Review

Synthèse

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The fainting patient: value of the head-upright tilt-table test in adult patients with orthostatic intolerance

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Abstract

THE HEAD-UPRIGHT TILT-TABLE (HUT) TEST IS USED primarily for the investigation of orthostatic symptoms. Although this test is frequently the gold standard for the evaluation of neurocardiogenic syncope, dysautonomia and postural orthostatic tachycardia syndrome, there is a debate over its diagnostic value and method. The authors review the physiologic basis of the HUT test, the method, patterns of response, indications and contraindications, and diagnostic validity. Despite its limitations, the HUT test is useful in patients with a variety of clinical manifestations induced by orthostatism. It is most useful in documenting objective measures of orthostatic hypertension that cannot be obtained in a clinical setting.

Syncope, fainting, dizziness, weakness and palpitations occurring in the upright position are not uncommon complaints and are associated with a variety of disorders (Table 1). New tools and concepts have been developed, resulting in the emergence of new diagnoses, such as postural orthostatic tachycardia syndrome (POTS)¹ and neurocardiogenic syncope,² and new scales, such as the composite autonomic scoring scale³ and orthostatic intolerance grading by symptoms.⁴ Modern technology has allowed us to improve sensitivity in detecting dysautonomia. The head-upright tilt-table (HUT) test, over half a century old, has retained a central place in the investigation of syncope of unknown origin,⁵⁻¹⁰ orthostatic intolerance and dysautonomia.^{11,12} However, the test is of debatable value and has been the subject of many articles in the past 10 years. We review the physiologic basis of the HUT test, the method, patterns of response, indications and contraindications, and diagnostic validity.

Physiologic basis

On standing, about 300 to 800 mL of blood is forced downward to the abdominal area and lower extremities.^{8,12} Within seconds of this sudden decrease in venous return, pressure receptors in the heart, lungs, carotid sinus and aortic arch are activated and mediate an increase in sympathetic outflow. Through vasoconstriction of capacitance and arteriolar vessels and through increased heart output, a healthy subject is able to reach orthostatic stabilization in 60 seconds or less. This neurally mediated mechanism is the only one by which we can adapt to the first few minutes of an upright position, and it remains the most important afterward. Orthostatic stress and sympathetic activity have been shown to increase with the angle of HUT testing.^{13–17} Hemodynamic and hormonal data suggest that this stress is exerted mostly between 60° and 90°.^{6,16}

Method

Tilt-table testing examines the neurocardiovascular orthostatic response in a maximally controlled environment. With passive orthostasis, stress is maximized on the sympathetic system by blocking the influence of inferior limb musculoskeletal contractions that could increase venous return. The table angle, duration of tilting and addition of pharmacologic stimulation are all under the examiner's control. The HUT test is a dedicated test in which the orthostatic challenge is much longer than can be allowed in an office setting, the controlled variables of the test maximize its value, and the partly automated setup enables the physician to pay more attention to the patient's symptoms.

Tilt-table testing has 2 main phases. It begins with supine resting for at least 30 minutes. This phase has great importance because it allows stabilization of the cardiovascular system

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and may increase the sensitivity of the test.¹⁸ In the second phase the patient is tilted upright for 30 to 45 minutes, usually at an angle of 60° to 80°. At this angle near-maximal passive orthostatic stress^{6,16} is exerted. A third phase, in which the test is repeated with pharmacologic stimulation, is sometimes used in the investigation of unexplained syncope. Isoproterenol is the most common provocative agent; edrophonium, nitroglycerine, adenosine triphosphate, epinephrine and nitroprusside⁶ have also been used. During the entire procedure the blood pressure and heart rate are measured regularly with an automated device, at least every 3 minutes while the patient is tilted.

Induced hemodynamic patterns

Four patterns can be identified during HUT testing (Fig. 1). The normal response consists of an increase in heart rate of approximately 10 to 15 beats/min, an elevation of diastolic pressure of about 10 mm Hg and little change in systolic pressure¹² (Fig. 1A). Abnormal responses are POTS and orthostatic hypotension. The POTS pattern (Fig. 1B) consists of a sustained increase in heart rate of at least 30 beats/min⁴ or a sustained pulse rate of 120 beats/min.¹⁹ Orthostatic hypotension is defined as a reduction in systolic blood pressure of at least 20 mm Hg or a reduction in diastolic blood pressure of at least 10 mm Hg.20 Neurocardiogenic syncope (Fig. 1C) usually appears as a symptomatic and sudden drop in blood pressure, often after 10 minutes or more of HUT testing and frequently with simultaneous bradycardia.5 An immediate and continuing drop in systolic and diastolic pressure without a significant increase in heart rate signals the presence of dysautonomia (Fig. 1D). A psychogenic reaction relates to symptoms unrelated to changes in heart rate or blood pressure.

Table 1: Principal causes of orthostatic symptoms

Orthostatic hypotension

| Resulting from dysautonomia Central (e.g., multiple system atrophy, Parkinson's disease) Spinal (e.g., transverse myelitis, spinal tumours) Peripheral (e.g., diabetic polyneuropathy, amyloidosis) |
|--|
| Resulting from vasovagal reactions Induced (e.g., pain, carotid hypersensitivity) Spontaneous: neurocardiogenic syncope |
| Resulting from cardiac malfunction Pump failure (e.g., severe chronic heart failure, valvular dysfunction) Arrhythmia (e.g., atrial fibrillation) |
| Resulting from absolute hypovolemia Acute (e.g., hemorrhage, acute dehydration) Chronic (e.g., adrenal insufficiency, salt-losing nephropathy) |
| Resulting from relative hypovolemia Generalized vasodilation (e.g., sepsis, systemic mastocytosis) Local venous pooling (e.g., severe venous insufficiency) |
| Resulting from extrinsic influences Drugs (e.g., antihypertensive drugs, antiparkinsonian drugs) Other (e.g., alcohol, heat) |
| Resulting from deconditioning (e.g., convalescent patients) |
| Postural orthostatic tachycardia syndrome |
| Psychogenic |
| |

Approaches to medical management will clearly be different depending on the response. The dysautonomic patient needs further investigation (e.g., for diabetes mellitus and extrapyramidal disorders), attention being given to attenuating venous pooling in the lower limbs and perhaps raising the blood pressure with drugs.²¹ The patient with neurocardiogenic syncope or POTS may also benefit from β -blockade, if not contraindicated.^{2,4}

Indications

HUT testing can be part of the investigation of any orthostatic symptom, especially in patients with no objective physical findings and no evidence of structural cardiovascular disease. Usually, it is part of the diagnostic algorithm of syncope or presyncope.^{6,9} The indications recommended by the American College of Cardiology⁶ are given in Table 2.

Contraindications and adverse effects

Contraindications to HUT testing are unstable cardio-

Table 2: Tilt-table testing for evaluation of syncope: principal indications

Tilt-table testing is warranted

- Recurrent syncope or single syncopal episode in a high-risk patient. Whether or not the medical history is suggestive of neurally mediated (vasovagal) origin, *and* (1) no evidence of structural cardiovascular disease *or* (2) structural cardiovascular disease is present, but other causes of syncope have been excluded by appropriate testing
- Further evaluation of patients in whom an apparent cause has been established (e.g., asystole, atrioventricular block), but in whom demonstration of susceptibility to neurally mediated syncope would affect treatment plans
- Part of the evaluation of exercise-induced or exercise-associated syncope
- Reasonable differences of opinion exist regarding the utility of tilt-table testing
- Differentiating convulsive syncope from seizures
- Evaluating patients (especially the elderly) with recurrent unexplained falls
- Assessing recurrent dizziness or presyncope
- Evaluating unexplained syncope in the setting of peripheral neuropathies or dysautonomias
- Follow-up evaluation to assess therapy of neurally mediated syncope **Tilt-table testing not warranted**
- Single syncopal episode, without injury and not in high-risk setting with clear-cut vasovagal clinical features
- Syncope in which an alternative specific cause has been established and in which additional demonstration of neurally mediated susceptibility would not alter treatment plans

Potential emerging indications

Recurrent idiopathic vertigo

Recurrent transient ischemic attacks

Chronic fatigue syndrome

Sudden infant death syndrome (SIDS)

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vascular disease, pregnancy and patient refusal. Many laboratories recommend that men older than 45 years and women older than 55 years undergo stress testing before tilt-table testing and that women of childbearing age have a pregnancy test.⁸

HUT testing is generally safe, but there have been occasional reports of coronary vasospasm,²² chest pain,⁵ hypertensive crisis⁵ and tachyarrhythmia.^{5,6} The most frequent adverse effects are hemodynamic changes, such as hypotension, tachycardia or bradycardia associated with orthostatic intolerance, presyncope or syncope. It is noteworthy that patients with neurocardiogenic syncope may rarely experience asystole (defined as ventricular pause of more than 5 seconds) or complete atrioventricular block during HUT testing. Lacroix and colleagues²³ reported 10 asystolic reactions (6%) (average duration 12 seconds) among 179 patients investigated for neurocardiogenic syncope; 8 patients needed cardiopulmonary resuscitation for 20 to 30 seconds. Dhala and associates²⁴ reported 19 asystolic reactions (9%) among 209 patients with suspected neurocardiogenic syncope and 3 asystolic responses (4%) among 75 healthy control subjects during HUT testing without pharmacologic stimulation. These subjects did not show a worse outcome than their nonasystolic counterparts during follow-up.24,25

Performance

We performed a MEDLINE search to identify studies of the reproducibility, sensitivity and specificity of HUT testing in adults using "orthostatic hypotension," "neurally mediated syncope" and "syncope" as key words. Articles providing details about the HUT test and patient selection were included. We found many studies on the topic, but study methods and populations were quite heterogeneous.

Reproducibility

Reproducibility is an important characteristic of a diagnostic tool. From studies in which data on HUT testing were obtained on at least 2 occasions, with a known time interval,^{23,26-35} we calculated an average reproducibility of 81%. However, as Behzad and collaborators²⁷ and other authors^{23,28} have highlighted, negative results are much more reproducible than positive ones (about 95% and 50% respectively). The reproducibility of HUT testing depends strongly on population selection as it is increased in patients with severe and frequent orthostatic symptoms. Clustering of orthostatic symptoms in time also heavily impairs the reproducibility of any 2 diagnostic tests significantly apart in time.

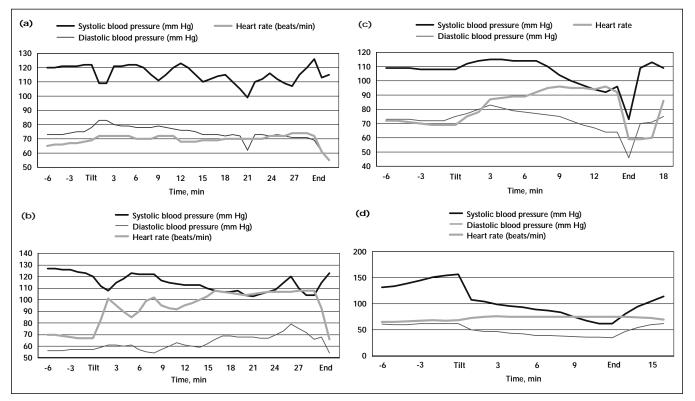


Fig. 1: Responses to head-upright tilt-table testing. A: Normal response is characterized by absence of significant decrease in blood pressure (more than 20 mm Hg systolic or 10 mm Hg diastolic), absence of significant and sustained increase in heart rate (more than 30 beats/min) and absence of orthostatic symptoms. B: Postural orthostatic tachycardia syndrome (POTS) is characterized by significant and sustained increase in heart rate. C: Neurocardiogenic syncope is characterized by significant and sudden decrease in blood pressure, frequently associated with sudden bradycardia. D: Dysautonomic response is characterized by immediate, progressive and significant decrease in blood pressure, frequently without appropriate increase in heart rate.

Diagnostic validity

Age, severity of symptoms, type of symptoms, proportion of subjects with dysautonomia and selection of subjects can influence pretest disease prevalence. The lack of a gold standard for assessing the value of the HUT test is an important limitation; patients with dysautonomia are frequently identified by positive results of HUT testing.

Studies attempting to assess the validity of the HUT test as a diagnostic test have used a combination of questionnaire, physical examination and paraclinical tests (excluding HUT testing) as the gold standard for comparison purposes. Not surprisingly, estimates of sensitivity (number of subjects with positive findings on HUT testing divided by the total number of symptomatic subjects tested) are quite variable.

Studies assessing the ability of the HUT test to diagnose neurocardiogenic syncope averaged a sensitivity of 35% without pharmacologic stimulation and 57% with pharmacologic stimultion.^{25,27–33,36–65} Studies using HUT testing within the boundaries set by the American College of Cardiology guide-lines⁶ averaged a sensitivity of 65%.^{31,38,48,53,58} It is noteworthy that the yield is not increased by repeating the test.²⁷

The specificity (number of subjects with negative results divided by the number of healthy subjects tested) of the HUT test for neurocardiogenic syncope was 92% on average without pharmacologic stimulation^{32,34,37,50–58,60–71} and 81% with pharmacologic stimulation.^{50,51,53,55–58,61,63,67,69} Two investigations in which HUT testing was used within the boundaries set by the American College of Cardiology guidelines⁶ both yielded a specificity of 100%.^{53,58}

Several investigations have established that abnormal results of tilt-table testing correlate with autonomic nervous system diseases^{72–76} and other tests of autonomic function.^{72,74–76} Axelrod and coworkers⁷⁷ tilted 10 patients with familial dysautonomia at an angle of 90° for 5 minutes and had positive results in all cases. Ward and Kenny⁷⁸ reported that 14 of 19 dysautonomic patients (74%) had orthostatic hypotension with a 70° tilt for 5 minutes. In the study by Khurana and Nicholas⁶⁵ 73% of 39 dysautonomic subjects were correctly identified within 5 minutes at a 90° tilt. Grubb and colleagues⁷⁹ identified patients with orthostatic intolerance and orthostatic tachycardia without full syncope (POTS) and studied HUT testing prospectively. A 45-minute 80° tilt resulted in a sensitivity of 100%.

Conclusion

Despite its limitations, the HUT test is useful in patients with a variety of clinical manifestations induced by orthostatism. It is most useful in documenting objective measures of orthostatic hypotension that cannot be obtained in a clinical setting.

Patients considered for HUT testing must be carefully selected to enhance diagnostic value. Abnormal hemodynamic response to the test in patients with clear clinical orthostatic symptoms is strong evidence for disease and should prompt changes in medical management, such as modification of lifestyle, use of compressive stockings or initiation of drug therapy.

Evaluation of treatment efficacy by serial HUT testing is still of unproven value. Despite the wide variability in orthostasis-related symptoms, the best indicator of treatment failure or success remains global evaluation of the symptoms experienced by the patient.

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