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#### Review

# Role of head-up tilt table testing in patients with syncope or transient loss of consciousness

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#### ARTICLE INFO

#### ABSTRACT

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Keywords: Tilt table testing Reflex syncope Pacemaker Italian protocol Management of syncope The tilt table test (TTT) is a useful method for the management of reflex syncope. However, the TTT is incomplete and has several problems. The indications for this test are established using guidelines. The TTT is not suitable for all syncopal patients. It is currently unclear (1) When should the TTT be used, (2) for which types of patients TTT should be performed, and (3) does the TTT provide useful information to guide indication for pacing therapy for reflex syncope. The answers to these questions appear in recent reports from two guidelines published by the European Society of Cardiology and the Japan Circulation Society. The indications for TTT do not apply to all syncopal patients, but selected patients. For patients with low risks and rare syncopal events, the TTT is not necessary, even when diagnoses are unconfirmed. The TTT is used not only for diagnosis of reflex syncope, but also for many clinical management of several conditions (i.e., exclusion of cardiac syncope). Positive TTT results cannot predict the effects of pacing therapy for reflex syncope. The decision to use pacing therapy should be based on documented electrocardiograms and other findings, including TTT results.

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#### 1. Introduction

The tilt table test (TTT) has been used to reproduce neurally mediated reflexes in laboratory settings for over 20 y [1]. In clinical settings, the TTT is useful for diagnosis of reflex syncope, and discrimination of reflex syncope from other transient losses of consciousness, including cardiac syncope and epilepsy [2,3]. However, the TTT has several problems, most importantly, its low sensitivity and specificity [4–7]. For example, a negative TTT result is often obtained in cases of typical vasovagal syncope (low sensitivity), whereas a positive TTT result is obtained in cases without any episodes of syncope (low specificity). Another drawback of the method is the cost of the TTT. For the TTT, single-purpose tools, such as a tilt table and a beat-to-beat blood pressure monitor, are needed [8]. In addition, a considerable amount of time is needed for testing. Thus, the following questions can be raised: should the TTT be applied to all syncopal patients, and which types of patients are suitable for the TTT. Recently published guidelines answer these questions, with the most important article being the 2009 European Society of Cardiology (ESC) guidelines [8].

#### 2. Methodology of the TTT

First, knowledge of the TTT protocols is required. Fig. 1 depicts the method of TTT. These protocols were reported with variations in the initial stabilization phase, duration, tilt angle, type of support, and pharmacological provocation since the first reports published by Kenny et al. [1]. The ESC guidelines recommend a tilt angle between  $60^{\circ}$  and  $70^{\circ}$  [8]. The most commonly used protocol is the low-dose intravenous isoproterenol test, that uses incremental doses to increase the average heart rate by 20–25% over baseline (usually < 3 µg/min) [9]. The next protocol, called the "Italian protocol", uses 300–400 mg of sublingual nitroglycerine after a 20-min passive phase [10]. The results from both protocols reveal similar rates of positive responses (61–69%), with a high specificity (92–94%). In the Italian protocol, however, a venous cannulation is not necessary, and the pre-tilt phase can be shortened to 5 min [8]. The protocol is simple and fast, saving

substantial time during busy clinical situations, and has few adverse effects, such as headache. In addition, no deaths were reported during either protocol. Our institute usually chooses the Italian protocol with few exceptions. TTTs with clomipramine are used for selected patients with syncope that is triggered by emotional distress [5,6]. These TTTs may be useful as biofeedback training for counter-pressure maneuvers in such patients [11].

#### 3. What situations require the TTT and which ones do not?

#### 3.1. Situations where the TTT is not performed for diagnosis

## 3.1.1. In situations where diagnosis of reflex syncope is already certain

In reflex syncope, the TTT is not necessary to confirm an already certain diagnosis. For example, vasovagal syncope can be diagnosed when a patient has a syncopal episode immediately after emotional distress (due to fear, pain, instrumentation, and venipuncture), that was associated with typical prodromes (symptoms before syncopal events) from autonomic activation (i.e., sweating, facial pallor, nausea, pupillary dilatation, slight palpitations, yawning, and/or hyperventilation) [8,11]. However, situational syncope can be diagnosed when the syncope is triggered by specific circumstances, which include the following: during or immediately after micturition, defecation, coughing, swallowing, laughing, eating, and vigorous activities or exercise [8]. When either type of syncope is diagnosed, it is considered a reflex syncope. In these situations, the TTT is not necessary for diagnosis confirmation.

#### 3.1.2. In situations where cardiac syncope is suspected

Criteria for risk stratification, particularly to identify patients with a suspicion of cardiac syncope, have been established [8]. In these patients, the first choice is to perform a cardiac evaluation; the TTT should not be performed initially. For these patients, the presence or absence of a heart disorder, which can manifest during syncopal attacks and cardiac arrhythmias, should be investigated [11]. Before the TTT, other cardiac tests, including an



**Fig. 1.** A. Outline of the tilt table test. Tilting angle of 60°. Beat-to-beat blood pressure monitor on the left arm (black arrow). For the patient's safety, support belts are necessary to prevent falling. If necessary, a venous cannulation was placed in the appropriate position. B. Monitoring during the tilt table test. Two-lead ECG of the upper area. Beat-to-beat BP monitor in the bottom area. In usual practice, twelve-lead electrocardiograms are rare. ECG = electrocardiogram, BP = blood pressure. C. Long asystole during syncope Induction of syncope with 12 s of asystole. ECG = electrocardiogram, BP = blood pressure.

electrophysiological study, are necessary for these patients. If patients' electrocardiograms (ECG) indicate inherited arrhythmias, genetic testing must be performed [12].

#### 3.1.3. In situations where diagnosis is not necessary

When the cause of the syncope remains unclear after initial evaluation, the subsequent management strategy depends on the risk of a cardiac syncope because the primary purpose of syncope managements is to prevent major cardiovascular events and/or sudden cardiac death [8]. The diagnostic flowchart from the ESC guidelines demonstrates that further evaluations are not necessary for patients with a low risk and rare episodes of the condition [8]. The management for these patients is similar to that for patients in whom diagnosis of reflex syncope is already certain. The TTT is not necessary for patients without symptoms of suspected cardiac syncope, electrocardiographic abnormalities, any cardiac diseases, injuries, and frequent episodes of syncope.

#### 3.2. Situations that require the TTT

The most important aspect of the TTT is the reproduction of reflex syncope in a laboratory setting. This test can also exclusively reproduce reflex syncope from a myriad of causes for syncope. Thus, the TTT can be useful for discriminating reflex syncope from other transient losses of consciousness, such as epilepsy and psychiatric problems [2,3]. If the TTT reproduces syncope with similar symptoms, the possibility of reflex syncope is increased [8].

### 3.2.1. In situations where reflex syncope is suspected; but, clinical presentations are atypical

The ESC guidelines state that the term "*atypical form*" applies to situations in which reflex syncope occurs with uncertain or absent triggers [8]. and prodromes are also absent. Thus, diagnosis from medical history review alone is difficult. However, exclusion of other syncope causes (i.e., absence of structural heart disease) and *reproduction of similar symptoms with the TTT* are useful for making a diagnosis. Unclear presentations may overlap with clear-cut occurrences within patients.

## 3.2.2. In situations where reflex syncope is suspected but other undeniable causes of syncope are found in clinical presentations and data

The ESC guidelines also states in sentence of tilt testing, "In patients with a high-risk profile for cardiovascular events or with data suggestive of arrhythmic syncope, *TTT has been reported to be useful* when a cardiovascular cause has been reasonably excluded by a comprehensive evaluation" [8]. For example, if a patient with syncopal events had typical reflex syncope, but his ECG indicated type II Brugada syndrome, TTT results can help in deciding future managements.

#### 3.2.3. In situations where reflex syncope occurs in special situations

The TTT indications change according to patients' situations. Special situations are defined as *injuries, anxiety, and occupational implications, such as those that occur in aircraft pilots* [8,13]. The TTT is indicated even for patients with single or rare confirmed reflex syncope in special situations.

## 3.2.4. In situations where diagnosis of reflex syncope is already certain, but the information from TTT results are useful for other clinical managements

According to the Japan Circulation Society (JCS) guidelines, the TTT is indicated for patients with reflex syncope to find out if syncope occurs very easily in such patients, to aid in further clinical management planning. The TTT is also indicated in patients in whom reflex syncope affects the therapy for cardiac syncope [14].

#### 4. Do TTT results help in deciding the indication for a pacemaker implantation?

Previous randomized controlled trials guided by TTT responses could not demonstrate the effectiveness of pacing therapy in patients with tilt-induced syncope due to long asystole [15-18]. The International Study on Syncope of Uncertain Etiology 3 demonstrated the effectiveness of pacing therapy in patients with asystole, documented using implantable cardiac monitors [19]. The patients were  $\geq$  40 y old. In this study, the patients with the most effective pacing had negative TTT results. The patients with positive TTT results, and documented similar asystole during spontaneous syncope, did not benefit significantly from the pacing therapy. The results in this group did not differ from those in untreated patients. Patients with positive TTT results and pacing therapy had a 55% recurrence rate during 2 y of follow-up [20]. Based on these studies, pacing therapy is useful for patients with documented asystole during spontaneous syncope and without syncope induced by the TTT. Conversely, there is no evidence that pacing therapy is effective for patients with syncope and long asystole induced by TTT. Therefore, patients with a positive TTT result should not receive pacemaker therapy. A negative TTT result suggests a need for prolonged cardiac monitoring, such as implantable cardiac monitoring to document asystole during spontaneous syncope. A recent report demonstrated the usefulness of a simple score for determining the mechanism of paroxysmal atrioventricular block [21]. A similar scoring system has the potential to guide the indication for pacemaker therapy.

#### 5. Conclusions

TTT is useful not for all syncopal patients but only for a few selected patients suffering from the condition. For patients with low risks and rare syncope episodes, the TTT is not necessary, even if diagnoses have not been confirmed. However, TTT can be used not only for diagnosis of reflex syncope, but also for several clinical management strategies, including ruling out a diagnosis of cardiac syncope. In addition, positive TTT results cannot predict the effects of pacing therapy in patients with reflex syncope. Pacing therapy should be administered based on documented electrocardiograms, TTT results (negative or positive), and other findings.

#### **Conflicts of Interest**

All authors declare no conflict of interest related to this study.

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