Longterm Physical Training in Rheumatoid Arthritis. A Randomized Trial with Different Training Programs and Blinded Observers

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The objective was to study the long-term effect (2 years) of different training programs in patients with rheumatoid arthritis.
The method was a randomized trial with 75 patients participating. The measured variables included morning stiffness, a pain score, number of swollen joints, a health assessment score, a functional score, ESR, Hb, the cost of medicine, and progression using X-rays of hands and feet.
The results showed no effect of training on the disease activity or on the progression of the disease.
The conclusion is that although most patients are in favour of training, the present study does not support that training lessons per se affect the disease activity or the progression of the disease.

Key words: physical training, rheumatoid arthritis, disease activity, X-ray score

Several studies (1, 2, 3) have shown that patients with rheumatoid arthritis (RA) may increase physical performance, aerobic capacity and muscle strength through physical training. In some studies the disease activity decreased after 2–3 months of training (2, 4) while in others it was unchanged (1, 3). Considering the duration of this chronic disease, the majority of studies have insufficient duration of observation. Nordemar (5, 6) claimed that RA patients who did physical training regularly during a period from 4–8 years had less progression of their disease than non-trained patients. The patients, however, were allowed to change from one group to another during the study, which may have influenced the results. In a recent long-term study (7), which included once-weekly intensive dynamic training in water, the only significant effects were a better grip strength of the right hands and fewer admittances for acute hospital care. However, also in this study the selection procedure may have influenced the results.

It is still unknown whether or not patients will benefit from a long-lasting training program, and which – if any – of the various approaches are preferable.

Our investigation was planned to elucidate these questions in a 2 year long, randomized, prospective study, using a blinded observer.

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Materials and Methods

The patients

King Christian X's Hospital is the only Department of Rheumatology in the county of South Jutland, serving approximately 250.000 inhabitants. Around 700 patients with RA are regularly seen at the hospital. All patients with definite or classical RA according to the ARA criteria (8) were asked to take part in the study provided that none of the exclusion criteria were present.

Exclusion criteria:
1. Functional stadium III and IV (9).
2. Age < 20 or > 60 years.
3. Diseases other than RA which contraindicated or made physical training impossible.
4. Already training 3 times a week or more.

The study was conducted in accordance with the second Declaration of Helsinki, and approved by the local ethical committee. Informed consent was obtained from all participating patients. Patients with functional stadium III and IV were excluded to ensure that the patients could meet the training demands.

A total of 75 patients were eligible for the study. There were 49 females and 26 males. The median age was 52 years (range 20–60). Thirty patients were working while 45 were unable to work or unemployed. The patients were allocated at random to one of 5 treatments:

A. Self training after instruction in the training program.
B. As A. plus training with a physiotherapist in general practice once a week.
C. As A. plus weekly group training in the hospital.
D. As C. but including training in a hot water pool.
E. No instruction in training.

Table I. Demografic data at start of the study.

Self training	Training in phys. practice	Group training	Group training + pool	No training
n = 15	n = 15	n = 15	n = 15	n = 15
Age of patients (medians with 25/75 percentiles)				
55 (44/58)	52 (46/58)	51 (42/56)	54 (44/56)	51 (46/57)
Sex (female/male)				
12/3	7/8	9/6	11/4	10/5
Disease duration (medians with 25/75 percentiles)				
7 (5/9)	7 (3/16)	7 (5/11)	5 (4/9)	8 (5/11)
Numbers with positive rheumatoid factor				
11	13	13	11	14
Numbers with erosions on X-rays				
12	13	15	12	14
Numbers on slow-acting drugs during the study				
10	11	11	9	11
Numbers on glucocorticoids				
0	1	1	1	1

The demografic data of the patients are given in Table I. The training groups B, C, and D were chosen because they represent the 3 types of training offered to RA patients by the Danish health system.

Training program

All patients in the groups A, B, C and D were given a written instruction in a 15 minutes overall training program. They were asked to do the exercises daily, followed by 30 minutes of conditioning training e.g. swimming, cycling, running or jogging. The minimum training should be 3 times a week with a maximum of 90 minutes daily and 330 minutes a week. The training intensity might be decreased if it caused severe pain or joint swelling. The patients were asked to keep a diary of their daily training and at the end of the trial they were asked to answer a questionaire about the amount of training they had done and about their physical activities in general.

The patients in group B met weekly in a physiotherapist practice where they did the 15 minutes standard program, followed by 15 min conditioning training on a bicycle, followed by 15 min of relaxation. The conditioning training on the bicycle was given in 4 periods of 4 minutes with 1 minute of relaxation in between. The patients should cykle with a revolution of 50 per minute and with a resistance which caused a pulse rate of 70% of maximum.

The patients in group C were trained weekly in the hospital in groups of maximum 5 persons. Otherwise they followed the same program as the patients in group B.

The patients in group D were trained in hospital like group C but used the hot water pool instead of bicycles for conditioning training. They were asked to swim or walk as fast as possible for 3 periods of 4 minutes each. The pool was 1.25 m deep and the temperature 35°C.

The patients in group E were not informed of the training program and served as a non-training control group.

Investigations

All the patients were examined by the same doctor and physiotherapist who were blinded with respect to the patients' training. The patients were told not to inform the examiner about their training.

Every third month the patients were examined by the doctor. The following variables were recorded:

1. Duration of morning stiffness in minutes.
2. Joint pain on a 10 cm long visual analogue scale.
3. The number of swollen joints (max. 40).
4. The medical treatment given and the patients' medicine expenses.
5. Health Assessment Questionaire (HAQ) score (10).
6. Erythrocyte sedimentation rate and blood-hemoglobin.

Every sixth month the patients were examined by the physiotherapist. The following variables were recorded:

1. Assessment of aerobic fitness as shown by Åstrand (11) by the use of a bicycle ergometer.
2. A functional score, with a range from 0–5 for each of 26 joints, 0 = normal function, 5 = no function left (12).
3. The maximum isometric muscle strength of the knee extensors, the elbow extensors and the shoulder abductors. The strength was measured in Kp by using a spring balance while the patients kept their knees in 75° flexion, the elbows

Table II. Medians and 25/75 percentiles at baseline and after 24 months according to treatment.

Month	Self training n = 14	Training in phys. practice n = 14	Group training n = 11	Group training + pool n = 13	No training n = 13
			ESR (mm)		
0	35	28	20	22	23
	13/46	14/32	6/42	14/27	12/32
24	22	19	17	16	28
	10/49	12/33	7/59	8/30	13/53
			Hb (mmol/l)		
0	7.0	8.0	8.0	8.0	8.0
	7.0/8.0	7.0/8.3	6.0/8.0	7.0/8.0	7.0/8.0
24	7.0	8.0	8.0	8.0	8.0
	7.0/9.0	7.0/9.0	7.0/9.0	8.0/8.0	7.0/8.0
			Number of swollen joints (0–40)		
0	3.5	3.2	2.3	3.6	3.8
	1.3/5.8	2.8/6.3	1.0/5.6	1.5/4.5	0.5/6.5
24	3.5	3.5	4.8	2.1	5.3
	0.2/6.5	0.4/5.8	0.4/8.0	1.1/5.9	0.3/12.5
			Pain score (0–10)		
0	1.6	1.8	1.9	1.9	1.9
	1.0/2.1	1.1/2.6	1.2/2.6	1.5/2.2	1.5/2.3
24	1.4	1.9	2.1	1.4	1.9
	0.9/2.0	1.4/2.3	1.6/2.6	0.9/2.5	1.1/2.3
			Morning stiffness (min)		
0	43	35	30	60	60
	11/60	4/60	10/60	25/90	13/80
24	30	30	20	20	60
	0/38	0/64	0/30	15/45	5/90
			HAQ-score (0–3)		
0	0.63	0.57	0.50	0.75	0.50
	0.38/0.88	0.35/0.88	0.50/0.75	0.47/0.94	0.13/0.88
24	0.25	0.69	0.87	0.50	0.62
	0.12/0.75	0.44/1.15	0.11/1.25	0.18/1.00	0.50/1.06
			X-ray score (0–130)		
0	40	49	37	33	68
*	13/79	30/62	17/76	17/85	58/89
24	50	56	46	48	74
	15/86	35/84	32/89	22/88	65/97
			Functional score (0–130)		
0	40	41	30	41	49
**	27/56	27/53	21/47	24/57	39/60
24	41	50	34	44	61
	29/64	36/60	26/50	20/81	50/69
			Max. isometric muscle strength of knee extensors (kp)		
0	29	40	31	34	29
**	24/44	24/55	26/38	22/42	19/35
24	38	63	57	54	45
	32/52	49/79	32/63	37/69	28/51
			Aerobic fitness (Watts)		
0	29	32	41	32	34
	26/37	30/35	34/44	27/38	30/40
24	26	28	36	31	29
	25/34	24/31	32/42	25/35	27/35
			Medicine cost/3 month (DKr)		
0	325	300	350	290	400
24	195/450	155/575	200/400	180/600	175/525
0	205	410	400	340	450
24	135/310	225/625	250/450	230/500	75/645

No statistically significant differences between the treatments.
* $P_{time} < 0.05$. ** $P_{time} < 0.01$.

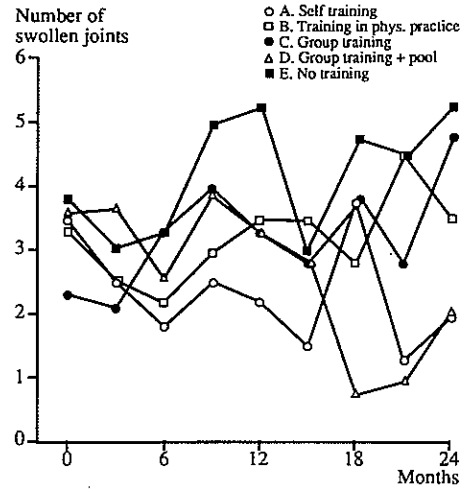

Fig. 1. The medians of number of swollen joints during 24 months according to treatment.

in 90° flexion and the shoulders in 15° abduction position.

Every twelth month an X-ray was taken of hands, wrists and feet. A score from 0–5 was given for each joint (0 = normal, 5 = maximum mutilating destructions) as described by Larsen (13). The X-rays were evaluated by a blinded roentgenologist.

After the end of the trial all patients answered a questionaire on their subjective evaluation of the training, and they were interviewed about their physical activities during the study. The physical activities were given scores from 0 to 6, where 0 = very low activity and 6 = maximum activity for each of 3 categories (housework, job, and sport) (14). A similar score (0–6) were used for the patients' reports on the physical training they performed during the study.

Statistical methods

Because some data were on ordinal measurement scales, the principal statistical method was a non-parametric model corresponding to the usual parametric two-way analysis of variance. The factors were time (repeated measures) and treatments. The model included a test for interaction between time and treatment, i.e. an evaluation with regard to the possibility that relationships between treatments were not constant through 24 months of observation.

Results

Out of the 75 patients 6 were lost to follow up, and in 4 patients the data at month 24 were incomplete. The data thus include the results from 65 patients. The attendance rate to the training sessions was > 50% for 6/14 in group B, 6/11 in group C, and 9/13 in group D.

There were no statistically significant effect of the training on any of the measured variables (Table II, fig. 1, and fig. 2). The results were the same if all patients were included or only those with an attendance rate of >50%. There was a progression with the time in joint destructions seen on X-rays and in the measured functional scores irrespectivly the type of treatment. The muscle strength increased with time in all groups although there was no change in the aerobic fitness.

In group A, 1 patient had a synovectomy and 3 patients had 3 intraarticular steroid injections during the 2 years. In group B, 2 patients had synovectomies, 1 patient a knee replacement and 6 patients had a total of 16 intraarticular steroid injections. In group C, 2 had foot operations and 3 had a total of 7 intraarticular steroid injections. In group D, 2 had synovectomies, 1 a knee replacement and 1 a foot operation. Six patients had a total of 10 intraarticular steroid injections. In group E, 1 had a synovectomy and 2 had foot operations. Only 1 patient had an intraarticular steroid injection.

The questionaire and interview after the trial indicated that 66% of all patients experienced a general improvement of disease activity or activity of daily living (Table III). Some patients found the training so inspirering that they engaged in new activities such as pony-riding, table-tennis etc. Twentyfive % would even like to intensify the treatment further, while only 6% would decrease the given training intensity. However, there were no statistically significant differences between the groups.

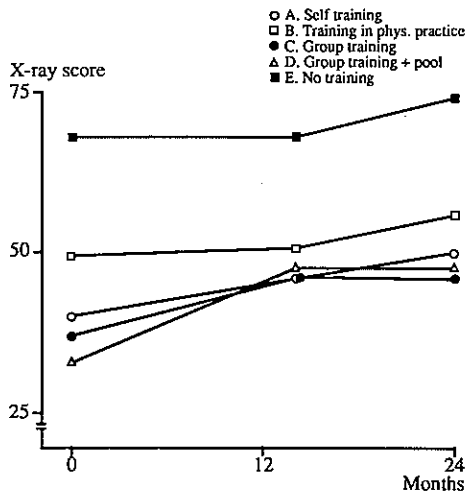

Fig. 2. The medians of X-ray score during 24 months according to treatment.

Table III. Patient questionaire about physical activities and the effect of the 2 year training program.

	Self training	Training in phys. practice	Group training	Group training + pool	No training
Followed training instructions?					
Yes	10	8	10	10	
No	4	3	1	3	
Unanswered		3			
Has the arthritis become:					
Much better	6	0	3	1	3
Little better	4	1	4	6	4
Unchanged	2	4	3	5	4
Little worse	2	5	1	1	2
Much worse	0	1	0	0	0
Has the general well-being improved?					
Yes	11	8	9	10	8
No	0	2	1	1	1
Don't know	3	1	1	2	4
Do you want to continue training?					
Yes, harder	4	0	6	1	6
Yes, unchanged	8	10	5	11	6
Yes, but less	2	1	0	0	0
No	0	0	0	1	1
Physical activity score (0–18) Medians (25/75 percentiles)	6.5 (3.4/7.3)	5.7 (3.9/7.0)	7.7 (6.0/8.6)	5.8 (4.8/7.1)	5.6 (3.5/6.3)
Exercise score (0–6) Medians (25/75 percentiles)	2.8 (2.1/3.3)	2.8 (1.9/3.3)	3.7 (2.9/4.6)	2.9 (2.3/3.5)	2.4* (1.8/3.0)

* $P_{treatment} < 0.05$.

Discussion

The effect of long-term physical exercises in RA is still questionable (15). Nordemar et al. (5, 6) claimed that training for a period of 4–8 years could inhibit the progression of X-ray changes, but they only examined the joints in the lower extremities which had ever shown any arthritic symptoms. Their study was invalidated by the fact that some patients were changed from the training group to the control group and vice versa after randomization.

It is interesting that our study showed no effect whatsoever on any of the measured variables, even when those patients who participated in less than 50% of the training lessons were excluded. It can be argued that the number of patients in each group was relatively small. The use of a 2-way analysis of variance on the results from the 65 patients, however, should have detected any clinically significant effect of training during the 2 year study. It could be argued that the patients in the no training group in fact did some self training as they had the same aerobic fittness as the patients in the training groups and showed the same increase in isometric muscle strength (Table II). However, the self reported exercise score was smaller in the no training group in comparison to the training groups (Table III). The lack of a detectable effect could also be due to an insufficient type or intensity of the training, but only 7 out of the 35 patients who went to weekly training sessions, wanted to continue with harder training (Table III). It thus seems unrealistic to introduce harder training as a long-term general treatment to all RA patients.

The apparent discrepancy between the present results and that of others (2, 4, 5, 6) may be explained by the long duration of the study, the true randomization and the omission of a selection of patients who were specially motivated for training. Most studies have been of relatively short duration (a few months) where the enthusiasm of the patients and the health professionals may have influenced the outcome. This does not reflect the true outcome in a chronic disease like RA.

It is possible that individually selected exercises would help some patients with specific problems, but the material was too small to study subgroups of patients with different outcomes. The statistical power was limited due to the small amount of patients. Accordingly minor differences may have been overlooked.

The increase in muscle strength after 24 months (Table II) seemed unrelated to the training which was given. This may reflect an effect of self training even in the group of patients who were not

given a specific training program. It is also possible, however, that the investigating physiotherapist, unaware of the patient groups, may have registered a higher score of muscle strength in all groups during the study by stimulating the patients to a better performance. It is thus noticable that the aerobic fittness did not increase (Table II).

Dynamic training may be superior to static training (16), and conditioning exercises may be superior to strengthening exercises (3). Exercise may increase intra-articular pressure, and repeated forceful muscle contractions have been associated with the formation of cysts in juxta-articular bone in RA (17). Thus, several years of training involving actively inflamed joints could be harmful and accelerate the erosive tendency. In our study a significant progression of joint erosions was found in all the five groups of patients, irrespectively of what type of training they received or if they did no training. Long-term training programs seem not to be harmful to inflamed joints, – neither do they seem to be helpful.

We focused on clinical disease activity markers such as joint pain and swelling, X-rays, and on laboratory values like ESR and Hb. They may, however, not be the true outcome measures of the effect of training. We found a discrepancy between the lack of treatment effect on these variables and the fact that most patients generally felt improvement. Outcome measures concerning quality of life, depression and anxiety may have been better suited to detect the general satisfaction of the patients (3). Harcom et al. (2) have shown that physical training improve fatique and the general feeling of well-beeing, which may be a better outcome measure than conventional variables used in studies of different drug treatments.

Whether the large amount of money currently beeing spent on exercise programs and hot water pools is truly cost-effective is still an unanswered question. We need more studies to elucidate which type of exercises should be given to which type of patients and what the long-term effect is.

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