Clinical Spectrum and Prevalence of Neurologic Events Provoked by Tilt Table Testing

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Background: Motor activity occurring during neurocardiogenic syncope can mimic true neurologic events.

Objective: To assess the prevalence and type of apparent neurologic events associated with tilt table testing.

Methods: The records of consecutive patients undergoing tilt table testing for the evaluation of syncope were reviewed. Patients underwent a 70° upright tilt for 40 minutes, followed by a 20-minute tilt while receiving isoproterenol hydrochloride. The results of tilt table tests were considered positive when clinical symptoms were reproduced in association with a decline in blood pressure. Clinical variables and neurologic events were analyzed.

Results: Tilt table tests were performed on 694 patients during the study period, and the results were positive in 222 of them. Eighteen patients (8%) had apparent neurologic events during tilt table testing. Eleven patients (5%) had apparent tonic-clonic seizure–like activity, and 7 patients (3%) had non–tonic-clonic neurologic events, including focal seizures (n = 3), dysarthria or aphasia (n = 2), unilateral extremity dysesthesia (n = 1), and reproduction of temporal lobe epilepsy symptoms (n = 1). The patients with tonic-clonic seizure–like activity had a significantly lower systolic blood pressure reading at the termination of tilt table testing than all other patients whose tilt table test results were positive (P = .04). The heart rate at the time of test termination was significantly lower in the patients with tonic-clonic seizure–like activity and non–tonic-clonic neurologic events (P < .01) than in those with positive test results and no provoked neurologic events, and asystole was provoked more frequently in these 2 patient populations (P = .03).

Conclusions: Neurologic events are common during episodes of neurocardiogenic syncope, and this diagnosis should be considered in the evaluation of unexplained seizure-like activity.

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for the evaluation of syncope over a 6-year period were reviewed. The results of tests performed for the evaluation of chronic fatigue symptoms or as follow-up to assess the efficacy of medical therapy were excluded. Positive test results, defined as a reproduction of the patient's clinical symptoms in association with a decrease in the systolic blood pressure level with or without relative bradycardia, were further analyzed.

Tilt table testing was performed with the patients in the unmedicated, fasting state. The patients were connected to a standard cardiac monitor for continuous evaluation of heart rate and to a standard sphygmomanometer for blood pressure measurement that was determined every 3 minutes. An intravenous catheter was inserted through which normal saline at 30 mL/h was infused to maintain catheter patency. After baseline measurements of heart rate and blood pressure levels, each patient was positioned at a 70° angle from horizontal for up to 40 minutes on a tilt table with a footboard made for weight bearing (Tri-W-G Inc, Valley City, ND). If syncope developed during the test, the table was rapidly lowered to the supine position. If the baseline tilt failed to yield a positive result, the patient was returned to the supine position for 5 minutes, and isoproterenol hydrochloride infusion was initiated at 2 ug/min. The dosage was increased by 1 ug/min to a maximum of 6 ug/min as needed to achieve a heart rate of greater than 100 beats/min and an increase of at least 25% above baseline. Upright tilt was then repeated for up to 20 minutes. A positive response was defined as syncope associated with hypotension with or without relative bradycardia.

Analyzed variables included patient age, sex, history of seizure, use of isoproterenol during protocol, duration of tilt table testing (at baseline and during isoproterenol infusion), initial and final heart rate and blood pressure reading, occurrence of asystole, and the type, if any, of neurologic events provoked. Asystole was defined as a pause lasting longer than 3 seconds. Tonic-clonic seizure–like activity was defined as tonic spasms with or without clonic movements occurring with loss of consciousness. Non–tonic-clonic neurologic events were defined as signs or symptoms consistent with a neurologic cause but not associated with tonic-clonic movements. The patients were divided into 3 groups for analysis: (1) those with positive tilt table test results with no provoked neurologic events, (2) those with positive tilt table test results with tonic-clonic seizure–like activity provoked, and (3) those with positive tilt table test results with non–tonic-clonic neurologic events provoked.

Comparisons of continuous variables between groups were performed with 1-way analysis of variance. Nominal variables were compared using χ² analysis or Fisher exact test; P < .05 was considered statistically significant. Continuous variables are expressed as mean ± SD.

Follow-up was performed by review of medical records and through discussions with the patients’ physicians. The study was approved by the institutional review board of Northwestern Memorial Hospital. Informed consent was obtained at the time of tilt table testing by an attending physician.

### Results

Tilt table tests were performed in 694 patients for the evaluation of syncope, and the results were positive in 222 patients (32%): 155 on baseline tilt (69.8%) and 67 (30.2%) with isoproterenol infusion. The duration of baseline tilt until a positive result was obtained was 26 ± 16 minutes, and the duration of isoproterenol tilt table testing until a positive result was obtained was 12 ± 10 minutes.

Eleven patients (5%) had tonic-clonic seizure–like activity provoked by tilt-table testing. Seven patients (3%) had other non–tonic-clonic neurologic events provoked by upright tilt, including focal seizure activity involving 1 extremity (n = 3), dysarthria or aphasia (n = 2), reproduction of unilateral extremity dysesthesia (n = 1), and reproduction of alteration of consciousness previously diagnosed as temporal lobe epilepsy (n = 1). All but 1 event resolved immediately or shortly after the patient’s return to the supine position with no postictal state; the single probable neurologic event was a prolonged period of aphasia that was ultimately diagnosed as a transient ischemic attack. All the apparent tonic-clonic seizure–like activity or non–tonic-clonic neurologic events occurred with baseline testing without isoproterenol.

Comparison of the 3 groups of patients with positive tilt table test results (positive tilt table test results with no neurologic events provoked, positive tilt table test results with tonic-clonic seizure–like activity provoked, and positive tilt table test results with non–tonic-clonic neurologic events provoked) revealed no significant differences in patient age, sex distribution, or initial heart rate and blood pressure reading (Table). Patients with positive tilt table test results and tonic-clonic seizure–like activity had a significantly lower systolic blood pressure reading at the time of termination of tilt table testing (37 ± 38 mm Hg for patients with positive tilt table test results and tonic-clonic seizure–like activity vs 56 ± 41 mm Hg for patients with positive tilt table test results and non–tonic-

### Table: Comparison of 3 Groups of Patients With Positive Tilt Table Test Results

<table>
<thead>
<tr>
<th>Variable</th>
<th>+ Tilt − Neuro</th>
<th>+ Tilt + TCS</th>
<th>+ Tilt + NTCN</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients, No. (%)</td>
<td>204 (92%)</td>
<td>11 (5%)</td>
<td>7 (3%)</td>
<td>...</td>
</tr>
<tr>
<td>Age, y</td>
<td>48 ± 20</td>
<td>38 ± 19</td>
<td>55 ± 31</td>
<td>.20</td>
</tr>
<tr>
<td>Sex, % male</td>
<td>47</td>
<td>18</td>
<td>57</td>
<td>.14</td>
</tr>
<tr>
<td>Seizure history, %</td>
<td>0.5</td>
<td>18</td>
<td>43</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Initial SBP, mm Hg</td>
<td>120 ± 22</td>
<td>121 ± 19</td>
<td>140 ± 19</td>
<td>.19</td>
</tr>
<tr>
<td>Final SBP, mm Hg</td>
<td>63 ± 32</td>
<td>37 ± 38</td>
<td>56 ± 41</td>
<td>.04</td>
</tr>
<tr>
<td>Final heart rate, beats/min</td>
<td>67 ± 26</td>
<td>38 ± 37</td>
<td>37 ± 30</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Asystole provoked, %</td>
<td>8</td>
<td>27</td>
<td>29</td>
<td>.03</td>
</tr>
<tr>
<td>Duration of asystole, s</td>
<td>14 ± 10</td>
<td>22 ± 25</td>
<td>11 ± 3</td>
<td>.52</td>
</tr>
</tbody>
</table>

Abbreviations: − Neuro, no neurologic events during tilt; + NTCN, non–tonic-clonic neurologic events during tilt; SBP, systolic blood pressure; + TCS, tonic-clonic seizure–like activity during tilt; + Tilt, positive tilt table test results.

*Data are given as mean ± SD unless otherwise indicated.
The major findings of the present study are the relatively high frequency of tonic-clonic seizure–like activity and non–tonic-clonic neurologic events in patients with positive tilt table results who were undergoing evaluation for syncope and the observed differences in hemodynamic profiles between the 2 groups at test termination.

Prior studies of neurologic events during tilt table testing have generally involved patient populations selected for a history of seizures that are often refractory to antiepileptic drug therapy, with seizure-like activity reported in as many as 25% to 66% of such patients.5,6,11 The frequency of neurologic events that occur during tilt table testing in an unselected population has not been well established. However, the prevalence of such events has been reported in a population of individuals during phlebotomy, a procedure that is well known to induce neurocardiogenic syncope in susceptible individuals. In a study of blood donors, retrospective and prospective analyses yielded incidences of 11.9% and 41.6%, respectively, of convulsive movements during syncope.12 The variation between retrospective and prospective results may be partially attributed to increased attentiveness during the prospective study. Although these observations did not take place in the more controlled setting of a tilt table test laboratory, it does give some indication as to the frequency with which syncope is associated with seizure-like activity.

The present study demonstrates that the hemodynamic changes in uncomplicated neurocardiogenic syncope are less marked than when the event is associated with tonic-clonic seizure–like activity and non–tonic-clonic neurologic events. As in the current study, significant bradycardia has been reported with seizure-like activity during tilt table testing.6 In a prior report involving patients with apparent recurrent transient ischemic attacks that could be reproduced on tilt table testing, the systolic blood pressure readings at the time of symptoms were similar to those of our patients with non–tonic-clonic neurologic events.7 Although the tonic-clonic seizure–like activity that may occur during neurocardiogenic syncope may appear similar to epileptic seizures, the mechanism is distinct. Simultaneous EEG and tilt table testing shows nonepileptiform theta and delta wave slowing during syncope.13 In patients with convulsive movements during tilt-induced syncope, EEG demonstrates similar diffuse slowing without spike or spike-wave activity.13 The adjuvant use of EEG with tilt table testing has been used to differentiate epileptic seizure and tonic-clonic activity during vasodepressor syncope from seizures of psychogenic origin that lack significant hemodynamic or EEG changes.14,15

Upright tilt table testing with simultaneous transcranial Doppler blood flow analysis demonstrates that sudden and transient loss of consciousness occurs when cerebral perfusion decreases to approximately half of the baseline flow velocity in most patients.10 Measurement of brain tissue oxygenation with noninvasive spectroscopy has shown a similarly consistent threshold level of oxygen saturation below which syncope occurs.17 These results have led some authors to conclude that cerebral autoregulation is ineffective at the extremes of systemic blood pressure levels or that some individuals have inherently less autoregu-
Symptomatic vasodepressor syncope is a common clinical entity, often associated with seizure-like symptoms. In a study of patients with vasodepressor syncope, 11,13 with the exception of the logic symptoms did not recur in those patients treated with antiepileptic medications. As in prior studies, neurologic symptoms did not recur in those patients treated for vasodepressor syncope.11,13 With the exception of the patient who had a dysthymic transient ischemic attack on tilt table testing, the patients in the current study who were followed up had no further episodes of primary neurologic-type events during adequate β-blocker or mineralocorticoid therapy, further supporting the concept that these events do not represent a manifestation of underlying central nervous system derangement.

Common neurologic events and follow-up were not available on all patients. While it is possible that some of these patients may have had a true seizure disorder, the absence of a postictal state after the tilt-induced event and the prevention of recurrent symptoms by β-blocker or mineralocorticoid therapy in all but 1 patient makes this unlikely. Furthermore, patients with a history of tonic-clonic seizure–like activity had experienced symptom persistence while taking antiepileptic medications before tilt table testing. Successful suppression of events may reflect the correct diagnosis of vasodepressor syncope presenting as a seizure, and more complete long-term follow-up would further support this hypothesis. In the absence of continuous and instantaneous hemodynamic monitoring, we cannot exclude the possibility that transient changes in blood pressure occurred in association with neurologic-type events but went undetected by our monitoring protocol.

The retrospective nature of this study may have resulted in inadequate documentation of all potential seizure-like or atypical neurologic events at the time of tilt table testing. However, given the standardized recording procedures used in our laboratory and the dramatic appearance of such events, a significant underestimate is unlikely. The patient population for this study excluded adolescents and children. The results, therefore, only apply to adults.

Finally, the observed frequency of neurologic events in this study is substantially lower than that seen in other studies and reflects the fact that this group was selected for the evaluation of syncope and not for seizure or other neurologic symptoms.19-21 Given the frequent occurrence of vasodepressor syncope in the general population and the frequency of neurologic events that may be associated with vasodepressor syncope, this diagnosis should be considered as a possible cause of seizure-like activity of all varieties for which an underlying neurologic cause is not identified, and tilt table testing should be considered early in the evaluation in such cases.

As described in this report, the diversity and frequency of seizure-like and other apparent neurologic events occurring in association with positive tilt table test results is clinically important. Apparent tonic-clonic seizures occurring during tilt table testing are due to profound reductions in cerebral perfusion pressure and need not suggest an underlying neurologic abnormality. Conversely, in patients with atypical neurologic events during tilt table testing, no significant reduction in systolic blood pressure levels at test termination was noted, suggesting that these patients represent a separate group that may require further investigation for an underlying abnormality. Thus, vasodepressor syncope should be considered as a possible cause of unexplained seizure-like activity of all varieties, and tilt table testing should be considered early in the evaluation of such patients.

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CONCLUSIONS

REFERENCES