pathways and the single patient with a right free wall pathway and subtle preexcitation, the AH intervals were short. These data pertain to a predominantly adult population. Only 1 of the patients was <12 years old. This patient showed a minimal preexcitation pattern and the pathway was in the left lateral region. These data cannot be extrapolated to the pediatric population, in general, who may have relatively shorter atrioventricular nodal conduction times, or to patients with decremental anterograde accessory pathways who may have longer accessory pathway conduction times. Nonetheless, the presence of a minimal preexcitation pattern in the adult with WPW syndrome is a useful first approximation to localizing the accessory pathway to the left lateral region.

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Comparison of Responses to Isoproterenol and Epinephrine During Head-Up Tilt in Suspected Vasodepressor Syncope

Hugh Calkins, MD, Alan Kadish, MD, Joao Sousa, MD, Shimon Rosenheck, MD, and Fred Morady, MD

Head-up tilt is known to play an important role in establishing the diagnosis of vasodepressor syncope in patients with syncope of unknown etiology.[1–5] Although passive head-up tilt alone may trigger a vasodepressor response, recent studies show that an infusion of isoproterenol significantly increases the sensitivity of head-up tilt in reproducing vasodepressor syncope.[1–5] However, isoproterenol is not endogenously produced and the role of endogenous catecholamines, such as epinephrine, in provoking vasodepressor syncope is unknown. Therefore, we compared the responses to isoproterenol and epinephrine during head-up tilt in patients suspected of having vasodepressor syncope.

Our subjects were 20 consecutive patients (13 men and 7 women, mean age ± standard deviation 52 ± 23 years) with syncope suspected to be of vasodepressor origin who underwent a tilt-table test. Clinical suspicion of vasodepressor syncope was based on the presence of (1) a history of syncope precipitated by a stressful situation; (2) a prodrome of nausea, warmth or diaphoresis; and (3) residual symptoms of nausea or fatigue. Twelve patients had no structural heart disease, 5 patients had coronary artery disease and 3 patients had hypertension. The number of syncopal episodes before referral ranged from 1 to 70, with a mean of 8 ± 16 syncopal episodes.

Passive head-up tilt to 70° was initially performed in the drug-free state for 10 minutes. If the patient's symptoms were not reproduced, a catecholamine infusion (isoproterenol or epinephrine at 50 ng/kg/min) was begun and head-up tilt was continued for an additional 10 minutes. The patient was then returned to the supine position and the catecholamine infusion rate was increased to 100 ng/kg/min. After 6 minutes of catecholamine infusion, head-up tilt was repeated. All patients requiring a catecholamine infusion were challenged with incremental doses of both isoproterenol and epinephrine. The sequence in which the 2 catecholamines were administered was randomized and the 2 tilt-table tests were performed sequentially, separated by a 20-minute rest period. The patient's blood pressure and heart rate were recorded noninvasively at 5-minute intervals and more frequently when symptoms developed. The electrocardiograph was monitored continuously throughout the procedure. In a subset of 7 patients, lower infusion rates of epinephrine (15 and 25 ng/kg/min) were used.

The epinephrine infusion rates used in this study were selected because previous studies demonstrated that these infusion rates result in plasma epinephrine concentration comparable to the levels achieved during a variety of pathophysiologic states.[6] A 25-ng/kg/min infusion of epinephrine results in plasma epinephrine concentrations similar to those occurring endogenously during mental stress, cigarette smoking and public speaking (178 ± 15 pg/ml), a 50-ng/kg/min infusion of epinephrine results in systemic levels similar to those during submaximal exercise or hypoglycemia (259 ± 24 pg/ml), and a 100-ng/kg/min infusion results in systemic levels similar to those produced during maximal exercise (484 ± 69 pg/ml).[6] The isoproterenol infusion rates used in this study were selected in order to equal epinephrine infusion rates and also because these infusion rates are similar to those used by other investigators in the evaluation of vasodepressor syncope.[1,2]

From the Division of Cardiology, Department of Internal Medicine, University of Michigan Medical Center, B1 F245 University Hospital, 1500 E. Medical Center Drive, Ann Arbor, Michigan 48109-0022.

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TABLE I Blood Pressure and Heart Rate Responses to Isoproterenol and Epinephrine

Pt. No.	Baseline HR (beats/min)	Peak HR Epinephrine (beats/min)	Peak HR Isoproterenol (beats/min)	Baseline Mean BP (mm Hg)	Peak Mean BP Epinephrine (mm Hg)	Peak Mean BP Isoproterenol (mm Hg)
1	70	93	139	83	94	77
2	72	116	161	82	82	94
3	72	100	136	89	87	87
4	64	102	167	93	84	83
5	68	120	104	97	85	98
6	79	86	104	93	105	102
7	99	163	162	111	118	104
8	68	113	145	91	88	95
9	91	128	130	110	81	87
10	50	96	107	94	85	77
11	69	113	166	110	108	96
12	92	96	145	101	106	105
Mean	75	112	139	97	94	92
±SD	±14	±21	±25	±9	±12	±10

BP = blood pressure; HR = heart rate; SD = standard deviation.

The criteria for a positive tilt-table test included the induction of syncope or presyncope in association with a systolic blood pressure <80 mm Hg and a relative bradycardia, defined as a >5 beats/min decrease in heart rate from the peak achieved heart rate.

All data are expressed as mean ± 1 standard deviation. Comparisons were performed with a paired t *test or by analysis of variance. A p value <0.05 was considered statistically significant.*

Seventeen patients (85%) had an abnormal response to tilt-table testing and 3 (15%) had a normal response. The tilt-table test was positive in the absence of a catecholamine infusion in 2 patients. Isoproterenol triggered a vasodepressor response in 15 patients, whereas epinephrine triggered a vasodepressor reaction in only 2 patients (p <0.01). No patient who had a negative tilt-table test during infusion of isoproterenol had an abnormal response during infusion of epinephrine. At the termination of the head-up tilt, the 15 patients with an abnormal response during isoproterenol infusion had a decrease in heart rate of 38 ± 27 beats/min and a decrease in mean blood pressure of 38 ± 14 mm Hg. During epinephrine infusion, these patients had a mean decrease in heart rate of 8 ± 13 beats/min (p = 0.02 vs isoproterenol) and a mean decrease in blood pressure of 3 ± 4 mm Hg (p <0.01 vs isoproterenol). The rhythm induced in patients with an abnormal response was junctional in 9 patients; complete heart block was induced in 1 patient, atrial fibrillation in 1, sinus tachycardia in 3, normal sinus rhythm in 1, and sinus bradycardia in 2.

The hemodynamic responses during isoproterenol and epinephrine infusions are listed in Table I. The 2 patients who had an abnormal response to head-up tilt in the absence of a catecholamine infusion and the 6 patients who were challenged with low-dose epinephrine infusions are excluded from this analysis. The baseline mean heart rate (supine) was 75 ± 14 beats/min. Isoproterenol resulted in a greater chronotropic response than did epinephrine. The mean peak heart rate achieved with isoproterenol before completion of the study or the development of a vasodepressor response was 139 ± 25 beats/min compared with 112 ± 21 beats/min with isoproterenol (p <0.01). Isoproterenol and epinephrine had similar effects on blood pressure. In the baseline state, mean blood pressure was 97 ± 9 mm Hg. During isoproterenol infusion, maximal mean blood pressure was 92 ± 9 mm Hg compared with 94 ± 12 mm Hg during epinephrine infusion.

The major finding of this study is that epinephrine, the primary endogenously produced circulating catecholamine, induces signs and symptoms of a vasodepressor reaction much less frequently than does isoproterenol during tilt-table testing. Only 2 of 15 patients who had a vasodepressor response with head-up tilt during isoproterenol infusion had a vasodepressor response during epinephrine infusion. Furthermore, no patient had a vasodepressor response only during epinephrine infusion. These findings suggest that epinephrine may not be the primary trigger of the vasodepressor response in humans.

The importance of the sympathetic nervous system in triggering vasodepressor syncope has been recognized for over 30 years. Early evidence consisted of the clinical observations that vasodepressor syncope frequently was precipitated by stress or anxiety.[7] Subsequent hemodynamic studies demonstrated a tachycardia response before the development of bradycardia and hypotension.[8] Catecholamine levels of patients before syncope provided additional evidence of the important role played by the sympathetic nervous system.[9] More recent studies report that infusion of isoproterenol during tilt-table testing significantly increases the yield of a vasodepressor response.[1,2,5]

The physiologic basis for the greater propensity of isoproterenol, compared with epinephrine, to trigger a vasodepressor response during head-up tilt is uncertain. Recently, ventricular mechanoreceptors with nonmyelinated vagal afferents have been identified.[10,11] Discharge of these fibers is influenced by contractility as well as by systolic and diastolic pressure. With an increase in pressure or contractility, the mechanoreceptors are stimulated, resulting in withdrawal of sympathetic tone and an increase in vagal tone, and this causes a vasodepressor

response. A hypercontractile ventricle with a small end-systolic volume may stimulate receptor discharge by inducing intraventricular pressure gradients. Within this physiologic framework, several mechanisms may explain isoproterenol's enhanced ability, compared with epinephrine, to trigger the vasodepressor response. First, isoproterenol has been demonstrated to reduce end-diastolic volume and increase stroke volume.[12] This effect on end-diastolic volume would be expected to be greater with isoproterenol than with epinephrine because of the greater chronotropic effects of isoproterenol. Second, isoproterenol may increase end-diastolic pressure to a greater degree than epinephrine because of a greater shortening of the diastolic filling period. Finally, once the vasodepressor response is triggered, isoproterenol may augment peripheral vasodilation because of its β_{-2} agonist properties, whereas epinephrine may counteract vasodilation through its α-agonist effects.

The precise role of epinephrine in precipitating vasodepressor syncope remains unknown. Although other studies report increases in circulating epinephrine in association with vasodepressor syncope, the results of this study suggest that additional factors are important. These factors may include a marked withdrawal of vagal tone in conjunction with an increase in circulating epinephrine, which together may lead to a more marked tachycardia and, in turn, trigger a vasodepressor response. It is also possible that a second neurohumoral substance, such as arginine vasopressin, may sensitize the mechanoreceptors and thereby lower the threshold for triggering the vasodepressor response.

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Frequency of Valvular Regurgitation by Color Doppler Echocardiography in Systemic Lupus Erythematosus

Katsuaki Enomoto, MD, Yoshikazu Kaji, MD, Takehito Mayumi, MD, Yasuo Tsuda, MD, Shozo Kanaya, MD, Kohei Nagasawa, MD, Takehiko Fujino, MD, and Yoshiyuki Niho, MD

We studied valvular regurgitation in patients with systemic lupus erythematosus (SLE) by color Doppler echocardiography. Because valvular regurgitation occurs frequently in normal subjects,[1,2] we matched the patients by age with a control group. Furthermore, the same person examined both patients and normal subjects using the same Doppler echocardiographic apparatus.

The patients were 43 women with stable SLE (18 to 29 years, 14; 30 to 39 years, 13; 40 to 49 years, 16). All fulfilled the 1982 American Rheumatism Association criteria for the diagnosis of SLE.[3] We judged as stable patients with SLE whose values of erythrocyte sedimentation rate and complements were normal or had not changed for a few months and whose clinical symptoms did not deteriorate. They underwent echocardiography, chest x-ray, standard 12-lead electrocardiography, phonocardiography, blood and urine analyses and serum chemistry analysis. Normal subjects comprised 93 women (18 to 29 years, 23; 30 to 39 years, 43; 40 to 49 years, 27) who had no history of heart disease, hypertension or other medical problems, and who underwent blood pressure measurement, urine analysis, chest x-ray and electrocardiography. M-mode, 2-dimensional and Doppler echocardiographic studies were performed with a SSH160A (Toshiba, Tokyo, Japan) using a 2-dimensional transducer (3.75 MHz) and a Doppler transducer (2.5 MHz). Echocardiography was performed on both patients and normal subjects in the partial left lateral decubitus position. The flow signal was judged as a regurgitation when it was observed as a regurgitant jet away from the valve by color Doppler echocardiography and when its duration was >100 ms by M-mode color-flow mapping. The severity of regurgitation was judged according to the classification by distance with pulsed-Doppler echocardiography.[4–7] Right ventricular systolic pressure was ascertained by measuring the pressure gradient between right ventricular and right atrial systolic

From the First Department of Internal Medicine, Faculty of Medicine, Kyushu University, Fukuoka, Japan, and the Institute of Health Science, Kyushu University, Fukuoka, Japan. Dr. Enomoto's present address is the Division of Cardiology, Department of Medicine, University of North Carolina, Burnett-Womack Building, Chapel Hill, North Carolina 27599-7075.

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