THERAPEUTIC VALUE OF GRADED AEROBIC EXERCISE TRAINING IN RHEUMATOID ARTHRITIS

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Women with rheumatoid arthritis performed 1 of 3 low intensity aerobic exercise protocols (15, 25, and 35 minutes) 3 times per week for 12 weeks. A nontraining group served as controls. All exercise groups improved their aerobic capacity, exercise time, and joint counts. Subjects described improvement in activities of daily living and reduced joint pain and fatigue. Exercise duration up to 35 minutes can be therapeutic, and as little as 15 minutes of exercise 3 times/week is sufficient to improve aerobic capacity in rheumatoid arthritis patients with severe limitations.

Recent experimental evidence has indicated that exercise training may be beneficial in rehabilitating patients with chronic diseases including spinal cord lesions (1), cardiovascular disease (2), obesity (3), obstructive lung disease (4), and diabetes mellitus (5). Rheumatoid arthritis (RA) results in muscle wasting, weakness, inactivity, and fatigue with resultant poor aerobic function (6). Exercise therapy in the past has been limited to range of motion and non-stress muscle strengthening coupled with appropriate rest, with the goal of preserving joint movement and strength (7). While this may be appropriate for acute flares of RA, recent studies suggest there may be a role for more vigorous conditioning exercise of a nontraumatizing nature in the long-term management of RA during nonacute or chronic stages (8–12).

Patients with RA have clearly demonstrated a very low level of physical performance ability when measured by aerobic capacity (6,8,9). It has been suggested that regular conditioning exercise can improve aerobic capacity, and improve their functional ability and sense of well-being with no apparent untoward effect on the joint symptoms (6,8–12). In addition, recent animal studies lend support to the theory that exercise is important for joint function. Salter (13) has shown that continuous passive motion favors healing and regeneration of damaged rabbit articular cartilage, and it has also been shown that joint motion with weightbearing is required to maintain normal articular cartilage in dogs (14).

This study was undertaken to evaluate more specifically the amount of exercise necessary to effect significant improvement in exercise tolerance, aerobic capacity, and functional ability without exacerbating joint symptoms. In order to determine appropriate exercise duration, 3 different exercise protocols were devised and a nonexercising group served as controls.

PATIENTS AND METHODS

Twenty women with definite or classic RA (15), American Rheumatism Association functional class II (16), age range 27–68 (mean ± SD, 52 ± 12), were enrolled in the study. Patients independently chose an exercise time slot convenient for them within a 4-hour block of time without knowledge of the protocol to which they would be assigned.

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Table 1. Joint evaluation key

Pain on motion or tenderness on pressure	
0 = none	
1 = minimal (positive response on questioning)	
2 = moderate (spontaneous response elicited)	
3 = severe (withdrawal by patient on examination)	
Swelling	
0 = none	
1 = mild (detectable synovial thickening without loss of bony contours)	
2 = moderate (loss of distinctness of bony contours)	
3 = severe (bulging synovial proliferation with cystic characteristics)	

The 4 different protocols were, in turn, randomly allocated to these time slots. This selection option was deemed necessary in order to facilitate attendance at exercise sessions considering the number of exercise sessions necessary. The control subjects were later informed they would not be attending exercise sessions. This method had the advantage of providing a random assignment of patients to protocols without restricting participation in the study because of scheduling difficulties.

Patients were selected from the large outpatient population followed at this institution and were willing to participate in the program with informed consent. All patients were on stable medical regimens, no major changes in drug therapy occurred during the study, and no intraarticular steroid injections were given. No patients had acute flares of joint symptoms at the time of entry into, nor during, the study. Self-administered questionnaires providing data on education, socioeconomic background, and duration of disease were completed by each subject. Using a modification of the Functional Status Index (FSI) (17), morning stiffness, sleep patterns, self care, ambulation, and activities of daily living were self-assessed by the subjects at baseline and at 2-week intervals during the study. At the end of the training program, subjects were asked to compare their perceptions of changes in fatigue, strength, ability to do housework, participation in social activities, overall mood, amount of joint pain, and tolerance of joint pain. This final inquiry was subsequently referred to as the global assessment. Grip strength, 50-foot walk time, and muscle strength measurement (knee flexors and extensors) using a Cybex II Isokinetic Dynamometer (Lumex Inc., Bay Shore, NY) were tested on all subjects (18). All joint count evaluations were performed by 1 investigator according to the criteria shown in Table 1.

Exercise tolerance tests which followed a standard graded protocol, beginning at 150 kilopond meters (kpm) and advancing by 150 kpm every 3 minutes, using a bicycle ergometer at 50 revolutions per minute (rpm) were performed on all subjects. Aerobic capacities ($\dot{V}O_2$ maximum) were calculated from values obtained using a Parkinson-Cowan Dry Gas Meter for volume determinations, and a Beckman LB-2 carbon dioxide analyzer and an Applied Electro-Chemistry oxygen analyzer for measuring expired CO_2 and O_2 gas composition.

Electrocardiographic rhythms were continuously monitored throughout the test, and heart rate and blood pressure measurements were taken at 1-minute intervals. Exercise was terminated when the subject was unable to maintain cycling cadence to the pace established by the metronome.

In a group setting, the subjects then began their program of bicycle ergometer exercise 3 times/week for 12 weeks, a period previously determined to improve aerobic capacity (19). Each session was supervised by physical education graduate students. The protocols differed in the initial length of total exercise time, the rate of progression, and the final total duration of activity achieved after 6 weeks (15, 25, 35 minutes) and patient groups labeled groups A, B, and C were assigned to the 3 protocols, respectively (Figure 1). The exercise intensity was measured by heart rate, and was maintained for all groups at 70% of the maximal heart rate measured during the baseline exercise tolerance test. The load on the bicycle ergometers was applied at a resistance which achieved and maintained 70% of the maximum heart rate at 50 rpm. Each total daily exercise session was divided into 5 bouts of exercise separated by 1-minute rest periods. Each session was preceded by a warmup and ended with a cool-down period and involved gentle, active, rhythmic range of motion exercises. Control subjects continued their routine daily activities without knowledge of any intervention.

At the end of the 12-week period, repeat exercise tolerance tests for aerobic capacities, joint count, muscle strength testing, walk time, grip strength, and repeat assessments of the FSI were performed exactly as done at baseline. Results were analyzed using the statistical programs of MIDAS for analysis of variance and Student's *t*-test (20).

RESULTS

These subjects, with similar socioeconomic backgrounds and educational levels, showed no differences at entry into the study in age group, duration of disease, aerobic capacity ($\dot{V}O_2$ maximum), exercise

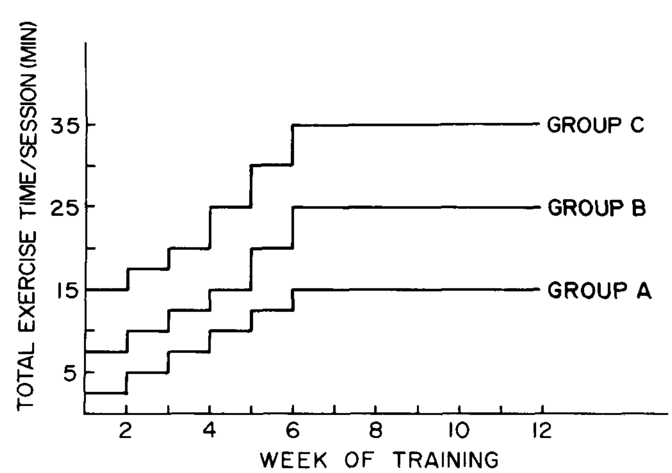

Figure 1. Training scheme. Bicycle ergometer rate at 50 revolutions per minute. Initial training duration, progression, and final training duration are shown. Each session was divided into 5 bouts with 1 minute of rest between bouts.

Table 2. Group means (±SD) for pre- and post-training parameters

	Group A (n = 4)		Group B (n = 3)		Group C (n = 4)		Controls (n = 6)	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Age	51.5 ± 3.1		47.3 ± 14.5		44.0 ± 18.3		45.1 ± 19.3	
Duration of disease (years)	12.2 ± 8.7		10.6 ± 5.5		5.6 ± 3.7		8.8 ± 10.1	
Aerobic capacity (ml/kg/minute)	14.6 ± 4.9	21.5 ± 6.5*†	20.3 ± 15.8	22.9 ± 17.9†	21.9 ± 9.0	29.1 ± 17.4†	18.5 ± 7.4	18.6 ± 8.3
Exercise maximum heart rate (beats/minute)	136.5 ± 21.4	151.3 ± 12.3	161.3 ± 44.3	161.3 ± 22.9	162.8 ± 31.3	156.0 ± 30.4	168.2 ± 18.7	162.5 ± 21.4
Exercise pressure rate product (systolic blood pressure × heart rate)/100	252.5 ± 81.7	291.5 ± 36.7	304.7 ± 83.1	318.3 ± 80.4	295.3 ± 56.8	280.5 ± 79.9	278.2 ± 39.4	240.7 ± 97.9
Exercise test time (minutes)	9.0 ± 2.5	12.3 ± 2.5†‡	9.0 ± 8.2	15.0 ± 6.1†	12.5 ± 3.9	14.3 ± 4.4†‡	9.83 ± 2.2	10.1 ± 2.92
Joint count	38.0 ± 21.7	24.0 ± 10.9†	26.0 ± 15.1	10.3 ± 7.0†	32.5 ± 19.4	23.0 ± 10.7†	27.5 ± 7.5	23.0 ± 8.46
Muscle strength (foot pounds)								
Isotonic extension	61.0 ± 17.1	58.5 ± 14.8	86.0 ± 3.5	82.0 ± 6.9	68.0 ± 11.7	61.0 ± 19.6	61.6 ± 13.4	70.6 ± 17.0
Isotonic flexion	35.0 ± 13.4	34.0 ± 6.3	46.6 ± 4.2	45.3 ± 3.1	38.0 ± 9.4	36.0 ± 7.7	35.6 ± 6.8	40.0 ± 10.0
Isometric extension	55.0 ± 13.7	56.0 ± 23.9	72.0 ± 10.4	86.7 ± 9.0*	60.5 ± 15.6	62.5 ± 22.9	63.6 ± 15.7	74.6 ± 13.6
50-foot walk time (seconds)	12.6 ± 3.2	13.5 ± 2.4	12.7 ± 1.5	13.0 ± 1.0	11.4 ± 2.5	12.3 ± 2.1	10.9 ± 1.8	9.55 ± 0.49
Grip strength (mm Hg)	117.8 ± 62.0	102.2 ± 42.2	132.7 ± 88.7	136.0 ± 75.6	101.0 ± 69.0	135.5 ± 45.2	116.35 ± 50.7	133.0 ± 50.3
Functional Status Index								
Self care	3.5 ± 3.1	4.8 ± 3.3	4.0 ± 5.2	5.3 ± 4.9	3.8 ± 3.3	4.7 ± 4.3	4.5 ± 5.3	3.6 ± 5.6
Ambulation	2.8 ± 1.3	4.0 ± 3.5	5.7 ± 3.1	4.7 ± 2.1	4.8 ± 2.2	7.5 ± 4.4	6.0 ± 4.7	5.2 ± 5.1
Activities of daily living	17.0 ± 6.1	14.2 ± 4.2	15.0 ± 14.0	9.7 ± 8.3	16.8 ± 8.3	16.0 ± 13.1	14.8 ± 10.2	14.8 ± 13.8

* $P < 0.05$ compared with baseline.
† $P < 0.01$ for groups A, B, and C combined compared with baseline.
‡ $P < 0.01$ compared with baseline.

maximum heart rates, pressure rate products, exercise test time, joint count, muscle strength, walk time, grip strength, or FSI scores (Table 2). Three patients, 1 from each exercise group, dropped out of the study for personal reasons not related to their disease or the exercise program.

Baseline $\dot{V}O_2$ maximum values were, in general, quite low, reflecting the severely unconditioned state of many of the subjects. Following training, as shown in Figure 2, there was an increase in $\dot{V}O_2$ maximum in all exercise groups compared with controls. While all exercising groups enhanced their aerobic capacities, these improvements only reached statistical significance in group A ($P < 0.05$, Table 2). Exercise tolerance, as measured by time to fatigue during exercise testing, also increased in all 3 exercise groups and was statistically significant for groups A ($P < 0.01$) and C ($P < 0.01$) (Table 2 and Figure 3).

The exercise group (groups A, B, and C combined) showed a significant reduction ($P < 0.01$) in joint counts at the completion of the study (Table 2). Scores for both pain and swelling decreased in the exercising group (Figure 4). The exercising subjects reported a reduction in morning stiffness (Figure 5) and an improvement in sleep patterns (Figure 6) during the study, while no subjective improvements in these parameters were noted by the nonexercising subjects.

Muscle strength, as tested by Cybex II, did not change in any of the groups except isometric extension at 90° in group B ($P < 0.05$) (Table 2 and Figure 7).

Subject assessment of particular aspects of self care, ambulation, and activities of daily living did not change in any general trend. However, in the global assessment of changes in fatigue, exercise tolerance, pain, strength, ability to do household chores, social activity, and overall mood, group A reported the most improvement, a lesser degree of improvement was shown for group B, and little or no change occurred in group C (Figure 8). This coincided with subjective assessments made by each subject as part of the final assessment.

When all exercise subjects were combined into 1 group (n = 11) for statistical purposes, significant improvements were noted on 3 important measures.

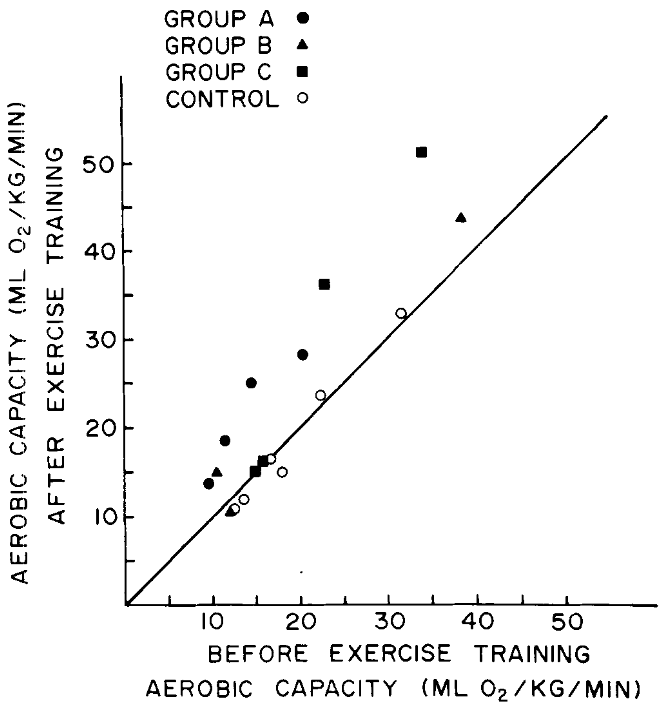

Figure 2. Oxygen uptake (aerobic capacity) for each subject before and after exercise training. $P < 0.05$ for group A.

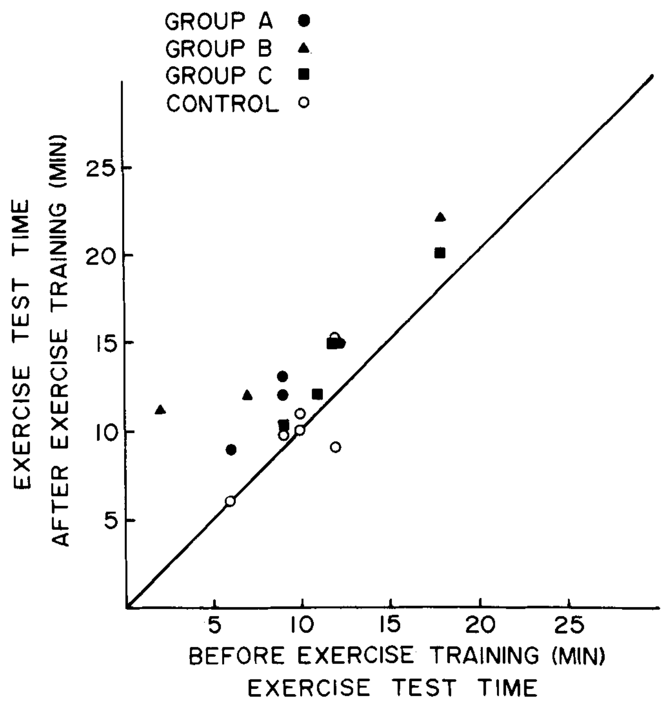

Figure 3. Exercise test time for each subject before and after exercise training. Test was ended when subject became fatigued and could not maintain 50 revolutions per minute. $P < 0.01$ for groups A and C compared with baseline values.

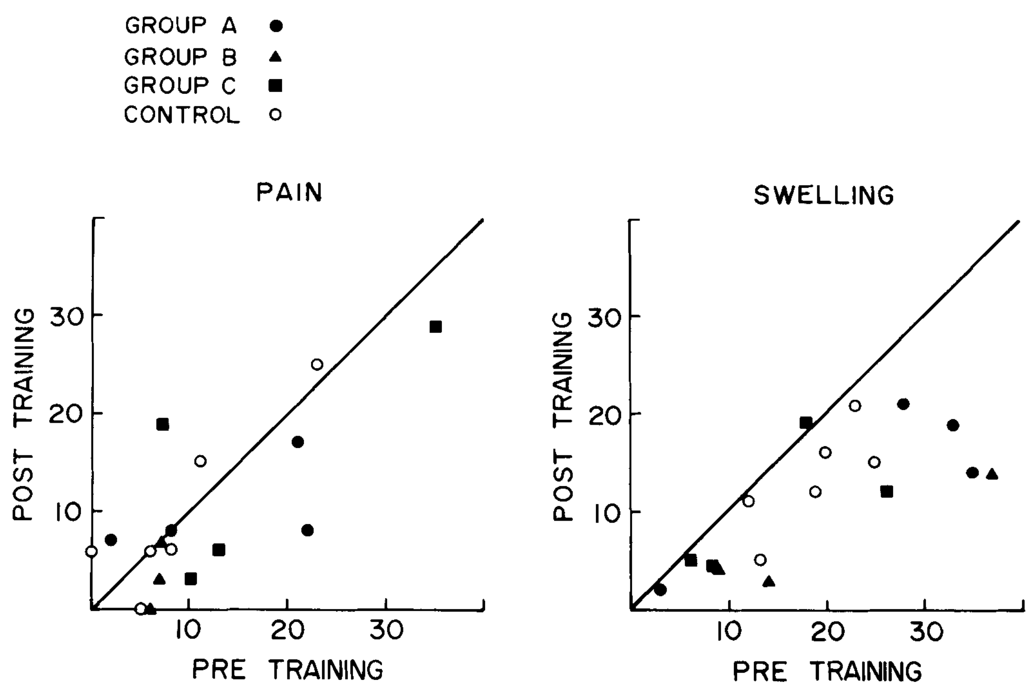

Figure 4. Joint count for each subject, scored for pain and swelling before and after exercise training.

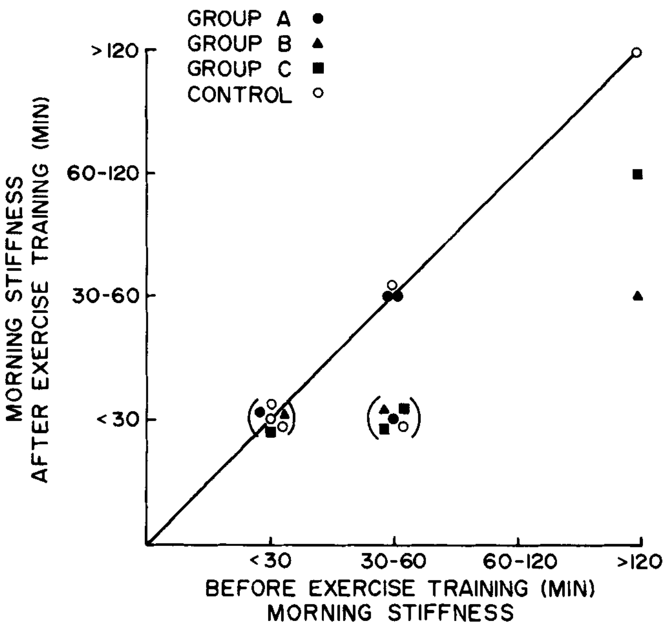

Figure 5. Duration of morning stiffness for each subject. No subject showed an increase in duration of stiffness, and 7 subjects showed a decrease.

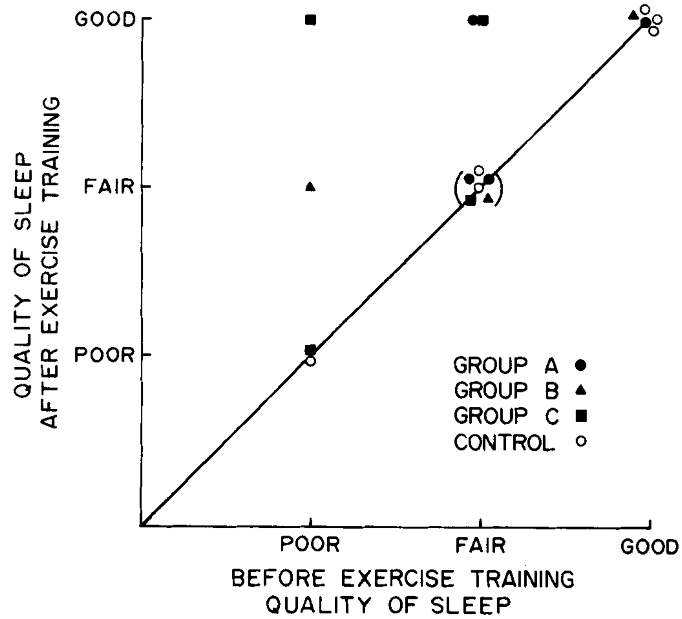

Figure 6. Quality of sleep for each subject. No worsening of sleep pattern was noted during or after training.

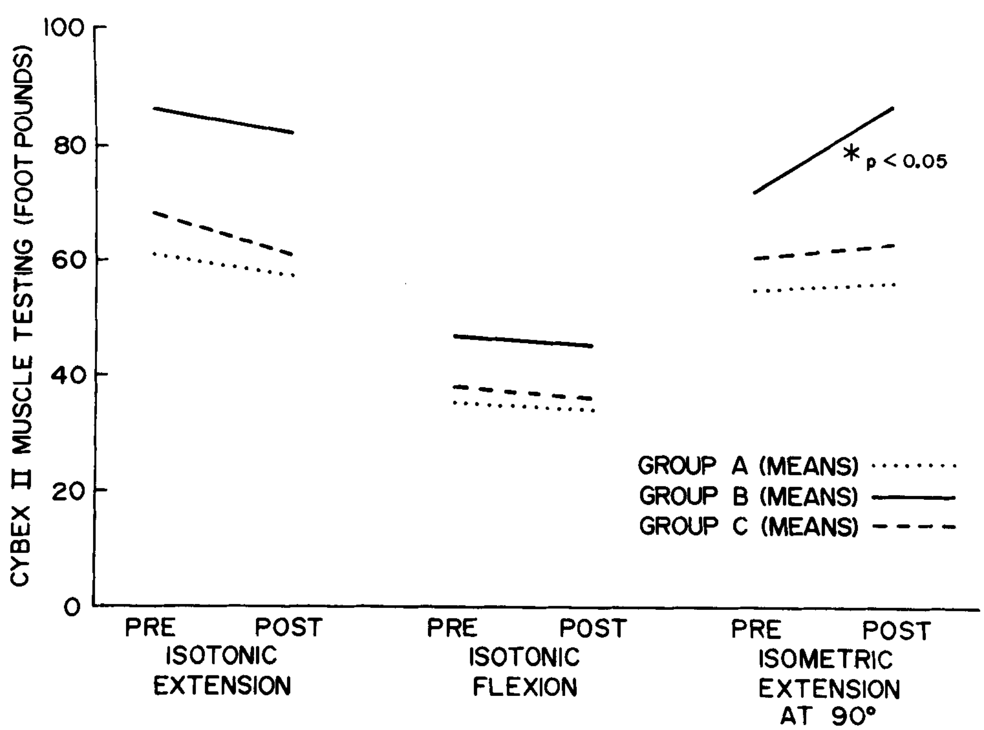

Figure 7. Knee flexors and extensors measured using Cybex II. Group means are shown.

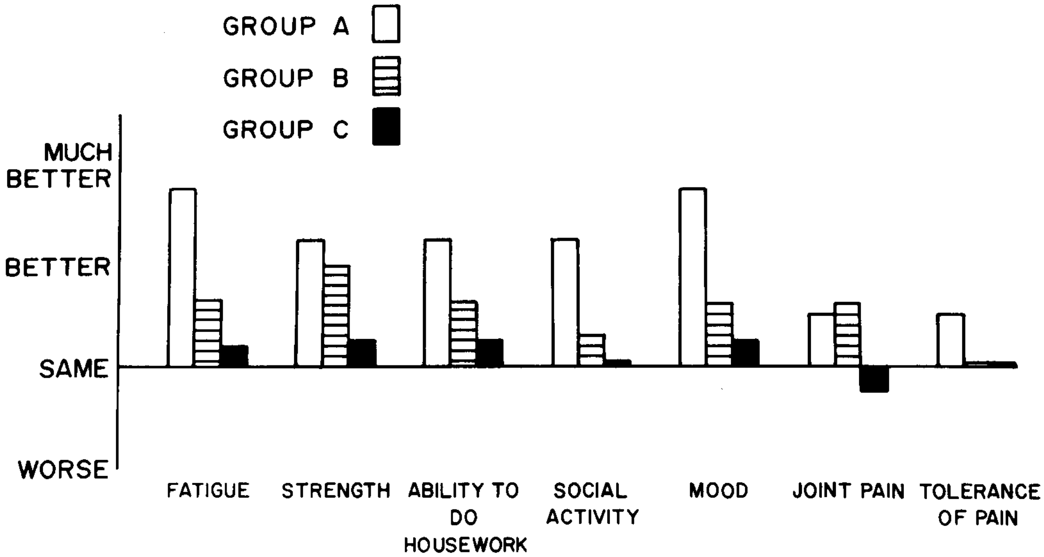

Figure 8. Global assessment by the subjects of changes in categories after completion of exercise training. Numerical assignments made to each level of change. Group means are shown.

Mean joint count decreased from 32.9 to 19.9 ($P < 0.01$); mean aerobic capacity increased from 18.5 to 24.7 ml/kg/minute^{-1} ($P < 0.01$); and mean exercise test time increased from 10.3 to 13.7 minutes ($P < 0.01$). No significant changes were noted for these measures in the control group.

DISCUSSION

In recent years, there has been increasing interest in the role of exercise as a part of various therapeutic programs. Experience with cardiovascular disease has more recently been followed by studies of exercise in chronic obstructive airway disease, diabetes mellitus, and juvenile rheumatoid arthritis (1–5).

Traditionally, and appropriately so, it has been conventional practice to rest inflamed joints and recommend energy conservation to patients with RA. However, it is possible that part of the fatigue and muscle weakness experienced after an acute flare has subsided is because of easily demonstrable poor aerobic capacity, perhaps in association with rheumatoid myositis (21).

This study was designed to evaluate in more specific terms the duration of exercise sufficient to achieve improvements of both an objective and subjective nature, and what duration of exercise might be excessive, causing aggravation of the underlying rheumatic disease. It is recommended that patients with cardiovascular disease exercise for 30 minutes, 3 times/week, at a heart rate of 70–80% of their maximal exercise attainable rates (2). No prior knowledge was available showing whether RA patients require exercise prescriptions similar to those for patients with cardiovascular diseases. Prior studies in RA have not quantified the duration, resistance load, intensity, or progression of exercise, information which is vital to determining a more precise "dosage" of exercise for patients with RA. The exercise protocols devised in this study resulted in increased exercise tolerance and aerobic capacity for all exercising subjects. Our data showed that RA patients initially had low levels of aerobic capacity, which is probably the reason only 15 minutes of exercise per session, the minimum time needed to train normal individuals (19), resulted in significant improvements. It would be expected that continued exercise beyond 12 weeks would cause even greater changes in aerobic capacity and exercise tolerance. The improvements in exercise tolerance were in accordance with improvement in objective scales and subjective comments regarding fatigue and ability to do housework and participate in social activities for longer periods.

In this study the FSI, which was given every 2 weeks and at the end of the study, showed variation in all patients from time to time. Generally, it appeared that the individual tasks evaluated in the index were accomplished without extreme difficulty or had been modified by the subject so that a change in ability to perform these specific tasks was not evident. The difficulty in correlating individual tasks with overall function was noted by Nordemar (10) as well, but changes in our subjects were reflected in more general descriptions, such as in the Global Assessment.

In the final global assessment (Figure 8), the subjects were asked to compare baseline and final self-evaluation of several parameters. Fatigue and general mood were definitely improved and the ability to participate in household and social activities was better for group A and for group B, but with little change for group C. Groups A, B, and C, who exercised 15, 25, and 35 minutes per session, respectively, were able to achieve aerobic, functional, and performance changes without exacerbation of joint discomfort or other symptoms.

The decrease in joint counts in this study was statistically significant for the subjects who exercised, a finding in agreement with those of Beals et al (8) and Ekblom and colleagues (9). The changes in reported pain and/or pain tolerance may be partly responsible for this effect, as well as an overall improvement in the sense of well-being. However, an increase in pain tolerance is not entirely responsible for the decreased counts, as swelling was also noted to be decreased. The role of exercise and its relationship to endogenous opioid peptides such as β endorphins in relief of joint pain remains to be elucidated. This factor may, in part, have influenced these subjective feelings since there is evidence of complex interactions of opioid peptides with exercise training, as well as appetite, thermoregulation, lipolysis, and reproduction (22). An important finding in this study was that all 3 exercise groups tended to have less morning stiffness and maintained or improved their sleep patterns. A concomitant sense of well-being following training may also have caused feelings of improvement, rather than a direct effect on the disease itself. In that our results did show exercise training to be beneficial, further studies need to delineate if this therapy influences synovial fluid and proteoglycan changes and whether it modifies the gelling phenomenon. Changes in pituitary hormones and adrenocortical response to exercise also need to be considered since they may also be responsible for improvements seen in joint count, morning stiffness, and overall enhancement of well-being (23–25).

The lack of improvement in muscle strength probably reflected the methods of training since the program did not involve high intensity isotonic or isometric extension, or flexion exercises that would isolate and specifically train certain muscle groups. Even though the least amount of resistance loading was used in order to avoid exacerbating the joint symptoms, group B still showed an increase in isometric extension at 90°.

A very interesting outcome of this study was the subjective commentary, both solicited and unsolicited, by the participants. In each exercise subject, the responses were uniformly positive, although varied. Comments generally correlated with the global assessment, that fatigue and participation in household, social, and shopping activities improved. The subjects' perceptions of self-image and abilities were better, many being quite surprised at what they could accomplish. The comment was made by several that in spite of control of joint symptoms by medical treatment, their fatigue had not improved until they increased their stamina during the exercise program.

It is apparent from this study that female subjects with nonacute RA in functional class II benefited from regular, supervised aerobic exercise, and this was accomplished without exacerbating joint symptoms. Also of importance is the observation that as little as 15 minutes per session produced improvement in aerobic capacity, exercise tolerance, and sense of well-being. Low intensity aerobic exercise, even at short durations, performed 3 times per week, is beneficial and may be an important adjunct in the long-term treatment of RA.

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