Effects of Exercise Training in the Elderly on the Occurrence and Time to Onset of Cardiovascular Diagnoses

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To examine the long-term effects of aerobic exercise on the occurrence and time to onset of cardiovascular diagnoses, 184 initially healthy older subjects were randomized into either a long-term exercise group (Group A, n = 80), a short-term exercise group (Group B, n = 42), or a contact control group (Group C, n = 62). After completion of two years in the study, data on new cardiovascular diagnoses and time to onset of these diagnoses in each of the three groups were compared. The occurrence rates for new onset diagnoses were as follows: Group A, 2.5%; Group B, 2%; and Group C, 13%; the average time to onset was greatest for the long-term exercisers and shortest for the contact control group ($P \leq .02$). The results suggest that a regular program of exercise may have cardiovascular benefits for those over 60 years of age. J Am Geriatr Soc 38:205–210, 1990

In the last decade there has been mounting experimental evidence of the physiologic benefits of exercise and the relationship between exercise and lowered incidence of age-related disorders.[1–8] The United States Department of Health and Human Services has responded to this evidence by setting the ambitious goal of having 50% of all older people exercise regularly by the year 1990,[9] and there have been endorsements of regular aerobic exercise for older people by the Surgeon General, the AMA, and other leading public health authorities.[9–12]

Available data from long-term observational studies, some of which include older subjects, suggest that regular physical activity is associated with lower incidence of cardiovascular disease.[13–20] Paffenbarger and Hale showed that longshoremen with low levels of work activity had a higher incidence of fatal myocardial infarction than those in more vigorous jobs.[16] In a more recent study of 16,936 Harvard University alumni, some of whom were in their ninth decade, Paffenbarger et al found that subjects with higher levels of physical energy expenditure had lower overall death rates, lower cardiovascular disease death rates, and a slightly increased longevity. Paffenbarger et al later showed that, by age 80, adequate exercise is associated with a one- to two-year increase in life expectancy.[18] The Framingham study has reported similar associations between exercise and decreased incidence of cardiovascular disease. The decrease in relative risk of death with increasing physical activity was most pronounced in subjects over age 60.[13] A secondary analysis of the Multiple Risk Factor Intervention Trial data showed that physical activity is also beneficial to those already at risk for coronary heart disease.[19] However, despite all the evidence for a beneficial relationship between physical activity and cardiovascular health, observational studies are limited to providing only correlational rather than causal evidence for the importance of exercise on future health.[20] Nonetheless, those noninterventional studies provide encouraging evidence that justifies the need for more rigorous examination of the relationship between physical activity and cardiovascular morbidity through controlled interventional studies.

To determine the direct influence of exercise on the onset of cardiovascular disease, a tightly controlled interventional study with adequate numbers of subjects is needed to assess whether exercise as a primary prevention protects against onset of cardiovascular disease. To date, no such studies exist. Some studies have examined the effects of an exercise program on cardiorespiratory fitness,[21,3] but did not examine the relationship between

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exercise and cardiovascular disease. Other studies addressed the role of exercise in the secondary prevention of cardiovascular events; however, the results ranged from favorable[22] to inconclusive to negative[23,24] and did not demonstrate that exercise prevents cardiac disease, especially in older adults. Our understanding of the influence of exercise on cardiovascular health would be enhanced by a large-scale study that included randomization and adequate control groups to examine the effects of exercise on the morbidity and mortality of healthy older people over time. To lay the groundwork for such a comprehensive study, we designed a longitudinal randomized three-group study of moderate size. This study allowed us to determine first whether older people could be recruited for a program of either exercise or contact control and comply with that program; second, whether physiological benefits could be derived from a moderate program of exercise; and third, whether health benefits occurred as a result of the exercise program. The successful answers to the first two questions have been discussed by us[25–27] and others[21] in previous publications. This study focuses on the third issue. Specifically, we evaluate the cardiovascular effects of a moderate program of exercise on previously nonexercising adults aged 60 to 86. This article reports the occurrence of cardiovascular diagnoses and the time to onset of new cardiovascular diagnoses between nonexercising older adults and two groups of older adults who pursued a supervised program of exercise.

METHODS

Data over a two-year interval exists for 184 subjects aged 60 years or older. The participants were recruited from senior citizen centers in the greater Philadelphia area. Volunteers responding to requests for subjects over age 60 in good health who did not exercise regularly underwent a multistage screening protocol to insure that they were healthy enough for this study. The screening protocol as previously described[25] included a medical history and physical examination, resting electrocardiogram, blood studies such as CBC, T_3 T_4 TSH, lipid profile, electrolytes and glucose, pulmonary function tests (spirogram, lung volumes, and single-breath diffusing capacity), and a progressive exercise test with continuous monitoring of electrocardiogram and expired gases. Volunteers with any of the following abnormalities (as could be diagnosed by the above tests or by the volunteers' physicians) were excluded from the study: cardiovascular disease (angina, myocardial infarction within the past two years, asymptomatic ischemic heart disease, hemodynamically significant valvular heart disease, arrhythmias, conduction disturbances, cardiomyopathy), moderate to severe pulmonary disease, musculoskeletal disease precluding bicycle ergometry, symptomatic peripheral vascular disease, uncontrolled metabolic disease (diabetes, anemia, thyroid disease), electrolyte abnormalities, blood pressure greater than or equal to 165/90 mmHg, or any other chronic diseases affecting the ability to exercise. Any volunteer whose exercise stress test was abnormal was also excluded from the study. An abnormality was defined as an ischemic response to exercise testing or other exercise-induced abnormality.[25] The screening process eliminated approximately 40% of the initial pool of volunteers. Subjects with controlled hypertension or history of myocardial infarction (silent or symptomatic) two or more years prior to the initiation of the study were eligible if the maximal exercise test was normal. The mean age of the subjects was 68.54 years, and the range was 60 to 86 years. Forty-three percent of the subjects were men, and 57% were women.

Subjects meeting eligibility requirements for the study were matched for sex and randomized into a training and home exercise group (Group A, or "long-term exercisers"), training-only group (Group B, or "short-term exercisers"), or attention control group (Group C). Subjects were randomized using a table of random digits. Spouses and siblings living together were randomized as a unit, but single men and women were randomized separately. The randomization procedure resulted in exercising and nonexercising groups that at baseline had equivalent values for age, weight, height (ie, all baseline analysis of variance tests were nonsignificant). Because subjects with controlled hypertension or history of myocardial infarction as described above were admitted into the study, we also examined the equivalence between the groups on the basis of cardiovascular problems. Again, no significant differences were found among the groups at baseline. During the first wave of data collection two-thirds of all subjects (Groups A and B) entered a supervised four-month aerobic exercise training program; one-third of subjects were assigned to the nonexercising attention control group. The second and third wave of data collection resulted in two thirds of the subjects being assigned to the long-term exercise group and one third being assigned to the attention control group. (This modification in design resulted from the lack of significant differences in structured exercise performed by the short-term exercise group and the control group after year one.) Subjects in the attention control group participated in a four-month lifestyle enrichment and discussion program designed to achieve equivalence with the exercise training groups in personalized attention, social interaction, and staff support.

Exercise Test Protocol Subjects performed maximal exercise testing three times during the study: at baseline, after the four-month exercise or contact control program, and at the conclusion of the first year. All subjects had been to the laboratory for one familiarizing session with the protocol prior to exercise testing. Exercise testing was conducted no sooner than two hours after a standardized light meal, and subjects were requested to refrain from cigarette smoking and consumption of caffeinated beverages on the day of the test. Three electrocardiographic leads (II, V_3, V_5) and blood pressure were monitored and recorded every minute during exercise and for 10 minutes during recovery. An electromagnetically braked ergometer (Meinhart KEM II) was used, with the subject pedaling at a constant speed of 60 rpm. After one minute of rest, exercise was initiated by two minutes of unloaded cycling and subsequent 15-watt per minute increases in workload until shortness of breath, exhaustion, or inability to move the pedals occurred. The workload increments were designed so that a subject would reach exhaustion within approximately 10 minutes of progressive work.[28]

Ventilation and gas exchange parameters were measured breath-by-breath using a computerized system (Medical Graphics, System 2000). Maximal oxygen uptake ($\dot{V}O_2max$) was determined as the average of all breaths within a 20-second period surrounding the highest recorded $\dot{V}O_2max$. Leveling off criterion was used when applicable; however, very few subjects demonstrated a "plateau" of oxygen uptake.

Training Program We utilized a three-group design to study the effects of exercise. Two groups followed a supervised program of exercise for differing lengths of time. The third group did not receive an exercise prescription, but attended weekly lectures instead. The volunteers were not provided any treatment other than the exercise or lectures by the project staff. All health treatment received by the volunteers during their participation in the study was given by their personal physicians who were unaware of the design of the study. After completion of the screening protocol and baseline testing, subjects in the exercise program, Groups A and B, were assigned to small groups ($n = 4-6$) for thrice weekly supervised exercise sessions for 16 weeks. Training was conducted on Monark bicycle ergometers (Model 868) and monitored by a physical trainer. Each training session began with measurement of resting heart rate and blood pressure and was followed by five minutes of unloaded cycling, 30 minutes of loaded cycling at training heart rate (which was the heart rate at 70% of the maximal attained oxygen uptake on the baseline exercise test), and ended with five minutes of unloaded cycling. Heart rate during training sessions was monitored continuously with a heart-rate meter. Workload (watts) was adjusted during each exercise session to maintain training heart rate. All heart-rate and blood pressure information was recorded on training logs. Compliance (as defined by attendance) to the four months of supervised exercise was 81%.

During the four months that the exercise groups were exercising, the attention control group subjects were attending weekly lectures that lasted approximately one hour. Topics of those lectures were designed not to have any physiological or health effects. During each session, blood pressure measurements were taken by project staff primarily to give the control subjects the same amount of attention to their health during the training period as the exercisers received. Compliance to the four months of attention control sessions was 67%.

Long-Term Follow-Up After completion of the four-month supervised exercise-training program, Group A exercisers received home cycles (Tunturi or MacLevy) and pulse-rate meters (Respironics Exersentry II or Americ 130) for continued home exercise. Group B exercisers were encouraged to exercise at home but were not given home exercise equipment.

Training heart rate was readjusted for home exercise subjects following the maximal exercise test at the conclusion of the supervised program. Subjects were instructed on the use of home cycles and pulse rate meters. The home bicyclers recorded heart rate meter reading at rest, after 15 and 30 minutes of loaded cycling, and a five-minute recovery heart rate.

After the life-style program, attention controls proceeded with their normal activity patterns. All subjects underwent repeat physiologic testing, including stress tests, pulmonary function tests, and blood lipid data at four months and 12 months after baseline testing, and were available for long-term follow-up telephone interviews throughout the second year of study participation. Home bicyclers were instructed to record heart rate meter readings at rest, after 15 and 30 minutes of loaded cycling, and a five-minute recovery heart rate. Heart-rate logs were returned monthly over the two-year period and examined by the exercise trainer. Home visits for repairing exercise equipment and telephone monitoring of exercise performance were conducted throughout the two-year period. The return rate for training logs was also high at 77% for the first year and 67% for the second year.

In addition to assessing long-term compliance to the exercise program through self-report methods (eg, training logs), compliance was evaluated on the basis of physiological parameters. Training effects are apparent when the maximal oxygen-uptake values are examined over the course of the first year. Those results are presented in Table 1 and are discussed more thoroughly in the results section. Those results, along with increased training workload ($t = -11.12$; df $= 125$, $P < .001$) from zero to four months, are evidence that subjects assigned to the long-term exercise treatment continued to comply with their exercise prescription throughout the first year. Another method of determining compliance through physiological parameters is to devise a compliance score based on frequency, intensity, and duration of exercise.[27] A compliance index was created as a function of intensity and frequency, and the value for this index was 65.5% for the entire year. No exercise stress-test data are available from the subjects after the

TABLE 1. MEAN MAXIMUM OXYGEN UPTAKE

	Long-Term Exercise	Short-Term Exercise	No Exercise	F_{int}
Time 1	22.70 (5.86)	22.35 (4.81)	22.24 (4.64)	2.91* (4,332)
Time 2	24.13 (6.11)	24.01 (5.20)	22.20 (5.19)	
Time 3	23.23 (6.43)	22.30 (5.42)	21.21 (5.14)	

Note: Oxygen uptake measured in units of mL/kg/min. Numbers in parentheses are standard deviations.
*$P < .05$

first year; therefore compliance estimates must be taken from the self-report measure described above.

Exercisers and controls were requested to maintain a daily record of physical activity and health behavior (including newly diagnosed cardiovascular conditions) over an eight-month period following intervention. Calendar recordings were returned monthly and verified by brief telephone interviews in which diary content was clarified and the presence of new physician-diagnosed conditions tracked. The return rate for calendar diaries averaged 94% during the first year. Second-year follow-up included quarterly telephone interviews to assess health behaviors and the onset of new medical conditions. For the 125 exercisers, 123 were contacted by phone during year two. For the control group, 59 of the 60 were contacted by phone. Compliance to supplying health information was higher than compliance to exercising because of the limited time and effort involved in supplying the health information.

All cardiovascular diagnoses were made by the subjects' physicians, who were unaware of the purpose of the research project in which their patients were enrolled. In fact, the subjects themselves were not informed as to the hypotheses under investigation. The exercisers were told only that the purpose of the study was to determine the effects of a regular program of exercise for older adults. The attention control subjects were only told that the study was focusing on the importance of lifestyle for older adults. All diagnoses were verified through each subject's medical records. No new diagnoses resulted from the exercise stress tests performed at four and 12 months after the subjects' entry into the project. New-onset cardiovascular conditions were defined as new-onset angina, myocardial infarction, symptomatic arrhythmias requiring treatment, congestive heart failure, hemodynamically significant valvular heart disease, cardiomyopathy, conduction disturbances, and other cardiovascular disease (ICCD codes, 414,429.2). Peripheral vascular disease, hypertension, and cerebrovascular disease were not included in this analysis. In the end, the new cardiovascular diagnoses uncovered were angina, atrial fibrillation, supraventricular arrhythmia, paroxysmal atrial tachycardia, and myocardial infarction.

RESULTS

In a repeated-measures MANOVA of maximal oxygen uptake, a significant group-by-time interaction ($P < .02$) was found. Subjects in the long-term exercise group increased maximal attained oxygen uptake after the four-month training program (see Table 1) and maintained that change over the course of a year with a home exercise program. Subjects in the short-term exercise group had an initial improvement in fitness levels but experienced a reversal of their fitness level following the completion of the supervised exercise program. Control subjects had unchanged fitness levels over the course of the year.

To keep training heart rate constant, work was increased as exercise subjects improved fitness. The work required to maintain training heart rate increased an average of 12.52 watts from the first to the last weeks of training. Compliance for subjects in the exercise group was computed each month as: (training frequency × training heart rate) ÷ prescribed heart rate. The sum of these monthly scores gave a final compliance score. According to this score, there was 71% compliance during the first four months of training and 60% compliance in the later seven months of training.

There were differences in the occurrence of new cardiovascular diagnoses between exercisers and nonexercisers during the two years under investigation (see Table 2). Control subjects (Group C) experienced a significantly higher number of new conditions ($n = 8$) than the long-term exercisers ($n = 2$) or the short-term exercisers ($n = 1$) ($\chi^2 = 7.99$, df $= 2$; $P < .025$). If one considers the two exercising groups together, 2.4% of the exercisers experienced a new-onset cardiac condition, whereas 12.9% of the control group did. There was a significant difference in time to onset of newly diagnosed cardiovascular conditions (Wilcoxon Breslow statistic $= 8.27$, df $= 1$ $P < .02$). The average time to onset of new cardiovascular condition was 728 days for the long-term exercisers, 715 days for the short-term exercisers, and 672 days for the attention control group.

Table 2 shows that the most frequent cardiac condition was arrhythmia ($n = 6$), followed by manifestations of coronary heart disease (angina and myocardial

TABLE 2. CASES OF NEW CARDIOVASCULAR CONDITIONS OVER TWO YEARS

Subject	Age at Initiation of Study	Sex	Interval (Days) Between Initiation of Study and Development of Condition	Condition	Previous History
Long-term exercise group					
1	73	M	720	Angina	Uncomplicated inferior wall myocardial infarction years before study
2	65	F	425	Angina	No
Short-term exercise group					
3	67	F	90	Atrial fibrillation	Frequent PACs on holter monitor
No exercise group					
4	85	F	60	Supraventricular arrhythmia	No
5	68	M	630	Supraventricular arrhythmia	No
6	78	M	180	Paroxysmal atrial tachycardia	No
7	66	F	227	Angina	No
8	75	M	300	Angina	No
9	64	M	300	Myocardial infarction	No
10	69	M	150	Atrial fibrillation	No
11	71	M	395	Atrial fibrillation	No

infarction) ($n = 5$). All arrhythmias were clinically significant and required treatment with medication and, in two cases, electrocardioversion was required.

DISCUSSION

This was a controlled randomized trial to study the effects of exercise in healthy, previously sedentary older people. The study revealed that a program of moderate exercise can improve fitness in a large group of healthy older people and that it affords some protection against the new onset of cardiac conditions. Previous large studies among older people have been observational. Such studies are subject to bias resulting from self-selection: subjects likely to participate in exercise are most likely to have less current disease and less risk of developing new disease. In principle, even prospective, controlled exercise trials are subject to bias: those subjects who are the most ill and frail are likely to be intolerant of exercise, so that exercise-completers might constitute a group selected on the basis of health. This study, however, was designed to preclude bias from this type of selection. All subjects present at the onset of intervention were followed and included in the analyses. (Three people dropped out of our study after randomization but before intervention and were not included in the results. One dropped out of each of the three experimental groups.) Once intervention began, data were collected on all subjects regardless of level of compliance.

The incidence of new-onset cardiovascular diagnoses in the control group (Table 2) at first inspection seems high. Incidence data from large national health surveys are not available for all of the cardiovascular conditions occurring in this study. However, in a five-year morbidity and mortality study of 263 initially healthy men and women (mean age, 72) conducted by Thomas et al,[29] 18.6% of subjects were diagnosed as having some form of new-onset heart disease by the end of the second year of the study. Of this group of subjects, 4.9% were noted to have ischemic heart disease; an additional 13.7% had other types of heart disease including cardiomegaly, congestive heart failure, aortic aneurysm, and problematic arrhythmias. Although some of the disease categories in the Thomas study differed from ours, the overall percentage of initially healthy subjects who subsequently developed heart disease was similar.

Our results show a protective effect of exercise primarily against the development of clinically significant arrhythmias, but not against the development of other cardiovascular conditions including angina and myocardial infarction. It is possible that the relatively small sample size and the relatively short follow-up have precluded the discovery of a protective effect of exercise against those conditions. It is also possible that the active lifestyles of our subjects (most of whom belonged to senior citizen's organizations) provided a level of protection against coronary artery disease such that our exercise program had no added effect. Such lifestyles are associated with a lower incidence of coronary artery disease.[15] It is also possible that a short program of moderate exercise simply does not protect against the development of myocardial infarction and angina.

This study demonstrates that a relatively large number of older exercisers and contact control nonexercisers will comply with program requirements. We also showed that the exercise program improves fitness and seems to afford some protection, even over the short term, against the development of new cardiac diagnoses. We believe these data demonstrate the feasibility of and justify the investment in more extensive, probably multicenter, studies on the health benefits of exercise among older adults.

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