# Global and Regional Left Ventricular Ejection Fraction Abnormalities During Exercise in Patients With Silent Myocardial Ischemia

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**Sixteen asymptomatic patients with coronary artery disease and silent myocardial ischemia were studied with exercise radionuclide ventriculography. Radionuclide ventriculograms were analyzed for changes in ejection fraction globally and in three regions. Results were compared with radionuclide ventriculograms in 24 symptomatic patients. Both groups (silent myocardial ischemia and angina) were similar in prevalence of multivessel disease and previous myocardial infarction, as well as in age and sex. Global ejection fraction decreased by 0.06 in both groups during exercise; regional ejection fraction also decreased by similar amounts in the two groups. Furthermore, the percent of regions with normal ejection fraction at rest that demonstrated a decrease during exercise was identical: 19 (60%) of 33 versus 26 (60%) of 46. These exercise radionuclide ventriculographic results suggest that abnormalities in regional and global left ventricular wall motion are similar in patients with coronary artery disease with and without silent myocardial ischemia.**

Few data are available concerning left ventricular ejection fraction abnormalities during exercise in patients with silent myocardial ischemia (1), yet such observations are of potential importance in improving our understanding of the pathophysiology of this syndrome. Silent myocardial ischemia has been attributed to: 1) different anginal pain thresholds in each person, 2) alterations in the central nervous system perception of pain, and 3) lesser amounts of myocardium at jeopardy during episodes of silent versus painful myocardial ischemia (2). One way to evaluate this latter possibility is by measuring changes in regional ejection fraction during exercise. Because new radioventriculographic techniques permit quantitative assessment of both global and regional ventricular function both at rest and during submaximal exercise, the present study was undertaken. In this study, 16 patients with silent myocardial ischemia underwent rest and exercise radionuclide ventriculography and the results of these studies were compared with those of 24 symptomatic patients.

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## Methods

**Study patients.** Group 1 included 16 consecutive patients with silent myocardial ischemia. Patients had to fulfill two selection criteria to be included in this group. First, they had to be asymptomatic (with or without a previous infarction) and on no antianginal medications. Second, they had to demonstrate ischemic ST segment depression on a recent graded exercise test in the absence of angina or its usual equivalents. Group 2 included 24 consecutive symptomatic patients whose condition was stable enough to permit discontinuance of antianginal medications for testing purposes. Patients in this group had both stable, chronic angina and readily provoked angina and ischemic ST depression during a recent graded exercise test.

**Cardiac catheterization studies.** All patients underwent standard right and left heart catheterization procedures, coronary arteriography and left ventriculography. Selective coronary arteriography was performed in multiple projections using either the Sones or Judkins technique. The arteriographic studies were analyzed without knowledge of the radionuclide studies. Significant coronary artery disease was defined as 70% or greater luminal stenosis.

**Radionuclide ventriculography.** Red blood cells were labeled in vivo by injecting unlabeled stannous pyrophosphate (5 mg Pyrolite, New England Nuclear Corporation), followed by injection of 15 to 25 mCi of technetium-99m as pertechnetate 15 to 20 minutes later.

*Rest gated radionuclide ventriculograms* were obtained utilizing an Anger scintillation camera with a high sensitivity straight bore, 30° slant hole collimator (Engineering Dynamics Corpora-



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tion) (3,4). Five minutes after injection of the radionuclide, the camera was positioned in the modified left anterior oblique projection (30° caudal tilt). Composite low count (400,000 counts) scintigrams were acquired until the camera obliquity that demonstrated the greatest separation of the right and left ventricles was found (typically between 35 and 45° obliquity). Ten million counts were acquired in matrix mode using a matrix size of 64 × 64 elements, collected on a magnetic disc and stored on magnetic tape using a digital computer (PDP 11/34, Digital Equipment Corporation) and commercially available software (GAMMA-11). Only those photo events falling within a 15% window centered on the photopeak of technetium-99m were recorded. Data acquisition was physiologically gated to the patient's electrocardiogram. The cardiac cycle was divided into 25 ms frames with data triggered by the patient's R wave.

*Global and regional ejection fractions* were obtained by manually tracing the left ventricular end-diastolic perimeter with an electronic cursor. A time-activity histogram was generated from this region of interest and end-diastolic and end-systolic frames were identified as those frames with the maximal and minimal counts, respectively, within the left ventricular perimeter. An automated computer algorithm (3,4) was used to generate background correction regions, as well as to divide the left ventricle into eight intraventricular subdivisions (Fig. 1). The two intraventricular subdivisions at the base of the heart (regions 1 and 8) were not included in the subsequent analysis of regional ejection fraction because 1) they tend to overlie the region of the mitral and aortic valves, and 2) precise definition of the superior border of these subdivisions was difficult because of the proximity to the left atrium and great vessels. As a result, background-corrected activity in these subdivisions during end-diastole was less than actual background activity in the majority of patients, probably resulting from inclusion of adjacent structures in the area. Regional ejection fractions for the remaining 6 subdivisions (in 3 anatomic regions formed by combining the subdivisions) are reported. Subdivisions 2 and 3 form an anteroseptal region, subdivisions 4 and 5 form an apical region, and subdivisions 6 and 7 are combined to form an inferoposterior region. Ejection fractions for the entire left ventricle, each of the 6 subdivisions and each of the 3 anatomic regions are calculated with use of the formula:

$$EF = \frac{ED - ES}{ED - B} \times 100\%,$$

where EF is ejection fraction, B is background and ED and ES are the end-diastolic and end-systolic counts, respectively.

*Exercise radionuclide ventriculography* (5) was performed after rest images were collected. Supine bicycle exercise was begun at 25 watt-seconds and increased by 12.5 watt-second increments at 1 minute intervals. When physician and patient detected any signs of fatigue, the load was increased to the next 12.5 watt-second load and continued at this final level for 3 minutes. Images were collected during the final 2 minutes of exercise. Generally, 2.5 to 3.0 million counts were collected during the 2 minute collection interval. During exercise, blood pressure was recorded by sphygmomanometry and a 12 lead electrocardiogram was continuously recorded. The rate-pressure product at peak exercise was obtained as the product of the peak heart rate and the peak systolic blood pressure. Global and regional ejection fractions were then obtained as described previously for studies at rest.

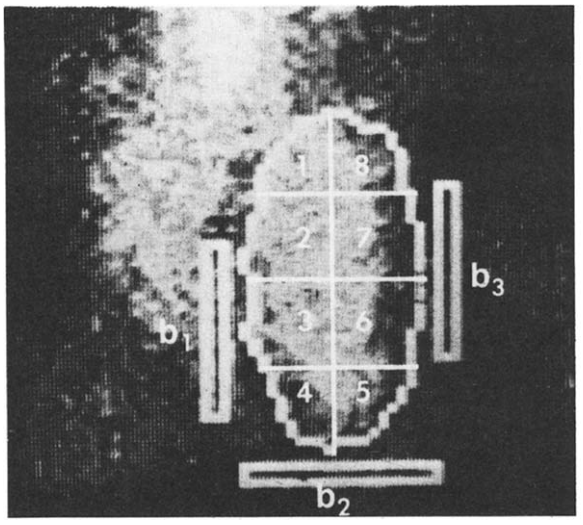


**Figure 1.** End-diastolic image of head in left anterior oblique position with hand-drawn left ventricular outline. Eight regions of interest (subdivisions within the left ventricle) are indicated by the numbers 1 to 8. Regions 2 and 3 represent the anteroseptal, 4 and 5 the apical and 6 and 7 the inferoposterior regions. Regions 1 and 8 are not used in analysis of regional ejection fraction because of the overlying cardiac valves and other structures (see text). Three background regions (rectangles $b_1$, $b_2$ and $b_3$ located outside the left ventricular perimeter) are constructed using an automated background correction algorithm.

## Results

**Clinical and arteriographic characteristics (Table 1).** Age and sex were similar in the patients with and without silent myocardial ischemia. Ten (63%) of 16 patients in Group 1 and 15 (63%) of 24 in Group 2 had a previous myocardial infarction. The prevalence of multivessel disease on coronary arteriography was also similar in both groups: 13 (81%) of 16 versus 18 (75%) of 24.

**Radionuclide ventriculograms (Table 2).** Global ejection fraction at rest was slightly higher in Group 1 (0.60)

**Table 1.** Clinical and Arteriographic Features in Patients With (Group 1) and Without (Group 2) Silent Myocardial Ischemia

| | Group 1 (16 patients) | p | Group 2 (24 patients) |
|---|---|---|---|
| Age (yr) | 55 ± 3* | NS | 54 ± 2 |
| Male | 13 | NS | 19 |
| Prior MI | 10 | NS | 15 |
| CAD | | | |
| 3 vessel | 7 | NS | 11 |
| 2 vessel | 6 | NS | 7 |
| 1 vessel | 3 | NS | 6 |

* = mean value ± standard error of the mean.
CAD = coronary artery disease, MI = myocardial infarction; NS = not significant; p = probability value

than in Group 2 (0.53), but this difference was not statistically significant. During exercise, global ejection fraction decreased by a similar amount (0.06) in both groups. The relative decreases were 9 and 12%, respectively (probability [p] value not significant). Analysis of each of the three regions also showed slightly (but not significantly) higher rest values in Group 1. With exercise, the reduction in regional ejection fraction was again similar when the two groups were compared. Furthermore, the percent of normal regions at rest (ejection fraction > 0.50) that demonstrated a decrease in ejection fraction during exercise was identical in both groups: 19 (60%) of 33 in Group 1 and 26 (60%) of 46 in Group 2.

## Discussion

The nature of the pathophysiologic mechanism in silent or painless myocardial ischemia remains obscure. The generation of the myocardial pain impulse is complex (6) and abnormalities in one or more stages of this process could account for the phenomenon. The magnitude of myocardium at jeopardy could also be a vital factor. This latter possibility has been suggested by the recent study of Chierchia et al. (7) in which hemodynamic changes measured during episodes of silent ischemia were found to be less severe than those seen in episodes of symptomatic ischemia. The present study has attempted to provide additional data concerning the amount of myocardium at jeopardy using a different approach: quantitative analysis of global and regional ejection fraction abnormalities with exercise. Because of the heterogeneous nature of coronary artery disease and the difficulties in qualitative analysis, our method for determining regional ejection fraction changes has proved useful in characterizing left ventricular function in patients with ischemic heart disease both at rest and during exercise (3–5).

*In the present study, patients were grouped according to their symptomatic status.* In Group 1, patients were either totally asymptomatic or asymptomatic after myocardial infarction. Equally important, all of these patients were free of symptoms during a positive graded exercise test; that is, they exhibited silent myocardial ischemia. In contrast, Group 2 patients had chronic stable angina and angina during positive graded exercise tests. None of the patients in either group was receiving antianginal medications at the time of the initial graded exercise test or during the subsequent rest and exercise radionuclide studies.

**Implications.** During the performance of the radionuclide studies, global and regional ejection fraction measurements were obtained. In these 40 patients with coronary artery disease with and without angina—in whom the prevalence of myocardial infarction and multivessel disease was similar—we could not discern any differences with this technique in the extent of wall motion abnormalities during exercise. Whether alterations in global and regional ejection fraction can accurately estimate the amount of myocardium at jeopardy is unclear; hence, the implications of these radionuclide studies must be interpreted with caution. They do suggest, however, that the extent of abnormalities in regional and global left ventricular wall motion is similar in patients with and without silent myocardial ischemia.

**Table 2.** Radionuclide Ejection Fraction in Patients With (Group 1) and Without (Group 2) Silent Myocardial Ischemia

| | Group 1 (16 patients) | p | Group 2 (24 patients) |
|---|---|---|---|
| Global | | | |
| Rest | 0.60 ± 0.04 | NS | 0.53 ± 0.04 |
| Exercise | 0.54 ± 0.04 | NS | 0.47 ± 0.04 |
| Anteroseptal region | | | |
| Rest | 0.60 ± 0.04 | NS | 0.51 ± 0.04 |
| Exercise | 0.56 ± 0.04 | NS | 0.45 ± 0.04 |
| Apical region | | | |
| Rest | 0.65 ± 0.06 | NS | 0.57 ± 0.05 |
| Exercise | 0.62 ± 0.06 | NS | 0.52 ± 0.05 |
| Inferoposterior region | | | |
| Rest | 0.70 ± 0.07 | NS | 0.66 ± 0.05 |
| Exercise | 0.64 ± 0.04 | NS | 0.59 ± 0.05 |

NS = not significant; p = probability value.

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