Shortened Head-Up Tilting Test Guided by Systolic Pressure Reductions in Neurocardiogenic Syncope

Mariavittoria Pitzalis, MD, PhD; Francesco Massari, MD; Pietro Guida, MS; Massimo Iacoviello, MD; Filippo Mastropasqua, MD; Brian Rizzon, MD; Cinzia Forleo, MD; Paolo Rizzon, MD

Background—Asymptomatic reductions in arterial pressure have been reported to occur before the onset of tilt-induced syncope. We investigated the predictive value of these reductions for a positive tilt result.

Methods and Results—In a first study, 238 consecutive healthy subjects with unexplained syncope underwent a passive tilt table test. Finger systolic arterial pressure (SAP) recordings made it possible to calculate how many of the beat-to-beat SAP values during the first 15 minutes of tilt were lower than the lowest value recorded at baseline. Neurocardiogenic syncope was diagnosed in 73 subjects; 28 fainted after 15 minutes of tilt and experienced more pressure reductions than did the subjects with a negative test (328±400 versus 119±284; P<0.01). More than 14 SAP reductions during the first 15 minutes of tilt allowed us to predict a positive test with 93% sensitivity, 58% specificity, and positive and negative predictive values of 28% and 98%, respectively. In a second prospective study (80 consecutive subjects), the online analysis of this criterion by visually inspecting a Finapres monitor showed 80% sensitivity, 85% specificity, and positive and negative predictive values of 57% and 94%.

Conclusions—In healthy subjects with unexplained syncope, the evaluation of SAP reductions during the first 15 minutes of tilt is a marker of systolic pressure instability preceding syncope and constitutes a simple and good predictor of tilt outcome that could be used to guide test duration. (Circulation. 2002;105:146-148.)

Key Words: blood pressure □ syncope □ cost-benefit analysis

Prolonged head-up tilt testing is widely used in the diagnosis of the neurocardiogenic origin of syncope, but it is time consuming. The lengthiness of the procedure is mainly due to the need to prolong the evaluation of subjects who will not faint in any case. The identification of parameters reflecting the changes in cardiovascular homeostasis preceding neurocardiogenic syncope would greatly help the diagnostic work-up. Since Lewis and O’Toole’s report, autonomic nervous system has been recognized to have a relevant role. Abnormal heart rate control was demonstrated to be predictive of tilt-induced syncope, however, what characterizes all neurocardiogenic syncope, regardless of heart rate changes, is a reduction in arterial pressure that may be the consequence of maladaptive arterial pressure control mechanisms. If these abnormalities are already operative during the first asymptomatic phase of tilting, the related changes in blood pressure may characterize subjects with a positive test. On the basis of these considerations, we analyzed early asymptomatic reductions in arterial pressure during head-up tilt testing in subjects referred for unexplained syncope and evaluated the ability of the reductions to predict the results of the test itself.

Study 1

The study involved 238 consecutive, medication-free subjects with unexplained syncope and no history of cardiovascular or any other disease that might affect the autonomic nervous system. Carotid sinus hypersensitivity was excluded. After 10 minutes’ rest in a supine position, each subject was tilted upwards to 70° for 45 minutes using a motorized tilt table with footplate support. Beat-to-beat heat rate (Hewlett-Packard 78354C) and arterial pressure signals (Finapres Ohmeda 2300) were continuously and simultaneously recorded. The tilt test was considered positive if the subjects experienced syncope (defined as a transient loss of consciousness) or presyncope (sensation of near-fainting).

A dedicated off-line computer program was used to analyze all beat-to-beat systolic arterial pressure (SAP) values recorded during the first 15 minutes of the test and to compare them with those recorded during the baseline period. SAP was considered reduced when its beat-to-beat value was lower than the lowest baseline value. The subjects experiencing syncope or presyncope within the first 15 minutes were excluded from further analysis.

Study 2

After the best predictive criterion had been established, we prospectively tested its predictive value in 80 consecutive subjects with characteristics similar to those in Study 1. This study was performed by one skilled registered nurse and one cardiologist. The latter was...
asked to record the lowest beat-to-beat SAP measured during the baseline evaluation by visually inspecting the Finapres monitor, and then to count whether the number of beat-to-beat SAP reductions during the first 15 minutes of tilt was higher or lower than the established criterion. In any case, the tilt was continued. Sensitivity, specificity, and predictive values were obtained by visual inspection and off-line by computer analysis (using the same method as that used in Study 1).

Variables are expressed as mean ± SD. The groups were compared using ANOVA, followed by the Newman-Keuls test, the $\chi^2$ test or the Mann-Whitney $U$ test, as appropriate. A value of $P<0.05$ was considered significant.

Results

Study 1

Neurocardiogenic syncope was diagnosed in 73 subjects (31%). Two subjects experienced psychogenic syncope before the 15th minute and were excluded from the analysis. The mean time to tilt-induced syncope was 14.5 ± 10.4 minutes. Table 1 shows the baseline characteristics of the population. A total of 45 subjects fainted within the first 15 minutes, and 28 fainted thereafter.

Heart rates and SAP values of the subjects who fainted after the 15th minute and those with a negative tilt are shown in Table 2. Baseline SAP did not differ between the 2 groups, but the tilt values were significantly lower in the subjects with syncope than in those without. At least 1 SAP reduction was observed during the first 15 minutes of tilt in 27 of the 28 subjects with syncope (96.4%) and in 118 of those with a negative test (72.4%). However, the phenomenon was more frequent in the subjects who fainted (328 ± 400 versus 119 ± 284; $P<0.01$) (example in the Figure). The median number of SAP reductions was 14 in the 191 subjects who reached the 15th minute of tilt, 8 in those with a negative test, and 107 in those with a positive test.

The value of SAP reductions in defining the subjects who would faint during the subsequent 30 minutes of the tilt and those who would not was related to the number of reductions (Table 3): The smaller the number of reductions, the higher

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<th>TABLE 1. Characteristics of Population in Study 1</th>
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<td>-----------------------------------------------</td>
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<tr>
<td>Number</td>
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<td>Age, y</td>
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<td>Sex, male/female</td>
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<td>Syncope in previous year</td>
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Values are mean ± SD or number.

* $P<0.0001$ vs both >15th-minute and negative tests.

<table>
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<tr>
<th>TABLE 2. Heart Rate and SAP Values in Study 1 Subjects</th>
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<td>Positive Tilt &gt;15th min</td>
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<tr>
<td>Baseline</td>
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<td>Heart rate, beats/min</td>
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<td>SAP, mm Hg</td>
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<td>First 15 minutes of tilt</td>
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<tr>
<td>Heart rate, beats/min</td>
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<td>Heart rate at 15th minute, mm Hg</td>
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* $P<0.001$ vs positive tilt.
the negative predictive value. The presence of >14 SAP reductions (i.e., the median number observed in the population) was chosen as the best predictive criterion because its negative predictive value for a positive test is still high (98%) and its specificity increases to 58% (Table 3).

**Study 2**
The mean age of the population (41 females) was 32±14 years. Tilt testing induced neurocardiogenic syncope in 21 subjects (26%), with 6 episodes occurring within the first 15 minutes. The sensitivity, specificity, and positive and negative predictive values of >14 SAP reductions as counted by means of online visual inspection were, respectively, 80%, 85%, 57%, and 94%. The accuracy of the online classification was 84%. The sensitivity, specificity, and positive and negative predictive values of >14 SAP reductions as counted by subsequent off-line analysis were, respectively, 80%, 70%, 40%, and 93%, with an accuracy of 72%.

**Discussion**
The precise classification of recurrent syncope requires the use of head-up tilt test, a diagnostic procedure that is burdened by its long duration and high incidence of negative results. Shortening the duration of the procedure in subjects who are not likely to faint could optimize tilt-related time and cost. This strategy involves detecting early signs that can predict tilt outcome.

We propose early, asymptomatic SAP reductions as a simple parameter that may help in guiding tilt duration. The rationale of this approach is based on pathophysiological considerations and the fact that it allows further investigation of the mechanisms leading to neurocardiogenic syncope. In 1968, Epstein et al observed large oscillations in arterial pressure before the development of tilt-induced syncope, thus suggesting that maladaptive arterial pressure control mechanisms play a role.

In our study, the subjects prone to fainting experienced a larger number of asymptomatic SAP reductions than did subjects who did not faint, and the absence of these reductions was more likely in subjects without than in those with syncope. We therefore hypothesize that early SAP reductions reflect changes in cardiovascular homeostasis before the occurrence of neurocardiogenic syncope. The presence of similar (but numerically less frequent) changes in a number of subjects who did not faint after continuing the tilt suggests that their cardiovascular system may also be abnormally controlled and that the effects are partially blunted by compensatory mechanisms that prevented the occurrence of syncope. Considering our findings together with those published by Mallat et al., who found that an abnormal heart rate increase during the first minute of tilt indicates a high probability of fainting, it can be hypothesized that a key role may be played by arterial baroreceptor activity.

The clinical implications of our findings are of primary importance because they allow the duration of tilt testing to be guided. In particular, the absence of SAP reductions during the first 15 minutes of tilt accurately identifies subjects who will not faint during the subsequent 30 minutes, thus suggesting that there is no advantage to continuing the test itself. The risk of stopping the test too early in subjects who later will experience syncope is very low, and it depends on the number of SAP reductions chosen as a marker of a negative tilt result; the smaller the number of reductions, the higher the negative predictive value. Stopping the test after 15 minutes only in the case of subjects with ≤14 SAP reductions made it possible to reduce the number of subjects who subsequently would faint to an acceptable minimum and to avoid prolonged testing in subjects who were unlikely to faint.

In the prospective evaluation, the accuracy of the online identification of more than or less than 14 SAP reductions in predicting tilt outcome even improved. This is probably because of better human identification of artifacts simulating what off-line analysis considers to be SAP reductions. This guided visual approach makes it possible to save 54% of the time traditionally used for syncope diagnosis. Vasoactive drugs are reported to increase positive test percentage, and they therefore are administered routinely in some laboratories. The 2 approaches (the one we propose and drug administration) have different objectives and are not mutually exclusive; their combined use may actually lead to a higher incidence of positive tests. We did not administer these drugs, and this may have limited the impact of the present study; the strategy of administering the drugs at the end of tilt to the subjects who have not fainted despite the presence of SAP reductions could be associated with better clinical results.

In conclusion, asymptomatic SAP reductions during the early phase of tilt reflect vasomotor instability preceding neurocardiogenic syncope and are an adequate means of guiding tilt duration in subjects with unexplained syncope.

**References**
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