Ischemia-modified albumin (IMA) is not useful for detecting myocardial ischemia during symptom-limited exercise stress tests

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Abstract

Background/Aims: We examined the ischemia-modified albumin (IMA) level during exercise in patients with coronary artery disease (CAD).

Methods: Forty patients with a history of chest pain underwent both symptom-limited treadmill exercise stress testing and coronary angiography within one week. During the treadmill tests, blood samples were obtained at baseline and 5 min after exercise to measure the serum IMA level.

Results: Of the 40 patients, fourteen (35%, CAD group) had significant coronary artery stenosis, while the other 26 (65%, non-CAD group) did not. The baseline and post-exercise IMA levels in the two groups did not differ significantly (105.2±7.2 vs. 107.7±6.7 U/mL at baseline and 93.1±10.1 vs. 94.8±5.7 U/mL at post-exercise in the CAD and non-CAD groups, p=0.29 and 0.57, respectively). The changes in IMA after exercise did not differ either (-10.4±7.5 vs. -14.0±7.6 U/mL in the CAD and non-CAD groups, respectively, p=0.10). Similarly, the change in IMA between the exercise ECG test positive (TMT positive, n=9) and negative (TMT negative, n=20) groups did not differ (-14.6±5.19, vs -8.50±9.01 U/mL, p=0.15, in the TMT positive and negative groups, respectively).

Conclusions: Our results suggest that IMA has limitation in detecting myocardial ischemia during symptom-limited exercise stress tests.

Key Words: Ischemia-modified albumin; Exercise ECG test; Ischemic heart disease

INTRODUCTION

Ischemia-modified albumin (IMA) has emerged as a useful diagnostic modality for evaluating chest pain, especially in patients with acute coronary syndrome. During an ischemic attack, a lack of oxygen in localized areas of the heart induces a series of reactions involving free radicals leading to an N-terminal structural change in albumin, producing IMA. Recently, several studies reported a high negative predictive value and high sensitivity for detecting patients with acute coronary syndrome presenting to the emergency department with chest pain. Other studies demonstrated that the serum level of IMA increased rapidly after transient balloon occlusion during percutaneous coronary intervention (PCI). In contrast, some studies have suggested that the change in IMA in...
response to ischemia in organs other than the heart is not the same as that in ischemic myocardium, such as in skeletal muscle ischemia and bowel ischemia\(^{11, 12}\). In reality, most patients with stable angina complain of effort-related chest pain, not resting pain. Several studies have examined the meaning of serum IMA in exercise-induced myocardial ischemia and reported that IMA was not useful for identifying myocardial ischemia during exercise\(^{13, 14}\); however, most of these studies used non-invasive tests, such as exercise stress tests, to provide evidence of myocardial ischemia. Such non-invasive tests are limited in their ability to address the issue because of false positive or negative results. Thus, in this study, we examined the meaning of the IMA level during exercise with greater precision by performing both exercise ECG testing and coronary angiography.

**MATERIALS AND METHODS**

The subjects included 40 patients with a history of chest pain. Patients with the following conditions were excluded from the study: (1) leg claudication; (2) a history of myocardial infarction; (3) a recent (within four weeks) history of PCI; (4) a history of stroke; (5) renal insufficiency (serum creatinine \(\geq 2\) mg/dL); (6) cancer or other active inflammation; and (7) baseline ECG abnormalities that might complicate the interpretation of exercise ECG test results, such as a left bundle branch block, Wolff-Parkinson-White syndrome, and ST depression. All of the patients underwent both symptom-limited treadmill exercise stress testing and coronary angiography within one week. During the treadmill tests, blood samples were obtained at baseline and 5 min after exercise to measure the serum IMA and lactate levels.

**Treadmill Exercise Stress Test (TMT)**

All of the patients underwent symptom-limited treadmill exercise ECG testing using the Bruce protocol\(^{15}\). The test was terminated if the patient complained of fatigue, marked dyspnea, exercise-limiting angina, dizziness with a documented systolic blood pressure drop of more than 20 mmHg, or marked ST-segment depression (\(> 3\) mm). The exercise ECGs were interpreted by an independent physician. The patients were declared positive for myocardial ischemia if they showed \(\geq 1\)-mm horizontal or down-sloping ST-segment depression at 80 ms after the J-point during the exercise or recovery period. If they showed no significant ST-segment change, the patients were declared negative for myocardial ischemia or placed in the indeterminate group depending on whether their heart rate (HR) reached more than 85% of the estimated maximum value. Blood samples were obtained before exercise (baseline) and 5 min after the cessation of exercise. The patients were assigned to the TMT positive or negative group according to their TMT result.

**Coronary Angiography**

Coronary angiography was performed within one week of the exercise treadmill test. The femoral or radial artery was used as the puncture site. Quantitative coronary angiography (QCA) was used to determine the degree of stenosis in the major branches of the coronary arteries. If a narrowing lesion with \(\geq 50\%\) stenosis was detected by QCA, coronary artery disease (CAD) with significant stenosis was deemed present. Patients were assigned to the CAD or non-CAD group according to whether they had significant CAD on the coronary angiogram.

**Analysis of Blood Samples**

Blood was collected in Vacutainer tubes (Becton Dickinson, Franklin Lakes, NJ, USA). The samples were frozen at \(-70\) °C within 2 h and stored until analysis. Serum IMA was measured using the Albumin Cobalt Binding (ACB) Test (Ischemia Technologies, Denver, CO, USA) using a Synchron LX20 chemical autoanalyzer (Beckman Coulter, Fullerton, CA, USA). The total intra-assay coefficient of variation (CV) was 2.36~3.29% while the inter-assay CV was 3.01~6.35% at 55-132 U/mL for the quality-control materials. The lactic acid concentration was measured using a Nova M7.

**Data Analysis**

The serum IMA and lactate levels before and after exercise were compared in both the CAD/non-CAD groups and the TMT-positive/negative groups.

**Statistical Analysis**

Student’s \(t\)-test was used to compare continuous variables (expressed as the mean±SD). For discrete variables, \(\chi^2\) analysis was used. For non-parametric testing, the Mann-Whitney U-test was used to compare continuous variables in two groups. All \(p\)-values less than 0.05 were considered statistically significant.

**RESULTS**

**Coronary Angiography**

Of the 40 patients, 26 showed no significant narrowing (the non-CAD group) whereas the other fourteen patients showed evidence of significant stenosis in at least one coronary artery (the CAD group). Age, sex, and the proportion of risk factors for CAD did not differ between the two groups. In the CAD group, nine patients (64.3%) had 1-vessel disease, two patients