any medication at the time of the tilt test had a more severe response when the tilt test was repeated when they were taking medication.<sup>7</sup>

Whether the presence of other accompanying diseases, such as hypertension, or the treatment being taken for these diseases, can influence the result of diagnostic tests in these patients is not yet known. Moreover, no study has yet analyzed the response to tilt testing in patients with hypertension, and the current indications for the performance of this test make no mention of the importance of coexisting hypertension, nor of its treatment, when assessing the result of the tilt test.<sup>3,4</sup>

In order to determine the influence of hypertension on the response to head-up tilt testing, we undertook a prospective study in a group of patients with syncope who underwent tilt testing because of a suspected vasovagal cause of their syncope.

## PATIENTS AND METHODS

### Patient Selection

We included prospectively all patients referred to our service with a clinical diagnosis of syncope having a possible vasovagal cause who underwent confirmatory head-up tilt testing between January 2003 and October 2004. The patients were studied in accordance with the protocols of our service and the ethical recommendations of our hospital.<sup>5,6</sup> The patients were grouped according to the absence (Group A) or presence (Group B) of accompanying hypertension.

### Tilt Testing

All the patients underwent tilt testing after an overnight fast, in a quiet room, between 9.00 and 14.00. We used the so-called "Italian protocol" for the tilt test in all the patients.<sup>8</sup> The tilt test was considered positive when the patient had a vasovagal response during its performance and recognized the induced syncope as similar to the clinical syncope.

### Definitions

Syncope was defined as the sudden loss of consciousness with inability to maintain posture and with spontaneous recovery. A vasovagal response during tilt testing was defined as the reproduction of syncope accompanied by hypotension, bradycardia, or both (decrease in systolic blood pressure [SBP] >50% and in heart rate >30% of the maximum value noted during standing). The time of development was defined as the number of months between the first episode of syncope and the performance of the tilt test. The patient was

considered to have hypertension if the SBP was  $\geq 140$  mm Hg or the diastolic blood pressure (DBP) was  $\geq 90$  mm Hg, or if the patient was taking anti-hypertensive medication. Based on previous data from our group, we divided the previous number of syncope episodes in <5 prior episodes or  $\geq 5$  prior episodes for the multivariate analysis.<sup>9</sup>

### Statistical Analysis

The results were analyzed with the statistical program SPSS, version 12.0 (SPSS, Chicago, IL). The qualitative variables were described according to relative or absolute frequencies; in the case of continuous variables, the description was done according to the mean  $\pm$  standard deviation or the median (interquartile range), according to whether the variable did or did not follow a normal distribution (with the Kolmogorov-Smirnov test). Comparison of the qualitative variables in Groups A and B was done with the  $\chi^2$  test or Fisher's exact test when necessary. The continuous variables (quantitative) were compared for Groups A and B with the Student *t* test when they followed a normal distribution and with the Mann Whitney U test when the distribution was not normal. To control for possible confusion bias in the tilt test responses, we undertook a logistic regression analysis in which the dependant variable was the response to tilt testing, and the independent variables were the presence or absence of hypertension, the number of syncope episodes (fewer or more than 5 previous episodes, as has recently been demonstrated),<sup>9</sup> the development time, the sex of the patient and the presence of diabetes mellitus. Values were considered to be statistically significant if the *P* was <.05.

## RESULTS

The study included a total of 338 patients with syncope, of whom 182 (53.8%) were women. Of the 338 patients, 243 did not have hypertension (Group A) and 95 did have hypertension (Group B). Table 1 shows the demographic characteristics of the 2 groups and their differences. No patient in Group A was taking vasoactive medication and all the patients in Group B who were taking anti-hypertensive medication took it on the day the tilt test was carried out. In the Group B patients, 12 (12.6%) were not taking any anti-hypertensive medication, 27 (28.4%) were taking 1 drug to control the hypertension, and 56 (58.9%) were taking 2 or more drugs for its control. The anti-hypertensive drugs taken by these patients were: angiotensin-converting enzyme inhibitors in 56 patients (58.9%), angiotensin II receptor antagonists in 50 (52.6%), diuretics in 50 (52.6%), beta-blockers in 36 (37.8%), calcium antagonists in 38 (40.0%), and other vasodilators in 10 (10.5%).

When we undertook the head-up tilt test, the mean supine SBP at the start of the test was  $128 \pm 12$  mm Hg in

**TABLE 1. Clinical Characteristics of the Study Population, Divided According to the Absence (Group A) or Presence of Hypertension (Group B)**

	Group A (n=243)	Group B (n=95)	P
Age, years, median (range)*	40 (23-57)	66 (57-73)	.0001
Women, n (%)	139 (57.2)	43 (45.3)	.048
Number of previous syncope episodes, median (range)*	3 (2-8)	3 (1-6)	.16
Duration of the symptoms, months, median (range)*	36 (12-102)	12 (2-48)	.0001
Diabetes mellitus, n (%)	6 (2.5)	20 (21.1)	.0001

\*Interquartile range.

Group A and  $162 \pm 14$  mm Hg in Group B ( $P=.0001$ ). The DBP was  $76 \pm 7$  mm Hg in Group A and  $97 \pm 6$  mm Hg in Group B ( $P=.0001$ ). No patient in Group B had a SBP < 140 mm Hg or DBP < 90 mm Hg; that is, none of the patients with hypertension in our series had their blood pressure controlled at the start of the tilt test, despite having taken their anti-hypertensive medication.

A total of 231 patients (68.3%) developed vasovagal syncope during the tilt test. Table 2 shows the results of the logistic regression analysis. No independent variable was significantly associated with a positive tilt test. The tilt test was positive in 168 patients from Group A (69.1%) and in 63 from Group B (66.3%) ( $P=.6$ ; NS). The tilt test was positive during the baseline phase of the protocol in 23 patients from Group A (13.7%) and in 10 from Group B (15.9%), and during the nitroglycerin phase in 145 from Group A (86.3%) and in 53 from Group B (84.5%). There were no differences in the phase of appearance of the response nor in the percentages between the 2 groups ( $P=.673$ ; NS). The time of the appearance of the vasovagal response was also analyzed; in the baseline phase the response in Group A appeared at minute 14 (range, 6-20) and in Group B at minute 11 (range, 8-18) ( $P=.69$ ; NS). In the nitroglycerin phase, the vasovagal response appeared in Group A at minute 3 (range, 3-5) and in Group B at minute 4 (range, 3-5) ( $P=.28$ ; NS).

Analysis of the types of positive response to the tilt test showed fewer type II responses and more type III responses in Group B ( $\chi^2=11.1$ ;  $P=.01$ ) (Table 3).

## DISCUSSION

Even though we had reason to suspect an association between the presence of hypertension, or the need for anti-hypertensive medication, and the results of head-up tilt testing, the data from this series fail to confirm this association. Groups A and B appear to contain 2 different populations, as seen from their clinical characteristics. The known associations between hypertension and age, and between hypertension and diabetes were present in our study group. However, we also detected other differences, as yet unreported, between persons with and without hypertension. Regarding sex, a lower percentage of women had syncope and hypertension (Group A, 57.4% as compared with Group B, 41.9%;  $P=.01$ ). This finding in our study group cannot be considered as definitive, and it should be evaluated in future confirmatory studies. Previous studies by our group have detected no influence of sex or age on the results of tilt testing.<sup>5,6</sup> The only previous study of patients with syncope admitted to hospital found differences regarding age in the presentation of the syncope; however, no differences were seen between sex (men and women) regarding a history of hypertension.<sup>10</sup> Nevertheless, the study population involved was different from our group and the findings are not therefore comparable.

The development time of the syncope episodes was also significantly different and was lower among the patients with hypertension (Group A, 36 months [range, 12-102] as compared with Group B, 12 months [range,

**TABLE 2. Multivariate Analysis of the Response to the Head-Up Tilt Table Test**

	P	OR	95% CI
Hypertension	.187	0.642	0.332-1.239
Age	.193	1.01	0.995-1.025
Sex	.992	1.003	0.603-1.666
Number of syncope episodes	.087	0.608	0.343-1.076
<5 previous episodes (reference)			
≥5 previous episodes			
Duration of the symptoms	0.358	1.001	0.999-1.003
Diabetes mellitus	0.958	0.975	0.377-2.521

\*OR indicates odds ratio; CI, confidence interval.

**TABLE 3. Distribution of the Types of Positive Responses to the Head-Up Tilt Table Test in the 2 Groups\***

	Group A Positive Responses (n=168)	Group B Positive Responses (n=63)
Type I (mixed)	58 (34.5%)	20 (31.7%)
Type II (cardioinhibition)	46 (27.4%)	6 (9.5%)
Type III (vasodepressor)	55 (32.7%)	31 (49.2%)
Other responses	9 (5.4%)	6 (9.5%)

\* $\chi^2=11.1$ ;  $P=.01$ .

2-48];  $P=.0001$ ). Whether taking anti-hypertensive medication was associated with this difference remains unknown. Moreover, as we were unable to find any references regarding this difference, it should be investigated in future studies. The logistic regression analysis confirmed that none of these variables were independently associated with the response to the tilt test. Accordingly, we conclude that with the control variables examined and the current sample size, no differences were found in the response between the syncope patients with and without hypertension. Studies including a greater number of patients should be designed in order to confirm this finding.

Analysis of the results of the tilt test in both groups showed interesting similarities. Not only did the 2 groups have a similar percentage of positive responses (69.1% vs 66.3%;  $P=.6$ ; NS), but these positive responses were distributed in the same way in both phases of the protocol (13.7% and 15.9% in the baseline phase, and 86.3% and 84.5% during the nitroglycerin phase, in Groups A and B, respectively;  $P=.673$ ; NS). This similarity in the percentage of positive responses and in the percentages in both phases has not been described previously. Only 1 study examined the response to this test in patients with hypertension after suspending treatment, but no comparisons were made with the patients without hypertension.<sup>11</sup> Accordingly, comparisons with our series can not therefore be made.

The only difference we found between the 2 groups was the higher percentage of patients with a pure vasopressor response (type III) and the lower percentage of patients with a pure cardioinhibitory response in Group B, the differences being statistically significant. This may indicate that, although the percentage of positivity did not vary according to whether the patients did or did not have hypertension or whether they were or were not taking anti-hypertension drugs, the type of positive response induced may be influenced by these factors. Notably, in spite of having taken their medication, all the patients in Group B had higher blood pressure levels at the start of the tilt test. Thus, the doubt remains as to whether the differences in the responses would still exist if the patients with hypertension had had normal blood pressure figures at the start of the tilt test.

### Study Limitations

Although no postural hypotension was seen during the tilt test in any of the patients, this etiology cannot be ruled out in all of them. We are unaware of the influence of the blood pressure values during the test in the Group B patients. As only 28.4% of the patients

in Group B were taking just one type of anti-hypertensive drug, it was not possible to analyze the possible differences between the different drugs. The data reported cannot be compared with previous series, and we will have to wait for future studies including a larger number of patients to recognize the data as definitive. The importance of the coexistence of left ventricular hypertrophy in the patients with hypertension was not evaluated in this study, and it will therefore be necessary to include this factor in future studies.

### CONCLUSIONS

The head-up tilt test produced similar results in patients with syncope, whether or not they also had hypertension, except for the type of response found. With the study variables included, no differences were found in the response between patients without and with hypertension.

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