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# Specificity and Sensitivity of Exercise-Induced ST Segment Elevation for Detection of Residual Viability: Comparison With Fluorodeoxyglucose and Positron Emission Tomography

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***Objectives.*** **We evaluated the sensitivity and specificity of exercise-induced ST segment elevation for the detection of residual myocardial viability.**

***Background.*** **Assessment of residual viability after myocardial infarction is relevant for establishing indication for revascularization. We have previously shown that exercise-induced ST segment elevation is a marker of residual viability.**

***Methods.*** **We studied 34 patients with a previous Q wave myocardial infarction (anterior in 21, inferior in 13) of whom 18 (group A) had exercise-induced ST segment elevation in more than one lead (mean [±SD] 1.8 ± 0.9 mm, range 1 to 4) and 16 (group B) did not. All patients underwent rest technetium-99m methoxyisobutyl isonitrile single-photon emission computed tomography (SPECT), fluorine-18 (F-18) fluorodeoxyglucose positron emission tomography and coronary angiography. The time elapsed between the infarction and the viability study was 72 ± 108 days (range 15 to 400) in group A and 516 ± 545 days (range 14 to 1,800) in group B.**

***Results.*** **The presence and site of previous infarction were confirmed by SPECT studies in all 34 patients. Uptake of F-18 fluorodeoxyglucose within the infarcted area was present in 18 of 18 patients in group A but in only 9 (56%) of 16 in group B ($p < 0.01$). In patients with an anterior infarction, the sensitivity, specificity and predictive accuracy of exercise-induced ST segment elevation for detection of residual viability were 82%, 100% and 86%, respectively (95% confidence intervals 46% to 83.5%, 59% to 100% and 55.6% to 87.1%, respectively).**

***Conclusions.*** **Exercise-induced ST segment elevation in infarct-related leads has a high specificity and acceptable sensitivity for detection of residual viability within the infarcted area.**

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The differentiation of myocardial regions with complete infarction from those containing viable, potentially salvageable ischemic tissue is of paramount importance for deciding whether revascularization may be indicated. Improved contraction of dysfunctional myocardium after nitroglycerin administration (1), ventricular ectopic beats (2), exercise (3) or inotropic agents (4) has been used to assess residual viability. Thallium-201 stress–redistribution (5) and reinjection (6) scintigraphy, as well as dipyridamole stress echocardiography (4), have also been used to differentiate reversible and irreversible damage. More recently, myocardial glucose metabolic imaging by positron emission tomography has been proposed as the reference standard technique for identification of severely ischemic yet metabolically active myocardium (7).

We previously showed (8) that exercise-induced ST segment elevation on infarct-related electrocardiographic (ECG) leads is almost invariably associated with a reversible perfusion defect on thallium-201 myocardial perfusion scintigraphy. On the basis of this observation we suggested that, at least in patients with recent myocardial infarction, transient ST segment elevation may indicate residual viability because the occurrence of reversible ischemia within the infarct zone implies, by definition, persistence of viable, potentially salvageable myocardium.

However, in the context of perinecrotic ischemia, the significance of postexercise thallium-201 redistribution is not fully understood (9). Furthermore, when compared with metabolic imaging with fluorine-18 (F-18) fluorodeoxyglucose positron emission tomographic conventional thallium-201 redistribution scintigraphy has a considerably lower sensitivity for detecting residual viability (10).

Therefore, to gain further insight into the significance of exercise-induced ST segment elevation, we undertook the present study aimed at correlating the occurrence of exercise-induced ST segment elevation with the presence of metabolically active tissue. To this end, we used F-18 fluorodeoxyglucose positron emission tomographic imaging, the reference

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standard investigation technique for detection of myocardial viability.

## Methods

**Patients.** We prospectively studied 34 consecutive patients (28 men, 6 women; mean [±SD] age 55 ± 9 years, range 33 to 75) with a Q wave myocardial infarction. The diagnosis was based on a history of typical and prolonged chest pain, serial ECG recordings and serum enzyme determinations. Diagnosis was confirmed by the echocardiographic demonstration of regional wall motion abnormalities in the region explored by the ECG leads with abnormal Q waves. Fourteen patients were studied during the hospital period after the acute infarction, and the remaining 20 were enrolled from our outpatient clinic to which they had been sent for prognostic stratification. All were in New York Heart Association functional class I or II.

Patients with left ventricular hypertrophy, valvular heart disease or left or right bundle branch block or taking drugs known to affect the ST segment were excluded. Those with overt diabetes or impaired glucose tolerance were also excluded.

The protocol was approved by the ethics committee of our institution, and each patient gave written informed consent to participate in the study.

**Exercise testing.** All patients underwent maximal exercise testing on a treadmill using a computer-assisted exercise system (Case 12 Marquette Electronics Inc.,) according to the modified Bruce protocol. Exercise was performed on the morning after an overnight fast. Antianginal medications were stopped at least 72 h before the test, and only sublingual nitrates were allowed for up to 6 h before the test to relieve chest pain. A 12-lead ECG and systolic and diastolic blood pressure (cuff sphygmomanometer) were recorded at rest, during the third minute of each exercise stage, at peak exercise, 1 min after exercise and every 2 min into recovery. Leads II, $V_1$ and $V_5$ were continuously monitored. The test was terminated when the target heart rate was achieved; when severe chest pain, dyspnea, fatigue, complex ventricular arrhythmias or hypotension occurred; or when ST segment depression >1 mm developed. ST segment elevation in infarct-related leads was not in itself considered a reason for exercise termination. Maximal predicted heart rate was calculated 220 minus age. Interpretation of ST segment deviation was performed in blinded manner by two independent observers. Disagreement was resolved by consensus. Exercise-induced ST segment elevation >1 mm above the baseline ST segment level (80 ms after the J point) in more than one ECG lead with abnormal Q waves was considered significant. When present, diagnostic ST segment depression on noninfarct-related leads was also noted.

**Positron emission tomographic studies of myocardial glucose metabolism.** Regional myocardial glucose metabolism was assessed by positron emission tomography, and F-18 fluorodeoxyglucose was synthesized according to the method described by Hamacher et al. (11) with a compact automated module connected to the cyclotron (CTI/Siemens RDS 112 cyclotron, Siemens/CPS). The labeled glucose analogue was used within 1 h of its preparation. Positron emission tomographic studies were carried out with an ECAT 931/04-12 tomograph (Siemens/CPS) equipped with germanium-68 retractable ring sources for transmission scans; transaxial and axial field of views were, respectively, 55.5 and 5.4 cm. Blood glucose and insulin levels were measured at the time of F-18 fluorodeoxyglucose injection. To enhance detection of ischemic and yet viable tissue, patients fasted overnight (15 h). This method has been shown to be very sensitive for detecting areas of viable myocardium (12,13). To correct for photon attenuation, two transmission scans were performed in the region encompassing the heart, previously identified on a rectilinear scan; indelible ink lines that defined the upper limit of the positron emission tomographic field of view were drawn on the torso. Two consecutive emission scans, each lasting 10 min, were carried out between 40 and 60 min after the intravenous administration of ~250 MBq of F-18 fluorodeoxyglucose. The two emission scans were performed by sliding the bed axially to acquire two sets of seven tomographic images of radioactivity distribution. Fourteen contiguous slices, 6.75 mm thick, were reconstructed in the transaxial plane using the Hann filter (cutoff frequency 0.5 cycles/pixel) on a 64 × 64 matrix. Under these conditions the spatial resolution in the transaxial plane was 0.8 cm full-width at half-maximum.

**Single-photon emission computed tomographic studies of myocardial perfusion.** Because the regional myocardial perfusion study was only meant to identify the infarct area potentially containing residual viable tissue, no attempt was made to quantify perfusion, which was assessed by single-photon emission computed tomography (SPECT) on the day after the positron emission tomographic metabolic study. Seven hundred forty megabecquerels of technetium-99m (Tc-99m) methoxyisobutyl isonitrile (MIBI) was injected intravenously. A standard cholecystokinetic fatty meal was provided 30 min after injection, and tomographic imaging was started within 90 min of tracer injection, using a large field of view, single-head rotating gamma camera (either a STARCAM 400 AC, General Electric or a 7500 Orbiter, Siemens, Erlangen, Germany) equipped with a high resolution, low energy parallel-hole collimator and interfaced with a dedicated computer. Just before the SPECT studies, radioactive external markers were placed on the torso at the level of the indelible ink lines that defined the upper limit of the positron emission tomographic field of view. Sixty-four angular projections (64 × 64 matrix) were obtained in ~40 min over 360°. Transaxial slices, 6.2 cm thick, were reconstructed using a filtered back-projection algorithm with a Butterworth filter (cutoff frequency 0.4 cycles/pixel). No attenuation correction was performed. Spatial resolution in the transaxial plane was 1.8-cm full-width at half-maximum.

**Combined positron emission tomographic and SPECT assessment.** A semiquantitative analysis was carried out on tomographic images of perfusion and metabolism by dividing the left ventricle into six segments: anterior, apical, inferior,

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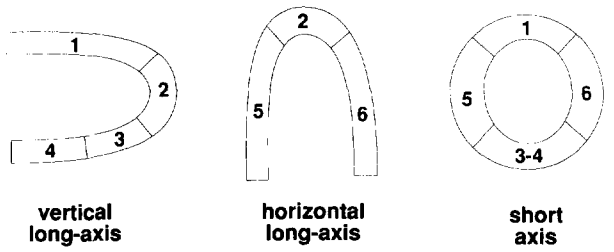


**Figure 1.** Subdivision of the left ventricle into six segments on tomographic images.

lateral, posterior and septal (Fig. 1). The positron emission tomographic and SPECT data were transferred to a SUN workstation (SUN 4/330, SUN Microsystem) for image processing and integration through an Ethernet network connection. The reconstruction of the SPECT transaxial slices was started from the level defined by the radioactive markers, consistent with the upper limit of the positron emission tomographic field of view, to match corresponding transaxial slices in the SPECT and positron emission tomographic studies. Images were decoded and converted to a standard file format. The SPECT and positron emission tomographic transaxial slices were realigned along the horizontal and vertical long and short axis with a commercially available software (Image tool, Siemens, Erlangen, Germany).

Corresponding positron emission tomographic and SPECT images were displayed on a color TV screen in random order and analyzed in blinded manner by two experienced observers for the presence of F-18 fluorodeoxyglucose uptake within underperfused areas.

Each F-18 fluorodeoxyglucose positron emission tomographic image was displayed together with the matching perfusion slice, and circular regions of interest, 1 cm in diameter, were drawn in the areas of the left ventricular wall corresponding to the underperfused region (Fig. 3). Counts/pixel were measured in each region of interest, and values from two to five discrete regions of interest from each segment were averaged to obtain a mean segmental value. A segmental index of F-18 fluorodeoxyglucose uptake was calculated by dividing the mean value of counts/pixel in each segment by the mean value of counts/pixel in the ventricular cavity. Underperfused tissue was defined viable when the F-18 fluorodeoxyglucose index was above the 95% confidence interval defined in six segments from five normal subjects studied in the fasting state.

**Left ventriculography and coronary angiography.** Selective coronary angiography and left ventriculography were performed by the Judkins technique. Biplane left ventriculography was performed in the 30° right anterior and 60° left anterior oblique projections. The left ventricular silhouette was divided into seven segments whose regional wall motion was scored according to the recommendations of the American Heart Association (14) using the following scale: *grade 0* = normal; *grade 1* = hypokinesia (reduced systolic wall motion); *grade 2* = akinesia (no systolic wall motion); and *grade 3* = dyskinesia (paradoxic systolic expansion). A global left ventricular dysfunction score was then obtained by adding the scores of single segments. The left and right coronary arteries were imagined in multiple views, including craniocaudal projections. Coronary artery stenosis was considered significant if the lumen diameter was narrowed by ≥50%. The extent of retrograde collateral opacification of occluded vessels was also assessed and graded according to the classification of Cohen and Rentrop (15). The studies were evaluated by two observers in blinded manner.

**Correlations between ST segment changes and positron emission tomographic imaging.** Using F-18 fluorodeoxyglucose positron emission tomography as the reference standard for determining the presence of tissue viability, the occurrence of ST segment elevation on the exercise ECG was considered a true positive result when the change involved leads with abnormal Q waves corresponding to an area with increased F-18 fluorodeoxyglucose uptake; a false positive when the ST segment elevation did not correspond to an area with increased F-18 fluorodeoxyglucose uptake; a true negative when no ST segment elevation and no F-18 fluorodeoxyglucose uptake in the corresponding area were observed; a false negative when no ST segment elevation was seen in the presence of increased F-18 fluorodeoxyglucose uptake in the infarct area. The sensitivity, specificity and predictive accuracy of exercise-induced ST segment elevation in detecting the presence of residual tissue viability within an area of Q wave myocardial infarction were determined using the following: *Sensitivity* = True positive/(True positive + False negative); *Specificity* = True negative/(True negative + False positive); and *Predictive accuracy* = (True positive + True negative)/(True Positive + True Negative + False positive + False negative).

**Statistics.** Data are presented as mean value ± SD. Statistical significance of continuous variables was determined with a two-tailed Student *t* test. Parametric variables were compared by the chi-square test. Regional myocardial wall motion, perfusion and metabolism were compared using two-way analysis of variance. Comparisons between subgroups concerning the time from infarction and patency of the infarct-related vessel were performed using Bonferroni probability procedures. Statistical significance was assumed when the null hypothesis could be rejected at $p = 0.05$.

## Results

**Clinical and ECG data.** Eighteen patients (15 men, 3 women; mean [±SD] age 57 ± 8 years, range 42 to 75) had exercise-induced ST segment elevation (mean 1.8 ± 0.9 mm, range 1 to 4) in more than one infarct-related lead and constituted group A (Table 1). Of these, 14 patients (78%) had an anterior and 4 (22%) an inferior myocardial infarction.

Sixteen patients (13 men, 3 women; mean age 54 ± 9 years, range 33 to 72), also with Q wave myocardial infarction (anterior in 7 [44%], inferior in 9 [56%]) but with no ST segment elevation in the infarct-related leads during exercise testing, constituted group B (Table 2). In both groups, the ST

**Table 1.** Clinical, Electrocardiographic, Scintigraphic and Angiographic Data for 18 Group A Patients With ST Segment Elevation

| Pt No. | Age (yr)/ Gender | Rest ECG Q Wave | Exercise Stress Test | | | Tc-99m MIBI SPECT | PET F-18 FDG Uptake | Coronary Angiogram (% stenosis) | LVWMA |
|---|---|---|---|---|---|---|---|---|---|
| | | | ST Elev | ST Dep | Chest Pain | | | | |
| 1 | 53/M | I, aVL, $V_1$–$V_5$ | I, aVL, $V_3$–$V_6$ | – | – | A, L, S | – | LAD 100%, RC 40%, Coll to LAD | (Ak)Ab, Al, Ap, S |
| 2 | 62/M | II, III, aVF, $V_6$ | III, aVF, $V_6$ | – | – | I, P | + | LAD 40%, RC 100%, Coll to RC | (Ak)I, Pb, (Hyp)Ap, S |
| 3 | 58/M | $V_2$–$V_5$ | aVL, $V_1$–$V_5$ | III, aVF | | A, S | + | LAD 60%, LCx 60% | (Ak)Al, Ap, S, (Hyp) |
| 4 | 44/M | $V_1$–$V_5$ | $V_3$–$V_5$ | – | – | A, S | + | LAD 100%, LCx 40%, Coll to LAD | (Ak)Al, S, (Dysk)Ap, (Hyp)I |
| 5 | 55/M | II, III, aVF, $V_5$, $V_6$ | II, III, aVF, $V_5$, $V_6$ | – | + | I, P | + | LAD 60%, LCx 100%, RC 100%, Coll to RC | (Ak), Pb, (Dysk)Ap, (Hyp)Pl |
| 6 | 50/M | $V_1$–$V_6$ | $V_2$–$V_6$ | – | + | A, Ap, S | + | LAD 100%, Coll to LAD | (Ak)Ap, I, S, (Dysk)Al |
| 7 | 67/M | II, III, aVF | III, aVF | I, aVL, $V_2$, $V_3$ | + | P, L, I | – | RC 100%, Coll to RC | (Ak)Ap, Pb, (Hyp)I, Pl |
| 8 | 53/M | II, III, aVF, $V_5$, $V_6$ | II, III, aVF | $V_2$–$V_6$ | – | I, P | + | LCx 40%, RC 100%, Coll to RC | (Ak)Pb, Pl, (Hyp)Al, Ap, I |
| 9 | 42/M | $V_1$–$V_3$ | $V_2$–$V_5$ | II, III, aVF | – | A, Ap | + | LAD 100%, Coll to LAD | (Ak)Ap, (Hyp)S |
| 10 | 55/F | aVL, $V_1$–$V_3$ | $V_1$–$V_4$ | – | – | S, A | + | LAD 75% | (Ak)Ab, Al, Ap |
| 11 | 60/M | $V_2$–$V_6$ | $V_3$, $V_4$ | – | + | A | + | LAD 100%, LCx 100%, Coll to LAD | (Ak)Al, Ap, S |
| 12 | 60/M | aVL, $V_1$–$V_3$ | aVL, $V_2$–$V_4$ | II, III, aVF, $V_6$ | – | S, A | + | LAD 90% | (Ak)Al, S, (Dysk)Ap |
| 13 | 65/M | aVL, $V_1$, $V_2$ | $V_1$, $V_2$ | II, III, aVF, $V_5$, $V_6$ | + | A, Ap, S | + | LAD 100%, LCx 50%, Coll to LAD | (Hyp)Al, Ap, S |
| 14 | 65/F | $V_1$–$V_2$ | $V_2$, $V_3$ | – | – | A, Ap, S | + | LAD 100%, LCx 40% | (Ak)Al, Ap, S |
| 15 | 59/M | $V_2$–$V_6$ | aVL, $V_2$–$V_5$ | – | + | A, I, P, Pl, S | + | LAD 60%, RC 60% | (Ak)Al, Ap, (Hyp)Ab, I |
| 16 | 75/M | $V_2$–$V_6$ | $V_3$, $V_4$ | – | – | I, S, A | + | LAD 100%, Coll to LAD | (Ak)Al, Ap, S, (Hyp)I |
| 17 | 51/M | $V_3$–$V_5$ | $V_2$–$V_5$ | – | – | A, Ap, S | + | LAD 100%, Coll to LAD | (Ak)Al, Ap, S |
| 18 | 50/F | $V_1$–$V_5$ | $V_2$–$V_5$ | – | – | A, L | + | LAD 100%, Coll to LAD | (Ak)Al, Ap, S |

A = anterior; Ab = anterobasal; (Ak) = akinesia; Al = anterolateral; Ap = apex; Coll = collateral vessels; (Dysk) = dyskinesia; ECG = electrocardiographic; F = female; F-18 FDG = fluorine-18 fluorodeoxyglucose; (Hyp) = hypokinesia; I = inferior; L = lateral; LAD = left anterior descending coronary artery; LCx = left circumflex coronary artery; LVWMA = left ventricular wall motion abnormality; M = male; MIBI = methoxyisobutyl isonitrile; P = posterior; Pb = posterobasal; PET = positron emission tomographic; Pl = posterolateral; Pt = patient; RC = right coronary artery; S = septal; ST Elev = ST segment elevation; ST Dep = ST segment depression; Tc-99m MIBI SPECT = technetium-99m MIBI single-photon emission computed tomography; – = absent; + = present.

segment on the infarct-related leads was isoelectric or only slightly (<1.0 mm) elevated at rest.

The time interval from infarction to enrollment was 72 ± 108 days (range 15 to 400) in group A and 516 ± 545 days (range 14 to 1,800) in group B ($p < 0.01$). Eight patients in group A (seven with an anterior, one with an inferior myocardial infarction) and seven in group B (four with an anterior, three with an inferior myocardial infarction) had received intravenous thrombolytic therapy within 4 h from the onset of chest pain.

Six patients (33%) in group A and six (38%) in group B had ST segment depression that involved noninfarct-related leads (p = NS). Six patients (33%) in group A and one (6%) in group B had angina during the test ($p = 0.05$). Total exercise time was 686 ± 252 s in group A and 844 ± 509 s in group B (p = NS). Rate-pressure product at peak exercise was 21,311 ± 4,789 beats mm Hg/min in group A and 23,560 ± 6,193 beats mm Hg/min in group B (p = NS).

**Myocardial perfusion and glucose metabolism.** All 34 patients in both groups had a perfusion defect consistent with the site of previous infarction. There was complete agreement between the two observers in all cases.

All 18 patients in group A had increased F-18 fluorodeoxyglucose uptake in the infarct area. Conversely, only 9 (56%) of the 16 patients in group B had evidence of within-infarct myocardial viability on the positron emission tomographic study ($p < 0.01$). When only anterior infarctions were analyzed in the two groups, all 14 patients in group A had F-18 fluorodeoxyglucose uptake, whereas only 3 of the 7 patients with an anterior infarction in group B had residual metabolic activity within the infarct area. A representative example of exercise ECG, SPECT and position emission tomographic data obtained in a group A patient is shown in Figures 2 and 3.

Using F-18 fluorodeoxyglucose positron emission tomography as the reference standard for determining the presence of tissue viability, the sensitivity, specificity and predictive accuracy of exercise-induced ST segment elevation for detecting the presence of residual tissue viability were 67%, 100% and 74% (95% confidence interval [CI] 46% to 83.5%, 59% to 100% and 55.6% to 87.1%, respectively) and for anterior infarctions, respectively, 82%, 100% and 86% (95% CI 56.6% to 96.2%, 39.8% to 100% and 63.7% to 97%, respectively).

**Table 2.** Clinical, Electrocardiographic, Scintigraphic and Angiographic Data for 16 Group B Patients Without ST Segment Elevation

| Pt No. | Age (yr)/ Gender | Rest ECG Q Wave | Exercise Stress Test: ST Elev | Exercise Stress Test: ST Dep | Exercise Stress Test: Chest Pain | Tc-99m MIBI SPECT | PET F-18 FDG Uptake | Coronary Angiogram (% stenosis) | LVWMA |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 51/M | II, III, aVF | – | – | + | I, L | – | LCx 100% | (Ak)I, Pl, (Hyp)Al, Ap, S |
| 2 | 54/M | aVL, $V_1$–$V_3$ | – | II, III, aVF | – | A, S | – | LAD 50% | (Hyp)Al, Ap, S |
| 3 | 48/M | II, III, aVF | – | – | – | I, P | – | RC 100%, Coll to RC | (Hyp)Ap, I, Pl |
| 4 | 57/M | $V_1$–$V_3$ | – | $V_4$–$V_6$ | – | I, S | – | LAD 75%, LCx 75%, RC 75% | (Hyp)Ap, I, S |
| 5 | 59/F | I, aVL, $V_1$–$V_5$ | – | – | – | A, S | – | LAD 100%, LCx 50%, RC 50%, Coll to LAD | (Ak)A, Ap |
| 6 | 62/M | $V_1$–$V_3$ | – | $V_5$, $V_6$ | – | A, Ap, I, S | + | LAD 75% | (Ak)Ap, S, (Hyp)Al, I, Po, Pl |
| 7 | 47/M | $V_2$–$V_6$ | – | – | – | Ap, A | – | LAD 100%, LCx 100%, Coll to LAD and LCx | (Ak)Al, (Hyp)Ap, S |
| 8 | 72/F | II, III, aVF, $V_5$, $V_6$ | – | – | – | L, P | + | LAD 60%, LCx 75%, Coll to RC | (Ak)Ap, I, Pl, (Hyp)Al, Pb, S |
| 9 | 47/M | II, III, aVF | – | – | – | S, I, L, P | – | LAD 95%, LCx 80%, RC 60% | (Ak)I, S, (Hyp)Al, Pb, S |
| 10 | 57/M | II, III, aVF | – | $V_5$, $V_6$ | – | I, L, P | + | LCx 40%, RC 60% | (Hyp)Ap, I, Pb, Pl |
| 11 | 55/M | II, III, aVF | – | $V_3$–$V_6$ | – | I, P | + | D1 100%, RC 100%, Coll to RC | (Ak)Pb, (Hyp)I, Pl |
| 12 | 33/M | II, III, aVF | – | – | – | I | + | LCx Irreg | (Hyp)I |
| 13 | 60/F | $V_1$–$V_6$ | – | – | – | A, Ap, S | + | LAD 100%, RC 50% | (Ak)Al, S, (Dysk)Ap |
| 14 | 56/M | $V_1$–$V_6$ | – | – | – | A, S | + | LAD 100% | (Ak)Al, S |
| 15 | 44/M | II, III, aVF | – | – | – | Ap, I, P | + | RC 50% | (Ak)Pb, Pl |
| 16 | 59/M | II, III, aVF | – | $V_3$, $V_5$ | – | I, P | + | LCx 100%, Coll to LCx | (Ak)I, Pb, Pl |

D1 = first collateral branch; Irreg = irregular; other abbreviations and symbols as in Table 1.

**Coronary angiography and left ventriculography.** On contrast ventriculography, all 34 patients had abnormal left ventricular wall motion in the area explored by leads with abnormal Q waves. Four patients (22%) in group A and one (6%) in group B had dyskinetic segments. On average, global left ventricular dysfunction was significantly greater in group A than group B (6.5 ± 1.6, range 3 to 9; 4.9 ± 2.1, range 1 to 9, respectively, $p < 0.02$).

Of the 18 patients in group A, 1 had three-vessel disease, 4 had two-vessel disease, and 13 had one-vessel disease. In 14 (78%) patient, the coronary artery supplying the infarcted territory was occluded. Retrograde filling of the occluded

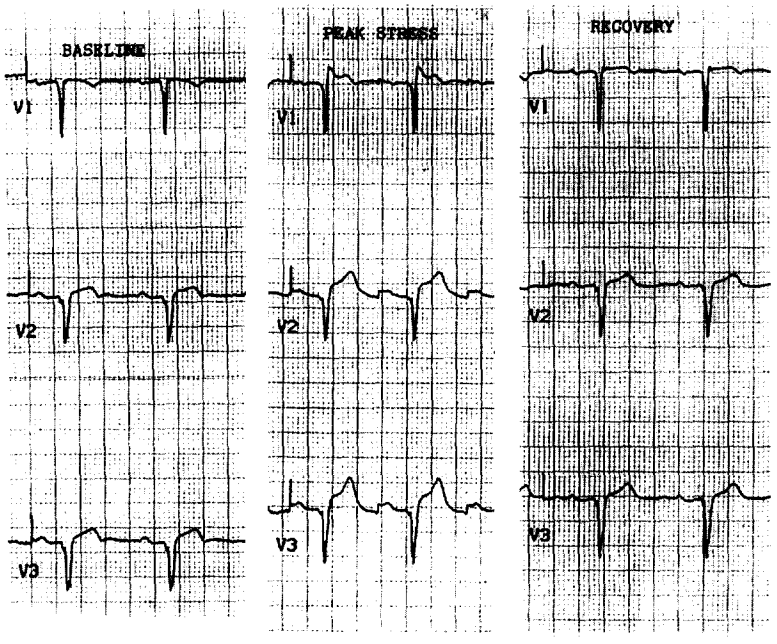


**Figure 2.** Patient 10. Electrocardiogram (leads $V_1$ to $V_3$) recorded at rest, at peak stress and after recovery; ST segment elevation is observed during exercise.

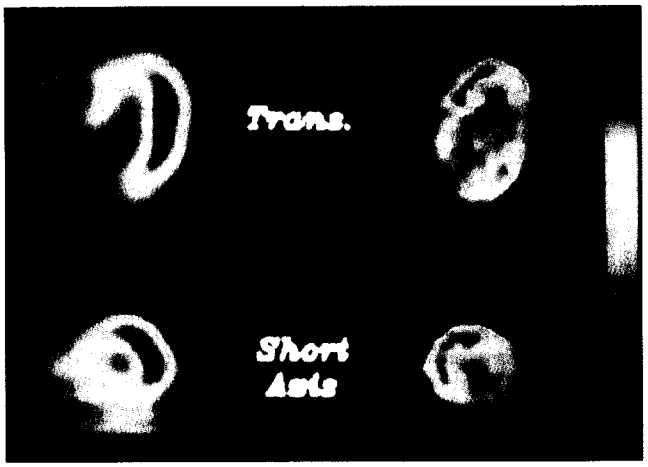


**Figure 3.** Patient 10. Rest myocardial perfusion (**left**) and positron emission tomographic (**right**) scans. **Left,** A perfusion defect involving the septum and anterior wall is evident on technetium-99m methoxyisobutyl isonitrile single-photon emission computed tomography. **Right,** Fluorine-18 fluorodeoxyglucose uptake is observed within the underperfused area at positron emission tomography. Trans = transaxial.

vessel by collateral flow was evident in 13 (93%) of these patients (grade 3 in 9 patients, grade 2 in 4). In the remaining four patients, the infarct-related artery was open, with critical residual narrowing (80 ± 8%).

Of the 16 patients in group B, 3 had three-vessel disease, 4 had two-vessel disease, and 8 had one-vessel disease ($p$ = NS vs. group A). The remaining patient had only minor irregularities of the infarct-related coronary artery. The infarct-related vessel was occluded in eight patients (50%), of whom five (63%) ($p \leq 0.05$ vs. group A) had angiographically visible collateral vessels (grade 3 in one patient, grade 2 in four).

## Discussion

The present study confirms and extends the results of our previous investigation (8) by showing that ST segment elevation that occurs during exercise testing on leads exploring Q wave myocardial infarction reliably indicates the presence of residual, within-infarct viable myocardium. This observation is of clinical relevance because it provides the background for the use of this simple, inexpensive and widely available diagnostic procedure for the identification of residual viability in the postinfarction period.

We investigated the significance of ST segment elevation in this context by using positron emission tomography with F-18 fluorodeoxyglucose, a marker of exogenous glucose uptake. In fact, this tracer has been shown (10) to detect residual metabolic activity even when other clinical tests suggest complete necrosis. During ischemia, myocardial metabolism is critically dependent on glucose utilization because fatty acid oxidation is impaired (16): When perfusion is severely reduced, anaerobic glycolysis may help support cell survival, although it is insufficient for maintaining contractility. Indeed, several investigators (4,7,13) have demonstrated that myocardial segments with severely depressed contractility and increased glucose uptake may contain significant amounts of viable myocardium that resume function on revascularization.

Most patients with ST segment elevation on infarct-related leads during exercise had a more recent infarction than those without ST segment elevation. This is not surprising because we previously showed (17) that residual tissue viability, as assessed by fluorodeoxyglucose uptake, cannot persist indefinitely after myocardial infarction. In fact, patients with a recent infarction have significantly larger areas of metabolically active myocardium within the necrotic region (17). The higher proportion of patients with collateral vessels to the infarcted area also suggests that retrograde flow might have contributed to preserve viability in group A.

Of the 18 patients in group A with ST segment elevation on exercise testing, only 6 experienced angina. Although the incidence of chest pain observed in our patients is lower than that reported in other studies (18), this percentage (33%) is in agreement with that described in patients with a recent myocardial infarction by Theroux et al. (19) and in a previous report by our group (20).

Whether ischemia or abnormal ventricular wall motion is the cause of ST segment elevation during exercise testing in patients with a Q wave myocardial infarction has been the subject of a number of investigations. Fox et al. (21) studied 24 patients with ST segment elevation after myocardial infarction. Because the ST segment change was abolished by coronary artery bypass surgery in 15 patients, Fox et al. suggested that the underlying mechanism was myocardial ischemia. Dunn et al. (22) and Sriwattanakomen et al. (23) concluded that ST segment elevation could be due to abnormal wall motion or peri-infarction ischemia, or both. Other investigators reported that ST segment elevation may result from left ventricular aneurysm (24,25), abnormal wall motion (26,27) and depressed left ventricular function (28).

Although no patient in the present study had a true ventricular aneurysm on ventriculography and two-dimensional echocardiography, our results suggest that exercise-induced ST segment elevation at the site of a previous Q wave myocardial infarction reliably indicates the presence of residual viable myocardium even when regional wall motion is severely abnormal. However, although ST segment elevation appears to be highly specific, its absence does not necessarily rule out persistence of viable tissue. In fact, >50% of the patients without ST segment elevation during exercise still had increased F-18 fluorodeoxyglucose uptake in the infarct area. The larger proportion of patients with inferoposterior myocardial infarction included in this group may partially account for the relatively high incidence of false negative results. Indeed, when analyzed separately, the results obtained in patients with an anterior myocardial infarction, both sensitivity and predictive accuracy increase to >80%.

Finally, the finding that left ventricular dysfunction was more severe in group A patients may be simply related to the much shorter interval elapsed from the myocardial infarction and therefore to a greater extent of myocardial stunning.

**Limitations of the study.** Our study has methodologic limitations in that groups A and B are not perfectly matched with

regard to site of infarction and time elapsed between its occurrence and enrollment. Furthermore, our results were obtained in a group of patients in whom the ST segment of the infarct-related leads was nearly isoelectric. The results might had been different had patients with rest ST segment abnormalities been enrolled.

Although F-18 fluorodeoxyglucose uptake is considered the reference standard for detection of myocardial viability, some problems related to its interpretation have to be considered (29,30). Unlike other investigations performed after glucose loading, our study used dietary suppression of F-18 fluorodeoxyglucose uptake in normal myocardium so that ischemic but metabolically active areas could be identified on the basis of an absolute increase in F-18 fluorodeoxyglucose uptake rather than by assessing flow/F-18 fluorodeoxyglucose activity ratios in the affected regions. With this technique, even small areas of ischemic tissue may show intense uptake of F-18 fluorodeoxyglucose compared with normal myocardium (31,32). Thus, under fasting conditions, myocardial F-18 fluorodeoxyglucose uptake may overestimate tissue viability, and this might at least partially explain the relatively high prevalence of glucose uptake within necrotic areas in our group B patients.

**Clinical implications.** The results of our study suggest that ST segment elevation that occurs on leads exploring an area of Q wave myocardial infarction during exercise testing is a specific marker of the presence of residual within-infarct viable tissue. Patients who exhibit ST segment elevation may benefit from revascularization procedures, even when regional wall motion is severely impaired. Prospective studies to test this hypothesis on the basis of objective measurements of left ventricular function are currently under way in our laboratory.

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