The prevalence and clinical significance of residual myocardial ischemia 2 weeks after uncomplicated non–Q wave infarction: a prospective natural history study

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ABSTRACT  Despite having smaller infarct size and better left ventricular function, patients with non–Q wave myocardial infarction (NQMI) appear to have an unexpectedly high long-term mortality that is ultimately comparable to that of patients with Q-wave myocardial infarction (QMI). Patients with NQMI may lose their initial prognostic advantage because there is more viable tissue in the perfusion zone of the infarct-related vessel, rendering myocardium more prone to reinfarction. We tested this hypothesis in a prospective study of 241 consecutive patients 65 years of age or younger with acute uncomplicated myocardial infarction confirmed by creatine kinase levels (MB fraction). All patients received customary care and none underwent thrombolytic therapy or emergency angioplasty. Predischarge coronary angiography, radionuclide ventriculography, 24 hr Holter monitoring, and quantitative thallium-201 (201TI) scintigraphy during treadmill exercise were performed 10 ± 3 days after infarction. Infarcts were designated as QMI (n = 154) or NQMI (n = 87) by accepted criteria applied to serial electrocardiograms obtained on days 1, 2, 3, and 10. The baseline Norris coronary prognostic index, angiographic jeopardy scores, and prevalence of Lown grade ventricular arrhythmias were similar between groups despite evidence for less necrosis with NQMI vs QMI, reflected by lower peak creatine kinase levels (520 vs 1334 IU/liter; p = .0001, 4 hr sampling), higher resting left ventricular ejection fraction (53% vs 46%; p = .0001), fewer akinetic or dyskinetic segments (1.2 vs 2.4; p = .0001), and fewer persistent 201TI defects in the infarct zone (0.9 vs 1.9; p = .0001). Patients with NQMI also had more patent infarct-related vessels (54% vs 25%; p < .0001) and a shorter time from onset of infarction to peak creatine kinase level (16.9 vs 22.5 hr; p = .0001). Importantly, the prevalence and extent of quantitatively determined 201TI redistribution within the infarct zone on exercise scintigraphy was greater in patients with NQMI vs those with QMI (60% vs 36%, p = .007; and 0.98 vs 0.53 myocardial segments, p = .0003); when the two groups were stratified on the basis of the infarct-related vessel, subset analysis revealed the same findings. During 30 months median follow-up, cardiac mortality was low, 8.4% in the QMI group and 9.2% in the NQMI group (p = NS). However, patients with NQMI had a higher reinfarction rate (18.4% vs 6.5%; p = .009), a higher rate of unstable angina necessitating hospitalization (36% vs 22%; p = .034), and had a greater incidence of subsequent bypass surgery or angioplasty (33% vs 19%; p = .018). Moreover, 88% of the recurrent infarctions in the NQMI group involved the same area as the original infarction compared with only 20% in the QMI group (p < .01). Thus, in a consecutive series of patients with uncomplicated myocardial infarction who were eligible for predischarge exercise testing, NQMI was characterized by: (1) similar long-term mortality despite a smaller infarct size and better left ventricular function, (2) a higher rate of reinfarction and incidence of angina and bypass surgery at 30 months, and (3) more evidence of residual infarct zone ischemia as compared to patients with QMI. Our data also suggest that the pathogenesis of NQMI may involve spontaneous reperfusion, since 47% of our patients had ST segment elevation on their admission electrocardiograms, the time to peak creatine kinase level was shorter than that in patients with QMI, and 54% of our patients with NQMI had patent infarct-related vessels during predischarge angiography.

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the electrocardiographic criteria employed in these studies for the diagnosis and characterization of acute infarction are not entirely consistent and only scant creatine kinase isoenzyme data are provided, it is generally believed that non-Q wave myocardial infarction (NQMI) is associated with less necrosis and a lower in-hospital mortality compared with Q-wave myocardial infarction (QMI). Despite this more favorable initial prognosis, long-term survival for patients with NQMI appears to be similar to or even less than that in patients with QMI. Moreover, several investigators have shown that the incidence of postinfarction angina,1-7 the rate of recurrent infarction,8-12 15-17, 21-22, 24 and possibly the risk of sudden death9 is higher after NQMI. These findings have understandably led some to recommend more aggressive evaluation and treatment strategies (e.g., early catheterization, angioplasty, or surgery) for survivors of NQMI, particularly since the benefit of prophylactic β-blockade is largely unproved in this subset of patients.25-27

The pathophysiologic basis of the apparent greater clinical instability after NQMI and the reason for loss of the initial prognostic advantage are not completely understood. One explanation that we and others have suggested15, 22, 28 is that patients with NQMI have more residual jeopardized myocardium within the perfusion zone of the infarct-related vessel than do patients with QMI. Because ischemic tissue remains, the heart may be more prone to recurrent ischemia and infarction. Also, if non-Q wave events result in a higher incidence of patent infarct-related vessels, the potential for a more unstable setting would exist.

We tested this hypothesis in an ongoing prospective natural history study of patients with uncomplicated QMI and NQMI. Unlike previous studies, each patient in the present cohort underwent predischarge coronary angiography, radionuclide ventriculography, 24 hr Holter recordings, and quantitative exercise thallium-201 (201TI) scintigraphy after informed consent as defined by our research protocol.29, 30 The primary objective was to determine in a group of patients with relatively well-preserved left ventricular systolic function whether the absence of Q waves identifies a distinct clinical subset with more remaining myocardium at risk for recurrent ischemic events.

Methods

Patient selection criteria. The study population was selected from 362 patients admitted consecutively to our coronary care unit between February 1979 and August 1984. Criteria for inclusion were (1) acute uncomplicated myocardial infarction31 diagnosed by typical history of chest pain and a rise and fall in creatine kinase isoenzyme level (MB fraction), (2) age 65 years or less, (3) absence of valvular, congenital, or cardiomyopathic heart disease or history of coronary bypass surgery, (4) absence of cardiogenic shock, ventricular septal defect, or papillary muscle rupture, (5) absence of left bundle branch block, and (6) the absence of serious noncoronary disease that might limit long-term follow-up. Of these patients, 273 (75%) gave written informed consent to undergo predischarge testing.

All 273 consenting patients were considered candidates for predischarge exercise testing. However, rest or effort angina in the antecedent 4 days, persistent left ventricular failure on physical examination, poorly controlled arrhythmias, or musculoskeletal handicap precluded cooperation with the stress examination in 12 (4%). Table 1 compares pertinent clinical findings in the 241 patients who constitute our study cohort, the 32 deemed ineligible for exercise testing, and the 89 candidates who declined to participate. Since these 89 patients were similar to those participating in the study, no obvious bias in the final patient selection was observed. During hospitalization, none of the 273 enrolled patients received thrombolytic therapy or emergency angioplasty. As expected, patients who became ineligible for predischarge exercise testing had more extensive underlying coronary artery disease and a lower left ventricular ejection fraction compared with those who were tested. Furthermore, during 22 ± 10 months of follow-up, nine of these 32 patients (28%) suffered cardiac death (n = 4) or reinfarction (n = 6) and 13 others (41%) underwent coronary bypass surgery (n = 12) or angioplasty (n = 1) because of unstable angina pectoris (n =

<table>
<thead>
<tr>
<th>TABLE 1</th>
<th>Comparison of clinical characteristics</th>
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<tbody>
<tr>
<td></td>
<td>Enrolled patients</td>
</tr>
<tr>
<td>Study cohort</td>
<td>SMTX ineligible (n = 241)</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>51 ± 8</td>
</tr>
<tr>
<td>Sex (males)</td>
<td>205 (85%)</td>
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<tr>
<td>No. risk factors*</td>
<td>2.3 ± 1.1</td>
</tr>
<tr>
<td>Prior angina pectoris</td>
<td>103 (43%)</td>
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<tr>
<td>Previous MI</td>
<td>42 (17%)</td>
</tr>
<tr>
<td>Norris index</td>
<td>2.8 ± 2.0</td>
</tr>
<tr>
<td>Location of acute MI</td>
<td></td>
</tr>
<tr>
<td>Anterior</td>
<td>83 (34%)</td>
</tr>
<tr>
<td>Inferior</td>
<td>84 (35%)</td>
</tr>
<tr>
<td>Lateral</td>
<td>19 (8%)</td>
</tr>
<tr>
<td>Other*</td>
<td>54 (22%)</td>
</tr>
<tr>
<td>Nonlocalizable</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>NQMI</td>
<td>87 (36%)</td>
</tr>
<tr>
<td>Maximum Killip class in CCU</td>
<td>1.5 ± 0.6</td>
</tr>
<tr>
<td>Peak creatine kinase</td>
<td>1042 ± 966</td>
</tr>
<tr>
<td>Multivessel CAD*</td>
<td>139 (58%)</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>49 ± 11</td>
</tr>
<tr>
<td>Range</td>
<td>20–74</td>
</tr>
</tbody>
</table>

SMTX = submaximal treadmill exercise test; MI = myocardial infarction; CCU = coronary care unit; CAD = coronary artery disease; LVEF = left ventricular ejection fraction.

*Includes hypertension, diabetes mellitus, hypercholesterolemia, smoking, family history of CAD ≤ 60 yr, and ≥ 25% ideal body weight.

*Includes anterior-inferior, inferolateral, posterolateral, and infero-posterolateral.

*≥ 50% stenosis in two or more major epicardial vessels.
11), left mainstem stenosis (n = 1), or severe three-vessel disease (n = 1). Only 10 patients (31%) in this group remained free of these events.

**Clinical evaluation.** A detailed clinical history was obtained from each patient upon admission. Subsequently, patients were evaluated daily by at least one staff cardiologist and a research nurse during hospitalization. Serum creatine kinase levels were measured upon admission and at 4 hr intervals for the next 24 hr, then daily until a normal value was obtained. Each patient was assigned by clinical criteria to Killip classes I through III, and for further characterization the Norris coronary prognostic index1 was calculated.

**Electrocardiographic evaluation.** Twelve-lead electrocardiograms (ECGs) were obtained on admission (day 1) and on days 2, 3, and 10 at a speed of 25 mm/sec and at a calibration of 1 cm = 1 mV. All four ECGs from each patient were interpreted blindly by two independent investigators; in cases of disagreement, a consensus reading with a third observer was used.

From the serial ECGs, all infarcts were classified as QMI or NQMI. This distinction was based on the presence or absence of new pathologic Q waves, i.e., Q waves of 30 msec or longer in duration in two or more of the anterior (V₁₋₃), inferior (II, III, or aVF), or lateral leads (V₄₋₆ or I, aVL). Patients with minimal-amplitude R waves (i.e., 0.25 mV or less) in infarct-related ECG leads and those with an R/S ratio of 1 or higher in V₁ were included in the QMI group.32, 33 Patients whose electrocardiographic changes were restricted to the ST segment or T wave throughout their hospital courses were designated as having NQMI. In all patients with a history of prior myocardial infarction, old ECGs were reviewed to ensure correct group assignment for those manifesting Q waves on the admission ECG.

Table 2 depicts the admission ECG findings in the 241 patients, which were recorded 4.7 ± 7.2 hr after onset of infarction.

**Exercise 201Tl imaging protocol.** All patients underwent submaximal exercise treadmill testing a mean of 10 ± 3 days after onset of infarction as previously described.30 Since it was anticipated that medications would be continued as long-term treatment, no attempt was made to alter drug therapy before testing. A dose of 1.8 to 2.1 mCi of 201Tl was injected intravenously, followed by a 10 ml saline flush as the patient approached either the target heart rate of 120 beats/min, 5 mets, or limiting symptoms. Exercise was continued for an additional 60 sec if symptoms, electrocardiographic changes, and blood pressure were stable.

**Quantitative analysis of 201Tl scintigrams.** Standardized image formation and quantification of relative 201Tl uptake and washout in six standard myocardial scan segments were performed by methods previously described.34 Criteria for designating a scan segment as abnormal and attributing it to disease in the left anterior descending (LAD), left circumflex (LCx), or right coronary artery (RCA) were identical to those already described.30, 35 All persistent 201Tl defects were classified as mild or severe based on the percentage of maintained decrease in myocardial 201Tl activity overtime. Those showing a 25% to 50% persistent reduction in relative activity were designated as having mild thallium defects and those with a greater than 50% constant decrease were recorded as having severe defects.36 Each patient study was also evaluated for the presence of one or more of the following “high risk” scintigraphic findings: (1) a multivessel disease scan pattern, (2) abnormally increased lung 201Tl uptake, and (3) redistribution. Based on prior work by our group and others, these scintigraphic abnormalities correlate strongly with the presence of functionally significant multivessel coronary artery disease,34, 37 reduced left ventricular reserve,38, 39 and residual ischemia,30, 34 respectively. All 201Tl images were examined by two independent, experienced observers without knowledge of clinical, electrocardiographic, or other test results. In cases of discordant interpretation, a reading by a third blinded observer was solicited and the majority opinion was accepted.

**Radionuclide ventriculography.** Immediately after the delayed 201Tl images were obtained, equilibrium gated blood pool imaging was performed in all patients at rest to determine left ventricular ejection fraction and segmental wall motion patterns.29, 40 For analysis of regional left ventricular function, 11 separate segments were assessed qualitatively from the anterior, 45 degree (or modified best septal view), and 70 degree left anterior oblique projections.40 Each segment was graded by three observers without knowledge of other data, and a consensus interpretation was obtained based on a five-point scale: 1 = hyperkinetic, 0 = segment not seen, 1 = normal, 2 = hypokinetic, 3 = akinetic, and 4 = dyskinetic. A total and regional wall motion score was derived as described previously by our group.29, 40

**Ambulatory electrocardiography.** In 220 of the 241 patients (91%), a double-channel 24 hr Holter tape recording was obtained during routine hospital activities within 72 hr of catheterization. Drug therapy was not specifically altered before Holter monitoring. Recordings were processed on either an Avionics Model 650 electrodioscanner or a Cardiodata MK3 system. Ventricular arrhythmias were printed out at normal paper speed (25 mm/sec), analyzed by a staff cardiologist, and categorized according to the modified criteria of Lown and Wolf41 without knowledge of infarct type or results of other tests. This classification system is hierarchical because if two or more types of ectopic rhythm occur, only the highest classification number, presumably reflecting the more serious form, is designated. For purposes of analysis, patients were categorized into simple or complex ventricular arrhythmia groups if Lown grades 0 to 2 or grades 3 to 5 ventricular arrhythmias were present, respectively.

**Coronary angiography.** All patients underwent selective coronary angiography in multiple oblique projections a mean of 11 ± 3 days after onset of infarction. Coronary anatomy was reviewed by two experienced blinded angiographers and the location of stenoses were recorded according to the 15 segment model recommended by the American Heart Association.42 The maximal luminal narrowing was established by caliper readings and an angiographically significant stenosis was designated if the narrowing was 50% or greater. Each patient was classified as having one-, two-, or three-vessel coronary artery disease. Significant stenoses in large diagonal or marginal branches were considered lesions of the LAD or LCx, respectively, and a left

<table>
<thead>
<tr>
<th>TABLE 2</th>
<th>Admission electrocardiographic findings in patients who evolved QMI and NQMI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>QMI (n = 154)</td>
</tr>
<tr>
<td>ST seg ≥ 1 mV (patients)</td>
<td>121 (79%)</td>
</tr>
<tr>
<td>ST seg ≥ 1 mV (leads)</td>
<td>2.9 ± 2.2</td>
</tr>
<tr>
<td>Σ ST seg ≥ (mV)</td>
<td>7.2 ± 7.6</td>
</tr>
<tr>
<td>ST seg ≥ 1 mV (patients)</td>
<td>78 (51%)</td>
</tr>
<tr>
<td>ST seg ≥ 1 mV (leads)</td>
<td>1.7 ± 2.1</td>
</tr>
<tr>
<td>Σ ST seg ≥ (mV)</td>
<td>3.0 ± 4.7</td>
</tr>
<tr>
<td>NSSTTWA (patients)</td>
<td>15 (10%)</td>
</tr>
<tr>
<td>Normal</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

^a = nonspecific ST-T wave abnormalities.
^p < .01 compared with QMI.
^p = .0001 compared with QMI.
The mainstem stenosis was recorded as disease in both the LAD and LCx. The extent of underlying coronary artery disease was further assessed by summing the total number of "jeopardized" angiographic segments. This was accomplished by the 15 segment model\textsuperscript{12, 14} with the assumption that all segments distal to a more proximal stenosis of 50% or greater were jeopardized. For example, a jeopardy score of 15 would result if significant stenoses were found in the most proximal portions of the RCA (i.e., segment 1) and in the main trunk of the left coronary artery (i.e., segment 5). By comparison, the score would be 2 if the disease was limited to segment 4 of the distal RCA and segment 10 of the LAD, which represents a diagonal branch.

All vessels were classified as patent or occluded. Patency was designated only if prompt and complete antegrade filling of the distal vessel was demonstrated during selective coronary injection. Vessels showing no antegrade flow beyond the point of occlusion were recorded as occluded, as were those with perceptually slow antegrade flow and only minimal or incomplete filling of the vessel past the obstruction. Finally, the vessel considered responsible for infarction was identified as the coronary artery supplying the area of maximal asynergy seen on the radionuclide ventriculogram and consistent with the electrocardiographically determined site of acute infarction.

**Clinical follow-up.** After hospital discharge, patients were managed by their primary physicians and no attempt was made to standardize therapy. All patients were asked to return to the Post-Myocardial Infarction Clinic for evaluation by the principal investigator (R. S. G.) 3 months after discharge and annually thereafter. For the 3% of eligible patients who did not return, follow-up information was collected by telephone interview. During follow-up, the incidence of cardiac death, recurrent myocardial infarction, rapidly progressive angina pectoris with minimal exertion (NYHA class III) or angina at rest (class IV) of sufficient clinical concern to warrant rehospitalization, and acute coronary bypass surgery or percutaneous transluminal coronary angioplasty (PTCA) was tabulated. Since we anticipated that results of predischarge testing might contribute to the decision to perform surgery or PTCA, the specific reason for revascularization was sought. The diagnosis of recurrent myocardial infarction was established as described above. Cardiac death was designated if it was sudden (occurring within 1 hr of onset of symptoms) or if it was associated with other cardiac complications for which the patient had been hospitalized.

**Data management and statistical analysis.** All data were compiled prospectively and stored in a computerized data bank using a VAX 11/750. Commercially available software (i.e., SAS) was used for statistical computations.

Continuous data are recorded as mean ± SD. Univariate analyses by a two-tailed Fisher exact test for discrete variables or \( t \) statistics for continuous variables were used to assess differences in characteristics between patients with QMI vs those with NQMI. Initially, group differences were determined based on the type of infarction (QMI vs NQMI) and then after stratification of patients within these two groups according to the identity of the infarct-related vessel.

Comparative event rates, including cardiac death, recurrent infarction, unstable angina requiring hospitalization, and coronary bypass surgery or PTCA, among the two groups were recorded as simple proportions, relative risks, and odds ratios.\textsuperscript{44}

To further evaluate differences in outcome, separate life tables (Kaplan-Meier) based on individual survival time were calculated for patients with QMI vs those with NQMI. Plots were constructed to show the cumulative event-free intervals subsequent to testing after myocardial infarction to the conclusion of follow-up; follow-up was terminated in the case of death or if the patient underwent either coronary bypass surgery or PTCA in this analysis. Equality of event probability between groups of patients based on the type of infarction was evaluated with the use of the Mantel-Cox statistic.

**Results**

As shown in table 3, patients with QMI and NQMI were remarkably similar with respect to almost all clinical characteristics and medication usage during the index hospitalization. The only notable exception to this otherwise even distribution of variables at baseline was a higher prevalence of prior angina and previous infarction in the NQMI group. Despite this finding, the Norris coronary prognostic index was similar between the two groups.

**Coronary angiographic findings.** The prevalence of normal coronary arteries and one-, two-, or three- vessel disease was similar between the two groups of patients. Also, no differences were found between patients with QMI and NQMI when the extent of anatomic coronary artery disease based on the mean number of jeopardized angiographic segments was tabulated (6.8 ± 3.5 vs 6.1 ± 3.6; \( p = \) NS). The same similarly

**TABLE 3**

<table>
<thead>
<tr>
<th>Variable</th>
<th>QMI (n = 154)</th>
<th>NQMI (n = 87)</th>
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<tbody>
<tr>
<td>Age (yr)</td>
<td>50.4 ± 8.6</td>
<td>52.2 ± 8</td>
</tr>
<tr>
<td>Range</td>
<td>29–65</td>
<td>31–65</td>
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<tr>
<td>Sex (males)</td>
<td>134 (87%)</td>
<td>71 (82%)</td>
</tr>
<tr>
<td>No. risk factors\textsuperscript{a}</td>
<td>2.2 ± 1.1</td>
<td>2.4 ± 1.1</td>
</tr>
<tr>
<td>Prior angina pectoris</td>
<td>54 (35%)</td>
<td>49 (56%)\textsuperscript{c}</td>
</tr>
<tr>
<td>Previous MI</td>
<td>21 (14%)</td>
<td>21 (24%)\textsuperscript{c}</td>
</tr>
<tr>
<td>Norris index</td>
<td>2.6 ± 1.8</td>
<td>3.1 ± 2.3</td>
</tr>
<tr>
<td>Time from MI onset to CCU admission (hr)</td>
<td>5.1 ± 8.3</td>
<td>4.0 ± 4.6</td>
</tr>
<tr>
<td>Admission Killip class</td>
<td>1.3 ± 0.5</td>
<td>1.4 ± 0.6</td>
</tr>
<tr>
<td>Maximum Killip class</td>
<td>1.6 ± 0.6</td>
<td>1.4 ± 0.6</td>
</tr>
<tr>
<td>Location of index MI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior</td>
<td>57 (37%)</td>
<td>26 (30%)</td>
</tr>
<tr>
<td>Inferior</td>
<td>59 (38%)</td>
<td>25 (29%)</td>
</tr>
<tr>
<td>Lateral</td>
<td>4 (3%)</td>
<td>15 (10%)</td>
</tr>
<tr>
<td>Other\textsuperscript{d}</td>
<td>34 (22%)</td>
<td>20 (23%)</td>
</tr>
<tr>
<td>Nonlocalizable</td>
<td>0 (0%)</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>Medication usage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low-dose heparin</td>
<td>93 (60%)</td>
<td>54 (62%)</td>
</tr>
<tr>
<td>Full-dose heparin</td>
<td>4 (3%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Warfarin</td>
<td>3 (2%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Aspirin</td>
<td>20 (13%)</td>
<td>9 (10%)</td>
</tr>
<tr>
<td>IV Nitroglycerin</td>
<td>51 (33%)</td>
<td>17 (20%)</td>
</tr>
<tr>
<td>Long-acting nitrates\textsuperscript{b}</td>
<td>54 (35%)</td>
<td>35 (40%)</td>
</tr>
<tr>
<td>( \beta )-Blocker\textsuperscript{b}</td>
<td>89 (58%)</td>
<td>54 (62%)</td>
</tr>
<tr>
<td>Calcium-entry blocker\textsuperscript{b}</td>
<td>28 (18%)</td>
<td>22 (25%)</td>
</tr>
<tr>
<td>Antiarrhythmic agent\textsuperscript{b}</td>
<td>6 (4%)</td>
<td>1 (1%)</td>
</tr>
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\textsuperscript{a}As in table 1.\textsuperscript{b}At time of discharge.\textsuperscript{c}p = .05 compared with QMI.
ties were observed when separate group comparisons were made for the 94 patients with LAD infarcts (6.8 ± 3.3 vs 5.5 ± 3.9; p = NS), for the 107 with RCA infarcts (6.7 ± 3.8 vs 6.3 ± 3.5; p = NS), and for the 40 patients with LCx infarcts (7.4 ± 3.0 vs 6.5 ± 3.3; p = NS).

Figure 1 illustrates that 54% of the patients with NQMI had patent infarct-related vessels 11 ± 3 days after onset of acute myocardial infarction compared with only 24.7% of the patients with QMI (p < .0001). As can be seen, this difference was caused by a higher patency rate in all three epicardial vessels but was particularly striking in the subset of 94 patients with LAD infarction (75% vs 29%; p < .0001). For those patients showing an open infarct-related vessel, the average residual stenosis was 73% for QMI and 76% for NQMI.

Creatine kinase data and scintigraphic measures of infarct size. The mean peak creatine kinase value was higher in the QMI group vs that in the NQMI group (1334 ± 996 vs 520 ± 540 IU/liter; p = .0001), implying less myocardial necrosis in NQMI patients. As figure 2 illustrates, a significant difference was observed in the LAD and RCA subsets but not the LCx subset. Of interest, compared with patients with QMI, those with NQMI had a shorter time from onset of symptoms to peak creatine kinase level (22.5 ± 8.7 vs 16.9 ± 10.0 hr; p = .0001). Moreover, this difference was statistically significant in both the LAD subset (21.5 ± 9.4 vs 14.2 ± 10.9 hr; p = .003) and the RCA subset (23.6 ± 8.5 vs 16.5 ± 8.7 hr; p = .0002) but not the LCx subset (21.2 ± 6.6 vs 22.3 ± 9.6 hr; p = NS).

In agreement with the creatine kinase data, the mean left ventricular ejection fraction at 10 ± 3 days was lower in patients with QMI vs that in patients with NQMI (46 ± 12% vs 53 ± 10%; p = .0001). Compared with the QMI group, the NQMI group had fewer akinetic segments (2.0 ± 1.7 vs 1.0 ± 1.3; p = .0001), fewer dyskinetic segments (0.4 ± 0.7 vs 0.2 ± 0.5; p = .023), and a lower total asynergy score, which was indexed to the number of segments analyzed in each patient (1.6 ± 0.4 vs 1.3 ± 0.3; p = .0001). When asynergy scores within the perfusion zone of the infarct vessel were compared, a significant difference between patients with QMI and those with NQMI was found in the LAD subset (2.3 ± 0.6 vs 1.6 ± 0.6; p < .01) and the RCA subset (1.8 ± 0.5 vs 1.6 ± 0.5; p = .04) but not the LCx subset (2.1 ± 0.6 vs 1.9 ± 0.6; p = .49).

Holter and exercise test findings. Complex ventricular arrhythmias defined as Lown grade 3 or higher during 24 hr of ambulatory monitoring were relatively rare in all patient subsets, including the LAD-QMI group (11 of 58 [19%]). Overall, the prevalence of these arrhythmias was 17% in the QMI group and 22% in the NQMI group (25 of 144 vs 17 of 76; p = NS).

Table 4 summarizes the results of treadmill stress testing. Although the test was submaximal by design, only 70 of the 241 patients (29%) achieved the target heart rate or workload without limiting signs or symptoms. No differences between the two groups were found in exercise treadmill time, workload achieved (mets), peak heart rate–blood pressure product, or the prevalence of exercise-induced ventricular arrhythmias. Compared with patients with QMI, fewer patients with NQMI exhibited exercise-induced ST segment elevation. Also, the magnitude of this change was less in patients with NQMI reflected by fewer leads with ST elevation and a lower ΣST elevation score. Despite finding that our two groups were similar with regard to ST segment depression and the prevalence of induced angina of any severity, more patients with NQMI experienced limiting angina (i.e., resulting in test termination) than did patients with QMI.

201Tl scintigraphy. Figure 3, A, compares the proportion of patients within each group with one or more of the predesignated high-risk 201Tl scintigraphic findings. As can be seen, the prevalence of a multivessel

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**FIGURE 1.** Prevalence of open infarct-related vessels 11 ± 3 days after onset of clinical infarction. Patency rates are higher for LAD and non-LAD (RCA and LCx combined) NQMI.
disease scan pattern was similar in the QMI group and in the NQMI group. Although these rates are somewhat lower than the actual prevalence of multivessel coronary artery disease angiography (59% for QMI and 54% for NQMI), they do confirm that the extent of malperfused myocardium was comparable between the two groups of patients. Abnormally increased lung uptake of 201Tl was twice as frequent in patients with QMI vs those with NQMI, implying greater reduction of left ventricular functional reserve in the QMI group. Finally, the overall frequency of 201Tl redistribution was higher in patients with NQMI compared with those with QMI; since the prevalence of redistribution outside of the infarct zone and the number of "remote" segments with redistribution was similar between the QMI and NQMI groups, this last difference was due to more 201Tl redistribution within the infarct zone of patients with NQMI.

The prevalence by type and the number of 201Tl defects within the perfusion zone of the infarct-related vessel for both groups of patients is depicted in figure 3, B and C, respectively. Compared with patients with QMI, those with NQMI were more likely to show redistribution defects (36% vs 60%; p = .007). As a group, patients with QMI had 0.53 ± 0.81 redistributing segments in the infarct zone vs 0.98 ± 0.99 for patients with NQMI (p = .0003). A difference of similar magnitude but in the opposite direction was found when persistent 201Tl defects were considered. Whereas 141 of 154 patients (92%) with QMI had at least one persistent defect, only 56 of 87 patients (64%) with NQMI demonstrated such perfusion abnormalities (p < .0001). Also, the mean number of segments in the infarct zone showing persistent 201Tl defects was 1.9 ± 1.1 in the QMI group vs 0.9 ± 0.9 in the NQMI group (p = .001). When analysis was restricted to severe persistent defects, we found that more patients with QMI had them (47% vs 17%; p < .0001) and more of them were demonstrated in the QMI vs the NQMI group (0.90 ± 1.2 vs 0.22 ± 0.6; p

**TABLE 4**

Results of predischARGE treadmill testing

<table>
<thead>
<tr>
<th>Exercise variable</th>
<th>QMI (n = 154)</th>
<th>NQMI (n = 87)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treadmill time (min)</td>
<td>7.3 ± 4.0</td>
<td>7.2 ± 4.6</td>
</tr>
<tr>
<td>Workload achieved (mets)</td>
<td>4.2 ± 1.9</td>
<td>4.3 ± 2.2</td>
</tr>
<tr>
<td>Rate-pressure product (×10⁵)</td>
<td>15.1 ± 4.5</td>
<td>16.4 ± 6.8</td>
</tr>
<tr>
<td>Ventricular arrhythmias</td>
<td>12 (8%)</td>
<td>9 (10%)</td>
</tr>
<tr>
<td>ST seg ↑ ≥1 mV (patients)</td>
<td>66 (43%)</td>
<td>16 (18%)</td>
</tr>
<tr>
<td>ST seg ↑ ≥1 mV (leads)</td>
<td>2.9 ± 2.2</td>
<td>1.3 ± 1.7</td>
</tr>
<tr>
<td>Σ ST seg ↑ score (mV)</td>
<td>7.3 ± 7.6</td>
<td>2.6 ± 4.9</td>
</tr>
<tr>
<td>ST seg ↓ ≥1 mV (patients)</td>
<td>45 (29%)</td>
<td>32 (36%)</td>
</tr>
<tr>
<td>Any angina</td>
<td>29 (19%)</td>
<td>26 (30%)</td>
</tr>
<tr>
<td>Limiting angina</td>
<td>14 (9%)</td>
<td>17 (20%)</td>
</tr>
</tbody>
</table>

*Frequent (≥5/min), multiform, or paired premature ventricular contractions.

*Necessitating termination of test.

*p < .05 compared with QMI.
pitalization occurred in 65 (27%), and 58 patients (24%) underwent either bypass surgery (n = 56) or PTCA (n = 2). As a group, the 58 patients who underwent revascularization had a higher mean NYHA angina class during follow-up than did the 183 patients who received only medical therapy (3.0 ± 1.3 vs 1.5 ± 1.4; p = .0001). Furthermore, in 47 (81%) of these 58 patients, the decision to perform surgery or PTCA was based on commonly accepted clinical indications, i.e., medically resistant class III or IV angina. For the remaining 11 patients in this group, the choice in favor of nonmedical treatment was significantly influenced by the results of baseline study testing; five of these patients had NQMI and six had QMI. Overall, nine of these 11 patients had severe three-vessel coronary artery disease, two had isolated 95% LAD stenoses (both underwent PTCA), and 10 (91%) exhibited $^{201}$TI redistribution on their predischarge scintigraphic studies.

Figure 4 shows the raw event rates for patients with QMI and NQMI. The mortality rate for both groups of patients with uncomplicated index infarctions who were eligible for predischarge exercise testing was low: 8.4% after QMI and 9.2% after NQMI (p = NS). However, patients with NQMI had a higher reinfarction rate (18.4% vs 6.5%; p = .009), were more likely to be hospitalized because of unstable angina (36% vs 22%; p = .034), and had a greater incidence of subsequent bypass surgery or PTCA (33% vs 19%; p = .018) than patients with QMI.

Figure 5 illustrates the relative probabilities of remaining event free during follow-up (top), remaining free of recurrent infarction (middle), and remaining

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**FIGURE 3.** A. Prevalence of high-risk $^{201}$TI scintigraphic patterns among patients with QMI and NQMI. B. Prevalence of $^{201}$TI redistribution and persistent defects in infarct-related scan segments. C. Number of scan segments in infarct zone with $^{201}$TI redistribution and persistent defects. See text.

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**FIGURE 4.** Incidence of death, recurrent myocardial infarction, unstable angina pectoris (USAP), and bypass surgery (CABG) or PTCA in 241 patients with uncomplicated acute infarction. Test of difference is between QMI and NQMI subgroup (solid bars) incidence. Relative risk values and odds ratios are presented as guides to the magnitude of the associations (e.g., the risk or odds of experiencing an event for patients with NQMI relative to patients with QMI). See text.
FIGURE 5. Kaplan-Meier probabilities for significant clinical events in patients with QMI (dotted line) and with NQMI (solid line); point comparisons of subgroup difference employed the method of Mantel-Cox. See text.

free of either reinfarction or unstable angina leading to bypass surgery or PTCA (bottom). As can be seen, the cumulative event-free probabilities for our two groups, which are adjusted according to the number of patients in each group still at risk, are different from 3 months of follow-up and beyond. Because of baseline differences in prior infarction and angina, evaluation of relative probabilities of remaining event free were examined for patients with QMI and NQMI after including prior infarction and angina as covariates. Prior infarction was not a predictor of outcome, but previous angina was a significant predictor (p = .0013). Cox-Weibull regression of QMI vs NQMI and previous angina showed that both NQMI and angina independently predicted future cardiac events (p = .0037 and p = .0151, respectively). Thus, although previous angina is an important predictor, QMI vs NQMI is independently predictive as well.

Cause-specific mortality. Twelve of the 21 cardiac deaths (57%) were sudden, presumably arrhythmogenic in origin, and nine (43%) were attributed to pump failure. The proportion of patients with NQMI who died suddenly was higher compared with patients with QMI (6/87 [6.9%] vs 6/154 [3.9%]), but despite this almost twofold difference, statistical significance was not achieved. Of interest, all patients who died had either two-vessel (n = 10) or three-vessel coronary artery disease (n = 11) and 18 (86%) showed evidence of residual ischemia by $^{201}$Tl scintigraphic or exercise test criteria. Only three patients (14%) exhibited exercise-induced ventricular arrhythmias at the time of hospital discharge, six (29%) had multiform or repetitive ventricular arrhythmias during Holter monitoring, and eight (38%) had left ventricular ejection fraction of less than 40%. Of the eight patients with ejection fractions under 40%, only one had NQMI and only two of the eight had complex ventricular arrhythmias on Holter monitoring.

Recurrent infarctions. Fourteen of the 16 recurrent infarctions in the NQMI group involved the perfusion zone of the index infarct-related vessel vs only two of 10 in the QMI group (88% vs 20%; p < .01). The reinfarctions in the QMI group tended to be larger as judged by peak creatine kinase values (1742 ± 1673 vs 510 ± 471 IU/liter; p = .08). Of the 16 patients who suffered recurrent myocardial infarction in the same region as the original injury, 15 (94%) showed $^{201}$Tl redistribution in the perfusion zone of the original infarct-related vessel.

Discussion

Much controversy and confusion continues to surround the issue of whether or not myocardial infarctions should be classified as Q wave and non-Q wave infarctions for prognostic purposes. Some authors vigorously denounce such dichotomization, pointing out that these electrocardiographic descriptors have no pathologic basis and do not delineate distinct subsets of patients. Others, however, believe significant differences do exist and that these differences in both short-term and long-term outcome have important therapeutic implications. The present prospective study provides data that strongly support the latter position,
i.e., that non-Q wave events represent incomplete infarctions and are harbingers of greater clinical instability caused by the presence of a larger residual mass of viable but jeopardized myocardium within the perfusion zone of the infarct-related vessel. Moreover, the results presented herein support the concept that in certain patients with NQMI, the pathophysiologic process may involve early spontaneous reperfusion and that patients with NQMI can experience sudden death despite well-preserved left ventricular function.

Descriptors of infarct size. We found that patients with NQMI had a higher ejection fraction at 10 ± 3 days and fewer asynergic ventricular segments than did patients with QMI. This observation is noteworthy because the prevalence of previous infarction was statistically greater in the NQMI group. Also, our data demonstrate that asynergy scores within the perfusion zone of the infarct vessel are lower after NQMI and this difference, which was highly significant, was due to lower scores in the subsets with LAD and RCA infarction. These results and the finding of lower peak creatine kinase values and fewer severe persistent 201Tl defects on exercise scintigraphy indicate that the area of infarct-related necrosis was smaller in patients with NQMI vs those with QMI.

Reasons for smaller infarct size with NQMI. Before speculating on reasons that might explain the smaller infarct size with NQMI, it seems important first to show that the amount of myocardium that presumably was at risk for infarction was similar between the QMI and NQMI groups. Unfortunately, neither the present study nor others can definitively address this issue, since such an answer would require that the potential infarct zone be defined before the index infarction. However, if we presume that both the area at risk and the initial event associated with NQMI are the same as in QMI (i.e., complete coronary occlusion51, 52), then early reperfusion as a result of either spontaneous thrombolysis or relief of spasm may represent the mechanism that limits infarct size in patients with NQMI. The results of the present study appear to support this hypothesis, including (1) the finding that 47% of our patients who evolved NQMI exhibited ST segment elevation on their admission ECG (table 2), (2) the time from onset of infarction to peak plasma creatine kinase level was shorter in patients with NQMI than in those with QMI,52 and (3) more open infarct vessels were found 11 ± 3 days after NQMI than after QMI. The last observation was particularly striking in the subset of 94 patients with LAD infarctions (75% vs 29%); of interest, these patients showed the greatest group differences among patients with NQMI and QMI with regard to peak creatine kinase levels and radionuclide indexes of systolic left ventricular function. Although other investigators have reported a similarly high prevalence of patent infarct-related vessels after NQMI,19, 54-56 our study differs from these in that we performed angiography before hospital discharge as part of a prospective natural history study and compared the results with those from a consecutive group of patients with QMI.

An open infarct-related vessel at 11 ± 3 days after onset of NQMI suggests that either the artery was never completely occluded or that spontaneous reperfusion had occurred. Since we did not perform early angiography, we cannot identify which patients in our study with patent vessels underwent spontaneous recanalization and which had a thrombus that subtotally occluded the infarct-related vessel at the onset of clinical infarction. Even if immediate angiography upon admission had been performed, the true prevalence of spontaneous recanalization may not have been defined, since reperfusion could have occurred before admission. Thus the concept is only speculative at present that NQMI is ushered in by complete coronary occlusion due to spasm, a platelet plug, or a thrombus but for some reason this occlusion is less sustained, leading to reperfusion and a smaller infarct size. Nevertheless, additional evidence from other studies supports the concept and deserves comment. Freifeld et al.57 have recently shown that contraction band necrosis, the histologic hallmark of reperfusion, and hemorrhage are more often found in patients who died with nontransmural than with transmural infarction. This finding, along with the observation that fatal nontransmural infarcts are less often associated with postmortem intracoronary thrombi,58-60 has led several investigators to conclude that transient occlusion followed by reflow may be important in the pathogenesis of NQMI.

An alternative to the reflow hypothesis is that NQMI is associated with subtotal occlusion from the outset and is precipitated by an increase in myocardial oxygen demand. However, we found no evidence for this in our study. At the time of hospital admission, patients with NQMI had a slightly lower heart rate and systolic blood pressure compared with those with QMI. Furthermore, the majority of patients in each group experienced onset of myocardial infarction at rest and this was equally distributed between the two groups. It is thus tempting to postulate, as Roberts61 has, that NQMI is caused by complete thrombotic occlusion but is transient either because of unsustained spasm, which may be necessary for clot stabilization, or because of an inherently more active fibrinolytic
system, which leads to early lysis. Obviously, further study is necessary to delineate the incidence and importance of abnormal platelet aggregation, intracoronary thrombus, and vasospasm in the NQMI syndrome.

**Characterization of NQMI by quantitative $^{201}$TI scintigraphy.** In this study, we identified persistent $^{201}$TI defects in 92% of our patients with QMI. These defects were often of the severe variety and usually involved several infarct-related scan segments. Because most persistent defects, particularly the severe ones, are associated with akinetic or dyskinetic wall motion and only a few show improved uptake after bypass surgery, it is reasonable to assume that these perfusion abnormalities represent myocardial scar. In contrast to our findings in the QMI group, only 64% of patients with NQMI had a persistent defect and the vast majority were of the mild variety and confined to a single infarct-related segment. As such, our results with quantitative $^{201}$TI scintigraphy are quite similar to those obtained with technetium-99m pyrophosphate imaging; in these studies, 90% or more of patients with QMI had abnormal infarct-avid scintigraphic studies compatible with acute myocardial necrosis compared with fewer than 50% after NQMI.

The prevalence of exercise-induced $^{201}$TI redistribution defects within the infarct zone was substantially higher and involved more scan segments in patients with NQMI compared with those with QMI. Based on much experimental and clinical data demonstrating that redistribution of thallium occurs under conditions of transient ischemia, this finding indicates that patients with NQMI have more remaining myocardium at jeopardy than do patients with QMI. Moreover, it helps clarify why a higher percentage of patients with NQMI experienced limiting angina at the time of their predischarge stress test. Because it has already been shown that this scintigraphic marker of ischemia correlates with an increased risk for future cardiac events, it was not surprising that redistribution defects were found in 94% of our patients who experienced reinfarction in the same area as the original injury. Furthermore, since redistribution of thallium predicts a highly favorable response to bypass surgery or PTCA, our data suggest the potential for greater ultimate myocardial salvage in patients with NQMI.

One other study has examined $^{201}$TI scintigraphic findings in patients with QMI vs those with NQMI. In this report, 41 subjects, including 16 with NQMI, were evaluated 10 days after onset of clinical infarction. In agreement with our data, this group of investigators found that patients with QMI had more persistent thallium defects (92% vs 50%; $p = .0007$). However, they were unable to show more peri-infarction redistribution abnormalities in the NQMI group (25% vs 38%; $p = \text{NS}$). The explanation for this discordant result is probably related to methodologic differences; only rest scintigraphy was employed by Wahl et al. rather than the more conventional stress-redistribution imaging protocol we used.

**Prevalence of predischarge ventricular arrhythmias after NQMI.** In this study, the overall prevalence of complex ventricular arrhythmias, as scored by the modified Lown scheme, was 18%, which is considerably lower than the 31% to 36% rates reported in other studies. Of interest, no differences in the frequency of these arrhythmias were found when patients were stratified according to their infarct-related vessel or type of infarction. To our knowledge, only two other studies have dichotomized data on ventricular arrhythmias based on infarct type. In these studies, which included only 28 and 10 patients with NQMI, respectively, the prevalence of multiform or repetitive premature ventricular contraction was 44% and 38% after QMI and 28% and 20% after NQMI ($p = \text{NS}$ for both studies).

The low arrhythmia rates were not unexpected, since all of our patients met criteria for uncomplicated infarction and the mean ejection fraction was 49 ± 11%. Moreover, only 21% of our patients had ejection fraction values under 40% and none exhibited signs of congestive heart failure beyond the fifth day after onset of infarction. Therefore, our finding that complex ventricular arrhythmias did not significantly predict subsequent cardiac death ($p = .31$) or sudden death ($p = .11$) was not surprising. However, it should be pointed out that our study may not have the power to reveal a significant correlation between predischarge arrhythmias and subsequent mortality, particularly because there were only 12 sudden deaths.

**Reasons for greater clinical instability after NQMI.** Our results demonstrate a significantly higher rate of recurrent myocardial infarction and unstable angina pectoris requiring hospitalization, as well as a greater likelihood of subsequent bypass surgery or PTCA in patients with NQMI. Even after analyzing our patients according to baseline clinical variables found to be distributed differently between the QMI and NQMI groups, we still found significant differences in the cumulative probabilities of these event end points. Thus the dichotomization of acute uncomplicated myocardial infarctions based on the presence or absence of Q waves appears to provide important prog-
nostic information of practical use because it identifies a subset of patients (i.e., NQMI) with substantially greater morbidity during a median of 30 months follow-up.

Our comprehensive data set included not only coronary angiographic variables but also quantitative physiologic information related to electrical, mechanical, and ischemic components of risk. In accounting for the observed difference in outcome between patients with QMI and NQMI, it appears that the greater clinical instability expressed as a high incidence of recurrent ischemia and infarction after NQMI is caused by more residual peri-infarction ischemia rather than by more extensive underlying coronary artery disease, greater depression in global or regional left ventricular function attributable to more prior infarcts that we and others observed in patients with NQMI or by a higher prevalence of complex ventricular arrhythmias.

Methodologic considerations. It is possible that medications administered during the index hospitalization might have influenced the infarct-related vessel patency rate, the prevalence of ventricular arrhythmias, and the radionuclide ejection fraction values. However, this did not seem to be the case, since drug therapies were comparable between the QMI and NQMI groups (table 3). It is also unlikely that choice of medical therapy during follow-up influenced subsequent outcome because medication use, risk factor modification, and rehabilitation strategies were similar in our two groups. As pointed out earlier, only 11 of the 58 patients (19%) who underwent bypass surgery or PTCA underwent these procedures for reasons other than medically resistant class III or IV angina pectoris; of these 11 patients, five were derived from the group of 87 with NQMI (5.7%) and six came from the group of 154 with QMI (3.9%; p = NS). Since many of these 58 surgical patients might have subsequently died or experienced reinfarction without revascularization (such patients were considered dropouts for purposes of data analysis), the result should, if anything, have detracted from the observed outcome differences between patients with QMI and those with NQMI given that more patients with NQMI underwent surgery or PTCA.

Data derived from the admission ECG and the predischarge radionuclide and angiographic evaluation permitted us to identify the coronary artery responsible for infarction in all but four (1.7%) of the 241 patients. These four patients had comparably severe occlusions of both the RCA and LCx vessels, and similar electrocardiographic and ventriculographic abnormalities. To maintain as much purity as possible in the LCx group, all four were designated as RCA infarctions. Despite this, our data show considerable overlap among patients with QMI and NQMI within the LCx subset with respect to multiple clinical and functional variables. Although our 201TI results identified differences, it appears that the standard electrocardiographic criteria employed in this study for infarct typing were not sufficiently stringent for the LCx group.

Clinical and therapeutic implications. The weight of evidence forthcoming from our study strongly supports the concept that uncomplicated QMI and NQMI are distinctly different clinical entities. The statement seems especially true for infarcts that are precipitated by LAD and RCA events because the clinical, angiographic, and functional differences were most striking in these subsets.

It appears on the basis of our data that some patients with NQMI should be considered for early cardiac catheterization and mechanical revascularization. This recommendation is particularly relevant for those patients who demonstrate significant ischemia, especially in the perfusion zone of the LAD, by exercise radionuclide methods. Implicit in this strategy is the hypothesis that knowledge of coronary anatomy beyond a “high-risk” exercise scintigraphic response (i.e., 201TI redistribution) improves clinical management. Although this issue was not the focus of the present study and remains to be determined, our data suggest that multiple angiographic stenoses may be an important covariate of risk. Thus it seems prudent to consider catheterization data. However, any recommendation in favor of early catheterization is predicated on the fact that revascularization with bypass surgery or PTCA will prevent reinfarction or prolong life in the subset of patients with NQMI and residual ischemia. Applying such aggressive therapy might be particularly difficult in patients who are asymptomatic during the recovery period. Currently, there are no controlled studies that show such a benefit.

There is evidence that suggests that NQMI and unstable angina pectoris share a common pathogenesis and that transient potentially reversible reductions in coronary blood flow caused by intracoronary thrombus formation and/or vasospasm occur in both syndromes. Since aspirin therapy inhibits cyclooxygenase and the secondary phase of platelet aggregation and calcium-channel blockers prevent vasoconstriction of diseased coronary segments, it seems reasonable to recommend carefully controlled clinical trials of such pharmacologic agents in patients recovering from NQMI. The purpose of such studies carried
out in a large enough sample to avoid a type II error.\(^\text{23}\) would be to determine whether prophylactic therapy with aspirin and/or calcium-channel blockade is as effective in decreasing recurrent cardiac events after NQMI as in unstable angina pectoris.\(^\text{20-22}\) Moreover, these studies may enhance our understanding of the relationship between dynamic obstruction and fixed atherosclerotic disease since successful therapy of the former might ameliorate the latter.

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