Tilt Table Testing: Concepts and Limitations

BLAIR P. GRUBB and DANIEL KOSINSKI

From the Electrophysiology Section, Division of Cardiology, Department of Medicine, The Medical College of Ohio, Toledo, Ohio

GRUBB, B.P., ET AL.: Tilt Table Testing: Concepts and Limitations. Recurrent unexplained syncope is a common and often frustrating clinical problem. Over the last decade, head upright tilt table testing has emerged as an important diagnostic method for the identification of individuals whose syncope is likely to be neurocardiogenic in origin. At the same time, tilt table testing, by providing syncopal episodes in a controlled setting, has allowed for a much greater understanding of these disorders. This article reviews the concepts behind tilt table testing, as well as the uses and limitations of the evolving diagnostic modality. (PACE 1997; 20[Pt. II]:781-787)

Tilt Table Testing, Neurocardiogenic Syncope

Introduction

Recurrent episodes of unexplained transient loss of consciousness (syncope) is one of the most common, and at the same time, one of the most perplexing of problems that the medical practitioner is called upon to evaluate. The vast quantity of possible causes and the difficulty in determining an exact etiology makes the evaluation of the patient with syncope a particularly challenging enterprise. Despite the relatively high prevalence of the problem (it has been estimated that up to 3% of adults suffer from recurrent syncope), there has not been an effective or organized approach to the evaluation and management of recurrent syncope. This has traditionally led to an extensive, expensive, and all too often fruitless series of tests that left at least 60% or more of patients without a diagnosis (and without an effective therapy). Over the years, it became evident to a number of investigators that many episodes of syncope occurred due to transient periods of autonomically mediated hypotension and bradycardia that were sufficiently profound to result in loss of consciousness (i.e., vasodepressor syncope). However, this traditionally has been a diagnosis of exclusion, as no method existed for reproducibly (and safely) provoking these syncopal episodes and thereby confirming the diagnosis. To help determine an individual’s susceptibility to these hypotensive episodes, it was suggested that a strong orthostatic stimulus such as prolonged upright posture could be used. Ever since the landmark studies of Kenny et al., tilt table testing has become a widely used method for the evaluation of patients with syncope of unknown origin. By providing a controlled orthostatic stress, head upright tilt table testing is used to uncover an individual’s predisposition to neurally mediated hypotension and bradycardia. In many ways, the test can be considered analogous to electrophysiological testing, where programmed electrical stimulation is used to identify the presence of the substrate for reentry and thereby assess an individual’s predisposition to either supraventricular or ventricular tachyarrhythmias. The ability to provoke hypotensive syncopal episodes using tilt table testing in a controlled laboratory setting has provided a unique opportunity to make detailed observations of the physiological changes that take place during these events. In the course of our investigations we have found that classic vasovagal (or neurocardiogenic) syncope is but one of a heterogeneous group of disorders of orthostatic intolerance that can be identified during head-up tilt table testing. In addition, a number of other potential uses for tilt testing, in addition to the evaluation of recurrent syncope and near syncope, have been identified. This article will review the

Address for reprints: Blair P. Grubb, M.D., Cardiology, The Medical College of Ohio, 3000 Arlington Ave., Toledo, OH 43699. Fax: (419) 381-3041.
underlying theory, the uses, and the limitations of head upright tilt table testing.

Pathophysiology

Prior to embarking upon a discussion on tilt table testing it would be useful to briefly review the mechanisms by which the human body adapts to upright posture. Mankind’s assumption of an upright stance is a relatively recent evolutionary adaptation, and appears to have placed a considerable burden upon a pressure control system that had originally developed to meet the needs of animals in the dorsal position. Indeed, the most complex and oxygen dependent of all organs, the human brain, became placed in the most tenuous of positions in relation to blood and oxygen supply. Over the last 50 years, physiologists have been fascinated by the responses of the human body to changes in position and posture. During the period, it was established that in a normal subject, assuming the upright position leads to a gravity-mediated pooling of 300–800 cc of blood to the dependent areas of the body, followed by a compensatory increase in heart rate and blood pressure. This response appears to be mediated by baroreceptors, specialized nerve endings that are distributed throughout the vasculature, which are sensitive to changes in intravascular pressure. As venous return to the ventricle and thorax diminishes, these mechanoreceptors are not stretched as much, and thus, afferent neural output to the brain stem diminishes. This in turn leads to a reflex increase in sympathetic stimulation, and diminished parasympathetic output. This response appears to be mediated by baroreceptors, specialized nerve endings that are distributed throughout the vasculature, which are sensitive to changes in intravascular pressure. As venous return to the ventricle and thorax diminishes, these mechanoreceptors are not stretched as much, and thus, afferent neural output to the brain stem diminishes. This in turn leads to a reflex increase in sympathetic stimulation, and diminished parasympathetic output. Therefore, the normal response to upright posture is an increase in heart rate, increase in diastolic blood pressure, and a slightly diminished systolic blood pressure. Any failure in these mechanisms could potentially compromise the maintenance of cerebral perfusion, leading to hypoxia and loss of consciousness. As previously mentioned, the failure of orthostatic compensation may take several forms, and our understanding of the mechanisms involved is still in a state of evolution. In the classic form of neurocardiogenic (or vasovagal) syncope, the degree of venous pooling is excessive, leading to a sudden drop in venous return to the heart. This precipitous fall in right ventricular return results in significant increase in inotropy. This increase in contractile force is felt to activate large numbers of ventricular mechanoreceptors that would normally only be activated by stretch, producing a surge in neural output to the brain stem. This surge in neural traffic to the brain stem (in particular to the nucleus tractus solitarius) is felt to mimic the conditions seen during extreme hypertension, and thereby provokes an apparently “paradoxical” sympathoexcitation with a subsequent decrease in heart rate and an increase in peripheral vasodilatation. The resultant hypotension, if sufficiently profound, leads to cerebral hypoxia and loss of consciousness. The reader interested in more detailed discussions of the pathophysiology of these disorders of orthostatic control are directed to several more complete discussions.

Since all of the aforementioned processes are under the domain of the autonomic nervous system, it would seem desirable to somehow measure the adequacy of this system in patients suffering from recurrent syncopal episodes. However, the location of the brain’s autonomic centers render them relatively inaccessible to direct measurement. Therefore, autonomic evaluations usually involve presenting the system with some form of a “stress” and then noting whether the body’s responses are appropriate. Thus, one attempts to “provoke” either a normal or abnormal autonomic response. In the past, a number of different maneuvers were used to trigger episodes of autonomic decompensation in predisposed individuals, which included carotid sinus stimulation, Weber’s maneuver, Valsalva’s maneuver, hyperventilation, neck suction, and ocular compression. However, each of these were eventually discarded due to their low sensitivity and reproducibility, concerns about patient safety, and poor correlation with clinical events.

Head Upright Tilt Table Testing

Tilt tables have long been used by physiologists to study the aforementioned changes occurring during movement from the supine to the head upright position. Later, these same techniques were utilized to study the changes that might occur during the stresses of aerospace travel. In the course of these investigations it was observed that a small number of the subjects studied would sud-
TILT TABLE TESTING

denly faint due to hypotension and bradycardia. It was not until the mid 1980s, however, that Kenny et al. used tilt table testing to provoke neurocardiogenic (vasovagal) syncope by providing a passive continuous orthostatic stress, resulting in decreased venous return and increased catecholamine levels. Since that time, tilt table testing has become a widely used modality to assess an individual’s susceptibility to neurally mediated hypotensive syncope.

Before continuing, however, it would be useful to consider some aspects of the nature of this sort of provocative testing. Much of the testing done in medicine could be described as “descriptive” in nature. This type of testing evaluates a relatively fixed (often anatomical) substrate that changes slowly. An X ray of an arm or a coronary angiogram both represent forms of testing where a specific area or condition is described. In contrast, provocative testing frequently tries to evaluate dynamic (often physiological) systems, which are by their very nature variable over shorter periods of time. Thus, provocative testing would be expected to show a higher degree of variability in results than descriptive testing. Electrophysiological studies using programmed stimulation are an example of provocative testing.

A group of observations has lent credence to the assertion that a positive head upright tilt table test reasonably represents the events taking place during a spontaneous syncopal episode. First among these is that both spontaneous and tilt induced syncopal episodes are associated with the same prodromal signs and symptoms, such as lightheadedness, pallor, diaphoresis, nausea, and loss of postural tone. Second, the progression of heart rate and blood pressure alterations seen are the same as those seen during spontaneous events. Last, the changes in serum catecholamine are essentially similar between tilt induced and spontaneous episodes.

Two principal methods of performing tilt table testing have been developed. The first uses head-up tilt alone to produce dependent venous pooling and thereby provoke the aforementioned reflexes in susceptible individuals. No pharmacological provocative agents are used.

Based on the previously mentioned observations that catecholamine levels rise significantly prior to the onset of syncope, the use of a concomitant isoproterenol infusion during head upright tilt table testing has been advocated by a number of centers as a way of increasing the sensitivity of the test. However, some investigators have cautioned that this increase in sensitivity may be purchased at the expense of a decrease in sensitivity. Recently, the use of a variety of other provocative agents has been explored. These agents include edrophonium, nitroglycerin, and adenosine triphosphate.

Tilt Table Testing in Control Populations

When used in the absence of provocative stimuli (other than gravity) tilt table testing can distinguish between asymptomatic control subjects and symptomatic patients with a level of precision considered acceptable for other clinically useful testing procedures. To review all of the data supporting this claim is beyond the scope of this article, and representative examples only will be given. Fitzpatrick et al. showed that a 60° tilt for 45 minutes caused syncope in only 7% of controls without a history of syncope. Raviele et al. noted no syncope among a group of 35 controls using a 60° tilt for 45 minutes. Grubb et al. have reported a low “false-positive” rate among both pediatric and geriatric patients. In regard to the use of isoproterenol as a provocative agent, Natale et al. investigated the influence of various tilt angles and different isoproterenol doses in a group of 150 control subjects without a history of syncope. They reported that tilt table testing at 60°, 70°, and 80° demonstrated specificities of 92%, 92%, and 80% in the presence of concomitant low dose isoproterenol provocation.

Thus, the literature would suggest that upright tilt table testing used without pharmacological provocation at angles between 60° and 80° demonstrates a specificity of approximately 90%. If concomitant low dose isoproterenol infusions are used, the majority of studies indicate a specificity of between 80% and 90%.

The exact sensitivity of head upright tilt table testing is difficult to determine because there is no real “gold standard” against which to compare it. However, in any discussion of the sensitivity of tilt table testing, one should keep in mind that it is largely dependent on the physiological mechanisms that result in neurally mediated syncope.
The physiological changes previously described could potentially occur in all individuals if a sufficient stimulus was delivered for a long enough period. In this way, tilt table testing does not so much identify a fixed underlying pathology (as does descriptive testing); rather, it demonstrates an exaggerated susceptibility to an otherwise normal reflex (much the same way an otolaryngologist uses rotary chair testing in assessing vestibular disorders). The true sensitivity of tilt table testing could potentially be underestimated due to the fact that healthy control subjects who have a false-positive tilt test may actually be more susceptible than other people to clinic syncopal episodes. This idea has been supported by Grubb et al., who reported that control subjects with tilt induced syncope (false-positives) later experienced spontaneous episodes of neurocardiogenic syncope.

Anyone who uses tilt table testing knows that it is not perfect (nor, for that matter, is any other test). It is impossible to exactly duplicate the clinical and environmental circumstances that may result in syncope in every patient. Indeed, orthostatic stress is only one of a number of stressors known to provoke syncope in patients with the neurally mediated disorders. Nonetheless, tilt table testing, if properly used, can be used to confirm one's clinical suspicions and can be used to establish a diagnosis where history, physical exam, and other testing have failed to determine a cause of recurrent syncope. As previously mentioned, the use of tilt table testing in syncope is analogous to the way electrophysiological testing is used. It determines whether the underlying substrate for a condition is present. The findings in either test are not taken in isolation; rather, they are evaluated in the context of the history, physical exam, and other pertinent data to come to a diagnosis and management plan appropriate for each individual patient. It should also be kept in mind that (unless one is fortunate enough to be monitoring during a spontaneous episode) the diagnosis of syncope is virtually always a "leap of faith" when it comes to applying the results of any laboratory test to the patient's actual condition. In few other areas of medicine is the interface between art and science so evident.

Uses of Head Upright Tilt Table Testing

The American College of Cardiology has issued an expert consensus document on the use of tilt table testing for assessing syncope. A table of principal indications is provided, and the interested reader is directed to that document for further details (Table I).

During the course of investigations into recurrent neurocardiogenic syncope, a variety of different response patterns were noted. In addition, it became evident that there were a number of potential uses for tilt table testing in addition to recurrent unexplained syncope.

In regard to the various response patterns seen during tilt table testing, we currently define five subgroups (Fig. 1). The first of these is the classic neurocardiogenic (or vasovagal) response pattern. Here there is a sudden drop in blood pressure, often followed by a fall in heart rate. In between episodes of syncope, these patients tend to be quite normal with few other complaints. The second pattern we have called "dysautonomic," and usually demonstrates a gradual decline in blood pressure to hypotensive levels leading to loss of consciousness. Frequently, these patients have other signs of autonomic dysfunction, such as abnormal sweating and thermoregulatory control. We have recently determined that a third pattern exists, which has been called "the Postural Orthostatic Tachycardia Syndrome" (POTS). These patients exhibit an increase of at least 30 beats/min (or a maximum of 120 beats/min) within the first 10 minutes of upright tilt, which is usually not associated with profound hypotension. It is felt that these patients have a milder form of autonomic dysfunction in which the principal problem is an inability to regulate peripheral vascular resistance adequately, which is then compensated for by an excessive increase in heart rate. These patients have, on occasion, been misdiagnosed as having an "inappropriate" sinus tachycardia. We have seen several patients who (at other centers) had undergone radiofrequency modification of the sinoatrial node, which eliminated their tachycardia, but left them with profound orthostatic hypotension. One of the principal complaints of pa-
TILT TABLE TESTING

Table 1.
Indications for Tilt Table Testing

I. General Agreement
   A. Recurrent syncope or single syncope episode in a high risk patient, whether or not the
      history indicates a neurocardiogenic cause and
      1. No evidence of structural heart disease, or
      2. Structural heart disease is present, but other causes of syncope have been excluded by
         appropriate testing
   B. In-department evaluation of patients in whom an apparent cause of syncope is identified
      (i.e., AV block, asystole), but in whom demonstration of a neurocardiogenic component
      would affect therapy
   C. As a part of the evaluation of exercise induced or associated syncope

Reasonable Differences of Opinion Exist
   A. Differentiating convulsive syncope from epileptic seizures
   B. Recurrent unexplained falls (especially in the elderly)
   C. Evaluation of recurrent dizziness or presyncope
   D. Evaluation of unexplained syncope in peripheral neuropathy and dysautonomia
   E. The follow-up assessment of therapy

Emerging Indications
   A. Recurrent idiopathic vertigo
   B. Recurrent transient ischemia attacks
   C. Chronic Fatigue Syndrome
   D. Sudden Infant Death Syndrome (SIDS)

Tilt Table Testing Not Warranted
   A. Single syncopal episode, without injury and not in a high risk setting with evident
      neurocardiogenic features
   B. Syncope where a specific cause has already been established and where demonstrating a
      neurocardiogenic component would not alter treatment plans

Modified from Benditt et al.19

Figure 1. Various responses to tilt table testing.
GRUBB, ET AL.

Tients with POTS is that of fatigue, and recent evidence has suggested that there may be considerable overlap between this condition and the chronic fatigue syndrome.\(^{23}\)

In the course of investigation into the pathophysiology of neurocardiogenic syncope it was noted that transcranial Doppler ultrasonography (TCD) would demonstrate evidence for cerebral vasoconstriction that would occur concomitant with (or on occasion precede) the development of hypotension and loss of consciousness.\(^{24}\) Recently, several groups have suggested that tilt-induced syncope may occur due to cerebral vasoconstriction alone (as determined by TCD) in the absence of systemic hypotension. This phenomenon has been dubbed "Cerebral Syncope."\(^{25,26}\)

Last, we have observed a group that has a psychogenic or psychosomatic response during tilt.\(^{27}\) In these individuals, the syncopal episode that occurs during head upright tilt table testing is not accompanied by any measurable change in blood pressure, heart rate, electroencephalographic pattern, or transcranial blood flow patterns. Patients who exhibit this response are frequently found to be suffering from underlying psychiatric disorders that range from conversion reactions to anxiety disorders and major depression. An additional classification system has been developed by a European working group, which is based on hemodynamic and heart rate responses seen during tilt table testing.\(^{28}\)

**Reproducibility of Tilt Table Testing**

Knowledge of the reproducibility of tilt table testing is quite desirable in the study of the pathophysiology of these disorders, the determination of their natural histories, and for the assessment of prophylactic therapeutic interventions. For prolonged passive head upright tilt table testing, the reproducibility of a positive test (as determined by various investigators using different protocols) has ranged from 62\%-80\% when performed over a period of 3-7 days.\(^{13,29,30}\) When tilt table testing is used concomitantly with an isoproterenol infusion (again by various groups using various protocols), the reproducibility of a positive test has varied between 67\% and 88\% when performed between 30 minutes and 2 weeks from the original test, with the reproducibility of an initially negative test ranging from 85\%-100\%.\(^{31-33}\) Taken together, the data suggest that the overall reproducibility of an initial test is roughly 80\% on subsequent testing.\(^{19}\) The data would also suggest that an initially negative study has a relatively low likelihood of becoming positive on repeat testing. It is important to realize there is some degree of variability in test results, as would be expected from the nature of provocative testing, and consistent with that observed during electrophysiological testing.\(^{12,19}\)

It is important to be aware of the exact reproducibility of a number of different test variables, especially given the inherent limitations of provocative testing. In isoproterenol tilt table testing the time to presyncope and lowest heart rate and blood pressure within groups have good reproducibility; on a patient-to-patient basis time to lowest heart rate and blood pressure have better reproducibility.\(^{34}\) The most dramatic response on tilt table testing, prolonged asystole, seems to have a reproducibility of 80\%.\(^{35}\)

**Conclusion**

Head upright tilt table testing has emerged as a new and exciting technique for evaluating episodes of autonomically mediated syncope. Although it has some limitations (as does virtually every other test ever developed by medical science), it is nonetheless a valuable tool for evaluating a number of disorders of orthostatic control. Continuing investigations will undoubtedly better clarify our understanding of these disturbances in autonomic regulation and further define the role of tilt table testing in their evaluation and management.

**References**


TILT TABLE TESTING
