Fig. 3. Histologic examination of coronary telangiectases after left ventricular endomyocardial biopsy demonstrated large, thin-walled vessels *(arrows)*, which were directly connected with the endocardium *(E)*. (Masson trichrome; ×250.)

Fig. 4. Histologic examination of subendocardial myocardium showed patchy areas of fibrous replacement *(arrows)*. (elastic van Gieson; ×250.)

2. Lande A, Bedford A, Schechter LS. The spectrum of arteriographic findings in Osler-Weber-Rendu disease. Angiology 1976;27:223-40.
3. Hachamovitch R, Wicker P, Capasso GM, Anversa P. Alteration of coronary blood flow and reserve with aging in Fischer 344 rats. Am J Physiol 1989;256:H66-H73.

Angiotensin-converting enzyme activity in myocardial ischemia during exercise testing

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Angiotensin-converting enzyme (ACE, kininase II) is a metal-zinc-peptidase with a molecular weight of 140,000 that converts angiotensin I into angiotensin II and participates in the degradation of bradykinin.[1,2] After it was identified and isolated in plasma,[3] ACE was found in other types of cells, most importantly the endothelial vesicle cells proximal to blood flow.[4-6] Since ACE is well represented in

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Table I. Results of exercise test in nonischemic and ischemic subjects

	Nonischemic	*Ischemic*	
Average total duration of exercise (min)	9.12 ± 1.90	4.90 ± 2.90	$p < 0.005$
Duration of exercise test at maximum (min)	1.55 ± 0.49	1.12 ± 0.33	$p < 0.05$
Average work load reached (W)	103.10 ± 14.90	66.60 ± 26.30	$p < 0.01$
SBP at maximum (mm Hg)	255.00 ± 11.18	224.40 ± 19.49	NS
DBP at maximum (mm Hg)	110.00 ± 7.00	106.60 ± 11.54	NS
MBP at maximum (mm Hg)	148.30 ± 6.86	145.80 ± 12.30	NS
HR at maximum (beats/min)	143.10 ± 3.90	122.50 ± 19.20	$p < 0.02$

SBP, Systolic blood pressure; *DBP*, diastolic blood pressure; *MBP*, mean blood pressure; *HR*, heart rate; *NS*, not statistically significant.

the endothelium of most organs[4] including the heart,[7] it can serve as a marker of endothelial cells.[8] In addition, ACE synthesis has been demonstrated in culture in the endothelial cells of the hog aorta,[9] and serum ACE (SACE) levels in experimental animals are correlated with the degree of vascular damage induced by hypertension-associated arterial disease.[4] In the light of these observations, we studied the SACE response to maximal exercise in patients with clinical and/or laboratory signs suggesting myocardial ischemia and we analyzed SACE modifications during myocardial ischemia as a result of exercise testing.

Methods. Eighteen patients, all men between 33 and 61 years of age (mean age ± SD 48 ± 9 years) who had been admitted to our clinic for suspected myocardial ischemia, were studied. None of them was in a state of athletic training. All subjects presented with clinical and physical signs of typical angina. Diagnosis was based on the presence of thoracic pain lasting less than 10 minutes and the recent onset of T wave depression or ST segment depression. None of the subjects presented clinical signs of either carotid vascular disease or peripheral vascular disease. Only one patient had had a myocardial infarction (posterior, 2 years previously). Patients with the following were excluded from the study: (1) left bundle branch block (LBBB) on baseline electrocardiogram (ECG) or an ECG pattern that did not permit an evaluation of transient myocardial ischemia; (2) previous transient ischemic attacks (TIA); (3) age greater than 70 years; (4) hemodynamically significant valvular heart disease; (5) arterial hypertension; (6) congestive heart failure; (7) sarcoidosis; (8) hyperthyroidism; (9) liver disease; or (10) diabetes mellitus. At the time of the study, no patients had coronary arteriography performed. All patients adhered to a diet containing 120 to 140 mEq/day of sodium and 40 to 60 mEq/day of potassium for at least 1 week. No patient was overweight. The stress test was administered 12 to 24 days after the onset of symptoms in hemodynamically stable fasting patients. All coronary vasoactive medications (nitrate derivatives, calcium antagonists) had been discontinued for at least 7 days. None of the patients had in the past used ACE inhibitors, β-adrenergic blocking agents, or diuretics. Before starting the test all patients had been in the recumbent position for 30 minutes; during this period (at 10 minutes of the preliminary rest period) venous samples (antecubital vein) were taken with a plastic syringe. In addition, a venous cannula was inserted to determine SACE levels. The bicycle ergometer exercise stress test (maximal) was then begun, with work loads increasing by 25 W every 2 minutes. A 12-lead ECG was obtained before the test began, each minute during the test, at maximum effort, and then at each minute during recovery. The criteria for interruption of the examination were: marked muscular fatigue, worsening angina, or systolic pressure above 250 mm Hg. Additional venous blood samples were taken at maximum effort, as well as during recovery. To determine SACE, the blood was immediately centrifuged at 4° C for 10 minutes and stored at −20° C. SACE was determined by evaluating the enzyme activity, using the colorimetric method of Kasahara et al.,[10] which utilizes p-hydroxy-benzoil-glycyl-L-histidyl-L-leucine as the substrate. In our laboratory, sensitivity of the method is 0.001 nmol/ml/min, and the intraassay and interassay precision is 5.0% and 14.5%, respectively. Data are given as mean ± SD. The statistical calculation was performed with an IBM personal computer (IBM Corp., Atlanta, Ga.) using Primer software (Biostatistics, S.A. Glantz, McGraw-Hill Inc., San Francisco, Calif.). The individual values were inserted by group on the spread sheet and were evaluated using the *t* test and multivariate analysis of variance test (MANOVA), whenever appropriate.

Results. Of the 18 patients examined, nine (50%) showed (during the test) ECG signs of myocardial ischemia (two of them with retrosternal pain). There was no difference between the age of the patients with a positive stress test (46.5 ± 7 years) and those with a negative stress test (48.5 ± 8 years). Values for the MANOVA test in subjects with a positive stress test were shown to be $F = 8.36$; $p = 0.000$. Patients with a negative stress test for myocardial ischemia exercised for significantly longer periods than those with a positive stress test. The latter patients interrupted the test because of the onset of ischemic signs or pain ($p < 0.005$) (Table I). Baseline SACE increased significantly during exercise testing (at maximum effort), and remained significantly elevated during recovery ($p < 0.01$) (Table II) only in those patients who showed ECG signs of myocardial ischemia ($p < 0.01$) during the test (Fig. 1).

Comments. This study showed that the serum level of angiotensin-converting enzyme (SACE) in patients with ischemic heart disease increases significantly during maximal stress testing for purposes of diagnostic work-up. The SACE was also significantly increased in those patients who developed signs of myocardial ischemia during the stress test; SACE remained unchanged during the test in those patients who did not develop ischemic signs. In fact,

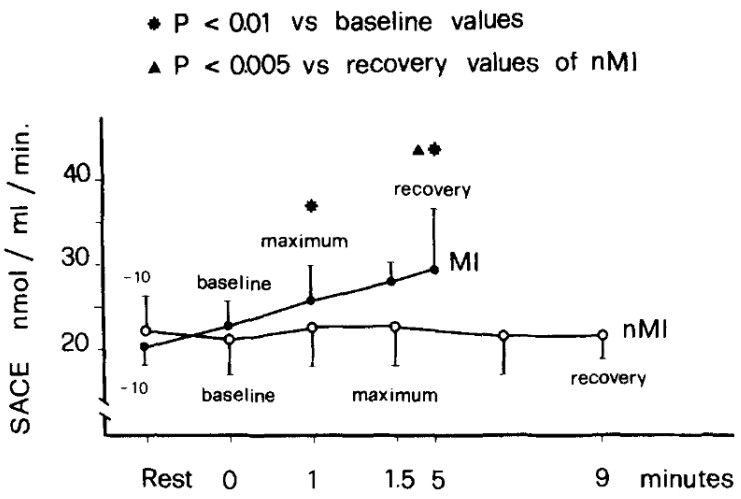

Fig. 1. SACE levels in ischemic *(MI)* and nonischemic *(nMI)* subjects during exercise test.

Table II. SACE activity during the exercise test

	SACE (nmol/ml/min)			
Groups	*−10*	*0*	*Maximum*	*Recovery*
Ischemic (n = 9)	20.78 ± 1.99	22.06 ± 2.17	25.18 ± 3.27*	28.95 ± 5.09*†
Nonischemic (n = 9)	21.80 ± 3.70	21.50 ± 4.80	23.30 ± 3.10	22.00 ± 3.40

*$p < 0.01$ versus baseline values.
†$p < 0.005$ versus nonischemic at recovery.

in the event of myocardial ischemia, SACE increases markedly at maximum effort as well as during recovery. Our data on SACE activity in nonischemic subjects support similar results obtained by Milledge and Catley,[11] who found SACE to remain unchanged during extended stress testing (up to 60 minutes) in normal healthy subjects. In light of our findings, we propose that SACE elevation could reflect acute endothelial vascular damage (both in general and in particular in the cardiac vasculature) in subjects with clinical and ECG signs of myocardial ischemia during stress testing (regardless of the duration of exercise).

REFERENCES

1. Erdos EG. The angiotensin I converting enzyme. Fed Proc 1977;36:1760-5.
2. Soffer RL. Angiotensin-converting enzyme and the regulation of vasoactive peptides. Ann Rev Biochem 1976;45:73-94.
3. Skeggs TL, Kahn JR, Shumway NP. The preparation and function of the angiotensin-converting enzyme. J Exp Med 1956;103:295-9.
4. Caldwell PRB, Seegal BG, Hsu RC, Das M, Soffer RL. Angiotensin converting enzyme vascular endothelial localization. Science 1976;191:1050-1.
5. Ryan JW, Ryan US. Correlation of pulmonary structure with pharmacokinetic function. Agents Actions 1976;4:510-4.
6. Studdy PR, Lapworth R, Bird R. Angiotensin-converting enzyme and its clinical significance: a review. J Clin Pathol 1983;36:938-47.
7. Wigger HS, Stalcup SA. Distribution and development of angiotensin-converting enzyme in the fetal and newborn rabbit. An immunofluorescence study. Lab Invest 1978;38:581-3.
8. Johnson AR, Erdos EG. Angiotensin I converting enzyme (kininase II) in human endothelial cells in culture. Adv Exp Med Biol 1978;120B:287-90.
9. Hayes LW, Goguen CA, Ching SF, Slakey LL. Angiotensin-converting enzyme: accumulation in medium from cultured endothelial cells. Biochem Biophys Commun 1978;82:1147-9.
10. Kasahara Y, Ashihara Y, Harada T. The method for determination of angiotensin I converting enzyme (ACE) activity. Clin Chem 1981;27:1114-8.
11. Milledge JS, Catley DM. Renin, aldosterone and converting enzyme during exercise and acute hypoxia in humans. J Appl Physiol 1982;52:320-3.

Protruding left ventricular thrombus formation following blunt chest trauma

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