Elderly Rheumatoid Arthritis Patients on Steroid Treatment Tolerate Physical Training Without an Increase in Disease Activity

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ABSTRACT. Lyngberg KK, Harreby M, Bentzen H, Frost B, Danneskiold-Samsøe B. Elderly rheumatoid arthritis patients on steroid treatment tolerate physical training without an increase in disease activity. Arch Phys Med Rehabil 1994;75:1189-95.

• The effects of physical training on elderly, fragile patients with rheumatoid arthritis (RA) who are on low-dose steroids were investigated. The controlled study included 24 patients who had been treated with low-dose steroids for 2 years. Each patient was assigned either to a treatment group receiving training or to an untrained control group. The training took place over a 3-month period and was based on a protocol using progressive interval training consisting of bicycle exercises, heel lifts, and step-climbing. The exercises were performed twice weekly for 45 minutes. Comparison of the two groups showed that disease activity did not increase in the trained group and that fewer, but not significantly fewer, swollen joints were observed in this group ($p = 0.06$). No significant changes were noticed in erythrocyte sedimentation rate, tender joints, or morning stiffness. The work capacity of the trained patients was doubled and the numbers of repetitions increased 76%. Individually adapted exercise programs can therefore be recommended for elderly rheumatoid arthritis patients on steroid treatment.

This study investigated possible changes in physical ability and disease activity when elderly patients with rheumatoid arthritis (RA), treated with low-dose glucocorticoids for at least 2 years, participate in a well-defined physical training program.

Physical training for RA patients, as opposed to rest therapy or bed rest is a matter of controversy.[1-3] Studies of the effects of physical training on moderately active RA patients show beneficial results[4-13] and some even show a decrease in disease activity in the dynamically trained patients.[11-13] Similarly beneficial effects have not been reported as a result of rest therapy or bed rest, in a comparable patient group.[14-17] Only in patients with very active disease have such beneficial effects from bed rest been reported.[14-17] No studies, moreover, have evaluated the effect on RA patients of detraining caused by bed rest. Reactions to immobilization by RA patients are probably similar to those of healthy persons,[18] where the need for training periods to regain physical function after immobilization is well-established.[19]

In general, RA patients die 10 to 15 years earlier than nonafflicted persons.[20] The cause of death may often be cardiovascular disease[20,21] but more often death is not attributable to any specific cause[22] for example, early ageing.[23] Recent studies indicate that a poor functional status is predictive of a higher mortality rate in RA patients.[20,22] In addition, the incidence of arteriosclerosis[24] and osteoporosis[25] is higher in patients receiving steroid treatment than it is in nonsteroid treated patients. Physical training of steroid-treated RA patients may produce beneficial effects similar to those found in other RA patients and in healthy persons.

Physical activity prevents coronary heart disease in healthy persons,[26] whereas training reduces mortality after cardiovascular disease.[27] Aerobic training increases the endogenous steroid production[28-29] and decreases anxiety and pain.[30] In nonsteroid-treated RA patients, physical training increases functional ability,[4-13] decreases disease activity,[11-13] reduces anxiety, depression, and pain,[31] reduces the need for hospital admissions,[7,32] and increases the circulating levels of beta-endorphin, beta-lipotropin, and corticotrophin-releasing factor.[33-34] No training studies have involved only RA patients on corticosteroids, even where the dosage was small, despite their lower muscle strength.[35-36] Steroid-treated RA patients may display both inactivity-induced muscle atrophy as an prednisone-induced myopathy,[36] conditions that can be reversed by physical training.[37]

The purpose of this study was to determine whether elderly patients with RA who were receiving low-dose steroid treatments could benefit and not be harmed by participating in physical training twice weekly over a 3-month period. The subjects were compared with blindly allocated controls. The physical training method had been shown to be effective and safe for nonsteroid-treated patients.[12,38]

METHODS

Approximately 50 RA outpatients (ARA criteria[39]) were on continuous, low-dose oral steroid treatment. The patients accepted for training had slight or moderate disease activity defined by the following four criteria: morning stiffness, erythrocyte sedimentation rate (ESR), painful and swollen

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joints. Table 1 describes the disease activity by median, range, mean, and SD. All the patients had been treated for at least 6 months with corticosteroid treatment, with the dose being unchanged for 3 months. If a disease-modifying drug (DMARD) was being given, the dose remained unchanged for 4 months. Patients with heart disease or a general inability to perform the exercises were excluded and patients with diseases that may cause sudden death, such as aortic stenosis, were excluded. After exclusion, only 24 of the patients, 2 men and 22 women, met the study criteria. The eligible patients were randomly assigned either to the training group or to the nontraining control group. The Helsinki declaration was followed and informed consent was obtained from all patients. Six patients in the trained group were receiving disease-modifying drugs; three were receiving gold; two sulfasalazine; and one penicillamine. In the control group one patient received penicillamine and another received aurothiomalat. None of the patients in either group had ever received pulse therapy. The NSAID treatment was continued unchanged. Patients in both groups received mostly ibuprofen in the form of three 400mg/day, and were allowed to adjust this medication according to need. Five patients, two in the training group and three in the control group, used additional nonprescribed analgetic (aspirin). Patients were allowed to continue with other physical activities that they usually performed, such as heat treatments and exercises in warm water. None of the patients had previously attended aerobic or strenuous strength exercise training.

Training

The training consisted of progressive interval training used in an earlier study.[12] Three exercises were performed, first, the aerobic training in the form of ergometer-bicycling, then the strengthening exercises, heel lifts, and step-climbing, and finally stretching of the trained muscles. The training was done in groups of four persons for 3 months in two weekly training sessions of 45 minutes each. To avoid extreme exhaustion, the number of repetitions was based on each person's individual ability. The heart rate during bicycling increased from 50% to 70% of predicted maximum pulse increment. The pulse increment was defined as the possible heart rate increase from resting heart rate to the age-related maximal heart rate for each person.[40] The 50% heart rate was determined as $\frac{1}{2}$ (maximal heart rate − resting heart rate) + (resting heart rate). The training load was decreased for patients who developed increased joint pain or inflammation. Heart rates, pain, complaints, the number of repetitions during strength training and frictional resistance to pedalling were recorded.

Testing Conditions

All tests of the 24 patients were performed in random order for 2 weeks before and 2 weeks after the training. Persons conducting the tests did not participate in the allocation of the patients, nor did they observe the patients during the training sessions. All patients were instructed not to tell the test persons to which group they belonged. To evaluate the disease activity, morning stiffness, number of swollen joints, number of tender joints, ESR, hemoglobin, trombocytes, and Fries' index[41] score were measured.

Clinical Assessment

All clinical assessments were made by the same rheumatologist, thus avoiding interobserver variations. The patients' functional impairment was classified according to Steinbrocker.[42] Joints were examined for soft tissue swelling, tenderness, and pain during motion. Forty-six joints were examined, the hip and the distal and proximal interphalangeal joints on the lower extremities being excluded. The number of swollen and tender joints was used as a joint count without any corrections or grading.[12]

Laboratory Assessment

Standard laboratory procedures were used for estimation of ESR (modified Westergren mm/h), potassium mmol/L, sodium mmol/L, creatinine mymol/L, hemoglobin gm/dL, leucocytes 10^9/L, thrombocytes 10^9/L, ferritin μg/L, fe μmol/L, and transferrin μmoL/L.

Functional Assessment

The functional abilities tested were, the time taken to walk 30 meters, grip strength, and stair-climbing (heights of 10, 20, 30, 40, and 50cm). Muscle strength was evaluated using the Cybex II Isokinetic Dynamometer[a], recording dynamic peak torque of the right and left knee extensors and ankle plantar flexors, measured isokinetically at an angular velocity of 30° per sec.[35] Aerobic work capacity as a submaximal Åstrand test[43] was measured on a Monark[b] ergometer bicycle starting at a workload of 25W and aiming for a minimum steady heart rate of 120/min and with a maximum heart rate of 80% of maximum increment.

Patients' Assessments

The patients' own assessments consisted of a report of the duration of their morning stiffness and the functional assessment according to Fries' index.[41]

Statistic

The results of this prospective unpaired randomly allocated trial were not all normally distributed and, except for data in table 1, are presented as medians and range. Nonparametric statistics were used in the hypothesis testings, the Wilcoxon signed rank test being used within the group, and the Mann-Whitney U test to compare the two groups. A 5% significance level was selected and the confidence limits of the median were calculated.

RESULTS

The results of our study showed that the physical effects of the training on the patients were beneficial and that the disease activity tended to decrease slightly in the trained group when compared with the control group.

Participation

The two groups of elderly RA patients were statistically comparable at base-line for age, functional class,[42] and duration of disease (table 1). Two patients were excluded from

Table 1: Patient Characteristics of the Two Groups of Steroid-Treated Rheumatoid Arthritis Patients, One Trained and One Untrained Control Group at Base-Line

	Trained Group	Control Group
No. of patients	12	12
Age of patients (yrs)		
Median, range	66 (40-84)	68 (54-80)
Mean, SD	65, ±10.8	68, ±7.2
Duration of disease (yrs)		
Median, range	10.5 (1-33)	7 (2-30)
Mean, SD	12.4, ±11.1	11.7, ±10.1
Morning stiffness (quarter hrs)		
Median, range	2 (0-8)	2 (0-8)
Mean, SD	2.7, ±2.6	2.9, ±3.0
Steinbrocher's functional class		
Median, range	2 (1-3)	2 (2-3)
Mean, SD	1.9, ±0.5	2.1, ±0.3
Swollen joints (number)		
Median, range	5.5 (1-14)	5.5 (0-21)
Mean, SD	5.8, ±3.8	5.6, ±5.6
Tender joints (number)		
Median, range	8.5 (2-29)	10 (0-26)
Mean, SD	11.5, ±9.4	10.4, ±8.2

the training group as one required surgery for an abdominal hernia, and the other patient, an 84-year-old woman, stopped because of her family's negative reaction to her training.

Medication

The medication was comparable in the two groups, both at base-line and after the 3-month study period (table 2), the median in the trained group being 7.5mg compared with 6.25mg in the control group. All patients continued without change in their medication, except for one in the trained group whose steroid medication was decreased from 12.5 to 7.5mg during the study period. Five trained patients and three untrained patients received intramuscular steroid injections of 20 or 40mg. The need for NSAID (ibuprofen) was insignificant lower in trained group at the end of the training period both within the group and compared with the control group.

Assessment of Disease

At base-line, the activity measures were comparable within the two groups, ie, the number of swollen joints ($p = 0.63$), the number of tender joints ($p = 0.77$), duration of morning stiffness ($p = 0.97$), and ESR ($p = 0.77$). The number of swollen joints decreased insignificantly in the trained group compared with the control group ($p = 0.06$)

Table 2: Medication of the Trained and the Untrained Group at Base-Line. Median and Range. All NS

	Steroid	Steroid	DMARD	NSAID
Group	Dose (mg/d)	Duration (yrs)	Gold, Penicillamine, Sulfasalazine	Ibuprofen, Naproxen
Trained	7.5 (2.5-12.5)	2 (.5-20)	6	6
Control	6.25 (3.75-15)	2 (.5-20)	2	7

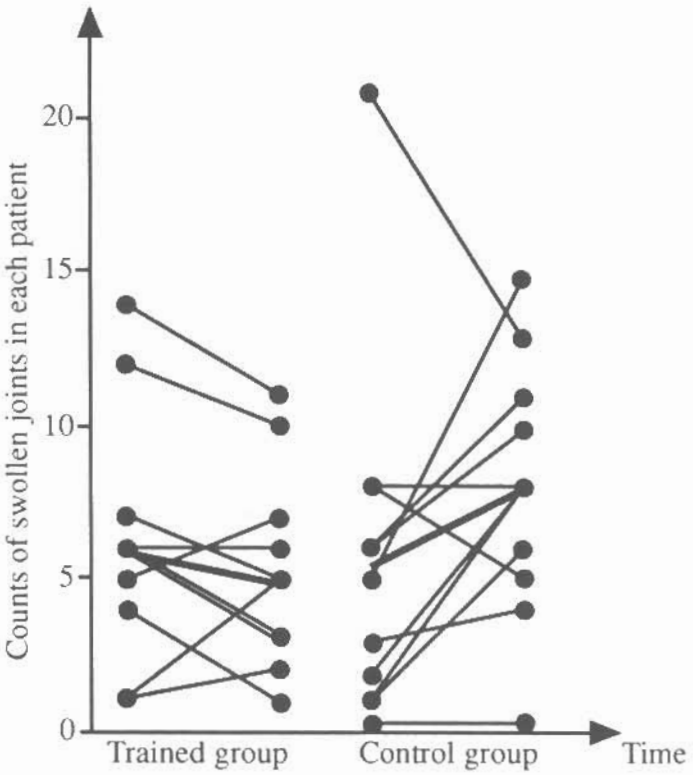

Fig 1—Counts of swollen joints and median in steroid-treated elderly patients with rheumatoid arthritis before and after receiving 3 months' physical training compared with a control group receiving no physical training.

(fig 1). Estimation of the 95% confidence intervals for the median difference of three swollen joints was 0 and 7. The number of swollen weight-bearing knee joints was 8 before and 10 after the study in the trained group, compared with 8 before and 12 after in the control group, whereas there were 5 swollen ankle joints before and 11 after the study in the trained group, and 11 swollen ankle joints before and 16 after in the control group (NS). Insignificant changes were found in morning stiffness (fig 2), the number of tender joints (fig 3), and other patient scores (table 3) in both groups. The laboratory assessment showed that ESR displayed a decreasing tendency ($p = 0.13$) in the trained group compared with the control group (table 4).

Functional Assessment

The number of missed training sessions per patient averaged 2 out of 28. Muscle torque and aerobic capacity were the same in the two groups at the start. During the training sessions the number of repetitions increased 76%. Step-climbing on right leg rose from 20 (9-36) to 36 (21-92), and on left leg it rose from 18 (7-50) to 36 (19-107). The number of heel lifts on right leg rose from 27 (7-39) to 45 (4-75), and on left leg it rose from 27 (7-39) to 45 (4-75). These were all significant increases. The changes in muscle torque at testing show that there was a statistically significant increase in the left plantar flexors and an insignificant change in the right plantar flexors, whereas the change in the knee

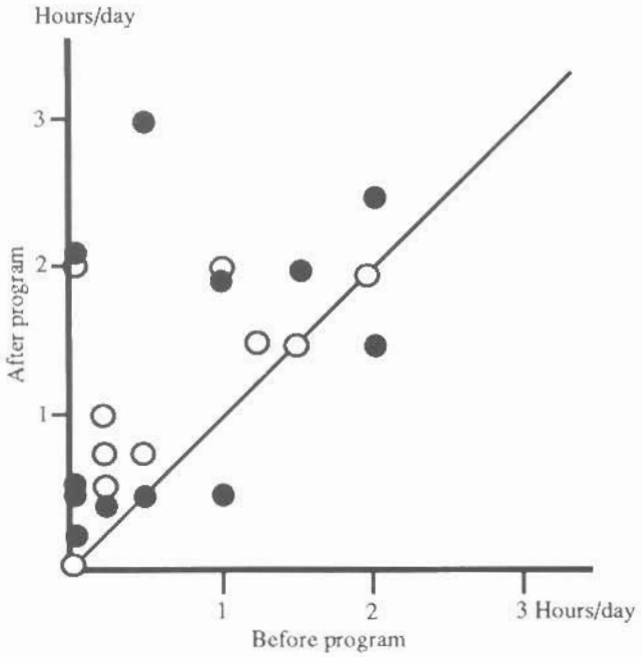

Fig 2—Duration of morning stiffness (hours) in two groups of steroid-treated rheumatoid arthritis patients: a test group undergoing 3-month's physical training program (○) and a control group with no physical training (●).

extensor strength was not impressive (table 5). During bicycling sessions the work intensity increased 100%, from 25W (25-48) at the start to 50W (45-90) at the end of training (Mann Whitney $p = .006$). The heart rate during the training sessions remained unchanged from median 127 (range 110-154) at the start to median 127 (range 107-169) at the end of the exercise periods (Fig 4). The test results of VO_2max showed no increase in oxygen capacity for either group (Mann Whitney $p = 0.67$). Median and range in the trained group before training were 2.6 (1.5-4.2) l/min and 2.7 (1.4-4.6) l/min after training, whereas in the control group the results were 2.8 (1.8-3.9) l per min before training and 2.7 (1.8-4.0) l per min at the end of the 3-month period. We note that our estimated results of VO_2 were much too high as the maximal values for this age group are greater than 2.40 in Åstrand.[40] The aerobic work capacity was evaluated using the adjusted nomogram from I Åstrand.[43] Only 11 patients fulfilled the required criteria during the test, and eight patients had pain resulting in broad variations in heart rate even during rest.

DISCUSSION

Our study showed that elderly RA patients on long-term steroid treatment in Steinbrocker's functional class I-III could endure and benefit from physical training without an increase in disease activity.

The assessment parameters selected to measure changes in disease activity during the study were the number of swollen joints, morning stiffness, the number of tender joints, and ESR. The number of swollen joints decreased insignificantly ($p = .06$) in the trained group compared with the control group. As earlier studies show,[11,12] we found that the joint count for the number of swollen joints was the most sensitive as a parameter for assessing decrease or increase in disease activity.

For the trained group, when compared with the control group, the results showed a tendency, albeit not a significant one, toward a reduction in morning stiffness, ESR, number of tender joints, hemoglobin, trombocytes, Fries' index and grip strength in the right hand (but not for the left hand). It can be concluded from this first study on steroid-treated patents that exercises given to RA patients on a low-dose steroids do not cause increased disease activity. This could be a reason the patients adhered to the training.

There was no correlation in the study between the initial number of swollen joints and the changes found during training, ie, patients with a high number of swollen joints at the start did not differ from those with a low number in their response to the training. In comparing the groups no change in inflammation in the trained knee or ankle joints was found. Slightly increased disease activity was found in both groups particularly in the control group. This finding may be explained by seasonal effects as the study was performed in the autumn and early winter.

The patients' physical abilities increased somewhat during training, although not as much as found in studies with non-steroid treated patients.[12,13] The effect of training on working capacity was clearly shown by a 100% increase. A significant increase was also found in the number of repetitions of step-climbing and heel lifts performed. Muscle torque in the knee extensors and left plantar flexors, VO_2, grip strength, walking speed, and Fries' index showed no significant changes, although a 28% increase was found in muscle torque in the

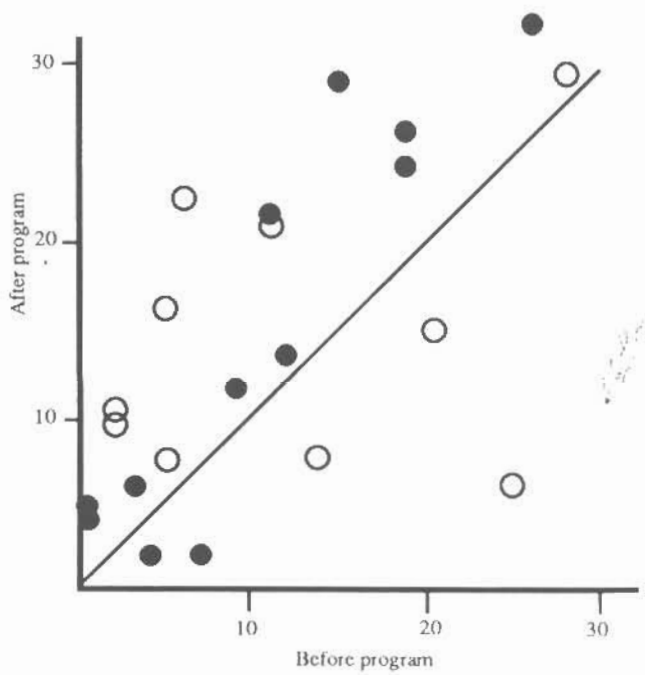

Fig 3—Number of tender joints in two groups of steroid-treated rheumatoid arthritis patients: a test group undergoing a 3-month physical training program (○) and a control group with no physical training (●).

Table 3: Pain and Physical Function in the Two Groups of RA Patients at the Start and at the End of the 3-Month Study. Medians and Range. All NS.

	Trained Group		Control Group	
	Before	After	Before	After
Joint pain numbers	9 (2-29)	13 (4-30)	10 (0-26)	13 (2-36)
Fries' index score	18 (6-30)	16 (0-31)	15 (0-37)	15 (0-49)
Right grip strength (mmHg)	82 (52-157)	82 (50-187)	100 (78-180)	110 (52-205)
Left grip strength (mmHg)	88 (40-187)	87 (30-170)	122 (80-194)	100 (50-180)
Right step height (cm)	45 (10-50)	50 (20-50)	30 (10-40)	20 (10-40)
Time for walking (30 msec $^{-1}$)	27 (16-89)	24 (12-43)	23 (19-30)	25 (20-39)

right plantar flexors of the foot. The training results may be explained by the low training intensity and short training period for this elderly patient group. Longer training periods are usually needed in elderly persons and may be especially necessary for such a fragile patient group.

The endogenous cortisol production increases during aerobic exercises in healthy persons.[28-29] It was therefore possible that the training had caused an increased cortisol production with a corresponding reduced need for corticosteroids in the trained group. However, it was not known whether the aerobic training was of sufficient intensity to increase cortisol production. No steroid-sparing effect was found.

No exercise-related injuries were noticed. Maximal exercise tests of rheumatic patients are not advised by the American College of Sports Medicine,[44] but in our study no heart-related problems were noticed during submaximal tests or when exercising. This could be because the training was moderate and adapted to the individual patient's ability. The exercise protocol consisted of bicycling as a warm-up and as an aerobic exercise followed by a considerable number of repetitions of strength exercises at moderate intensity. The program ended with stretching of the exercised muscles. The program thus consisted of the same kind of exercises for arthritis that have been recommended by Pothier.[45]

One patient with osteoporosis in the trained group developed a compression fracture at home but was able to continue training. Inactivity[46] or low-dose prednisone therapy may increase the frequency of vertebral spine compression fractures.[47-48] As exercise programs have been shown to increase bone mass in postmenopausal healthy women,[49] the osteoporotic RA patient continued the training.

Submaximal exercises tests were found not to be suitable for this group of patients. This could be because the patients were extremely deconditioned and therefore had higher heart rates at start of project than later compared with healthy persons as found by Piha.[50] The patients had difficulty staying on a high exercise level for the 5 to 7 minutes to achieve a steady state result. Pain also increases the heart rate. To achieve the most reliable test-result, we recommend that the specific performed exercise performed is measured.

Friis[51] postulates that early aging is preventable because cardiac reserve, pulmonary reserve, physical strength, and physical endurance are trainable. In adults, exercise reduces the risk of coronary heart disease,[26] conserves bone mass after the menopause,[49] increases HDL which is important for arteriosclerosis,[52] and decreases all-cause mortality.[53] During our study both the working capacity and the number of repetitions performed were increased. Whether these improvements in functional status can predict any increase in expected life-length is still unknown, but in two long-term studies a poor functional status was correlated with increased mortality[20,22] especially in steroid treated patients.[54]

The problem of defining which patients should be prescribed bed rest and which should perform exercises is now closer to a solution. In the Alexander study,[14] the patients' responses to bed rest treatment were evaluated according to disease activity. The patients with the least disease activity had deteriorated during the study period. Conversely, the patients with the greatest disease activity, defined as evaluation index, articular index, morning stiffness, and visual analogue score improved significantly after rest therapy. Other studies show the same results.[15-17] In Lee's[55] study in which only very active patients were included, the response was a significant improvement for 50% of the patients after bed rest and hospitalization, compared with a control group treated as outpatients.

Exercises that improve physical strength or condition may therefore only be prescribed when the acute disease activity diminishes as agreed by Hicks.[56] Early mobilization can especially be advised for juvenile RA patents on steroid treatment.[57]

This first study with only steroid treated patients showed the same result as have former studies on nonsteroid treated patients,[11-13,58] the fear of increasing disease activity by exercising moderately active RA patients has been exaggerated and that exercise programs should be based on the individual

Table 4: The Hematologic Results at Start and End of the 3-Month Study in Trained and Untrained RA Patients. Medians and Range. All NS

	Trained Group		Control Group	
	Before	After	Before	After
ESR (mm/h)	33 (2-97)	22 (2-60)	17 (6-48)	23 (6-50)
Thrombocytes (10^9/L)	372 (203-584)	352 (279-597)	358 (171-440)	361 (176-458)
Hemoglobin (g/dL)	13.0 (11.7-14.8)	13.2 (11.1-14.8)	13.0 (10.6-15.6)	12.6 (10.6-15.2)

Table 5: Muscle Torque in the Right and Left Foot Plantar Flexors and the Knee Extensors Before and After the Training Period in the Trained and Control Groups Measured Isokinetically at an Angular Velocity of 30° per sec. Median and Range. Mann Whitney *p*, for Difference Between the Two Groups in the Change in Torque (Before/After)

	Trained Group		Control Group		
	Before	After	Before	After	*p*
Right ankle (Nm)	35 (9-80)	45 (23-68)	26 (20-62)	25 (5-42)	0,06
Left ankle (Nm)	28 (10-54)	26 (6-41)	41 (21-94)	22 (3-42)	0,04
Right knee (Nm)	89 (37-174)	86 (37-174)	76 (20-112)	46 (7-98)	0,09
Left knee (Nm)	69 (32-133)	66 (37-183)	74 (32-137)	62 (11-132)	0,22

patient's own functional ability.[38] Long-term (2- and 4-year) training studies have now confirmed that no deterioration occurs in the joints during training.[32,59] However, the effectiveness of training was only slight.

The mechanism by which bed rest effects RA patients may be a sparing effect on the paretic limb emanating from the nervous system.[60] The effect of exercising may be caused by stimulating of the immune system[61-62] or hormonal system.[33-34]

Several questions need to be answered. How do we define which RA patients to exercise? Do patients with other connective tissue diseases respond in the same way? Which exercises should be preferred, aerobic or strengthening exercises? How intensively should patients exercise?

Our study showed that this mild program of physical training could be safely recommended for the treatment of elderly low-dose steroid patients especially where there is moderate disease activity. The effect obtained after 3 months of training was a 100% increase in working capacity and a 76% increase in the numbers of repetitions.

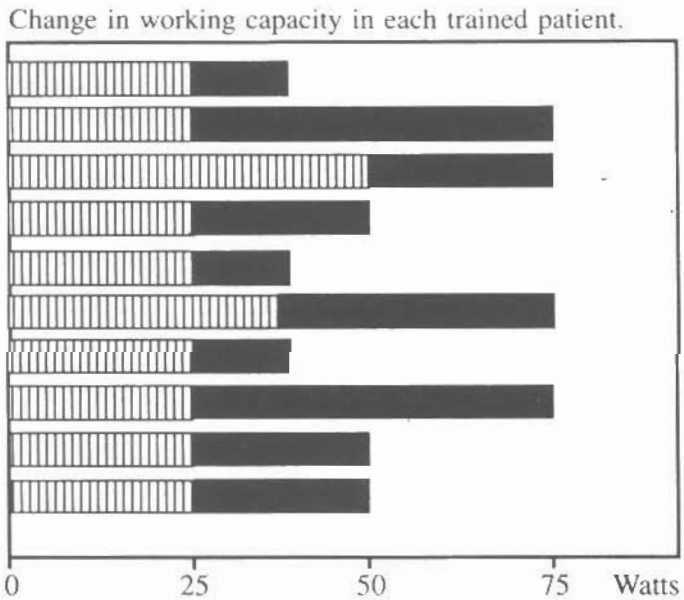

Fig 4—The working capacity, expressed as the intensity at which the patients trained at same HR, increased 100%, range 50% to 200%, in steroid-treated RA-patients. Working capacity in the individual patients at start ▥, and at completion of training ■.

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Suppliers

a. Cybex II Isokinetic Dynamometer, Lumex Incorporated, New York.
b. Monark ergometer bicycle, AB, 43282 Varberg, Sverige.