

EDITORIAL

Tilt-table testing: transient loss of consciousness discriminator or epiphenomenon?

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Introduction

Syncope accounts for 1–1.5% of emergency room visits and up to 6% of general hospital admissions.^{1–4} Patients with syncope present with a blackout,⁵ or transient loss of consciousness (T-LOC), and may present in family practice, cardiology, general medicine, accident and emergency, neurology, geriatric medicine, and psychiatry. Generally, a patient with T-LOC can only give limited details of the event, covering premonition and aftereffects. An eye-witness account is essential for filling in details during T-LOC. However, there are important causes of T-LOC other than syncope, e.g. generalized epilepsy and psychogenic blackouts. When patients present having had T-LOC, clinicians seek a test that will discriminate between these important causes. Is tilt-table testing such a test?

Tilt testing is a simple, non-invasive test with a low risk of complications.⁶ The physiological and pathophysiological effects of orthostatic stress by tilt testing have been known for 60 years.⁷ In 1986, Kenny *et al.*⁸ observed a high rate of tilt-induced syncope, with hypotension and bradycardia, in patients with syncope of previously unknown origin when compared with controls. Subsequently, many reports profiled the use of the test, and guidelines and recommendations emerged.⁶ However, clinical practice featured a very variable yield from a wide range of protocols, varying in duration and angle of tilt, the use of drug provocation to increase yield, and most importantly, the type of patients studied. Such factors presumably underlie the variable yield of tilt-table testing, which is from 26 to 87%.⁹ The overall reproducibility of a negative response (85–94%)^{10–14} is higher than that of an initial positive response (31–92%). The impact of these variations in protocol and patient clinical types, and their effect on the interpretation of a test result for T-LOC discrimination, is considered below.

What types of patients were studied?

Most studies using tilt testing have done so in patients who have already been labelled with 'syncope', not 'T-LOC'. Few have studied unselected T-LOC patients in order to evaluate tilt testing as a discriminator of the underlying cause of T-LOC. The evidence that tilt testing can discriminate between causes of T-LOC is limited. In one study¹⁵ of 145 unselected patients with T-LOC of uncertain cause presenting to the emergency department, the overall yield of tilt testing was only ~20%, was little enhanced by drug provocation, and was clearly dependent on the clinical features of patients. High rates of positive tests (~70%) were seen in elderly patients with recurrent T-LOC and no structural heart disease. No positive tests were found in young patients with T-LOC and repaired congenital heart disease. These findings indicated that the pre-test clinical characteristics of patients tended to determine the outcome of the test, and also that the sensitivity was imperfect—e.g. the cause of T-LOC in the 30% of elderly patients with a negative tilt remained unclear. In another study, a 'positive' test could be achieved in an important group, but without reproduction of syncope. In patients with suspected psychogenic blackouts, apparent T-LOC could be induced on tilt-table testing, but without any change in the heart rate, blood pressure, or electroencephalographic (EEG) recordings.¹⁶ The positive response appeared to be more likely if suggested to the patient prior to tilting and could even predict the time of the apparent T-LOC.

Even positive responses are poorly reproducible

When patients with a positive tilt test are restudied by tilting, 50% of them will become negative, irrespective of whether they have received treatment or not.^{17–19} This poor reproducibility is unexplained, but goes hand-in-hand with the less than perfect sensitivity in groups with a high pre-test likelihood of a positive tilt, i.e. patients with

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recurrent syncope and no structural heart disease. It seems that a tilt test may be positive one day and negative the next and may be subject to unknown day-to-day variables, even in susceptible patients.

Drug provocation increases sensitivity, but reduces specificity

Drug provocation has been used in an attempt to improve the sensitivity of the test but necessarily reduces the specificity at the same time.²⁰ When a standard tilt test is negative, the European Society of Cardiology⁶ recommends drug provocation with intravenous isoprenaline or sublingual nitroglycerin.⁶

Using isoprenaline shortens the time required for a tilt test, but an increase in yield is at the expense of a decrease in specificity.²¹ The response to isoprenaline may be non-specific. Kapoor and Brant²² subjected 20 patients with syncope of unknown aetiology and 40 controls to tilt testing and isoprenaline infusion. Positive response to tilt testing in patients was 75% (95% CI 55–95%) and among controls 55% (CI 20–86%). Tilt-induced symptoms were similar in patients and controls. Such high rates of false-positive results indicate that drug-provoked tilt testing is unlikely to discriminate between causes of T-LOC. Other drugs have similar shortcomings. The use of nitroglycerin also increases the sensitivity of the test but, like isoprenaline, at the cost of decreased specificity.^{23–25}

Low specificity and poor reproduction of spontaneous features

Englund *et al.*²⁶ tilted patients with bifascicular block with and without symptoms of T-LOC. Symptomatic patients with bifascicular block had similar rates of positive tilt to asymptomatic patients (28 vs. 32%, $P = \text{ns}$), further questioning the specificity of the test. In addition, the false-negative rates are also likely to be high, as high as 14–30%.²⁷ Importantly, the mechanism of tilt-induced syncope is frequently different from that of spontaneous syncope recorded with an implantable loop recorder.^{27,28} More patients were found to have a bradycardic or asystolic response on an implantable loop recorder than that found during tilt-table testing. The positive predictive value was 80% for an asystolic response during tilt testing, predicting a similar response during spontaneous episodes documented by an implantable loop recorder.²⁸

Value of tilt testing in guiding treatment

Results of the tilt-table test cannot be used to predict response to treatment. Sud *et al.*²⁹ performed a meta-analysis to determine whether permanent pacemaker therapy prevents refractory vasovagal syncope. Nine randomized trials (two double blind, seven open label or single blind) were analysed. Although permanent pacing reduced the risk of recurrent syncope in unblinded studies, and in studies comparing pacemaker algorithms, no effect was seen in double-blind trials. Patients in these trials were recruited on the basis of the results of the tilt-table test. However, the above results did not change even when the analysis was restricted to patients with marked

cardio-inhibitory response on the tilt-table test. The meta-analysis concluded that the treatment effect of pacemakers in patients with reflex syncope has been overestimated and that the apparent response was due to a strong expectation response to pacing. In contrast, preliminary studies using asystolic episodes causing spontaneous syncope recorded on implantable electrocardiogram (ECG) loop recorders do appear to predict a good response to pacing.³⁰ Further studies are required, and planned, to confirm this, but it may be that an asystolic response to tilt is an unreliable guide to the application of pacing, and that the recording of spontaneous asystole is required to ensure a confident recommendation of pacing.

Is tilt testing better than clinical assessment?

The importance of a good history in the evaluation of patients presenting with T-LOC was assessed in the Syncope Symptom Study, in which a uniform 118-item historical questionnaire was administered to 671 patients who were referred to three academic centres in Canada and Wales. On the basis of the questionnaire, a point score was developed. The cause of loss of consciousness was known satisfactorily in 539 patients and included seizures ($n = 102$; complex partial epilepsy and generalized epilepsy) and syncope [$n = 437$; tilt positive vasovagal syncope (267 patients), ventricular tachycardia (90 patients), and other diagnoses such as complete heart block and supraventricular tachycardia (80 patients)]. The point score based on symptoms alone correctly classified 94% of the patients, diagnosing seizures with 94% sensitivity and 94% specificity.³¹ A further study from the same group administered this questionnaire to 418 patients with syncope and no apparent structural heart disease.³² The point score correctly classified 90% of the patients, diagnosing vasovagal syncope with 89% sensitivity and 91% specificity. The decision rule used in the study suggested that 68% of an additional 95 patients with T-LOC and a negative tilt-table test had vasovagal syncope. Moreover, this study suggested that there is a close symptomatic similarity between most patients with negative and positive tilt tests, which would be consistent with the idea that most patients with negative tilt tests have false-negative tests. The results of the recently published Fainting Assessment Study³³ showed that attending physicians could make a diagnosis based on the initial evaluation in 63% of the patients with T-LOC, with an overall diagnostic accuracy of 88%. Furthermore, the conclusion was that the use of additional testing beyond history, physical examination, and ECG could be avoided in many patients presenting with T-LOC. A lower sensitivity for arriving at a diagnosis of T-LOC was found for a combination of these three modalities (a good history, physical examination, and an ECG) by Linzer *et al.*³⁴ in an earlier meta-analysis of six population-based studies. These studies suggest that clinical features are a good diagnostic predictor in T-LOC and that a good history is probably better than a tilt-table test. These studies also suggest that an ideal test for the cause of T-LOC would be one that measures physiological parameters such as ECG, blood pressure and EEG, or their surrogates, during a spontaneous attack. This would be superior to provoked testing, such as the tilt-table test, with its high rates of false-positive and false-negative results. However, given the infrequent symptoms of most patients with

T-LOC, opportunities to capture all these physiological parameters are necessarily limited at present.

So should we abandon tilt testing?

The European Society of Cardiology⁶ currently recommends tilt testing (Class I) in the following situations.

1. In the case of unexplained single syncopal episode in high-risk settings (e.g. occurrence of, or potential risk for, physical injury or with occupational implications), or recurrent episodes in the absence of organic heart disease, or, in the presence of organic heart disease, after cardiac causes of syncope have been excluded.
2. When it will be of clinical value to demonstrate susceptibility to neurally mediated syncope to the patient.

In a patient with Reflex Syncope, the reproduction of and the measurement of physiological variables during symptoms while undergoing a tilt test are likely to be reassuring to the patient for a number of reasons: (i) the patient is reassured that a medical professional has had a chance to observe their symptoms; (ii) the abnormal physiological parameters observed during a positive test provide a ready and logical explanation to the patient about the mechanism of their symptoms; and (iii) in those with a true positive tilt test, patients are relieved to know that their symptoms are nothing more serious than a common faint.

As already mentioned earlier, tilt testing is useful in patients with psychogenic blackouts, presenting with apparent T-LOC. Tilt testing may also be useful in the diagnosis of orthostatic intolerance.³⁵

Carotid sinus hypersensitivity is an important cause of syncope in elderly patients.^{6,36} Cardio-inhibitory and mixed types of carotid sinus hypersensitivity are amenable to permanent pacing with a decrease in syncopal events by 80%.^{37,38} Parry *et al.*³⁹ demonstrated that undertaking the carotid sinus massage in the supine position only, as opposed to an upright position (on a tilt-table test), underestimated the frequency of a positive response and prevents pacing being offered to a significant group of patients.

Tilt testing may be useful not as a discriminator of T-LOC but as a form of therapy. Tilt training (tilting to a 60° angle daily until syncope or until a maximum of 45–90 min) has been advocated as a treatment for recurrent reflex syncope.^{40,41} The medium- and long-term results of this treatment appear to be mixed. Gurevitz *et al.*⁴² found no benefit of tilt training in 46 patients over a 1-year period, whereas Reybrouck *et al.*⁴³ found that 81% of the 38 patients remained free of syncope over a period of 43 ± 7.8 months.

Another therapeutic area where tilt testing is likely to be useful is in the demonstration of the use of counter-pressure manoeuvres to abort an impending episode. Brignole *et al.*⁴⁴ showed that performance of the isometric arm counter-pressure manoeuvre during tilt testing at the onset of the prodromal phase of Reflex Syncope resulted in a significant increase in systolic blood pressure with the abolition of symptoms in 63% of the patients (vs. 11% in the control arm, $P=0.01$). Similar beneficial effects of counter-pressure manoeuvres during tilt testing have also been demonstrated by Krediet *et al.*⁴⁵

Conclusions

The evidence base suggests that the usefulness of tilt-table testing in the management of patients with syncope is limited by poor specificity, sensitivity, reproducibility, and misleading characteristics for guiding treatment. As the evidence base has been acquired almost entirely in patients with suspected syncope, rather than T-LOC, tilt-table testing is unlikely to be of value in the discrimination of the cause of T-LOC. A skilled and thorough clinical evaluation is always required, backed up by an ECG in all cases, to exclude high-risk structural or electrical heart disease, and if done diligently, may be less misleading than tilt testing. Implantable ECG recorders seem to hold promise for determining when T-LOC is caused by, or associated with, asystole, and when it is, guiding the appropriate use of pacemakers. However, some patients with epilepsy have associated asystole during seizures⁴⁶, therefore a finding of asystole is not a guarantee that the diagnosis is reflex asystolic syncope. Improved implantable diagnostics that sample multiple physiological parameters during a spontaneous T-LOC are required and may be the way forward for discrimination between the causes of T-LOC.

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