Preinfarction Angina as a Major Predictor of Left Ventricular Function and Long-Term Prognosis After a First Q Wave Myocardial Infarction

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Objectives. The purpose of this study was to assess the prognostic significance of preinfarction angina after a first Q wave myocardial infarction. Patients with anterior or inferior myocardial infarction were compared.

Background. The effect of preinfarction angina on prognosis after anterior and inferior myocardial infarction remains unclear.

Methods. A total of 291 patients with a first Q wave anterior (n = 171) or inferior (n = 120) myocardial infarction were examined to assess the effect of preinfarction angina on short- and long-term prognosis. The relation between predischarge left ventriculographic findings and preinfarction angina was also examined.

Results. The presence of preinfarction angina was associated with lower peak creatine kinase activity, a lower in-hospital incidence of sustained ventricular tachycardia and fibrillation and a lower incidence of pump failure and cardiac mortality in patients with either anterior or inferior infarction. Among patients with anterior infarction, preinfarction angina was associated with a lower incidence of cardiac rupture and less need for readmission for heart failure within 1 year after the onset of infarction. In this subgroup it was also associated with a higher ejection fraction, a smaller end-diastolic volume and a lower incidence of aneurysm formation noted on ventriculography during convalescence. In patients with inferior infarction, these variables did not differ significantly in the presence or absence of preinfarction angina. Multivariate analysis confirmed that the presence of preinfarction angina was an independent predictor of development of ventricular aneurysm, late phase heart failure and 1-year cardiac mortality.

Conclusions. The presence of preinfarction angina has a favorable effect on infarct expansion and late phase left ventricular function, especially in patients with anterior myocardial infarction. The mechanisms responsible for this phenomenon are not known but may be secondary to limitations of infarct size through unidentified mechanisms other than collateralization (e.g., ischemic preconditioning).

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Angina pectoris preceding acute myocardial infarction is a prognostic predictor for survival in patients with myocardial infarction. We (1) have reported that patients with preinfarction angina have a better clinical outcome than do those without angina before their first myocardial infarction. This finding contrasts with several previous studies (2-5) demonstrating an unfavorable effect of preinfarction angina. However, the majority of those studies assessed the prognostic significance of preinfarction angina without regard to prior myocardial infarction, risk factors, multivessel coronary artery disease, presence or absence of Q waves and location of infarction. Prior myocardial infarction, multivessel coronary artery disease and non-Q wave infarction are more common in patients with than in those without preinfarction angina. Therefore, the prognostic significance of preinfarction angina remains unclear. Our previous study (6) demonstrated a favorable effect of preinfarction angina on short-term prognosis and left ventricular function after a first Q wave anterior myocardial infarction, despite uniform patient characteristics, coronary angiographic findings and prevalence of acute reperfusion therapy between patients with and without angina. However, it is unknown whether preinfarction angina affects long-term prognosis or other locations of infarction in patients with acute myocardial infarction. Recent data (7-11) suggest that left ventricular remodeling is related to long-term prognosis particularly in patients with anterior infarction. If preinfarction angina influences ventricular remodeling, the effects on long-term prognosis would be expected to vary with the location of infarction. The primary aim of this study was to confirm the effects of preinfarction angina on long-term prognosis after a first Q wave myocardial infarction. A comparison

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was made among preinfarction angina, anterior and inferior infarction and left ventricular function.

Methods

Study group. A total of 291 consecutive patients experiencing a first Q wave anterior (n = 171) or inferior (n = 120) myocardial infarction were examined. They ranged in age from 19 to 87 years (mean 62) and were admitted to Keio University Hospital within 7 days of the onset of myocardial infarction between May 1985 and September 1994. The group included the 153 patients with anterior myocardial infarction assessed in our previous study (6). A diagnosis of Q wave anterior myocardial infarction was established if new abnormal Q waves (≥30 ms) existed in at least two adjacent precordial leads and were associated with at least one of the following criteria: chest pain lasting >30 min or an increase in the serum creatine kinase MB fraction (2). The diagnosis of Q wave inferior myocardial infarction was established if abnormal Q waves (≥30 ms) were noted in leads II, III and aVF and were associated with at least two of the preceding criteria. No patient had a prior history of myocardial infarction. The history of preinfarction angina was obtained on admission by the patient's physician. Preinfarction angina was defined as the presence of typical chest pain occurring at rest or during exercise and relieved by sublingual nitroglycerin. Patients unable to provide a clear clinical history were excluded from the study. The patients were classified into subgroups according to the absence or presence of preinfarction angina in each infarction location. The pattern of preinfarction angina was divided into three types according to the classification of Harper et al. (2): 1) new onsets angina, defined as angina developing during the month preceding infarction; 2) chronic angina with unstable pattern, defined as angina that had been present for >1 month before infarction but associated with an increase in severity of symptoms in the month before infarction; and 3) chronic stable angina, defined as angina present for >1 month before infarction with no change in anginal pattern.

Variables assessed. The following data were obtained: age; gender; presence of coronary risk factors (cigarette smoking, hypertension as defined by the fifth report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure [12]; diabetes mellitus as defined by the World Health Organization Study Group [13]; hypercholesterolemia, defined as a cholesterol level >220 mg/dl); use of beta-adrenergic antagonists, calcium channel blockers or angiotensin-converting enzyme inhibitors before and after the onset of myocardial infarction; time from onset of infarction to arrival at the hospital, use of and success rate of revascularization therapies during the early phase of infarction, including thrombolytic therapy, angioplasty or bypass surgery, peak serum creatine kinase level obtained by serial blood sampling every 6 h; incidence of complications, and in-hospital mortality. Pump failure was defined as a hemodynamic status categorized as class ≥2 according to Killip et al. (14) or subset ≥II according to Forrester et al. (15). Recurrent ischemia was defined as the presence of two or more of the following criteria: typical chest pain, transient electrocardiographic ST-T wave changes or increases in the MB fraction of the serum creatine kinase level (16). Follow-up data were obtained during direct contact at an outpatient clinic or during a mail interview an average of 25 months after infarction. The incidence of readmission to the hospital for heart failure, unstable angina, or recurrent myocardial infarction, history of percutaneous transluminal coronary angioplasty or coronary artery bypass graft surgery and cardiac death including sudden death were assessed in patients who survived the acute phase of infarction.

Angiographic analysis. Selective coronary angiography was performed with the use of multiple projections. The degree of coronary artery stenosis was determined by the caliper method and classified according to the American Heart Association system (17). Significant angiographic coronary artery stenosis was defined as an area of narrowing >75%. Coronary collateral channels were estimated according to the method described by Rentrop et al. (18) and based on emergency coronary angiography showing Thrombolysis in Myocardial Infarction (TIMI) (19) grade 0 or grade 1 flow in the infarct-related artery. During the convalescence period, contrast left ventriculography was performed in the 30° right anterior and 60° left anterior oblique projections. Global left ventricular ejection fraction and end-diastolic left ventricular volumes were estimated from the right anterior oblique projection according to the method of Kasser and Kennedy (20). The right and left anterior oblique views were also used to detect left ventricular aneurysm formation. A left ventricular aneurysm was considered to be present only if the following criteria initially described by Meizlish et al. (21) were met: the presence of a well localized region of the left ventricle exhibiting either akinesia or dyskinesia; a discrete deformity occurring in both systole and diastole, and a normally contractile segment of myocardium adjacent to the area of regional dysfunction. Catheterization data were interpreted jointly by two experienced observers who had no prior knowledge of the patient's history.

Statistical analysis. Data were expressed as mean value ± SD. Patients with and without preinfarction angina were compared by using an unpaired t test. Differences in prevalence were assessed by the chi-square test. Statistical significance was defined as a p value < 0.05. Multiple logistic regression analysis was used to examine the determinants of in-hospital and 1-year cardiac mortality, development of left ventricular aneurysm and cardiac events occurring within the 1st posthospital year after the onset of infarction. All statistical analyses were performed on a Macintosh Centris 650 computer with use of the JMP 2.0 program (SAS Institute, Inc.).

Results

Patient characteristics. The incidence of angina before the development of a first Q wave myocardial infarction was 65%
Table I. Patient Characteristics and Coronary Angiographic Findings in Patients With Anterior or Inferior Infarction With and Without Preinfarction Angina

<table>
<thead>
<tr>
<th>Patient characteristics</th>
<th>Anterior Infarction</th>
<th>Inferior Infarction</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No Angina</td>
<td>Angina</td>
<td>Value</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>63 ± 15</td>
<td>62 ± 12</td>
<td>NS</td>
</tr>
<tr>
<td>Male (%)</td>
<td>76 (45/59)</td>
<td>83 (93/112)</td>
<td>NS</td>
</tr>
<tr>
<td>Cigarette smoking (%)</td>
<td>56 (31/55)</td>
<td>51 (86/109)</td>
<td>NS</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>33 (18/55)</td>
<td>42 (46/109)</td>
<td>NS</td>
</tr>
<tr>
<td>Diabetes mellitus (%)</td>
<td>20 (11/56)</td>
<td>20 (22/110)</td>
<td>NS</td>
</tr>
<tr>
<td>Hypercholesterolemia (%)</td>
<td>18 (10/55)</td>
<td>22 (24/109)</td>
<td>NS</td>
</tr>
<tr>
<td>Use of beta-blockers</td>
<td>Before MI (%)</td>
<td>5 (3/56)</td>
<td>6 (6/99)</td>
</tr>
<tr>
<td>After MI (%)</td>
<td>41 (24/59)</td>
<td>55 (62/112)</td>
<td>NS</td>
</tr>
<tr>
<td>Use of ACE inhibitors</td>
<td>Before MI (%)</td>
<td>5 (3/56)</td>
<td>0 (0/99)</td>
</tr>
<tr>
<td>After MI (%)</td>
<td>15 (9/59)</td>
<td>13 (14/112)</td>
<td>NS</td>
</tr>
<tr>
<td>Use of calcium channel blockers</td>
<td>Before MI (%)</td>
<td>16 (9/56)</td>
<td>20 (20/99)</td>
</tr>
<tr>
<td>After MI (%)</td>
<td>29 (17/59)</td>
<td>38 (42/112)</td>
<td>NS</td>
</tr>
<tr>
<td>Arrival within 6 h of symptom onset (%)</td>
<td>49 (29/59)</td>
<td>50 (55/110)</td>
<td>NS</td>
</tr>
<tr>
<td>Revascularization therapies (%)</td>
<td>34 (20/59)</td>
<td>38 (42/112)</td>
<td>NS</td>
</tr>
<tr>
<td>Intravenous rt-PA (%)</td>
<td>3 (2/29)</td>
<td>2 (2/112)</td>
<td>NS</td>
</tr>
<tr>
<td>Intravenous UK (%)</td>
<td>0 (0/59)</td>
<td>2 (2/112)</td>
<td>NS</td>
</tr>
<tr>
<td>Intracoronary UK (%)</td>
<td>10 (6/59)</td>
<td>18 (20/112)</td>
<td>NS</td>
</tr>
<tr>
<td>Rescue PTCA (%)</td>
<td>12 (7/59)</td>
<td>7 (8/112)</td>
<td>NS</td>
</tr>
<tr>
<td>Direct PTCA (%)</td>
<td>9 (5/59)</td>
<td>9 (10/112)</td>
<td>NS</td>
</tr>
<tr>
<td>Angiographic success rate (%)</td>
<td>78 (14/18)</td>
<td>92 (35/36)</td>
<td>0.016</td>
</tr>
<tr>
<td>Peak creatine kinase level (IU/liter)</td>
<td>2,819 ± 2,515</td>
<td>1,824 ± 1,458</td>
<td>0.016</td>
</tr>
</tbody>
</table>

Coronary angiographic findings

<table>
<thead>
<tr>
<th>No. of diseased vessels (%)</th>
<th>Anterior Infarction</th>
<th>Inferior Infarction</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n = 38)</td>
<td>(n = 85)</td>
<td>(n = 40)</td>
</tr>
<tr>
<td>0</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>1</td>
<td>71</td>
<td>65</td>
</tr>
<tr>
<td>2</td>
<td>13</td>
<td>15</td>
</tr>
<tr>
<td>3</td>
<td>16</td>
<td>15</td>
</tr>
<tr>
<td>Left main lesion (%)</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Acute phase collateral circulation (%)</td>
<td>(n = 18)</td>
<td>(n = 28)</td>
</tr>
<tr>
<td>Absent</td>
<td>66</td>
<td>50</td>
</tr>
<tr>
<td>1</td>
<td>17</td>
<td>21</td>
</tr>
<tr>
<td>2</td>
<td>17</td>
<td>29</td>
</tr>
<tr>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Data are expressed as mean value ± SD or percent (number of patients with characteristic/number of patients studied). ACE = angiotensin-converting enzyme; MI = myocardial infarction; PTCA = percutaneous transluminal coronary angioplasty; rt-PA = recombinant tissue-type plasminogen activator; UK = urokinase.

and 55%, respectively, in the subgroups of patients with anterior and inferior infarction. The respective values were 39% and 26% for new onset angina; 15% and 12% for chronic angina with an unstable pattern, and 10% and 17% for chronic stable angina. Thus, 84% of the patients with angina and anterior infarction and 70% of patients with angina and inferior infarction had an unstable anginal pattern that included either new onset angina or chronic angina with an unstable progression during the month before infarction.

There were no significant differences between patients with and without preinfarction angina in either of the subgroups based on infarct site with respect to age, gender, coronary risk factors, use of beta-adrenergic blockers, angiotensin-converting enzyme inhibitors or calcium channel blockers before and after infarction, percent arriving at the hospital within 6 h after the onset of infarction or use of or angiographic success rate of emergency revascularization therapies on admission. In both subgroups, the peak creatine kinase activity was lower in patients with than in those without preinfarction angina (Table 1).

In-hospital complications. Patients with anterior myocardial infarction. In this subgroup, the incidence of pump failure (22% vs. 49%, p = 0.0003), ventricular septal perforation or free wall rupture (1% vs. 17%, p = 0.0001) and sustained ventricular tachycardia or fibrillation (8% vs. 24%, p = 0.004) was significantly lower in patients with than in those without preinfarction angina. The rate of recurrent ischemia in this subgroup was similar between patients with and without preinfarction angina (18% vs. 14%, p = 0.47).
Patients with inferior myocardial infarction. In this subgroup, the incidence of pump failure, including right ventricular infarction (18% vs. 38%, p = 0.01) and sustained ventricular tachycardia or fibrillation (3% vs. 13%, p = 0.04), was also lower in the patients with than in those without preinfarction angina. However, there was no significant difference in the incidence of cardiac rupture between angina groups (0% vs. 5%, p = 0.05). The rate of recurrent ischemia was higher in patients with than in those without angina (26% vs. 11%, p = 0.04) (Fig. 1).

In-hospital mortality. Figure 2 demonstrates that in patients with myocardial infarction at either site, the presence of preinfarction angina was associated with a lower in-hospital cardiac mortality than the absence of angina (anterior, 8% vs. 27%, p = 0.0008; inferior, 3% vs. 13%, p = 0.045). In patients with anterior infarction, the total number of deaths from cardiac rupture was lower in patients with than in those without preinfarction angina (1% vs. 15%, p = 0.0001). However, in patients with inferior infarction, death from cardiac rupture occurred more commonly in those with preinfarction angina (0% vs. 4%, p = 0.12). Multiple logistic regression analysis confirmed that the absence of preinfarction angina (relative risk 2.03, p = 0.0007) and the anterior location of myocardial infarction (relative risk 1.56, p = 0.049) were significant predictors of in-hospital cardiac mortality. The other variables examined, including absence of successful revascularization therapies and the presence of multivessel coronary disease, were not significant determinants of in-hospital cardiac mortality.

Coronary angiographic findings. Coronary angiography was performed in 123 patients (72%) in the anterior infarction subgroup and in 85 patients (71%) in the inferior infarction subgroup a mean of 9 days after the onset of infarction (Table 1). The prevalence of multivessel coronary artery disease was not different between patients with or without preinfarction angina in either the anterior or the inferior infarction subgroup. In patients with anterior infarction, the prevalence of a no. 6 lesion (proximal to the first septal branch) as a culprit lesion was similar in patients with and without preinfarction angina (51% vs. 57%, p = 0.54). In patients with inferior infarction, the infarct-related artery was assumed to be the right coronary artery in 66 patients (78%) and the left circumflex artery in 16 patients (19%); in the remaining 3 patients, the infarct-related artery could not be precisely determined. There was no difference with respect to the prevalence of right coronary artery lesions between patients with and without preinfarction angina (87% vs. 73%, p = 0.12). The prevalence of a no. 1 lesion (proximal to the right ventricular branch) as a significant predictor of myocardial infarction.
The culprit lesion was also similar among the two groups (31% vs. 41%, p = 0.37).

The extent of coronary collateral circulation was estimated in 46 patients with anterior and 21 patients with inferior myocardial infarction. These data are based on results from emergency coronary angiography performed early after the onset of infarction. Although the prevalence and degree of the collateral circulation were not significantly different between patients with and without preinfarction angina, the presence of grade 2 collateral circulation was somewhat more common in the patients with preinfarction angina, especially in those with inferior infarction (p = 0.17).

**Left ventricular function.** Left ventriculography was performed in 78 patients with anterior and 51 patients with inferior myocardial infarction a mean of 12 days after the onset of infarction. The left ventricular end-diastolic volume and ejection fraction were similar in patients with anterior and inferior infarction (end-diastolic volume 79 ± 16 vs. 77 ± 20 ml/m², p = 0.61; ejection fraction 52 ± 13% vs. 55 ± 11%, p = 0.25). In patients with anterior infarction, the left ventricular end-diastolic volume was lower, whereas the left ventricular ejection fraction was higher in those without preinfarction angina (end-diastolic volume 76 ± 14 vs. 88 ± 18 ml/m², p = 0.002; ejection fraction 55 ± 13% vs. 44 ± 12%, p = 0.0008). No significant difference was noted among these variables in patients with inferior infarction (end-diastolic volume 75 ± 20 vs. 79 ± 20 ml/m², p = 0.50; ejection fraction 54 ± 11% vs. 55 ± 11%, p = 0.63) (Fig. 3).

The prevalence of left ventricular aneurysm was higher in patients with anterior than in those with inferior myocardial infarction (35% vs. 16%, p = 0.018). In patients with anterior infarction, the prevalence of aneurysm formation was lower in the presence than in the absence of preinfarction angina (27% vs. 55%, p = 0.020). This finding was not observed in patients with inferior myocardial infarction (13% vs. 19%, p = 0.58) (Fig. 3). Multiple logistic regression analysis revealed that the absence of preinfarction angina (relative risk 1.61, p = 0.035) as well as the anterior location of infarction (relative risk 1.97, p = 0.0097) were independent predictors of left ventricular aneurysm formation. The extent of coronary collateral circulation, the presence of successful revascularization therapies, hypertension or multivessel coronary disease, patient age and postinfarction use of beta-adrenergic blockers and angiotensin-converting enzyme inhibitors were not significant determinants of aneurysm formation.

**Clinical follow-up.** Follow-up data were obtained in 212 of the 233 patients who survived the acute phase of myocardial infarction. These patients were followed up for a minimum of 1 year (120 patients with anterior and 92 patients with inferior myocardial infarction; follow-up rate 91%). In the patients with anterior infarction, the presence of preinfarction angina was associated with a lower incidence of readmission for heart failure within 1 year (2% vs. 11%, p = 0.038), a higher incidence of readmission for unstable angina (19% vs. 3%, p = 0.023) and a greater likelihood of undergoing coronary angioplasty (16% vs. 3%, p = 0.040); the prevalence of reinfarction and coronary artery bypass graft surgery was similar between patients with and without preinfarction angina. In the patients with inferior myocardial infarction, none of these variables differed between the two groups (Fig. 4).

The posthospital 1-year mortality rate was 3% in patients with anterior and 0% in patients with inferior myocardial infarction. In patients with anterior infarction, this rate did not differ between patients with and without preinfarction angina (3% vs. 4%, p = 0.83). However, the 1-year mortality rate including the in-hospital cardiac deaths was lower in patients with than in those without preinfarction angina regardless of
infarct site (anterior 13% vs. 31%, \( p = 0.0067 \); inferior 2% vs. 15%, \( p = 0.014 \)).

Multiple logistic regression analysis revealed that the absence of preinfarction angina was the most important predictor of readmission for heart failure (relative risk 2.50, \( p = 0.030 \)) among the variables, including the absence of successful revascularization therapies, the anterior location of infarction and use of beta-adrenergic blockers or angiotensin-converting enzyme inhibitors. Furthermore, the absence of preinfarction angina (relative risk 1.85, \( p = 0.003 \)) was the most important predictor of 1-year cardiac mortality among the other predictors, including the anterior location of infarction (relative risk 1.83, \( p = 0.010 \)) and the absence of successful revascularization therapies (relative risk 1.76, \( p = 0.047 \)).

**Discussion**

**Incidence of preinfarction angina.** The incidence of antecedent angina before a first Q wave anterior or inferior myocardial infarction was 61%. This finding is similar to that observed by others (2-5, 17). There was no difference in the incidence of preinfarction angina between patients with anterior or inferior myocardial infarction; in each of these two subgroups, \( \sim 80\% \) of patients with preinfarction angina had an unstable anginal pattern.

**Effect of preinfarction angina on clinical outcome.** Most previous studies (2-5) have demonstrated poorer short- and long-term prognoses in patients with than in those without preinfarction angina. The discrepant results in the present study may be attributable to the fact that previous studies noted prior myocardial infarction, multiple risk factors, severe multivessel coronary artery disease and anterior location of myocardial infarction more commonly in patients with than in those without preinfarction angina. The effect of preinfarction angina alone, however, is not known. In our study, after excluding patients with a previous infarction, there was no difference between the two groups with respect to patient characteristics and coronary angiographic findings including the degree of collateralization, the site of the culprit lesion and the number of diseased vessels. The presence of preinfarction angina was associated with a lower incidence of in-hospital complications and mortality and a lower peak creatine kinase activity in both subgroups based on infarction site. Multivariate analysis revealed that the absence of preinfarction angina was an independent predictor of in-hospital cardiac mortality. These findings suggest that preinfarction angina has a protective effect against myocardial damage after abrupt coronary occlusion. This myocardial protective effect results in limitation of infarct size at both sites of myocardial infarction. Regarding long-term prognosis, the present study demonstrated that the absence of preinfarction angina is a major predictor of cardiac mortality at 1 year and readmission for heart failure during the 1st year after the onset of infarction.

The present study, however, also revealed that the posthospital ischemic events were more prevalent in patients with than in those without preinfarction angina, particularly in the subgroup with anterior myocardial infarction. In patients with inferior infarction, the incidence of posthospital ischemic events was not different between patients with and without preinfarction angina; however, the incidence of in-hospital ischemic events was higher in the group with preinfarction angina. Midwall et al. (3) observed that preinfarction angina was associated with a greater prevalence of postinfarction angina in a study involving 97 patients with a first Q wave anterior or inferior myocardial infarction. The left ventricular ejection fraction in these patients was similar in those with and without preinfarction angina. The investigators suggested that a greater prevalence of multivessel coronary disease may have led to the higher observed incidence of postinfarction angina in patients with than without preinfarction angina. In the present study, the prevalence of multivessel coronary disease did not differ in the groups with and without preinfarction angina; however, the peak creatine kinase activity was lower and the left ventricular ejection fraction was higher in patients with preinfarction angina. These findings suggest that limitation of infarct size may be associated with a considerable amount of viable myocardium that is exposed to further ischemia in the presence of critical coronary artery stenosis. The difference observed in the period for development of ischemic events between patients with anterior and inferior myocardial infarction was
tion is not clear. It is possible that a large segment of ischemic myocardium as seen in patients with anterior myocardial infarction leads to regional denervation and results in subclinical ischemia during the in-hospital period and in subsequent symptomatic ischemia after hospital discharge.

Effect of preinfarction angina in anterior and inferior myocardial infarction. Although the effect of preinfarction angina on reducing the incidence of pump failure and malignant ventricular arrhythmias during the acute phase was observed in patients with infarction at both sites, the effect of preinfarction angina on reducing the incidence of cardiac rupture and late phase heart failure was observed only in patients with anterior infarction. Furthermore, predischarge left ventriculography revealed that the presence of preinfarction angina was associated with better global left ventricular function, lesser degrees of ventricular enlargement and a lower incidence of ventricular aneurysm formation in patients with anterior but not in those with inferior infarction.

The favorable effect of preinfarction angina on left ventricular function has been previously reported (7,9,22,23). However, these studies generally did not focus on differences with respect to location of myocardial infarction. Cortina et al. (22) examined 39 patients with total occlusion of the infarct-related artery (19 patients with left anterior descending artery involvement and 20 with right coronary artery involvement). Their study showed the beneficial effects of preinfarction angina on overall and regional left ventricular function according to a scoring system of segmental wall motion. These positive effects were evident in patients with anterior as well as inferior myocardial infarction. However, a quantitative analysis of ventricular volume was not made with respect to site of infarction. In the present study, the beneficial effect of preinfarction angina in preventing aneurysm formation and ventricular enlargement was evident in patients with anterior infarction but not in those with inferior myocardial infarction.

Left ventricular aneurysm formation occurs because of infarct expansion and consists of disproportionate dilation and wall thinning in the infarct area, which are more commonly observed in anterior than inferior myocardial infarctions (7,9–11,23). In patients with anterior infarction, aneurysm formation typically involves the apical myocardium because of the high wall stress observed in this region. The small radius of the curvature in the ventricle in this segment has a greater propensity for infarct expansion relative to other regions (Laplace law). In the present study the prevalence of cardiac rupture, an extreme form of infarct expansion (24,25), was also lower in patients with than in those without preinfarction angina in the subgroup with an anterior infarction but not among patients with an inferior infarction. In addition, multivariate analysis confirmed that the absence of preinfarction angina and anterior location of infarction were significant predictors for the development of a left ventricular aneurysm. Therefore, the protective effects of preinfarction angina against infarct expansion are apparent in patients with anterior myocardial infarction and contribute to preservation of global left ventricular function.

Mechanisms responsible for the beneficial effects of preinfarction angina. Left ventricular aneurysm formation has been reported to develop early in the course of acute myocardial infarction when infarcted tissues are structurally the weakest. Necrotic myocardium predominates during this period and little scar tissue has formed. If an aneurysm is to develop, it is generally apparent by the time of hospital discharge. No new developing aneurysm and resolution are noted by 3 months of follow-up after discharge (21). Experimental studies (26) have demonstrated that delayed geometric changes do not appear to occur after healing and fibrosis have taken place. Therefore, left ventricular aneurysm formation, which is noted during predischarge left ventriculography, appears to reflect irreversible ventricular contour changes that will lead to further ventricular enlargement, or ventricular remodeling (21,27,28). Meizlish et al. (21) observed that left ventricular aneurysm formation is associated with a high risk of death within the year after infarction and that this risk is independent of left ventricular ejection fraction. Recent studies (29,30) have shown that left ventricular remodeling as estimated by chamber enlargement is among the most important predictors of poor survival after myocardial infarction. It is possible that the effects of preinfarction angina on ventricular remodeling are related to long-term clinical outcome.

Infarct size, like infarct healing and ventricular wall stress, is a major determinant of ventricular remodeling (31). Reduction of myocardial necrosis by acute reperfusion therapy has been demonstrated to prevent infarct expansion (32–34). It is possible that preinfarction angina prevents infarct expansion and ventricular remodeling through limitation of infarct size, especially in patients with anterior myocardial infarction. Patients with anterior infarction are at increased risk for impairment of ventricular remodeling relative to that of patients with inferior infarction. However, the long-term effects of preinfarction angina on ventricular remodeling, including elongation of noninfarct regions, were not determined in this study.

The mechanisms responsible for limitation of infarct size in the presence of preinfarction angina are not clear, although, ischemic preconditioning, previously described in experimental models (35–38), is presumed to be a possible mechanism. However, the clinical evaluation of ischemic preconditioning is difficult because the risk area for myocardial infarction is diminished by the presence of coronary collateral circulation that develops as a result of previous ischemia (39–42). When assessing the effects of ischemic preconditioning, one must exclude the influence of collateral circulation during coronary obstruction. The degree of collateralization has previously been reported (7,22,43,44) to be higher in the presence than in the absence of preinfarction angina. However, all previous studies estimated the collateral circulation later, after the onset of infarction, despite patency of the infarct-related artery. Collateral vessels are prominent if the infarct-related artery has little or no anterograde flow, and they may develop gradually after the onset of myocardial infarction. In the present study, collateral vessels were assessed during early phase coronary angiography and TIMI grade 0 or 1 flow (19).
was shown in the infarct-related artery. Thus, grade 3 collateral circulation (18) was not observed in our patients with a Q wave infarction and no significant difference was noted in the grade of collateral circulation between our patients with and without preinfarction angina. Multivariate analysis revealed that preinfarction angina is a significant predictor of short- and long-term prognosis and infarct expansion. This association is independent of the grade of collateral circulation. We cannot exclude the effects of collateral channels during the acute phase of infarction because of the limited number of the acute catheterization studies assessed for collateral circulation. However, limitation of infarct size may be achieved in patients with preinfarction angina by a mechanism other than collateralization, such as ischemic preconditioning.

**Limitations of the study.** Our study showed that the presence of preinfarction angina is a major determinant of short- and long-term prognosis after a first Q-wave myocardial infarction; however, we have not proved that preinfarction angina directly affects clinical outcome. We cannot completely exclude the possibility that the association may reflect other variables that are influencing outcome or that there were differences between the patients with and without preinfarction angina that were not accounted for in this study.

**Conclusions.** The presence of preinfarction angina is associated with a favorable in-hospital course and survival. These positive effects are seen in patients either anterior or inferior myocardial infarction. Furthermore, these beneficial effects persist up to 1 year after infarction, particularly in patients with an anterior infarction. Limitation of infarct size results in prevention of ventricular remodeling through unidentified mechanisms other than collateralization (e.g., ischemic preconditioning) and is presumed to be responsible for this phenomenon.

**References**


