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The relationship between ischemia-induced left ventricular dysfunction, coronary flow reserve, and coronary steal on regadenoson stress-gated ^{82}Rb PET myocardial perfusion imaging

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Abstract

Background—Gated rubidium-82 (^{82}Rb) positron emission tomography (PET) imaging studies are acquired both at rest and during pharmacologic stress. Stress-induced ischemic left ventricular dysfunction (LVD) can produce a significant decrease in left ventricular ejection fraction (LVEF) from rest to stress. We determined the prevalence on PET of stress LVD with reduced ejection fraction (EF) and its association with absolute global and regional coronary flow reserve (CFR), and with relative perfusion defect summed difference score (SDS).

Methods and Results—We studied 205 patients with known or suspected coronary disease (120 M, 75 F, age 69 ± 13 years) who had clinically indicated rest/regadenoson stress ^{82}Rb PET/CT studies. Data were acquired in dynamic gated list mode. Global and 17-segment regional CFR values were computed from first-pass flow data using a 2-compartment model and factor analysis applied to auto-generated time-activity curves. Rest and stress LVEF and SDS were quantified from gated equilibrium myocardial perfusion tomograms using Emory Cardiac Toolbox software. LVD was defined as a change in LVEF of -5% from rest to stress. A subgroup of 109 patients also had coronary angiography. Stress LVD developed in 32 patients (16%), with mean EF change of $-10 \pm 5\%$, vs $+6 \pm 7\%$ for patients without LVD ($P < .0001$). EF was similar at rest in patients with and without stress LVD ($57 \pm 18\%$ vs $56 \pm 16\%$, $P = .63$), but lower during stress for patients with LVD ($47 \pm 20\%$ vs $61 \pm 16\%$, $P = .0001$). CFR was significantly lower in patients with LVD (1.61 ± 0.67 vs 2.21 ± 1.03 , Wilcoxon $P = .002$), and correlated significantly with change in EF ($r = 0.35$, $P < .0001$), but not with SDS ($r = -0.13$, $P = .07$). The single variable

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Conflict of interest

John Votaw and Kenneth Nichols receive royalties from Synterm, Inc. in relation to cardiac software used in this investigation.

most strongly associated with high risk of CAD (i.e., left main stenosis $\geq 50\%$, LAD $\geq 70\%$ stenosis, and/or 3-vessel disease) was stress EF ($\chi^2 = 17.3$, $P < .0001$). There was a higher prevalence of patients with territorial CFR values ≤ 1.0 , consistent with coronary steal, in the LVD group than in the non-LVD group (39% vs 12%, $P = .001$).

Conclusions—LVD developed in 16% of patients undergoing ^{82}Rb PET myocardial perfusion imaging, and was associated with multivessel coronary artery disease. There was a significant relationship between LVD and coronary blood flow during stress, with LVD corresponding to a low CFR. Territorial CFR ≤ 1.0 was more common in patients with LVD than those without, suggesting that coronary steal is an important pathophysiologic mechanism contributing to pharmacologic stress-induced LVD.

Keywords

PET/CT; left ventricular dysfunction; myocardial perfusion imaging; PET; coronary flow reserve; quantification; rubidium isotopes

INTRODUCTION

Left ventricular ejection fraction (LVEF) is an important parameter in the evaluation of patients with coronary artery disease (CAD). Resting LVEF is the strongest predictor of prognosis in a wide variety of clinical populations, including post-CABG and angioplasty patients, and those being managed without intervention.¹ Exercise or stress LVEF, and the change (Δ) in ejection fraction (EF) from rest to stress, also are important predictors of outcomes in CAD patients.² Studies using equilibrium or first-pass blood pool imaging have shown that a change in LVEF of $\geq 5\%$ from rest to stress, or low absolute stress LVEF, identifies subgroups of patients who have high risk three-vessel or left main coronary disease and an adverse prognosis.³ LVEF obtained from SPECT myocardial perfusion imaging (MPI) also has diagnostic and prognostic value.⁴ Using current technology, however, SPECT-gated wall motion studies assess LVEF at rest and 30–60 minutes following exercise or pharmacologic stress.⁵ Consequently, SPECT MPI wall motion studies may not detect stress-induced changes in LV function of shorter duration.

In contrast, with gated rubidium-82 (^{82}Rb) positron emission tomography (PET/CT), perfusion imaging and wall motion studies are acquired at rest and *during* pharmacologic stress, a more sensitive approach to detect stress-induced changes in LVEF.

Previous ^{82}Rb PET studies have shown that stress LVEF, and ischemic left ventricular dysfunction (LVD), are prognostically important in CAD,⁶ and can identify a subset of patients with three-vessel or left main CAD.⁷ However, the relationships between LVD and quantitatively determined absolute rest and stress myocardial blood flow (MBF) and coronary flow reserve (CFR) have not been determined.

Our objectives were to determine (1) the prevalence of stress LVD in a representative population of patients referred for PET imaging, (2) the relationship between LVD and conventional scintigraphic perfusion parameters such as relative perfusion defect scores, and (3) the relationship of coronary blood flow and CFR to LVD and its pathophysiology.

METHODS

Patients

This was a retrospective investigation of 205 consecutive patients (120 males, 85 females, age 69 ± 12 years) referred for rest/regadenoson stress CT attenuation-corrected ^{82}Rb -gated PET MPI between Jan 1, 2010 and June 30, 2011 to evaluate known or suspected coronary disease. This investigation was approved by the St. Francis Hospital Institutional Review Board. All data were handled in compliance with the Health Insurance Portability and Accountability Act of 1996.

Imaging and Stress Testing Protocol

Pharmacologic stress testing was performed using regadenoson in all patients.⁸ Stress testing procedures, including patient preparation, duration of fasting, abstention from caffeine, and withholding of cardiac medications, conformed to accepted standard protocols.⁵ Blood pressure, heart rate, and cardiac rhythm were monitored throughout the procedure. At rest, an activity of 1.30–1.67 GBq (35–45 mCi) of ^{82}Rb from a strontium-rubidium generator, which measured the delivered dose using a beta probe, was infused over 20–30 seconds (Bracco Diagnostics Inc., Princeton, NJ, USA).⁹ Initial quality control checks were performed immediately during the first-pass data acquisition phase by having the supervising cardiologist monitor the beta-probe readout of count rate changes during injection; only data for which count rates were consistent with an effectively delivered bolus of injected activity were analyzed. At peak pharmacologic stress, when hemodynamic steady state was achieved, an isotope dose with activity similar to that used for rest imaging was infused.

PET studies were performed on a GE Discovery VCT 64, PET/CT (General Electric, Milwaukee, Wisconsin, USA), a 24-slice LYSO system with a 14 cm field of view. CT scan transmission data were used to correct for attenuation using the manufacturer's iterative reconstruction software, which also corrected for scatter and random events. The correction for cascade gammas was not employed, as this feature was not available for this device.

All data were acquired in gated list mode and reconstructed by OSEM (20 subsets; 2 iterations; z axis filter = "standard"; post-filter = 2.57 mm FWHM), as recommended by the manufacturer.

Image Processing

For MBF, first-pass PET perfusion data were re-binned into 20 3-second frames, 5 12-second frames, and 7 30-second frames. Semi-automated algorithms (Emory University, Atlanta, GA) generated the longitudinal axis of the transaxial slices, the limits of the LV myocardium, and the LV epicardial and endocardial borders. A medical imaging physicist (KJN) adjusted these limits when necessary. The algorithms identified right ventricular and LV blood pools on dynamic first-pass PET data, and isolated regions of the LV myocardium using curve-fitting factor analysis.¹⁰ Regional myocardial time-activity curves were generated for rest and stress data. Factor analysis was used to correct for spillover effects.¹¹ Using a two-compartment model for ^{82}Rb kinetics,^{12,13} we applied a partial volume

correction and then used the Yoshida extraction fraction correction specific to ^{82}Rb ,¹⁴ to calculate rest and stress MBF for each of the 17 standard AHA/ACC segments. We noted that the Emory algorithm's method for setting myocardial limits could result in marked variability and low values for blood flow in standard AHA segments 1–3, possibly due to their proximity to the left ventricular outflow tract. Consequently, these segments were excluded from the blood flow analysis. Resting MBF values were adjusted for resting cardiac work, using the method of Czernin et al,¹⁵ according to the formula¹⁶:

$$\text{Resting MBF corrected for rate-pressure product} \\ = \text{resting MBF} \times 10,000 / ((\text{heart rate at rest}) \times (\text{systolic blood pressure at rest})). \quad (1)$$

CFR was computed using the following formula¹⁶:

$$\text{CFR} = \text{stress MBF} / \text{resting MBF corrected for rate pressure product}. \quad (2)$$

Minimal coronary vascular resistance (CVR) was computed as mean arterial pressure divided by MBF, using the following formula^{16,17}:

$$\text{CVR} = 0.33 \times ((2 \times \text{diastolic pressure}) + \text{systolic pressure}) / \text{MBF}. \quad (3)$$

The regional CFR values of the 14 segments were grouped into mean CFR values for the LAD, LCX, and RCA coronary territories.

Equilibrium myocardial perfusion portions of the data were re-binned as gated tomograms at 8 frames/R-R interval. Rest and stress LVEF's and volumes were calculated using Emory Cardiac Toolbox software (Emory University, Atlanta, GA).¹⁸ To check the consistency of the placement of limits for the apex, base, and myocardial walls, we evaluated the agreement between myocardial mass values computed from rest and stress data.

Stress-induced LVD was defined as a change in LVEF of $\geq 5\%$ from rest to stress.^{7,19–21} In patients who demonstrated LVEF decreases of $\geq 5\%$, but whose rest EF was $> 60\%$, careful visual examinations of wall motion cines were conducted to confirm a genuine reduction in cardiac performance, and exclude possible EF errors due to partial volume effects.²² Since an increase from rest to stress of LV end-systolic volume (ESV) is associated with increased mortality,²³ we also tabulated change in ESV.

Because a mean CFR ≤ 1.0 in a coronary territory has been associated with coronary steal, we evaluated the frequency of this finding in patients with and without LVD.^{24,25}

Polar perfusion maps using normal limits specific to ^{82}Rb for relative perfusion distributions were generated using Emory Cardiac Toolbox algorithms to determine summed stress score (SSS), summed rest score (SRS), and summed difference score (SDS).

Reproducibility of CFR Values

To determine reproducibility of ^{82}Rb PET computations of MBF and CFR, a reanalysis of data was performed in 33 patients chosen at random. Data were analyzed twice on two separate occasions by a medical imaging physicist (KJN), and once by another medical physicist at Emory University (TF). All computations were performed in a blinded fashion.

Coronary Angiography

A subgroup of 109 patients underwent coronary angiography at the discretion of their responsible physicians with a median interval of 3.5 days between PET and angiography. No known clinical events or coronary revascularization occurred between PET studies and angiography. Angiographic results were obtained from the clinical reports. Stenoses $\geq 70\%$ were defined as hemodynamically significant. In patients with previous coronary bypass surgery, the degree of stenosis in a coronary territory supplied by a saphenous vein graft was considered the degree of stenosis in that graft. If the graft was free of disease or had only a minor, non-obstructive blockage, then the degree of stenosis in that coronary territory was equal to the degree of stenosis in the native vessel, distal to the vein graft insertion. In patients who had angioplasty, the degree of stenosis in that vascular territory was the maximal degree of stenosis in the stent, or in the native vessel proximal or distal to it.

Statistical Analysis

Statistical analyses were performed using commercially available software ("Medcalc," Version 7.5.0.0., Medcalc Software, Inc., Mariakerke, Belgium). Values are reported as mean $\pm$ one standard deviation. Continuous variables were tested by the Kolmogorov-Smirnov test to determine if they were normally distributed. The paired or unpaired t test, as appropriate, was used to compare values between groups for continuous variables that were normally distributed; otherwise, the Wilcoxon test was used. Frequencies and percentages were used to characterize categorical variables. Chi-squared analysis of proportions was used to compare ratios between subgroups.

Receiver operating characteristic (ROC) curves were generated from continuous variables, using LVD ($\text{EF} \leq -5\%$) as the reference standard. The threshold for abnormality generated by ROC curve analysis for variables were used to dichotomize methods from which sensitivity, specificity, accuracy, positive predictive value, and negative predictive value were determined. Linear regression was used to analyze relationships between continuous variables and change in LVEF from rest to stress. Univariate logistic regression analyzed associations with LVD of discrete and continuous variables. Angiographic study correlations were assessed using the rank correlation test of continuous variables vs the number of vessels judged by angiographers visually to have occlusions of $\geq 70\%$.

For all tests, probability (P) $< .05$ was defined as statistically significant.

RESULTS

Patient Population

There was a high prevalence of known CAD, coronary risk factors, and history of revascularization in the group (Table 1). LVD was present in 16% (32/205) of patients. There were no differences in age, gender, or other clinical characteristics between patients with and without LVD (Table 1), although women had a higher mean EF response than men ($EF = 5 \pm 7\%$ vs $2 \pm 8\%$, $P = .02$). There were no differences in resting hemodynamics or response to vasodilator between the groups (Table 2).

Patients with LVD had a mean change in LVEF from rest to stress (EF) of $-10 \pm 5\%$ vs $+6 \pm 7\%$ for patients without LVD ($P < .0001$). Resting EF was similar in patients with and without LVD, but was lower during stress in patients with LVD (Table 3). Resting LV end-diastolic volume (EDV) was significantly higher in patients with LVD than those without LVD. With vasodilator stress, EDV did not change in LVD patients but increased significantly in non-LVD patients. LV ESV at rest was similar for both groups. Stress ESV increased significantly in the LVD group, and decreased slightly in the non-LVD group (Table 3). LV mass values were similar for rest and stress (121 ± 37 vs 124 ± 49 grams, $P = .45$) and correlated closely with one another ($r = 0.94$, $P < .0001$), which confirmed the consistency of LV limits used to generate LV volumes.

MBF and CFR Calculations and Their Reproducibility

For the entire group resting MBF was 0.86 ± 0.54 mL/g/minute, and stress MBF was 1.65 ± 0.95 mL/g/minute, with flow reserve 2.12 ± 1.00 (Table 4). Pearson coefficients for rest MBF, stress MBF, and CFR were $r = 0.99$, 0.99 , and 0.93 for intra-rater correlations, and 0.93 , 0.95 , and 0.94 for inter-rater correlations. Bland-Altman analysis for CFR values indicated no intra-rater difference (median = 0.00 ; range = -0.50 to 0.51), and no inter-rater difference (median = 0.00 ; range = -0.52 to 0.51).

Relationships Between LVEF, LVD, MBF, and Flow Reserve

Resting global MBF was similar in patients with and without LVD (0.93 ± 0.64 vs 0.84 ± 0.52 mL/g/minute, $P = .40$), as was stress MBF (1.49 ± 1.26 vs 1.67 ± 0.89 mL/g/minute, $P = .33$), but global CFR was significantly lower in patients with LVD (1.61 ± 0.67 vs 2.21 ± 1.03 , Wilcoxon $P = .002$). Minimal CVR during stress was significantly higher for patients with LVD (97 ± 57 vs 72 ± 45 mmHg/mL/g/minute, Wilcoxon $P = .03$) (Table 4). By ROC analysis, global CFR 1.47 predicted LVD with a sensitivity of 52%, specificity of 81%, and accuracy (area under the ROC curve) of $69 \pm 5\%$. There was a significant correlation between EF and CFR ($r = 0.35$, $P < .0001$) (Figure 1). EF was also significantly correlated with minimal CVR during stress ($r = -0.22$, $P = .002$) (Figure 2), and with MBF during stress ($r = 0.14$, $P = .047$) (Figure 3).

There was a significantly higher prevalence of patients with CFR values ≥ 1.0 in at least one coronary territory in the LVD group than in the non-LVD group (39% vs 12%, $P = .001$). MBF during stress was significantly lower for territories with CFR < 1.0 than all other territories (0.82 ± 0.58 vs 1.67 ± 0.99 mL/g/minute, $P < .0001$).

Relation Between Relative Perfusion Scores, LVEF, and LVD

All quantified perfusion scores were greater than values expected for a normal population.²⁶ Relative perfusion scores were significantly different in patients with LVD (Table 3). There were significant correlations between EF and SSS ($r = -0.22$, $P = .002$), and SRS ($r = -0.18$, $P = .01$), but not SDS ($r = -0.13$, $P = .07$). Univariate logistic regression analysis demonstrated that the variable most closely associated with LVD was CFR ($\chi^2 = 10.3$, $P = .01$; regression relationship: $-0.18 - (0.81 \pm 0.28) \times \text{CFR}$).

Angiographic Subgroup

For the subgroup of 109 patients who underwent coronary angiography, 19 patients had LVD, and LVD was significantly associated with the number of diseased vessels ($\chi^2 = 6.79$, $P = .01$). In patients with 0–1 vessel disease, EF increased from rest to stress while in patients with 2–3 vessel disease EF decreased ($+5 \pm 8\%$ vs $-2 \pm 10\%$, $P = .0002$) (Figure 4), with Spearman Rank correlation = -0.25 ($P = .01$).

The numbers of patients who had prior coronary revascularization or CABG were 26 with 0-vessel, 9 with 1-vessel, 9 with 2-vessel, and 7 with 3-vessel CAD. More patients had prior revascularization or CABG who had 0-vessel than 3-vessel CAD ($P = .0006$). In patients with prior revascularization or CABG, EF increased from rest to stress for those with 0-vessel disease but fell for those with 3-vessel CAD ($+5 \pm 10\%$ vs $-4 \pm 13\%$, $P = .047$).

We also analyzed the PET parameters that correlated with high risk coronary of CAD, which was defined as left main stenosis $\geq 50\%$, proximal to mid vessel LAD stenosis $\geq 70\%$, or 3-vessel CAD with $> 70\%$ stenoses present in all vessel and at least one-vessel having a 70% stenosis in its proximal portion (first one-third of vessel).⁷ There were 31 patients who had high risk coronary anatomy. By univariate logistic regression analysis, the variable most strongly associated with high risk of CAD was stress EF ($\chi^2 = 17.3$, $P < .0001$; regression relationship: $+1.98 - (0.053 \pm 0.015) \times \text{stress EF}$) (Table 5). There were 11/31 patients with high risk of CAD who had LVD, vs 8/78 without high risk of CAD who had LVD ($\chi^2 = 8.1$, $P = .004$). Moreover, the negative predictive value of EF $> -5\%$ to exclude high risk of CAD was 89%.

DISCUSSION

This study was undertaken to investigate the prevalence and pathophysiologic correlates of stress-induced LVD detected by pharmacologic ^{82}Rb PET myocardial perfusion imaging. Previous studies have reported a relationship between reversible perfusion defects (SSS and SDS) and stress-induced LV dysfunction.⁷ The salient finding from our investigation is documentation of a direct correlation between quantitatively determined CFR and EF.

LVEF Response to Stress

Historically, the change in LVEF from rest to stress was measured using exercise-gated radionuclide ventriculography (RNV).^{27,28} A decrease in LVEF from rest to stress was associated with functionally significant CAD and adverse cardiac events.³ Gated SPECT myocardial perfusion imaging largely supplanted RNV, as it provided both perfusion and

LV functional information. Since gated SPECT wall motion data are acquired at rest and 30–60 minutes post-stress, LV volume and EF values at both time points are comparable in most patients. In patients with severe stress-induced ischemia, however, there may be a decrease in LVEF and persistent regional asynergy post-stress, relative to rest.²⁹

Gated ⁸²Rb PET has several advantages over SPECT for analyzing stress-induced changes in LV function. Because of the short half-life of the radionuclide, stress data are acquired simultaneously with administration of the pharmacologic agent, so that acute and transient changes in LVEF and wall motion are detected.⁷ PET also provides quantification of absolute global and regional MBF and flow reserve.³⁰

Pathophysiology of EF Response

Regadenoson is an A2A adenosine receptor agonist that produces vasodilation in peripheral and coronary vascular beds.³¹ Peripheral vasodilation leads to reduced afterload, and baroreceptor-mediated sympathetic stimulation, both of which result in improved ventricular performance and increased EF.³² Coronary vasodilation and increased blood flow also may cause enhanced ventricular performance.³³ Previous investigations have found that patients uniformly increased EDV, or preload during coronary vasodilation,⁷ suggesting that increased LVEF results in part from a Frank-Starling mechanism. In our investigation, the group with LVD had significantly larger EDV at rest, which did not change during stress. This suggests that patients with LVD already require a high preload at rest in order to maintain ventricular function. Patients without LVD did increase EDV from rest to stress, as noted by others.⁷ Our non-LVD patients may have had less serious heart disease, and an adequate preload reserve to allow a Frank-Starling effect.

Dorbala et al⁷ found that women had a greater LVEF response to vasodilators than men. This same gender effect also was seen in our population, even though the prevalence of LVD was similar in both sexes.

The pathophysiologic mechanisms of pharmacologic stress-induced LV dysfunction have not been fully established. Previous studies have shown correlation between reversible perfusion defects (SSS, SDS), CAD extent, and LVD.^{7,19} In patients with no or mild CAD by angiography, LVEF increased with stress, while in patients with 3-vessel/left main disease, LVEF decreased. Our results are in general agreement with these observations. SSS was greater in patients with LVD, and there was an inverse correlation between SSS and

EF. Other studies found a stronger correlation of SDS with EF than did ours,^{7,19} and the current study found a stronger correlation of SRS with EF. These differences may arise from several possible sources: Our patient population had more extensive CAD, with a 28% incidence of MI. Our perfusion scores were derived from automatically applied normal limits, while other investigators have used visually assessed perfusion scores.^{7,19} Our study utilized regadenoson as the vasodilator, the peak hyperemic effect of which is 2.5 minutes, shorter than that of dipyridamole (although, in using ⁸²Rb as the radionuclide, most of the count data are acquired in the first 3 minutes after injection, given the short half-life of the radionuclide).

As in other studies, our patients with no or mild CAD (0–1 vessels) by angiography increased LVEF in response to vasodilators, while those with 2–3 vessel involvement did not.

Our data extend further the relationship between CAD and stress-induced LVD by demonstrating significant correlation between quantitative CFR and LVD. We found that CFR was significantly lower in the LVD group, and that there is a significant correlation between EF and CFR. CFR was a strong univariate predictor of LVD.

Coronary vasodilators increase overall blood flow, and would be expected to improve LV performance. Reversible perfusion defects result from nonhomogeneity of augmented regional perfusion rather than from ischemia.³⁴ True ischemia (with ECG changes and angina) is not common with pharmacologic stress.³⁵ Ischemia may occur in patients who develop coronary steal, which is a decrease in absolute blood flow from rest to stress in a coronary territory.³⁶ In PET imaging, coronary steal is detected as a mean flow reserve less than 1.0 in a coronary distribution.^{33,34} In our investigation, patients with LVD were three times more likely to demonstrate steal than those without LVD. Coronary steal is sometimes associated with a positive electrocardiographic ischemic response, which was uncommon in our LVD group. However, steal may also occur in patients with high grade coronary stenoses,²⁵ (which was common in our LVD group). Alternatively, coronary vasodilators may produce myocardial ischemia through endocardial steal, as coronary blood flow is rerouted from subendocardial to epicardial vessels.²⁵ Subendocardial ischemia may result in the less pronounced systolic shortening and relatively increased ESV.^{37,38} The increase in ESV in our LVD patients may reflect subendocardial steal. Our data thus suggest that true ischemia due to coronary steal, which is regional or subendocardial, is important mechanistically in causing LVD in coronary disease patients.

CONCLUSIONS

LVD, which was present in approximately 16% of the patients in our investigation, was associated with multivessel CAD and correlated with a low CFR. Segmental CFR < 1.0 was significantly more common in patients with than in those without LVD, which suggests that coronary steal is an important pathophysiologic mechanism producing pharmacologic stress-induced LVD.

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Figure 1.
Change in EF from rest to stress vs CFR.

Figure 2.
Change in EF from rest to stress vs minimal CVR during stress.

Figure 3.
Change in EF from rest to stress vs MBF during stress.

Figure 4.
Change in EF from rest to stress vs number of vessels involved in CAD.

Table 1

Characteristics for all patients, and for the subgroups with LVD (LVD+) and those without LVD (LVD-)

Characteristic	All (N = 205)	LVD+ (N = 32)	LVD- (N = 173)	P
Age (years)	69 ± 12	72 ± 9	68 ± 13	.13
Gender (% female)	42	25	44	.07
Body mass index (kg/m ²)	30.1 ± 7.6	28.1 ± 7.3	30.5 ± 7.6	.12
Diabetes mellitus (%)	31	34	31	.69
High blood pressure (%)	82	90	81	.24
History of smoking (%)	32	28	33	.57
Cholesterol (%)	77	70	79	.25
Family history of coronary disease (%)	7	3	7	.43
Angina (%)	37	38	37	.95
CAD (%)	53	45	54	.35
Cath (%)	52	59	50	.46
History of myocardial infarction (%)	28	24	28	.64
History of percutaneous coronary intervention (%)	32	24	33	.36
History of coronary artery bypass graft (%)	22	17	23	.51
Abnormal (ischemic) stress electrocardiogram (%)	4	4	4	.75

Table 2

Hemodynamic characteristics

	All (N = 205)	LVD+ (N = 32)	LVD- (N = 173)	P
Rest systolic BP (mmHg)	136 ± 21	141 ± 27	136 ± 20	.22
Stress systolic BP (mmHg)	133 ± 19	139 ± 21	133 ± 18	.07
systolic BP (mmHg)	-3 ± 14	-2 ± 14	-3 ± 14	.63
Rest diastolic BP (mmHg)	70 ± 13	70 ± 16	70 ± 13	.94
Stress diastolic BP (mmHg)	71 ± 11	69 ± 14	71 ± 11	.34
diastolic BP (mmHg)	+1 ± 15	-1 ± 11	+1 ± 16	.54
Rest heart rate (BPM)	70 ± 12	69 ± 12	71 ± 12	.44
Stress heart rate (BPM)	91 ± 15	90 ± 19	91 ± 14	.81
heart rate (BPM)	30 ± 22	31 ± 29	30 ± 21	.62
Rest MAP (mmHg)	92 ± 12	94 ± 13	92 ± 12	.30
Stress MAP (mmHg)	92 ± 10	93 ± 9	92 ± 11	.40
Rest RPP (mmHg/minute)	9,575 ± 2,045	9,755 ± 2,281	9,542 ± 2,005	.60
Stress RPP (mmHg/minute)	11,979 ± 2,680	12,337 ± 3,579	11,914 ± 2,492	.43

LVD+, Patients with left ventricular dysfunction; LVD-, patients without left ventricular dysfunction; BP, blood pressure; , change from rest to stress; BPM, beats per minute; MAP, mean arterial pressure; RPP, rate-pressure product.

Table 3

Function and perfusion indices

	All (N = 205)	LVD+ (N = 32)	LVD- (N = 173)	P
Stress end-diastolic volume (mL)	109 ± 55	121 ± 51	107 ± 56	.18
Rest end-diastolic volume (mL)	101 ± 50	120 ± 51	97 ± 50	.02*
end-diastolic volume (mL)	+9 ± 20	+1 ± 20	+10 ± 20	.02*
Stress end-systolic volume (mL)	52 ± 49	72 ± 52	48 ± 48	.01*
Rest end-systolic volume (mL)	51 ± 44	59 ± 48	49 ± 44	.24
end-systolic volume (mL)	+1 ± 14	+13 ± 15	-1 ± 13	< .0001*
Stress EF (%)	59 ± 17	47 ± 20	61 ± 16	.0001*
Rest EF (%)	56 ± 16	57 ± 18	56 ± 16	.63
EF (%)	+4 ± 9	-10 ± 5	+6 ± 7	< .0001*
SSS	9.8 ± 10.5	15.2 ± 11.6	8.8 ± 9.9	.001*
SRS	4.8 ± 7.3	8.0 ± 9.1	4.2 ± 6.7	.01*
SDS	5.0 ± 7.1	7.1 ± 7.1	4.6 ± 7.1	.03*

* $P < 0.05$ for LVD+ vs LVD-.

, Change from rest to stress.

Table 4

Blood flow and CFR

	All (N = 205)	LVD+ (N = 32)	LVD- (N = 173)	P
Uncorrected MBF at rest (mL/g/minute)	0.80 ± 0.56	0.93 ± 0.91	0.78 ± 0.48	.14
MBF at rest corrected for rate-pressure product (mL/g/minute)	0.86 ± 0.54	0.93 ± 0.64	0.84 ± 0.52	.40
MBF at stress (mL/g/minute)	1.65 ± 0.95	1.49 ± 1.26	1.67 ± 0.89	.33
CFR	2.12 ± 1.00	1.61 ± 0.67	2.21 ± 1.03	.002*
CVR at rest (mmHg/mL/g/minute)	147 ± 81	142 ± 81	148 ± 81	.71
CVR during stress (mmHg/mL/g/minute)	76 ± 47	97 ± 57	72 ± 45	.03*

* $P < 0.05$ for LVD+ vs LVD-.

Univariate logistic regression analysis results of perfusion and function stress, rest, and rest-stress change parameters that are predictive of high risk of CAD in 31 patients for a subgroup of 109 patients with angiography, i.e., left main stenosis 50%, proximal to mid vessel LAD stenosis 70%, and/or 3-vessel disease with at least one-vessel with a 70% stenosis in its proximal portion (first one-third of vessel)

Table 5

	<u>Stress (N = 109)</u>		<u>Rest (N = 109)</u>		<u>Rest-stress change (N = 109)</u>	
	χ^2	P	χ^2	P	χ^2	P
EF	17.3	<.0001*	8.0	.005*	8.8	.003*
MBF	10.7	.001*	4.8	.03*	7.9	.005*
Perfusion scores	10.3	.001*	7.4	.006*	2.7	.10
End-systolic volume	7.6	.006*	7.7	.005*	2.1	.15
End-diastolic volume	3.4	.07	7.3	.007*	2.3	.13

* P <0.05 for statistical significance of factors predictive of high risk of CAD.