Efficacy of exercise training in patients with coronary artery disease who are taking propranolol

LAWRENCE J. LASLETT, M.D., LINDA PAUMER, M.A., PATTI SCOTT-BAIER, R.N.,
AND EZRA A. AMSTERDAM, M.D.

ABSTRACT  The effects of β-adrenergic blockade on the efficacy of exercise training in patients with coronary artery disease were assessed in a community-based cardiac rehabilitation program. Twenty-five patients took no β-adrenergic–blocking agent and 17 patients took a constant dose of propranolol during the 3 month study period. Individual exercise prescriptions consisted of an intensity of 70% of maximal workload monitored by heart rate, performed 20 min each session, three sessions per week. Both groups improved in maximal exercise capacity: from $8.7 \pm 1.9$ (mean ± SD) to $9.7 \pm 2.1$ mets ($p < .01$) in those not taking propranolol and from $6.6 \pm 1.5$ to $7.7 \pm 1.8$ mets ($p < .01$) in those taking the drug. At a workload of 70% of maximal achieved at pretraining testing, heart rate decreased with training from $123 \pm 19$ to $113 \pm 17$ beats/min ($p < .01$) in those not taking propranolol and from $97 \pm 14$ to $92 \pm 12$ beats/min ($p < .05$) in those taking the drug. At a workload of 85% of pretraining maximum, heart rate similarly was lowered with training from $138 \pm 17$ to $126 \pm 17$ beats/min ($p < .01$) in those not taking a β-blocker and from $107 \pm 13$ to $102 \pm 13$ beats/min ($p < .02$) in those taking propranolol. Thus patients with coronary disease who take propranolol have the same potential to benefit from physical training as patients who do not take β-blockers, and exercise does not need to be modified because of the drug. *Circulation* 68, No. 5, 1029–1034, 1983.

AEROBIC exercise training is widely used in the rehabilitation of patients with coronary heart disease. This therapy is prescribed in formal supervised programs and is part of counseling for informal exercise training of selected patients. The intensity of exercise undertaken for cardiac rehabilitation is usually monitored by heart rate response and is prescribed at the submaximal level produced by a workload of approximately 70% of an individual’s maximum. Treatment of many patients with coronary heart disease includes β-adrenergic antagonists, which characteristically reduce both maximal and submaximal heart rates. Little attention has been directed to the utility of an exercise prescription based on heart rate limited by β-adrenergic blockade, and the sparse data available are conflicting. Especially lacking is information regarding the effect of training on submaximal exercise parameters in patients taking the β-adrenergic blocker propranolol compared with the results in patients not taking this drug.

Methods

All patients admitted to the community-based University of California–Davis Medical Center cardiac rehabilitation program were considered for inclusion in this study. Patients were excluded if they did not complete 3 full months participation or, if taking propranolol, their dose of the drug varied during the study period, including initial and final testing. No patients took other β-blockers. Of the 65 patients entering the program, nine were excluded because they changed from taking propranolol to not taking it or from not taking the drug to taking it, or because they were taking another β-blocker; four were excluded because follow-up data could not be obtained on time, and 10 dropped from the program on their own volition.

Forty-two patients comprised the study group (table 1). Twenty-five of the patients (23 men, two women; mean age 57 years) took no propranolol and 17 (14 men, three women; mean age 58 years) took a constant dose of the drug during 3 months of exercise training. The mean dose of propranolol among those receiving it was $91 \pm 69$ mg/day (mean ± SD); the range was 20 to 240 mg/day. All patients qualified for participation in the rehabilitation program because of the presence of a previous myocardial infarction, recent coronary artery bypass surgery, angiographically documented coronary artery disease, or classic history of angina. In patients who had had myocardial infarction or coronary bypass surgery, the interval from these events into the program was at least 12 weeks.

Of the 23 patients excluded from analysis, 10 took propranolol and 13 did not at entry into the program. Of those not taking propranolol, all were men (mean age 51 years, range 30 to 64) and nine had suffered a myocardial infarction, four had undergone coronary bypass surgery, and six were experiencing angina. Among those using propranolol, all but one were men (mean age...
age 53 years, range 38 to 71), nine had experienced a myocardial infarction, four had undergone coronary bypass surgery, and two had angina.

Treadmill assessment made at entry into the program provided data on initial functional capacity and heart rate and blood pressure responses to exercise. A modified Balke protocol was used, which had been altered to allow more flexibility in accommodating widely varying patient exercise capacities than permitted by published standardized protocols. Initial speed was individualized between 1.7 and 2.6 mph; initial slope was 0 degrees. These parameters were increased every 2 min by amounts depending on individual response. Functional capacity was taken at the highest symptom-limited workload attained and was expressed in terms of estimated oxygen consumption. For convenience, these values were converted to mets (1 met = 3.5 cc/kg/min).

Based on initial treadmill testing, an individual exercise prescription was designed for each patient. This prescription included a target heart rate equal to that produced by a workload approximately 70% of maximal, which was to be maintained for at least 20 min each exercise session. Medically supervised training sessions were performed three times weekly. Exercise included walking, jogging, or running as appropriate. After 3 months of training, patients were reassessed by treadmill testing. The effect of training was evaluated by alteration in maximal functional capacity, and in heart rate and double product (heart rate \times\text{ systolic blood pressure}) at submaximal workload during this second test relative to the first.

Results were analyzed separately for each group. Data are presented as mean ± SD. Student’s t test for paired data was used to assess the statistical significance of differences between group means of pretraining and posttraining functional capacity and of heart rate and double product at maximal workload and workloads corresponding to 70% and 85% of initial maximal values. Student’s t test for unpaired data was used to analyze the difference of the independent means of the two groups for percent improvement in functional capacity. The significance of differences in noncontinuous data was analyzed by the chi-square method. Differences were considered significant at p < .05.

Results

Patient characteristics. The group of patients taking propranolol was not statistically different from the group not taking a \( \beta \)-adrenergic blocking drug in age, sex distribution, percent exercise sessions attended, and proportions with angina, prior myocardial infarction, and coronary bypass surgery (table 1). Those excluded from analysis were similar to those analyzed, although they were slightly younger, had a higher incidence of angina, and had a higher incidence of myocardial infarction among those taking propranolol. The proportions of patients taking propranolol within the excluded and analyzed populations were similar.

Effective \( \beta \)-adrenergic blockade was reflected by a significantly (p < .01) lower mean entry maximal heart rate in patients taking propranolol (118 ± 19 beats/min) compared with those not taking this drug (151 ± 19 beats/min) (table 2).

Functional capacity. At entry, patients taking propranolol had a mean functional capacity of 6.6 ± 1.5 mets, which increased significantly (p < .01) with training to 7.7 ± 1.8 mets. In patients not taking this drug, training was associated with a significant (p < .01) increase in functional capacity from 8.7 ± 1.9 to 9.7 ± 2.1 mets (figure 1). There was no significant difference in the relative improvement in mean functional capacity between the two groups: 19 ± 26% in those taking propranolol and 13 ± 12% in those not taking propranolol. Absolute improvement was also not statistically different between the two groups; mean improvement was 1.1 mets among those taking propranolol and 1 mets among those not taking propranolol (table 2). Of the 17 patients taking propranolol, 13 (76%) experienced an increase in functional capacity by at least 0.5 met, compared with 21 of 25 patients (84%) not taking propranolol (p = NS). When only those patients taking at least 80 mg/day propranolol are considered, the increase in functional capacity is significant, from 6.4 ± 1.3 to 7.4 ± 1.8 mets (p < .05).

Maximal heart rate and double product. There was no significant change in heart rate or double product at maximal workload with training in either group (table 2). Among those not taking propranolol, the maximal heart rate was 151 ± 19 beats/min before training and 152 ± 20 beats/min after training; the maximal double products were 264 ± 49 \times 10^2 and 271 ± 59 \times 10^2 beats/min/mm Hg before and after training, respectively. Those taking propranolol had a maximal heart rate of 118 ± 19 beats/min before training and 122 ± 19 beats/min after training. Their pretraining and posttraining double products were 200 ± 54 \times 10^2 and 216 ± 57 \times 10^2 beats/min/mm Hg, respectively.

Submaximal heart rate and double product. Among those not taking a \( \beta \)-blocker, training resulted in significant reduction (p < .01) in submaximal heart rate (figure 2) and double product (table 2). The mean

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\(\text{MI} = \text{myocardial infarction}; \text{CABG} = \text{coronary artery bypass graft surgery.}\)

\(^a\)No statistically significant difference between groups for any characteristic listed.
Alterations in pretraining and posttraining heart rate and double product at a workload of 70% of entry-test maximum were 123 ± 19 beats/min and 196 ± 46 × 10² beats/min/mm Hg, respectively. After training, these values at the same absolute workload were reduced to 113 ± 17 beats/min and 172 ± 4 × 10² beats/min/mm Hg, respectively. The mean pretraining heart rate and double product at a workload of 85% of entry-test maximum declined from 138 ± 17 beats/min and 223 ± 46 × 10² beats/min/mm Hg, respectively, to 126 ± 17 beats/min and 204 ± 45 × 10² beats/min/mm Hg, respectively.

In the group taking propranolol there was also a significant reduction in submaximal heart rate with training (figure 2, table 2). At a workload of 70% of entry-test maximum, mean heart rate of 97 ± 14 beats/min at program entry decreased to 92 ± 12 beats/min after training (p < .05). Similarly, at a workload of 85% of entry-test maximum, mean heart rate fell from 107 ± 13 beats/min before training to 102 ± 13 beats/min after training (p < .02). Of the 17 patients taking propranolol, 13 (76%) had a reduction in heart rate at this workload, compared with 22 of 25 patients (88%) not taking propranolol (p = NS). Reductions in double product produced at 70% and 85% of pretraining maximal workload also occurred in the group using propranolol. Although these reductions were similar in relative magnitude to the reductions achieved in the group not taking the drug, they were not statistically significant (table 2).

Ischemic evidence during exercise. Among the 17 patients taking propranolol, 12 had angina or ischemic ST segment depression at initial exercise testing. After training, these changes occurred at a lower heart rate in five, at a higher heart rate in three, and were absent in four. Among the 25 patients not taking propranolol, angina or ischemic ST segment depression was present in two at initial testing and four at final testing. In these cases, the heart rate at occurrence was lower after training.

Discussion

Formal programs of exercise training for patients with ischemic heart disease were begun in this country during the 1960s and have markedly increased in popularity and application during this past decade. These cardiac rehabilitation programs have clearly been shown to improve maximal functional capacity and lower cardiac work (as estimated by heart rate or double product) associated with submaximal workloads in patients taking propranolol or not taking propranolol.

![Functional Capacity (Mets)](image-url)

**Figure 1.** Effect of exercise training on maximal functional capacity in coronary artery disease patients. One group took no β-adrenergic blocker and the other group took a constant dose of propranolol during training.
patients with angina, previous myocardial infarction, or prior coronary artery bypass surgery. The safety of these supervised programs has been demonstrated.

In cardiac rehabilitation programs, each patient is given an individual prescription for exercise based on his or her pretraining work capacity as assessed by graded treadmill testing. A training effect can usually be expected from performing aerobic exercise (e.g., walking, jogging, or bicycling) three times per week for 20 min per session at an intensity of 70% of maximal capacity. Since a linear relationship exists between heart rate and workload at submaximal levels, the training intensity is often prescribed for convenience at approximately 75% of maximal heart rate or at the heart rate produced by approximately 70% of maximal workload.

With the widespread use of the β-adrenergic blocking agent propranolol by cardiac patients who were candidates for cardiac rehabilitation, uncertainty arose as to whether an exercise prescription based on a maximal heart rate that had been reduced by this drug would be effective, or whether the prescription should be based on the heart rate that would exist (known or predicted) in the absence of propranolol. Studies of this question are sparse and conflicting. Hossack et al. reported only minor changes in the linear relationship between submaximal heart rate and workload, but they did not evaluate the efficacy of training with propranolol-limited heart rates. Obma et al. found that propranolol-treated angina patients did have increased maximal exercise capacity after training at a "level equivalent to 65% to 80% of angina threshold," but whether this level was in terms of workload or heart rate and how it related to maximal heart rate were not defined. Malmborg et al. found no statistically significant improvement in exercise capacity from training in patients taking pindolol. This lack of benefit may have been due to a twice weekly rather than thrice weekly training program. In a recent report, Pratt et al. did show a significant improvement in maximal exercise capacity from training of coronary disease patients taking propranolol. Another current study by Sable et al. failed to demonstrate improvement in exercise capacity with training in subjects taking propranolol, but they evaluated only healthy young volunteers. None of these studies evaluated the effect of training on heart rate response to submaximal exercise in patients taking propranolol. This unaddressed issue is important, since most activity of coronary patients is at submaximal levels and reduction in the cardiac work needed to accomplish submaximal activity should be functionally and symptomatically beneficial.

Our study demonstrates that exercise prescriptions based on propranolol-limited maximal heart rates in coronary disease patients have similar efficacy to exercise prescriptions for patients not taking propranolol. The improvements in maximal exercise capacity were statistically significant and there was no significant difference in the changes in the two groups in either relative or absolute terms. Additionally, we demonstrate that comparable reductions in heart rate produced by submaximal workloads occurred after training in patients taking propranolol and in those not using the drug. That these average improvements of the group taking propranolol reflected generalized individual improvement is demonstrated by the fact that more than three-fourths of patients in both groups demonstrated functional capacity improvement and lowered submaximal heart rate, the groups not differing significantly in this respect. To evaluate whether im-

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**FIGURE 2.** Effect of exercise training on heart rate of coronary artery disease patients at maximal and submaximal exercise levels. One group took no β-adrenergic blocker and the other group took a constant dose of propranolol during training. n.s. = not statistically significant.
provements in the propranolol group were favorably weighted by the patients on low doses of the drug that perhaps were not physiologically effective, the 11 who were taking at least 80 mg/day were evaluated separately. The maximum exercise capacity and submaximal heart rate were also improved significantly in this group. Thus we have shown that patients with coronary disease may expect to achieve the same beneficial training effects at both maximal and submaximal workloads, whether or not they are taking propranolol.

An efficacious exercise prescription may therefore be based on the same criteria for both groups of patients.

The double product associated with workloads of 70% and 85% of pretraining maximal capacity were similarly lowered by training. In the group not taking propranolol, this reduction was statistically significant. In the group taking propranolol, statistical significance was not achieved. The lack of statistical significance in reduction of double product in the latter group may be related to the smaller number of patients and the imprecision of indirect measurement of the blood pressure component of double product during exercise. On the other hand, there may be a real difference in the double product response to training between patients taking and those not taking propranolol due to attenuation by this drug of the expected training-induced reduction in blood pressure response to exercise. Pratt et al.4 did find, for instance, that propranolol reduced peak heart rate response to exercise both before and after training but did not reduce peak systolic blood pressure response. This same lack in peak blood pressure reduction may likewise pertain to submaximal blood pressure response. To our knowledge, this important question of the effect of propranolol on submaximal blood pressure response to training has never been directly investigated. Further studies involving larger numbers of patients are needed to clarify this point.

The group not taking propranolol had little change in mean maximum heart rate after training, which is usually observed. Those taking propranolol demonstrated the same finding, although the maximum heart rates were significantly lower. We speculate that a constant dose of this drug exerts a relatively uniform influence on sinus node depolarization frequency and the adrenergic influence of maximal exercise is also uniform throughout the training period.

It has been shown that patients recovering from a myocardial infarction experience spontaneous improvement in functional capacity during the first 11 weeks even if not trained.15 Such spontaneous improvement, however, would not be expected in our postinfarction patients, since all infarctions occurred more than 12 weeks before training began.

Among those patients taking propranolol, training was not associated with any consistent improvement or deterioration in the heart rate at which evidence of exercise-induced ischemia occurred. The number of patients with ischemic manifestations in the group not taking propranolol was too small to be reliably analyzed. The fact that relatively few patients in this latter group had exercise-induced ischemia is of interest and probably consistent with their being more stable than the former group, hence often not requiring medical therapy such as propranolol.

No attempt was made in this study to evaluate any possible effect that other interventions, such as other prescribed drugs, may have had on exercise capacity or on indicators of cardiac work, because all patients were under the care of other physicians not related to the exercise training program and standardization of their nonexercise care was not feasible. It is also possible that clinical characteristics of the two groups may have differed in ways not described in table 1, so that being placed on propranolol was a marker of other factors influencing likelihood of training success. Such a lack of control of multiple treatment and patient factors, however, is typical of community-based cardiac rehabilitation programs and this study’s results are applicable to patients presenting to most existing programs.

We conclude that treatment by β-adrenergic blockade of a patient with coronary disease who is a candidate for exercise training does not limit the expectation of improvements that patient should experience from training. Additionally, the intensity of the exercise prescribed should be based on an appropriate proportion of maximal workload, regardless of whether the associated heart rate is limited by propranolol therapy.

References


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