Radionuclide assessment of regional left ventricular function in acute myocardial infarction

To determine changes in global and regional left ventricular function following acute myocardial function, 17 patients underwent radionuclide angiography at 3 and 10 days post infarction. Five patients had nontransmural myocardial infarction and 12 had transmural infarction (six anterior and six inferior). There were no previous infarctions in 16 (94%) patients. Regional ejection fractions were calculated by dividing the left ventricle into four quadrants using the geometric center of the left ventricle on the end-diastolic frame as a reference point. At 3 days post infarction, 8 of 17 (47%) patients had an abnormality of global left ventricular ejection fraction (LVEF), whereas 16 of 17 (94%) patients had abnormalities of one or more regional ejection fractions ($p < 0.01$). Between 3 and 10 days, global LVEF did not change (51% to 49%, p = NS). However, there were significant changes in 23 of 68 (34%) regional LVEFs. These changes did not relate to type, ECG location, creatine kinase (CK) size of infarction, or initial global LVEF. These data suggest that regional LVEF is a sensitive technique for identifying segmental dysfunction associated with myocardial infarction. In addition, significant changes occur in regional LV function during acute myocardial infarction despite stable serial global LV performance. (AM HEART J 111:36, 1986.)

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Acute myocardial infarction produces variable left ventricular regional damage.[1] Depending on the extent and severity of the ischemic insult, global left ventricular function may be affected. However, in some cases, the extent of myocardial necrosis is limited and left ventricular global function is preserved. In these cases, left ventricular ejection fraction may be normal, but abnormalities of regional function may be present. Therefore, the quantitative assessment of regional left ventricular function may aid in the detection of acute infarction, particularly if global function is maintained.

In recent years, the development of radionuclide angiography has provided the ability to assess noninvasively left ventricular performance in acute myocardial infarction. Previous investigators[2-5] have suggested that left ventricular function remains relatively stable during the acute in-hospital phase. However, serial changes in quantitative regional functional analysis have not been reported following

acute myocardial infarction without acute coronary reperfusion intervention. Since infarction is usually a regional process, and since global analysis may mask changes in regional function, we investigated 17 consecutive patients during their in-hospital course to study the effect of infarction on changes in global and quantitative regional function during this period.

METHODS

The study population consisted of 17 consecutive patients, 16 men and 1 woman, with acute myocardial infarction. The mean age was 55 years (range 29 to 71 years). The diagnosis of myocardial infarction was based on the following criteria: (1) ischemic chest pain lasting at least 30 minutes, (2) typical abnormalities of myocardial enzymes including elevation of the MB fraction of creatine kinase, and (3) evolutionary ECG abnormalities. Only 1 patient of the 17 had had a previous infarction. Myocardial infarction was transmural by ECG in 12 patients (six anterior, six inferior) and nontransmural in five. Infarct size was measured with serial 4-hourly creatine kinases (CK) according to the method of Shell et al.,[6] and mean infarct size was 23 CK gm Eq/m^2 (range 6 to 49 CK gm Eq/m^2). At the time of presentation, 13 patients were Killip class I, three patients were Killip class II, and one patient was Killip class III.

At approximately 3 (mean 3.4 ± 1.2 days) and 10 (mean 9.8 ± 2.4 days) days post infarction, each patient under-
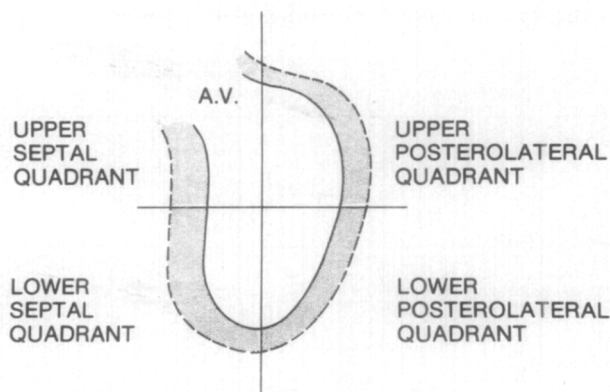
Fig. 1. A schematic representation of the assessment of regional ejection fraction. The end-diastolic geometric center was used as a fixed reference point.

Fig. 2. Percentage of patients with abnormalities of regional left ventricular ejection fraction *(LVEF)* and global LVEF at 3 days and 10 days post infarction.

went radionuclide angiography following in vivo labelling of red blood cells with 25 mCi of Technetium-99m pertechnetate. Resting studies were performed using a single crystal gamma camera (Searle Pho/Gamma IV, Des Plaines, Ill.) with a low-energy, all-purpose collimator, and a dedicated Nuclear Medicine computer (A^2, Medical Data Systems, Ann Arbor, Mich.). A total of 250,000 counts per frame were collected over 22 frames with ECG gating in the left anterior oblique projection. Left ventricular ejection fraction was derived using commercially available software, as the background corrected left ventricular stroke counts divided by background corrected left ventricular end-diastolic counts.

Following derivation of left ventricular ejection fraction, regional ejection fraction was determined using commercially available software. This program divides the left ventricle in the left anterior oblique projection into 4, 8, or 16 equal seqments using radial axial coordinates and the geometric center of the left ventricular end-diastolic frame. For the purpose of the present study, four regions, or quadrants, were used following division of the left ventricle by vertical and horizontal cursors at perpendicular angles through the center of the diastolic left ventricular frame. We labelled the four quadrants: upper septal, lower septal, upper posterolateral, and lower posterolateral (Fig. 1). Regional ejection fractions were calculated using background corrected time-activity curves.

Validation studies of regional ejection fraction. Regional ejection fractions were calculated in 10 normal healthy volunteers (mean age 27 years) to establish 95% confidence limits for each quadrant. The lower limit of normal was 38% for the upper septal quadrant, 61% for the lower septal quadrant, 34% for the upper lateral quadrant, and 67% for the lower lateral quadrant.

To determine reproducibility of the regional ejection fraction, 25 patients with stable coronary disease underwent two radionuclide studies on the same day, 1 to 2 hours apart. The patients were repositioned beneath the scintillation camera for the second study. The average variabilities of the regional ejection fractions are summarized in Table I. Mean initial and repeat regional ejection
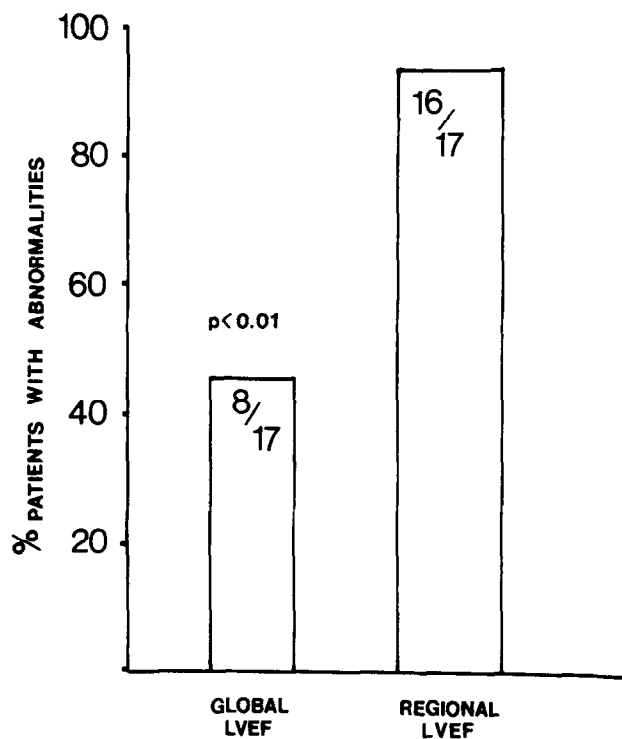
fractions for the upper septal quadrant were 43.1 ± 21.5% vs 44.8 ± 22.5%, p = NS; for the lower septal quadrant 38.1 ± 28.5% vs 33.2 ± 26.5%, p = NS; for the lower posterolateral quadrant 46.6 ± 26% vs 46.4 ± 23.5%, p = NS; and for the upper posterolateral quadrant 56.6 ± 21.0% vs 55.0 ± 19.0%, p = NS. There were no differences in regional ejection fraction variabilities in patients with normal and abnormal global ejection fraction (Table I). Using the data from these reproducibility studies, the 95% confidence limits were established as 2 standard deviations of the mean absolute variability.

The operator reprocessed the entire study on two separate occasions in 17 studies to determine observer variability. The operator was not aware of the initial processing results at the time of reprocessing. The mean variability of regional ejection fraction was: 0.9 ± 1.2% for the upper septal quadrant, 1.2 ± 2.5% for the lower septal quadrant, 0.7 ± 1.2% for the lower posterolateral quadrant, and 0.8 ± 1.2% for the upper posterolateral quadrant. The correlation between initial and repeat regional ejection fraction determinations for each quadrant was 0.99.

Statistical analysis. All data were expressed as mean ± standard deviation. Standard statistical techniques including analysis of variance, paired t testing, and chi square testing, were used to test the null hypothesis.

RESULTS

Global left ventricular ejection fraction. At 3 days post myocardial infarction, mean global left ventric-

Table I. Variabilities of serial regional ejection fraction in patients with normal and abnormal global ejection fractions

	Upper septal	Lower septal	Lower posterolateral	Upper posterolateral
All patients (n = 25)	6.6 ± 4.5	8.3 ± 6.0	8.5 ± 8.5	10.0 ± 9.0
LVEF > 55% (n = 9)	4.7 ± 3.6	8.7 ± 8.4	8.3 ± 6.6	9.1 ± 8.7
LVEF < 55% (n = 16)	7.6 ± 4.4	8.1 ± 4.4	8.6 ± 9.6	10.5 ± 9.6
p value*	NS	NS	NS	NS

LVEF = Left ventricular ejection fraction.
*p values for comparison of serial change in regional ejection fraction for patients with and without normal global ejection fractions.

Table II. Global and regional ejection fractions at day 3 post infarction

	Regional ejection fractions				Global ejection fraction
	US	LS	UPL	LPL	
Anterior TM MI (n = 6)	29 ± 15†	20 ± 19†	58 ± 18	51 ± 24	37 ± 7*
Inferior TM MI (n = 6)	54 ± 14	49 ± 29*	57 ± 21	43 ± 19*	51 ± 17
NTM MI (n = 5)	61 ± 22	77 ± 20	61 ± 24	70 ± 17	67 ± 15
Normal (n = 10)	68 ± 16	79 ± 10	72 ± 19	80 ± 6	74 ± 10

LPL = lower posterolateral; LS = lower septal; MI = myocardial infarction; NTM = nontransmural; TM = transmural; UPL = upper posterolateral; US = upper septal.
*p < 0.05 compared to normal.
†p < 0.01 compared to normal.

Table III. Serial changes in global and regional ejection fractions

	Day 3					Day 10				
	Global EF	Regional EF				Global EF	Regional EF			
		US	LS	UPL	LPL		US	LS	UPL	LPL
Anterior TM MI (n = 6)	37 ± 7	29 ± 15	20 ± 19	58 ± 18	51 ± 25	36 ± 11	30 ± 10	26 ± 12	61 ± 21	32 ± 30
Inferior TM MI (n = 6)	51 ± 17	54 ± 14	49 ± 29	57 ± 21	43 ± 19	49 ± 14	46 ± 16*	45 ± 24	62 ± 19	51 ± 14
NTM MI (n = 5)	67 ± 15	61 ± 22	77 ± 20	61 ± 24	70 ± 17	63 ± 16	59 ± 20	60 ± 22	65 ± 29*	68 ± 21

LPL = lower posterolateral; LS = lower septal; MI = myocardial infarction; NTM = nontransmural; TM = transmural; UPL = upper posterolateral; US = upper septal.
*p < 0.05 compared to day 3.

ular ejection fraction for the group was 51%. Left ventricular ejection fraction was significantly depressed in those with anterior myocardial infarction compared to those with inferior or nontransmural myocardial infarction (Table II).

Regional ejection fraction. Regional ejection fraction data are summarized in Table II. Regional ejection fraction in the subgroup with anterior myocardial infarction was significantly depressed in the upper and lower septal quadrants. Regional ejection fraction was significantly reduced in the lower septal and lower posterolateral quadrants in the subgroup with inferior myocardial infarction. There was no localization of infarction by regional ejection fractions in the nontransmural infarct subgroup.

At 3 days post infarction, abnormal regional ejection fractions were found in 15 of 24 (63%) regions

in patients with anterior myocardial infarction, in 11 of 24 (46%) regions in those with inferior infarction, and in 4 of 20 (20%) regions in those with nontransmural infarction. In addition, at 3 days post infarction, a significantly greater number of patients had abnormalities of regional function as compared to the number with abnormalities of global function. Eight of 17 (47%) patients had an abnormality of global left ventricular ejection fraction, whereas 16 of 17 (94%) patients had abnormalities of one or more regional ejection fractions (p < 0.01) (Fig. 2).

Serial changes in function. Between 3 and 10 days, two patients with anterior myocardial infarction and global ejection fraction less than 30% developed increasing congestive heart failure requiring therapy. One additional patient with nontransmural myocardial infarction whose ejection fraction fell from
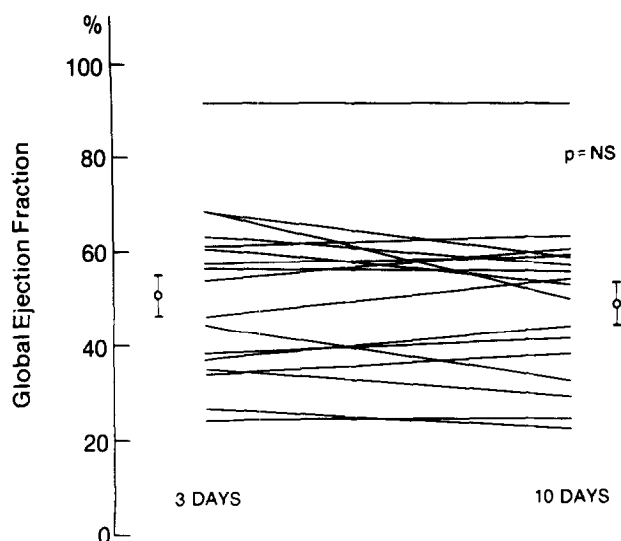
Fig. 3. Global ejection fraction at 3 days and 10 days post infarction.
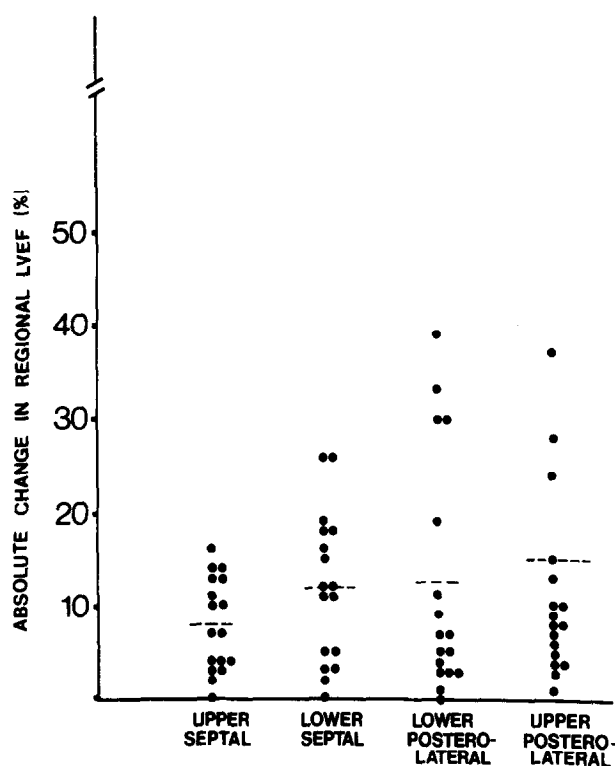

Fig. 4. Absolute change in regional left ventricular ejection fraction *(LVEF)* for the four regions. The 95% confidence limits of reproducibility in each region is indicated by the *dashed line.* The data points above the 95% confidence limits of reproducibility indicate significant change in regional LVEF.

68% to 49% developed ventricular tachycardia. Otherwise, there were no significant clinical events in this period. In addition, there were relatively few changes in medications: four patients had digitalis added, three patients had nitrates withdrawn, and 10 patients had no change in medications.

In the interval between 3 and 10 days post infarction, global left ventricular ejection fraction did not change for the group. Initial ejection fraction was 51% at 3 days and 49% at 10 days (Fig. 3). There was significant variation in global left ventricular ejection fraction (greater than 5%) in six patients. Group changes in global and regional ejection fractions for different infarct subsets are summarized in Table III. There were no changes in global ejection fractions in any group. However, there were significant changes in regional ejection fractions in patients with inferior and nontransmural myocardial infarction.

Individual regional ejection fraction changes are illustrated in Fig. 4. There were significant changes in regional ejection fraction in 23 of 68 (34%) regions in the interval between 3 and 10 days. These changes did not relate to location or size of infarction or resting global ejection fraction. Fourteen of 17 (82%) patients had changes of one or more regional ejection fractions compared to 6 of 17 (35%) patients who had a change in global ejection fraction $(p < 0.01)$ (Fig. 5).

DISCUSSION

Our results indicate that global left ventricular performance remains unchanged during the acute phase of myocardial infarction, but that there is significant variability of regional left ventricular function. These changes in regional function may relate to various mechanisms that operate during this phase of infarction which include, among others, changes in compliance in the infarcted segments, alterations in catecholamine and other neurohumoral substances, spontaneous coronary recanalization and redistribution phenomena, and changes in regional loading conditions.[7-9] Whatever the mechanism, it is important to realize that spontaneous variation in regional ejection fraction may make interpretation of response to acute intervention during this period difficult unless a control group is studied.

Regional ejection fraction. Regional ejection fraction is an accurate and reproducible method of analyzing regional left ventricular function.[10-13] Previous reports have correlated this technique to contrast left ventriculograms, but it is important to appreciate the differences in these methods.[13] With radionuclide angiography, tracers circulate in the blood pool and provide direct "three-dimensional" data from activity contained in the left ventricle.
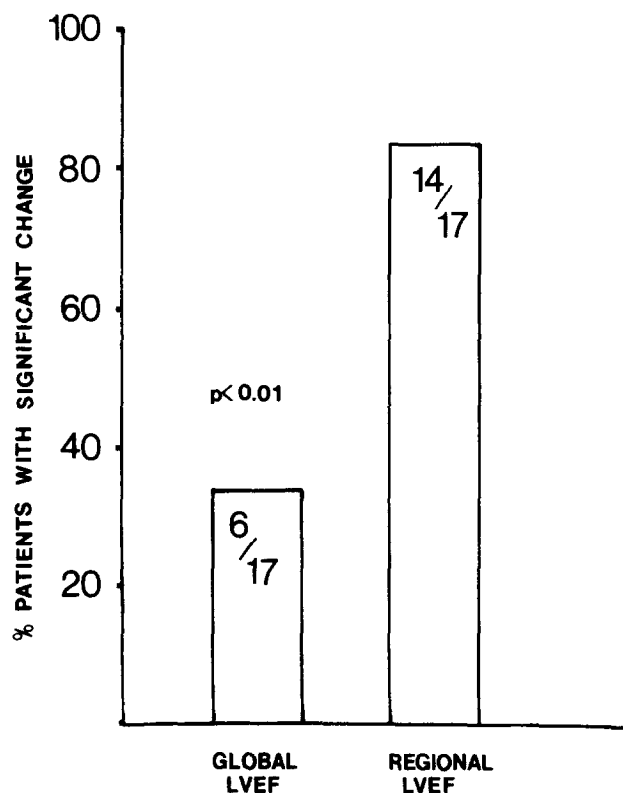
Fig. 5. Percentage of patients with significant change of global left ventricular ejection fraction *(LVEF)* and regional LVEF.

The radionuclide technique is free of geometric constraints regarding left ventricular shape and derives estimates of function from changes in tracer activity. On the other hand, contrast angiography silhouettes the left ventricular cavity with radiopaque dye and provides a tomographic image of the left ventricle in a two-dimensional plane. Various algorithms incorporating geometric assumptions have been used to estimate volume and function. As a result of these inherent differences in these two imaging techniques, correlation studies of regional left ventricular function have compared regional ejection fraction by radionuclide angiography to regional area shortening by contrast angiography. Although the correlations between these techniques have been good, they have been less than excellent because of their basic differences.[13] The radionuclide method may provide a more accurate representation of regional information, since it analyzes regional function from "three-dimensional" data.

Regional functional abnormalities in acute myocardial infarction. Regional left ventricular function abnormalities occurred significantly more frequently than global abnormalities. This is not surprising, since infarction would be expected to produce regional dysfunction more commonly than global abnormali-

ty.[15-17] The extent and severity of this regional dysfunction contributes to subsequent global abnormality. Therefore, the detection of regional abnormality is important in diagnosing localized ischemic or infarcted areas, particularly when global function is normal.

Regional ejection fraction has been examined previously in patients with myocardial infarction. Wynne et al.[14] found that regional function was significantly depressed in the zone of infarction localized by electrocardiography. In addition, they found abnormalities in electrocardiographically noninfarcted zones which contributed to global dysfunction. In their study, the left ventricle was divided into three regions which corresponded to ECG sites of infarction. Our study differed from that of Wynne et al.,[14] in that, four regions were examined. Regional ejection fraction was derived from the "three-dimensional" data that was contained in each region. In the present study, anterior infarctions had significant depression of regional ejection fractions affecting the upper and lower septal regions; inferior infarctions had decreased regional ejection fractions of the lower septal and lower posterolateral regions; and nontransmural infarction had no specific regional ejection fraction localization.

Previous serial studies[2-5] of global left ventricular function during the in-hospital phase of myocardial infarction have suggested that global function remains relatively stable, and this concurs with our findings. However, none of these studies have commented on significant variability of regional function. This is likely related to the fact that regional function was evaluated qualitatively in a manner similar to contrast ventriculographic assessment. This method of judging regional function is imprecise and is subject to significant inter- and intraobserver variability.[18] The quantitative approach to regional function used in the present study minimizes these difficulties.

Study limitations. There are some limitations which need to be addressed in this study. There are intrinsic technical problems related to regional ejection fraction determination including variable background definition, placement of the centroid and axial division, geometric overlap of structures, and difficulty in defining anatomic localization.[19] For example, the interference of the high posterolateral quadrant by left atrial activity may certainly have contributed to the increased variability of this segment. Nevertheless, this technique should be valid following the definition of confidence limits of technical variability. Thus, in our studies, change in

regional ejection fraction was defined as that which exceeded the intrinsic variability of the technique. An additional limitation in our study is the possibility that changes in medications may have contributed to the change in regional ejection fraction. Although we cannot confidently exclude this possibility, it seems unlikely, since few changes in medications occurred and since the patients with medication changes were otherwise indistinguishable from those without medication alterations.

Clinical implications. Our results indicate that it is possible to have major changes in regional function during the course of myocardial infarction without altering left ventricular global ejection fraction. This implies that various compensatory mechanisms may be acting on a regional basis to maintain global function. That is to say, global left ventricular ejection fraction may remain unchanged despite improvement in left ventricular efficiency. For example, an akinetic infarcted segment may improve, and another segment which was previously hyperkinetic as a compensatory mechanism to maintain global function, may become normokinetic. Thus, the overall efficiency of pump performance is improved without major change in global ejection fraction. Furthermore, the analysis of regional function has important implications in the study of acute coronary reperfusion interventions during myocardial infarction; these interventions probably preserve relatively small amounts of regional myocardium. Changes produced by acute interventions may not affect left ventricular ejection fraction, but may improve regional performance and overall left ventricular efficiency.[20] In view of the spontaneous variability of regional function demonstrated in the present study, the interpretation of regional changes following acute coronary reperfusion should be made with caution in the absence of appropriate controls.

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