ACC EXPERT CONSENSUS DOCUMENT

Tilt Table Testing for Assessing Syncope

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Preamble

Topic selection. The present document is an Expert Consensus. The type of document is intended to inform practitioners, payers and other interested parties of the opinion of the American College of Cardiology (ACC) concerning evolving areas of clinical practice or technologies, or both, that are widely available or are new to the practice community. Topics chosen for coverage by Expert Consensus documents are so designated because the evidence base and experience with the technology or clinical practice are not sufficiently well developed to be evaluated by the formal ACC/American Heart Association (AHA) Practice Guidelines process. Thus, the reader should view the Expert Consensus documents as the best attempt of the ACC to inform and guide clinical practice in areas where rigorous evidence is not yet available. Where feasible, Expert Consensus documents will include indications and contraindications. Some topics covered by Expert Consensus documents will be addressed subsequently by the ACC/AHA Practice Guidelines process.

Document review. Documents reviewed for purposes of this Expert Consensus report included all English language peer-reviewed publications between 1985 and 1995 identified by means of a Medline search using index words as described in Method of Data Collection and Analysis, as well as publications available in the personal files of the Writing Committee members.

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Introduction

Need for Document

Head-up tilt table testing has become a widely accepted tool in the clinical evaluation of patients presenting with syncopal symptoms. Currently, there is substantial agreement that tilt table testing is an effective technique for providing direct diagnostic evidence indicating susceptibility to vasovagal syncope (1-13). Previously, apart from the presence of a "classic" clinical history, the diagnosis of vasovagal syncope and other neurally mediated syncopal syndromes could be addressed only indirectly by careful exclusion of other causes of syncope. In essence, tilt table testing has become the "gold standard" among clinical laboratory diagnostic studies in this setting.

Given the relatively recent evolution of head-up tilt testing, it is not surprising to find differences of opinion with respect to various aspects of the technique. Furthermore, some third-party payers are sufficiently uncertain of the utility of tilt table testing to decline reimbursement for its performance. Consequently, this Expert Consensus document was developed with the goals of reviewing the current status of tilt table testing to decline reimbursement for its performance. Consequently, this Expert Consensus document was developed with the goals of reviewing the current status of tilt table testing (including its rationale, methodology, indications and alternatives) and providing an up-to-date basis for practitioners and payers to use in considering the role of such testing in patient care.

Rationale for Use of Tilt Table Testing

Scope of the problem. Syncope is a relatively frequent symptom, and its evaluation is an important aspect of medical practice (14-22). In terms of hospital visits, syncope has been reported to account for ~3% of emergency room visits and from 1% to 6% of general hospital admissions in the United States (19-22). A conservative estimate suggests that at least 3% of the population can be expected to experience a syncopal
episode during an approximate 25-year period of observation (14).

Many individuals who experience a solitary syncopal event probably do not seek medical attention. However, recurrences are common after an initial syncopal event, occurring in ~30% (14-18). In such cases, it is more likely that physician advice will be sought. Furthermore, even single syncopal events, when associated with physical injury or occurring in individuals with high risk occupations or avocations (e.g., pilots, commercial drivers, surgeons, window washers) or accompanying certain high profile activities (e.g., competitive athletics), may warrant assessment.

The vasovagal faint is believed to be the most common cause of syncope, especially if there is no evidence of underlying structural cardiac or cardiovascular disease (15,23-26). In reports derived from various hospital services (emergency rooms, intensive care units, in-patient services), the proportion of patients with this diagnosis has ranged from 10% to 40% (19,20,21,24,25,27). More recently, in a long-term follow-up study of 433 patients with syncope, a cause of syncope was assigned in 254 (57%). Neurally mediated syncope was the single most frequent diagnosis (76 [30%] of 254). This diagnosis may have been more frequent had additional diagnostic testing such as tilt table studies been available.

Nomenclature. 1) Neurally mediated syncope and the neurally mediated syncope syndromes are the terms used in this document to refer to a variety of clinical scenarios (e.g., vasovagal syncope, carotid sinus syndrome, postmicturition syncope) in which the triggering of a neural reflex results in a vasovagal faint. Alternative terms used in published reports, such as "neurocardiogenic" syncope and "cardioneurogenic" syncope have been avoided for purposes of consistency. 2) Vasovagal syncope is the term used to denote one of the clinical scenarios (the most common) within the category of neurally mediated syncope syndromes.

Head-up tilt testing. The importance of identifying susceptibility to vasovagal reactions in patients with syncope is readily evident given the frequency with which vasovagal syncope appears to be responsible for patient symptoms. To date, the head-up tilt table test is the only diagnostic tool to have been subject to sufficient clinical scrutiny to assess its effectiveness in this setting.

Several observations suggest that symptomatic hypotension-bradycardia associated with a "positive" head-up tilt test response is comparable to the spontaneous neurally mediated vasovagal syncope (28,29). 1) Both induced and spontaneous syncopal episodes tend to be associated with similar premonitory symptoms (e.g., nausea, diaphoresis) and signs (e.g., marked pallor, loss of postural tone). 2) The temporal sequence of blood pressure and heart rate changes during tilt-induced syncope is parallel those reported for spontaneous episodes (30). 3) Plasma catecholamine levels measured before and during spontaneous and tilt-induced syncope exhibit important similarities. In particular, premonitory increases in circulating catecholamine levels appear to characterize both the spontaneous vasovagal faint (31,32) and tilt-induced hypotension-bradycardia (33).

Head-up tilt table testing in asymptomatic control subjects. Tilt table testing, especially when undertaken in the absence of provocative pharmacologic agents, appears to discriminate between symptomatic patients and asymptomatic control subjects with a level of precision considered acceptable for other clinically useful medical testing procedures. For example, deMey and Enterling (34) reported only eight instances of hypotension-bradycardia among 40 apparently normal subjects (20%). In a follow-up report these investigators noted abnormal responses in 7 (20%) of 35 subjects. Fitzpatrick et al. (35,36) indicated that a 60° upright tilt for 45 min was accompanied by development of syncope in only 7% of 27 subjects without a history of syncope (mean time to syncope 35 ± 5 min). Similarly, during a 45-min drug-free tilt at 60°, Raviele et al. (37) noted that among 35 control subjects, none developed syncope. Grubb et al. (10,13) have also observed a relatively low "false-positive" rate associated with tilt testing in both elderly and young patients. Finally, with regard to the potential impact of pharmacologic agents on specificity of tilt testing, Natale et al. (38) examined the outcome of tilt testing at various angles and with various doses of isoproterenol provocation in 150 volunteers with no prior history of syncope or presyncope. They found tilt table testing at 60°, 70° and 80° to exhibit specificities of 92%, 92% and 80% respectively, when low doses of isoproterenol were used.

In summary, most studies suggest that tilt table testing at angles of 60° to 70°, in the absence of pharmacologic provocation, exhibits a specificity of ~90%. In the presence of pharmacologic provocation, test specificity may be reduced, although the magnitude of this reduction is unclear. For instance, in the case of isoproterenol provocation, Kapoor and Brant (39) noted that almost 50% of control subjects exhibited a positive response during a tilt protocol consisting of a 15-min 80° baseline tilt with subsequent isoproterenol provocation if needed. In contrast, in a relatively large population, Natale et al. (38) reported a specificity of 80% using a relatively steep tilt (80°) and low dose isoproterenol, and an even higher specificity (90%) when less steep tilt angles were used.

Head-up tilt studies in suspected neurally mediated syncope. The response to upright tilt table testing in patients with suspected neurally mediated syncope differs from that observed in patients with syncope in whom other diagnostic studies have provided a firm basis for symptoms (see also Short- and Long-Term Outcomes). By way of example, in an early report advocating the use of upright posture during conventional electrophysiologic testing to assess the hemodynamic impact of observed arrhythmias, Hammill et al. (40) noted that only the six patients with histories most compatible with vasovagal syncope developed hypotension-bradycardia-related syncopal symptoms during head-up tilt. Similarly, Fitzpatrick et al. (35) found that 60° upright tilt reproduced symptoms in 53 (75%) of 71 patients with unexplained syn-
cope; 40 exhibited both hypotension and bradycardia, whereas 13 manifested primarily a vasodepressor response.

**History of Tilt Table Testing and Prior ACC Documents**

Head-upright tilt table testing has been used over the past 50 years by physiologists and physicians to study the human body's heart rate and blood pressure adaptations to changes in position; for modeling responses to hemorrhage; as a technique for evaluation of orthostatic hypotension; as a method to study hemodynamic and neuroendocrine responses in congestive heart failure, autonomic dysfunction and hypertension; and as a tool in drug research (32-34,41–46). Occasionally, during such studies it was noted that some individuals would develop vasovagal reactions, including syncope. On the basis of these latter observations, and largely beginning with the report by Kenny et al. (1), drug-free passive head-upright tilt table testing began to be evaluated as a method for the provocation of neurally mediated hypotension and bradycardia in subjects believed to be susceptible to vasovagal syncope. Subsequently, pharmacologic provocation (e.g., isoproterenol, nitroglycerin, edrophonium) was introduced in an attempt to enhance the diagnostic yield (3,37,45,46).

This Expert Consensus document is the first official ACC report addressing tilt table testing. Its focus is on the use of tilt table testing for the assessment of syncope (principally vasovagal syncope), with only brief mention of certain related disorders. Detailed assessment of potential tilt table testing applications for the management of other conditions (e.g., orthostatic hypotension) is beyond the scope of this document.

**Description of Current Tilt Table Technology and Its Principal Variations**

**Basic Technology and Protocols for Head-Up Tilt Table Testing**

To utilize head-up tilt table testing effectively (see Indications), careful consideration must be given to the laboratory environment, the nature of medical/nursing supervision and testing protocols (Table 1). Here, we have attempted to identify those elements of tilt table testing in which there has been evolution of a consensus and those in which reasonable differences of approach remain. Absolute agreement on all aspects should not be deemed essential for the procedure to be of clinical value. As is the case for many useful diagnostic procedures in medical practice, there may not be a single "correct" protocol that is appropriate for all laboratories. This Expert Consensus document attempts to outline an accepted range of options for various aspects of the tilt table testing procedure.

**Laboratory environment.** Overview of laboratory environment. The laboratory environment in which tilt testing is undertaken is important. The room should be quiet, at a comfortable temperature and as nonthreatening as possible. The lighting should be dim and the patient permitted to rest in the supine position for ~20 to 45 min before beginning the test (28,30,36,47). The equilibration period is particularly important and should tend toward the longer duration if an arterial line is positioned as part of the study (28,47).

**Patient.** Patients are usually instructed to fast overnight in preparation for early morning studies or for several hours before tilt table testing in the case of studies scheduled later in the day. As a consequence, susceptibility to gravitationally induced hypotension may be increased. To diminish the possibility of “false positive” tests, it is reasonable to consider provision of parenteral fluid replacement before initiating the procedure. In adult patients this can usually be achieved by infusing normal saline in a volume approximately equivalent to 75 ml for each hour of the fasting period. For initial diagnostic studies, all nonessential drugs should be withheld for a period exceeding several drug half-lives.

**Recordings.** A minimum of three electrocardiographic (ECG) leads should be recorded simultaneously and continuously throughout the study. Beat-to-beat blood pressure recordings, using the least intrusive method possible, should be...
obtained and recorded continuously during the entire study. Very slow recording speeds are quite effective.

Currently, the finger plethysmographic measurement method is the least intrusive available technique for documenting blood pressure changes in this setting (48,49). In the application of this technique, each laboratory should establish procedures to verify measurement accuracy by periodic comparison with other methods (e.g., intraarterial recordings). Intraarterial recordings are also useful for documenting beat-to-beat pressures during tilt table testing. However, concern has been expressed that vascular instrumentation may alter the specificity of the test in older patients (47). Consequently, if intraarterial recordings are used, an appropriate precaution is the provision of an adequate equilibration period (30 min is often used) for the patient to recover from the vascular cannulation procedure. In principle, intermittent sphygmomanometer pressure recordings are less desirable than the aforementioned techniques due to the limited number of blood pressure recordings that can be obtained during the course of the procedure and their being inherently more disturbing to the patient. Nonetheless, the sphygmomanometer continues to be widely used in clinical practice, especially in the evaluation of children.

Table design. An appropriate tilt table permits calibrated upright tilt angles ranging from 60° to 90°. Typically, the transition from supine to upright position should be achieved smoothly and relatively rapidly (e.g., 10 to 15 s). The table permits the patient to be gently secured to prevent falling and veins, have been associated with an excessively high incidence

be widely used in clinical practice, especially in the evaluation of children.

be either manually or electronically operated.

Only tilt tables of the foot-board support type are appropriate for syncpe evaluations. Tables with saddle support, probably by virtue of excess compression of leg and pelvic veins, have been associated with an excessively high incidence of a positive test response in control subjects (8 [67%] of 12 [36]). To maximize passive gravitational stress, patients should be instructed to avoid flexing ankles, knees or lower extremity muscles.

Tilt angle. Available evidence suggests that the physiologic effects of passive upright posture are comparable for tilt angles ≥60°. Less severe angles (i.e., 30° to 45°) do not seem to provide sufficient orthostatic stress and result in a lower yield of positive test responses in patients with syncope (3 [30%] of 10 vs. 53 [75%] of 71 [36]). Consequently, tilt angles in the 60° to 80° range have become the most widely used, and in the absence of pharmacologic provocation there does not seem to be any substantial difference between these values from a testing outcome perspective. In contrast, especially in the setting of isoproterenol provocation, the positivity rate appears to be higher and the specificity lower at steeper tilt angles (80° vs. 60°) (38,50). Angles <60° have been used in some laboratories as an intermediate step in the test protocol before proceeding to steeper values (4). This intermediate step may

be useful to exclude other causes of syncope, especially subtle forms of severe orthostatic hypotension (4).

Chronobiologic factors. It seems likely, given the tendency for spontaneous vasovagal events within individual patients to cluster in time, that chronobiologic factors play a role in the emergence of the condition. Similarly they may be expected to contribute to the occurrence of vasovagal symptoms under provocative tilt table testing conditions. Consequently, although the role of repeat tilt testing for evaluation of treatment remains to be clarified, it is reasonable to assume that if such an approach is elected, the time of day in which testing is undertaken should be relatively constant for each patient. Further, the relationship between testing and the dosing of concomitant medications should be fixed.

Medical/nursing supervision. Physicians of various disciplines (e.g., cardiologists, pediatricians and internists) undertake tilt table testing. It is reasonable to expect that physicians accepting the responsibility for such testing be knowledgeable of the broad differential diagnosis associated with syncopal symptoms, be aware of the range of studies and appropriate order of testing for evaluation of such symptoms and be sufficiently dedicated to the understanding of the tilt table testing technique to become cognizant of both its uses and limitations.

Optimally, a registered nurse or medical technician experienced in tilt table testing technique and the management of its outcomes and potential complications should be in attendance during the entire procedure. These individuals would benefit from having had prior experience caring for patients during other types of invasive cardiovascular laboratory procedures. The need for a physician to be present throughout the tilt test procedure is well established because the risk to patients of such testing is very low. Nevertheless, serious bradycardia and hypotension requiring resuscitative action, as well as tachyarrhythmias, have been reported (51–53). Consequently, it is prudent for a physician to be physically in attendance in the room throughout the test or in sufficient proximity so as to be immediately available should a problem arise. As a rule, the tilt table laboratory should provide medical supervision and supply the level of resuscitative equipment expected of cardiovascular exercise testing laboratories (54).

Tilt table test protocols. Definition of a positive test response. Interpretation of the clinical significance of a tilt table test outcome (i.e., whether vasovagal symptoms adequately account for the patient’s clinical picture) requires careful consideration of the tilt test result (including the temporal relationship of heart rate and blood pressure changes and the nature of the patient’s symptoms) in the context of all historical and clinical data in that patient. In general, a tilt test response is deemed to be positive for vasovagal syncope if syncopal symptoms are reproduced by the provocation of neurally mediated hypotension or bradycardia, or both, as a result of the procedure. The test response may also be considered positive if syncope occurs due to hypotension or bradycardia, or both (even though the patient is unable to attest to reproduction of symptoms), or if hypotension or
bradycardia, or both, is of sufficient severity that the associated presyncopal symptoms lead the attending physician to believe that true syncope is inevitable (1-4,6-10,36-38,45,55). Currently, in the absence of appropriate symptoms, heart rate or blood pressure changes alone cannot be accepted as constituting a positive test response, however. Present medical care necessitates careful monitoring for excessive bradycardia or hypotension throughout the procedure, and termination of the test if their occurrence is deemed potentially hazardous (e.g., patients with known cerebrovascular disease).

**Tilt duration.** The duration of upright posture is probably the most critical determinant of the sensitivity and specificity of the tilt test; time periods of 10 to 60 min have been advocated by various investigators (1-4,6-13,36,45). Recently, most published reports have tended to favor relatively long drug-free tilt durations (usually 45 min) initially (28,36,37). Pharmacologic interventions are reserved for a second stage if the initial drug-free tilt is nondiagnostic. This sequential approach is clearly preferable when questions of pathophysiology and treatment efficacy are being addressed. Alternative approaches, using pharmacologic interventions at an early stage of diagnostic testing in an attempt to shorten the overall duration of the procedure, have been proposed and are being evaluated (see later).

The optimal duration for tilt table testing has yet to be determined. However, in the absence of pharmacologic provocation, tilt test durations of 30 to 45 min at 60° to 80° have become widely accepted in laboratories evaluating older adolescents and adult patients. The longer period (45 min) tends to be favored currently by most clinical investigators (28,36,37). Shorter periods of upright posture may be favored for evaluation of syncope in children. Thereafter, if the test remains nondiagnostic, pharmacologic provocation may be used (see Pharmacologic provocation and Important Variations). The 45-min tilt duration is supported by the results of Fitzpatrick et al. (36) (i.e., the mean value for time to syncope [24 min] in their study plus two standard deviations [assuming a normal distribution]).

**Pharmacologic provocation.** Pharmacologic provocation during head-up tilt testing is a useful additional tool for eliciting susceptibility to hypotension—bradycardia (3,7,10,11,56-61), and several agents are currently utilized. Many laboratories have found the administration of isoproterenol to be useful in facilitating recognition of susceptibility to neurally mediated syncope (3,7,10,11,55-59). One report has expressed concern regarding the use of isoproterenol (39). Other provocative pharmacologic agents, especially nitroglycerin and edrophonium, appear to be promising (37,59-61).

The rationale for isoproterenol provocation rests on the notion that variability in the magnitude of epinephrine/norepinephrine release may in part account for the unpredictable nature of spontaneous neurally mediated syncopal events and consequently may affect the diagnostic reliability of the tilt test. Provision of exogenous catecholamine may facilitate recognition of susceptible patients. In this context the most widely used protocol initiates each level of isoproterenol infusion (see usual dosing discussed later [Important Variations]) while the patient is supine and continues the infusion during sequential 10-min tilt test procedures. Bolus isoproterenol administration has also been reported to be effective (46).

Although isoproterenol appears to be the preferred sympathetic agent for infusion during tilt table testing, only one study has compared its effect with that of epinephrine. A crossover comparison of isoproterenol and epinephrine showed that isoproterenol is associated with a significantly greater sensitivity for reproducing the patient's symptoms (59).

**Tilt table testing in pediatric patients: differences from adults.** In general, children ≤6 years old can undergo successful tilt table testing (11,12,56,62-63). Younger patients may also undergo such testing successfully if cooperative. In contrast to studies in adult patients, there are fewer reports of tilt testing data in pediatric patients. Consequently, all the problems that exist in reaching a consensus and making recommendations for adult patients are magnified for pediatric practice. Moreover, given the absence of data in pediatric patients, certain consensus recommendations made for adult patients may not be applicable to the pediatric setting: 1) Finger plethysmographic methods for blood pressure recording require verification in children, whereas sphygmomanometer measurements have been widely used in pediatric practice to document susceptibility to neurally mediated syncope. 2) The issue of tilt duration has not been assessed in the pediatric population. Given the lower center of gravity in children, it is possible that the orthostatic stress during tilt is less in children than in adults. As is largely true for adults, tilt table testing may not be necessary for the further evaluation of syncope in pediatric patients who present with a normal physical examination, absence of abnormal laboratory findings and a medical history characteristic of vasovagal syncope.

**Important Variations**

Most laboratories undertaking tilt table testing utilize, as necessary, both "drug-free" passive tilt and passive tilt with pharmacologic provocation. Some laboratories, particularly those evaluating pediatric patients, have reported results with a "standing" test (essentially an "active" tilt). The latter variation is now infrequently used and is not discussed further.

**Drug-free passive head-up tilt table testing** refers to upright tilt without exogenous pharmacologic stimulation. Pharmacologic provocation during tilt testing is generally used if symptoms are not elicited during the drug-free phase. In such cases, isoproterenol is the most widely used provocative (see above). However, there has also been limited experience with other agents, such as adenosine triphosphate, edrophonium, epinephrine, nitroglycerin and nitroprusside (37,45,59-61).

With regard to the use of isoproterenol provocation, there are several approaches to drug administration. The most widely used protocol entails returning the patient to the supine position after the drug-free phase of the tilt procedure has proved nondiagnostic. At that time a continuous isoproterenol infusion is initiated with an empirically determined dose of
1 μg/min. After a reequilibration period (usually 10 min), the patient is again tilted (usually for 10 min in duration) while maintaining a constant drug infusion rate. Subsequently, if the test remains nondiagnostic, this same procedure (i.e., return to supine at each stage) is repeated using further dose tiers (usually three and, if necessary, 5 μg/min) (3,9,10). An alternative approach to empirical isoproterenol dose selection is dose adjustment based on isoproterenol-induced heart rate increment. In this case, isoproterenol is administered during a 10 to 15-min supine phase at doses sufficient to increase heart rate by 20% to 30%. The upright tilt is then conducted at that dose.

Certain variations of the isoproterenol infusion protocol have been proposed. It has been suggested that isoproterenol administration (either by infusion or by bolus) be initiated while the patient remains in the upright posture (46). Although this approach may save time, Kapoor and Brant (39) suggest that its specificity is poorer. A second, less common variation has been the use of isoproterenol provocation without a period of drug-free passive tilt. This variation may further diminish the overall duration of the testing procedure, although the potential for an increased number of false positive test results is a concern.

Method of Data Collection and Analysis

A Medline search was performed for English language articles published between 1985 and 1995 about tilt table testing and syncope. The term tilt table testing was used alone and in conjunction with the terms vasovagal, neurally mediated and neurocardiogenic syncope. Articles from peer-reviewed journals were selected if they documented the use of tilt table testing in the diagnosis and management of unexplained syncope and other disorders. Findings were individually compared because a true statistical analysis of combined data was inappropriate due to differences among studies in patient selection, testing and follow-up.

Indications and Recommendations for Use of Tilt Table Testing in the Assessment of Syncope and Closely Related Disorders

Tilt table testing has emerged as a valuable diagnostic technique in the evaluation of the basis of syncope. In particular, tilt table testing has been demonstrated to be highly effective for the provocation of neurally mediated hypotension and bradycardia in subjects susceptible to vasovagal syncope. For practical purposes the indications for tilt table testing can be divided into three general categories (Table 2): specifically, those conditions in which there is overall agreement that tilt table testing is warranted; those conditions in which there remain differences of opinion regarding the utility of tilt table testing; and certain potentially emerging indications where further study is needed. In addition, a number of scenarios can be identified in which tilt table testing is not warranted and in some cases may be contraindicated.

Table 2. Tilt Table Testing for Evaluation of Syncope: Summary of Principal Indications

<table>
<thead>
<tr>
<th>Indication</th>
<th>Notes</th>
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<tr>
<td>Recurrent syncope or single syncopal episode in a high risk patient,</td>
<td>whether or not the medical history is suggestive of neurally mediated</td>
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<tr>
<td>whether or not the medical history is suggestive of neurally mediated</td>
<td>(vasovagal) origin, and</td>
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<td>Structural cardiovascular disease is present, but other causes of</td>
<td>or</td>
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<td>syncope have been excluded by appropriate testing</td>
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<tr>
<td>Further evaluation of patients in whom an apparent cause has been</td>
<td>established (e.g., asystole, atrioventricular block), but in whom</td>
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<td>demonstrated susceptibility to neurally mediated syncope would affect</td>
<td>demonstration of susceptibility to neurally mediated syncope would</td>
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<tr>
<td>treatment plan</td>
<td>affect treatment plan</td>
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<tr>
<td>Part of the evaluation of exercise-induced or exercise-associated syncope</td>
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<td>Reasonable differences of opinion exist regarding utility of tilt table testing</td>
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<tr>
<td>Differentiating convulsive syncope from seizures</td>
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<td>Evaluating patients (especially the elderly) with recurrent unexplained</td>
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<tr>
<td>falls</td>
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<tr>
<td>Assessing recurrent dizziness or presyncope</td>
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<td>Evaluating unexplained syncope in the setting of peripheral neuropathies</td>
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<td>or dysautonomias</td>
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<tr>
<td>Follow-up evaluation to assess therapy of neurally mediated syncope</td>
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<tr>
<td>Tilt table testing not warranted</td>
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<tr>
<td>Single syncopal episode, without injury and not in a high risk setting</td>
<td>with clear-cut vasovagal clinical features</td>
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<td>in which alternative specific cause has been established and in which</td>
<td>Syncope in which an alternative specific cause has been established</td>
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<tr>
<td>additional demonstration of a neurally mediated susceptibility would</td>
<td>and in which additional demonstration of a neurally mediated</td>
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<tr>
<td>not alter treatment plans</td>
<td>susceptibility would not alter treatment plans</td>
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<tr>
<td>Potential emerging indications</td>
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<tr>
<td>Recurrent idiopathic vertigo</td>
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<td>Recurrent transient ischemic attacks</td>
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<td>Chronic fatigue syndrome</td>
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<tr>
<td>Sudden infant death syndrome (SIDS)</td>
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</table>

a. Patients in whom there is no history of or overt evidence for organic cardiovascular disease and in whom the historical aspects are suggestive of vasovagal episodes (i.e., episodes tend to occur while standing or sitting; are associated with prodromal symptoms, such as dizziness, diaphoresis, nausea, weakness, or a "flushed feeling") (1,2,4,6,9).

b. Patients in whom organic cardiovascular disease is present, but in whom historical aspects are suggestive of vasovagal episodes (see above) and in whom other
causes of syncope have not been identified by appropriate testing (including conventional electrophysiologic study).

c. As part of the overall evaluation of unexplained syncope despite absence of historical features suggesting a diagnosis of vasovagal syncope in i) patients without a history of or overt evidence for organic cardiovascular disease and in whom vasovagal syncope may be a potential cause (9,45,63-65); ii) in patients with concomitant cardiovascular disease after appropriate testing to rule out other potential causes of syncope.

2. The further evaluation of patients in whom an apparent specific cause of syncope has been established by physiologic recordings either during a spontaneous event or by demonstration of reproduction of symptoms during electrophysiologic/hemodynamic study (e.g., apnoeole, high grade atrioventricular (AV) block), but in whom the demonstration of susceptibility to hypotension-bradycardia of a neurally mediated origin may affect treatment plans (e.g., use of education, reassurance or pharmacologic therapy instead of or in conjunction with implantable pacemaker therapy).

3. Evaluation of recurrent exercise-induced syncope when a thorough history and physical examination, 12-lead ECG, echocardiogram and formal exercise tolerance testing demonstrate no evidence of organic heart disease (66-68).

Conditions in Which Reasonable Differences of Opinion Exist Regarding Tilt Table Testing

1. Differentiating convulsive syncope from epilepsy in patients with recurrent unexplained loss of consciousness with associated tonic-clonic activity in the setting of repeated normal electroencephalographic findings and failure to respond to antiseizure medications (69,70). Tilt table testing is further supported if other aspects of the episodes suggest vasovagal syncope, such as a provocative situation or environment, occurrence in standing or sitting positions or prodromal symptoms, as described earlier.

2. Evaluating patients (especially the elderly) in whom recurrent falls remain unexplained and in whom a history of premonitory symptoms compatible with vasovagal symptoms is not obtained.

3. Recurrent near-syncopal spells or dizziness, presumed to be neurally mediated in origin in subjects in whom clinical aspects otherwise conform to those described in the general agreement section above.

4. The evaluation of unexplained syncope in patients in whom peripheral neuropathies or dysautonomias may contribute to symptomatic hypotension (2).

5. Follow-up evaluation of therapy to prevent syncope recurrences (3,10,13,65-68)

a. Tilt table testing may be helpful in assessing the ability of a particular therapy (e.g., pharmacologic, physical maneuvers) to prevent syncope.

b. Tilt table testing may be helpful in determining whether temporary dual-chamber cardiac pacing would be useful in preventing or lessening symptoms in patients with neurally mediated bradycardia or asystole before permanent dual-chamber pacemaker implantation (71,72).

Conditions in Which Tilt Table Testing Is Not Warranted

1. Single syncopal episode, without injury and not in a high risk setting (see above), in which clinical features clearly support a diagnosis of vasovagal syncope.

2. Syncope in which an alternative specific cause has been established by physiologic recordings either during a spontaneous event or by demonstration of reproduction of symptoms during electrophysiologic/hemodynamic study and in which the potential additional demonstration of a neurally mediated contribution to the etiology would not alter treatment plans.

Conditions in Which a Relative Contraindication to Tilt Table Testing Exists

1. Syncope with clinically severe left ventricular outflow obstruction.

2. Syncope in the presence of critical mitral stenosis.

3. Syncope in the setting of known critical proximal coronary artery stenoses.

4. Syncope in conjunction with known critical cerebrovascular stenoses.

Apart from the more conventional uses for tilt table testing summarized above, several additional applications have begun to emerge: 1) Tilt table testing may be useful in the evaluation of recurrent idiopathic vertigo in patients in whom clinical aspects (see description under General Agreement section 1a.) suggest the possibility of neurally mediated hypotension-bradycardia as a cause and in whom extensive evaluation has failed to disclose an otolaryngologic source (73). 2) Some older patients may experience episodic neurally mediated hypotension and bradycardia of sufficient degree to cause transient neurologic dysfunction (e.g., recurrent transient ischemic attacks) but not full syncope (74). These patients should be considered for tilt table testing if clinical settings are suggestive of a neurally mediated origin and especially if Doppler ultrasound, carotid angiography and transesophageal echocardiography have failed to disclose an etiology for the symptoms. 3) Preliminary observations suggest that in some individuals with chronic fatigue syndrome, neurally mediated hypotension-bradycardia may contribute to the symptom complex. Head-up tilt table testing may help to identify a subgroup of patients in whom therapy directed at the neurocardiogenic disorder may be of benefit (75). 4) Recent findings suggest that severe bradycardic episodes may be reproduced in some survivors of sudden infant death syndrome (SIDS) using upright tilt table testing (76,77). Potentially, neurally mediated hypotension-bradycardia may play a role in certain SIDS deaths, and tilt table testing may play a role in developing a better understanding of this troublesome problem.
Frequency of Use of Diagnostic Tilt Table Testing

National Statistics on Utilization

Currently there are no reliable data concerning the use of tilt table testing or on potential variations in the geographic penetration of such testing. However, based on the widespread origins of current published reports, it seems that most full-service clinical electrophysiologic testing laboratories in the United States, Canada, Western Europe and the Pacific Rim now offer such testing. Additionally, tilt table testing is undertaken in neurology and cardiovascular laboratories specializing in the evaluation of a wide variety of autonomic disorders.

Utilization Over Past Several Years

Other than in a few investigative centers that began to use tilt table testing for evaluation of syncope in the early 1980s, this application of the technique remained relatively limited until after publication of several key studies later in that decade (1-4,46). Subsequently, use of tilt table testing for evaluation of syncope spread rapidly.

According to Medicare statistics (based on CPT code 93660 data), the application of tilt table testing in the United States increased dramatically from 1992 (5,800 procedures) to 1994 (14,350 procedures). Further, in these 3 years charges increased from $440,000 to $1,730,000. By contrast, this same time period saw a decline in the proportion of these procedures carried out by physicians who identified themselves in the Medicare data base as cardiologists (71% and 59%, respectively) and an increase in the proportion provided by those identified as internists (12% and 25%, respectively).

Short- and Long-Term Outcomes

Success and Failure Rates

Diagnostic capability. Numerous published reports provide a substantial base of experience supporting the diagnostic utility of tilt table testing in patients with unexplained syncope (1-3,6,8,35,65). For instance, in a seminal study examining the diagnostic role of tilt table testing (40° without pharmacologic provocation) in patients with syncope, Kenny et al. (1) found that 10 (67%) of 15 patients with unexplained syncope had a positive tilt test response at 29 ± 12 min. Subsequently, from the same group of investigators, Fitzpatrick et al. (35) noted that whereas 60° head-up tilt table test responses were positive in 53 (75%) of 71 patients with unexplained syncope, such test responses were rarely positive among patients with syncope due to AV block (19% positive), sick sinus syndrome (11% positive) or inducible tachyarrhythmias (0% positive). Findings from other centers have tended to confirm these observations. Thus, a report from the Cleveland Clinic indicated that tilt table testing studies reproduced symptoms in 27 (79%) of 34 patients with previously unexplained syncope (2). Almqquist et al. (3), in an early report using a much shorter tilt test duration (10 min) than is currently recommended, noted that 80° upright tilt (using isoproterenol infusion as an adjunctive provocative measure when necessary) reproduced symptoms in 9 of 11 patients with suspected but previously undocumented neurally mediated syncope. In contrast, among nine patients with syncope in whom conventional electrophysiologic testing provided alternative explanations for syncope, only two (22%) developed symptoms during tilt testing. Strasberg et al. (6) evaluated 40 patients with unexplained syncope and 10 control subjects using 60° head-up tilt. Symptoms were reproduced in 15 patients (38%) with a mean tilt duration of 42 ± 12 min. None of the control subjects fainted. Similarly, Raviele et al. (8) observed positive tilt outcomes in 15 (50%) of 30 of such patients, whereas Sra et al. (65) reported a diagnostic test response in 34 (40%) of 86 patients.

On the basis of studies in control subjects discussed earlier, it is clear that tilt able testing exhibits a high level of diagnostic specificity (10,13,34-38). Sensitivity, in contrast, is a more difficult issue. Apart from tilt table testing itself, there is no clear-cut, accepted "gold standard" for establishing a diagnosis of neurally mediated (and especially vasovagal) syncope against which diagnostic procedures can be measured. The sensitivities of conventional diagnostic approaches (e.g., medical history, carotid sinus massage) have long been suspect. As a result, in terms of identifying susceptibility to neurally mediated vasovagal syncope, the tilt table test is currently as close to a gold standard as exists. In this regard, tilt table sensitivity (measured against a classic presentation in most cases) has been reported to range from 32% to 85% (with the median being closer to the higher number), thereby placing it in a similar category with many widely accepted diagnostic tests (e.g., ECGs, conventional exercise stress tests).

Reproducibility. The reproducibility of tilt table testing is a crucial factor in determining the usefulness of the test as both a diagnostic tool and a means of evaluating treatment options. Both short- and long-term reproducibility have been the subject of study.

Among the earliest studies of short-term reproducibility, Cher et al. (78) reported outcomes of two sequential (~1 h apart) 80° head-up tilt tests (potentiated by isoproterenol when necessary) in 23 patients (6.5 to 74 years old, mean age 24) undergoing evaluation for recurrent syncope of unknown origin. Overall, 15 (65%) of 23 patients developed syncope in either the first or second tilt procedure, whereas 8 remained asymptomatic. Importantly, the findings in the two tests were concordant (i.e., positive in both tests or negative in both tests) in 20 (87%) of 23 of patients. However, the level of concordance was somewhat less among patients with an initial positive test response (12 [80%] of 15) because 3 patients were tilt positive during tilt 1 only. In contrast, none of the eight patients who were tilt negative in the first study developed syncope on the second tilt exposure (100% concordance).

Fish et al. (79) used a protocol similar to that reported by Chen et al. (78) to examine short-term reproducibility of tilt testing in young patients (8 to 19 years old, mean age 14.2). Findings revealed that syncope or presyncope was reproduced in 14 of 21 patients, with a further 4 patients exhibiting milder...
The long-term reproducibility of tilt table tests has been studied at intertest intervals ranging from 1 day to several years (8, 36, 57, 58, 72, 81). For instance, Raviele et al. (8) performed a second tilt test after 1 to 13 days (mean 3) in 14 patients with a positive response to an initial 60°, 60-min head-up tilt without pharmacologic provocation. They observed a test reproducibility of 71%. A similar but somewhat lesser degree of reproducibility (62%) was reported by Blanc et al. (81) in 13 patients studied at a mean period of 7 days between tests. Grubb et al. (58) also examined tilt test reproducibility with 3- to 7-day separations in 21 patients using 80°, 30-min tilts with subsequent isoproterenol provocation if needed. In the first study, 14 patients were tilt positive (6 at baseline, 8 during isoproterenol). During the second study, 19 patients exhibited concordant outcomes (90%); however, the level of provocation necessary differed in 5 patients (24%) between the two tests. Sheldon et al. (57) examined reproducibility at 1 to 6 weeks in 46 patients. The protocol comprised sequential 80°, 10-min tilts, initially in the baseline state and thereafter using graded isoproterenol infusions. Among patients who were initially tilt negative, findings were reproduced in 85%. Finally, in the longest intertest interval yet reported (~4 years), Petersen et al. (72) noted a 64% reproducibility in a group of 11 patients with predominantly cardioinhibitory vasovagal syncope.

In summary, apart from one report in which the reproducibility of tilt table testing was ~35% (82), most studies suggest that test reproducibility is in the 65% to 85% range whether repeat testing is conducted on the same day or substantially later. In addition, with current protocols an initial negative response differed in 5 patients (24%) between the two tests. Sheldon et al. (57) examined reproducibility at 1 to 6 weeks in 46 patients. The protocol comprised sequential 80°, 10-min tilts, initially in the baseline state and thereafter using graded isoproterenol infusions. Among patients who were initially tilt negative, findings were reproduced in 85%. Finally, in the longest intertest interval yet reported (~4 years), Petersen et al. (72) noted a 64% reproducibility in a group of 11 patients with predominantly cardioinhibitory vasovagal syncope.

Utility of tilt testing for prediction of treatment effectiveness. Because a positive initial tilt test response may not be reproducible in ~15% to 35% of patients, tilt testing may be less effective for predicting treatment efficacy than it is as a diagnostic tool. Consequently, if tilt table testing is used to assess treatment, a reasonable approach currently is to interpret an apparently effective "therapeutic" outcome with caution (83, 84). Studies using careful correlation of tilt test observations with long-term clinical follow-up are needed to address this issue further.

Alternative Approaches

Overview of Alternative Approaches

A detailed medical history and a complete physical examination are essential elements in the evaluation of all patients with syncope whether or not they ultimately undergo tilt table testing. However, especially in the case of vasovagal syncope, the history and physical examination may be considered "diagnostic" if the findings are "classical" and other causes of syncope are appropriately excluded. In reported studies in which history and physical examination were used as sole determinants of vasovagal syncope, there has been a wide variation in the diagnostic clinical criteria. In this regard, diagnostic criteria have variously included all or a combination of some of the following: the presence of a precipitating event (18); fainting occurring in an emotional setting, with warning in patients <60 years old (20); and the presence of associated autonomic symptoms (19, 85, 86). Overall, the sensitivity of history and physical examination for diagnosis of vasovagal syncope is believed to be relatively low. However, it is probably reasonable to conclude that when the history and physical findings are unequivocal, the need for other diagnostic testing (including tilt table testing) is largely obviated.

Although the medical history and physical examination are central elements in the assessment of syncope and may be the least costly method of diagnosing vasovagal syncope, many physicians may not feel confident with their ability to identify the cause of syncope definitively using the history and physical examination alone. This uncertainty may be of particular concern when patients have experienced recurrent syncope, syncope complicated by injury, urinary incontinence or seizure-like activity or when symptoms occur in a high risk setting (see above). Additional diagnostic testing may then be deemed appropriate. In such circumstances, the medical history, physical examination and other diagnostic procedures (possibly including tilt table testing), are reasonably utilized in a complimentary fashion.

Certain clinical laboratory studies are often used as part of the overall evaluation strategy in the patients with syncope (e.g., ambulatory ECG recordings). In a sense these may be considered "alternatives" to tilt table testing, although they are frequently complementary. For practical purposes these alternatives are considered to comprise three categories: 1) ECG recordings; 2) assessment of vagal tone by heart rate variability; and 3) other measures. The sensitivity of these or other diagnostic techniques in vasovagal syncope is less well established than is the case for tilt table testing. Nonetheless, on the basis of clinical experience, certain general statements appear to be valid.

Electrocardiographic monitoring. Although only rarely available, ECG documentation during spontaneous syncopal events may provide sufficient evidence for the basis of syncope (e.g., ventricular or supraventricular tachycardia) such that no further diagnostic testing is needed. However, even these recordings may not be definitive. For example, documented periods of symptomatic AV block or sinus arrest may be due to
either intrinsic conduction system disease or a neurally mediated event. Distinguishing between these may require tilt table testing. Similarly, in the setting of a documented tachyarrhythmia, tilt table testing may nonetheless be helpful in view of recent evidence supporting the probable role of neural reflex effects in the development of hypotension in these conditions. Finally, even the absence of an apparent arrhythmia during a hypotensive event does not exclude a neurally mediated vasodepressor syncope since “relative” bradycardia may be easily overlooked.

Conventional ambulatory ECG (Holter) monitors continue to play a role in the evaluation of patients with recurrent syncope. However, given the fact that spontaneous events are usually infrequent, and current systems necessitate replacement of magnetic tapes every 24 to 48 h, the evaluation of syncope by these recorders tends to be relatively inefficient. Event recorders, particularly those that operate in a continuous loop mode, may be more useful. However, even these systems have the drawback that abrupt loss of consciousness may preclude the patient from triggering the recorder memory. Recently, an implantable ECG recorder for use in patients with syncope has been described (87). It is too early to ascertain the ultimate utility of such an instrument. In any case, outpatient ECG monitoring leaves patients exposed to the risks associated with recurrence of syncope in an uncontrolled environment.

Electrocardiographic recording during formal exercise testing has limited utility in the evaluation of syncope. However, such testing may permit detection of unsuspected myocardial ischemia that may form the substrate for cardiac arrhythmia. Additionally, rate-dependent AV block, exertionally related tachyarrhythmias or certain forms of exercise-associated neurally mediated syncope may come to light.

Heart rate variability. Analysis of heart rate variability to measure cardiac autonomic function has been used to investigate autonomic function in patients with syncope who have a positive response to upright tilt testing (88-95). There are two major categories of indexes of heart rate variability: time and frequency domain indexes. The time domain indexes assess the overall magnitude of heart rate variability by using mean successive differences between consecutive RR intervals, standard deviation of RR intervals, coefficient of variance and other relatively simple measures. The frequency domain indexes assess the magnitude of individual components of the heart rate power spectrum, which include a high and low frequency component. High frequency power appears to be modulated primarily by parasympathetic tone, whereas low frequency oscillations appear to reflect both sympathetic and parasympathetic effects. Investigations of heart rate variability in syncope have evaluated patients with a positive tilt test response compared with those with a negative tilt test response or control subjects without syncope (88,89,92-94). These studies have shown abnormalities of sympathovagal balance in patients with vasovagal responses to tilt testing. At the current time, there is insufﬁcient evidence to determine the role of the tests for heart rate variability for establishing a diagnosis of vasovagal syncope.

Other tests. Several other tests are available in the assessment of autonomic function, but they have not been systematically studied for diagnosis of vasovagal syncope. These tests include Valsalva maneuver, vascular responses to lower body negative pressure and eyeball compression. At the current time, there is insufﬁcient evidence to suggest the use of any of these other tests of autonomic function as alternates to tilt table testing in unexplained syncope. Future research is needed to determine the role of these tests in the evaluation of neurally mediated syncope syndromes.

Advantages of Alternative Approaches

Ambulatory ECG recordings offer the possibility of documenting spontaneous events economically. However, given the infrequent occurrence of syncope in most patients, extended periods of recording may be needed.

The advantages of analysis of heart rate variability and other tests of autonomic function for assessing susceptibility to neurally mediated syncopal events are that they are noninvasive and may potentially be used to evaluate the effect of therapy on autonomic function in vasovagal syncope. However, at present little is known regarding the potential value of such tests in the evaluation of patients with suspected vasovagal syncope.

Disadvantages of Alternative Approaches

It is estimated that in >50% of the patients ultimately diagnosed as having vasovagal syncope, history and physical examination are nondiagnostic. This observation alone supports the need for the availability of additional diagnostic tools, such as tilt table testing. Additionally, widely agreed-on clinical criteria for establishing a diagnosis of vasovagal syncope are not available. There is a need for research on clinical rules and correlates of vasovagal syncope.

In regard to use of ambulatory ECG recordings alone, the cost and inconvenience associated with prolonged outpatient monitoring are a major deterrent. Furthermore, in the absence of practicable and widely available recorders capable of correlating cardiac rhythm and systemic blood pressure, conclusions made from ECG evaluation alone may be erroneous. In the end, the desired economic advantage may be lost while exposing patients to potentially hazardous symptom recurrences in uncontrolled circumstances.

The analysis of heart rate variability and other tests of autonomic function may provide information on mechanisms involved in vasovagal syncope. Although these tests have the potential to become useful in the diagnosis of vasovagal syncope, greater insight into their sensitivity, speciﬁcity and predictive values is needed. There are no data on the cost-effectiveness of alternative testing strategies.

In general, alternative diagnostic techniques have received less study than tilt table testing. Ultimately, failure to establish
a diagnosis results in leaving patients at risk of a recurrence. Further, unsuccessful investigations increase cost of diagnostic testing with no benefit. Consequently, until alternatives are more thoroughly assessed, tilt table studies appear to be the most effective diagnostic approach in the setting of suspected neurally mediated vasovagal syncope.

Cost-Effectiveness and Economic Impact
Analysis of Cost-Effectiveness in Patient Subsets

Currently there are no data specifically addressing the cost-effectiveness of tilt table testing in various subsets of patients with syncope. However, certain general principles will most likely hold true. Tilt table testing is likely to be most cost-effective for establishing a diagnosis of vasovagal syncope in patients with syncope without evidence of cardiovascular disease. In such cases, diagnostic tilt testing is warranted if the diagnosis is not already established unequivocally by history and physical findings. In patients with syncope in whom structural cardiovascular abnormalities are present, tilt table testing may prove cost-effective for establishing the basis of syncope when preceding conventional cardiac electrophysiologic testing has proved nondiagnostic. In such cases, excepting those patients with residual abnormal neurologic findings on physical examination, tilt testing is far more likely to be of value than are neurological studies, such as electroencephalography or magnetic resonance imaging (MRI). With regard to other patient subsets presenting with symptoms such as dizziness, vertigo or chronic fatigue syndrome, the cost-effectiveness of tilt table testing is more speculative.

Comparison of Cost-Effectiveness With Alternate Approaches

In 1982, Kapoor et al. (96) pointed out the need for a more cost-effective approach to the evaluation of syncope. At that time it was estimated that the average cost for evaluating syncope patients was U.S. $2,600. Furthermore, because in relatively few cases was the actual etiology found, the overall cost was approximately U.S. $24,000 per specific diagnosis. In view of inflation and the more widespread availability of various neurologic imaging procedures, conventional electrophysiologic testing, it is reasonable to assume that the per-patient cost will have at least doubled in the past decade, an estimate approximately confirmed by Calkins et al. (97). In contrast, the increased frequency with which a specific diagnosis is made most likely offsets the increased per-patient cost. The impact of improvements in diagnostic precision on both the cost per specific diagnosis and on the potential for improved patient well-being, leading to financial savings as a result of fewer subsequent medical problems during follow-up, remains to be quantified.

With regard to current cost-effectiveness of diagnosis and treatment of neurally mediated syncope, a few general comments are pertinent. Neurally mediated syncope is the most common cause of transient loss of consciousness and may account for at least 20% of patients referred to tertiary medical centers for evaluation of syncope (97). The average cost for a diagnostic workup before referral to one university hospital for a group of such patients approached $4,000 in the early 1990s (97). Testing often included multiple neurologic and cardiovascular tests despite the fact that many if not most of these syncopal spells were neurally mediated in origin. Consequently, in the setting of an appropriate history and physical examination (especially in patients without structural heart disease), early use of tilt table testing is likely to be more cost-effective in the evaluation of syncope than are many currently widely selected tests, such as electroencephalography or MRI or computed tomography of the head alone or in combination, and should be part of the preferred diagnostic strategy. In the long run, prospective study is needed to assess the cost-effectiveness of this recommendation.

Conclusions

Until recently, attempts to substantiate a diagnosis of suspected neurally mediated vasovagal syncope have been indirect, time-consuming, expensive and often unrewarding. Head-up tilt table testing has markedly altered this picture by providing a means for assessing susceptibility to vasovagal syncope directly (in essence, becoming “the gold standard” for laboratory testing). In this regard, the technique has clearly moved beyond the realm of clinical investigation to become both a widely available and important diagnostic tool in medical practice. Findings from numerous published reports attest to the diagnostic utility of the technique and substantiate its valuable role in the clinical evaluation of patients with syncope of uncertain origin. By providing the ability to establish the diagnosis unequivocally, tilt table testing permits physicians to counsel patients and relatives with greater certainty, offering reassurance where appropriate and initiating therapy when necessary.

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