

## Is there an indication for coronary angiography in patients under 60 years of age with no or minimal angina pectoris after a first myocardial infarction?

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**SUMMARY** Coronary angiography and exercise stress tests were performed in 91 consecutive patients under 60 years of age having either no or only mild angina pectoris with or without medication after a first myocardial infarction. Nine (10%) patients had angiographic high risk coronary artery disease defined as three vessel disease, left main stenosis, or proximal stenosis of the left anterior descending artery. Eighteen patients had a positive electrocardiographic exercise stress test, including eight of the nine patients with angiographic high risk coronary artery disease.

It may be concluded therefore that coronary angiography to detect high risk coronary artery disease in this group can be restricted to patients with a positive exercise stress test. This policy would obviate the need for about 80% of coronary angiograms performed in this age group.

The indication for coronary angiography in patients after a first myocardial infarction, with no or only mild angina pectoris, remains controversial.<sup>1-6</sup> In patients with severe angina, there is a clear indication for coronary angiography to determine their suitability for surgery. Although patients with no or only mild angina pectoris are not candidates for coronary artery bypass surgery on the basis of symptoms, severe coronary artery disease may be present despite their apparently minor symptoms.<sup>6-8</sup> In some cardiac centres all patients under a certain age with evidence of coronary artery disease in the absence of specific contraindications are examined by coronary angiography in order to detect high risk disease.

High risk coronary artery disease is defined as: three vessel disease, proximal stenosis of the left anterior descending artery, or stenosis in the left main coronary artery (see methods). In these patients surgery has been shown to prolong life expectancy.<sup>9-16</sup> Our study was performed in order to determine the incidence of high risk coronary artery

disease in patients under 60 years of age without or with only mild angina pectoris after a first myocardial infarction and whether or not the existence of high risk coronary artery disease could be predicted from the results of electrocardiographic exercise stress testing.

### Patients and methods

#### PATIENT SELECTION

Only patients, under 60 years of age, who sustained a first transmural myocardial infarction in the period January 1982 to October 1983, with no or with only mild angina pectoris (New York Heart Association functional class I or II for angina pectoris) irrespective of treatment were considered eligible. Patients with valvar heart disease, congestive heart failure, left bundle branch block, or associated severe non-cardiac disease such as malignancy, insulin dependent diabetes, or severe hypertension were excluded from the study. Cardiac catheterisation and coronary angiography were performed about two months after acute myocardial infarction. Ninety one patients entered the study. Before cardiac catheterisation and coronary angiography all patients underwent electrocardiographic exercise testing. If patients were receiving medication this was not withdrawn.

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## EXERCISE TESTING

All patients underwent a symptom limited exercise stress test to detect a possible discrepancy between subjective and objective signs of coronary insufficiency. The stress test was performed using either a treadmill (with the graded multistage exercise protocol of Bruce) or a graded bicycle ergometric exercise test (10 W/min). Every three minutes a complete 12 lead electrocardiogram was recorded and blood pressure measured.

In the absence of electrocardiographic signs of coronary insufficiency, irrespective of whether or not patients reached 85% of the predicted maximal heart rate, the stress test was considered to be negative. The test was considered to be inconclusive if the electrocardiogram showed ST segment elevation in leads over the infarcted area accompanied by reciprocal ST segment depression. Several authors have attributed these ST segment elevations to abnormal left ventricular wall motion.<sup>17-19</sup>

Electrocardiographic signs of coronary insufficiency were defined as: (a) J point depression of  $\geq 0.1$  mV relative to the end of the PQ segment, with horizontal or downward sloping ST segment,<sup>20,21</sup> or (b) U wave inversion,<sup>22</sup> or (c) a slow upsloping ST segment depression  $\geq 0.2$  mV for at least 0.08 s beyond the J point,<sup>23,24</sup> or (d) an increase of  $\geq 0.2$  mV for at least 0.08 s after the J point in cases of preexisting ST segment depression.

## LEFT VENTRICULOGRAPHY AND CORONARY ANGIOGRAPHY

The left ventricle was visualised in the frontal and lateral projections. The segmental contractility was classified as normal, hypokinetic, akinetic, or dyskinetic. Coronary angiography was performed by either the Sones' or Judkins' technique. In addition to the standard posterior-anterior and oblique projections, angulated views were also used.

In patients with normal coronary arteries an ergonovine provocation test was performed 48 hours after stopping all medication. Increasing doses of 0.05, 0.1, and 0.2 mg ergonovine maleate were injected intravenously under electrocardiographic control and recording of symptoms.

Coronary stenoses resulting in more than a 70% reduction of luminal diameter in any projection were considered to be haemodynamically important.<sup>25,26</sup> Only the most severe narrowing in each coronary artery was counted. Left main stenosis was counted as two vessel disease and was considered to be present when the luminal diameter was reduced by more than 50%, as commonly accepted. Stenoses of angiographically large diagonal or marginal branches were considered as lesions of the left anterior descending and circumflex coronary arteries respectively. Patients

were classified as having one vessel, two vessel, or three vessel disease.

High risk coronary artery disease was defined as: (a) three vessel disease—all vessels having a narrowing  $> 70\%$ , (b) left main stenosis  $> 50\%$ , (c) proximal stenosis of the left anterior descending artery with a 70–99% narrowing before take off of the first large septal perforator without prior anterior wall infarction, and (d) any combinations of the above.

## STATISTICAL METHODS

The results were analysed by the  $\chi^2$  test. A p value  $< 0.05$  was considered to be significant.

## Results

## CLINICAL CHARACTERISTICS

The mean age of the 91 patients (88 men, three women) was 48 (range 34–59) years. Of these, 51 sustained an inferior wall infarction and 40 an anterior wall infarction. Seventy patients were in NYHA functional class I and 21 in functional class II for angina pectoris (Table 1).

## FINDINGS AT CORONARY ANGIOGRAPHY

Table 2 summarises the findings.

*All patients*—Four patients had completely normal vessels, including one with an aberrant origin of the right circumflex artery. Another patient had  $< 70\%$  stenoses. All these patients underwent an ergonovine provocation test, which appeared to be negative in all cases. High risk coronary artery disease was present in nine patients; four had left anterior descending artery stenosis and five three vessel disease, including two patients with associated left main stenosis.

*Functional class*—High risk coronary artery disease was present in five out of 70 asymptomatic patients (class I) and in four out of 21 with mild angina pectoris (class II). This difference is not significant. Two patients with left main artery stenosis were asymptomatic.

*Site of infarction*—Seven out of nine patients with high risk coronary artery disease had sustained an inferior wall infarction: four patients had proximal stenosis of the left anterior descending artery and three had three vessel disease, including the two patients with left main stenosis. None of the patients

Table 1 NYHA functional class of symptoms related to the site of the infarction

Site	No of patients	Class I	Class II
Inferior	51	39	12
Anterior	40	31	9
Total	91	70	21

Table 2 *Angiographic findings*

No of diseased vessels	No of patients	Including stenosis of:	
		Left anterior descending artery	Left main artery
<i>All patients (n=91)</i>			
0	5	—	—
1	63	—	—
2	18	4*	—
3	5*	—	2*
<i>Patients in class I (n=70)</i>			
0	5	—	—
1	49	—	—
2	14	3*	—
3	2*	—	2*
<i>Patients in class II (n=21)</i>			
0	0	—	—
1	14	—	—
2	4	1*	—
3	3*	—	—
<i>Patients with inferior infarction (n=51)</i>			
0	1	—	—
1	36	—	—
2	11	4*	—
3	3*	—	2*
<i>Patients with anterior infarction (n=40)</i>			
0	4	—	—
1	27	—	—
2	7	—	—
3	2*	—	—

\*High risk coronary artery disease.

with previous anterior wall infarction had left main disease or proximal stenosis of the left anterior descending artery in the sense of high risk disease. If the left anterior descending artery was occluded or supplied the infarcted area this was not considered to be in the high risk category. The difference in the incidence of high risk disease between patients with previous inferior or anterior wall infarction was not significant.

#### EARLY COMPLICATIONS OF CARDIAC CATHETERISATION

Three patients developed early complications after catheterisation: one required surgical correction of a pseudoaneurysm of the femoral artery, and two had reversible glottic oedema and shock attributable to an allergic reaction to the contrast material.

Table 3 *Results of exercise stress test in relation to functional class and number of diseased vessels*

Variable	No of patients	Test result:		
		Positive	Negative	Inconclusive
<b>Functional class:</b>				
I	70	9	49	12
II	21	9	9	3
Total	91	18	58	15
<b>No of diseased vessels:</b>				
0	5	0	5	0
1	63	6	46	11
2	18	7*	7†	4
3	5	5	0	0

\*Including three patients with stenosis of the left anterior descending artery.

†Including one patient with stenosis of the left anterior descending artery.

#### FINDINGS AT EXERCISE STRESS TESTING

Nine of the 70 patients who were in functional class I had a positive stress test as did nine of the 21 patients in class II (Table 3). This difference is significant ( $p < 0.01$ ). All patients showed a normal blood pressure response during exercise. No attempt was made to record the differences between maximal heart rate and duration of exercise in relation to the method of stress testing used.

Only six patients with one vessel disease had a positive stress test, whereas all the patients with three vessel disease, including two with left main stenosis, had a positive exercise response. Three of the four patients with proximal stenosis of the left anterior descending artery had a positive stress test. None of the patients with an inconclusive test had high risk disease.

In 18 patients the exercise test was positive, including eight of the nine patients with high risk disease. Only one patient with high risk disease had a negative stress test. The difference in incidence of high risk disease in patients with a positive exercise test compared with those with a negative test is significant ( $p < 0.001$ ).

Thirteen of 15 patients with an inconclusive test had previously sustained an anterior wall infarction and two an inferior wall infarction. After previous anterior wall infarction 10 patients had one vessel disease and three two vessel disease. Of the remaining two patients after inferior wall infarction, one had one vessel disease and the other two vessel disease. At left ventriculography dyskinesia of the infarcted area was found in 12 patients and akinesia in three.

#### Discussion

This study was performed to document angiographically the incidence of high risk coronary artery disease in patients under 60 years of age having no or only mild angina pectoris after first transmural myocardial infarction and to relate this to the results of exercise stress testing.

Previous studies—the European coronary surgery study group,<sup>12</sup> the Veterans Administration study,<sup>10</sup> the Seattle Heart Watch,<sup>11</sup> and Sheldon *et al*<sup>16</sup>—suggest that life expectancy might be prolonged by operation in patients with stable angina pectoris and associated left main stenosis, three vessel disease, or proximal left anterior descending stenosis. On the other hand the latest Coronary Artery Surgery Study fails to show an improved five year survival after coronary artery bypass surgery in patients with no or mild angina pectoris with either three vessel disease or proximal left anterior descending artery stenosis.<sup>27</sup> Nevertheless, as only 37% of the patients who were eligible were actually studied, the question of whether these results are valid remains.

Comparison of our results with other reported studies is hampered by differences of definition as to what constitutes a haemodynamically important stenosis (Table 4). Mautner and Phillips considered a >70% cross sectional narrowing haemodynamically important, corresponding to a 50% narrowing in luminal diameter.<sup>28</sup> Vanhaecke *et al* considered a >50% diameter narrowing as haemodynamically important.<sup>29</sup> For the purposes of this study we chose a >70% reduction in luminal diameter as being haemodynamically important. These differences probably explain the lower incidence of three vessel disease in our study, which is similar to that reported by Roubin *et al*<sup>30</sup> (Table 4). The higher incidence of one vessel disease in our series might possibly be due to our criteria for patient selection. Firstly, all patients were under 60 years of age (mean 48 years). Chaitman *et al* reported a higher incidence of multivessel disease in patients over 55 years.<sup>31</sup> In David's series, 18% of patients under 40 years of age had normal coronary angiograms.<sup>32</sup> Secondly, all patients had recently sustained a first infarction. Roubin *et al* found a higher incidence of three vessel disease after second infarction.<sup>30</sup> Thirdly, our patients had only mild or no angina, whereas Vanhaecke *et al* and

Chaitman *et al* found a higher incidence of three vessel disease in patients with more severe symptoms.<sup>29,31</sup>

In the present study five of 70 patients without angina pectoris had high risk disease compared with four out of 21 with mild angina. This difference is not significant.

Several reports suggest a higher incidence of multivessel disease in patients after inferior wall infarction.<sup>31,33</sup> In our study 14 out of 51 patients who sustained inferior wall infarction had multivessel disease, including three with three vessel disease. Although nine of 40 patients after anterior wall infarction had multivessel disease, including two with three vessel disease these differences are not significant, as confirmed by Roubin *et al*, who also found no difference in the incidence of multivessel disease in patients with inferior wall infarction compared with patients with anterior wall infarction.<sup>30</sup>

Although the risk of morbidity related to cardiac catheterisation is low 2–3%,<sup>34,35</sup> the mortality, nevertheless, amounts to 0.2%.<sup>34,35</sup> Bourassa and Noble found that mortality was closely related to the presence of left main coronary artery stenosis.<sup>35</sup> In our study no patient died, and the complication rate was 3%.

All patients with three vessel disease, including the two with left main stenosis, had a positive exercise stress test, even when taking medication. This agrees with the results of Weiner *et al*, who, using only a horizontal ST segment depression of >0.1 mV, found that 97% of the patients with left main stenosis and 96% of the patients with three vessel disease had a positive result.<sup>36</sup> Similarly three of the four patients with a proximal left anterior descending artery stenosis had a positive stress test, which is in accordance with the results of Chaitman *et al*, who found a positive test in 86% of the patients with proximal left anterior descending artery stenosis.<sup>31</sup>

It would, therefore, appear that the existence of left

Table 4 Review of published studies

Author	No of patients	Definition of significant stenosis	Patient characteristics	% Of patients with*:			
				Normal vessels	One vessel disease	Two vessel disease	Three vessel disease
Roubin <i>et al</i> <sup>30</sup>	202	>70% diameter narrowing	No, mild, or severe angina, <60 years	7	62	24	7
Mautner and Phillips <sup>28</sup>	31	>70% cross sectional narrowing	No or only mild angina, <65 years	7	32	32	29
Vanhaecke <i>et al</i> <sup>29</sup>	59	>50% diameter narrowing	No angina, <45 years	51		49	
Present study	91	>70% diameter narrowing	No or only mild angina, <60 years	5½	69	20	5½

\*Although the use of percentages calculated from populations of <100 is often misleading, vessel involvement is given as a percentage for comparison.

main stenosis, three vessel disease, and in most cases also proximal left anterior descending artery stenosis can be predicted on the basis of a positive exercise test.

#### CONCLUSION

The indication for coronary angiography in patients under 60 years who have sustained a first myocardial infarction and who subsequently are either asymptomatic or have only mild angina pectoris is still controversial. Our study suggests that high risk coronary artery disease is seldom encountered in such patients. The presence of high risk disease is almost always associated with a positive exercise stress test. Although no mortality was associated with angiography in this study group, a 3% early complication rate cannot be overlooked. Thus, bearing in mind both patient safety and cost containment, we conclude that in this patient population coronary angiography to detect high risk disease should be limited to patients with a positive exercise test. This policy could be expected to save approximately 80% of angiograms in this patient population.

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