Exercise testing provides additional prognostic information in angiographically defined subgroups of patients with coronary artery disease

Helmut Gohlke, M.D., Ladislaus Samek, M.D., Peter Betz, M.D., Ph.D., and Helmut Roskamm, M.D.

ABSTRACT We examined whether exercise testing with measurement of cardiac output during maximal exercise can provide additional prognostic information for medically treated patients in whom left ventricular function and extent of coronary artery disease are known. We followed 1034 patients with normal or mildly impaired left ventricular function; 410 of these patients (group 1) had single-vessel disease, 316 had double-vessel disease (group 2), and 308 had triple-vessel disease (group 3). In addition, 204 patients with double- or triple-vessel disease and moderately impaired left ventricular function (group 4) were followed. Mean follow-up in these 1238 patients was 4.5 years. End point of follow-up was death. Groups 1, 2, and 3 were divided into terciles according to the maximally achieved values of the following exercise variables: exercise tolerance, angina-free exercise tolerance, maximal heart rate, and cardiac output during maximal exercise. Group 4 was divided into halves accordingly. Survival curves (according to the method of Cutler and Ederer) for group 2 showed a 15% difference in 5 year survival rate between the highest and lowest terciles (p < .005) by use of the noninvasive variables exercise tolerance, angina-free exercise tolerance, and maximal heart rate (95% vs 80%). The separation into terciles according to cardiac output during maximal exercise resulted in a significant difference in survival rates between the highest and lowest terciles (halves) in all groups of patients. The differences in 5 year survival rates were 9% (p < .05), 16% (p < .05), and 19% (p < .005) for groups 1, 2, and 3, respectively, and 22% for group 4 (p < .005). We conclude that noninvasive exercise parameters can separate high- and low-risk subgroups of patients with double-vessel disease and good left ventricular function. Determination of maximal cardiac output allowed identification of low- and high-risk subgroups in all four angiographically defined groups.


RETROSPECTIVE AND PROSPECTIVE studies have shown that the extent of coronary artery disease and left ventricular dysfunction are important factors determining the prognosis of patients with coronary artery disease.1-7 Also, the results of exercise testing correlate with the subsequent development of coronary events in a normal population,8 in patients in the chronic phase of coronary artery disease,9 and in patients after myocardial infarction.10-14 The correlation of the results of exercise testing with subsequent cardiac events has been related to the fact that exercise tests are more often positive in patients with multivessel disease,11 and patients with multivessel disease are more likely to have a poor prognosis. The objectives of the present study are to analyze whether exercise testing can give additional prognostic information in patients with angiographically determined left ventricular function and extent of coronary artery disease.

Materials and methods

Patient selection. Between 1975 and 1978, 2883 patients underwent coronary angiography for suspected coronary artery disease or for preoperative evaluation. Of these patients, 757 underwent bypass surgery within 6 months after angiography. In 1772 of the remaining 2126 patients, coronary angiograms and results of exercise tests were available for review. These patients were followed up for a mean of 4.5 years (table 1).

Patients included in this study were not part of a randomized or controlled study; medical management of patients with significant coronary disease was chosen because anginal symptoms were adequately controlled with antianginal medication and/or modification of life-style or because coronary anatomy did not appear suitable for bypass surgery.

Coronary angiography. Coronary angiography was performed with the Sones technique in the majority of patients...
TABLE 1

<table>
<thead>
<tr>
<th>Patient selection and characteristics</th>
<th>No. of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angiography for suspected coronary artery disease or for preoperative evaluation between 1975 and 1978</td>
<td>2883</td>
</tr>
<tr>
<td>Bypass surgery within 6 mo after angiography</td>
<td>757</td>
</tr>
<tr>
<td>Exercise test not available</td>
<td>414</td>
</tr>
<tr>
<td>Patients managed medically, exercise test and angiography available</td>
<td>1772</td>
</tr>
<tr>
<td>Male/female</td>
<td>1595/177</td>
</tr>
<tr>
<td>Mean age at angiography (yr ± 1 SD)</td>
<td>49.9 ± 6</td>
</tr>
<tr>
<td>Mean follow-up after angiography in yr (range)</td>
<td>4.5 (3–7)</td>
</tr>
</tbody>
</table>

(90%) and with the Judkins technique in the remainder. Sublingual nitroglycerin was usually given before angiography. The right and left coronary system were visualized in sufficient projections to delineate the morphologic characteristics of the entire coronary system. Angled caudocranial views were used routinely.

Lesions in the coronary arteries were analyzed by measuring the reduction in luminal diameter with an optical gauge in reference to the size of the artery just proximal to the obstruction. A luminal diameter reduction of more than 50% was considered significant.

Left ventricular angiography. Left ventricular angiography was performed in the right anterior oblique projection (30 degree) at 50 frames/sec in all patients. The left ventricle was divided into five segments according to American Heart Association recommendations. Sublingual nitroglycerin was usually given before angiography. The right and left coronary system were visualized in sufficient projections to delineate the morphologic characteristics of the entire coronary system. Angled caudocranial views were used routinely.

Lesions in the coronary arteries were analyzed by measuring the reduction in luminal diameter with an optical gauge in reference to the size of the artery just proximal to the obstruction. A luminal diameter reduction of more than 50% was considered significant.

Left ventricular angiography. Left ventricular angiography was performed in the right anterior oblique projection (30 degree) at 50 frames/sec in all patients. The left ventricle was divided into five segments according to American Heart Association recommendations. The systolic contraction pattern of each of the five segments was numerically scored: 1 = normal, 2 = mildly hypokinetic, 3 = severely hypokinetic, 4 = akinetic, and 5 = dyskinetic. The left ventricular score is the sum of the points of these five segments.

The left ventricle was considered to be normal when there was only mild hypokinesia in one segment (score 5 to 6). Left ventricular function was considered mildly impaired when there was akinnesia in one segment and mild hypokinesia in a second segment (score 7 to 9). Moderately impaired left ventricular function was present when there was at least akinnesia in one segment and severe hypokinesia or akinnesia in a second segment (score 10 to 14). Patients with severe hypokinesia of nearly all segments had a left ventricular score of 15 or more and were not included in this analysis. A similar scoring system was used in the CASS Registry. In 90% of patients the left ventricular angiogram was performed with a Swan-Ganz catheter, and ventricular premature beats were common during contrast injection. We obtained a regular sinus beat with full opacification of the left ventricle in only 43% of the patients; therefore, ejection fraction values were not considered in this analysis.

Exercise electrocardiogram and hemodynamics. All patients underwent exercise testing in the postabsorptive state after all antianginal drugs had been discontinued for at least 12 hr. Eleven percent of patients had taken digitalis within the week before exercise testing. The prevalence of exercise-induced ST segment depression was 47.3% in patients who used digitalis and 49.6% in patients who did not use digitalis (p > .5).

Exercise tests were performed with an electrically braked bicycle ergometer (Siemens Elephant) with the patient in the supine position. The shoulders of the patient were fixed by padded bars. A No. 5F Swan-Ganz catheter was inserted percutaneously into an antecubital vein and was advanced to the pulmonary artery without fluoroscopic control. Pulmonary artery and pulmonary capillary wedge pressure were measured in patients at rest. A nine-lead electrocardiogram (ECG) (I, II, III, aVR, aVL, aVF, V2, V4, and V6) was recorded before and immediately after exercise. During exercise, leads V2, V4, and V6 were recorded at the end of each minute at 50 mm/sec. Exercise was started at 25 or 50 W, depending on the previously tested exercise tolerance of the individual patient. The work load was increased by 25 or 50 W every 6 min until fatigue, severe angina pectoris, more than 0.3 mV ST segment depression occurred, or 80% of the age-predicted maximal heart rate was reached.

Pulmonary artery pressure was recorded throughout exercise, and pulmonary capillary wedge pressure was measured in a relative steady state after 4 to 5 min on each exercise level. The oxygen saturation in the central pulmonary artery was determined in patients at rest and after 6 min on each exercise level. Arterial oxygen saturation was determined from the hyperemic earlobe. Cardiac output was determined in patients at rest and in a relative steady state after 6 min on each exercise level with Fick’s principle. Because oxygen consumption for a given work load shows very little variation with supine bicycle ergometry, oxygen consumption was not measured but taken from a table of previously established normal values for age, sex, and external work load. Although measurement of oxygen uptake might have been more accurate, this is difficult to accomplish in clinical routine work; it also makes it more difficult for the patient to relate the development of discomfort or chest pain to the physician supervising the exercise test.

The following variables were analyzed: age of the patient, heart size (mL/m² body surface area), exercise tolerance in watts, angina-free exercise tolerance in watts, peak heart rate during exercise, peak systolic blood pressure, the peak heart rate–blood pressure product, occurrence and severity of angina pectoris (scale of 0 to 3), occurrence and degree of ST segment depression, pulmonary capillary wedge pressure in patients at rest and during maximal exercise, and cardiac output in patients at rest and during maximal exercise.

Follow-up. Follow-up was obtained by questionnaires sent out in September 1982 or by means of repeat visits to our outpatient clinic. Follow-up was 98% complete in patients with significant coronary artery disease regardless of the number of vessels involved. End point for follow-up was death of the patient. The causes of death were not analyzed in detail; a previous study has shown that total survival rates and cardiac survival rates correlate very closely in patients with angiographically determined coronary disease up to 5 years after angiography. In case of bypass surgery after 6 months of follow-up, the patient was withdrawn from the study at the time of surgery.

Statistical analysis. Survival curves were computed according to methods of Cutler and Ederer. Following a recommendation of Collins et al., we tested the comparison of the survival rates between the different groups according to the method of Mantel and Haenszel. A probability level of less than .05 was considered significant. The correlation between the exercise parameters and subsequent death was determined by use of multivariate analysis of noninvasive and invasive parameters with the proportional hazards regression model of Cox. Calculations were performed on a PDP 11/45 computer.

Results

There were 403 patients with either normal coronary arteries or less than 50% luminal diameter narrowing in a major coronary artery. The number of patients...
PATHOPHYSIOLOGY AND NATURAL HISTORY—CORONARY ARTERY DISEASE

FIGURE 1. Survival curves of patients with zero-, single-, double-, and triple-vessel disease independent of left ventricular function (p < .0001, global testing for differences in survival). n = number of patients in each group at the beginning of the indicated year of follow-up.

with single-, double-, or triple-vessel disease was 495, 413, and 461, respectively. The mean age increased from 47.3 ± 7 years in patients with normal coronary arteries or less than 50% stenosis to 52.3 ± 6 years in patients with triple-vessel disease. During a mean follow-up of 4.5 years 182 patients died.

The gross survival rates for up to 6 years after angiography in these patients are shown in figure 1, and the rates illustrate the typical trend to less favorable survival with increasing number of diseased vessels (p < .0001).

If the patients are grouped according to the degree of left ventricular dysfunction (figure 2), the difference in survival rates between those with normal left ventricular function (score 5 to 6) and patients with severe left ventricular dysfunction (score ≥15) becomes greater than the difference in survival rates between patients with zero- and triple-vessel disease; however, the number of patients with severe left ventricular dysfunction is small (p < .001).

Because patients with angiographically determined poor left ventricular function are known to have a poor prognosis, we confined our analysis of the prognostic importance of exercise parameters to the following subgroups of patients (table 2): Those with normal or only mildly impaired left ventricular function (score 5 to 9) were divided into three groups, according to the number of vessels diseased (groups 1, 2, and 3). In addition, patients with double- or triple-vessel disease and moderately impaired left ventricular function were grouped together (group 4) because of the smaller number of patients available for analysis (table 3). The ejection fraction could be determined in 43% of patients. It was 72 ± 11% in patients with normal left ventricular function (score 5 to 6), 59 ± 12% in patients with mildly impaired left ventricular function (score 7 to 9), and 47 ± 11% in patients with moderately impaired left ventricular function (score 10 to 14). The survival curves in the four groups analyzed are shown in figure 3.

The previously seen trend to less favorable survival rates for patients with more severe disease is seen again, but the difference in rates between patients with single- and triple-vessel disease (groups 1 and 3) is slightly less after patients with severe left ventricular dysfunction have been excluded. The difference in survival rates among the four groups remains highly significant (p < .0001).

We examined the prognostic importance of the noninvasive and invasive exercise parameters in these four groups. According to the distribution of each exercise variable, the patients in groups 1, 2, and 3 were divid-

---

TABLE 2
Definition of groups 1–4 based on angiographic assessment

<table>
<thead>
<tr>
<th>Group</th>
<th>No. of patients</th>
<th>No. of diseased vessels</th>
<th>LV function and LV score</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>410</td>
<td>One</td>
<td>Normal or mildly impaired; LV score: 5–9</td>
</tr>
<tr>
<td>2</td>
<td>316</td>
<td>Two</td>
<td>Moderately impaired; LV score: 10–14</td>
</tr>
<tr>
<td>3</td>
<td>308</td>
<td>Three</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>204</td>
<td>Two or three</td>
<td></td>
</tr>
</tbody>
</table>

*Patients with single-vessel disease and moderately or severely impaired left ventricular function and patients with double- or triple-vessel disease and severely impaired left ventricular function are not included.*
ed into three approximately equal-sized groups. Thus, in group 1 the third of patients with the highest exercise tolerance was grouped together (the highest tercile) and compared with the third of patients with the lowest exercise tolerance (the lowest tercile) (table 3).

The survival curves for patients in these terciles were computed. The survival curves of the middle terciles were between those of the highest and the lowest tercile for all variables. Patients in group 4 were divided into halves based on the exercise variables because of the smaller number of patients available. The p value refers to global differences of the survival curves of the three terciles or of both halves of the corresponding variable; only the 5 year survival rates of the highest and lowest tercile (halves) are shown in table 3.

By use of the noninvasive exercise variables such as maximal exercise tolerance, angina-free exercise tolerance, and maximal heart rate achieved, there was a trend to better survival rates in the highest tercile in all subgroups. This trend, based on noninvasive parameters, reached statistical significance only for patients in group 2. Survival rate was significantly better for patients in group 2 with higher exercise tolerance, higher angina-free exercise tolerance, and for those achieving a higher maximal heart rate. The magnitude of this difference in 5 year survival rates between the highest and the lowest tercile for patients with double-vessel disease is comparable to the difference in survival rates between patients with single- and triple-vessel disease, i.e., approximately 15%.

In group 1 the overall mortality was low, and the trend to better survival rates in the highest terciles did not reach statistical significance. In group 3 mortality was high even for patients in the highest tercile of the exercise parameters. Here again the difference in mortality did not reach statistical significance (table 3).

Analysis of the invasive exercise parameters (maximal cardiac output and pulmonary capillary wedge pressure obtained during maximal exercise testing) revealed a significant difference in survival rates for all three groups between those in the lowest and the highest tercile of those with maximal cardiac output and those in the higher and lower half in group 4 (table 3). The differences in 5 year survival rates between those in the highest and lowest terciles were 9% (p < .05), 16% (p < .05), and 19% (p < .005) in groups 1, 2, and 3, respectively. Among patients in group 4 the difference in survival rates between those in the higher and the lower half was 22% (p < .005).

Univariate analysis (table 4) of noninvasive exercise parameters with the proportional hazards regression model of Cox showed that in patients with single-vessel disease (group 1), age correlated best with subsequent death, and the maximal double product was only second, followed by maximal heart rate and exercise tolerance. In patients with double-vessel disease (group 2), univariate analysis with this model shows that age is no longer important, and the parameters of exercise testing become determinants of survival; maximal exercise tolerance is the most significant factor.

In patients with triple-vessel disease (group 3) the occurrence of ST segment depression correlates with subsequent death. In patients with double- or triple-vessel disease and moderately impaired left ventricular function (group 4), exercise tolerance is the most important noninvasive variable for the prediction of subsequent death.

If the invasive exercise parameters, maximal cardiac output, and maximal pulmonary capillary wedge pressure, are included in the univariate or multivariate analysis, maximal cardiac output is the most important variable that correlates with subsequent cardiac death in all four groups (table 4). However, age in group 1 and exercise-induced ST segment depression in group 3 remain of independent importance. In group 4 the maximal cardiac output and the maximal pulmonary capillary wedge pressure are independent prognostic factors.

Thus, when noninvasive parameters are used, exercise testing is able to differentiate, among patients with double-vessel disease and normal or mildly impaired left ventricular function, those at low risk for death during a 5 year follow-up period from those at substantially higher risk for death during the follow-up time. When cardiac output is used as an invasive parameter
TABLE 3

Five year survival in highest and lowest terciles (halves) of exercise parameters in groups 1–4

| Group | No. of patients | Tercile | Exercise tolerance (watts) | Cut points | 5 yr survival (%) | Non-invasive | Invasive | Cut points | 5 yr survival (%) | Non-invasive | Invasive | Cut points | 5 yr survival (%) | Non-invasive | Invasive | Cut points | 5 yr survival (%) | Non-invasive | Invasive | Cut points | 5 yr survival (%) | Non-invasive | Invasive |
|-------|----------------|---------|---------------------------|------------|-------------------|-------------|----------|------------|-------------------|-------------|----------|------------|-------------------|-------------|----------|------------|-------------------|-------------|----------|------------|-------------------|-------------|----------|------------|-------------------|-------------|----------|
| 1     | 410            | Highest | >110                      | 97 ± 2     | NS                | >90         | 95 ± 2   | NS         | >140              | 97 ± 2     | NS       | >15        | 96 ± 2            | NS           |           | >12        | 87 ± 4            | NS           |           | >14        | 96 ± 2            | NS           |           |
|       |                | Lowest  | ≤90                       | 92 ± 3     | NS                | ≤60         | 93 ± 2   | ≤110       | 93 ± 2            | NS           |           | ≤12        | 87 ± 4            | NS           |           | ≤10        | 80 ± 6            | NS           |           | ≤9         | 92 ± 3            | NS           |           |
| 2     | 316            | Highest | >110                      | 95 ± 2     | NS                | >70         | 96 ± 2   | NS         | >125              | 95 ± 2     | NS       | >14        | 96 ± 2            | NS           |           | >10        | 80 ± 6            | NS           |           | >9         | 92 ± 3            | NS           |           |
|       |                | Lowest  | ≤90                       | 81 ± 5     | NS                | ≤40         | 78 ± 5   | ≤110       | 90 ± 2            | 83 ± 2     | NS       | ≤14        | 92 ± 3            | MS           |           | ≤10        | 73 ± 5            | NS           |           | >13        | 90 ± 3            | NS           |           |
| 3     | 308            | Highest | >90                       | 86 ± 4     | NS                | >70         | 88 ± 4   | NS         | >110              | 88 ± 3     | NS       | >14        | 92 ± 3            | NS           |           | >10        | 80 ± 6            | NS           |           | >13        | 90 ± 3            | NS           |           |
|       |                | Lowest  | ≤60                       | 79 ± 4     | NS                | ≤40         | 82 ± 3   | ≤100       | 82 ± 4            | NS           |           | >10        | 73 ± 5            | NS           |           | ≤10        | 80 ± 6            | NS           |           | >14        | 90 ± 3            | NS           |           |
| 4     | 204            | Higher half | >60                       | 88 ± 4     | NS                | >40         | 80 ± 5   | NS         | >105              | 83 ± 4     | NS       | >11        | 90 ± 3            | NS           |           | >11        | 85 ± 5            | NS           |           | >12        | 87 ± 4            | NS           |           |
|       |                | Lower half | ≤60                       | 62 ± 5     | *                 | ≤40         | 78 ± 5   | ≤105       | 75 ± 5            | NS           |           | ≤11        | 68 ± 5            | NS           |           | ≤11        | 59 ± 4            | NS           |           | ≤10        | 92 ± 3            | NS           |           |

*aSurvival rates are ± SD. Groups 1–3 were divided into terciles and group 4 was divided in half as determined by noninvasive exercise parameters and maximal cardiac output. Separation into two or three equal-sized groups was based on the cut points of the exercise variables.

All p values refer to the differences of the survival curves of the terciles or halves in the corresponding groups rather than only to the 5 year survival rates shown in this table. *p < .05; †p < .005.

obtained during exercise testing, a significant difference in survival rates becomes evident in all four groups between those in the lowest and the highest tercile (groups 1, 2, and 3) or half (group 4), respectively.

Discussion

The classification of patients with coronary artery disease into subgroups according to the number of vessels diseased has gained wide acceptance despite its limitations. Several authors have developed a scor-

TABLE 4

Chi-square analysis

<table>
<thead>
<tr>
<th></th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>Group 4</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Multivariate</td>
<td>Multivariate</td>
<td>Multivariate</td>
<td>Multivariate</td>
</tr>
<tr>
<td></td>
<td>Univariate</td>
<td>Non-invasive</td>
<td>Invasive</td>
<td>Non-invasive</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>8.69</td>
<td>5.51</td>
<td>4.93</td>
<td>3.89</td>
</tr>
<tr>
<td>Heart size (ml/m² BSA)</td>
<td>0.00</td>
<td>0.05</td>
<td>0.06</td>
<td>0.92</td>
</tr>
<tr>
<td>Exercise tolerance (W)</td>
<td>3.64</td>
<td>0.26</td>
<td>0.27</td>
<td>5.61</td>
</tr>
<tr>
<td>Angina-free exercise tolerance (W)</td>
<td>2.29</td>
<td>0.03</td>
<td>0.37</td>
<td>6.38</td>
</tr>
<tr>
<td>Severity of angina (0–3)</td>
<td>0.02</td>
<td>1.46</td>
<td>0.92</td>
<td>0.93</td>
</tr>
<tr>
<td>Degree of ST segment depression (mV)</td>
<td>0.29</td>
<td>0.41</td>
<td>0.04</td>
<td>0.63</td>
</tr>
<tr>
<td>Maximal heart rate (beats/min)</td>
<td>5.49</td>
<td>0.04</td>
<td>0.02</td>
<td>6.05</td>
</tr>
<tr>
<td>Maximal blood pressure (mm Hg)</td>
<td>3.42</td>
<td>0.21</td>
<td>0.06</td>
<td>0.52</td>
</tr>
<tr>
<td>Maximal double product (HR × mm Hg)</td>
<td>6.32</td>
<td>3.14</td>
<td>1.02</td>
<td>4.59</td>
</tr>
<tr>
<td>Maximal cardiac output (l/min)</td>
<td>8.62</td>
<td>4.86</td>
<td>6.29</td>
<td>1.37</td>
</tr>
<tr>
<td>Pulmonary capillary wedge pressure (mm Hg)</td>
<td>2.73</td>
<td>0.09</td>
<td>2.14</td>
<td>0.98</td>
</tr>
<tr>
<td>Global chi-square</td>
<td>10.7</td>
<td>12.2</td>
<td>6.0</td>
<td>6.0</td>
</tr>
</tbody>
</table>

Results of univariate and multivariate analysis of noninvasive and invasive variables correlating with subsequent death (Cox regression model) by chi-square analysis. Different variables are important in groups 1–4 with univariate analysis; age is the most important variable in group 1, angina-free exercise tolerance in group 2, and maximal cardiac output in groups 3 and 4. Maximal cardiac output is significantly correlated with subsequent death in all four groups. Except in group 2 the invasive variables improve the global chi-square obtained by use of the noninvasive variables.

*aChi square values of 3.84 correspond to p = .05, 6.63 to p = .01, and 10.83 to p = .001.

Vol. 68, No. 5, November 1983 983
ing system that can give a more precise picture of the
test of coronary artery disease in a given patient or
in groups of patients.

Despite the theoretical advantage of a more precise
classification with one of these scoring systems, the
simple original classification of patients into groups
with single-, double-, and triple-vessel disease has
been used in most of the major studies such as the
Veterans Administration study,8 the European Coro-

nary Surgery Study,24 and in the Coronary Artery Sur-
gery Study (CASS) registry.7

The evaluation of left ventricular function in our
study was subjective, i.e., it was done by visual in-
spection of the segmental wall motion in the right
anterior oblique projection. Our method is very similar
to the method used in the CASS registry.7 The data
from the CASS registry show that subjective evalua-
tion of left ventricular function from left ventricular
angiography predicts late survival as well as the ejection
fraction.

Other studies have suggested that the left ventricular
ejection fraction is the most important determinant of
survival in patients with coronary artery disease.5,24
However, ejection fraction cannot be determined in all
patients because of the frequent occurrence of prema-
ture ventricular contractions during left ventricular an-
giography. Hammermeister et al.5 and Vlietstra et al.24
had to exclude between 28% and 45% of their patients
from analysis because ejection fraction was not or
could not be determined. In the CASS registry, 30% of
patients with a left ventricular score had no ejection
fraction recorded.7 Therefore, grading of left ventricu-
lar function according to a scoring system based on
segmental wall motion appears to be a valid alternative
to the determination of ejection fraction. The 5 year
survival rates of our groups 1, 2, and 3 are similar to
those reported in the CASS registry for patients with
comparable left ventricular function; the 5 year survi-
al rates of groups 2 and 3 are also similar to those of
medically treated patients with double- and triple-ves-
sel disease in the European Coronary Surgery Study, in
which only patients with ejection fractions above 50% were randomized.24 Thus, the 5 year survival rate of
patients with good left ventricular function is related to
the number of vessels diseased and is similar in the
United States and in Europe.

Previous studies have correlated the results of exer-
cise testing with subsequent cardiac events or subse-
quently death in a normal population of patients in the
chronic phase of myocardial infarction and of patients
early after myocardial infarction.11,25,26 The results of exercise testing allow a classification of high-

risk subgroups in each category of individuals or
patients. The prediction of a future event is enhanced if

a normal exercise test becomes abnormal on repeat
examination.8 The correlation of the results of exercise
testing has been related to the fact that exercise tests
are more likely positive in patients with multivessel
disease or with severe left ventricular dysfunction,11
and these patients in turn are more likely to have a poor
prognosis.2

We excluded patients with severely impaired left
ventricular function as determined by angiography be-
cause these patients are known to have a poor pro-

gnosis. Thus, exercise testing was able to delineate
high- and low-risk subgroups of patients in whom
angiography revealed similar results. Noninvasive
exercise parameters appear particularly useful in the
group of patients with double-vessel disease and good
left ventricular function to separate those with a good
prognosis (5 year survival rate of 96%) from those with
a markedly reduced prognosis (5 year survival rate of
81%). The difference in survival rates between the
highest and lowest terciles in group 2 is similar to or
even greater than the difference in survival rates be-
tween patients with single- and triple-vessel disease. In
patients with triple-vessel disease, the prognosis for
patients with better exercise capacity, higher angina
threshold, or those achieving higher heart rates is
slightly but not significantly better than the prognosis
for patients in the lower terciles. Patients in group
4 with a higher exercise tolerance had a significantly
better prognosis than patients with a lower exercise
tolerance, but the differences that occur when the other
noninvasive exercise parameters are used are not sig-
nificant.

By use of the invasively obtained exercise param-
eters (maximal cardiac output and maximal pulmonary
capillary wedge pressure) a significant difference in
survival rates is evident in all four groups of patients
between those in the lowest and the highest tercile or
half of cardiac output. In patients in group 4 the maxi-
mal pulmonary capillary wedge pressure is of inde-
pendent prognostic importance in multivariate step-
wise regression analysis and probably reflects the
degree of left ventricular dysfunction during exercise.

The magnitude of the difference in survival rates
between those in the lowest and the highest tercile of
cardiac output increases with the extent of coronary
disease. The difference in survival rates between those
in the lowest and the highest tercile was significant
even in patients with single-vessel disease (group 1).
In patients in group 2, noninvasive parameters reached
a similar differentiation of high- and low-risk sub-

CIRCULATION
PATHOPHYSIOLOGY AND NATURAL HISTORY—CORONARY ARTERY DISEASE

groups. In patients in group 3 and 4 maximal cardiac output was able to identify patients with a markedly impaired prognosis. The difference in survival rates between the high- and low-risk groups was almost twice as large as the difference in survival rates between patients with single- and triple-vessel disease.

Thus exercise testing is not only a means to quantitate the limitation of exercise capacity, but in conjunction with the angiographic findings it provides additional prognostic information. The power of exercise testing to differentiate between high- and low-risk subgroups is similar to that of coronary angiography. Both tests, coronary angiography and exercise testing, provide complementary information, and exercise testing should not be considered redundant even if performed after coronary angiography.

We thank Monika Hofman for her assistance in preparation of the manuscript and Hans-Joachim Heinz for preparation of the figures.

References

15. AHA Committee report: A reporting system on patients evaluated for coronary artery disease. Circulation 51: 5, 1975
Exercise testing provides additional prognostic information in angiographically defined subgroups of patients with coronary artery disease.

H Gohlke, L Samek, P Betz and H Roskamm

Circulation. 1983;68:979-985
doi: 10.1161/01.CIR.68.5.979

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1983 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/68/5/979

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/