Prediction of Multivessel Disease after Inferior Myocardial Infarction

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SUMMARY We correlated clinical parameters with angiographic findings in 108 men with a previous isolated inferior myocardial infarction, to determine if these parameters could predict accurately which patients had multivessel disease.

Of 71 men in angina class 2–3, 42 had three vessel disease versus only seven of the 37 who were either asymptomatic or angina class 1 (P < 0.001). Multivessel disease was present in 35 of the 36 who had anterior ST-T abnormalities at rest (P < 0.001) and 16 of the 17 with cardiomegaly. Among men 55 years and older, the incidence of multivessel disease was 94% compared to 70% in men less than 55 (P < 0.03).

We conclude that functional angina class, age, and the presence of resting anterior ST and T abnormalities are highly predictive of associated left system disease in survivors of inferior infarction.

CORONARY ARTERY BYPASS SURGERY relieves angina in approximately 80% of patients surviving operation.1,2 In symptomatic patients with significant left main coronary artery stenosis, bypass surgery prolongs life, compared to nonoperated controls.3,4 Some evidence5 suggests that surgery also may prolong life in the subgroup of patients with three vessel involvement and good ventricular function; however, prospective randomized studies in patients with stable angina have failed to demonstrate improved survival in operated patients.6,7 Definitive studies which may resolve this question have yet to be completed; therefore, the ultimate indications for bypass surgery, and thus coronary arteriography, remain to be clarified.

Survivors of inferior myocardial infarction represent a large, easily-defined subgroup of patients with coronary artery disease. It has been suggested that most of these patients should undergo coronary arteriography even if they are asymptomatic.8 This point of view is highly controversial, however. Selzer et al.9 have recently outlined the case against performing coronary arteriography in most subgroups of asymptomatic patients, including those with a previous uncomplicated myocardial infarction.

If noninvasive clinical parameters correlated well with the extent and severity of coronary artery disease in this subgroup of patients, coronary arteriography could be reserved for those likely to be surgical candidates.

The purpose of this study was to evaluate various clinical parameters as predictors of the extent and severity of coronary artery involvement in a group of men with previous inferior myocardial infarction.

Methods

Patient Material

The study population consisted of 108 consecutive men with an isolated inferior myocardial infarction who underwent coronary arteriography at the Montreal Heart Institute between August 1974 and February 1977. Patients with unstable angina, cardiomyopathy, malignant hypertension, valvular or congenital heart disease were excluded.

Inferior myocardial infarction was diagnosed on the basis of the electrocardiogram recorded one day prior to coronary arteriography. Sixty patients met definite criteria and the remaining 48 probable criteria for inferior infarction according to the Minnesota code.10,11 Those with coexistent anteroseptal infarctions were excluded. As illustrated in table 1 no significant clinical or angiographic differences could be detected between men with definite and probable criteria for infarction; therefore, in subsequent analyses the two groups are not considered separately.

No clinical history of previous myocardial infarction could be elicited from 13 patients but in the remaining 95 a typical clinical history was documented. Of these 95 men, infarction occurred within the year prior to arteriography in 51, between one and three years in 16 and greater than three years previously in 28. Confirmation of infarction by serial enzyme studies was not available for all patients, since many were referred from distant centers. Men with silent infarction or a long interval between infarction and subsequent coronary arteriography displayed similar clinical and angiographic features to the entire group and thus are not analyzed separately.

Clinical Parameters

On the day preceding coronary arteriography a complete description of the patient's symptoms and risk factors were recorded. All patients were then classified according to the Canadian Heart system12 which differs slightly from both the New York Heart Association and the American Heart Association classifications. Thirty-seven of the 108 men were either asymptomatic or Canadian Heart anginal class 1 and the remaining 71 were anginal class 2 or 3. Patients with unstable angina, anginal class 4 or unprovoked angina at rest were excluded from the study.

A family history was considered positive when one or more family members had a well documented coronary event before age 55. Smoking more than ten cigarettes daily was counted as a risk factor. Diabetes was considered present if a fasting blood glucose was greater than 140 mg% or if the patient was already being treated with hypoglycemic agents. Hypertension was defined as a cuff pressure above 150/100 and was also accepted as being present if the patient had a history of hypertension and was receiving antihyper-
tensive drug therapy. Hyperlipidemia was diagnosed when the serum cholesterol exceeded 250 mg% or the triglycerides 150 mg% following an overnight fast.

A standard postero-anterior chest film and a twelve lead electrocardiogram were also done on the day preceding coronary arteriography and were interpreted without knowledge of the clinical or angiographic findings. When the cardiothoracic ratio exceeded 0.50 cardiomegaly was considered present. Anterior ST-T wave abnormalities were diagnosed by Minnesota code criteria.16 17

Exercise Testing

On the day preceding coronary arteriography all patients had an exercise test using a Bruce protocol18 modified by a three minute warmup at 1.7 mph with a 5% grade. A bipolar precordial lead (CMs) was monitored continuously and recorded each minute during and for five minutes following exercise. Cuff blood pressure was measured at each minute throughout the test. Exercise was continued until incapacitating fatigue, dyspnea, progressive angina, an important arrhythmia or horizontal or downsloping ST-segment depression of 3 mm occurred. In the absence of these end points exercise was continued to at least 85% of the age-predicted maximum heart rate. The criteria for a positive test were the development of horizontal or downsloping ST-segment depression ≥ 1 mm or a slowly upsloping ST segment depressed ≥ 2 mm at 0.08 seconds after the J point, compared to the resting tracing.14 15

Maximal ST-segment response, maximal exercise capacity, maximal heart rate and pressure-rate product were calculated; however data from all patients were not suitable for analysis. In 74 of the 108 men maximal ST-segment response was evaluated. Excluded were the four men without significant coronary stenoses, seven who could not be tested adequately because of a physical handicap, three in whom digitalis or procainamide could not be stopped prior to testing and twenty who stopped with negative tests before 85% of the age predicted maximum heart rate (three because of serious arrhythmias, six because of fatigue and eleven because of angina). Maximal exercise capacity, maximal heart rate and pressure-rate product were calculated for these 74 patients, with the exception of nine in whom propranolol could not be discontinued because of the severity of their angina. In these 74 men, the end points for exercise testing were chest pain in 31, dyspnea in 23, fatigue in 16, 3 mm of horizontal or downsloping ST-segment depression in three and dizziness in one; all of these men either developed positive tests or reached 85% of their age predicted heart rate.

Cardiac Catheterization

The coronary arteriogram was performed by a percutaneous transfemoral approach using preformed catheters as previously described.19 Each artery was filmed in four to six projections including special angulated views.17 Stenotic vessels were coded according to the criteria of the Ad Hoc Committee on Coronary Artery Disease Reporting.19 For the purposes of this study, stenoses ≥ 70% of the arterial intraluminal diameter were considered significant lesions. Stenoses of large diagonal or marginal branches were counted as lesions of the left anterior descending and circumflex coronary systems, respectively. A proximal lesion in the left anterior descending coronary artery was defined as a stenosis which occurred before the first septal branch.

A vessel was considered operable if its diameter distal to the significant stenosis was 1 mm or greater and if it irrigated an area of myocardium subjectively evaluated as large enough to support a bypass graft. Revascularization was considered complete when all stenoses ≥ 70% could be bypassed, optimal when all major stenotic vessels could be bypassed and suboptimal if a major vessel was not operable.

Left ventriculography was filmed in the 30° right anterior oblique projection before the coronary arteriogram. Ejection fraction was calculated by the area-length method19 and wall motion abnormalities were assessed by techniques previously described.20

All angiographic documents were interpreted without knowledge of the patient’s clinical status.

Statistical Analyses

A Chi-square analysis was used to determine the statistical significance of nonquantitative differences between groups. Quantitative differences between groups were analyzed using an unpaired Student’s t-test.

Results

Angiographic Findings

Significant single vessel disease occurred in 18%, two vessel disease in 32% and three vessel disease in 45% of the 108 men in the study. The remaining four men had no coronary lesions ≥ 70%. Of the other 104 men, 100 had significant right coronary lesions and 63 right coronary arteries were completely occluded. Proximal left anterior descending coronary stenoses occurred in 40 men and five had left main coronary lesions.

The mean ejection fraction (N = 94) was 0.45 ± 0.01 (SEM). Inferior wall motion abnormalities were present in 90% (85 of 94) and 46% of these (39 of 85) exhibited akinesis or dyskinesis. Figure 1 illustrates the relationship between the number of significantly stenosed arteries and ejection fraction. Of the 79 men with multivessel disease for whom ejection fraction could be calculated, only 30% (24) had a
normal ejection fraction, 54% (49) had a moderately depressed ejection fraction (0.30-0.49) and 8% (6) had an ejection fraction of less than 0.30. No patient with single vessel disease had an ejection fraction below 0.30.

Clinical Parameters

Functional Anginal Class

The relationship between functional anginal class and the extent of coronary disease is illustrated in table 2. Fifty-nine percent of the patients in anginal class 2 to 3 had three vessel disease compared to only 21% of those in anginal class 0 to 1 (P < 0.001). Only 13% of patients in anginal class 2 to 3 had single vessel disease compared to 33% in anginal class 0 to 1 (P < 0.05). Although the difference is not statistically significant, anginal classes 2 and 3 were more frequently associated with proximal left anterior descending disease than anginal classes 0 and 1: 45% (32 of 71) compared to 24% (8 of 33). All five patients with left main coronary artery stenosis were anginal class 2 or 3.

Risk Factors

In table 3, the number of risk factors per patient is compared to the number of diseased arteries. The risk factors evaluated were hypertension, hyperlipidemia, diabetes, cigarette smoking and a positive family history of coronary disease. The number of risk factors per patient appears to be unrelated to the number of arteries involved and thus risk factors, when evaluated in this manner, are of no value in predicting the severity of disease in this population. It is possible that a more detailed risk factor analysis, structured to consider the severity of each factor, might yield different results.

The patient’s age, however, correlates with the severity of the disease. Among men 55 years of age and older the incidence of multivessel disease was 94% (32 of 34), compared to 70% (52 of 74) in men less than 55 years old (P < 0.03); 62% of these older men had proximal left anterior descending coronary artery stenosis compared to only 26% of the younger men (P < 0.005).

Cardiomegaly

Only 17 of the 104 men with significant coronary disease had a cardiothoracic ratio greater than 0.50 on chest X-ray. Twelve (71%) of these had three vessel disease, four (24%) had two vessel disease and one (5%) had only single vessel disease. The absence of cardiomegaly was associated with three vessel disease in 37 (43%) patients, with two vessel disease in 31 (36%) and with single vessel involvement in 19 (21%). Although three vessel disease occurred much more frequently when cardiomegaly was present, the difference did not attain statistical significance. Cardiomegaly on chest X-ray was not invariably associated with a low ejection fraction since four of 14 patients with this finding had an ejection fraction greater than 0.45.

Resting Electrocardiogram

Thirty-six of the 108 men had electrocardiographic ST and T abnormalities at rest in the precordial leads. The relationship between the number of arteries with significant disease and these abnormalities is illustrated in figure 2. Sixty-nine percent (25 of 36) of the patients with this finding had three vessel disease compared to only 35% (24 of 68) of those with normal anterior ST and T waves (P < 0.005). Only one of the 36 patients with anterior ST and T abnormalities had single vessel disease. Fifty-six percent (20 of 36) of the men with this finding had proximal left anterior descending or left main coronary stenosis compared to 37% of those without this finding (P = NS).

Treadmill Exercise Test

In table 4 the extent of coronary disease is compared to the ST-segment response to exercise for the 74 patients with adequate tests. Negative tests (< 1 mm) occurred in 93% (13 of 14) of men with one vessel disease, 44% (12 of 27) of those with two vessel disease and 24% (8 of 33) of those with three vessel disease (P < 0.005). All 13 patients with 3 or more

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**Table 2. Functional Anginal Class and Extent of Coronary Disease**

<table>
<thead>
<tr>
<th>Functional class</th>
<th>No. pts</th>
<th>Number of vessels with stenosis ≥ 70%</th>
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<tr>
<td>0</td>
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**Table 3. Coronary Risk Factors**

<table>
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<th>Number of vessels with stenosis ≥ 70%</th>
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</thead>
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<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
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</tbody>
</table>

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**Figure 1.** Although a great deal of overlap exists, the average ejection fraction of patients with multivessel disease was less than those with single vessel disease (P < 0.05). Of 79 men with multivessel involvement, 55 (70%) had an ejection fraction < .50.
mm of ST depression had multivessel disease; 11 had three vessel disease and ten had proximal left anterior descending or left main coronary artery stenosis. Therefore, profound ST depression indicated severe disease in this population.

Maximal exercise capacity also correlated with the extent of coronary disease, as illustrated in figure 3. The average treadmill time for men with one vessel disease was greater than for those with multivessel disease (P < 0.01). All patients with one vessel involvement entered Bruce stage III compared to only 52% of those with two vessel disease and 37% of those with three vessel disease. However, 23% (12 of 52) of the patients with multivessel disease entered stage III and had negative tests, indicating that single lead exercise testing as performed in this study is not a sensitive detector of severe disease in this population. Analysis of maximal heart rate and pressure-rate product provided no additional predictive data.

Twenty-one patients were unable to complete Bruce stage I because of angina, dyspnea or profound ST depression; 19 had positive ST segments. This degree of incapacity was associated with three vessel disease in 16 and two vessel disease in the remaining five. Proximal left anterior descending coronary stenosis was present in 13 and left main coronary disease in two.

![Graph](image_url)

**Figure 2.** Only 1 (3%) patient with resting anterior ST-T wave abnormalities had isolated right coronary disease compared to 19 (28%) without a precordial ECG abnormality. Anterior ST-T wave abnormalities indicated three vessel disease in 25 (69%) cases.

Multivariate Analysis

The most useful independent predictors of severe coronary disease in this population were functional anginal class, age and the presence of resting anterior ST and T abnormalities. The results of exercise testing and radiographic cardiomegaly also correlated with severe coronary disease, but added little additional information. Risk factors were of no value in predicting the extent of disease; for example, both patients with four risk factors had only isolated right coronary disease.

Ninety percent (62 of 71) of the patients in anginal class 2 and 3 had multivessel disease. Eighty percent (32 of 40) of the men with proximal left anterior descending coronary stenosis and all five with left main coronary stenosis were in this group. The inability to complete Bruce stage I identified a group of patients with multivessel disease; however, this was already strongly suspected since all of these 21 patients were in anginal class 2 or 3. A negative exercise test in anginal class 2 or 3 was still associated with multivessel disease in 9 of 14 instances, indicating that with this combination of factors exercise testing also was of little additional predictive value once functional class was known.

Forty percent (17 of 37) of patients in anginal class 0 and 1 had single vessel disease. Exercise testing was not helpful in detecting multivessel disease in anginal class 0 and 1: of eight patients with positive tests, two had no coronary stenosis ≥ 70%, two had isolated right coronary disease and only four had multivessel disease. The findings in those with negative tests were similar: of 19 men in class 0 or 1 without resting anterior ST and T abnormalities with an adequate negative test, nine had multivessel disease and three of these had proximal left anterior descending coronary stenosis.

The patient's age and resting electrocardiogram were useful predictors of multivessel disease in anginal class 0 and 1. All four men with resting anterior ST and T abnormalities had multivessel disease including two with negative exercise tests. Similarly all four patients 55 years of age and older had multivessel disease and three had proximal left anterior descending coronary artery stenosis.

Twenty-nine men were anginal class 0 or 1, less than 55 years old and without resting anterior ST and T abnormalities. Three had three vessel disease, ten had two vessel disease and three of these 13 had proximal left anterior descending coronary stenosis. Thus severe disease is not
elaborated even by the most favorable combination of predictive factors.

Operability

Table 5 depicts the potential for coronary artery bypass surgery in several subgroups of this population. Although at least one vessel could be bypassed in 75 of the 84 men, complete or optimal revascularization was possible in only 32 (39%). Among the 43 men in whom a suboptimal revascularization was possible, 21 would have had residual unbypassed left coronary disease. Functional anginal class appeared unrelated to the potential degree of revascularization; in anginal class 2 and 3, slightly less than half of the patients were good surgical candidates.

**Table 5. Operability of Patients with Multivessel Disease**

<table>
<thead>
<tr>
<th>Anginal class 0-1</th>
<th>Complete</th>
<th>Optimal</th>
<th>Sub-optimal</th>
<th>Not possible</th>
<th>Total</th>
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</thead>
<tbody>
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<td>2</td>
<td>10</td>
<td>0</td>
<td>14</td>
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<tr>
<td>3 vessel</td>
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<td>1</td>
<td>4</td>
<td>1</td>
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<tr>
<td>Total</td>
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<td>3</td>
<td>14</td>
<td>1</td>
<td>21</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Anginal class 2-3</th>
<th>Complete</th>
<th>Optimal</th>
<th>Sub-optimal</th>
<th>Not possible</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 vessel</td>
<td>9</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>21</td>
</tr>
<tr>
<td>3 vessel</td>
<td>3</td>
<td>10</td>
<td>25</td>
<td>4</td>
<td>42</td>
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<tr>
<td>Total</td>
<td>12</td>
<td>14</td>
<td>29</td>
<td>8</td>
<td>63</td>
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</tbody>
</table>

The long term prognosis for hospitalized patients surviving inferior infarction has been reported to be better than that predicted by the angiographic findings in our study. The mortality between two months and five years following a transmural inferior myocardial infarction in veterans was 28% in a study by Beard et al. Cole et al. reported a ten year mortality rate of 54% in survivors of inferior infarction. Both of these studies were completed before the introduction of coronary bypass surgery; therefore, recent therapeutic advances do not explain these excellent long term results. Although spontaneous variations in patient populations could partly explain the difference in prognosis between our patients and those in the aforementioned studies, it is more likely that we have selected patients with somewhat more severe disease than the average survivor of an isolated inferior infarction.

The extent and distribution of coronary disease in our patients is similar to that described by Hamby et al. and Williams et al. in their catheterized patients with previous inferior infarction. Neither claimed that their patients were representative of all survivors of inferior infarction. On the other hand, Miller et al. have described a group of 84 survivors of uncomplicated inferior infarction in NYHA class I or II with similar or slightly more severe disease. On the basis of their data they conclude that previous inferior myocardial infarction, even when associated with few symptoms, is a marker of advanced coronary disease, and they recommend coronary arteriography for the majority of patients with inferior infarction. The distribution and extent of coronary disease will not be known precisely until a consecutive series of patients hospitalized with inferior infarction undergoes coronary arteriography. Such a study would be useful since the projected mortality based on angiographic studies exceeds that found in clinical studies, probably because relatively fewer asymptomatic patients undergo coronary angiography.

Predictors of Severe Disease

Functional anginal class, the patient's age and the presence of resting anterior ST and T abnormalities are highly predictive of associated left system disease in survivors of inferior infarction, according to the results of this study. Younger men without moderate or severe angina or resting anterior ST and T abnormalities usually have single vessel disease. Since the number of false positives and false negatives associated with a predictor depends upon the prevalence in a population of the abnormality being measured, the quantitative results of this study, for example, the exact percentage of multivessel disease associated with a certain parameter, may not be valid in other populations. This would be particularly so if the patients in our study have more severe disease than the average survivor of isolated inferior myocardial infarction. Nevertheless, the association of moderate to severe angina with anterior ST and T abnormalities in older survivors of inferior infarction will, in general, be highly predictive of important left anterior disease.

This study suggests that exercise testing can predict the
extent of coronary disease in this population but that it adds little to what can already be inferred from the patient's age, functional anginal class and resting electrocardiogram. However, exercise testing has other uses in these patients; it aids in both rehabilitation and the detection and characterization of arrhythmias and it is an objective means of evaluating functional class in a patient with vaguely defined symptoms. The use of multiple lead systems increases sensitivity without sacrificing specificity in selected patients undergoing exercise testing. The usefulness of exercise testing as a predictor of the severity of coronary disease might have been increased if multiple leads had been used in the present study.

Which Patients Should Undergo Coronary Arteriography?

Since coronary artery bypass surgery relieves angina in most patients who survive surgery, we recommend coronary arteriography for survivors of inferior myocardial infarction who are limited to functional class 2 or 3 because of angina. This study indicates that for nearly half of such patients complete or near-complete revascularization will be possible. For a small minority with no bypassable vessels surgery will be contraindicated and for a larger minority surgery could be performed, but with suboptimal revascularization. All patients with significant left main coronary stenosis in our study were in anginal class 2 or 3 and therefore would be referred for coronary arteriography by this criterion.

Because no presently available data prove that surgery prolongs life in patients with multivessel coronary disease, we believe that coronary arteriography is not routinely indicated in survivors of inferior infarction in anginal class 0 or 1. Coronary arteriography in certain instances is necessary to establish a prognosis, to help either the patient or his physician in the management of the disease. A further indication for arteriography in this subgroup might be the infrequent patient in whom left main coronary artery stenosis is suspected on the basis of profound exercise-induced ST depression, although in this study no patient in anginal class 0 or 1 exhibited this finding.

These recommendations may undergo important changes as more data accumulate documenting the effect of coronary bypass surgery on the natural history of coronary artery disease.

Acknowledgment

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