

# Exercise-Induced ST-Segment Elevation in ECG Lead aVR Is a Useful Indicator of Significant Left Main or Ostial LAD Coronary Artery Stenosis

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**OBJECTIVES** The authors tested the hypothesis that exercise treadmill testing (ETT)-induced ST-segment elevation (STE) in electrocardiographic lead aVR is an important indicator of significant left main coronary artery (LMCA) or ostial left anterior descending coronary artery (LAD) stenosis.

**BACKGROUND** Although STE in lead aVR is an indicator of LMCA or very proximal LAD occlusion in acute coronary syndromes, its predictive power in the setting of ETT is uncertain.

**METHODS** Rest and stress electrocardiograms, clinical and stress test parameters, and single photon-emission computed tomographic myocardial perfusion imaging (MPI) data, when available, were obtained in 454 subjects (378 with MPI) who underwent cardiac catheterization and standard Bruce ETT  $\leq$  6 months before catheterization. Patients were selected for LMCA or ostial LAD disease ( $\geq$ 50% stenosis) with or without other coronary artery disease (CAD), CAD ( $\geq$ 70% stenosis) without significant LMCA or ostial LAD, or no significant CAD. Univariate followed by multivariate logistic regression analyses of clinical, electrocardiographic, stress test, and single photon-emission computed tomographic MPI variables were used to identify significant correlates of LMCA or ostial LAD stenosis. Bayesian analysis of the data also was performed.

**RESULTS** LMCA (n = 38) or ostial LAD (n = 42) stenosis occurred in 75 patients (5 patients had both). The remainder had CAD without LMCA or ostial LAD stenosis (n = 276) or no CAD (n = 103). In multivariate analysis, the strongest predictor was stress-induced STE in lead aVR (p < 0.0001, area under the curve 0.82). Both left ventricular ejection fraction (after stress) and percent reversible LAD ischemia on single photon-emission computed tomographic MPI also contributed significantly in multivariate analysis (p < 0.005 and p < 0.05, respectively, areas under the curve 0.60 and 0.64, respectively). Although additional electrocardiographic, stress test, and MPI variables were significant univariate predictors, none was statistically significant in multivariate analysis. At 1-mm STE in lead aVR, sensitivity for LMCA or ostial LAD stenosis was 75%, specificity was 81%, overall predictive accuracy was 80%, and post-test probability increased nearly 3 times from 17% to 45%.

**CONCLUSIONS** Stress (ETT)-induced STE in lead aVR is an important indicator of significant LMCA or ostial LAD stenosis and should not be ignored. (J Am Coll Cardiol Img 2011;4:176–86) © 2011 by the American College of Cardiology Foundation

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Prior studies have demonstrated that ST-segment elevation (STE) in electrocardiographic (ECG) lead aVR in the setting of acute coronary syndromes may indicate the presence of severe stenosis or occlusion of the left main coronary artery (LMCA) or proximal left anterior descending coronary artery (LAD) (1–10). Data re-

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garding the significance of STE in lead aVR in the setting of exercise treadmill testing (ETT), however, are limited. Indeed, current practice guidelines indicate that it should be disregarded in the interpretation of exercise ECG findings (11), notwithstanding reports suggesting that STE in lead aVR may be predictive of hemodynamically significant LMCA or very proximal LAD stenosis in this setting (12–14). Accordingly, in the present study, we tested the hypothesis that ETT-induced STE in lead aVR is a useful indicator of hemodynamically significant LMCA or ostial LAD stenosis.

## METHODS

**Patient population.** A database search of patients undergoing cardiac catheterization at our institution between January 2008 and July 2009 was performed to identify 3 groups of patients: 1) those with significant LMCA or ostial LAD disease ( $\geq 50\%$  luminal diameter reduction) in addition to any other coronary lesions ( $\geq 70\%$  luminal diameter reduction for mid and distal LAD segments); 2) those with coronary artery disease (CAD) ( $\geq 70\%$  luminal diameter reduction) but not LMCA or ostial LD disease; and 3) those free of significant CAD (LMCA and all 3 major vessels free of any stenosis  $\geq 50\%$ ). Ostial LAD stenosis included any lesion proximal to the first septal perforator. All patients had undergone ETT according to the standard Bruce protocol with ( $n = 378$ ) or without ( $n = 76$ ) myocardial perfusion imaging (MPI; rest/stress 99mTc-methoxyisobutylisonitrile [MIBI])  $\leq 6$  months before the clinically indicated cardiac catheterization. LMCA ( $n = 38$ ) or ostial LAD stenosis ( $n = 42$ ) was present in 75 patients (5 patients had both). The remainder had either CAD of varying severity that did not involve the LMCA or ostial LAD ( $n = 276$ ) or no significant CAD ( $n = 103$ ). All were consecutive cases in that they were included in unbiased fashion in the order in which they were encountered in the database search, provided they met study entry criteria.

Patients with acute coronary syndromes or prior coronary artery bypass grafting were excluded. Patients who had undergone pharmacological stress in conjunction with MPI also were excluded, as were those whose baseline ECG studies indicated left bundle branch block, intraventricular conduction delays  $\geq 120$  ms, left ventricular hypertrophy with marked strain pattern (down-sloping ST-segment depression [STD]  $\geq 1$  mm with biphasic or inverted T waves), or marked anterior T-wave inversions (the Wellens pattern) concerning for active ischemia or possible LMCA or proximal LAD stenosis. Leads  $V_1$  to  $V_3$  were not used for ischemia assessment in patients with right bundle branch block, although inferior leads and leads  $V_4$  to  $V_6$  were if the baseline was isoelectric. No patient had STE in lead aVR on rest electrocardiography. Mild STD ( $< 1$  mm) in 1 or more leads on rest electrocardiography was not cause for exclusion.

Pertinent clinical details of the study population are provided in Table 1. The study received institutional review board approval.

### Single photon-emission computed tomographic (SPECT) MPI acquisition and analysis.

**IMAGE ACQUISITION.** SPECT MPI using 99mTc-MIBI ( $n = 370$ ) or thallium ( $n = 8$ ) was performed according to standard 1-day protocols and image acquisition guidelines (15). A dual-head Siemens gamma camera (E-CAM or C-CAM; Siemens Medical Systems, Erlangen, Germany) equipped with a low-energy, high-resolution collimator (32 views per camera head in a  $64 \times 64$  matrix) was used for image acquisition. The patient performed treadmill exercise according to the standard Bruce protocol (11). One minute before completion of symptom-limited exercise (test end point as defined in current practice guidelines [11]), radiotracer was injected intravenously. Gated images were obtained 30 to 45 min later in the same fashion as noted previously.

**SPECT MPI DATA AND IMAGE ANALYSIS.** Rest and stress myocardial perfusion images were analyzed objectively, in a quantitative fashion, using a standard 17-segment model (15) and a commercially available SPECT image analysis program (4DM-SPECT; Invia Medical Imaging Solutions, Ann Arbor, MI). Analysis was performed blinded to the

## ABBREVIATIONS AND ACRONYMS

<b>AUC</b>	= area under the curve
<b>CAD</b>	= coronary artery disease
<b>ECG</b>	= electrocardiographic
<b>ETT</b>	= exercise treadmill testing
<b>LAD</b>	= left anterior descending coronary artery
<b>LCx</b>	= left circumflex coronary artery
<b>LMCA</b>	= left main coronary artery
<b>LVEF</b>	= left ventricular ejection fraction
<b>MIBI</b>	= methoxyisobutylisonitrile
<b>MPHR</b>	= maximal predicted heart rate
<b>MPI</b>	= myocardial perfusion imaging
<b>1VD</b>	= single-vessel disease
<b>ROC</b>	= receiver-operating characteristic
<b>RPP</b>	= rate-pressure product
<b>SPECT</b>	= single photon-emission computed tomographic
<b>STD</b>	= ST-segment depression
<b>STE</b>	= ST-segment elevation
<b>3VD</b>	= triple-vessel disease
<b>TID</b>	= transient ischemic dilation
<b>2VD</b>	= double-vessel disease

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