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Head Up Tilt Testing: An Appraisal of Its Current Role in the Management of Patients with Syncope

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Abstract

Head up tilt testing (HTT) is now commonly used to investigate otherwise unexplained syncope and presyncope. This test has been used for over 20 years primarily to diagnose neurally mediated syncope, but HTT's exact role in the diagnostic process remains uncertain. Recognized limitations include poor reproducibility, lack of prognostic role, and insufficient randomized studies to guide therapeutic choice. In this review, we describe the indications and methods recommended by present guidelines on utilizing HTT. In addition, present criticisms and limitations of this test, along with future perspectives, are outlined.

Introduction

ASyncope is a common problem, accounting for up to 6% of emergency room visits and 3% of hospital admissions.[1, 2] The causes of syncope are varied, ranging from potentially fatal arrhythmia to the common, relatively benign syndrome of neurally mediated syncope.[3] The varied significance of this syndrome coupled with the transient nature of symptoms gives rise to major questions on how best to evaluate a patient with syncope. In order to evaluate the possible role of arrhythmia, long term monitoring is frequently employed. However, symptoms occur infrequently, and the small but significant possibility of a fatal event being associated with the next time symptoms occur limit the usefulness of monitoring. Since neurally mediated mechanisms are the most common cause of syncope, a popular approach is to perform head up tilt testing (HTT). With HTT, if the patient's exact symptoms complex, including prodrome and the loss of consciousness is reproduced, the value of such a positive test is obvious.[4, 5]

In 1986, Kenny et al described for the first time the utility of HTT for investigating patients presenting with syncope of a probable vasovagal origin.[6] They observed that the exposure to 60 degree tilting for 60 minutes would trigger a vasovagal reflex in 66% of patients with unexplained syncope. Since then, shorter protocols have been tested with and without drugs with the purpose of improving the sensitivity, specificity, and ease of conducting the test.

Recently, this test has been target of many critics regarding its low sensitivity and variable specificity rates reported in different studies.[7, 8] Furthermore, the reproducibility of positive results seems

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to be low and the therapeutic implications are not well-defined. In this review, we will address the HTT indications, currently used methodology and upcoming protocols, interpretation of results, pitfalls, and clinical implications of the test.

Indications

While the 2006 American Statement of Syncope did not recommend HTT for syncope investigation, this document, as discussed below, has been criticized.[9,10] In current clinical practice, the indications advocated by the 2009 Guidelines for the Diagnosis and Management of Syncope, published by the European Society of Cardiology (ESC), are often used.[5] These guidelines recommend that HTT should be used as a diagnostic tool in the following situations:

Class I recommendations:

In young adults without evident or suspected heart disease presenting with recurrent unexplained syncopes when the history is not sufficiently typical of neurally mediated syncope;
• In cases of an isolated episode of unexplained syncope when it happens in a high risk setting or when it has occupational implications;
• In cases of recurrent syncopal episodes in the absence of structural heart disease, or if the patient has a diagnosed cardiac disease, and cardiac causes for the syncope have been already excluded;
• When the demonstration of susceptibility to neurally mediated syncope is clinically relevant.

Class II recommendations:

• For differentiating reflex syncope from delayed orthostatic hypotension;
• For the differential diagnosis of convulsive syncope;
• For evaluating patients with recurrent unexplained falls;
• For investigating recurrent syncopal episodes in patients with psychiatric diseases.

In accordance to these guidelines, HTT has not been recommended for assessing treatment efficacy nor for performing the test in patients with a typical clinical history of vasovagal syncope when the clinical diagnosis is sufficient and independent of the HTT result. Nevertheless, in some cases the correlation between spontaneous symptoms and the induced manifestations during HTT can be helpful for counseling patients and improving treatment adherence.

The aforementioned guidelines also affirm that whenever HTT is indicated and no heart disease is suspected, a positive result with the reproduction of the spontaneous syncope is enough to diagnose a neurally mediated syndrome. A practical diagnostic flow diagram is shown (Figure 1).

The evolution of the protocol

EBefore describing the different available protocols, some terms have to be defined. In previous studies, the use of "sensitivity" and "positivity" brought up some confusion because of the absence of a gold-standard test to diagnose vasovagal syndrome. When considering the clinical diagnosis as the gold-standard test, the term "sensitivity" can be correctly used and means the capability of identifying the sick patients in this diagnosed population. When HTT is done in patients with unexplained syncope, the term "positivity" or "positive result" is often used. However, for this review, the term "sensitivity" was standardized to facilitate the description and comparison of studies, although one should recognize that it may mean "positivity" in some situations. Although utilizing the clinical diagnosis as a gold-standard is subject to criticism due to the subjectivity inherent to human judgment, there is no other method proven to have better accuracy in this situation.

Passive tilting, a prolonged tilt duration without any provocative drugs, was first recommended. In five studies that evaluated the exposure to passive orthostasis in the tilt table for at least 40 minutes, the observed sensitivity rates were 13%, 25%, 31%, 35% and 75% (median of 31%).11-14 In contrast to the low sensitivity, the specificity rates were 100%, 100%, 95%, 92% and 89%, respectively (mean of 95%).

In order to augment the diagnostic accuracy of HTT, various provocative drugs to raise sensitivity have been tested. After a negative passive phase, a drug is administered to potentiate the ap-

pearance of a vasovagal reflex. For this purpose, nitroglycerin and isoproterenol are the most commonly used drugs in the current practice. In a variety of studies, the observed sensitivity while utilizing nitrates is between 57.5% and 87% and the specificity is between 70% and 100%.[11, 13, 15-17] Similarly, the rates while utilizing isoproterenol are between 42% and 69% and between 70% and 90 %, respectively. Nitrates have been used less due to the need for a venous access and the side effects, which can be serious in patients with ischemic cardiomyopathy.[18]

Initially, nitrates were used in the form of intravenous nitroglycerin, when it was associated with a sensitivity of 53% and a specificity of 92% in the potentiated phase.19 Subsequently, the effect of a sublingual nitroglycerine was evaluated.12 A passive phase of 45 minutes was tested and, if no positive results were elicited, 300 µg of sublingual nitroglycerin was administered. A low sensitivity (25%) and high specificity (100%) in the passive phase was encountered. On the other hand, the drug challenge allowed a positive response in 26% of the patient group and 6% of the control group, resulting in a final specificity of 94%. Comparable

Table 1 Methodology and results in different studies using a drug-sensitized head-up tilt testing.

Authors	N	Tilt angle	Drug	Passive Phase	Sensitized phase (min)	Sensitivity (%)	Specificity (%) p-value	Accuracy (%)
Raviele et	235	60º	NTG 300 µg	45	20	51(65)	94	56(67)
Aerts et al 1997	32	70º	ISDN 5mg	45	15	87	70	81
Del Rosso et al 1998	202	60º	NTG 400 µg	20	25	70(74)	94(82) `	81(83)
Ammirati et al 1998	73	60º	ISDN 1,25mg	30	15	57(71)	57(71)	NA
Aerts et al 2005	38	70º	NTG 400 µg	-	30	82	84	83
Oraii et al 1999	65	70º	GTN 400µg ISOP 1-4µg	45	20 10-40	71 69	85 90	NA
Hermosillo et al 2000	120	70º	ISDN 5mg ISOP 4µg	30 30	12 10	83 51	88 70	84 71
Nava et al 2004	128	70º	NTG 400 µg ISOP 1-3µg	15 30	15 20	60,9 42,2	NA NA	NA NA

N= sample size; NTG= nitroglycerin. ISDN= isosorbide dinitrate; GTN= glyceryl trinitrate; ISOP= isoproterenol; NA= non-available

data was presented in other studies in the following years.[11, 17, 20] A summary of drug-potentiated HTT protocols is shown is Table 1.

The 2004 ESC Guidelines on Management of Syncope included an analysis of studies which included 20 or 45 minutes of a passive phase, followed by administration of nitrate.[2] It showed that the sensitivity was not significantly reduced with the shorter passive phase (69% versus 62%), and there was no specificity loss (94%). Since those guidelines were published, it has been recommended that HTT should be performed with at least 20 minutes of a passive phase and 20 minutes after a drug challenge (nitroglycerin or isoproterenol). Furthermore, the 2009 ESC Guidelines suggest that for older patients, the passive phase could be suppressed to improve compliance.5 Increasing sensitivity for the test by using nitrate reproduces the same vasovagal responses as those elicited by the passive tilting: mixed, cardioinhibitory and vasodepressor.[21] Nevertheless, the mechanism by which nitrate induces vasovagal reflex in not well understood yet. The hypotheses are 1) vasodilatation; 2) fall in cardiac output; 3) sympathetic inhibition and increased vagal activation; 4) direct effect on the central nervous system (CNS); and 5) effect on the CNS via neurohormone.[21-25]

Current Recommended Methodology

HTT should be done in a quiet room with dim lights and comfortable temperature. The test is performed by a nurse and/or by a physician, but the presence of two professionals in the room enables a better monitorization. The room should have cardiopulmonary resuscitation equipment, although its use is rarely necessary. It is not recommended that a patient's family member watch the testing.[26]

The patient should fast for four hours prior to the test and must be in the supine position, resting for at least five minutes immediately before tilting. If there is a need for venous access, for example if isoproterenol will be administered, the resting period should be increased to 20 minutes.[5]

and blood pressure (BP) monitoring. The best method for BP measure is the continuous beat-to-beat finger arterial BP measurement, but this is not widely available. In such situations, manual intermittent measures using a sphygmomanometer are acceptable and should be performed within short intervals, especially when the patient is presenting pre-syncope symptoms (Figure 2).

For patients above 40 years old presenting with syncope, it is recommended that a carotid sinus massage should be performed during tilt. It has been demonstrated that the orthostasis allows a higher sensitivity to that technique, and there is also the opportunity to evaluate the vasodepressor component.[28]

Responses to HTT

Table 2 Classification of the positive responses during the head-up tilt testing.

Type 1 or mixed	Fall in HR during syncope, without reaching 40bpm. If the HR falls under 40bpm, it lasts less then 10 seconds. The BP falls before the HR does.
Type 2A or cardioinhibitory without asystole	The HR falls to bellow 40bpm for more than 10 seconds. The BP falls before the HR does.
Type 2B or cardioinhibitory with asystole	Occurrence of asystole that lasts more than 3 seconds. The BP falls occurs before or during the fall in HR.
Type 3 or vasodepressor	Fall in BP. There is an increase in HR or a fall that does not exceed 10% of the peak HR.
Exception 1- chronotropic incompetence	No significant increase in HR after tilting (i.e., less the 10% of the baseline HR)
Exception 2 – Postural Tachycardia Syndrome (POTS) .	Excessive increase in HR (i.e., to above 130 bpm) from the beginning and throughout the tilting until the occurrence of syncope

Different practical guidelines characterize a positive vasovagal response when there is reproduction of the spontaneous symptoms associated with hemodynamic collapse.[5, 26] In this context, there is some debate whether the test can be aborted before the occurrence of syncope. Many studies advocate that HTT can be interrupted when syncope seems to be imminent – the presyncopal period – and that there is no justification for submitting the patient to extended discomfort when the hypotension and/or bradycardia are sufficient to classify a vasovagal response.[2, 29, 30] Subsequently, most recent studies consider as positivity criteria the induction of syncope or presyncope associated with hypotension and/or bradycardia.[15, 16, 29, 31]

The modified VASIS classification (Vasovagal Syncope International Study) is the most often used to characterize HTT responses, which are a) type 1 or mixed; b) type 2A or cardioinhibitory without asystole; c) type 2B or cardioinhibitory with asystole; and d) type 3 or vasodepressor (Table 2, Figure 3).[32] Otherwise, the type response to HTT does not necessarily reproduce the spontaneous pattern, according to studies that used the loop recorder.33, 34 The finding of a mixed or vasodepressor type does not exclude the occurrence of a cardioinhibitory response during spontaneous syncope. Therefore, there is no evidence that the hemodynamic pattern at HTT should guide treatment.

Other diagnoses obtained through HTT

Besides the vasovagal response, HTT enables the diagnosis of different forms of dysautonomia and orthostatic intolerance. Carotid sinus hypersensitivity is confirmed if, during carotid sinus massage, there is ventricular asystole equal to or greater than 3 seconds or a fall in systolic BP equal to or greater than 50 mmHg.[5] Performing the massage under passive orthostasis increases the diagnostic yield. Half of the diseased pa tients would have been missed if the test was done only in the supine position. In a retrospective study including 1,719 patients, carotid sinus hypersensitivity was diagnosed in 226 patients when the maneuver was performed in the supine position. However, 217 patients were diagnosed only after the maneuver was repeated in the tilted position.[28] Furthermore, the continuous BP monitoring during HTT enables the evaluation of the vasodepressor component which is essential for diagnosing the majority of cases in which there is concomitant fall in heart rate (HR) and in BP, or mixed response.

Another potential diagnostic finding is Postural Tachycardia Syndrome (POTS), characterized by palpitations, dizziness, and presyncope related to orthostasis. HTT is important to confirm this diagnosis, which is made by the reproduction of symptoms associated with an increase in HR of at least 30 bpm, reaching at least 120 bpm, maintained during orthostatic exposure.[35] On the other extreme, there is also chronotropic incompetence, defined as the inability to increase the HR during tilt, i.e. when there is no increment or it is less than 10% of the baseline HR.[32] This diagnosis cannot be made if the patient is on negative chronotropic drugs.

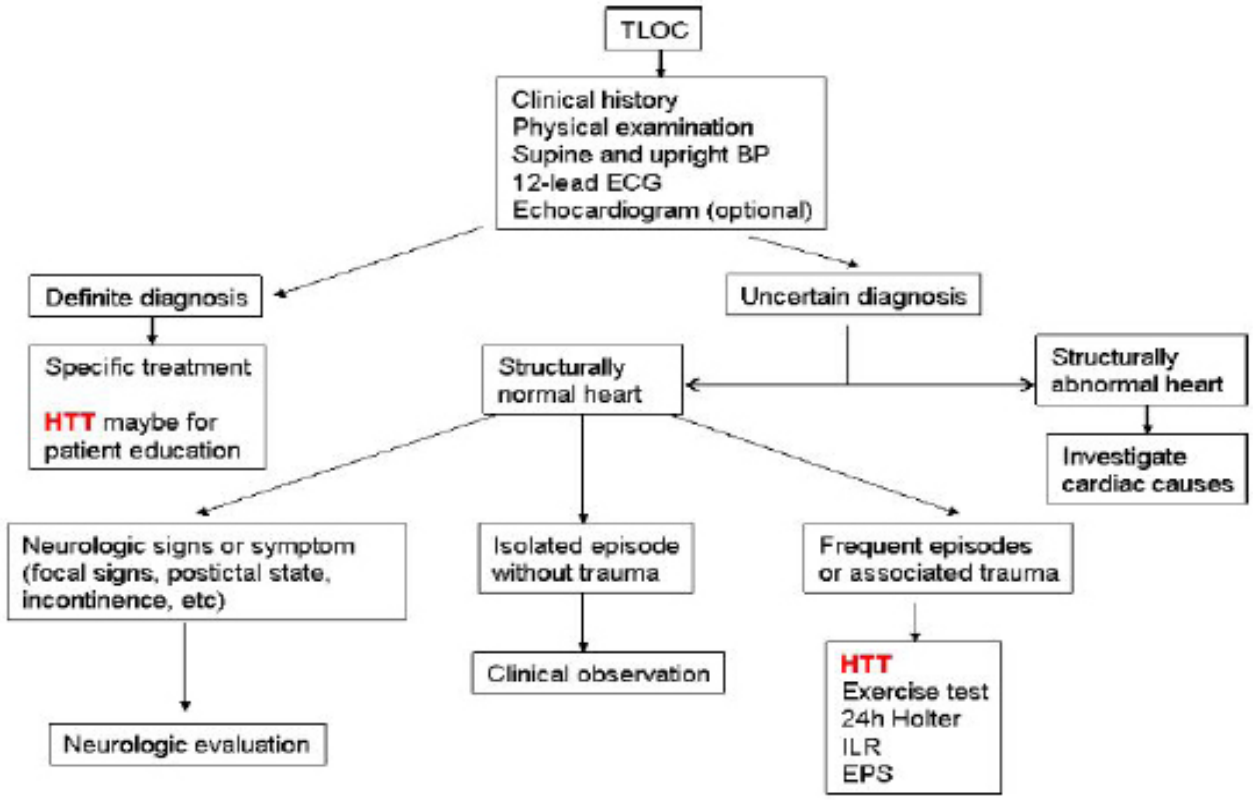
HTT can also reveal another form of orthostatic intolerance called dysautonomic response. There is a slow and progressive fall in systolic BP to less than 80 mmHg, without a fall in HR, accompanied by symptoms of arterial hypotension, such as sweating, dizziness, and blurred vision.[32] The manifestations last at least five minutes without syncope, and then the test should be stopped.

The primary autonomic nervous system disorders, such as pure autonomic failure, Shy-Drager Syndrome and multisystem atrophy, or the secondary autonomic insufficiencies associated with diabetes mellitus or amyloidoses, for example, can be evaluated by HTT as well.[36] They are characterized by supine hypertension and orthostatic hypotension. Depending on the magnitude of the autonomic impairment, orthostatic hypotension can also be associated with insufficient HR increase.

When is HTT most helpful?

NBecause HTT is able to reproduce the patient's symptoms while simultaneously inducing hemodynamic alterations in a laboratory, it has been used to confirm the diagnosis of VVS for more than 20 years. It is indicated in the investigation of

Figure 1: Flow diagram for differential diagnosis of patients with transient loss of consciousness (TLOC)



This algorithm shows when HTT is most useful and it is not intended to encompass every TLOC etiologies. ILR= implantable loop recorder; EPS= electrophysiologic study.

unexplained syncopes, presyncope, dizziness, unexplained falls, and repeated seizures. Although patients with syncope and no cardiac disorders have a good prognosis, many of them are troubled by the absence of a definite diagnosis, and this anxiety can in turn result in recurrent symptoms. Therefore, a positive HTT response can be reassuring and help in treatment compliance. It also has a role in educating patients to recognize the prodrome symptoms, which enables them to perform specific maneuvers in time to avoid fainting. Guida et al showed that was no difference between the premonitory symptoms elicited by HTT or by the spontaneous episode.[37] Moreover, they analyzed the length of the period between the appearance of each symptom and the occurrence of syncope. These analyses could be very useful in counseling the patient and improving his awareness of imminent syncope.

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Also HTT is important in the investigation of abrupt syncope after a cardiac cause has been excluded. The test can reproduce the syncope without prodromes, either because the patient is insensitive to the fall in BP or HR, or because the hemodynamic collapse develops too fast.

VVS is responsible for less than 35% of syncopal events in elderly people, as opposed to 68% in patients under 40 years old.[38, 39] In older patients, it is especially important to rule out a cardiac cause before performing HTT. After a negative cardiac evaluation, tilt testing can reveal diagnoses like VVS, orthostatic hypotension and carotid sinus hypersensitivity. The latter accounts for 20% of syncopal events in the elderly, and HTT increases the chance of identifying a positive response.[40] Especially in this population, the correct diagnosis and early appropriate treatment can possibly prevent falls and consequent complications, such as fractures and subdural intracranial hematoma.

HTT is also very useful to differentiate between convulsive syncope and epilepsy.[41] During tilting, the spontaneous prodrome symptoms and seizures can be reproduced and, if associated with a typical vasovagal reflex, supports the diagnosis of VVS with convulsive fainting. The disabling diagnosis of epilepsy can be cleared, and the anti-convulsive drugs and all their associated side effects can be discontinued.

It may be possible to characterize psychogenic syncope during HTT when the patient faints without any concomitant hemodynamic alteration.[42] Other diagnoses, such as orthostatic intolerance and POTS can also be confirmed by the tilt testing.

Complications

HTT is a safe test if performed as recommended and after exclusion of cardiac causes of syncope when necessary. Importantly, before ordering the test, physicians should obtain a detailed clinical history regarding the syncopal event and other symptoms, and whenever a cardiac cause is suspected specific investigation should proceed.[43] Leman et al reported an occurrence of ventricular fibrillation during HTT while using isoproterenol at 5 μg/kg/min.[18] The patient was 80 years old, had past myocardial infarction, and was being investigated for a syncopal event. No echocardiogram or ischemic test had been performed previously to HTT. After successful defibrillation, a coronary angiogram was done and revealed 99% obstruction within the circumflex coronary artery.

Figure 2: Tilt table test with a footboard and upper limb supports. The velcro strips are used to restrict the patient in case there is a lost in postural tone. Other necessary equipment is (from right to left): beat-to-beat non-invasive blood pressure monitoring and monitors to view ECG and BP tracings

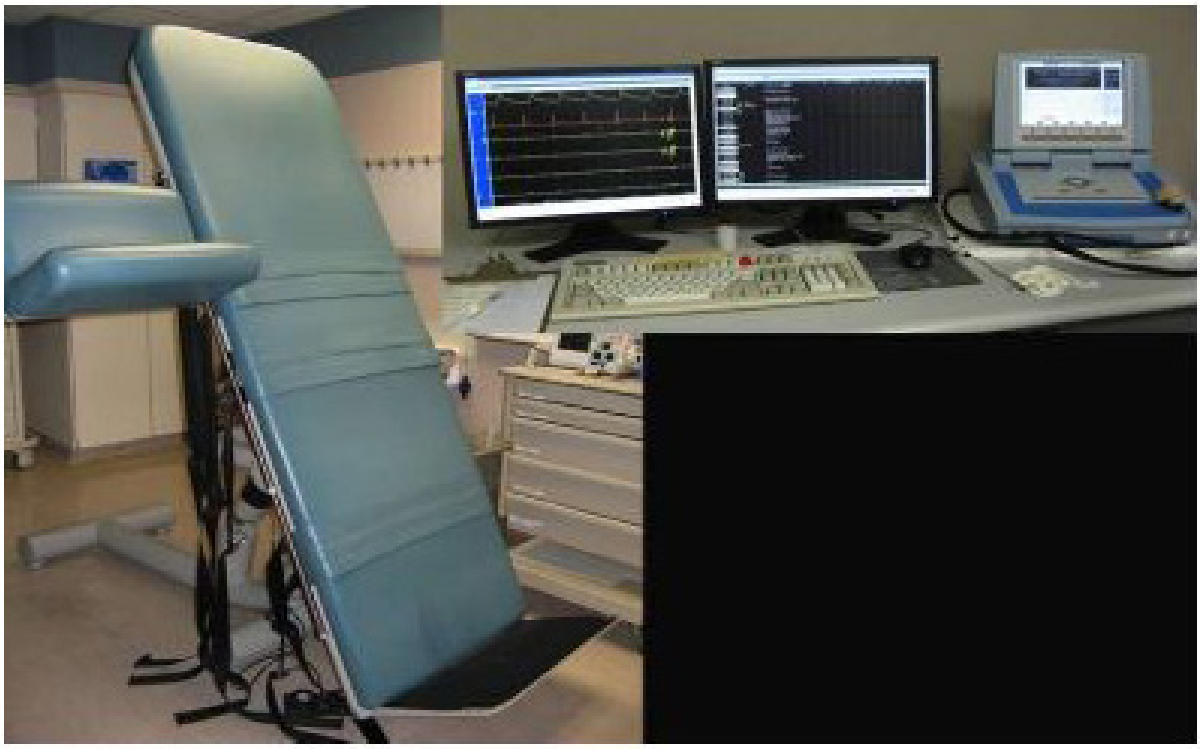

Figure 3: Efficacy comparison among the studied drugs

A= Cardioinhibitory with normal carotid sinus massage; B= POTS; C= Mixed or type 1 vasovagal response; D= Vasodepressor or type 3 vasovagal response

Otherwise, a British study which included 1,969 patients older than 60 years, 44% of which older than 75 years, who were exposed to passive tilting with or without nitrate challenge attested to HTT safety.[44] Only one patient presented atrial fibrillation after 26 minutes of passive orthostasis, the only reported cardiovascular event, and no neurologic events were observed. Another study done in Spain did not demonstrate any complication related to the performance of 1,219 tests, with both young and elderly patients, in which the isoproterenol was used when necessary.[45] It is not uncommon to observe a prolonged asystole as a result of the vasovagal reflex induced by HTT. However, in most of the cases the return to a supine or to a Trendelenburg position is sufficient for recovery of hemodynamic conditions and consciousness, and rarely are resuscitation maneuvers needed.

Previously, an asystole of 73 seconds was reported, which was reverted with cardiac massage and atropine, without any sequelae after the test.[46] The observed pauses usually last less than 30 seconds; longer pauses are not considered complications but exaggerated responses.

Limitations

Because HTT allows the reproduction of the patient's symptoms simultaneously to induction of

fore administering the potentiating drug, the passive phase lasts longer than 30 minutes. Protocols consisting of a shorter passive phase, or even an absent passive phase, followed by nitrate or isoproterenol challenge are associated with specificities from 84% to 97% ,[20, 31, 48] while protocols with prolonged passive phases show specificities from 48% to 70%.[11, 13, 17] Indeed, limiting the total duration of the test seems to guarantee a good specificity.

Finally, if one considers that the use of drugs increases HTT sensitivity significantly and that the loss in specificity is acceptable, the potentiated protocol is the most appropriate to clinical practice.

Use of HTT for evaluating prognosis:

Some studies have been done in order to analyze the capability of HTT results to predict clinical outcomes. Hachul et al described that, after initiating treatment for VVS, a negative HTT result was associated with a lower rate of symptom recurrence compared to a positive result (4.9% versus 52.4% in 12 months, $p< 0.0001$).[49] Bastos et al assessed the utility of this test to predict the recurrence of syncope after suspending medication, and observed that 84% of patients with a positive HTT post-treatment would present with symptoms within 12 months.[50] Furthermore, the mean time of first recurrence was significantly lower in patients with a positive result.

Some studies concluded otherwise. In the ISSUE-2 study, patients with suspected vasovagal syncope received an implantable loop recorder and also performed HTT. It was found that the HTT results were not predictive of syncope recurrence in [12] months of follow-up.[33] In the positive HTT group, the ECG recorded during spontaneous syncope did not correlate with the type of response during tilt testing. However, the loop recorder did not measure BP fall, which limited its capability of detecting the mixed and vasodepressor response. Furthermore, whether vasovagal episodes always occur in the same manner in patient is unknown.

In a recent study, 276 patients with a clinical diagnosis of VVS were followed for two years.[51] HTT was positive in 37% of patients. The predictive factors of syncope recurrence were the number

hemodynamic alterations in laboratory, it has been used to confirm the diagnosis of VVS for more than 20 years. It is also indicated in the investigation of unexplained syncopes, presyncopes, dizziness, unexplained falls, and repeated seizures.

In 2006, the American Society of Cardiology published a statement in which it was suggested that HTT would have poor utility for investigating syncope.9 The criticisms were regarding its sensitivity, specificity, accuracy, and reproducibility.

However, few references were included in that document and even the European guidelines were not mentioned. Later, the Ad Hoc Syncope Consortium affirmed that the statement was incomplete, enabled only partial evaluation of the disease context, and had missed some important and updated documents, including the European guidelines.[10]

Other studies also question the test's value.[7, 8] Regarding the sensitivity and specificity, some consider the results too diverse depending on the protocol used, such as the angle of tilting, passive phase duration, use of potentiating drugs, and the characteristics of the studied sample. Indeed the wide range of results is explained by the comparison of very different protocols, which led the scientific community to standardize methodology in the 2004 European guidelines.

The sensitivity of the passive phase alone is widely variable, but most of the previous studies found that it was low. When this phase lasts between 40 and 45 minutes, the reported sensitivites were 13%, 25%, 31% and 35% in different studies.[11-13, 29] Only when the duration was increased to 60 minutes did the sensitivity rise to 75%, yet the specificity fell to 89%.[14] Otherwise, in the nitrate-potentiated protocols, the sensi tivity varied between 53% and 87%.[11, 13, 15-17, 19, 29]

Petkar and Fitzpatrick criticized the low specificity when HTT was done with administration of an inducing drug,7 describing one study that encountered 55% of false positives when the test was potentiated with isoproterenol.[47] However, the angle used in this protocol was 80 degrees, which certainly reduces the specificity, and therefore is not recommended. Moreover, recent studies indicate there is a significant loss of specificity when, be-

of previous syncopal events, female gender, and bronchial asthma. HTT response had no predictive value.

In conclusion, based on current scientific evidence, the HTT result does not seem useful in the prognostic evaluation of patients with syncope.

HTT for evaluating the response to treatment

Regarding the use of HTT to evaluate the response to therapy, the main problem is the absence of an established and efficacious treatment for VVS. In this context, the selection of patients with a positive HTT in a study to analyze the effect of metoprolol has been used to justify the failure of that medication.[52] However, a randomized and controlled study with another beta blocker, atenolol, also did not show a reduction in symptom burden, despite the fact that the patients were selected by clinical history of VVS independent of HTT results.[53]

Again, the unsuccessful outcomes of pacemaker implantation in this population have been attributed to the selection of patients with bradycardia in HTT.[7, 54] An ongoing study is evaluating the role of pacing in vasovagal patients who presented significant asystolic pauses during a loop recording.[55] So far, this therapy has a class IIb recommendation for patients with refractory and abrupt syncopal episodes.[5]

In order to analyze the usefulness of HTT in evaluating therapy success, the efficacy of treatment has to be proven first. The clinical outcome will probably be a better parameter than the HTT result itself.

Future Trends and Perspectives

In order to improve the specificity of HTT and patients' tolerance to the test, shorter pro tocols have been studied. Reducing the passive phase duration or even abolishing it has been tested, but the results are controversial.

In patients with unexplained syncope, Bartoletti et al compared the outcomes of passive tilting for 45 minutes versus a passive phase of only five minutes followed by a nitrate-potentiated phase.[48] They observed a significantly higher sensitivity with the conventional method (51% versus 35%, p=0.04), suggesting the need for a longer passive phase. Nevertheless, this conclusion is contrary to other studies. Aerts et al assessed nitrate-sensitized HTT preceded by the following passive phases: 45 minutes, 30 minutes, or no passive tilting,56 encountering sensitivities of 87%, 77%, and 76%, respectively, and specificities of 83%, 83%, and 82%, respectively. There was a small difference in the accuracy (78%, 80% and 71%), without statistical significance though. Moreover, in this study, the observed sensitivities were higher than those encountered by Bartoletti et al, probably due to the selection of patients with typical clinical history of VVS.

More recently, Aerts and Dendale analyzed the accuracy of HTT without the passive phase.31 Thirty-eight patients and 30 healthy subjects underwent a HTT potentiated by 400 μg sublingual nitroglycerin, for a maximum duration of 30 minutes. They observed a sensitivity of 82%, specificity of 84% and accuracy of 83%. It was also demonstrated that after 15 minutes of tilting, those results reached a plateau, suggesting that the test could be shorter without a loss of sensitivity. In addition, the observed sensitivity was elevated compared to other studies, which was attributed that to the selection of patients with a high clinical suspicion of VVS.

The frequency of false-positives is lower, although it has been shown that it can reach 15% even when the recommended protocols are used. Clarifying the pathophysiologic mechanisms and the limits between a normal and a pathological response can facilitate interpreting the test.

Other studies are necessary to define the utility of HTT in evaluating prognosis and guiding treatment. Before HTT can be tested as a tool to evaluate the response to a given therapy, the treatment has to be proven efficacious. So far, the randomized and controlled studies have failed to demonstrate efficient medications or pacemaker devices for treating VVS.

Conclusion

HTT continues to be widely used and retains significant utility in the investigation of unexplained syncope. To maximize this test's value in clinical

practice, physicians need to be aware of its limitations and correlate clinical information and other testing data with the HTT results.

Although the test's methodology has been somewhat refined in recent years, false positives, as well as false negatives, are still significant. Further studies with protocol-based variants in test duration and the use of provocative agents may improve accuracy.

The value of the test in educating and reassuring the patient in terms of a likely positive diagnosis of a neurally mediated syndrome is often underappreciated. Further, understanding the predominant hemodynamic or rhythm alteration during the reproduced syndrome may guide treatment.

HTT is a low risk, noninvasive test that, despite limitations, when used in the appropriate clinical context and following established guidelines remains valuable in the management of patients with unexplained syncope.

Abbreviations

i) HTT - Head Up Tilt Testing
ii) HR - Heart Rate
iii) BP - Blood Pressure
iv) VVS - Vasovagal Syncope
v) CNS - Central Nervous System

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