Post–Myocardial Infarction Exercise Testing

Non–Q Wave Versus Q Wave Correlation With Coronary Angiography and Long-term Prognosis

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Background. The presence or absence of baseline diagnostic Q waves has been believed to compromise the accuracy of standard exercise electrocardiography in identifying severe coronary artery disease (three-vessel and/or left main disease); therefore, a retrospective analysis was performed using a personal computer data base of exercise test responses and cardiac catheterization results to evaluate this premise, and follow-up was performed to observe how Q waves and/or severe coronary disease impacted on survival.

Methods and Results. Two hundred fifty-three male patients who had survived a myocardial infarction were studied. Patients on digitalis, those with left bundle branch block or left ventricular hypertrophy on their baseline electrocardiogram, those with previous revascularization procedures, and those with significant valvular or congenital heart disease were excluded. All patients performed either a low-level predischarge or a sign/symptom limited exercise test and underwent diagnostic coronary angiography within 32 days of each test (range, 0–90 days). Long-term follow-up on patients was performed for an average of 45 months (±17 months). Group NQMI comprised 103 post–myocardial infarction patients lacking Q waves at the time of exercise testing and group QMI comprised 150 patients who developed Q waves with their myocardial infarction. The cut points of ≥1 mm ($\chi^2=14.39, p<0.001$) and ≥2 mm ($\chi^2=26.11, p<0.001$) of exercise-induced ST segment depression were reliable markers of severe coronary disease in Q wave infarct survivors. This was also true for non–Q wave infarct survivors as ≥1 mm ($\chi^2=6.02, p=0.01$) and ≥2 mm ($\chi^2=4.37, p=0.04$) of ST segment depression were reliable markers of severe coronary disease. Receiver operating characteristic curve analysis revealed that exercise-induced ST segment depression had discriminating power for the identification of severe coronary artery disease in both the Q wave myocardial infarction patients (area=0.735, $z=4.47, p<0.001$) and the non–Q wave infarct patients (area=0.700, $z=3.20, p<0.001$). After 4.4 years of cumulative follow-up, patients with severe coronary disease had an infarct-free survival rate of 72% (95% CI, 50.0–86.0%), whereas those without severe disease had an 86% (95% CI, 76.5–91.5%) infarct-free survival rate (Cox $\chi^2=4.00, p=0.045$). Non–Q wave patients had an infarct-free survival rate of 81% (95% CI, 66.0–89.5%), whereas those with Q waves had an infarct-free survival rate of 85% (95% CI, 73.9–91.3%) (Cox $\chi^2=0.0005, p=NS$).

Conclusions. The presence or absence of diagnostic Q waves has no significant effect on the ability of the exercise electrocardiogram to identify severe coronary artery disease in survivors of myocardial infarction. Long-term infarct-free survival of patients with myocardial infarction is more related to the presence of severe coronary disease rather than if they suffered a non–Q wave or Q wave infarction. (Circulation 1991;84:2357–2365)

With the development and availability of aggressive cardiovascular revascularization techniques,1–4 one of the goals of post–myocardial infarction risk stratification is to identify which patients have extensive coronary disease because survivors with multivessel disease have an increased risk of early5 and late mortality6–9. Those recognized should then be referred for diagnostic coronary angiography10 so that those with appropriate anatomy may benefit from revascularization. Prior studies have suggested that patients with

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Q waves on their baseline electrocardiogram who have severe angiographic coronary disease may not be identified by post-myocardial infarction exercise testing.11–13 This could be due to exaggerated ST segment shifts associated with infarct-related intraventricular conduction defects (false positives)11 and/or to the reciprocal effect of ST segment elevation over Q waves (false negatives).12,13

This study was therefore undertaken to ascertain if the presence or absence of Q waves on the baseline electrocardiogram in the post–myocardial infarction patient affects the ability of exercise-induced ST segment depression to predict severe coronary artery disease (three-vessel and/or left main disease) and how Q waves and severity of coronary disease relate to prognosis.

Methods

Patient Selection

Patients were selected from a group of 3,047 who underwent routine clinical exercise testing from April 1984 to June 1989. Their data were entered into a personal computer data base (R:BASE, Micromin, Redman, Wash.) in a prospective fashion with the analysis made retrospectively. Of these, approximately 30% also underwent coronary angiography within 3 months of testing. After excluding women, patients on digitalis, those with left bundle branch block or criteria for left ventricular hypertrophy on their baseline electrocardiogram, those with previous revascularization procedures (coronary artery bypass or percutaneous transluminal coronary angioplasty), and those with significant valvular or congenital heart disease, 476 patients remained. These patients were then classified by clinical history or electrocardiographic evidence of prior myocardial infarction. The diagnosis of myocardial infarction was made if at least two of the following criteria were fulfilled: 1) chest pain pattern consistent with myocardial infarction; 2) evolutionary Q wave, R wave, or ST segment changes; and/or 3) a typical rise and fall pattern of CK-MB isoenzymes. At the time of exercise testing, Q waves were considered diagnostic if they occurred in two adjacent leads and were 40 msec in duration and 25% in amplitude of the following R wave. The electrocardiographic diagnosis of left ventricular hypertrophy was made using the criteria outlined by the point-score system of Romhilt and Estes.14 Three groups were formed in the following priority: one group comprised 223 patients who had no clinical or electrocardiographic evidence of prior myocardial infarction (NOMI), one group of 103 patients had survived a myocardial infarction without the formation of Q waves (NOMI), and the final group of 150 patients formed Q waves as a result of their myocardial infarction (QMI).

Exercise Testing

A standard exercise test was performed using a Mortara EliXR treadmill system and the Balke-Ware protocol. Blood pressure was measured noninvasively using manual sphygmomanometry at rest in the supine and standing positions every 2 minutes during exercise, immediately after exercise, and at 2 minutes and 5 minutes into recovery while in the supine position. A baseline standing 12-lead electrocardiogram was obtained before the onset of exercise. Leads II, V1, and V5 were monitored continuously during exercise, and a 12-lead electrocardiogram was obtained every 2 minutes during exercise and recovery. Sign/symptom–limited postdischarge maximal tests were performed at least 21 days after the index infarction and used standard criteria for stopping, including serious dysrhythmias, a drop in systolic blood pressure below rest, greater than 4 mm ST segment depression or elevation, severe angina pectoris, or central nervous system complaints. Low-level predischarge exercise tests were performed within 20 days of the index infarction and had the same end points noted for sign/symptom–limited tests but also included end points of the attainment of a heart rate of 130 beats per minute (110 if on a β-blocker), a Borg level of 15, or 5 METs, whichever came first. When the end point was reached, the treadmill was stopped abruptly and the patient was placed supine within 1 minute.

If patients performed both predischarge and postdischarge exercise tests, only the postdischarge test was considered because a greater stress was imposed. Most of the patients who performed only a low-level predischarge exercise test had a revascularization procedure, died, or did not return for a postdischarge test. Most of the patients who performed only a sign/symptom–limited postdischarge exercise test had a history of remote myocardial infarction or were hospitalized at another hospital for their acute myocardial infarction and were followed afterward at the Long Beach Veterans Affairs Medical Center.

The exercise electrocardiogram was considered abnormal if the patient developed ≥1 mm of horizontal or downsloping ST segment depression measured at the J-point using the PQ segment for the baseline even in patients with early repolarization. An additional 1 mm ST segment depression was required in patients with baseline ST segment depression. The occurrence of typical angina pectoris during the test was determined by a cardiologist or a cardiology fellow who supervised the test.

Coronary Angiography

A significant coronary artery stenosis was defined as ≥75% narrowing of the diameter of one of the major epicardial coronary arteries or its branches or ≥50% narrowing of the left main coronary artery, measured visually in at least two angiographic projections. Left ventricular volumes and ejection fractions were computed from the single-plane contrast ventriculogram in the 30° right anterior oblique projection using the area-length method of Dodge et al.15 Angiography was performed within an average of 32 days (range, 0–90 days) of the exercise test and
was not routinely performed on all myocardial infarction survivors (i.e., only those patients who were believed to be at higher risk clinically were studied).

Follow-up

All patients were followed up by clinic visit, telephone interview, and/or medical chart review. Overall follow-up was 99% complete (only two lost to follow-up). The average length of follow-up was 45 months (±17 months).

Statistical Analysis

Univariate statistical analysis for categorical variables was performed using the \( \chi^2 \) test, and the quantitative variables were analyzed using the Student’s \( t \) test. Differences were considered significant at a probability value of 0.05 or less. Receiver operating characteristic curves were generated with the TRUE EPISTAT software (version 4.0, TRUE EPISTAT Services, Richardson, Tex.), and the areas of receiver operating characteristic curves were compared with the area of 0.50 (area under a straight line that represents no discrimination) using the \( z \) statistic.\(^{16-18} \) Confidence intervals were calculated according to Gardner and Altman.\(^{19} \)

Kaplan-Meier estimates were used to generate infarct-free survival curves from the day of exercise testing\(^{20} \) with the use of EGRET software (version 0.26.6, Statistics and Epidemiology Research Corporation, Seattle, Wash.). Infarct-free survival was defined as those patients who had not expired or suffered a subsequent myocardial infarction. All patients were considered to be medically treated at the initiation of follow-up. The follow-up of 71 patients (28%) undergoing percutaneous transluminal coronary angioplasty (26 patients) or coronary artery bypass grafting (45 patients) was included up to the date of the intervention; these patients were then censored from further survival analysis at that point. Statistical comparisons between survival curves were performed using Cox regression analysis and the log-rank statistic.

Results

Table 1 gives the clinical, exercise, and angiographic results of the three groups. Probability values are given only for differences between the NQMI and QMI groups. The NQMI group had a higher prevalence of no significant coronary artery disease than the QMI group. As expected, the QMI group had a higher left ventricular end-diastolic volume index and a lower left ventricular ejection fraction than the NQMI group. There were no other statistically significant differences between the two types of infarct groups.

Table 2 is a breakdown and comparison of \( \beta \)-blocker use and exercise test responses between patients with and without severe coronary disease in each subset of patients. There were no statistically significant differences in exercise test response between any groups nor was there any difference in percentage of patients who performed a low-level predischarge test or in the use of \( \beta \)-blockers. Angina and exercise-induced ST segment depression occurred more frequently in the group without a prior myocardial infarction who had severe coronary disease. Angina was not discriminatory for severe coronary disease in both the Q wave and non-Q wave myocardial infarction survivors. However, 1 or 2 mm of additional exercise-induced ST depression were statistically significant discriminators for the diagnosis of severe coronary disease in non-Q wave and Q wave infarction survivors.

Table 3 lists the sensitivities, specificities, and positive and negative predictive values for 1 or 2 mm or greater of additional exercise-induced ST segment depression in each of the groups studied for the diagnosis of severe coronary artery disease (three-vessel and/or left main disease). Exercise-induced ST segment depression of ≥1 mm (\( \chi^2=6.02, p=0.01 \)) and ≥2 mm (\( \chi^2=4.37, p=0.04 \)) were statistically significant markers for severe coronary disease in survivors of non-Q wave infarction. This was also true for survivors of Q wave infarctions: ≥1 mm (\( \chi^2=14.39, p<0.001 \)) and ≥2 mm (\( \chi^2=26.11, p<0.001 \)). These cut points, of course, were also statistically significant markers for severe coronary disease in patients without a prior myocardial infarction: ≥1 mm (\( \chi^2=17.08, p<0.001 \)) and ≥2 mm (\( \chi^2=29.93, p<0.001 \)) of exercise-induced ST segment depression.

Receiver Operating Characteristic Curve Analysis

Figure 1 is a comparison of receiver operating characteristic curves of exercise-induced ST segment depression for the diagnosis of severe coronary artery disease in survivors of a myocardial infarction with (QMI) or without (NQMI) Q waves on their baseline electrocardiogram; the curve for patients without prior myocardial infarction (NOMI) is included for comparison. Both curves had a statistically significant greater area than 0.50 (area under a straight line that represents no discrimination): QMI curve (area=0.735, \( z=4.47, p<0.001 \)) and NQMI curve (area=0.700, \( z=3.20, p<0.001 \)). The NOMI curve had an area of 0.763 (\( z=6.45, p<0.001 \)).

Anterior Q Waves

The specific effect of anterior Q waves on the diagnostic accuracy of exercise testing was also evaluated. There were 54 patients in the study group with anterior Q waves that comprised 36% (54 of 150) of the Q wave patients. The exercise test had a sensitivity of 56% (five of nine), a specificity of 69% (31 of 45), and a negative predictive value of 89% (31 of 35) for the diagnosis of severe coronary disease. Because there were only nine patients with three-vessel and/or left main coronary disease who also concomitantly had anterior Q waves, we were unable to perform a receiver operating characteristic curve analysis in this group; such a small number of patients would make the analysis unreliable. However, we could generate an analysis for the identification of
multivessel coronary disease as there were 28 patients who had multivessel disease and concomitant anterior Q waves. The area under the receiver operating characteristic curve for the identification of multivessel coronary disease during exercise testing in patients with anterior Q waves was 0.686 ($z=4.365$, $p<0.001$). This indicates that exercise-induced ST segment depression is a reliable marker for multivessel disease in the patient who has survived an anterior Q wave myocardial infarction.

**Long-term Prognosis**

During follow-up, 19 patients suffered cardiovascular death, 21 patients had nonfatal myocardial infarctions, one patient developed congestive heart failure, 45 patients proceeded to coronary artery bypass grafting, and 26 patients underwent percutaneous transluminal coronary angioplasty. No patients were counted twice, and death took precedence if a patient suffered two different events. One hundred thirty-nine patients did not suffer a cardiac event and two were lost to follow-up.

The infarction-free survival curve for Q wave and non-Q wave infarction patients is shown in Figure 2. At 4.4 years of cumulative follow-up, non-Q wave patients had an infarction-free survival rate of 81% (95% CI, 66.0–89.5%), whereas those with Q waves had a rate of 85% (95% CI, 73.9–91.3%) of infarct-free survival, which was not a statistically significant difference (Cox $\chi^2=0.983$). In contrast, the prognosis of myocardial infarction survivors with severe coronary disease (three-vessel and/or left main) was significantly worse than those without severe coronary disease as shown in Figure 3; the infarction-free survival rate of patients with severe coronary disease was only 72% (95% CI, 50.0–86.0%), whereas those without severe disease had an infarction-free survival rate of 86% (95% CI, 76.5–91.5%) (Cox $\chi^2=4.00$, $p=0.045$). The Cox hazard risk ratio for sustaining either another infarct or dying was 2.29 if a patient had severe coronary disease compared with patients without severe disease ($p=0.052$).

**Discussion**

**Major Finding of Present Study**

The presence or absence of Q waves on the baseline electrocardiogram in survivors of a myocardial infarction determine long-term prognosis.
Dial infarction had no significant effect on the ability of exercise-induced ST segment depression during standard exercise testing to identify severe coronary artery disease. Long-term infarct-free survival was related more to the presence of severe coronary disease rather than if the patient suffered a non-Q wave or Q wave infarction.

**Reasons and Needs for Study**

It has been shown that survivors of a myocardial infarction with multivessel coronary artery disease have an increased risk of early as well as late mortality. Muller et al showed that in the era of reperfusion therapy for myocardial infarction, the number of diseased vessels was the strongest independent predictor of in-hospital mortality. In a prospective study, Schulman and colleagues showed that survivors of a myocardial infarction with three-vessel coronary disease had only a 38% cardiac event-free survival over 5 years; cardiac events were defined as death, recurrent myocardial infarction, or coronary bypass surgery. On the other hand, single-vessel coronary artery disease after myocardial infarction is generally associated with a better prognosis. These results are supportive of the present study, in which it was found that the presence of severe coronary disease correlated with long-term prognosis. Obviously, a reasonably accurate noninvasive test that would help to identify severe coronary disease in survivors of myocardial infarction, for triage to diagnostic coronary angiography, would be quite useful. This would be a more cost-effective

**TABLE 2. Clinical and Exercise Characteristics of Study Groups Divided by Presence or Absence of Severe Coronary Disease**

<table>
<thead>
<tr>
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<th>NOMI</th>
<th>NQMI</th>
<th>QMI</th>
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<tbody>
<tr>
<td>N3VD/3VD/LM</td>
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<tr>
<td>(n=184)</td>
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<tr>
<td>NQVD/LM</td>
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<td>(n=39)</td>
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<tr>
<td>p</td>
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<tr>
<td>β-Blocker</td>
<td>39 (21%)</td>
<td>14 (36%)</td>
<td>0.07</td>
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<tr>
<td>Exercise response</td>
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<tr>
<td>No. with low level test</td>
<td>20 (24%)</td>
<td>8 (38%)</td>
<td>NS</td>
</tr>
<tr>
<td>No. with maximal test</td>
<td>62 (76%)</td>
<td>13 (62%)</td>
<td>NS</td>
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<tr>
<td>Avg maximal HR (bpm)</td>
<td>129±22</td>
<td>124±18</td>
<td>NS</td>
</tr>
<tr>
<td>Avg maximal SBP (mm Hg)</td>
<td>171±29</td>
<td>160±27</td>
<td>NS</td>
</tr>
<tr>
<td>Avg METs</td>
<td>7.2±3.0</td>
<td>6.0±2.3</td>
<td>NS</td>
</tr>
<tr>
<td>No. with angina during test</td>
<td>28 (37%)</td>
<td>23 (59%)</td>
<td>0.01</td>
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<tr>
<td>No. with ≥1 mm additional ST depression</td>
<td>84 (46%)</td>
<td>32 (82%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>No. with ≥2 mm additional ST depression</td>
<td>48 (26%)</td>
<td>28 (72%)</td>
<td>&lt;0.001</td>
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<tr>
<td>N3VD/3VD/LM</td>
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<td>(n=82)</td>
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<tr>
<td>NQVD/LM</td>
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<td>(n=21)</td>
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<td>Exercise ECG performance using criterion of additional ≥1 mm ST segment depression</td>
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<tr>
<td>Sensitivity (%)</td>
<td>82</td>
<td>71</td>
<td>76</td>
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<tr>
<td>Specificity (%)</td>
<td>54</td>
<td>59</td>
<td>62</td>
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<tr>
<td>Positive predictive value/posttest probability of disease (%)</td>
<td>28</td>
<td>31</td>
<td>36</td>
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<tr>
<td>Negative predictive value (%)</td>
<td>93</td>
<td>89</td>
<td>90</td>
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<tr>
<td>Exercise ECG performance using criterion of additional ≥2 mm ST segment depression</td>
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<tr>
<td>Sensitivity (%)</td>
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<tr>
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<td>74</td>
<td>76</td>
<td>87</td>
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<tr>
<td>Positive predictive value/posttest probability of disease (%)</td>
<td>37</td>
<td>33</td>
<td>55</td>
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<tr>
<td>Negative predictive value (%)</td>
<td>93</td>
<td>85</td>
<td>87</td>
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NOMI, group without prior myocardial infarction; NQMI, non-Q wave myocardial infarction patients undergoing post-MI exercise testing; QMI, Q wave myocardial infarction patients undergoing post-MI exercise testing; ECG, electrocardiography.
strategy than routine coronary angiography for all postinfarction survivors.23

However, there have been conflicting studies on the use of standard exercise testing in survivors of a

myocardial infarction. One study of exercise testing that was correlated with coronary angiography found an abnormal ST segment response, with or without concurrent angina, to predict multivessel, three-vessel, and/or left main disease in post–myocardial infarction patients.24 In contrast, though, Ahnve and associates11 found that in the presence of anterior Q waves, ST segment changes could not distinguish between patients with and without ischemia, with ischemia defined as a reversible perfusion defect on 201Tl perfusion scanning. Furthermore, Ellestad and coworkers12,13 suggested that patients with transmural infarction can have an electrocardiographic cancellation of exercise-induced ST segment depression by the reciprocal ST segment elevation over Q waves, producing a false negative response. Therefore, the present study was performed to ascertain if the presence of Q waves compromised the ability of standard exercise testing to identify severe coronary disease.

Comparison With Other Studies

Exercise Testing After Myocardial Infarction. Griffith and associates25 performed a prospective study of 123 patients, correlating predischarge exercise test results with coronary arteriography. They found that 50% (36 of 72) of their patients with multivessel disease did not have exercise-induced ST segment depression with exercise, giving the exercise test an overall sensitivity of only 50%. However, in comparison, the present study had a higher sensitivity at 61% (78 of 128 patients) for the diagnosis of multivessel disease. Despite the retrospective nature of the present study, the prevalence of multivessel coronary disease was similar at 51% (128 of 253 patients) to the prevalence in Griffith’s study at 59% (72 of 123 patients). Differences between the studies can be found in that Griffith’s study did not exclude patients on digitals or those with left ventricular hypertrophy, which can decrease both the sensitivity and specificity.
of exercise testing; all exercise tests in Griffith's study were low-level predischarge tests, whereas only 29% of the present study's tests were low-level, and it has been shown that symptom-limited exercise tests after infarction precipitate more prognostic end points such as angina or ST segment depression than low-level tests; only 75% of their patients with negative exercise tests underwent coronary angiography; and finally, the present study encompasses over twice as many patients (253 compared with 123). Castellanet et al studied 43 patients with prior anteroseptal Q wave infarctions and found the exercise test to have a sensitivity of 52%, a specificity of 90%, and a negative predictive value of only 36% for identifying additional ischemia outside the infarct-related artery. The present study had a much higher negative predictive value of 89% for the identification of three-vessel and/or left main disease. Differences between the studies that may account for the disparate results are that Castellanet's study used only three electrocardiographic leads for monitoring the ST segment in 82% of their patients and only one lead in the remaining 18% of patients, whereas the present study used 12 leads, and multiple-lead systems have been shown to improve the sensitivity of exercise testing, and we excluded upsloping ST segment elevation as an abnormal response because the consideration of slope has been shown to have a significant impact on the accuracy of exercise testing.

There have been numerous studies of standard exercise testing and coronary angiography in the setting of non-Q wave, Q wave, and all combined myocardial infarctions. In a composite review of five previous studies, plus the present study, a total of 220 patients with non-Q wave myocardial infarction were studied, and standard exercise testing had a positive predictive value of 50% (54 of 108 patients) for the identification of either multivessel, three-vessel, and/or left main coronary disease. In a review of 13 studies (including the present study) evaluating 1,094 Q wave myocardial infarction survivors, exercise testing compared favorably with a positive predictive value of 70% (335 of 481 patients). For comparison, 15 studies totaling 1,330 patients (including the present study) used exercise testing in both types of myocardial infarction survivors (non-Q wave and Q wave) revealed a positive predictive value of 71% (437 of 618 patients). These results agree with the present study in that Q waves do not significantly compromise the predictive value of exercise testing in survivors of myocardial infarction.

Comparison Between Q Wave and Non-Q Wave Myocardial Infarctions

Gibson performed a review of previous clinical studies of non-Q wave infarctions compared with Q wave infarctions and found that the extent of underlying atherosclerotic coronary disease and long-term mortality were not significantly different in the two groups. Our results are congruent with these findings and suggest that the early survival advantage of non-Q wave infarct survivors is lost over time and that perhaps we should concentrate less on the distinction between Q wave and non-Q wave infarctions and more on the identification of which patients have severe underlying coronary disease.

Limitations of the Study

Retrospective analyses permit only the generation of hypotheses, and proving them can only be done with prospective studies and/or comparison and validation with other data bases. The preferential selection of patients based on an abnormal exercise test response for referral to coronary angiography to verify coronary disease ("workup bias") may result in an apparent increase in sensitivity and decreased specificity in this study. The present study also did not compare residual left ventricular function (i.e., left ventricular ejection fraction) with severe coronary disease as to which was the stronger predictor of adverse cardiovascular events. This was not done because the point of the study was to correlate exercise test results with the identification of severe coronary disease because severe coronary disease is related to long-term mortality. Finally, the exclusion of women from this study confines its conclusions to men.

Conclusions

The presence or absence of Q waves on the baseline electrocardiogram in men with a recent myocardial infarction does not alter the overall diagnostic accuracy of standard exercise testing for the diagnosis of severe coronary artery disease. Long-term prognosis is related to the presence of severe coronary disease irrespective of whether the patient suffers a non-Q wave or Q wave myocardial infarction. Post-myocardial infarction exercise testing continues to be an integral component of a cost-effective strategy to identify patients with severe coronary disease.

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References


KEY WORDS • exercise test • myocardial infarction • coronary angiography
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