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INVITED REVIEW

Tilt table testing, methodology and practical insights for the clinic

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Abstract

Tilt table testing (TTT) has been used for decades to study short-term blood pressure (BP) and heart rate regulation during orthostatic challenges. TTT provokes vasovagal reflex in many syncope patients as a background of widespread use. Despite the availability of evidence-based practice syncope guidelines, proper application and interpretation of TTT in the day-to-day care of syncope patients remain challenging. In this review, we offer practical information on what is needed to perform TTT, how results should be interpreted including the Vasovagal Syncope International Study classification, why syncope induction on TTT is necessary in patients with unexplained syncope and on indications for TTT in syncope patient care. The minimum requirements to perform TTT are a tilt table with an appropriate tilt-down time, a continuous beat-to-beat BP monitor with at least three electrocardiogram leads and trained staff. We emphasize that TTT remains a valuable asset that adds to history building but cannot replace it, and highlight the importance of recognition when TTT is abnormal even without syncope. Acknowledgement by the patient/eyewitness of the reproducibility of the induced attack is mandatory in concluding a diagnosis. TTT may be indicated when the initial syncope evaluation does not yield a certain, highly likely, or possible diagnosis, but raises clinical suspicion of (1) reflex syncope, (2) orthostatic hypotension (OH), (3) postural orthostatic tachycardia syndrome or (4) psychogenic pseudosyncope. A therapeutic indication for TTT in the patient with a certain, highly likely or possible diagnosis of reflex syncope, may be to educate patients on prodromes. In patients with reflex syncope with OH TTT can be therapeutic to recognize hypotensive symptoms causing near-syncope to perform physical countermanoeuvres for syncope prevention (biofeedback). Detection of hypotensive susceptibility requiring therapy is of special value.

KEYWORDS

initial evaluation, orthostatic hypotension, postural tachycardia syndrome, psychogenic pseudosyncope, reflex syncope, syncope, vasovagal syncope

1 | INTRODUCTION

Tilt table testing (TTT) is a diagnostic procedure primarily used to assess the cause of unexplained syncope, near-fainting episodes or orthostatic intolerance. Whereas originally developed for physiological studies of the human haemodynamic response to orthostatic provocation, the test has been used clinically in syncope evaluation for four decades (Anne Kenny et al., 1986). Besides provoking and reproducing vasovagal syncope (VVS), or any form of transient loss of consciousness (TLOC), TTT is used to diagnose conditions of chronic orthostatic intolerance not necessarily including TLOC, postural orthostatic tachycardia syndrome (POTS) and orthostatic hypotension (OH). It may also be used for education of the patient with these conditions (Thijs et al., 2021).

Briefly, TTT involves tilting a specially designed table to a specific angle to simulate a change in position from lying to erect position, which can trigger symptoms of fainting in individuals with certain conditions. During the test, the patient is first secured on the table by Velcro straps and then tilted to 60°–80°. The patient's heart rate (HR), blood pressure (BP) and symptoms are monitored throughout the test, which typically lasts between 20 and 45 min. The objective of TTT is to evaluate the body's response to a change in position and identify any underlying conditions that may be contributing to loss of consciousness and/or orthostatic intolerance. The diagnostic accuracy for identifying VVS can be enhanced by adding sublingual nitroglycerine (NTG) after the passive phase, this approach is the most commonly used 'Italian protocol' (Bartoletti et al., 2000).

Despite being in clinical use for four decades and by some even being seen as the 'Holy Grail' of syncope evaluation, there is still uncertainty for some clinicians about TTT and its most appropriate use. One reason may be that TTT is usually performed in tertiary syncope centres, unlike most other cardiovascular examinations, nonspecialists may never encounter TTT firsthand. In contrast, most patients undergoing TTT are referred by clinicians working outside a tertiary syncope centre. Importantly, while TTT adds valuable information, it is not a substitute for the initial syncope evaluation which includes thorough history taking of the current event and previous events, physical examination including supine and standing BP, and a standard 12-lead electrocardiogram (ECG) (Brignole et al., 2018a) (Figure 1). An abnormal TTT result provides the most information if the provoked event reproduces the symptoms that the patient has spontaneously experienced (Thijs et al., 2021).

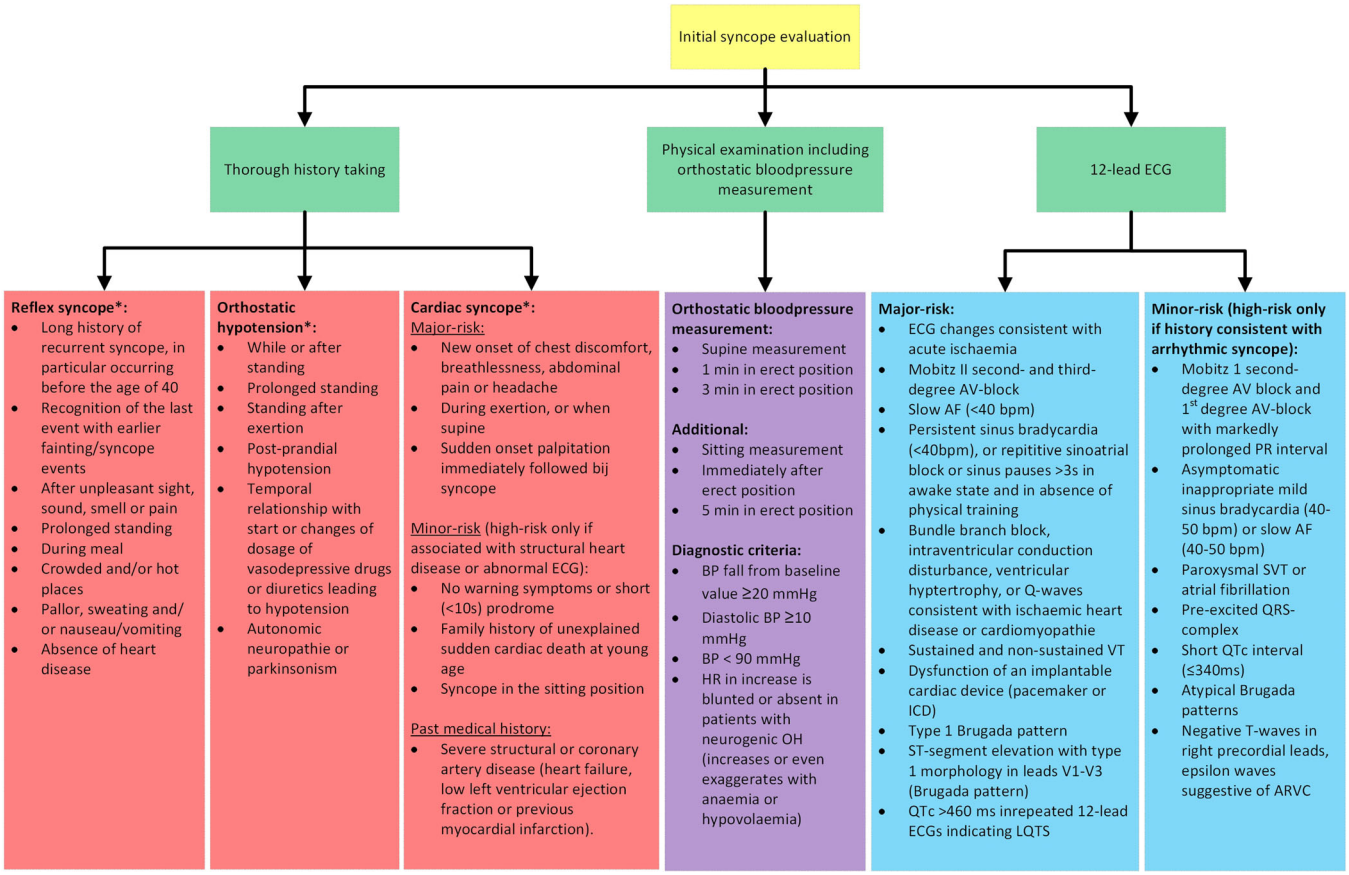

FIGURE 1 Header: Overview of the initial syncope evaluation. The figure comprises important questions for history taking for the general physician (building a history instead of taking history) and show the importance of orthostatic BP measurement and 12-lead ECG. *European Society of Cardiology guideline. AF, atrial fibrillation; ARVC, arrhythmogenic right ventricular cardiomyopathy; AV, atrioventricular; BP, blood pressure; bpm, beats per minute; ECG, electrocardiogram; ICD, implantable cardioverter defibrillator; LQTS, long QT syndrome; SVT, supraventricular tachycardia; VT, ventricular tachycardia.

This review intends to fill the gap in knowledge for healthcare professionals that may exist for TTT and describes the basics of TTT in terms of practical knowledge, indications and interpretation. The authors aim to provide the reader, for example, physicians, (specialized-) nurses, nurse practitioners and physician assistants, with a comprehensive yet clear and concrete overview of TTT that may further guide the appropriate use of TTT in clinical practice.

2 | WHAT IS NEEDED FOR TTT?

For clinical value, TTT must be well performed by diligent observant staff members using the best equipment possible to yield quality data.

2.1 | Staff

Performance of TTT by physicians should not be obligatory but they should have access to detailed test data for posttest interpretation, if appropriate. Tests must be safe but safety can be equally well delivered by nurses, nurse practitioners, physician assistants and technicians who should have, however, access to a physician, if needed. These latter groups are particularly well-suited to perform TTT because they are trained in resuscitation and in being observant of clinical physiology. Moreover, they have demonstrated that they are better at following protocols than most physicians. Only one staff member is needed to perform a TTT but two are optimal for detailed test documentation, as it relies on observing both the patient and the monitor at the same time. There may be special occasions when a very experienced clinical physician is able to deliver more than any other staff. For example, in patients where a TTT is being repeated because of doubt over details in a previous nondiagnostic test.

The monitoring staff member must reassure the patient, if anxious, prevent the patient from moving, and document events such as symptoms directly on the continuous beat-to-beat recording device as they occur (which the equipment must facilitate). Also, the staff member must be sympathetic and reassuring throughout and especially during recovery from syncope. In patients with Parkinson's disease, cold hands, autonomic failure, for example, it may be helpful to prewarm the hands for several minutes which will favour peripheral vasodilatation, thus benefitting the test.

In the case of the need to establish a certain, highly likely or possible diagnosis after initial evaluation (Brignole et al., 2018a), staff members must be aware that the tilt must be pursued to complete loss of consciousness so that asystole and its exact timing can be revealed, if present (van Dijk et al., 2022; Saal et al., 2017). This requires some steely nerves at first and not being compliant with patient's wishes to stop before a full test including syncope is achieved (Russo, Parente, Rago, et al., 2022). A complete loss of consciousness is important for therapy decisions, being possibly cardioneuroablation, even if still under evaluation for the younger and pacemaker for the older patient (Aksu et al., 2023). In some patients, after performing TTT, while the patient is still attached to monitoring or when there is a certain, highly likely or possible diagnosis after initial evaluation, biofeedback might be given so the patient can observe the added value of performing physical countermanoeuvres (Figure 2) while watching their haemodynamic parameters on the monitor. This may also be performed during an active standing post-TTT.

2.1.1 | Staff involved in the interpretation

The majority of syncope units have a multidisciplinary approach where cardiology and neurology are the specialties most involved in studying syncope patients. These two specialties are aware of the complete differential diagnosis of unexplained TLOC, and the need to separate syncope from nonsyncopal mimics. Such an approach might be also preferable to distinguish benign from malign causes of TLOC and either to reassure the patient or prescribe appropriate therapy (van Zanten et al., 2023).

2.1.2 | Equipment

Tilt table

This must be efficient and regularly serviced to be sure that it will tilt down at the single press of a button. Tilt-down time is very important. Studies have shown that slow tilt-down, >12 s, is associated with a greater likelihood of asystole and its prolongation (Zyśko et al., 2016). While provocation of asystole is not thought to be dangerous carrying no adverse prognosis (Sau et al., 2016), its prolongation may be harmful such as infratentorial brain lesions, including hyperintense brainstem lesions and cerebellar infarcts (Kruit et al., 2013).

The table requires retention straps (Velcro) to prevent the patient from falling from the table in the event of syncope. The table should be able to tilt up to angles of 60°–80° (Brignole et al., 2018a). Table motors must not cause interference in physiological records such as the ECG.

Monitoring

ECG should be a continuously recording system, employing at least three leads, feeding into the beat-to-beat monitor to be simultaneously in view with the haemodynamic parameters. BP should also be a continuous noninvasive beat-to-beat system which, at optimum, offers the possibility of extraction of stroke volume from the waveform of the output. The monitor requires the ability to review the tracings, if possible, with the variability of the display speed to permit detailed analysis of the event. The manual sphygmomanometer is inadequate for this purpose as it compares so poorly with beat-to-beat recordings. The manual method performed at its most dextrous will yield measurements every 40 s when during such intervals so much may occur. For example: BP may be near normal at the onset of cardioinhibition and the patient be asystolic with no recordable BP within 40 s. In addition, this method may be very inconvenient for the patient.

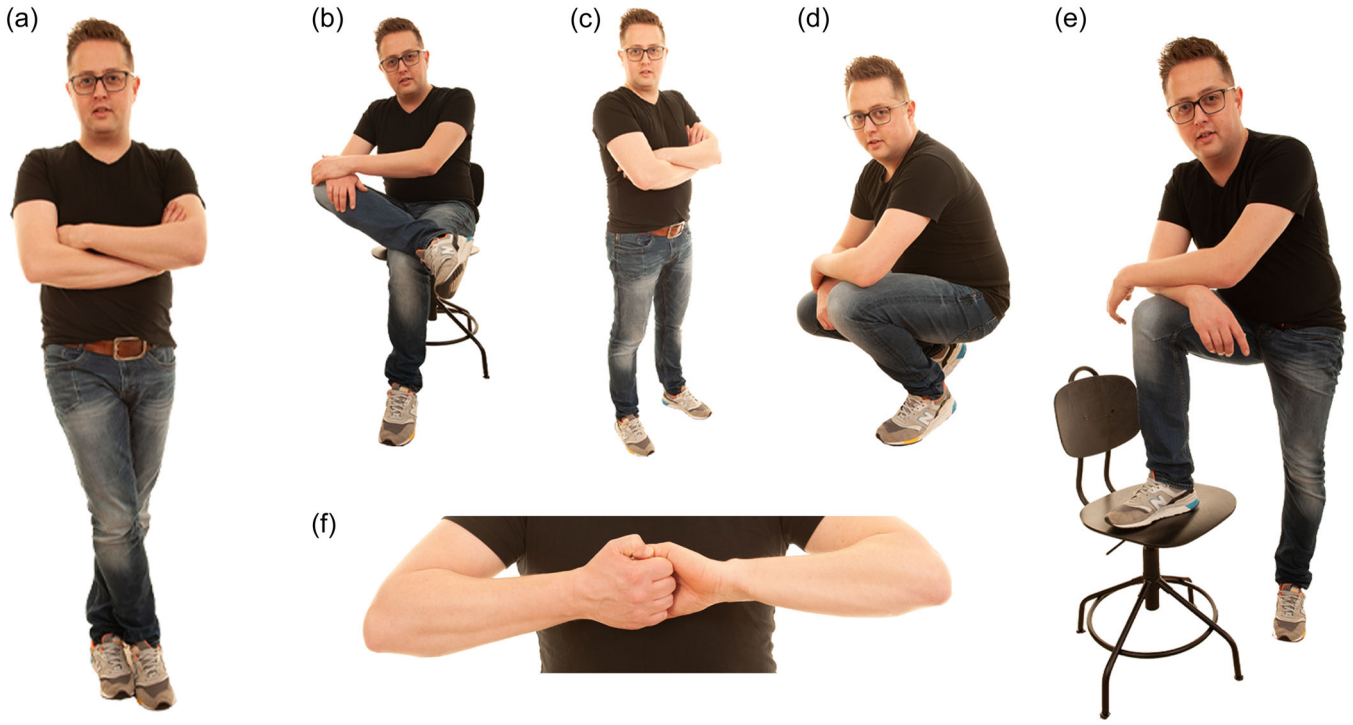

FIGURE 2 Header: Overview of performing countermanoeuvres. Countermanoeuvres: Education should be done on different physical countermanoeuvres as a result of which venous return to the heart leads to rise in blood pressure. (a) Tensing lower body muscles while crossing arms and legs, (b) place one leg on top of the other and applying pressure with the arms, (c) whole body tensing, (d) squatting, (e) raising a leg and put onto a raised surface and apply pressure with the arms and (f) arm tensing. The man in the photo gave fully informed consent for publication.

It is also of potential importance to select a beat-to-beat BP monitoring system that favourably permits the demonstration of the oscillation of BP. When present, its existence indicates the autonomic BP control is under stress and often precedes its collapse (Hausenloy et al., 2009). Some monitoring systems appear to suppress this phenomenon.

ECG and BP are the minimum physiological parameters to be recorded. Additional data may prove valuable in interpretation.

Video recording of the patient so as to determine the precise moment of loss of consciousness (head-flop) is a valuable addition (de Lange et al., 2023). It is necessary to feed this stream into the recording computer for precise timing of the moment of (apparent-) loss of consciousness or recognition of symptoms without complete loss of consciousness. The methodology has recently been described and is now available obviating the need for an electroencephalogram (EEG) recording (de Lange et al., 2023) (Figure 3).

Assessments of cerebral perfusion are considered to be research techniques but they are becoming more commonly used in clinical settings. Middle cerebral artery blood flow velocity (Van Lieshout et al., 2003), less frequently, posterior cerebral artery blood flow velocity and cerebral oxygenation (Bachus et al., 2018). This latter technique may be used in conjunction with cerebral artery blood flow velocity. At present, a fall in cerebral perfusion has been clearly demonstrated at syncope but may occur much earlier. Also, demonstration of successive decreases in cerebral saturation on tilt despite preserved BP parameters may help diagnosing orthostatic intolerance in the absence of significant BP fall. This may have a role in assessing of orthostatic reflex syncope susceptibility and symptom generation in OH or POTS (Bachus et al., 2018).

Respiration monitoring is potentially easier and cheaper but strain gauges are inherently unreliable. There may be value in separating respiratory changes from the oscillation of BP. Oscillation may also be detectable on ECG but those in the BP trace seem to be the most clinically valuable.

NTG

300–400 mcg at 20 min of tilt. NTG causes haemodynamic changes of peripheral vasodilation further unloading the heart as already in part achieved by the upright posture of tilt combined with the lack of leg muscle pump for venous return that happens in normal standing. NTG also stimulates a compensatory rise in HR. These changes are expected and should be attributed to the drug not to the evolution of VVS. A recent development has been put forward to shorten the test by reducing the passive phase from 20 to 10 min. In a large number of patients, this has been shown not to prejudice the test but offers an advantage in busy clinical environments to permit the testing of more patients. (Russo et al., 2023). It may be anticipated that this is likely to become the new norm.

Carotid sinus massage (CSM)

CSM should be performed in patients older than 40 years of age in which the underlying mechanism of syncope is unexplained after

FIGURE 3 Header: View of the setup for a tilt-table test. The patient is performing a physical counterpressure manoeuvre as described in Figure 2. *Using Open-Acces-Video-TTT (de Lange, et al., 2023). The woman in the picture gave complete informed consent for publication. BP, blood pressure; ECG, electrocardiogram; NTG, nitroglycerine; TTT, tilt table test.

initial evaluation (Rivasi et al., 2018) (Figure 1). The use of the TTT with noninvasive beat-to-beat monitor is aimed at detecting abnormal BP and/or HR response with every heartbeat. CSM may be performed before or after TTT. A positive test reproduces the patient's syncope. CSM is performed, first on the right carotid artery followed by the left in the supine position and when this is nondiagnostic, it is repeated with the patient in a head-up tilt position. The two carotids should be massaged sequentially for 10 s in each position to allow symptoms to develop. 'The method of symptoms' involving intravenous atropine should be used to eliminate bradycardia (Brignole et al., 2018b). This way is better to evaluate the vasodepressor component (Rivasi et al., 2018).

In some patients, especially older men affected by cardiovascular disease (≤40%), carotid sinus hypersensitivity is a common finding without a history of syncope. Syncope is induced in 5% of asymptomatic persons older than 65 years of age (Kerr et al., 2006). Carotid sinus syndrome is diagnosed when there is syncope with a ventricular pause lasting longer than 3 s and/or a fall in systolic BP of 50 or more mmHg in patients with a history of syncope. However, when there is no such history of syncope, the positive finding implies carotid sinus hypersensitivity which is not recognized as a disease and its prognosis is not known.

Complications such as provocation of TIA are very rare. However, it is necessary to be careful with patients with previous TIA, stroke or known carotid stenosis of more than 70% (Brignole et al., 2018a).

2.2 | Storage of data and printouts

The whole test should be stored in the patient's electronic medical record, if possible. If not possible, retention in a dedicated computer may prove very valuable if any future review is required. Paper printouts or Compact Disk/Digital Versatile Disk, if available, are valuable ways to offer details to the referring physician and sometimes in explaining to the patient what has happened.

2.3 | The patient

The patient should be nil-by-mouth for a limited time before the test, perhaps 2 h for water, and 4 h for food. A middle road is ideal between avoidance of dehydration and having nothing substantial to vomit in the event of nausea. At the advent of tilt testing, overnight fasting was prescribed which may have increased the positive yield (Anne Kenny et al., 1986).

The patient must be well-prepared so that there is confidence in what will happen combined with the best possible compliance. The patient should understand that loss of consciousness may occur and be instructed not to tense any muscle groups or to move the legs. In some healthcare environments, formal consent is required. Patients are advised to arrange for someone to escort them home as symptoms may recur after TTT.

2.4 | The laboratory

The room for the test must be at normal room temperature, quiet, free from telephones, call systems and any kind of interruption. 'No Entry Tilt test in Progress' is a good label to have on the door but the door should not be locked. During daylight, means of darkening the room should be available and may help to relax the patient. Full resuscitation equipment close by is mandatory. All requirements can be found in Figure 3.

3 | WHAT ARE THE INDICATIONS FOR TTT?

TTT is currently used in specialized centres and diagnostic clinics with a variety of protocols, variants and sometimes combined with additional testing. Recent guidelines and consensus documents recommend the use of TTT in the workup for disorders that may cause TLOC or orthostatic intolerance (Brignole et al., 2018a; Thijs et al., 2021). TTT should be used only when the initial evaluation (Figure 1) failed to yield a certain, highly likely or possible diagnosis (de Jong et al., 2021) but implies a form of reflex syncope, OH, POTS or psychogenic pseudosyncope (PPS). TTT may then add to the history of events but does not replace history taking nor should it be used in isolation from patient's history as a 'stand-alone' test (Brignole et al., 2018a). However, it must be accepted that at least in some geographic areas, knowledge of syncope and its management is not good and some cardiologists will prefer to refer their patients without work-up rather than perform this themselves. Figure 4 shows a flowchart when to perform a TTT.

The primary indication for TTT is to permit complaint recognition and correlate them with physiological measurements. Complaint recognition can be either from the patient or by an eyewitness during TTT. When the initial evaluation does not reach a conclusive or possible diagnosis, these aspects are of paramount importance. Sometimes both patients and/or physicians are in dilemma and want to be certain of their diagnosis, while there may also be events in sitting or supine position. Recognition of prodromes or syncope during TTT should always correlate with the findings from the history.

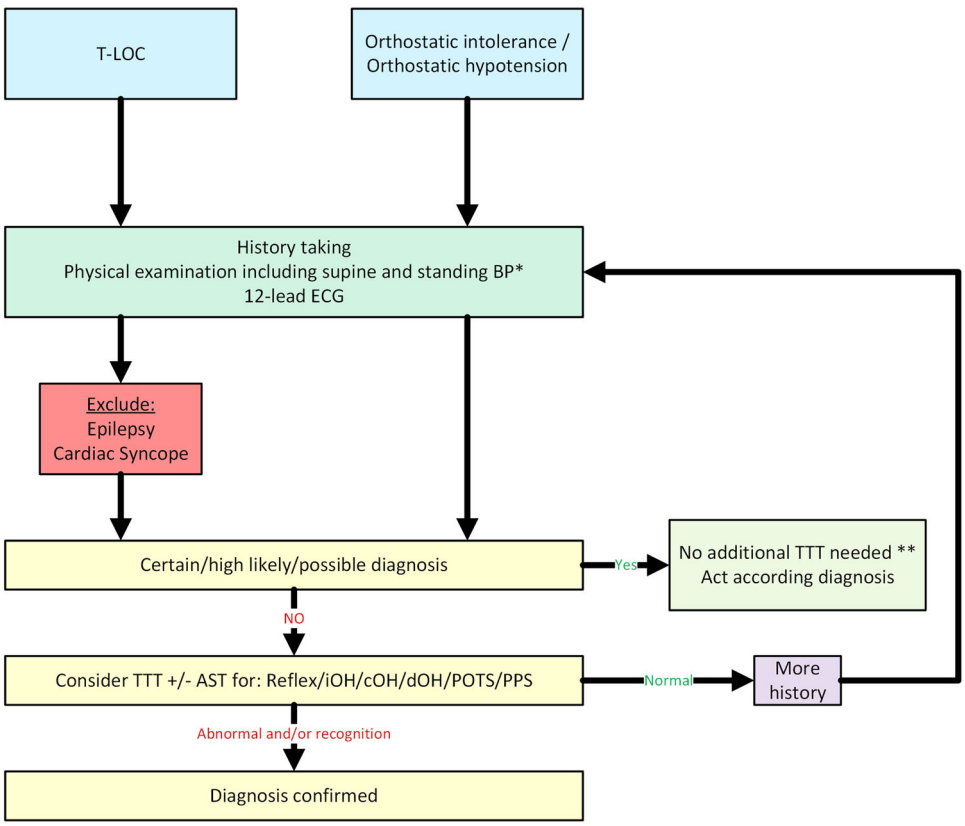

FIGURE 4 Header: A pragmatic flowchart, starting with the initial evaluation of TLOC and orthostatic intolerance. This includes (1) complete and thorough history taking, (2) physical examination including orthostatic BP measurement in office or at bedside and (3) perform a 12-lead ECG. *Orthostatic blood pressure measurement includes RR/HR after 5 min in the supine position and after 1 and 3 min standing in the erect position. **TTT may be useful to recognize hypotensive symptoms and to perform counterpressure manoeuvres as biofeedback. AST, active standing test; BP, blood pressure, cOH, classic orthostatic hypotension; dOH, delayed orthostatic hypotension; ECG, electrocardiogram; iOH, initial orthostatic hypotension; POTS, post orthostatic tachycardia syndrome; PPS, psychogenic pseudosyncope; T-LOC, transient loss of consciousness; TTT, tilt table test.

3.1 | Reflex syncope

TTT in diagnosing reflex syncope is not needed in the majority of the cases presenting with unselected syncopal episodes (de Jong et al., 2021; Sheldon, 2005; Sutton & Brignole, 2014; van Dijk et al., 2008). This is mainly due to the low sensitivity (overall 59%; 95% confidence interval: 53%–65%; range 21%–72%) in confirming the diagnosis. Moreover, one should bear in mind that TTT reveals a hypotensive susceptibility in any predisposed individual, which is exemplified by hypotension due to low stroke volume or inadequate vasoconstriction during orthostatic stress when the tilt table is in the upright position (Brignole et al., 2021; Sutton & Brignole, 2014). Thus, in some, TTT may provoke hypotension and syncope without a direct correlation with the episode in question or in a patient with a previously unknown tendency to reflex syncope (Petersen et al., 2000).

The pathophysiology of reflex syncope has recently been defined more precisely than before, very much due to the availability of better measurement equipment. The initial paper with a more precise description of the pathophysiological events was by Jardine et al. (2018). This work has been followed by a series of papers from van Dijk's group in Leiden. With these papers, we see the slow onset of vasodepression with the ultimate intercession by much more rapid cardioinhibition. (van Dijk et al., 2020, 2022), please see also under interpretation).

The results of the TTT should always be interpreted in the context of all the elements of the initial evaluation (Brignole et al., 2018a). TTT results rely predominantly on the orthostatic stress in the upright position and thus the indications are limited to conditions with orthostatic intolerance. Most often patients suffering from reflex syncope also suffer from orthostatic intolerance even when they do not faint (Saal et al., 2016).

3.2 | Orthostatic intolerance

Besides orthostatic VVS, TTT can be also of additional use in patients suffering from orthostatic intolerance, which includes all forms of OH and POTS. OH comprises: initial orthostatic hypotension (iOH), classical orthostatic hypotension (cOH) and delayed orthostatic hypotension (dOH). iOH is, however, not well suited to examination by TTT and is much better examined by the Active Stand Test (AST) but with the same beat-to-beat monitoring (see also later under interpretation).

Interestingly, forms of reflex syncope that have specific triggers like cough syncope, are also susceptible to orthostatic VVS (Humm & Z'Graggen, 2015; Mereu et al., 2016) and many of their symptoms are most likely to occur in the upright position.

3.3 | PPS

TTT can be very helpful in confirming the diagnose of PPS when video documentation is available (LaFrance et al., 2013; de Lange et al., 2023). Also, in this case, description by the patient or eyewitness with subsequent recognition is important to establish and confirm the diagnosis. PPS can also be confirmed on clinical grounds when the physician witnesses the event on TTT and observes features favouring PPS, including mild acceleration of HR and a rise in BP together with the apparent loss of consciousness. Video recordings provide the most convincing evidence to diagnose PPS since history taking often raises a strong suspicion of PPS but may not always be reliable enough to rule out other causes of TLOC (LaFrance et al., 2013). Video recording with EEG is important to exclude epilepsy when the event is accompanied by muscle jerks or strong motor phenomena. A normal EEG during a recognized event on TTT excludes epilepsy that presents as TLOC, that is, tonic, clonic and tonic–clonic seizures (van Dijk et al., 2009). When TTT is negative for an event, this does not exclude PPS, then catching an event by the camera (e.g., on smartphone) by an eyewitness should be the next step to confirm the diagnosis of PPS. It must be kept in mind that at least 30% of PPS patients also have a susceptibility to VVS (Blad et al., 2015).

3.4 | Complications

These have recently been reviewed by Zysko et al., 2023.

TTT is a safe procedure. However:

1. Autonomic tests have been suggested to be avoided within 3 months of stroke or myocardial infarction as these conditions disturb autonomic function for many months after they occur.
2. Prolonged bradycardia could cause arrhythmic complications such as ventricular tachyarrhythmias although very rarely.
3. Vomiting.
4. Severe weakness/tiredness for several hours.
5. Convulsive syncope (it is common that there are a few seconds of extremity myoclonus before consciousness returns). This is not a complication but may be, in some cases, considered so by patients.
6. Headache (especially after NTG).
7. Atrial fibrillation (especially in older patients or in those with paroxysms).

3.5 | Contraindications

Known pathophysiology of the presenting syncope which renders a further test unnecessary. Simply, redemonstrating previously shown pathophysiology is a futile exercise. However, there may be other good reasons for repeating a TTT, please see Section 2.1 early in this paper.

Importantly, any severe medical condition such as anaemia, aortic stenosis and hypertrophic obstructive cardiomyopathy.

4 | HOW TO INTERPRET TTT?

Appropriately performed and recorded TTT offers quality data which is an absolute necessity for accurate interpretation of TTT results and for the understanding of syncope and orthostatic intolerance aetiology.

In this discussion, we include both tilt positivity in the passive and drug-challenge phases. Classification of syncopal test outcomes was hoped to lead to the prescription of optimal therapy for each patient. The first attempt at classification for reflex syncope was the Vasovagal Syncope International Study (VASIS) presented in 1992 (Sutton et al., 1992). It is still widely followed but it must be understood that its clinical value is limited. The hope that specific therapies would go with every type has not been realized. One recently detected limitation is that the test must be pursued to loss of consciousness, collapse or the occurrence of asystole without which false assumptions can be made including denying potential pacemaker therapy when it will offer patient benefit demonstrated in a specific population (Russo, Parente, Groppelli, et al., 2022).

Recently, a comprehensive analysis of a large number of tilt test records (Russo, Parente, Groppelli, et al., 2022) has shown that pursuing the test to complete loss of consciousness occurring due to haemodynamic collapse (usually asystole as a result of severe cardioinhibition or primary BP drop as a result of a form of vasodepression or mixed with some cardioinhibition) which appears to be close to the observed collapse on implantable loop recorder (Moya et al., 2001) has prompted many syncope specialists to adopt this as standard testing. It will be recalled that the original report on clinical diagnostic tilt testing required exactly this induction of syncope (Anne Kenny et al., 1986). There may be circumstances when induction of syncope is not absolutely necessary, for example, when the diagnosis is clear to the caring physician but a test is being performed to 'teach' the patient about warning symptoms (Sutton et al., 2021).

In daily practice, some tests are conducted only to presyncope which fail to demonstrate the extent and severity of the cardioinhibitory and vasodepressor components of the reflex. From its clinical origins, TTT was intended to reproduce the patient's syncope. If this is not done much important clinically valuable information will be missing. TTT is always prolonged beyond the decision moment to stop the test by the tilt-down time which must be short <12 s as stated above in the equipment section. (Zyśko et al., 2016)

The original VASIS classification of positive tilt tests, without full detail, was (Sutton et al., 1992):

1. Class 1: Mixed with both HR and BP fall.
2. Class 2A: Pronounced HR fall but not asystole, associated BP fall.
3. Class 2B: HR fall to asystole, associated BP fall.
4. Class 3: BP fall with minimal but not zero HR fall.

This classification was clarified in 2000 (Bartoletti et al., 2000; Brignole et al., 2000) and focused on HR behaviour, assuming that a significant fall in BP is a necessary prerequisite for syncope:

1. Type 1 mixed: Fall in HR but not below 40 beats per minute (bpm) or below 40 bpm but for less than 10 s.
2. Type 2A: Fall in HR below 40 bpm with duration over 10 s but without asystole.
3. Type 2B: Fall in HR leading to asystole >3 s with fall in BP that precedes or occurs simultaneously with asystole.
4. Type 3 vasodepressor: Fall in HR not more than 10%.

If VASIS is used as a summary of the interpretation, the latter is the one to employ. However, a detailed description of the findings is always superior and sufficient without the use of VASIS.

The interpreter is required to examine every detail of the recording from beginning to end. A detailed report should note the HR and BP in the supine period before tilt and note if oscillation of BP is present which is very predictive of a positive outcome (Hausenloy et al., 2009).

Of course, tilt-up will cause haemodynamic change in almost all individuals. The expected change is a rise in both HR and BP which is normal (Petersen et al., 2000).

4.1 | Reflex syncope

VVS may be preceded by BP oscillation (Hausenloy et al., 2009). BP fall never occurs in the first 3 min of tilt in VVS. Typical VVS occurs at about 23 min of passive tilt (Fitzpatrick & Sutton, 1989). The 'Italian protocol' for tilt (Bartoletti et al., 2000), which is the most widely applied, allows more than 20 min by administering sublingual NTG 300–400 mcg at 20 min of tilt, as mentioned before. VVS commences its collapse with HR fall (cardioinhibition) which occurs relatively rapidly compared with the slow development of BP fall over the preceding ~8 min (van Dijk et al., 2020, 2022).

The behaviour of VVS is, thus, characteristic. The difficulty arises in distinguishing VVS from dOH as their timing of onset and initial onset overlap. However, the critical discrimination factor is a fall in HR or cardioinhibition, plus characteristics of the fall and form of recovery (Ghariq et al., 2021).

Treatment approaches for patients with reflex syncope are listed in Figure 5.

4.2 | OH

OH can be studied by TTT but is more often screened at the bedside. The consensus on diagnostic criteria for cOH is a fall in systolic BP by 20 and/or 10 mmHg in diastolic BP on adopting the erect position (Fedorowski et al., 2022; Freeman et al., 2011; Ricci et al., 2015). Early symptomatic fall in BP indicates immediate/iOH followed by quick (<15 s) recovery (van Wijnen et al., 2016) which is common in the young and over fasted. This may be the only finding but it reveals the diagnosis. Immediate OH is better demonstrated in the AST but beat-to-beat BP is mandatory, as manual BP measurement takes about 40 s which could easily miss

Reflex Syncope	Orthostatic hypotension (tailored approach)	POTS (tailored approach)	PPS
- Patients must lie down if they feel symptoms of syncope coming on. If this is not possible, sit down and make counter-pressure manoeuvres such as squatting. ○ Counter-pressure manoeuvres are tensing large muscles in the body like pressing the buttocks together and straightening the knees forcefully or making fists and tensing arm muscles or crossing legs and pressing them together (Figure 2) - Drink at least 2L of fluid per day - Do not use salt sparingly unless BP is raised - Inform associates what to do during a spell e.g., raise legs high. - Invasive treatments (pacemaker implantation or cardioneuroablation) are reserved for very symptomatic 'often older' patients who have followed all of the above and remain symptomatic.	- Early recognition and avoidance of triggering events - Medication review (Midodrine/Droxidopa reduce hypotensive) - Counter-pressure manoeuvres - Drink at least 2L of fluid per day ○ Start the day with 500ml fluid ○ Bolus water drinking (500ml ingested in 2–3 min) elicits, within 5 to 10 min, an increase in BP - Mediated by the sympathetic nervous system: this effect lasts for 30–45 min. - Eating frequent small meals and decreasing alcohol intake - Increasing dietary salt intake unless hypertension, heart failure or kidney failure are present - Avoidance of physical deconditioning - Minimizing orthostatic stress in provoking situations - Slower changes of posture - Avoid the supine position during the dvay - Sleep with the head of the bed raised at night by 25cm. This requires attention to the foot end of the bed to be sure that the patient does not slip off the bed during the night. - Putting a chair in the shower room to allow a sitting position - Compression stockings - Start medication (only patients with severe orthostatic hypotension, who remain symptomatic and the treatment above has no benefit).	- Compression stockings or abdominal binders (waist high compression garments) - Strength training of lower extremities to promote skeletal muscle increase - Counter-pressure manoeuvres (Figure 2) - Similar measures to those in OH - Pharmacological (Midodrine, Droxidopa) - Augmenting plasma volume with 3 months of exercise training, mild-moderate intensity endurance training 3-5 times per week at 30-45 min, at first in supine or sitting position - Drink more than 2L per day (often 3L per day is advised) - Salt 5mg/d (2 teaspoons per day - Withdrawing medications that worsen POTS (e.g., SSRIs and SNRIs) - Pharmacological: ○ If standing HR very high (propranolol 10-20mg 4 times a day ○ If standing HR very high and B-blocker is contraindicated (Ivabradine 5mg 2 times per day ○ If standing HR is not too high and BP is low (Midodrine 5mg orally every 4 hours, 3 times per day (8am, noon, 4 pm)	- Professional psychotherapy (cognitive behavioral therapy) - Go through the description of the events with the patient and caregiver - Explaining the condition for the patient and relatives with its uncontrolled character (patient is not "faking" syncope and cannot control the attacks) - Console the patient in case there is a cluster of attacks - Inform others who may witness the attack about its character, so they know beforehand what to do - Inform the healthcare workers about the condition, to avoid unnecessary examinations and anxiety. - There is not a medical emergency, the attacks will pass by themselves (the heart and brain are not at risk). If the patient has not been injured, there is no need to call a doctor or ambulance.
(Brignole et al., 2018b; Wieling et al., 2022)		*(Mar & Raj, 2020; Raj et al., 2022)*	*(Alciati et al., 2020; Brignole et al., 2018b)*

FIGURE 5 Overview of the different treatment options. BP, blood pressure; HR, heart rate; OH, orthostatic hypotension; POTS, postural orthostatic tachycardia syndrome; PPS, psychogenic pseudosyncope; SNRI, serotonin-norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor.

the iOH event. In cOH BP starts falling within the first minute of tilt and continues, HR rises or remains stable (Brignole et al., 2018a, 2018b). In dOH, BP starts to fall later, at a variable time, after 3 min of tilt is usually quoted. It is accompanied by an HR rise although perhaps not fully compensatory; this is not an HR fall as should this occur the likely cause is vasovagal. Some investigators prefer to employ the AST with beat-to-beat BP as an alternative to TTT in all cases of OH but this policy has its limitations when there is, for example, dOH. In interpreting the results of TTT for OH, one might consider the fact that systolic BP drop is often sufficient for the diagnosis, and analysis of diastolic components rarely leads to reclassification or clinically significant conclusions (Fedorowski et al., 2017).

Tailored treatment approaches for OH are listed in Figure 5 for patients with OH.

Residual problems occur where VVS has a mixed pattern with only slight cardioinhibition. It must be accepted currently that a few cases will be left with an unclear diagnosis (Fedorowski et al., 2017). Many experts will be inclined to attribute the diagnosis to VVS because dOH is considered to be quite rare, although the proportion of cOH and dOH seems to be equal (Torabi et al., 2020). These remarks emphasize the attention to detail required in tilt result interpretation. One centre has suggested that TTT could be prolonged >35 min in cases where the history implies such a need (Gibbons et al., 2017). It is also necessary to assess a 'normal' fall in BP caused by NTG and separate this from dOH. Again, an HR rise is expected with the 'normal' BP fall. If it is absent, thought should turn to dOH.

As all forms of OH fluctuate in severity, a single negative test without BP decline meeting standard criteria may not be conclusive in the context of the history being suggestive of OH. Moreover, there might be variations in compensatory mechanisms depending on the level of hydration, use of cardiovascular drugs and concomitant conditions.

4.3 | False positive and false negative tests

False positives have been suggested in the use of NTG in TTT but evidence (Brignole et al., 2000) from close observation is against this, as similar haemodynamic changes are found in nonsyncopal patients. The mechanism is simply haemodynamic thereby further decreasing venous return which may be the trigger for VVS but also the compensatory tachycardia may be the trigger against a background of low cardiac volume.

False negative tests undoubtedly occur (Hausenloy et al., 2009). Repeat testing can reveal this but is not usually necessary. If the patient's history strongly points toward reflex syncope. This can be assumed to be the aetiology. In such cases, the reflex may be milder than when it presents during TTT.

4.4 | POTS

POTS can be diagnosed by other methods than TTT. Both a simple stand test or a more formal AST with beat-to-beat BP are more likely to be selected than TTT. However, when there is a history of syncope, TTT should be preferred to give a clear understanding of what happens to the patient. The standard criteria for diagnosis are an HR rise of 30 bpm within 10 min. of becoming erect without a fall in BP but with symptoms of orthostatic intolerance (Brignole et al., 2018a; Johansson et al., 2019; Low et al., 1995).

If there is a history of syncope, TTT should be performed using a standard protocol (Bartoletti et al., 2000). We give preference to the 'Italian protocol'. Tailored treatment approaches for patients with POTS are listed in Figure 5.

4.5 | PPS

PPS is best investigated by TTT notably with accompanying video (Brignole et al., 2018a; de Lange et al., 2023; van Wijnen et al., 2016). Neurologists will use an EEG probably also with video. A positive test is recorded when the patient appears to lose consciousness with a small rise in HR (up to about 15%) accompanied by a small rise in BP. The head flop will either be different with a seemingly active movement (unlike the passive head flop of true syncope) or most likely there will be none. Occasionally, there may be excessive movements which are unlike epilepsy termed psychogenic non-epileptic seizure. This is much more likely to present to a neurologist. In PPS, attacks usually last longer than syncope, the eyes are typically closed (open in syncope), and there are no colour changes or other autonomic changes, such as sweating. If an EEG is recorded in PPS, the findings will be close to normal and very different from the slow-flat-slow wave pattern in syncope. The combination of mild haemodynamic changes, eyes closed and no EEG change makes the diagnosis of PPS. Many cardiologists will be willing to accept video evidence as an alternative to EEG.

5 | CONCLUSIONS

Tit testing remains a valuable asset to those concerned with diagnosing and treating patients with unexplained syncope, orthostatic intolerance and related conditions. Another review without the practical details contained here is available for further study if needed (Sutton et al., 2021).

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The authors would like to thank the woman in Figure 3 for her informed consent for publication. In Figure 3, the authors used a Finapres Nova® from Finapres Medical Systems to give an overview of the tilt table test. In the computer, we use the Open Broadcaster Software (OBS®) to view the video of the camera beside the outcome in the Finapres Nova®.

CONFLICTS OF INTEREST STATEMENT

Artur Fedorowski: Consultancy fees: Medtronic Inc. (syncope), ArgenX BV and Antag (POTS and Long COVID) and lecture fees: Medtronic Inc. (syncope), BMS (syncope) and Finapres Medical Systems (syncope and POTS). Frederik J. de Lange: Reports speakers/consultancy fees from Biotronik, Medtronic and St. Jude Medical. The remaining authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

No datasets were generated or analysed during this review. Review publication in open access.

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