Coronary Anatomy and Prognosis After Myocardial Infarction in Patients 60 Years of Age and Younger

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SUMMARY Two hundred twenty-nine hospital survivors of acute myocardial infarction (MI) age 60 years or younger underwent coronary arteriography a median of 2 weeks after infarction and were followed a median of 24 months (range 6–62 months). For 62%, MI was the first presentation of coronary disease and 75% were in clinical Killip class I. Overall outcome was good: 96% survival at 1 year and 95% survival at 2 years. This was due to the high prevalence of patients with one-vessel disease (58%), with a survival of 99% at 1 year and 96% at 2 years. Only 9% of patients had three-vessel disease and they had an 85% survival at 1 year. Eleven patients died and 23 had coronary bypass surgery. In this cohort of younger patients (mean age 51 years), prophylactic therapy may not be justified because of the low mortality and should be reserved for identifiable high-risk groups.

RECENT trials have suggested that β-adrenergic blocking drugs reduce mortality in survivors of myocardial infarction (MI).1-3 as have previous trials with antiplatelet drugs.4 The inference in these studies is that all patients who survive MI should be treated with an appropriate drug to reduce death rate. Before this axiom is translated into clinical practice, it is pertinent to reexamine the natural history of survivors of MI, which Kannel et al.5 described as “inconsistent, fragmentary and inadequate.”

The purpose of this study is to relate coronary anatomy—the number of arteries obstructed—to outcome in posthospital survivors of MI age 60 years and younger.

Methods

Patient Selection

From October 1976 to June 1981, 229 survivors of MI age 60 years or younger underwent coronary arteriography a median of 2 weeks (range 10 days to 16 weeks) after the onset of infarction and formed the study cohort. Patients gave informed consent for angiography and follow-up. Two hundred fifty-seven patients were eligible for the study and 229 (89%) underwent catheterization. The remaining 28 patients did not undergo coronary arteriography because they or their cardiologist did not consent to it. Patients younger than 60 years admitted initially to this hospital and who did not have other life-threatening disease were eligible for this study. Patients with cardiogenic shock and those who had previously undergone coronary bypass surgery were not eligible. Patients transferred from other hospitals were also excluded to avoid significant bias, as this hospital is a tertiary referral center, which receives many patients with complications of infarction. MI was diagnosed by the presence of two of the following criteria: a typical history of chest pain, the development of new pathologic Q waves on the ECG and a typical rise in serum CK enzyme, including a CK-MB fraction.

Clinical Data

Clinical data were collected prospectively on each patient and entered into a computerized information system. This consisted of a detailed history, daily physical examination throughout the hospital stay, chest x-ray and ECG.

Coronary arteriography and left ventriculography were performed by the Sones or Judkins technique in the right and left anterior oblique projections and read by two independent observers. Left ventricular ejection fraction (EF) was calculated for each patient using the area-length method.6 In the right, left anterior descending and circumflex arteries, narrowing of greater than 70% of luminal diameter in any projection agreed upon by two observers was considered significant. Left main disease (LMD) greater than 50% was considered significant. Only the most severe narrowing of each coronary artery was recorded, and patients were classified as having one-, two- or three-vessel disease. After discharge, patients were followed at 3-month intervals to a median of 24 months; the minimum follow-up time was 6 months. All patients were referred back to their physicians and no attempt was made to influence management. Probability of survival was estimated using Kaplan-Meier life tables, and log-rank analysis was used to compare survival between groups. Patients who underwent surgery remained in the analysis up to that time.

Results

Clinical Characteristics

The median age of the 229 patients was 51 years (range 27–60 years). One hundred ninety-five were males and 34 were females. Twenty-four patients (11%) had a history of MI and 85 (38%) had a history of angina pectoris. The site of infarction on the ECG was anterior in 114 patients,
TABLE 1. Coronary Anatomy in 229 Survivors of Myocardial Infarction

<table>
<thead>
<tr>
<th></th>
<th>No. of pts</th>
<th>Mean EF (± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>One-vessel disease</td>
<td>132 (58%)</td>
<td>54 ± 12%</td>
</tr>
<tr>
<td>Two-vessel disease</td>
<td>60 (26%)</td>
<td>47 ± 16%</td>
</tr>
<tr>
<td>Three-vessel disease</td>
<td>20 (9%)</td>
<td>43 ± 16%</td>
</tr>
<tr>
<td>Left main disease</td>
<td>3 (1%)</td>
<td></td>
</tr>
<tr>
<td>(&gt; 50% stenosis)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insignificant disease</td>
<td>14 (6%)</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviation: EF = ejection fraction.

inferior in 108, and indeterminate in six. New Q waves developed during infarction in 148 patients (65%). One hundred seventy-three patients (75%) were in Killip class I, 40 (18%) in class II and 16 (7%) in class III.

Angiographic Data

The coronary anatomy of the group is shown in table 1. One hundred thirty-two patients (58%) had one-vessel disease, 60 (26%) two-vessel disease and 20 (9%) three-vessel disease; 14 patients (6%) had insignificant disease or normal coronary arteries. Three patients had left main stenosis > 50% luminal diameter; two of them underwent coronary artery bypass surgery after angiography and are alive. The other was not operable and is alive 34 months after infarction.

Left ventricular EF measured at angiography ranged from 20–80% (median 52%). The left ventricular EF was 43 ± 16% in patients with three-vessel disease, 47 ± 16% in patients with two-vessel disease and 54 ± 12% in patients with one-vessel disease.

Relation of Clinical Characteristics to Angiography

Age

None of the 28 patients younger than age 40 years had three-vessel disease and only five (18%) had two-vessel disease, whereas 40% of the patients age 40 years or older had two- or three-vessel disease. The prevalence of one-, two- and three-vessel disease and the mean left ventricular EF were not significantly different in 40–50-year-old patients compared with 50–60-year-old patients.

History of Coronary Disease (table 2)

Six of 24 patients (25%) who had a history of MI had three-vessel disease, compared with 7% without previous infarction. In contrast, 62% of patients without previous MI had one-vessel disease, compared with 25% with previous infarction (p < 0.05). Left ventricular EF was significantly lower in patients with previous MI than in those without (40 ± 23% vs 52 ± 13%, p < 0.001).

In patients with no history of angina (62%), one-vessel disease was more common (p < 0.05). Thirteen percent of patients with a history of angina had three-vessel disease, compared with 6% of patients with no history of angina. Left ventricular EF was not different in these two groups.

Killip Classification and Electrocardiographic Variables (table 3)

The number of patients with three-vessel disease increased with each Killip class (I, 6%; II, 15%; III, 25%) and the EF decreased. The distribution of one-, two- and three-vessel disease was not different in anterior and inferior infarction. The mean ejection fraction in anterior infarction was significantly lower than in inferior infarction. Similarly, when Q-wave and non-Q-wave infarcts were compared, the number of vessels involved was not different, but EF was lower in patients with Q-wave infaracts. In patients who developed ventricular tachycardia or fibrillation in the coronary care unit, the prevalence of three-vessel disease was higher and the EF lower than in those who did not have these arrhythmias.

Outcome

The median follow-up period was 24 months (range 6–62 months). There were 13 deaths, 11 of which were cardiac related. Twenty-three patients underwent coronary artery bypass surgery. The cumulative life-table survival for all 229 patients was 96.4 ± 1.4% (± SEM)

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Total</th>
<th>3 (&gt; 70% stenosis)</th>
<th>2</th>
<th>1</th>
<th>0+</th>
<th>Mean left ventricular ejection fraction (%)†</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 40</td>
<td>28 (12%)</td>
<td>0</td>
<td>5 (18%)</td>
<td>20 (71%)</td>
<td>3 (11%)</td>
<td>54 ± 9</td>
</tr>
<tr>
<td>41–50</td>
<td>78 (35%)</td>
<td>8 (10%)</td>
<td>17 (22%)</td>
<td>48 (62%)</td>
<td>5 (6%)</td>
<td>52 ± 14</td>
</tr>
<tr>
<td>51–60</td>
<td>120 (53%)</td>
<td>12 (10%)</td>
<td>38 (32%)</td>
<td>64 (53%)</td>
<td>6 (5%)</td>
<td>50 ± 15</td>
</tr>
<tr>
<td>Previous MI</td>
<td>24 (11%)</td>
<td>6 (25%)</td>
<td>12 (50%)</td>
<td>6 (25%)</td>
<td>0</td>
<td>40 ± 15</td>
</tr>
<tr>
<td>No previous MI</td>
<td>202 (89%)</td>
<td>14 (7%)</td>
<td>48 (24%)</td>
<td>126 (62%)</td>
<td>14 (7%)</td>
<td>53 ± 13</td>
</tr>
<tr>
<td>History of angina</td>
<td>85 (38%)</td>
<td>11 (13%)</td>
<td>30 (35%)</td>
<td>42 (49%)</td>
<td>2 (3%)</td>
<td>50 ± 16</td>
</tr>
<tr>
<td>No previous angina</td>
<td>141 (62%)</td>
<td>9 (6%)</td>
<td>30 (21%)</td>
<td>90 (64%)</td>
<td>12 (9%)</td>
<td>52 ± 13</td>
</tr>
</tbody>
</table>

Three patients with left main coronary artery disease were excluded from this table.

†Normal coronary arteries and stenosis < 70%.

Abbreviation: MI = myocardial infarction.
TABLE 3. Killip Class, Electrocardiographic Site of Infarction, Type of Infarction and Ventricular Tachycardia or Ventricular Fibrillation in the Coronary Care Unit Related to Extent of Coronary Obstruction and Left Ventricular Ejection Fraction

<table>
<thead>
<tr>
<th>Ejection fractions</th>
<th>No. of vessels with significant (&gt; 70%) stenosis</th>
<th>Mean left ventricular ejection fraction (%)*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total†</td>
<td></td>
</tr>
<tr>
<td>Killip class</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>170 (75%)</td>
<td>54 ± 12</td>
</tr>
<tr>
<td>II</td>
<td>40 (18%)</td>
<td>45 ± 15</td>
</tr>
<tr>
<td>III</td>
<td>16 (7%)</td>
<td>37 ± 13</td>
</tr>
<tr>
<td>Anterior</td>
<td>114 (51%)</td>
<td>50 ± 14</td>
</tr>
<tr>
<td>Inferior</td>
<td>108 (49%)</td>
<td>54 ± 14</td>
</tr>
<tr>
<td>Q wave</td>
<td>148 (65%)</td>
<td>48 ± 14</td>
</tr>
<tr>
<td>Non-Q wave</td>
<td>78 (35%)</td>
<td>57 ± 12</td>
</tr>
<tr>
<td>VT or VF in CCU</td>
<td>28 (12%)</td>
<td>47 ± 18</td>
</tr>
<tr>
<td>No VT or VF in CCU</td>
<td>198 (88%)</td>
<td>52 ± 13</td>
</tr>
</tbody>
</table>

*Values are mean ± sd.
†Excluding three patients with left main coronary artery disease.
‡Normal coronary arteries and stenosis < 70%.
§Four patients in whom site not determined electrocardiographically.
Abbreviations: VT = ventricular tachycardia; VF = ventricular fibrillation; CCU = coronary care unit.

at 1 year, 95.8 ± 2.1% at 2 years and 95.8 ± 2.5% at 3 years (fig. 1). Figure 2 shows outcome for one-, two- and three-vessel disease. Figure 3 shows outcome in patients with and without previous MI.

The median age of the 11 patients who died of heart disease was 51 years. Three had three-vessel disease, four had two-vessel disease and four had one-vessel disease. The mean EF in this group was 44 ± 20% (± sd). Five patients died within 6 months of entering the study, two between 6 and 12 months, two between 12 and 24 months, one patient at 40 months and one at 42 months. Three of these patients died from severe heart failure, with a further MI as the terminal event. Eight patients died suddenly; in two of these patients, ventricular arrhythmia was documented.

The median age of the 23 patients who underwent surgery was 49 years. Three had a history of MI. Seventeen were in Killip class I, four in class II and two in class III. Two had left main, five had three-vessel, 10 had two-vessel and six one-vessel disease. The mean left ventricular EF for the group was 57 ± 14% (± sd). Eleven patients had surgery within 3 months of infarction, six within 6 months, four at 12 months and one at 13 months and 19 months. Of the 11 patients who were operated on in the first 3 months, the indication was severe angina in seven and severe multivessel disease in the others.

Relation of Clinical Findings to Outcome

Patients with reduced 1-year survival were those in
Killip class III (76 ± 10%), with previous MI (90 ± 7%) or ventricular tachycardia or ventricular fibrillation in the coronary care unit (92 ± 5%).

Males and females had the same survival. One-year survival was 100% in patients 40 years or younger, compared with 94% in patients older than 50 years (NS). A history of angina, anterior infarction and Q-wave infarction were also associated with a lower 1-year survival. None was statistically significant.

Relation of Angiographic Data to Outcome

Coronary anatomy predicted survival (fig. 2). The cumulative survival for one-vessel disease was 99 ± 1% (± SEM) at 1 year, 96 ± 1% at 2 years and 96 ± 3% (± SEM) at 3 years. Cumulative survival for two-vessel disease was 92 ± 4% (± SEM) at 1 year, 92 ± 5% (± SEM) at 2 years and 92 ± 6% (± SEM) at 3 years. Patients with three-vessel disease had a lower survival 85 ± 11% (± SEM) (p < 0.005) at one year. Because only 10 patients remained after 1 year, further analysis was not done.

Survival in patients with a left ventricular EF > 50% was 99.0 ± 1% at 1-year compared with 93 ± 3% at 1 year for left ventricular EF < 50% (NS) (fig. 4). Survival in patients with one-vessel disease with EF > 50% was 100% at 1 year and 97 ± 2% when EF was less than 50% (fig. 5).

Discussion

This study in survivors of MI age 60 years or less attempts to relate mortality to the degree of coronary artery obstruction and to left ventricular function. These patients originate from the normal emergency intake of a hospital servicing the surrounding community; transfers from other hospitals were not eligible. This policy was an attempt to simulate the patient population with myocardial infarction at community hospitals, where most such patients are treated, in contrast to the population in a tertiary referral center where complicated transfers with a higher mortality may bias the sample. In addition, patients with other significant disease such as severe hypertension, renal failure, or valvular disease that might influence outcome were not eligible.

Although prognosis in patients with angina pectoris has been related to coronary anatomy,7,8 few prospective studies are available relating coronary anatomy to prognosis after myocardial infarction. In our study, posthospital mortality is low, partly because of the high prevalence of one-vessel disease. This finding is...
in contrast to two reported studies. 9,10 Taylor et al. 9
reviewed patients age 65 years or younger with >
50% stenosis. They did not mention whether transfer
patients were included and only 39% of eligible pa-
tients underwent coronary arteriography, compared
with 89% in our study. In the second prospective
study, a similar percentage of eligible patients was
studied, but those age 70 years or younger were in-
cluded and transfers were not discussed. These two studies
showed a prevalence of one-vessel disease of 26% and
23%, in contrast to 58% in our study; the prevalence of
multivessel disease was 73% and 66.5%, in contrast to
35% in our study. The younger age of our patients,
exclusion of referred patients, the fewer patients with
previous infarction and the different definition of sig-
nificant coronary artery obstruction may explain these
differences.

In one study of 50 survivors of MI, 60% had mul-
tivessel disease but 80% were catheterized for angina,
which was unstable in 66%. 11 In another study of pa-
tients younger than 45 years who survived a first in-
farction, coronary arteriography done within 12
months showed that 64% had multivessel disease.
Again, most of these patients were referred for study
because they developed angina. 12 In a study with a
16% sudden death rate, at 1 year after infarction, 27%

had suffered a previous MI and 12% cardiac failure. 13
As coronary arteriography has not been routinely per-
formed on patients who are asymptomatic after infarc-
tion, these studies, like many other nonprospective
studies, tend to be biased toward high-risk patients.
This emphasizes the difficulties of retrospective analy-
ses to define the natural history of myocardial infarc-
tion. In a prospective study of patients age 60 years or
younger who underwent angiography after a second MI,
the annual mortality was 3–4%, which agrees with
our results. 14

Age is an important prognostic variable, 15,16 and
mortality increases exponentially beginning at age 55
years. 15 However, age was not as important in this
study because patients older than 60 years were not
included. The small but significant difference in out-
come between the younger and older patients in this
study were almost certainly due to differences in coro-
nary anatomy. The Coronary Artery Surgery Study
(CASS) in patients with chronic stable angina also
emphasized the relationship between age and severity
of coronary disease. 17 Sixty years of age was chosen as
the upper age limit for our study because, when it
began, coronary arteriography was not accepted as a
usual procedure early after infarction in asymptomatic
patients. In addition, we were interested in the out-

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**Figure 4.** Life-table survival in patients with ejection fraction (EF) > 50% and < 50%. There was no significant difference in survival at 12 months. Bars indicate SEM.

**Figure 5.** Life-table survival in patients with one-vessel disease and ejection fraction (EF) > 50% and < 50%. Bars indicate SEM.
come of patients who suffered complications of premature atherosclerosis.

This group of patients represents a particular profile of early symptomatic presentation of coronary artery disease that has not been emphasized or appreciated previously. The mean age was low (51 years). Myocardial infarction was the first symptomatic presentation of coronary artery disease in 60% of all patients; 37% had a history of angina and only 11% previous infarction. This early presentation of coronary disease has a favorable outcome because of the high prevalence of one-vessel disease and good left ventricular function associated with first infarction. Much of the literature on the natural outcome of coronary artery disease is derived from referred patients with angina pectoris or retrospective analyses of patients who have suffered infarction. A community-based study, the Framingham survey, showed that 50% of patients had myocardial infarction as the first symptom of coronary disease; the death rate was 5% at 1 year and 7% at 2 years. These figures are similar to those in our prospective study.

Inferior myocardial infarction is said to be associated with a high prevalence of multivessel disease, i.e., 64–80%. In our study, inferior myocardial infarction was associated with an 13% prevalence of three-vessel disease, 26% prevalence of two-vessel disease and 1- and 2-year survival of 98% and 96%. Similarly, non-Q wave infarction has been said to be associated with a high prevalence of multivessel disease and high mortality. Nearly 35% of our patients suffered non-Q wave infarction. This group had a 6% prevalence of three-vessel disease and a 26% prevalence of two-vessel disease; the 1- and 2-year survival rates were 100% and 98 ± 2%. Previous studies of non-Q wave and inferior infarction were not prospective and were biased because patients were usually referred for angiography for persistent angina, which suggests a more advanced type of coronary disease than seen in our series.

In our study, poor outcome was best predicted clinically by a history of MI and Killip class III. In both of these groups, the prevalence of three-vessel disease was increased and left ventricular EF was decreased. This is consistent with the data from the clinical indices used by Peel et al., Norris et al. and Killip and Kimball, which indirectly reflect both the severity of coronary artery obstruction and degree of left ventricular impairment. Few of our patients had suffered a previous MI or were in Killip class III, emphasizing that our group reflects the earlier presentation of coronary artery disease. EF is thought to be an independent prognostic factor after MI. Our data tend to suggest that a low EF only enhances mortality in association with two- or three-vessel disease, but not with one-vessel disease; this finding has not been emphasized previously.

Apart from differences in age distribution, the cohort of survivors of MI in our series closely resembles the patient populations recruited for trials of secondary prevention. In the Norwegian Multicenter Trial of timolol, exclusion criteria were similar to those used in our study, only 48% of patients surviving to 11 days being entered into the trial. In the Anturane Reinfarction study, only patients in Killip class I or II who had survived for 3 weeks after MI were entered. The placebo group in this trial had a mean age of 56 years and their 1-year survival was 93.5%.

The reported 1-year mortality in posthospital survivors of MI varies; 5% is commonly quoted. If subsets are considered, 1-year mortality varies from as high as 66% in patients with poor left ventricular function and ventricular dysrhythmia to as low as 1% in patients with one-vessel disease and good left ventricular function, as is shown in this study. These figures illustrate the complex heterogeneous population that may be included in a group of survivors of myocardial infarction. Of the 23 patients who had surgery in this group, many had severe multivessel obstruction, and outcome in this series may have been influenced by surgery, as 17 underwent surgery within 6 months of infarction. Most patients were operated on for symptoms, which is accepted management for patients with coronary artery disease. Surgery may influence outcome after infarction, although to what extent is not known.

Patients not operated on were followed by their physicians and no attempt was made to influence therapy. At some time during follow-up, 105 patients received β-blocking agents. However, there was no difference in outcome between patients who received β blockers and those who did not.

In clinical practice, coronary arteriography is being done more often in younger survivors of MI, and it provided valuable prognostic information in this study. It is the only reliable means of accurately identifying the amount of coronary artery stenosis and at the same time assessing left ventricular function — the two major determinants of prognosis. High-risk subsets can be identified early after MI and managed by appropriate medical or surgical therapy. Trials of secondary prevention have shown significant differences in survival, and there is considerable pressure on physicians to treat all patients with β blockers after infarction. To recommend β-blockade therapy for all patients after MI disregards the heterogeneous nature of this disease and presents a dilemma of inevitable medical therapy for very low risk subsets who do not require it or creates a false means of security for high-risk groups (i.e., left main disease patients who require operation rather than any medical therapy).

The present study suggests that when MI patients age 60 years or younger from the surrounding community are followed and treated by their physicians, 3-year survival is good because of the high prevalence of one-vessel disease. Prophylactic therapy may not be indicated for all.

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