Transcranial Doppler monitoring during head upright tilt table testing in patients with suspected neurocardiogenic syncope

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Abstract The aim of the present study was to evaluate the mechanism of cerebrovascular autoregulation in patients with neurocardiogenic syncope using bilateral transcranial Doppler (TCD) monitoring during head upright tilt table testing (HUT). Two hundred and six patients were prospectively studied. One hundred and fifty-nine subjects (77%) had a prior history of syncope and 47 (23%) had presyncope. Ninety-nine patients (48%) had syncope or presyncope during HUT with a 76% fall in diastolic middle cerebral artery blood flow velocity (D-MCA-BFV). Systolic MCA-BFV (S-MCA-BFV) fell by 33%. Deepening of the dicrotic notch in the Doppler waveform always preceded the fall in D-MCA-BFV. Patients without syncope or presyncope (n = 96) had smaller changes in cerebral blood flow velocities during HUT and only twenty-two subjects had transient deepening of the dicrotic notch. Eleven subjects had presyncope during HUT due to an exaggerated response to nitrates with progressive arterial hypotension without bradycardia and changes during TCD monitoring that were intermediate between positive and negative HUT.

In conclusion, patients with neurocardiogenic syncope have changes in cerebral blood flow during the event. TCD monitoring during HUT helps to assess these alterations.

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Introduction

Syncope is a transient loss of consciousness with inability to maintain postural tone due to cerebral hypoperfusion. Recovery is typically spontaneous. The most frequent cause of syncope is a dysfunction
of the autonomic nervous system (i.e., neurocardiogenic syncope) [1]. Its pathophysiological mechanisms are not fully understood. Syncope is the result of transient arterial hypotension, with or without bradycardia, after triggering of sympathetic inhibition and adrenomedullary discharge, associated or not with parasympathetic upregulation [2]. This autonomic pattern may be mediated by peripheral mechanisms involving the Bezold–Jarisch reflex or central mechanisms with release of serotonin or endogenous opiates. A rapid decrease in venous return associated with increased ventricular inotropism triggers most episodes [3–5].

The head upright tilt table test (HUT) objectively helps to identify patients with neurocardiogenic syncope. The pathophysiology of neurocardiogenic syncope still poses several unanswered questions. One of them is the role of cerebral autoregulation.

In 1982, Aaslid et al. [6] introduced a transcranial Doppler technique that allowed real time assessment of blood flow velocities in intracranial cerebral arteries. This technique provides anatomical

Figure 1  Mean ± SD of percentage fall from baseline in diastolic (gray bars) and systolic (white bars) MCA-BFV during HUT. P, positive test patients; N, negative test patients; E, exaggerated response to nitrates patients. *p < 0.0001 vs. N and E, **p < 0.0001 vs. N.

Figure 2  Patient with positive HUT. (A) MCA-BFV at baseline. (B) Normal cerebral autoregulation at the beginning of the test. Diastolic velocity decreases less than systolic velocity. (C) Dicrotic notch is deepened and diastolic velocity decreases more than systolic velocity. (D) Graphic representation of the fall in systolic and diastolic velocities during testing.
as well as functional information including cerebral autoregulation [7].

We evaluated cerebral blood flow dynamics using transcranial Doppler during HUT in patients with suspected neurocardiogenic syncope.

**Methods**

Two hundred and six patients with a suspected diagnosis of neurocardiogenic syncope referred to our laboratory between August 1999 and December 2001 were analyzed. Syncope was defined as a sudden transient loss of consciousness with inability to maintain postural tone, with spontaneous recovery. Presyncope was defined as the presence of premonitory symptoms (i.e., dizziness, sweating, and nausea) not followed by loss of consciousness. All patients received a detailed medical history including neurological and cardiological clinical examinations and electrocardiogram (ECG). Ancillary diagnostic tests were performed when medically indicated. A photoplethysmographic device (Colin 7000, San Antonio, TX, USA) allowed accurate continuous noninvasive monitoring of systolic and diastolic blood pressure and heart rate during the procedure.

HUT was performed following a 3-h fasting period. After baseline measurements of heart rate and blood pressure, each patient was positioned at an angle of 60° from supine on the tilt table for as long as 45 min. If syncope did not occur during the initial tilt, patients received 2.5 mg of sublingual isosorbide dinitrate [8–14]. A positive test was defined as syncope associated with hypotension with or without bradycardia. Positive tests were classified as: Type 1 (*mixed*), blood pressure fall with heart rate reduction to no lower than 40 beats per minute;

![Figure 3](image-url)

**Figure 3** Patient with a positive HUT. (A) Baseline. (B) Patient asymptomatic with the typical transitory stage of deepening of dicrotic notch. (C) Seconds later, symptoms appear, diastolic velocity falls with bradycardia and hypotension.
Type 2 (cardioinhibition), heart rate fall to a ventricular rate less than 40 beats per minute; and Type 3 (vasodepressor), blood pressure fall without bradycardia [15].

Blood flow velocities of both middle cerebral arteries (MCA-BFV) were continuously monitored at a depth of 55 mm through the transtemporal window using a transcranial Doppler device (Multi Dop X4, Sipplingen, Germany). We recorded systolic and diastolic MCA-BFV (S-MCA-BFV and D-MCA-BFV). For data analysis purposes, we selected recordings from the side with the best ultrasonic signal.

We analyzed the data using standard statistical procedures. We compared percent change in BFV during HUT using paired $t$-tests. Comparisons of percent change in MCA-BFV during HUT between positive test, negative test, and exaggerated response to nitrates groups were done using Student’s $t$-test for unpaired data. All statistical levels quoted ($p$ values) are two-sided. Results are given as mean ± SD and were considered statistically significant when the $p$ value was $<0.05$.

**Results**

We studied 206 consecutive subjects, aged 40 ± 22 years (range 5–85 years). There were 129 females and 77 males. One hundred and fifty-nine subjects had a history of syncope and 47 had presyncope. On average, subjects had $5.7 ± 6.1$ episodes (1.5 ± 2.0 episodes in the previous 30 days). Dizziness was the most frequent prodromal symptom ($n = 110$). Thirty patients had abnormal movements (seizur-like activity) during the episode, 48 sustained trauma, 26 had urinary incontinence, and 32 lost consciousness without a prodrome. No patient had a history of cardiac disease or ECG abnormalities.

HUT was positive in 99 patients (48%), negative in 96 (47%) and the remaining 11 (5%) had an exaggerated response to nitrates. Systolic and diastolic MCA-BFV fell significantly in the three groups. However, the magnitude of the fall, especially in diastolic values, was larger in patients with positive tests (Fig. 1). Test responses in the positive group were vasodepressor in 19, cardioinhibitory in 12, and mixed in 68 cases.

![Head-upright tilt table test](image1)

**Figure 4** Sonogram in a patient with syncope during HUT and during hyperventilation. Note the different shapes of the waveforms.
In the positive group, S-MCA-BFV decreased by 33.1 ± 23.2% (p < 0.0001 vs. negative group) and D-MCA-BFV fell by 76.0 ± 15.2% (p < 0.0001 vs. negative and exaggerated response to nitrates groups) (Fig. 2). MCA-BFV changes preceded symptom appearance in all cases by less than 2 min. Symptoms always resolved and MCA-BFV returned to baseline values immediately after placing the patient back to supine position, overlapping with the recovery of consciousness and normalization of systemic blood pressure.

Besides the change in velocities, a typical pattern of changes in the MCA-BFV waveform preceded the fall in blood pressure and onset of symptoms in every syncopal case. This consisted of a slight deepening of the dicrotic notch, transient at the beginning (Fig. 3) and permanent later. This pattern was different from changes normally elicited during hyperventilation/hypocapnia (Fig. 4). Similar changes were seen in 22 of the 96 negative HUT patients. However, they were only transient.

In patients with positive HUT, heart rate fell by 9.3 ± 49.8%. In patients with negative HUT, heart rate was increased by 30.5 ± 25.7% (p < 0.0001). Systolic and diastolic blood pressure diminished by 56.3 ± 18.7% and 57.7 ± 27.4%, respectively, in the positive group, and by 9.6 ± 11.9% and 2.2 ± 19.5%, respectively, in the negative group (p < 0.001) (Fig. 5).

The 11 patients with presyncope during HUT due to an exaggerated response to nitrates had progressive arterial hypotension without bradycardia. TCD monitoring demonstrated a fall in MCA-BFV that was intermediate between the values of the positive and negative groups, without substantial morphological changes from baseline (Fig. 6). In these patients, heart rate increased by 53.0 ± 31.7% while systolic and diastolic blood pressure diminished by 41.8 ± 15.1% and 31.8 ± 12.8%, respectively.

Discussion

The normal brain is able to regulate its blood flow through a homeostatic vasomotor mechanism [16].
Previous studies have documented the ability of this physiological system to maintain a relatively constant cerebral blood flow within a wide range of mean arterial blood pressure (50–170 mmHg). TCD monitoring assesses "real time" cerebral blood flow velocities and can rapidly detect haemodynamic responses to acute blood pressure changes [17].

Grubb et al. [18] demonstrated that patients with neurocardiogenic syncope had "paradoxic cerebral vasoconstriction" just before loss of consciousness due to a marked fall in cerebral blood flow mean velocity. This pattern was not observed in controls and negative HUT patients. These findings have since been confirmed by other authors [19–22].

Bondar et al. [23] evaluated the changes that occur in the cerebral circulation in different ranges of reduced blood pressure using TCD monitoring. They demonstrated that the sympathetic nervous system was a key factor in cerebral blood flow autoregulation. Sympathetic intracranial nerve activation served as a protective mechanism during systemic hypertension to maintain the cerebral blood flow constant. A critical reduction of blood volume may activate the sympathetic nervous system, causing cerebral vasoconstriction. If vasoconstriction overcomes metabolically induced vasodilatation, cerebral hypoperfusion and syncope can follow. Schondorf et al. [24] documented that the main finding in patients with neurocardiogenic syncope is a decrease in diastolic cerebral blood flow velocity, and that the selective loss of diastolic flow is due to a collapse of downstream vessels.

The present study demonstrated that TCD monitoring of MCA-BFV during HUT was technically feasible in presumed syncope cases. Since this is a noninvasive, painless test, it does not affect method sensitivity and appears to allow better assessment of these patients.

We confirmed the presence of a marked decrease in D-MCA-BFV during HUT and characterized the temporal profile of these changes in patients with neurocardiogenic syncope. In addition, we described a typical pattern of waveform changes preceding syncope in patients with positive tests. It consisted of transitory deepening of the dicrotic notch. We hypothesize that this pattern is due to the effect of
the respiratory cycle on the cerebral blood flow velocities during conditions of relative hypovolemia as seen during the Valsalva manoeuvre, especially in susceptible patients. Patients with negative tests did not exhibit this waveform pattern except for 22 subjects, who did so transiently. The recognition of this pattern has 2 important implications: (1) it shows objective evidence of altered cerebral blood flow regulation preceding systemic haemodynamic changes; and (2) it identifies patients who may later have neurocardiogenic syncope.

TCD monitoring also allowed for better identification of patients with exaggerated response to nitrate stimuli. Despite a moderate fall in S- and D-MCA-BFV velocities, this group did not exhibit the typical deepening of the dicrotic notch found in positive HUT patients. We believe that this feature may help to differentiate these patients from those with true vasodepressor syncope.

The disproportionate change in diastolic compared with systolic velocities suggests that simply monitoring the mean MCA-BFV may not reflect the actual magnitude and quality of changes in cerebral circulation. Cerebral vessels of patients with neurocardiogenic syncope may have impaired reactivity, making them susceptible to sustain transient hypoperfusion. The evidence for this was the finding of an early deepening of the dicrotic notch with lowering of D-MCA-BFV preceding changes in blood pressure.

In conclusion, patients with neurocardiogenic syncope have changes in cerebral blood flow regulation during the event. TCD monitoring during HUT helps to assess these alterations. Since TCD changes precede the fall in blood pressure, heart rate and symptoms, this technique may, in the future, allow early interruption of HUT before symptoms arise, preventing the unpleasant experience for the patients. TCD monitoring may also help to differentiate patients with exaggerated response to nitrates from those with true neurocardiogenic vasodepressor syncope. TCD during HUT may improve the well-known usefulness of the method for the diagnosis of neurocardiogenic syncope.

References