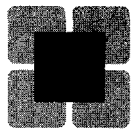

# Using the tilt test to diagnose cause of syncope

THE HEAD-UP TILT TEST has become widely used to determine the cause of unexplained syncope. In this issue of the *Cleveland Clinic Journal of Medicine*, Kapoor[1] addresses the value of this test, reviewing the pathophysiology of vasovagal syncope, the commonly used testing procedures and protocols, the sensitivity, specificity, and reproducibility of the test, and the common therapeutic approaches to this disease.

## PRINCIPLES

Simple and noninvasive, the head-up tilt test allows determination of the cardiovascular response to the effect of gravity on the venous circulation and cardiac preload. After the level and duration of tilting and whether to use saddle support have been decided, a set of data is collected that includes the blood pressure, heart rate, and degree of arteriolar vasoconstriction and adrenergic neural stimulation (measured directly by microneurography or indirectly by plasma catecholamine levels). The normal response consists of a 10-mm Hg reduction in systolic blood pressure, a 5-mm Hg increase in diastolic blood pressure, a heart rate acceleration of 10 to 15 beats per minute, and a doubling of the plasma norepinephrine level. A variety of abnormal patterns have been recognized (*Table*).

These changes are part of a physiologic response that maintains adequate cardiac output despite the fall in stroke volume. The cardiac and arterial responses to the reduction of venous return are regulated by various factors, including the autonomic nervous system, the arteriolar vascular reactivity to reflex adrenergic drive and other vasoconstrictive stimuli, and the pump function of the heart.

## ISSUES AND CONCERNS

The response to head-up tilting is, therefore, complex, and the operator's task is to detect the various changes in an accurate fashion to allow adequate interpretation of the results. Accurate and frequent measurements of blood pressure and heart rate are essential. Ideally, these data should be recorded continuously. However, for practical reasons and in order to keep the test noninvasive, compromises have become acceptable.

The heart rate is easy to monitor continuously with electrocardiography (one to three leads), and a strip can be recorded every minute or whenever an event is observed. Noninvasive blood pressure recording is more difficult. First, the technique of recording should be consistent; use of the guidelines recommended by the American Heart Association[2] obviates most errors. The cuff must be of appropriate size and centered over the brachial artery, and both the arm and the measuring device must remain at the level of the heart throughout the procedure. Observer bias should be avoided, such as preference for readings ending in the digit zero. Automated electronic blood pressure-measuring devices with a digital display were thought to eliminate this problem. However, these have their own pitfalls and should be validated and well calibrated before use. A beat-by-beat arterial pressure recording is ideal, but no sensitive, noninvasive, and reliable device is widely available yet that can be used at different levels of tilt in clinical practice.

Whether intra-arterial blood pressure recording predisposes to syncope is controversial and should be discussed in relation to the merits and drawbacks of this technique. Intra-arterial blood pressure recording, although invasive, is the gold standard for

**TABLE**
PATTERNS OF ABNORMAL RESPONSE TO THE HEAD-UP TILT TEST*

| Definition of response | Blood pressure | Heart rate |
|---|---|---|
| Vasovagal reaction | Sudden decrease | Sudden decrease after initial increase |
| Vasodepressor reaction | Sudden decrease | Increase |
| Venous pooling or autonomic insufficiency | POH† | Increase |
| Venous pooling | POH | Marked increase |
| Autonomic insufficiency | POH | No change |
| Chronotropic insufficiency | Normal response | No change |

*Other abnormal responses are premature beats and electrocardiographic ischemic changes
†POH = progressive orthostatic hypotension

blood pressure determination and for the validation of any noninvasive blood pressure technique. Further, once the arterial catheter is in place, no known hemodynamic or neurally mediated events have been ascribed to the presence of the catheter itself. In published reports, ambulatory intra-arterial blood pressure monitoring (using the brachial artery) did not increase the incidence of fainting.[3,4]

As a first step in screening for the cause of syncope, the tilt test is a powerful technique that defines the cardiovascular response and delineates the pathway for achieving a definite, accurate diagnosis. Unfortunately, there are no standard definitions of hypotension and bradycardia in studies of vasovagal syncope, as Kapoor mentions. It is also well known that clinically normal subjects may experience vasovagal syncope during the passive tilt test; they are said to have "false-positive" results. Conversely, patients with a history suggestive of vasovagal syncope may have a completely normal ("false-negative") response to the passive tilt test. In general, the sensitivity and specificity of the tilt test for vasovagal syncope varied among studies, as Kapoor discusses in depth. The question is: are these results truly false-positive and false-negative? The problem becomes compounded when pharmacological agents are incorporated in the passive head-up tilt procedure. Infusion of isoproterenol in this test has become quite popular in recent years, even though it does not increase the positive response rate as compared to passive testing alone at the same angle of tilt.[5] In fact, the specificity of tilt testing is less when isoproterenol is used, as Kapoor points out.

## NEEDED: A MATRIX OF DIAGNOSTIC INFORMATION

The problem is that the tilt test, as it is performed now, does not examine all the events that occur in the heart and the circulatory system during the procedure. Furthermore, the level of tilt is not an accurate measure of the stimulus imposed on the cardiovascular system. The exact reduction in preload varies from person to person at the same angle and duration of tilt depending on the venous capacitance function; a person with a highly compliant venous system will exhibit substantial venous pooling in the dependent part of the body (below heart level) when assuming the upright posture.[6] Indeed, the mechanism of increased translocation of blood volume in the peripheral venous system may not be the same in all patients presenting with accentuated venous pooling. Traditionally, it was thought that increased venous pooling always resulted from a sedentary life that led to loss of skeletal muscle tone and of the supporting function of the skeletal muscles.[7–9] However, athletes may develop venous pooling, and this abnormality may play an important role in postexercise syncope.[10,11] The mechanism could be related to damage in the venous valves, but this assumption is purely speculative at present.

The relationship between the total blood volume and the response to head-up tilting is controversial. Our initial clinical impression was that chronic hypovolemia is a common precipitating cause of the vasovagal response to upright posture.[12,13] However, further analysis of data from a larger series of our patients showed that the distribution of blood volume is more important,[14,15] unless the hypovolemia is severe (< 75% of average laboratory values for normal subjects of the same gender).

The poor reproducibility of the tilt test in patients with syncope of undetermined cause is another limitation of the test. This variable response may be related to the changeable nature of the underlying hemodynamic and neural factors[16,17] and of

their interactions relative to changes in endogenous and exogenous environmental conditions.

Used by itself, the tilt test cannot conclusively identify the problem underlying the syncopal event or classify the type of syncope. A complementary cardiovascular hemodynamic and neurohumoral evaluation should be considered and should involve determination of intravascular blood volume and its distribution, venous capacitance, arteriolar vascular reactivity, integrity of autonomic reflexes, alterations in plasma norepinephrine and dopamine levels, and cardiac pump function.[18] Together, these parameters form a matrix that specifies the cause of syncope and, possibly, the severity of the abnormality. As Kapoor suggests, this algorithm may help define individuals who are disease-free vs those who have not had syncope in their lifetime but are predisposed to it.

The multiplicity of the drugs and devices used for treating syncope of undetermined etiology attests to their lack of specificity. The results of the study of Brignole and colleagues[19] underscores the concern about the efficacy of these treatments when used empirically. The determination of the exact cause of syncope is therefore essential for targeting a specific form of therapy.

What we need to do is to develop a diagnostic matrix in which all pieces of the puzzle are entered and a final diagnosis is based on the recognition of the emerging pattern. Perhaps a computer program may achieve this goal independently of human interpretation bias.

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## REFERENCES

1. **Kapoor WN.** Evaluating unexplained syncope with upright tilt testing: a review. Cleve Clin J Med 1995; **62:**305-310.
2. **Kaplan NM.** Measurement of blood pressure. In: Kaplan NM, Neal WW, editors. Clinical hypertension 6th edition. Baltimore: Williams & Wilkins, 1994:23–45.
3. **Bevan AT, Honour AJ, Stott FH.** Direct arterial pressure recording in unrestricted man. Clin Sci 1969; **36:**329–344.
4. **Pagani M, Furlan R, Lombardi F, et al.** Technique for 24 hour recording of continuous high fidelity arterial pressure and electrocardiogram in ambulatory patients. Clin Exper Hypertens [A] 1985; **7:**401–405.
5. **Kapoor WN, Brant N.** Evaluation of syncope by upright tilt testing with isoproterenol. Ann Intern Med 1992; **116:**358–363.
6. **Ulrych M, Frohlich ED, Tarazi RC, Dustan HP, Page IH.** Cardiac output and distribution of blood volume in central and peripheral circulations in hypertensive and normotensive man. Br Heart J 1969; **31:**570–574.
7. **Tyberg JV.** Venous modulation of ventricular preload. Am Heart J 1992; **123:**1098–1104.
8. **Streeten DHP.** Pathogenesis of hyperadrenergic orthostatic hypotension: evidence of disordered venous innervation exclusively in the lower limbs. J Clin Invest 1990; **86:**1582–1588.
9. **Epstein SE, Stampfer M, Beiser GD.** Role of the capacitance and resistance vessels in vasovagal syncope. Circulation 1968; **37:**524–533.
10. **Fleg JL, Asante AVK.** Asystole following treadmill exercise in a man without organic heart disease. Arch Intern Med 1983; **143:**1821–1822.
11. **Huycke EC, Card HG, Sobol SM, Nguyen NX, Sung RJ.** Postexertional cardiac asystole in a young man without organic heart disease. Ann Intern Med 1987; **106:**844–845.
12. **Fouad FM, Tadena-Thome L, Bravo EL, Tarazi RC.** Idiopathic hypovolemia. Ann Intern Med 1986; **104:**298–303.
13. **Abi-Samra F, Maloney JD, Fouad-Tarazi FM, Castle LW.** The usefulness of head-up tilt testing and hemodynamic investigations in the workup of syncope of unknown origin. PACE 1988; **11:**1202–1214.
14. **Jaeger FJ, Maloney JD, Castle LW, Fouad-Tarazi FM.** Is absolute hypovolemia a risk factor for vasovagal syncope. PACE 1993; **16:**743–750.
15. **Schutzman J, Jaeger F, Maloney JD, Fouad-Tarazi FM.** Head-up tilt and hemodynamic changes during orthostatic hypotension in patients with supine hypertension. J Am Coll Cardiol 1994; **24:**454–461.
16. **Panza JA, Epstein SE, Quyyumi AA.** Circadian variation in vascular tone and its relation to alpha-sympathetic vasoconstrictor activity. N Engl J Med 1991; **325:**986–990.
17. **Linsell CR, Lightman SL, Mullen PE, Brown MJ, Causon RC.** Circadian rhythms of epinephrine and norepinephrine in man. J Clin Endocrinol Metab 1985; **60:**1210–1215.
18. **Fouad-Tarazi FM.** A strategy for the syncope work-up. Cleve Clin J Med 1993; **60:**184–185.
19. **Brignole M, Menozzi C, Gianfranchi L, Lolli G, Bottoni N, Oddone D.** A controlled trial of acute and long-term medical therapy in tilt-induced neurally mediated syncope. Am J Cardiol 1992; **70:**339–342.