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COOPERATIVE STUDIES

# Prognostic Significance of Location and Type of Myocardial Infarction: Independent Adverse Outcome Associated With Anterior Location

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**To determine the relative prognostic significance of location (anterior or inferior) and type (Q wave or non-Q wave) of infarction, the hospital course and follow-up outcome (mean duration 30.8 months) of 471 patients with a first infarction were analyzed. Analyses were performed grouping the patients according to infarct location (anterior, n = 253; inferior, n = 218), infarct type (Q wave, n = 323; non-Q wave, n = 148), and both location *and* type (inferior non-Q wave, n = 85; inferior Q wave, n = 133; anterior non-Q wave, n = 63; and anterior Q wave, n = 190).**

**Patients with anterior infarction had a substantially worse in-hospital and follow-up clinical course compared with those with inferior infarction, evidenced by a larger infarct size (21.2 versus 14.9 g Eq/m$^2$ creatine kinase, MB fraction [MB CK], $p < 0.001$), lower admission left ventricular ejection fraction (38.1 versus 55.3%, $p < 0.001$) and higher incidence of heart failure (40.7 versus 14.7%, $p < 0.001$), serious ventricular ectopic activity (70.2 versus 58.9%, $p < 0.05$), in-hospital death (11.9 versus 2.8%, $p < 0.001$) and total cumulative cardiac mortality (27 versus 11%, $p < 0.001$). Patients with Q wave infarction similarly experienced a worse in-hospital course compared with patients with non-Q wave infarction, evidenced by a larger infarct size (20.7 versus 12.7 MB CK g Eq/m$^2$, $p < 0.001$), lower admission left ventricular ejection fraction (43.7 versus 50.6%, $p < 0.001$), and a highe. incidence of heart failure (31.9 versus 21.6%, $p < 0.05$) and in-hospital death (9.3 versus 4.1% $p < 0.05$). However, there was no increased rate of reinfarction or mortality in hospital survivors with non-Q wave infarction compared with those with Q wave infarction, and total cardiac mortality was similar (16 versus 21%, p = NS).**

**To evaluate the role of infarct location and type independent of infarct size, patients were grouped according to quartile of infarct size, and outcome was reanalyzed within each group. Patients with anterior infarction demonstrated a lower left ventricular ejection fraction on admission and after 10 days than did patients with inferior infarction, even after adjustment for infarct size, as well as a higher incidence of congestive heart failure and cumulative cardiac mortality. When patients were evaluated on the basis of both location *and* type of infarction, those with anterior infarction exhibited a worse hospital course and cumulative cardiac mortality than did those with inferior infarction, whether the infarction was non-Q wave or Q wave in type. Life-table analysis of cardiac mortality using the Cox proportional hazards regression model demonstrated that location, but not type, of infarction exerted an independent prognostic effect.**

**Thus, patients with anterior infarction experience a more complicated hospital and follow-up course than do patients with inferior infarction despite adjustment for infarct size and regardless of type of infarction (Q wave or non-Q wave). The disparity between outcomes in patients with anterior as opposed to inferior infarction may be due to coexistent right ventricular infarction in patients with inferior infarction, resulting in less left ventricular impairment relative to the total MB CK released, as well as to differences in topographic responses to infarction between the two sites.**

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The relative prognostic significance of *location* (anterior versus inferior) and *type* (Q wave versus non-Q wave) of infarction remains controversial. Most previous studies have addressed the prognostic significance of location or type separately, but few studies have combined the analyses to identify the group or groups at greatest risk. Conclusions have often been conflicting: Some (1–5) have suggested that patients with anterior infarction have a worse outcome than patients with inferior infarction, but others (6) have found that the increased mortality in patients with anterior infarction is due solely to the increased size of anterior infarcts and not to their location. The controversy concerning the significance of type of infarction is also unresolved. Most studies (7–14) show that patients with Q wave infarction experience higher in-hospital mortality and morbidity than do patients with non-Q wave infarction and that patients with non-Q infarction exhibit a higher rate of recurrent infarction and mortality in the follow-up period. Other investigators (15–17), however, indicate that the differences in outcome between infarct types are minor and not clinically useful, and some (18,19) even suggest that the entire clinical and anatomic distinction between Q wave and non-Q wave infarction is meaningless. Many of the studies are flawed by utilization of small sample sizes or patients with previous infarction.

The purpose of this study, therefore, was to analyze the prognostic significance of location *and* type of infarct in a large group of patients with a first infarction who were well characterized in terms of baseline features, hospital course and subsequent outcome. Analyses were performed by separately categorizing patients according to infarct location and type, then categorizing infarct location with each infarct type. To adjust for differences in infarct size between anterior and inferior infarcts, the total cohort was divided into quartiles of infarct size and the significance of infarct location was evaluated.

## Methods

**Patient population.** The patients studied were a subgroup of those enrolled in the Multicenter Investigation of the Limitation of Infarct Size (MILIS), a study (20) designed to determine the effect of the administration of propanolol or hyaluronidase on the size of acute myocardial infarction. Patients were eligible for enrollment in MILIS if they satisfied the following inclusion and exclusion criteria and if they and their physician provided informed consent. The inclusion criteria were: age <76 years, at least 30 min of pain typical of myocardial ischemia, and demonstration of electrocardiographic (ECG) criteria of acute myocardial ischemia or evolving infarction (new Q waves >30 ms in width and ≥0.2 mV in depth or ST segment elevation or depression ≥0.1 mV in at least two related leads) or left bundle branch block or idioventricular rhythm. Patients were excluded from MILIS if they were in cardiogenic shock (Killip class IV), had an advanced or terminal illness, had an artificial cardiac pacemaker, or had had an infarction or major surgery within the previous 2 weeks. Other exclusion criteria, guidelines for standard care and procedures for the administration of hyaluronidase or propanolol have been reported (20).

*Patients were identified retrospectively for this study* only if their index myocardial infarction had been confirmed by the Creatine Kinase Core Laboratory, if the index infarction was their first infarction and if the infarction could be characterized on the basis of ECG location (anterior or inferior) and type (Q wave or non-Q wave). "Anterior" location was defined as leads I, aVL, $V_1$-$V_6$ on the standard 12 lead ECG and "inferior" location was defined as leads II, III, aVF, and included a true posterior location with R/S wave ratio in lead $V_1$ >1.0. Patients with a combination of anterior and inferior infarction were excluded. The presence of Q waves was defined as a negative deflection >30 ms in width and ≥0.2 mV in depth. The categorization of type and location of infarction was assigned at the ECG Core Laboratory after review of the ECGs obtained at randomization and 3 days and 10 days later without knowledge of the patient's outcome.

**Data collection.** After enrollment, but before randomization, baseline measurements were obtained, including a 12 lead ECG and a rest radionuclide ventriculogram. Blood samples for measurement of total and MB creatine kinase were collected hourly during the initial 4 h, at 2 h intervals for the next 4 h, and at 4 h intervals for the subsequent 72 h throughout the remaining hospital stay, as previously reported (20). Radionuclide ventriculography was repeated on day 10. The left ventricular ejection fraction from multigated equilibrium blood pool scintigraphy was calculated by a standard technique using a background-corrected count method from the left anterior oblique view (21). A subjective analysis of left ventricular regional wall motion was performed with the left ventricle divided into 11 segments from the anterior and left anterior oblique projections, as previously described (22). A 12 lead ECG was obtained at 90 min and at 72 h after initiation of therapy and again on day 10. A 24 h Holter ECG recording was performed on the day 10. "Serious" ventricular ectopic activity was defined as the presence of >6 ectopic beats/h, bigeminy, multiform configuration or ≥3 consecutive ectopic beats. Historical and physical examination data, a summary of daily clinical events, vital signs and the results of special procedures and routine laboratory tests were recorded throughout the hospitalization.

*Follow-up visits to assess interval history and physical examination* were scheduled at 3 and 6 months for all enrolled patients. At 3 months, a rest and exercise radionuclide ventriculogram was performed and at 6 months a treadmill exercise test was performed. Subsequently, the

**Table 1.** Analysis of Type and Location of Myocardial Infarction Separately

| Patient Characteristics | Location of MI | | | Type of MI | | |
|---|---|---|---|---|---|---|
| | Anterior (n = 253) | Inferior (n = 218) | p | Non-Q wave (n = 148) | Q wave (n = 323) | p |
| Age | 57 | 55 | NS | 56 | 56 | NS |
| History of cigarette smoking in last 6 months (%) | 50 | 72 | < 0.001 | 65 | 58 | NS |
| History of hypertension (%) | 50 | 47 | NS | 48 | 49 | NS |
| History of diabetes mellitus (%) | 19 | 9 | 0.004 | 19 | 12 | 0.05 |
| History of angina (%) | 32 | 24 | NS | 33 | 26 | NS |
| Female (%) | 28 | 26 | NS | 35 | 23 | 0.007 |
| Family history of MI (%) | 39 | 39 | NS | 39 | 39 | NS |

MI = myocardial infarction.

vital status of all patients was ascertained at 6 month intervals by a questionnaire administered by telephone.

*Total plasma creatine kinase activity* was assessed by the Rosalki method (23) and creatine kinase, MB fraction (MB CK) both by the glass bead batch adsorption technique (24) and by radioimmunoassay (25). Myocardial infarction was confirmed if one or more of the following criteria were met: 1) MB CK values ≥13 IU/liter in two or more sequential plasma samples obtained within a 12 h period; 2) an MB CK value ≥13 IU/liter in one plasma sample, if representing a threefold increase above the previous values; or 3) a single MB CK value >13 IU/liter if only one sample was analyzed. Infarct size was estimated from changes in plasma MB CK (26).

**End point analyses.** The baseline characteristics, hospital course and clinical outcome of patients were compared separately on the basis of both location (anterior or inferior) and type (Q wave or non-Q wave) of infarction and then in combination (Q wave anterior or inferior; non-Q wave anterior or inferior). Because infarct size was significantly different between anterior and inferior infarcts and Q wave and non-Q wave infarcts, differences in clinical outcome may result from the size of infarct alone and can be relatively independent of infarct type or location. Patients were therefore categorized by quartiles of infarct size index, mortality and outcome were then compared on the basis of location and type of infarction.

**Statistical methods.** *t*-tests were used to analyze differences in continuous-type variables, chi-square and Fisher's exact tests were used for categorical data and life-table methods used for survival analyses (27). The Cox proportional hazards regression model was used to assess the relative effects of location and type of infarction on mortality (28).

## Results

**Study patients.** Among the 985 patients randomized to MILIS, 849 (86%) developed a myocardial infarction confirmed by the Creatine Kinase Core Laboratory. Of these, 625 patients (74%) experienced a first infarct. The location of the infarct was anterior in 253 patients (40%), inferior in 218 (35%) and a combination of anterior and inferior in 154 (25%). Only the 471 patients with either an anterior or an inferior infarct location are included in this report. The 218 patients with inferior infarction include 185 patients (85%) with ECG changes only in the inferior leads, 30 (14%) with inferior and true posterior changes and 3 (1%) with true posterior changes only. Among the 471 patients, 148 (31%) experienced non-Q wave infarction and 323 (69%) experienced Q wave infarction; there were 85 patients with inferior non-Q wave infarction, 133 with inferior Q wave infarction, 63 with anterior non-Q wave infarction and 190 with anterior Q wave infarction.

### *Analysis on the Basis of Type and Location of Myocardial Infarction Separately*

**Patient characteristics (Table 1).** Patients with inferior infarction had a higher incidence of recent cigarette smoking compared with patients with anterior infarction (72 versus 50%, $p < 0.001$), whereas patients with anterior infarction had a higher incidence of diabetes mellitus (19 versus 9%, $p < 0.01$). Patients with non-Q wave infarction were more likely to be female than were patients with Q wave infarction (35 versus 23%, $p < 0.01$) and also had a higher incidence of diabetes mellitus (19 versus 12%, $p < 0.05$).

**Hospital course (Table 2).** Patients with anterior infarction experienced a substantially worse clinical course in the hospital than did patients with inferior infarction. They had a larger infarct size (21 versus 15 g Eq/m$^2$, $p < 0.001$) and a lower left ventricular ejection fraction on admission (38 versus 55%, $p < 0.001$) and at 10 days (41 versus 57%, $p < 0.001$) compared with patients with an inferior infarct. They also had a higher incidence of heart failure (41 versus 15%), serious ventricular ectopic activity (70 versus 59%, $p < 0.05$), cardiac arrest (19 versus 5.5%) and in-hospital death (12 versus 3%, all $p < 0.001$).

**Table 2.** Analysis by Type and Location of Myocardial Infarction Separately

| Hospital Course | Location of MI | | | Type of MI | | |
|---|---|---|---|---|---|---|
| | Anterior (n = 253) | Inferior (n = 218) | p | Non-Q wave (n = 148) | Q wave (n = 323) | p |
| ISI-MB CK (g Eq/m$^2$) | 21 | 15 | <0.001 | 13 | 21 | <0.001 |
| Early peak MB CK (≤15 h, %) | 26.5 | 20 | NS | 30 | 20 | 0.02 |
| LVEF admission (%) | 38 | 55 | <0.001 | 51 | 44 | <0.001 |
| LVEF 10 day (%) | 41 | 57 | <0.001 | 55 | 45 | <0.001 |
| "Serious VEA" on 10 day Holter (%)* | 70 | 59 | 0.02 | 60 | 67 | NS |
| Infarct extension (%) | 12 | 7 | NS | 13 | 8 | NS |
| CHF in-hospital (%) | 41 | 15 | <0.001 | 22 | 32 | 0.02 |
| Cardiogenic shock (%) | 8 | 4 | 0.04 | 5 | 6.5 | NS |
| Cardiac arrest (%) | 19 | 5.5 | <0.001 | 5 | 16 | 0.001 |
| Ventricular arrhythmias (%) | 78 | 72 | NS | 74 | 75.5 | NS |
| Atrial arrhythmias (%) | 34 | 22 | 0.005 | 26 | 29 | NS |
| In-hospital death (%) | 12 | 3 | <0.001 | 4 | 9 | 0.05 |
| In-hospital CABG (%) | 5 | 3 | NS | 7 | 2.5 | 0.03 |

*"Serious VEA" is defined as the presence of ventricular ectopic depolarizations >6/h, bigeminy, multiform configuration or ≥3 consecutive ectopic beats. CABG = coronary artery bypass surgery; CHF = congestive heart failure; ISI = infarct size index; LVEF = left ventricular ejection fraction; MI = myocardial infarction.

Compared with patients with Q wave infarction, patients with non-Q wave infarction exhibited a significantly smaller infarct (12.7 versus 20.7 g Eq/m$^2$, $p < 0.001$), and a better preserved left ventricular ejection fraction on admission (51 versus 44% $p < 0.001$) and at day 10 (55 versus 45%, $p < 0.001$). Patients with non-Q wave infarction also exhibited a higher incidence of an early peak (≤15 h after onset of symptoms) in the MB CK (30 versus 20%, $p < 0.05$). They had less heart failure (22 versus 32%, $p < 0.05$), fewer cardiac arrests (5 versus 16%, $p < 0.001$) and a lower in-hospital mortality (4 versus 9%, $p < 0.05$) than did patients with Q wave infarction, but more patients with non-Q wave infarction underwent coronary artery bypass surgery during the index hospitalization (7 versus 2.5%, $p < 0.05$). The perioperative mortality rate for those patients undergoing bypass surgery during the hospitalization was extremely high: 4 (40%) of the 10 patients with non-Q wave infarction and 3 (38%) of the 8 patients with Q wave infarction.

**Exercise treadmill test performance 6 months after myocardial infarction.** At the time of the 6 month follow-up visit, 281 patients performed an exercise treadmill test: 146 patients with anterior infarction, 135 with inferior infarction; 90 with non-Q wave infarction and 191 with Q wave infarction. There was no difference in exercise duration, peak rate-pressure (double) product achieved or percent of patients developing angina during the test in any group. Patients with anterior infarction had a much higher incidence of developing ST segment elevation than did patients with inferior infarction (35 versus 4%, $p < 0.001$) as did patients with Q wave infarction compared with patients with non-Q wave infarction (26 versus 7%, $p < 0.001$).

**Clinical outcome (Table 3, Fig. 1).** Over a mean follow-up of 30.8 months (range 0 to 48 months), the total cumulative

**Table 3.** Follow-Up Analysis by Type and Location of Myocardial Infarction Separately*

| | Location of MI | | | Type of MI | | |
|---|---|---|---|---|---|---|
| | Anterior (n = 253) | Inferior (n = 218) | p | Non-Q wave (n = 148) | Q wave (n = 323) | p |
| Cardiac mortality (%)† | 27 | 11 | <0.001 | 16 | 21 | NS |
| Recurrent MI (%)† (excludes in-hospital extension) | 17 | 13 | NS | 16 | 14 | NS |
| Coronary bypass surgery (excludes in-hospital surgery) (%) | 11 | 9 | NS | 10 | 10 | NS |

*Mean duration 30.8 months (range 0 to 48 months); †life-table methods used for significance tests. MI = myocardial infarction.

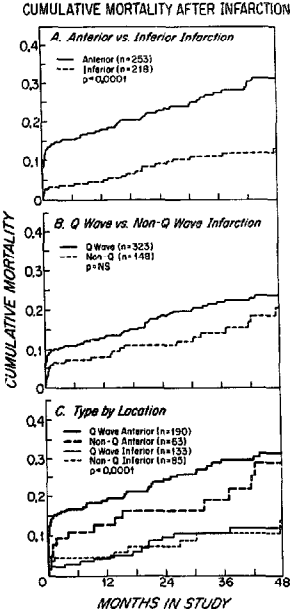


**Figure 1.** Cumulative mortality after myocardial infarction. **A.** In patients with anterior or inferior infarction. **B.** In patients with non-Q wave or Q wave infarction. **C.** In patients with anterior non-Q wave infarction, anterior Q wave infarction, inferior non-Q wave infarction or inferior Q wave infarction. Patients with anterior infarction exhibited a significantly worse mortality than did those with inferior infarction ($p < 0.0001$) regardless of Q wave or non-Q wave type. There was no significant difference in mortality between those with Q wave and those with non-Q wave infarction.

cardiac mortality was higher in patients with anterior infarction compared with those with inferior infarction (27 versus 11%, $p < 0.001$). This difference in mortality was evident both during the index hospitalization (12 versus 3%, $p < 0.001$) as well as among hospital survivors (17 versus 8%, $p < 0.01$). In contrast, although patients with Q wave infarction had a higher *in-hospital mortality* than patients with non-Q wave infarction (9 versus 4%, $p < 0.05$), there was no difference in cardiac mortality between those with Q wave and those with non-Q wave infarction among patients who survived the index hospitalization (12 versus 13%, p = NS) nor was there a difference in total cumulative cardiac mortality (21 versus 16%, p = NS).

*There was no difference in the rate of recurrent fatal or nonfatal infarction after hospital discharge* between patients with anterior compared with inferior infarction (17 versus 13%, p = NS), nor between patients with initial Q wave or non-Q wave infarction (16 versus 14%, p = NS). There was also no difference in the incidence of coronary bypass surgery after hospital discharge between patients with anterior or inferior infarction, or between patients with non-Q wave or Q wave infarction. None of the patients who underwent bypass surgery during the index hospitalization or in the follow-up period experienced a subsequent infarction.

To determine whether the increased rate of bypass surgery during the index hospitalization among patients with non-Q wave infarction affected outcome, the analysis of outcome was repeated excluding the 18 patients who underwent bypass surgery (10 with non-Q wave and 8 with Q wave infarction). The rate of recurrent infarction and mortality was virtually the same whether these patients were included or excluded.

***Analysis of outcome independent of infarct size (Tables 4 to 7).*** To identify whether location and type of infarction exerted an effect on outcome *independent* of infarct size, the total cohort of patients was divided into quartiles of infarct size, and outcome was then determined within categories of location and type. Among patients with infarcts of comparable size, those with anterior infarction consistently manifested a significantly lower left ventricular ejection fraction on admission than did patients with inferior infarction (Table

**Table 4.** Left Ventricular Ejection Fraction on Admission Stratified by Infarct Size

| | Location of MI | | | Type of MI | | |
|---|---|---|---|---|---|---|
| Quartile of ISI* | Anterior (n = 215) | Inferior (n = 197) | p | Non-Q wave (n = 128) | Q wave (n = 24) | p |
| I. ISI-MB CK ≤8.44 (n = 91) | 48% | 58% | 0.004 | 54.5% | 52% | NS |
| II. ISI-MB CK 8.45–15.87 (n = 85) | 39% | 55% | <0.0001 | 50% | 47% | NS |
| III. ISI-MB CK 15.88–24.27 (n = 93) | 34% | 55% | <0.0001 | 49% | 44% | NS |
| IV. ISI-MB CK >24.27 (n = 75) | 34% | 49% | <0.0001 | 44% | 37% | NS |

*Infarct size index (ISI) (MB CK in g Eq/m²) could be calculated in 412 (87%) of the 471 patients and forms the basis of division into quartiles. Of those with an infarct size index, 344 (83%) patients had a radionuclide ventriculogram. Abbreviations as in Table 2.

Table 5. Congestive Heart Failure In-Hospital Stratified by Infarct Size

| Quartile of ISI* | CHF by Location of MI | | | CHF by Type of MI | | |
|---|---|---|---|---|---|---|
| | Anterior (n = 215) | Inferior (n = 197) | p | Non-Q wave (n = 128) | Q wave (n = 284) | p |
| I. ISI-MB CK ≤8 (n = 103) | 18% | 10% | NS | 17% | 10% | NS |
| II. ISI-MB CK 8–16 (n = 103) | 27% | 16% | NS | 19% | 21% | NS |
| III. ISI-MB CK 16–24 (n = 103) | 39% | 15% | 0.006 | 20% | 28% | NS |
| IV. ISI-MB CK >24 (n = 103) | 62% | 26% | 0.001 | 50% | 53% | NS |

*Infarct size index (ISI) (MB CK in g Eq/m$^2$) could be calculated in 412 (87%) of the 471 patients. Abbreviations as in Table 2.

4) and consequently exhibited a higher in-hospital incidence of congestive heart failure (Table 5). Left ventricular ejection fraction remained depressed at 3 months in patients with anterior infarction compared with those with inferior infarction, regardless of infarct size (Table 6), and the cumulative cardiac mortality was also increased in patients with anterior infarction (Table 7). Despite the increased incidence of serious ventricular ectopic activity on the 10 day Holter recording in patients with anterior infarction compared with those with inferior infarction (Table 2), there was no significant increase in the incidence of sudden death in the patients with anterior infarction: the incidence of sudden death over the mean follow-up period was 5% among patients with anterior non-Q wave infarction, 5% among those with anterior Q wave, 6% among those with inferior non-Q wave and 2% among those with inferior Q wave infarction.

*In contrast to the consistently poor outcome of patients with anterior infarction compared with those with inferior infarction,* there was no consistent difference in outcome when patients with a comparable infarct size were categorized into with a non-Q wave or Q wave type of infarction (Tables 4 to 7). In both groups, left ventricular ejection fraction was lower on admission and at 3 months and the incidence of heart failure was higher with increasing infarct size.

### *Analysis of the Interaction Between Type and Location of Infarction*

The hospital course and follow-up of patients categorized by location within each type of infarction is displayed in Table 8. Especially among patients with Q wave infarction, those with anterior infarct location manifested a lower left ventricular ejection fraction on admission and at 10 days, more congestive heart failure in the hospital and a higher in-hospital mortality compared with patients with inferior infarction. The pattern of increased cardiac mortality in patients with anterior infarction persisted among hospital survivors (anterior non-Q wave 18 versus inferior non-Q wave 7%, $p < 0.05$; anterior Q wave 17 versus inferior Q wave 8%, $p < 0.05$), such that the cumulative cardiac mortality was at least twice as great in patients with anterior as in patients with inferior infarction, both in patients with Q wave and non-Q wave infarction.

Patients with anterior infarction manifested a significantly higher cardiac mortality rate than did patients with inferior infarction, regardless of Q wave or non-Q wave type (Fig. 1). The plots of Figure 1 also show that anterior infarction was a much stronger predictor of cardiac mortality than was Q wave infarction. Indeed, Cox regression analysis testing both location and type of infarction simultaneously as prognostic factors revealed that location had a highly significant effect on cardiac mortality ($p < 0.001$), but that the type of infarct had no independent effect.

## Discussion

There has been renewed interest and controversy concerning the relative prognostic significance of location and type of myocardial infarction. The usefulness and validity of distinguishing infarctions on the basis of the development of Q waves on the surface ECG continues to be debated

Table 6. Left Ventricular Ejection Fraction at 3 Months Stratified by Infarct Size

| Quartile of ISI* | EF by Location of MI | | | EF by Type of MI | | |
|---|---|---|---|---|---|---|
| | Anterior (n = 215) | Inferior (n = 197) | p | Non-Q wave (n = 128) | Q wave (n = 284) | p |
| I. ISI-MB CK ≤8 (n = 73) | 51% | 59% | 0.01 | 57% | 54% | NS |
| II. ISI-MB CK 8–16 (n = 74) | 43% | 54% | <0.0001 | 50% | 49% | NS |
| III. ISI-MB CK 16–24 (n = 68) | 37% | 52.5% | <0.0001 | 53% | 43% | 0.02 |
| IV. ISI-MB CK >24 (n = 67) | 33% | 48% | <0.0001 | 36% | 38% | NS |

*Infarct size index (ISI) could be calculated in 412 (87%) of the 471 patients, and of these, 380 (92%) were alive at 3 months. Of these, 282 (74%) patients had radionuclear ventriculography performed 3 months after the index myocardial infarction. EF = ejection fraction; other abbreviations as in Table 2.

**Table 7.** Cardiac Mortality Stratified by Infarct Size

| Quartile of ISI* | Mortality by Location of MI: Anterior (n = 215) | Mortality by Location of MI: Inferior (n = 197) | p | Mortality by Type of MI: Non-Q wave (n = 128) | Mortality by Type of MI: Q wave (n = 284) | p |
|---|---|---|---|---|---|---|
| I. ISI-MB CK ≤8 (n = 103) | 22% | 3% | 0.006 | 13% | 10% | NS |
| II. ISI-MB CK 8–16 (n = 103) | 16% | 10% | NS | 14% | 12% | NS |
| III. ISI-MB CK 16–24 (n = 103) | 22% | 11% | NS | 20% | 15% | NS |
| IV. ISI-MB CK >24 (n = 103) | 33% | 22% | NS | 21% | 31% | NS |

*Infarct size index (ISI) could be calculated in 412 (87%) of the 471 patients. Abbreviations as in Table 2.

(18,19), although clear differences in clinical behavior between infarctions associated with a Q wave and those not associated with a Q wave are acknowledged (8–14). Recent reports (2–6) also differ on conclusions regarding prognostic significance of the site of infarction, that is, anterior versus inferior. None of the reported series, however, have addressed the larger scope of the relative importance of both type *and* location of infarction on subsequent prognosis. The present study indicates that patients with anterior infarction, whether Q wave or non-Q wave in type, exhibit an increased cardiac mortality and morbidity compared with patients with inferior infarction, even when the increased size of the anterior infarct is taken into account. Although both type of infarction and infarct size influence prognosis, location of infarction is the more important determinant of prognosis after a first infarction.

**Significance of location of infarction: anterior versus inferior.** Previous studies concerning the prognostic significance of infarct location have been conflicting. In an early study of 173 patients with a first infarction, Geltman et al. (6) observed that late mortality was significantly higher in the 61 patients whose infarct was anterior in location as compared with the 79 whose infarct was inferior (but they found no difference between patients with a Q wave versus a non-Q wave type). Multivariate analysis in this relatively small study, however, indicated that the differences in mortality between anterior and inferior infarction were due to the larger size of the anterior infarcts (33.2 versus 23.6 CK MB g Eq/m$^2$, $p < 0.01$) and not to an independent prognostic effect of infarct location. In contrast, Thanavaro et al. (2), using a larger data base, noted that among patients with a first transmural infarction, those with an anterior location

**Table 8.** Analysis of Interaction Between Type and Location of Myocardial Infarction

| Hospital Course | Non-Q wave MI: Anterior (n = 63) | Non-Q wave MI: Inferior (n = 85) | p | Q wave MI: Anterior (n = 190) | Q wave MI: Inferior (n = 133) | p |
|---|---|---|---|---|---|---|
| ISI-MB CK (g Eq/m$^2$) | 13 | 13 | NS | 24 | 16 | <0.001 |
| Early peak MB CK (≤15 h, %) | 37 | 26 | NS | 23 | 16 | NS |
| LVEF on admission (%) | 43 | 57 | <0.001 | 36 | 54 | <0.001 |
| No. abnormally contracting chords on admission | 6 | 3 | <0.001 | 7 | 3 | <0.001 |
| LVEF on day 10 (%) | 50 | 59 | <0.001 | 38 | 55 | <0.001 |
| Infarct extension (%) | 16 | 11 | NS | 11 | 5 | 0.05 |
| CHF in-hospital (%) | 29 | 17 | NS | 45 | 14 | <0.001 |
| Cardiogenic shock (%) | 5 | 6 | NS | 9.5 | 2 | 0.01 |
| Cardiac arrest (%) | 8 | 4 | NS | 23 | 7 | <0.001 |
| Ventricular arrhythmias (%) | 81 | 69 | NS | 77 | 74 | NS |
| Atrial arrhythmias (%) | 33 | 21 | NS | 34 | 23 | 0.03 |
| In-hospital death (%) | 5 | 4 | NS | 14 | 2 | <0.001 |
| In-hospital CABG (%) | 10 | 5 | NS | 3 | 1.5 | NS |
| Follow-up | | | | | | |
| Cardiac mortality (%) | 22 | 11 | 0.05 | 28 | 11 | <0.001 |
| Recurrent MI (%) (excludes in-hospital extension) | 22 | 12 | NS | 15 | 13 | NS |
| CABG (%) (excludes in-hospital surgery) | 13 | 9 | NS | 10 | 9 | NS |

Abbreviations as in Table 2.

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had a worse prognosis even after stratification by height of enzyme rise. Logistic regression analysis showed that both peak enzyme elevation and infarct location exerted an independent effect on prognosis. Hands et al. (4) recently confirmed the independent prognostic significance of location of infarction in 798 patients with a first infarction, although they did not distinguish patients on the basis of type of infarction (Q wave versus non-Q wave). Our results confirm the findings of the latter two studies (2,4), that cardiac mortality is increased in patients with anterior infarction compared with inferior infarction despite adjustment for infarct size.

**Significance of type of infarction: Q wave versus non-Q wave.** Although the clinicopathologic correlation between the classification of infarction as Q wave or non-Q wave on the basis of the surface ECG and the histologic extent of actual transmural or nontransmural infarction is poor (18), the distinction between Q wave and non-Q wave infarction is considered to be of value in terms of patient management and the observed outcome (7–14). Furthermore, coronary anatomy early in the course of infarction is distinctly different in the two types of infarction: patients with non-Q wave infarction often exhibit subtotal coronary occlusion in the infarct-related artery (29), whereas patients with Q wave infarction generally exhibit a total coronary occlusion (30). The concept has been proposed, therefore, that differences in morbidity and mortality between Q wave and non-Q wave infarcts are due to an incompleted process in patients with non Q-wave infarction (11,31). This concept is supported by the observations (7,8,10–13,32) that patients with Q wave infarction have a worse in-hospital outcome than do patients with non-Q wave infarction, but that patients with non-Q wave infarction remain in persistent jeopardy that is manifested by more frequent angina, more frequent ischemic responses on an exercise test, increased rate of reinfarction and higher late mortality. Others (6,9,15,16,33) have observed that the greatest difference between Q wave and non-Q wave infarction is in the hospital course and that the outcome during the later follow-up period is similar.

Much of the early controversy concerning the clinical course of patients with Q wave or non-Q wave infarction was due to inclusion of patients with previous infarction in the study population so that the natural history of the index infarction was confounded by baseline differences in the population. In the overall MILIS study 14% of patients with a Q wave infarction had had a previous infarction, compared with 19% of patients with a non-Q wave infarction (p = NS). More recent studies have restricted their focus on patients with a first infarction, although the results nevertheless remain somewhat controversial. Thanavaro et al. (2) similarly observed that although the 621 patients with a first Q wave infarction experienced a higher in-hospital morbidity and mortality than the 124 patients with a first non-Q wave infarction, these differences were solely due to the larger infarct size associated with Q wave infarction. When patients were classified by terciles of infarct size, as estimated by peak serum glutamic oxaloacetic transaminase (SGOT), adverse outcomes such as death, cardiomegaly, heart failure and ventricular ectopic activity were all related to infarct size and not to infarct type (Q wave versus non-Q wave). When these patients were followed up over a period of 8 years, those with Q wave infarction experienced higher mortality in the first 6 months than did those with non-Q wave infarction, although there was no difference in overall survival between the two groups (14). The complexity and variable expression of factors responsible for outcome following myocardial infarction are underscored by the observations by Krone et al. (9) that the variables predictive of death in the 12 months after a first infarction among 593 patients were those of infarct size, whereas those predictive of death during later follow-up were age, initial non-Q wave type and peak lactate dehydrogenase level.

Our results support the concept that patients with Q wave infarction have a more malignant and complicated in-hospital course than do patients with non-Q wave infarction. However, there were no differences in late outcome between patients with Q wave versus non-Q wave infarction and there was no "catch-up" phenomenon observed of increased incidence of recurrent infarction and late fatality in the patients with initial non-Q wave infarction. Although a greater number of patients with non-Q wave infarction underwent coronary artery bypass grafting during the index hospitalization than did patients with Q wave infarction (7 versus 2.5%), it is unlikely that this intervention had a major effect on the natural history of type of infarction since very few patients underwent this procedure and the incidence of bypass surgery was similar in the two groups after hospital discharge. Furthermore, the outcome results were virtually the same whether the patients who underwent bypass surgery during the index hospitalization were included or excluded from the outcome analysis. It appears that, although there are differences in outcome between patients with a first Q wave or non-Q wave infarction, these differences are not as important clinically as has been suggested, especially after adjustment for infarct size is made. It is possible that subsequent cardiac events such as reinfarction in patients with non-Q wave infarction could have occurred late after the index event (9), after the mean follow-up period of 30.8 months, and thereby may have yielded a difference in outcome between patients with the two types of infarction. Most studies (7,8,12,13,32) that have demonstrated a difference in late outcome between the two infarct types, however, utilized a shorter follow-up duration than the one in this study and it therefore seems unlikely that our follow-up period was insufficient to detect meaningful differences in outcome.

**Significance of both location and type of infarction.** Our results indicate that the location of infarction (anterior

versus inferior) is of greater prognostic significance than is type of infarction (Q wave versus non-Q wave), independent of infarct size. The adverse outcome associated with anterior infarction regardless of infarct size appears to be due to a disproportionate reduction in left ventricular ejection fraction and consequent manifestations of heart failure and death compared with the outcome associated with inferior infarction. The increased mortality in patients with anterior infarction is not due to an increased incidence of sudden death.

The reason that loss of myocardium with an anterior infarct confers a worse outcome than does loss of a similar amount of myocardium during an inferior infarct remains unknown. One explanation may be that the topographic consequences of anterior compared with those of inferior infarction are distinctly different: disproportionate dilation and transmural thinning in the infarct zone (expansion) are much more common after anterior infarction than after inferior or posterior infarction (34). The differences in topographic responses are unexplained, but may be due to differences in wall stress within the left ventricular chamber, differences in normal myocardial thickness between apical and other portions of the left ventricle, with consequent propensity to dilate, and differences in the supporting or buttressing structures such as the septum, papillary muscle, mitral valve or pericardium (35). In addition, a comparison of anterior versus inferior infarcts of similar "size," as estimated enzymatically, may be complicated by the fact that patients with inferior infarction often exhibit involvement of the right ventricle, although it may be clinically undetected (36,37). Necrosis of portions of the right ventricle contributes to the total release of MB CK, but does not contribute to the extent of left ventricular dysfunction; the better prognosis after inferior infarction may therefore be due to disproportionately less left ventricular dysfunction compared with that in anterior infarction of equivalent size (38). Animal studies (39) confirm that infarcts in the anterior myocardium (left anterior descending artery occlusion), with damage confined to the left ventricle, result in a greater decrease in left ventricular ejection fraction than do infarcts of comparable size in the inferior myocardium (circumflex artery occlusion), with damage involving both left and right ventricles, regardless of histologic type or extent of infarction (that is, transmural versus subendocardial). In the present study, right ventricular involvement in the patients with inferior infarction could not be directly confirmed because right ventricular function was not evaluated as part of the MILIS protocol.

**Limitations of the study.** The observations made in this study are derived from the data base accumulated for the MILIS study, which was designed both to determine the effect of two pharmacologic interventions on infarct size and to establish a data base to study the natural history of acute myocardial infarction. Because of the number of statistical comparisons that were made, some statistically significant relations may have been due to chance and may not constitute true biologic significance. Therefore, we have emphasized those concepts that were supported by a large number of statistically significant and internally consistent relationships.

**Clinical implications.** Identification of the location and type of myocardial infarction based on the surface ECG provides useful prognostic information. Patients with anterior infarction experience a more complicated hospital and follow-up course than do patients with inferior infarction, despite adjustment for infarct size and regardless of type of infarction (Q wave versus non-Q wave). More detailed investigation and aggressive intervention may therefore be warranted in the high risk group of patients with anterior infarction. This concept is supported by the recent studies (40–42) of early administration of thrombolytic therapy in the course of acute infarction, which have suggested that an improved outcome from thrombolytic therapy occurs in patients with anterior but not inferior infarction.

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## Appendix

**Multicenter Investigation of the Limitation of Infarct Size (MILIS) Study Personnel**

**Clinical Centers**

**Barnes Hospital, Washington University School of Medicine, St. Louis, MO.** Allan S. Jaffe, MD, Principal Investigator; Robert Roberts, MD, Principal Investigator; Edward Geltman, MD, Co-Investigator; Dan Biello, MD, Nuclear Medicine Coordinator; Rosanne Wettach, RN, MNP, Research Nurse Coordinator; Data Coordinators: Ava Yeaguire, Susan Payne and Linda Wilson.

**Massachusetts General Hospital, Boston, MA.** Herman K. Gold, MD, Principal Investigator; Robert C. Leinbach, M.D., Principal Investigator; Tsunehiro Yasuda, MD; Research Nurse Coordinators: Wendy Werner, RN and Mary McHugh, RN; Harry Garabedian, Data Coordinator.

**Medical Center Hospital of Vermont, University of Vermont College of Medicine, Burlington, VT.** Daniel S. Raabe, Jr., MD, Principal Investigator; Walter Gundel, MD; Research Nurse Coordinators: Marian Dornell, RN, Maureen Huxley, RN, Patricia Beecher, RN, Kathleen Cornell, RN and Karen Helminger, RN; Raina Maynard, Data Coordinator.

**Brigham & Women's Hospital, Harvard Medical School, Boston, MA.** Eugene Braunwald, MD, Principal Investigator; Clinical Unit Directors: Peter H. Stone, MD, Joseph S. Alpert, MD and Robert Rude, MD; Research Nurse Coordinators: Nancy E. Taplin, RN, Kathryn Shea, RN and Debbie Shiner, RN.

**Parkland Memorial Hospital, University of Texas Health Science Center at Dallas, TX.**

James T. Willerson, MD, Principal Investigator; Robert E. Rude, MD, Clinical Unit Director; Charles Croft, MD, Robert Dillon, MD, Kevin Wheelan, MD, Christopher Wolfe, MD; Research Nurse Coordinators: Barbara Moses, RN and Sandra Cochran, RN; Marvin Akers, RN, Joan Reinert Corey, RN, Vicki Gillespie, RN and Barbara Fitzpatrick, RN; Kris Kraft, Unit Clerk.

**Creatine Kinase Core Laboratory**

**Washington University School of Medicine, St. Louis, MO.** Burton E. Sobel, MD, Principal Investigator; Robert Roberts, MD, Principal Investiga-

tor; Allan Jaffe, MD; Cynthia Ritter, Laboratory Coordinator; Steven Mumm, Laboratory Technician.

**Cardiovascular Pathology Core Laboratory**

**Duke University Medical Center, Durham, NC.** Donald B. Hackel, MD, Principal Investigator; Raymond E. Ideker, MD, PhD; Keith A. Reimer, MD, PhD, Eileen Mikat, PhD.

**Technetium-99m Pyrophosphate Myocardial Scintigram Core Laboratory**

**University of Texas Health Science Center at Dallas, Dallas, TX.** James T. Willerson, MD, Principal Investigator; Samuel E. Lewis, MD, Laboratory Director; Robert W. Parkey, MD, Laboratory Co-Director; Irma Dobbins, Laboratory Coordinator.

**Holter Recording Core Laboratory**

**Washington University School of Medicine, St. Louis, MO.** Lewis J. Thomas, Jr., MD, Principal Investigator; Robert Roberts, MD, Co-Principal Investigator; Kenneth W. Clark, Laboratory Director; Kathleen Madden, Laboratory Coordinator; J. Phillip Miller, Biostatistician.

**Radionuclide Ventriculogram Core Laboratory**

**Massachusetts General Hospital, Boston, MA.** H. William Strauss, MD, Principal Investigator; Nathaniel M. Alpert, MD, Co-Principal Investigator; Kenneth A. McKusick, MD, Clinical Director, Nuclear Medicine Division; Tsunehiro Yasuda, MD; Karen Kelly, Laboratory Coordinator; Annali Kiers, Laboratory Coordinator and Nuclear Medicine Technician; Leander Blakeman, Laboratory Coordinator and Nuclear Medicine Technician; Merrill Griff, Laboratory Coordinator and Nuclear Medicine Technician.

**ECG Core Laboratory**

**Harvard Medical School/Brigham & Women's Hospital, Boston, MA.** Eugene Braunwald, MD, Principal Investigator; John D. Rutherford, MD, Laboratory Director; Zoltan G. Turi, MD, Laboratory Director; James E. Muller, MD, Laboratory Co-Director; Peter H. Stone, MD, Laboratory Co-Director for ETT Analysis; Laboratory Coordinators: Gail Z. Alymer, Susan G. Albert, PA, Jennifer Forage and Michael Miller; Programmers/Analysts: Neil Rhodes, Matthew Levine, Jeremy Pool and John Rees; Computer Operators: Jane Soukup and David Mayberry.

**Data Coordinating Center**

**Research Triangle Institute, Research Triangle Park, NC.** W. Kenneth Poole, PhD, Principal Investigator; Tyler D. Hartwell, PhD, Co-Principal Investigator; Corette Parker, MSPH, Project Coordinator, Biostatistician; Data Coordinators: Connie Hobbs, Norma Fox, MPH and Susan Warwick, RN; Priscilla Rigby, RN, Data Management Coordinator; Computer Programmers: Thomas S. Farrell and Debra Fleischman; Statisticians: Nancy Gustafson, MS, Susan K. Settergren, MS, B.J.G. York, MS, James H. Crowder, MPH, Carolyn Stuart, MSPH and Vicki Davis, MS; Statistical Clerk: Lee Larsen.

**Clinical Coordinating Center**

**Harvard Medical School/Brigham & Women's Hospital, Boston, MA.** Eugene Braunwald, MD, Principal Investigator; James E. Muller, MD; Zoltan G. Turi, MD; Ellenjane Schreiner, Project Coordinator; Norman R. Stein, Financial Administrator.

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**MILIS Policy Advisory Board**

William L. Ashburn, MD; Eugene Braunwald, MD; Paul Canner, PhD; Robert L. Frye, MD (Chairman); Lawrence E. Hinkle, Jr., MD; Andrew Z. Keller, DMD; Paul Meier, PhD; Leroy Walters, PhD; Nanette Wenger, MD.

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