Results of a Multicenter Randomized Clinical Trial of Exercise and Long-Term Survival in Myocardial Infarction Patients

The National Exercise and Heart Disease Project (NEHDP)

Joan Dorn, PhD; John Naughton, MD; Dai Imamura, MA; Maurizio Trevisan, MD; for the NEHDP Project Staff

Background—This study examined whether a supervised exercise program improved 19-year survival in 30- to 64-year-old male myocardial infarction patients.

Methods and Results—The men (n=651) were participants in the National Exercise and Heart Disease Project, a 3-year multicenter randomized clinical trial conducted in the United States (1976–1979). The treatment group (n=315) exercised for 8 weeks in a laboratory. Thereafter, they jogged, cycled, or swam in a gymnasium/pool setting guided by an individualized target heart rate. Participants in the control group (n=319) were to maintain normal routines but not participate in any regular exercise program. Participants were followed up until their death or December 31, 1995. Cox proportional hazards analysis revealed the all-cause mortality risk estimates (95% CIs) in the exercise group compared with controls to be 0.69 (0.39 to 1.25) after an average follow-up of 3 years, 0.84 (0.55 to 1.28) after 5 years, 0.95 (0.71 to 1.29) after 10 years, 1.02 (0.79 to 1.32) after 15 years, and 1.09 (0.87 to 1.36) after 19 years. Cardiovascular disease (CVD) mortality risk estimates (95% CI) for the same follow-up periods were 0.73 (0.37 to 1.43), 0.98 (0.60 to 1.61), 1.21 (0.79 to 1.60), 1.14 (0.84 to 1.54), and 1.16 (0.88 to 1.52). However, each 1-MET increase in work capacity from baseline to the end of the original trial resulted in consistent reductions in all-cause and CVD mortality risk at each follow-up period, regardless of initial work-capacity level.

Conclusions—These findings indicate exercise-program participation resulted in nonsignificantly reduced mortality risks early in the follow-up period. Benefits diminished as time since participation increased, which suggests that the protective mechanisms associated with the program may be short term. Contamination between groups over time could also explain the diminished effects, because increased work capacity provided survival benefits up to 19 years. **(*Circulation*. 1999;100:1764-1769.)**

Key Words: exercise ■ survival ■ myocardial infarction

Each year, more than 1 million Americans will experience a coronary event.[1] For some, this will be the first event; for others, a repeat attack. There has been a decline in coronary heart disease (CHD) mortality rates in recent years.[2] This fact, coupled with aging of the population, has resulted in nearly 14 million individuals living with a history of myocardial infarction (MI) or angina pectoris.[1] Exercise programs are often recommended as part of therapy after MI. The goals of these programs are to return patients to a lifestyle that is productive and of high quality and to reduce risk of subsequent cardiac events or death.

Results of individual exercise cardiac rehabilitation studies generally show favorable short-term effects of exercise on morbidity and mortality,[3–10] but due to small sample sizes, findings are seldom statistically significant. Meta-analysis of 10 randomized clinical trials of cardiac rehabilitation indicated pooled ORs favoring exercisers of 0.76 (95% CI 0.63 to 0.92) for all-cause mortality and 0.75 (95% CI 0.62 to 0.93) for cardiovascular disease (CVD) death.[11] Interventions included exercise only, as well as comprehensive programs of exercise with various components of risk-factor management. The duration of individual programs ranged from 6 weeks to 48 months, and follow-up periods ranged from 24 to 60 months.

After 10 years of follow-up, significantly lower cardiac mortality rates in participants in comprehensive rehabilitation programs compared with control subjects were reported in 2 studies.[12,13] In both studies, 10-year all-cause mortality rates were also lower in treatment-group participants than in controls, but only in the Swedish study[12] were differences

Received May 7, 1999; revision received June 21, 1999; accepted July 9, 1999.

From the Department of Social and Preventive Medicine, State University of New York at Buffalo, Buffalo, NY.

Correspondence to Joan Dorn, PhD, Department of Social and Preventive Medicine, 270 Farber Hall, SUNY at Buffalo, Buffalo, NY 14214. E-mail jdorn@acsu.buffalo.edu

Circulation **is available at http://www.circulationaha.org**

statistically significant. In that study, differences between groups occurred primarily in the second 5 years of the study.[12] Whether any survival benefits in terms of specific cause or overall mortality are maintained beyond 10 years remains unknown.

The National Exercise and Heart Disease Project (NEHDP) was a standardized 3-year multicenter randomized clinical trial conducted in male MI survivors between 1976 and 1979. Previous findings indicated a nonsignificant 37% reduction in total mortality after 3 years in men in the exercise group compared with controls.[14] The present study extends the follow-up of the NEHDP to 1995, enabling investigation of the long-term (19-year) effects of participation in the study on survival of the participants. Given the increasing prevalence of CHD survivors, this study has important public health implications regarding long-term benefits of exercise participation in MI patients.

Methods

Study Design and Patients

A detailed description of the design and conduct of the NEHDP has been published previously.[15] Briefly, a total of 651 men 30 to 64 years of age were enrolled at 1 of 5 centers in the United States during 1976. The men had to have a documented MI ≥8 weeks but <3 years before being enrolled. Other eligibility criteria included the ability to exercise at an intensity level ≥3 metabolic equivalents (METs) and a supine resting diastolic blood pressure <100 mm Hg. Patients were considered ineligible if they had any other significant coexisting CVD or other disease likely to be fatal in the near future, uncontrolled diabetes mellitus, complete heart block with or without ventricular pacemaker, or emotional or physical impairments that would make participation and adherence difficult, or if they were already participants in a formal exercise program.

After completion of a 6-week, low-level-exercise–program run-in period, the men were randomly assigned to the exercise-treatment group (n=323) or nonexercising control group (n=328). An additional 280 men did not meet eligibility criteria or failed to successfully complete the 6-week program and were excluded. Signed informed consents and personal physician agreement were obtained for all participants.

Exercise Testing

Before enrollment and every 6 months during the study, the men completed a medical history interview and physical examination and performed an ECG-monitored treadmill multistage graded exercise test (MSET). Stage 1 began at a level of ≈2 METs (1 MET approximates oxygen uptake at rest, that is, 3.5 mL · kg^{-1} · min^{-1}). Each subsequent stage imposed a 1-MET increase in workload. A test was terminated when a patient reached his age-predicted maximal heart rate, reported symptoms such as angina pectoris or shortness of breath, or developed abnormal ECG or blood pressure changes. The stage and MET level at the termination point were designated as each patient's maximal physical work capacity (PWC). For the present study, a change in PWC was determined as the difference between the maximal attained stage of the prerandomization MSET and the last MSET completed before the end of the trial.

Exercise Prescription and Training Program

For participants enrolled in the exercise-training group, an exercise prescription was developed on the basis of each patient's MSET results. An exercise target heart rate guided the prescription and was determined as 85% of the peak heart rate achieved on the test. This group performed brisk physical activity in the laboratory for 8 weeks, exercising 1 hour per day, 3 days per week. The patients were supervised and underwent continuous ECG monitoring. Each individual exercised for 4 minutes on each of 6 stationary machines with a 2-minute rest interval between machines. Attainment of the target heart rate was the goal for every 4-minute exercise period. Exercise was stopped if patients experienced any adverse signs or symptoms or ECG abnormalities.

After 8 weeks, participants exercised in a gymnasium or swimming pool without ECG monitoring, although exercise heart rates were periodically checked. Activities consisted of 15 minutes of continuous jogging, cycling, or swimming, followed by 25 minutes of recreational games. The activities were performed at an intensity level enabling each participant to reach his individually prescribed target heart rate. The men were encouraged to attend 3 sessions per week but in some situations were allowed to exercise on their own. Both the laboratory and gymnasium/pool phases were focused solely on exercise, with no formal education/targeting provided regarding other lifestyle habits such as cigarette smoking, diet, or weight loss.

Participants in the nonexercising control group were encouraged to maintain normal routines but not to participate in any regular exercise program.

All participants were evaluated at 2 and 6 months after randomization and semiannually thereafter. Each evaluation consisted of a physical examination, MSET, and interval medical history. Individual exercise prescriptions were updated for the exercise participants on the basis of subsequent MSET results. The original clinical trial was terminated as of December 1, 1978, with morbidity and mortality follow-up completed as of May 31, 1979.

Long-Term Mortality Follow-Up

A search of the National Death Index was used to determine vital status and date of death in the deceased participants starting in 1979 and continuing until December 31, 1995. Because the original NEHDP investigators previously monitored participants from 1976 to 1979, the National Death Index alone was sufficient to determine the vital status of all participants. Death certificates were retrieved from the state in which the death occurred, and the underlying cause of death was recorded. The primary outcomes of the present study are all-cause and CVD mortality. International Classifications of Disease (ICD9) codes 390 through 450 were classified as CVD deaths. Death due to stroke was also examined, with sample-size limitations taken into consideration. ICD9 codes 430 through 439 were used to define stroke.

The present study was approved by the University at Buffalo Institutional Review Board. All procedures were in accordance with institutional guidelines.

Statistical Analysis

Intention-to-treat methodology was used in all primary analyses. Cox proportional hazards model[16] was used for survival/failure time analysis, to determine the risk of all-cause, CVD, and stroke mortality over time, from the initial examination until completion of long-term follow-up (December 31, 1995), according to treatment-group status. With the exception of stroke, similar analyses were conducted to examine differences in mortality between groups at different intervals throughout the follow-up (3, 5, 10, 15, and 19 years).

A number of secondary analyses were also performed. We examined the effectiveness of the exercise program in terms of all-cause mortality for various subgroups of the study population by comparing percent differences in mortality rates between those with high and low levels of various risk factors, (ie, smoking status).[17] Percent differences in mortality between the treatment and control groups were calculated as follows: (percent deceased in treatment group−percent deceased in control group)/percent deceased in treatment group×100. The effect of changes in PWC on all-cause and CVD mortality was also examined in the entire cohort by use of the Cox proportional hazards model.[16] All secondary analyses were repeated for follow-up periods of 3, 5, 10, 15, and 19 years. Statistical significance was declared at $P<0.05$ (2-tailed).

Results

Vital status was determined for 634 (97.4%) of the original 651 participants. Seventeen men (8 exercise group partici-

TABLE 1. Characteristics of NEHDP Study Population at Baseline

	Exercise Treatment Group (n=315)	Control Group (n=319)	*P*
Age, y	51.5±7.4	52.1±7.2	0.29
Education, y	14.3±2.8	14.4±2.9	0.72
Family income, $	23 844±13 991	23 090±13 287	0.60
Smoking, packs/d	1.40±0.92	1.51±0.98	0.17
Body weight, kg	79.6±11.2	79.4±14.9	0.87
Resting systolic blood pressure, mm Hg	125.0±16.1	124.8±15.8	0.85
Resting diastolic blood pressure, mm Hg	82.1±9.4	81.5±9.5	0.46
Resting heart rate, bpm	63.0±10.3	61.2±10.5	0.04
Body mass index (wt/ht^2)	26.0±3.3	26.0±4.3	0.99
Cholesterol, mg/dL	221.6±39.6	219.9±38.1	0.61
Triglycerides, mg/dL	186.7±168.9	180.4±169.5	0.65
Body fat, %	20.8±3.4	20.9±3.6	0.64
Interval since qualifying MI, mo	14.4±9.8	14.3±9.3	0.87
Previous MI (not including QMI), n	1.0±0.87	1.1±0.90	0.64
Work capacity, METs	7.8±2.1	7.8±2.2	0.93
Married, n (%)	285 (91.9)	291 (91.5)	0.85
Use alcohol, n (%)	199 (65.0)	212 (67.3)	0.55
Working (≥10 h/wk), n (%)	300 (95.5)	300 (94.9)	0.72
White, n (%)	294 (93.3)	301 (94.4)	0.76
Complicated MI, n (%)	151 (47.9)	149 (46.7)	0.76
Angina in past 3 months, n (%)	91 (29.2)	86 (27.3)	0.60
ST-segment changes with exercise, n (%)	40 (12.8)	43 (13.5)	0.55
History of hypertension, n (%)	98 (31.5)	108 (34.0)	0.51
Father died of MI, n (%)	100 (38.9)	97 (37.9)	0.81

QMI indicates Q-wave MI.
Values are mean±SD or n (%).

pants, 9 controls) were not located and were excluded from the present analysis. Characteristics of the remaining study population at baseline according to treatment-group status are displayed in Table 1. The men were well educated (14 years on average), married, working at least part time, and predominantly white. The average time interval between enrollment and qualifying MI was 14 months, and nearly 50% of the men reported ≥1 complication with that episode. The average work capacity was 7.8 METs. With the exception of resting heart rate, which was on average lower in control subjects than in the exercise group, no significant differences were noted between the groups for any of the baseline characteristics.

As of December 31, 1995, 162 (51.4%) exercise-group participants and 150 (47.0%) control subjects were deceased. The majority of deaths were due to CVD (64.2% in exercisers, 72.7% in controls). The difference between groups is mainly accounted for by excess stroke deaths in control subjects (7 versus 2). Cause of death for 29 men remains unknown.

The risk of mortality from all causes according to treatment-group status is displayed in Figure 1. Initially, enrollment in the exercise group appeared to offer survival benefits compared with control-group assignment, although none of the relative risks were statistically significant. At 3 years of follow-up, exercisers were at an ≈30% lower risk of death (relative risk [RR] 0.69, 95% CI 0.39 to 1.25) than men in the control group. These findings are similar to those reported by Shaw[14] at the end of the trial. The nonsignificant lower point estimates of risk for exercisers continued up to 10 years of follow-up, but the reduction in risk was attenuated as time since the trial increased. By 15 years, the RR for exercisers compared with controls was >1 (RR 1.02, 95% CI 0.79 to 1.32), and at the end of follow-up, it had increased to 1.09 (95% CI 0.87 to 1.36).

With regard to death due to CVD (Figure 2), a benefit in favor of the exercise group (RR 0.73, 95% CI 0.37 to 1.43)

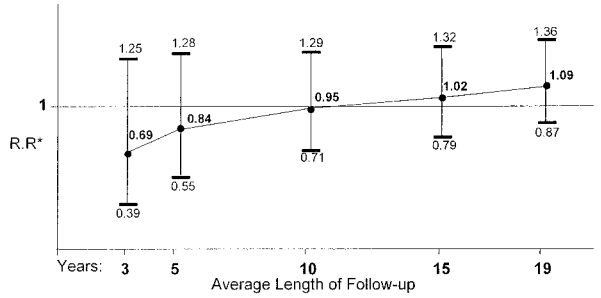

Figure 1. Risk of all-cause mortality in exercise-treatment group compared with control subjects at various follow-up periods. *RR, bars represent 95% CIs.

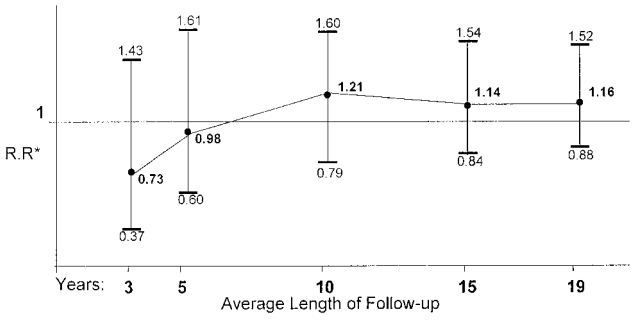

Figure 2. Risk of CVD mortality in exercise-treatment group compared with control subjects at various follow-up periods. *RR, bars represent 95% CIs.

was detected only in the earliest years of the study. At 5 years of follow-up, the relative risk approached unity. A nonsignificant elevated risk for CVD death associated with exercise-group assignment became evident at year 10 and leveled off thereafter.

After 19 years of follow-up, 7 controls and 2 exercise group participants died of stroke, resulting in an RR (95% CI) of 0.32 (0.07 to 1.56) ($P=0.16$) in favor of the exercise-program participants. Sample-size limitations prohibited us from examining this association further.

At the end of the original trial (1979), results were suggestive of a differential effect of the exercise program in individuals in various categories of CVD risk factors.[14] As a secondary hypothesis, we examined the long-term follow-up stratified by specific risk-factor levels to determine whether any of these differences persisted over time (Table 2). Younger men, cigarette smokers, and those with a low initial PWC (<7 METs) generally derived more benefits from the exercise program than men who were older, nonsmokers, or had a high PWC. However, the only statistically significant differences in effectiveness of the program were between smokers and nonsmokers at the 10-year follow-up period.

A final secondary analysis examined the relation between changes in PWC and both all-cause and CVD mortality. The results are illustrated in Table 3 after adjustment for age alone and for age as well as baseline PWC. Each single-stage (1 MET) increase in PWC of the MSET was associated with a reduction in all-cause mortality risk in the range of 8% to 14%, depending on the time period examined. The age-adjusted RRs were significant at every follow-up period except 5 years, for which the upper bound of the 95% CI was equal to 1.00. Additional adjustment for baseline levels of PWC attenuated the risk estimates slightly, but at every follow-up period, the RRs remained <1. CVD mortality risks were similar to those observed for all-cause mortality.

Discussion

The NEHDP represents the first study to examine survival effects of exercise on MI patients over a period of nearly 20

TABLE 2. Deaths and Percent Differences in Study Groups According to Risk Factor Levels

	Follow-up, y									
	3		5		10		15		19	
Risk Factor	No. Dead (%)	% Diff.	No. Dead (%)	% Diff.	No. Dead (%)	% Diff.	No. Dead (%)	% Diff.	No. Dead (%)	% Diff.
Age, y										
<50										
TX (n=124)	7 (5.6)	−48	13 (10.5)	−40	25 (20.2)	−27	35 (28.2)	−11	50 (40.3)	−5
Co (n=109)	9 (8.3)		16 (14.7)		28 (25.7)		34 (31.2)		46 (42.2)	
≥50										
TX (n=191)	12 (6.3)	−37	26 (13.6)	−5	58 (30.4)	11	85 (44.5)	2.4	112 (58.7)	15.7
Co (n=210)	18 (8.6)		30 (14.3)		57 (27.1)		82 (39.0)		104 (49.5)	
Cigarette smokers										
No										
TX (n=220)	15 (6.8)	−4.4	31 (14.1)	4.3	64 (29.1)	17.5*	87 (39.6)	11.9	112 (50.9)	10.8
Co (n=238)	17 (7.1)		32 (13.5)		57 (24.0)		83 (34.9)		108 (45.4)	
Yes										
TX (n=93)	4 (4.3)	−186.9	8 (8.6)	−101	19 (20.4)	−70	33 (35.5)	−14.6	49 (52.7)	1.5
Co (n=81)	10 (12.3)		14 (17.3)		28 (34.6)		33 (40.7)		42 (51.9)	
PWC baseline										
≥7 METs										
TX (n=239)	9 (3.8)	−5.3	24 (10.0)	12.0	54 (22.6)	19.6	80 (33.5)	14.6	109 (45.6)	12.1
Co (n=227)	9 (4.0)		20 (8.8)		43 (18.9)		65 (28.6)		91 (40.1)	
<7 METs										
TX (n=76)	10 (13.2)	−48.5	15 (19.7)	−43.7	29 (38.2)	−19.6	40 (52.6)	−5.3	53 (69.7)	8.0
Co (n=92)	18 (19.6)		26 (28.3)		42 (45.7)		51 (55.4)		59 (64.1)	

Diff. indicates difference; TX, exercise-treatment group; and Co, control group.
*$P<0.01$.

TABLE 3. RR of All-Cause Mortality According to PWC Change at Various Follow-Up Periods: The NEHDP (n=634)

Average Length of Follow-Up, y	Age-Adjusted All-Cause Mortality, RR (95% CI)	Age- and Baseline PWC-Adjusted All-Cause Mortality, RR (95% CI)	Age-Adjusted CVD Mortality, RR (95% CI)	Age- and Baseline PWC–Adjusted All-Cause Mortality, RR (95% CI)
3	0.86 (0.76–0.98)	0.91 (0.78–1.07)	0.87 (0.74–1.02)	0.94 (0.78–1.13)
5	0.91 (0.82–1.00)	0.97 (0.86–1.09)	0.91 (0.81–1.03)	0.97 (0.85–1.11)
10	0.88 (0.83–0.95)	0.92 (0.85–0.99)	0.89 (0.82–0.96)	0.92 (0.84–1.01)
15	0.89 (0.84–0.95)	0.92 (0.86–0.98)	0.90 (0.83–0.96)	0.93 (0.86–1.01)
19	0.92 (0.87–0.97)	0.96 (0.90–1.01)	0.93 (0.87–0.99)	0.96 (0.96–1.03)

PWC change=maximal attained stage final MSET minus maximal attained stage baseline MSET.
Note: 238 men (73.7%) increased their PWC at least 1 MET.

years. The results of this long-term follow-up of a 3-year multicenter randomized clinical trial suggest that men randomized to the exercise group may have experienced early survival benefits but that any protective effect of the program per se diminished over time. An increase in PWC from the beginning until the end of the trial, on the other hand, was associated with a consistent reduction in mortality throughout the entire 19 years of follow-up.

Other types of clinical trials have benefited from extended follow-up periods. In the Coronary Drug Project,[18] a beneficial effect of niacin use on all-cause mortality did not emerge until after nearly 6 years of follow-up, and the largest difference was achieved ≈12 years after initiation of that regimen (nearly 5.8 years after treatment was discontinued).

In the Multiple Risk Factor Intervention Trial (MRFIT),[19] all-cause and CHD mortality rates were comparable for participants receiving usual care and those receiving a special intervention program (eg, dietary advice and stepped-care hypertension treatment) after an average follow-up of 7 years. However, in the posttrial years, after ≈10.5 years of follow-up, all-cause and CHD mortality rates were 7.7% and 10.6% lower, respectively, in the intervention than in the usual-care group.

In a Swedish cardiac rehabilitation program, no mortality differences between study groups were observed during the first 5 years of the study.[12] Only during the second 5 years of follow-up did survival benefits in favor of the treatment group become evident and significant.

We did not find significant increased survival benefits with exercise-program participation over time. In fact, with each extended follow-up period, estimates of all-cause and CVD mortality risk were rather consistently attenuated. Even among subgroups within which there were strong early protective effects associated with randomization to the exercise group (ie, current smokers), survival benefits decreased as length of follow-up increased.

The implications of these findings are that exercise after an MI must be performed on a continuous and regular basis to provide long-term survival benefits. This notion concurs with previous research in healthy men[20,21] showing that protective effects of physical activity cannot be stored, and activity must be performed regularly to offer protection, at least against CHD.

Contamination between study groups may also explain our findings, because analyses were performed with intention-to-treat methodology. The investigators of the original trial noted that by the end of 2 years, 23% of the treatment group had stopped attending sessions and did not report exercising elsewhere, whereas 31% of the control group reported they were exercising regularly.[14] It is likely that contamination between study groups became even greater after the trial was completed, which could possibly attenuate estimates of the true benefits of exercise.

Our point estimates of all-cause mortality risk up to 5 years of follow-up fall within the 95% CIs (OR 0.76, 95% CI 0.63 to 0.92) reported by Oldridge et al[11] in a meta-analysis of 10 randomized clinical trials and by O'Connor et al[22] in an overview of 22 trials of cardiac rehabilitation (OR 0.80, 95% CI 0.66 to 0.96). Among these combined studies, the longest follow-up period was 60 months.

At 10 years, the effectiveness of the NEHDP to reduce overall mortality was considerably less than that observed 10 years after participation in comprehensive cardiac rehabilitation programs reported by Hedback et al[12] or Hamalainen et al.[13] In both of those studies, the treatment group received educational programs and counseling regarding other heart disease risk factors, including diet and cigarette smoking, in addition to intense exercise. These additional interventions may have contributed to study group differences in survival beyond any effects of exercise. Such risk-factor interventions were not provided in the NEHDP.

Another important finding in this long-term follow-up of the NEHDP cohort is that improvement in PWC resulted in consistent survival benefits throughout the entire 19 years. Regardless of length of follow-up, age-adjusted estimates of all-cause and CVD mortality risk were similar, which indicates that every single-stage increase (1 MET) in PWC resulted in an ≈10% reduction in mortality, regardless of study-group assignment. When baseline PWC levels were taken into consideration, there was still a consistently lower risk of death throughout the follow-up period. Increased PWC likely reflects actual exercise performance during the trial. If this is the case, our results indicate that exercise performed at a level sufficient to increase PWC may have long-term survival benefits in MI survivors. These findings are in agreement with those of Blair et al,[23] who showed that in nearly 10 000 healthy and unhealthy men, increased physical fitness, measured by exercise treadmill time, was associated with a reduction in all-cause mortality. Men who increased

their PWC may also have been more likely to continue to exercise in the years to follow, and this consistency of exercise performance could be directly related to improved survival. Cautious interpretation of these findings is advised because the analyses were performed outside the original randomized study design. Nevertheless, these data have physiological plausibility and imply that it may be possible to gain long-term survival benefits after MI if exercise is performed in a manner sufficient to increase PWC, regardless of initial work-capacity levels.

Limitations of the present study include the lack of information regarding effects of the program on hospitalizations, procedures (ie, coronary bypass surgery), nonfatal events, unstable angina, and quality of life after MI. These are important end points that may be favorably affected by the program. We also do not have follow-up measures of exercise and other lifestyle habits or other medical or pharmacological interventions after completion of the original trial. Treatment differences between groups in 1 or more of these factors could have explained our findings. We do know that during the original trial, differences in β-blocker use between men in the 2 groups increased over time, with control subjects having a nonsignificantly higher prevalence of use at the end of the study (22.8% versus 16.0%; $P=0.22$).

In summary, this extended follow-up of the NEHDP examined effects of enrollment in an exercise clinical trial on the long-term survival of male MI patients. The greatest benefits to exercise-program participants were realized during the trial and only during the earliest years of follow-up, yet increased PWC was associated with improved survival throughout the entire 19 years. The public health implications of this report are that in MI survivors, as in healthy individuals, the effects of exercise cannot be stored, and exercise must be maintained to offer survival benefits. No conclusions can be drawn with regard to the effects of exercise participation on subsequent nonfatal cardiac events or quality of life, 2 important areas that require additional study.

Acknowledgment

This project was supported by a National Heart, Lung, and Blood Institute First Independent Research Support in Transition award (R29-HC54874-02).

References

1. American Heart Association. *1998 Heart and Stroke Facts*. Dallas, Tex: American Heart Association; 1997.
2. Braunwald E. Shattuck Lecture: cardiovascular medicine at the turn of the millennium: triumphs, concerns and opportunities. *N Engl J Med*. 1997; 337:1360–1369.
3. Kentala E. Physical fitness and feasibility of physical rehabilitation after myocardial infarction in men of working age. *Ann Clin Res*. 1972;4(suppl 9):1–84.
4. Wilhelmsen L, Sanne H, Elmfeldt D, Grimby G, Tibblin G, Wedel H. A controlled trial of physical training after myocardial infarction: effects of risk factors, nonfatal reinfarction, and death. *Prev Med*. 1975;4:491–508.
5. Palatsi I. Feasibility of physical training after myocardial infarction and its effect on return to work, morbidity and mortality. *Acta Med Scand*. 1976;559:1–84.
6. Kallio V, Hamalainen H, Hakkila J, Luurila O. Reduction in sudden deaths by a multifactorial intervention programme after acute myocardial infarction. *Lancet*. 1979;2:1091–1094.
7. Carson P, Philips R, Lloyd M, Tucker H, Neophytore M, Buch N, Gelson A, Lawton A, Simpson T. Exercise after a myocardial infarction: a controlled trial. *J R Coll Physicians Lond*. 1982;16:141–147.
8. Rechnitzer PA, Cunningham DA, Andrew GM, Buck CW, Jones NL, Kavanagh T, Oldridge NB, Parker JO, Shepard RJ, Sutton JR, Donner AP. Relation of exercise to recurrence rate of myocardial infarction in men: Ontario Exercise-Heart Collaborative Study. *Am J Cardiol*. 1983; 51:65–69.
9. Roman O, Guitierrez M, Luksic I, Chavez E, Camuzzi A, Villalon E, Klenner C, Cumsille F. Cardiac rehabilitation after myocardial infarction: nine year controlled followup study. *Cardiology*. 1983;70:223–231.
10. Vermueulen A, Lie K, Durrer D. Effects of cardiac rehabilitation after myocardial infarction: changes in coronary risk factors and long-term prognosis. *Am Heart J*. 1983;105:798–801.
11. Oldridge NB, Guyatt GH, Fischer ME, Rimm AA. Cardiac rehabilitation after myocardial infarction: combined experience of randomized clinical trials. *JAMA*. 1988;260:945–950.
12. Hedback B, Perk J, Wodlin P. Long-term reduction of cardiac mortality after myocardial infarction: 10-year results of a comprehensive rehabilitation programme. *Eur Heart J*. 1993;14:831–835.
13. Hamalainen H, Luurila OJ, Kallio V, Knuts L-R, Arstila M, Hakkila J. Long-term reduction in sudden deaths after a multifactorial intervention programme in patients with myocardial infarction: 10-year results of a controlled investigation. *Eur Heart J*. 1989;10:55–62.
14. Shaw LW. Effects of a prescribed supervised exercise program on mortality and cardiovascular morbidity in patients after a myocardial infarction: the National Exercise and Heart Disease Project. *Am J Cardiol*. 1981;48:39–46.
15. Naughton J. The National Exercise and Heart Disease Project: development, recruitment, and implementation. In: Wenger NK, ed. *Exercise and the Heart*. Philadelphia, Pa: FA Davis Co; 1978:205–222.
16. Cox DR. Regression models and life tables. *J R Stat Soc*. 1972;34: 187–220.
17. Fleiss JL. *Statistical Methods for Rates and Proportions*. 2nd ed. New York, NY: John Wiley & Sons Inc; 1981:165–168.
18. Canner P, Berge K, Wenger N, Stamler J, Friedman L, Prineas R, Friedewald W. Fifteen year mortality in Coronary Drug Project patients: long-term benefit with niacin. *J Am Coll Cardiol*. 1986;8:1245–1255.
19. Multiple Risk Factor Intervention Trial Research Group. Mortality after 10½ years for hypertensive participants in the Multiple Risk Factor intervention Trial. *Circulation*. 1990;82:1616–1628.
20. Paffenbarger RS Jr, Wing AL, Hyde RT. Physical activity as an index of heart attack risk in college alumni. *Am J Epidemiol*. 1978;108:161–175.
21. Paffenbarger RS Jr, Hyde RT, Wing AL, Steinmetz CH. A natural history of athleticism and cardiovascular health. *JAMA*. 1984;252:4:491–495.
22. O'Connor GT, Buring JE, Yusuf S, Goldhaber SZ, Olmstead EM, Paffenbarger RS Jr, Hennekens CH. An overview of randomized trials of rehabilitation with exercise after myocardial infarction. *Circulation*. 1989;80:234–244.
23. Blair SN, Kohl HW III, Barlow CE, Paffenbarger RS Jr, Gibbons LW, Macera CA. Changes in physical fitness and all-cause mortality: a prospective study of healthy and unhealthy men. *JAMA*. 1995;273: 1093–1098.