High or Low Intensity Aerobic Fitness Training in Fibromyalgia: Does It Matter?

MARIJKE van SANTEN, PAULIEN BOLWIJN, ROBERT LANDEWÉ, FRANS VERSTAPPEN, CARLA BAKKER, ALITA HIDDING, DÉSIRÉE van der HEIJDE, HARRY HOUBEN, SJEF van der LINDEN

ABSTRACT. ***Objective.*** To determine the efficacy of training in fibromyalgia (FM), we compared the effects of high intensity fitness training (HIF) and low intensity fitness training (LIF).

Methods. Thirty-seven female patients with FM were randomly allocated to either a HIF group (n = 19) or a LIF group (n = 18). Four patients (1 HIF group, 3 LIF group) refused to participate after randomization but before the start of the intervention. They were excluded from the analysis. Assessments were performed at baseline and after 20 weeks of HIF or LIF. The primary outcome was patient's global assessment [on 100 mm visual analog scale (VAS)]. Secondary endpoints were pain, number of tender points, total myalgic score, physical fitness, health status, and psychological distress.

Results. One patient in the HIF group (n = 18) and 2 in the LIF group (n = 15) stopped training sessions during the course of the study. Nine of 18 patients in the HIF group compared to 8 of 15 patients in the LIF group achieved a participation rate of 67% or more. Most important reasons for nonadherence were postexercise pain and fatigue, time consumption, and stress. The VAS for global well being improved slightly from 64 to 56 mm in the HIF group, and did not change in the LIF group (58 to 61 mm) (p = 0.07). The W_{max} (physical fitness) changed modestly from 110 to 123 watt in the HIF group, and from 97 to 103 watt in the LIF group (p = 0.3). VAS for pain increased from 53 to 64 mm in the HIF group and from 52 to 54 mm in the LIF group. The large standard deviations around mean change in global assessments, number of tender points, total myalgic score, and psychological distress (by SCL-90) severely influenced the power to detect within- and between-group differences. Analysis limited to those patients who accomplished a high attendance rate (> 67%) showed similar results.

Conclusion. High intensity physical fitness training compared to low intensity physical fitness training leads to only modest improvements in physical fitness and general well being in patients with FM, and does not positively affect psychological status and general health. (J Rheumatol 2002;29:582–7)

Key Indexing Terms:
FIBROMYALGIA
PHYSICAL FITNESS
RANDOMIZED CLINICAL TRIAL
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Fibromyalgia (FM) is a common condition of unknown etiology characterized by chronic, widespread musculoskeletal pain and tenderness at specific anatomic locations. Treatment is often considered unsatisfactory, although fitness training appeared to be effective in relieving some symptoms of FM[1-11]. However, high dropout rates[2,4,9] and different outcome measurement techniques[1,8] used in these studies interfere with a valid judgment about the merits of fitness training as a therapeutic modality for FM. In a randomized clinical trial (RCT) we have shown that fitness training was not better than either biofeedback or usual medical care[11]. A possible fallacy of this trial was that it failed to reveal any aerobic training effect after 24 weeks of training, which may imply that positive effects on well being could not be expected at all[12].

The only RCT of efficacy of high intensity fitness training (HIF) thus far measured a 25% increase in physical fitness and a 50% improvement in global well being after 20 weeks of training[1]. Based on these positive findings, the primary hypothesis of this study was that HIF in patients with FM will lead to a measurable improvement of physical fitness, along with an improvement of global well being, pain, and health status.

From the Department of Internal Medicine, Division of Rheumatology, University Hospital, Maastricht; University of Limburg, Maastricht; Department of Rheumatology, Atrium Medical Center, Heerlen; and Institute for Rehabilitation Research, Hoensbroek, The Netherlands.

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M. van Santen-Hoeufft, MD, Rheumatologist; C. Bakker, MSc, PhD; D. van der Heijde, MD, Professor of Rheumatology; S. van der Linden, MD, Professor of Rheumatology, Division of Rheumatology, University Hospital, Maastricht; P. Bolwijn, MSc; F. Verstappen, MD, PhD; H. Houben, MD, PhD, Consultant Rheumatologist, University of Limburg; R. Landewé, MD, PhD, Rheumatologist, University Hospital, Maastricht, Atrium Medical Center, Heerlen; A. Hidding, MSc, PhD, Senior Researcher, Institute for Rehabilitation Research, Hoensbroek.

Address reprint requests to Dr. M. van Santen-Hoeufft, Department of Internal Medicine, Division of Rheumatology, University Hospital Maastricht, PO Box 5800, NL-6202-AZ, Maastricht, The Netherlands. E-mail: msa@sint.azm.nl

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We decided to copy the high intensity fitness protocol described by McCain, *et al*[1], and to compare it with low intensity fitness training (LIF), as described[11]. We report the results of a RCT in which the effects of HIF were compared to the effects of LIF in female patients with FM.

MATERIALS AND METHODS

Recruitment of patients. Patients were recruited from a central registry for the diagnosis of rheumatic diseases. Within one year the department of rheumatology in Maastricht had assembled 163 patients with a clinical diagnosis of FM (20% of all newly referred outpatients). For practical reasons only female patients aged 18 to 60 years and living within 30 km from Maastricht were invited to participate. Additional prescreening of the 128 medical case records left was performed to exclude subjects with known cardiopulmonary (n = 1) or psychiatric comorbidity (n = 4). The remaining 123 patients were informed about the study, in which it was clearly stated that the interventions might be arduous and time consuming. This proved to be the most frequently stated reason to refrain from participation: only 43 patients gave written informed consent. Before the study patients were seen by one of us (MvS) to confirm a diagnosis of FM according to the American College of Rheumatology (ACR) criteria[13] and to check for any exclusion criteria (ischemic heart disease, arrhythmia, exercise induced asthma, unsettled disability compensation disputes, or incapacitating psychological distress). Four patients did not meet the ACR criteria for FM, one was excluded because of a psychiatric score on the Symptom Checklist-90-Revised (SCL-90R), and one patient was not able to spend the time required. A total of 37 patients were eligible for the study (Figure 1).

Study design. The 37 eligible patients were randomized to either a high intensity physical fitness group (n = 19) or to a low intensity group (n = 18). All patients were allowed to continue their basic treatment (medication, physiotherapy).

Fitness training. *Low intensity training*. Participants who were to receive LIF were coached together by one professional female instructor. They trained in a private fitness center twice weekly under close supervision by the instructor during 60 min for 20 consecutive weeks. Subjects were encouraged to exercise during an additional third, unsupervised, 60 min weekly session and to use the sauna and/or swimming pool after all the sessions. Each session comprised a 10 min warmup period with aerobic exercises and postural muscle stretching, followed by intensive aerobic exercises alternating with general flexibility and balance exercises for 30 min. Thereafter, isometric muscle strengthening was done (10 min), followed by a cooling-down period with aerobic, stretching and relaxation exercises (10 min). This protocol is in accord with the guidelines of the American College of Sports Medicine to develop and maintain cardiorespiratory and muscular fitness[14]. It should be noted, however, that the training intensity was left up to each patient. That is, an individual patient was allowed to stop or interrupt this process of exercising whenever she felt too tired or experienced too much pain.

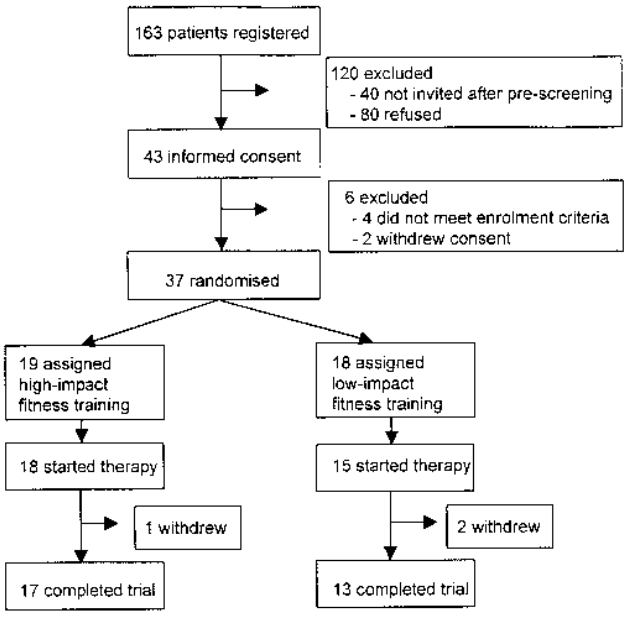

Figure 1. The fitness training trial profile.

High intensity training. The participants allocated to HIF were divided into 2 subgroups. Each group exercised 3 times weekly for 60 min at the physical therapy exercise room of the University Hospital of Maastricht. Each session was guided by 2 physiotherapists who were instructed to encourage the patients during the training sessions to increase the individual training intensity as much as possible. Warmup consisted of 10 to 15 min of ball games and stretching exercises of lower extremities. The remaining 45 min per session was used for bicycling on an ergometer. According to the high intensity protocol used by McCain, *et al*[1] the ultimate goal was to subject patients to sustained heart rate elevation training to aim at a maintenance heart rate above 150 beats per minute for at least 20 to 30 min using a bicycle ergometer. We corrected for age and stated that training intensity should at least reach and maintain a heart rate level of 70% of the maximum heart rate achieved on the baseline graded exercise test. Monitoring of the heart rate was done by a digital pulse meter.

Assessments. Before the start of the study 5 endpoints were defined as most relevant: patient's global assessment of well being, pain, physical fitness, health status, and psychological distress. Global assessment of well being was considered the primary outcome measure.

Measurements. All measurements were performed at baseline and after 20 weeks by the same assessor, who was unaware of the treatment allocation. Patients were asked not to discuss the allocation with the assessors. Followup assessment for each patient was scheduled at the same time of the day as the baseline assessment to control for diurnal fluctuation.

Divided over one day the following measurements were done: self-reported questionnaires (requiring up to 1 h to complete), the number of tender points and their pain threshold by dolorimetry (10 min), and fitness tests (up to 30 min).

Instruments. *Patient global assessment*. Subjects indicated the global assessment of their general sense of well being on a 100 mm visual analog scale (VAS) (0 = the best imaginable, 100 = the worst imaginable).

Pain. Pain was measured on a 100 mm VAS, on which the patients marked the pain they had experienced during the previous week (0 = no pain, 100 = the worst pain imaginable).

In addition, the assessor palpated tender and control points, and carried out dolorimetry. The 18 tender points according to the ACR criteria for classification of FM[12] were scored as positive when the patient noted pain at thumb pressure of about 4 kg. A dolorimeter with a 9 kg scale, 1.0 kg calibrations, and a pressure area of 1.54 cm^2 (Chatillon, New York, NY, USA) was used to measure pain threshold. The assessor applied vertical force with the instrument at a rate of roughly 1 kg/s and instructed the subject as follows: "Tell me when this becomes painful." As described by McCain, *et al* dolorimetry was performed at 5 tender point pairs. The sum of these individual scores in kg/cm^2 was denoted "total myalgic score" (TMS).

Physical fitness. Peak workload was measured using an electronically braked bicycle ergometer (Jaeger ER800, Breda, The Netherlands). The saddle height was adjusted to the patient's height. The internal power delivered by the bicycle remained constant over a pedaling range of 45 to 75 rpm. The protocol started at 50 watt for 5 min as a warmup. The resistance

level was increased by 10 watts every minute until subjective maximum workload (W_{max}). Heart rate was monitored continuously by a pulse watch recorder (Sports tester PE3000, Finland) and registered at a steady state level at 50 watts and at W_{max}. The fitness test was interrupted if the heart rate exceeded 200 beats/min or the patient developed chest pain. Perceived exertion was scored after 5 min and at the end of the test by applying the Borg scale (range 6–20; 6 = extremely easy, 20 = extremely heavy; the Borg score should be equal to the heart rate divided by 10)[15].

Health status. Functional ability was assessed by self-report using the Dutch Arthritis Impact Measurement Scales (Dutch-AIMS)[16]. The Dutch-AIMS consists of 53 items categorized into 11 subscales covering physical, psychological, and social well being.

Psychological distress. To assess somatic and psychological discomfort the Symptom Checklist-90-Revised (SCL-90R)[17] was used. This self-report inventory evaluates 9 primary symptom clusters (phobic anxiety, anxiety, depression, somatization, obsession/compulsion, interpersonal sensitivity, hostility, sleep, and psychoticism) that can be summed to a global severity index of psychological distress.

Reliability assessment. Test-retest reliability was assessed one week after baseline for the following instruments: patient global assessment (VAS), number of tender points, total myalgic score, pain (VAS), fitness (W_{max}), and health status (AIMS).

Statistics. Sample size calculation was based on the patient's global assessment (100 mm VAS) for well being. In a previous study a 10% improvement in global well being after low intensity physical fitness was found[10]. Based on these data, a sample size of 18 per group was calculated as sufficient to significantly detect a true difference of 20% in favor of the high intensity physical fitness group [alpha (2 tailed) = 0.05 and beta = 0.90].

Analysis. An intention-to-treat as well as a completers analysis was performed. It was decided that only patients who had participated in the allocated program at least once should be analyzed by intention-to-treat. In addition, an explorative analysis was performed for those patients who had participated in at least 67% of the training sessions.

Data were summarized as means and standard deviations, 95% confidence intervals of change scores, and, if appropriate, as medians and ranges. At 20 weeks, differences in change scores between both groups were tested by 2 sample t test.

The study was approved by the Ethics Committee of the University Hospital of Maastricht.

RESULTS

Demographic data. Group comparisons before treatment. There were no relevant differences between the study groups, although patients in the HIF group were somewhat younger than patients in the LIF group (Table 1). Baseline scores for the outcome measurements were comparable between both groups (Tables 2–4). The regular use of medication and physiotherapy preceding the study was similar in both groups.

Reliability. Intraclass correlation coefficients were fairly high for W_{max} (0.86) and total myalgic score (0.85), moderate for pain VAS and AIMS (0.70), and poor for the number of tender points (0.51). The unweighted kappa statistic for patient's global assessment was marginally satisfactory at 0.66.

Premature discontinuations. Figure 1 shows the procedure of the study. Altogether 37 female patients were randomized; before the intervention started, 4 declined to participate. Reasons were too much stress (n = 3) and the death of a child (n = 1). These patients were excluded from further analysis. Of the 33 remaining patients 18 received the HIF program and 15 the LIF program.

One patient in the HIF group and 2 in the LIF group did not complete the entire protocol, and dropped out [for family reasons (n = 2) and stress (n = 1)].

Nine of 18 patients in the HIF group and 8 of 15 in the LIF group achieved a participation rate of 67% or more.

Outcomes. The intention-to-treat analysis gave the same results as the completers analysis in all outcome measures, so that we only report the latter here.

Table 2 summarizes the effects of both treatment modalities on the primary and secondary outcome measures. It is obvious that neither intervention led to important improvements between baseline and 20 weeks. The most important change was a 20% *increase* in pain in the HIF group, which was statistically significant (p = 0.02). All other changes in both groups were less than 20% compared to baseline. The VAS for patient global well being decreased (improved) with 8 mm in the HIF group, and increased (worsened) with 3 mm in the LIF group. The between-group difference was not statistically significant (p = 0.07).

One important objective of this study was to investigate whether patients with FM could really improve their physical fitness measurably by performing fitness exercises. W_{max} indeed improved, with 13 watt (12%) in the HIF group and 6 watt (6%) in the LIF group, but again the between-group difference was not statistically significant.

The Borg-max score at baseline was 17 in both groups, indicating that patients in both groups perceived their exertion as "heavy." Their perception was not changed during the study. As noted above, the VAS for pain increased with 11 mm in the HIF group and 2 mm in the LIF group, suggesting that high intensity fitness training provoked pain in these patients.

Table 3 summarizes the Dutch-AIMS scores before and after the interventions. In general there was very little improvement in any of the subscales of the Dutch-AIMS in

Table 1. Demographic characteristics.

	HIF Group, n = 18	LIF Group, n = 15
Age , yrs, mean (range)	39 (20–54)	45 (25–58)
Duration of complaints, yrs, mean (range)	9 (2–27)	12 (1–36)
Marital status, %		
Married	72	93
Divorced	6	0
Single	16	7
Widow	6	0
Education, %		
< 7 yrs	6	33
7–12 yrs	88	60
> 12 yrs	6	7

Table 2. Outcomes.

	HIF Group, n = 17		LIF Group, n = 13		
	At Study Entry	Change After 20 Weeks	At Study Entry	Change After 20 Weeks	p**
Patient global, VAS mm	64 (14)	8 (0 to 16)*	58 (11)	– 3 (–10 to 4)	0.07
Pain, VAS mm	53 (15)	–11 (–19 to –3)*	52 (19)	–2 (–14 to 10)	0.22
No. of tender points	9 (6)	–1 (–4 to 2)	11 (6)	0 (–3 to3)	0.65
Total myalgic score, kg/cm^2	171 (46)	6 (–14 to 26)	164 (65)	14 (–11 to 39)	0.62
Fitness, W_{max}	110 (33)	13 (5 to 21)*	97 (30)	6 (–4 to 16)	0.28
Borg-max	17 (2)	–1 (–2 to 0)	17 (1)	–1 (–2 to 0)	1.00

Values are the mean (SD). Positive net change implies improvement. VAS: visual analog scale for pain: 0 = no pain, 100 = worst pain imaginable; W_{max}: maximal watt bicycle ergometer; Borg-max: Borg scale at W_{max} (range 6–20: 6 = extremely easy, 20 = extremely heavy). * p for within-group change < 0.05. ** p for between-group difference (2 sample t test on the change scores).

Table 3. Health status.

AIMS Dimension	HIF Group, n = 17		LIF Group, n = 13		p*
	At Study Entry	Change After 20 weeks (95% CI)	At Study Entry	Change after 20 Weeks (95% CI)	
Mobility	0.6 (1.4)	–0.4 (1.2 to 0.4)	0.2 (0.7)	0.0 (–0.9 to 0.9)	NS
Physical activity	4.3 (2.0)	0.3 (–0.9 to 1.5)	3.5 (2.4)	1.1 (0.1 to 2.1)**	NS
Dexterity	2.5 (2.9)	0.0 (–1.2 to 1.2)	1.2 (1.0)	–0.8 (–0.7 to 2.3)	NS
Social role	1.0 (1.3)	–0.3 (–0.6 to 0)**	0.9 (1.0)	–0.1 (–0.5 to 0.3)	NS
Social activities	3.8 (1.7)	0.0 (–0.7 to 0.7)	5.0 (1.5)	0.9 (0.2 to 1.6)**	NS
Activities of daily living	0.3 (0.6)	0.9 (0.6 to 1.2)**	0.3 (0.6)	0.1 (–0.4 to 0.6)	NS
Pain	6.0 (1.9)	0.5 (–0.1 to 1.1)	6.3 (1.8)	–0.7 (–1.7 to 0.3)	0.04
Depression	3.3 (1.6)	–0.2 (–0.7 to 0.3)	2.7 (1.5)	0.2 (–0.7 to 1.1)	NS
Anxiety	4.4 (2.3)	0.0 (–0.6 to 0.6)	4.3 (2.0)	0.9 (0.0 to 1.8)**	NS
Health perception	4.6 (2.0)	–0.4 (–1.4 to 0.6)	4.6 (2.0)	–0.5 (–1.3 to 0.3)	NS

Baseline values are mean score (SD). Change scores are mean changes from baseline (95% CI). Negative changes indicate improvement; positive changes indicate worsening. *p for between-group difference (2 sample t test on change scores). **p value for within-group change < 0.05.

Table 4. Psychological measures.

SCL-90 Dimension	HIF Group, n = 17		LIF Group, n = 13		p*
	At Study Entry	Change After 20 Weeks (95% CI)	At Study Entry	Change after 20 Weeks (95% CI)	
Global severity of psychological distress	149 (43)	–0 (–12 to11)	168 (51)	5 (–21 to 31)	NS
Phobic anxiety	9 (3)	1 (–0 to 1)	10 (4)	1 (–1 to 3)	NS
Anxiety	16 (7)	0 (–2 to 2)	19 (7)	1 (–2 to 4)	NS
Depression	26 (10)	1 (– 2 to 4)	31 (12)	3 (–3 to 8)	NS
Somatization	28 (9)	–2 (–4 to 1)	32 (8)	2 (–2 to 6)	NS
Obsession/compulsion	17 (4)	–0 (–2 to 2)	19 (7)	0 (–3 to 4)	NS
Interpersonal sensitivity	26 (9)	1 (–1 to 3)	28 (11)	1 (–6 to 8)	NS
Hostility	8 (3)	0 (–1 to 1)	8 (3)	–1 (–2 to 1)	NS
Sleep	8 (3)	0 (–1 to 2)	10 (4)	–0 (–2 to 1)	NS
Psychoticism	12 (4)	0 (–1 to 1)	12 (5)	–2 (–5 to1)	NS

Baseline values are means (SD). Change scores are means (95% CI). Positive change implies improvement. NS: not statistically significant. * p for between-group difference (2 sample t test on change scores).

both treatment arms, and between-group differences were not statistically significant, except for the "pain" dimension. Pain had improved in the LIF group, but deteriorated in the HIF group, and the between-group difference was statistically significant. There was a nonsignificant trend toward less worsening in the LIF group with respect to the "activities of daily living" subscale. The HIF group scored better than the LIF group with respect to the social activities subscale.

Table 4 summarizes the SCL-90 scores and subscales. Again, very little change was noticed in both groups.

DISCUSSION

The starting point of this study was to investigate whether we could reproduce the significant improvements in physical fitness and global assessment of well being by a high intensity cardiovascular training program that were described by McCain, *et al*[1]. We compared this high intensity fitness with a low intensity fitness program primarily using the outcome measures reported in the study by McCain, *et al*, which seemed to be sensitive to change. The main conclusion of our study is disappointing: HIF led to increased fitness as measured by W_{max}, but it was not experienced as such by the patients. For instance, the finding that they did not perceive their exertion as less heavy after the 20 weeks HIF (Borg scale) indicates that the gain was not sufficient to activate the body's own endogenous opioid system, to which the sense of feeling better is usually ascribed. We did not find measurable benefits with respect to health status, as has been well documented after HIF progams in healthy people and in patients after myocardial infarction[12,13]. In addition we did not see an improvement in any of the psychological dimensions, such as level of anxiety or depression, other subjects have shown as a consequence of better physical fitness[18-22]. The patients in the cardiovascular training group of the McCain study had better compliance and achieved a higher fitness level. This might be the main reason we could not replicate the positive results of their study. Other studies aimed at promoting fitness encountered more or less the same problems leading to critically low participation rates as in our study[2,4,9]: refusal to participate, dropping out, and inability to comply indeed have seriously deflated statistical power to detect even large differences. We tried hard to prevent it, but despite continuous encouragement by the study instructors, about 50% of the participants in both groups were not able to fully comply with the training sessions. As the main reason for this, patients in the HIF group stated that they felt completely "broken-down" for more than 24 hours after the training session and that they had hardly recovered before the next training session was due. It took about a month after study start before all participants cycled on the desired high level of intensity. Although the post-exercise pain and stiffness decreased in the last month of the study, suggesting the duration of the study was too short to achieve positive results, almost all participants of both groups judged their fitness training as too time consuming, painful, and stressful. In some studies with more or less vigorous activities the occurrence of post-exercise pain and stiffness was not seen as a problem[1,5]. The exercise program of Mengshoel, *et al*[2] is the only study in which extra attention was paid to prevent post-exercise pain and fatigue by frequently changing the activated muscle groups, in combination with avoiding eccentric and static muscle work.

Whether a 20 week training course as monotherapy is insufficient to attain improvements or not, it appears that a high intensity training for patients with FM is only tolerated for a limited period of time; our results in this respect are in accord with those of Meyer, *et al*[9]. The participants in the HIF group experienced no sense of pleasure during the training: on the contrary, it was hard work and it hurt, which was reflected by the only relevant and statistically significant between-group difference we found, i.e., an increase in pain.

Fibromyalgia research suggests that greater levels of physical activity strongly relate with greater perceived control of symptoms and health related quality of life[6,23]. To determine which kind of exercise program enhances physical fitness most and has the highest longterm adherence rate is difficult: direct comparisons between studies of physical activity cannot be made because of differences in training methods, intensity, and above all in measurements. The different training modalities studied include cycling[1,3,8], pool exercises[3,7,10], walking[3,4,6,8,9], dancing[2], jogging[8], aerobics[11], muscle strength exercises[4,6,18], and stretching exercises[3,6,11]. The frequency of training varied from 3 times weekly to once monthly, from 35 minutes to one hour, in studies varying from 6 weeks' duration to 2 years, with most studies suffering a high dropout rate. This diversity in methodology requires caution in interpreting the results. Finally, the many different outcome measurements used, the large standard deviations, and the low sensitivity to change, especially for symptom outcomes, make comparison of treatment modalities difficult. Another problem is whether statistically significant results are clinically meaningful as well: a positive change score of 13 in W_{max} in our HIF group versus 6 in the LIF group resulted in a between-group difference of 7, which was statisticallly significant but in our opinion hardly relevant. Not to mention that the difference might even be smaller taking into account that the high intensity cycling group was more used to the cycle ergometer than the low impact aerobic exercise group!

Despite all critical remarks we believe that a less intense, more pleasant program of longer duration might be most effective in FM treatment, as the studies of Mannerkorpi, *et al*[10] and Buckelew, *et al*[6] have shown. It is conceivable that a fitness program with a training intensity titrated on the individual's threshold for pain and fatigue, as described by Mannerkorpi, *et*

al, may improve physical and psychosocial symptoms. Further, there is some evidence that additional educational sessions aimed at coping strategies are valuable[6,10].

Our study did not reproduce the substantial improvements found by McCain, *et al*[1] in physical fitness and global assessment. On the contrary, high intensity fitness training was found to provoke instead of relieving pain. We do not advocate a time consuming, expensive high intensity fitness training program for fibromyalgia.

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REFERENCES

1. McCain GA, Bell DA, Mai FM, Halliday PD. A controlled study of the effects of a supervised cardiovascular fitness training program on the manifestations of primary fibromyalgia. Arthritis Rheum 1988;31:1135-41.
2. Mengshoel AM, Komnaes HB, Forre O. The effects of 20 weeks of physical fitness training in female patients with fibromyalgia. Clin Exp Rheumatol 1992;10:345-9.
3. Burckhardt CS, Mannerkorpi K, Hedenberg L, Bjelle A. A randomized, controlled clinical trial of education and physical training for women with fibromyalgia. J Rheumatol 1994;21: 714-20.
4. Martin L, Nutting A, MacIntosh BR, Edworthy SM, Butterwick D, Cook J. An exercise program in the treatment of fibromyalgia. J Rheumatol 1996;23:1050-3.
5. Wigers SH, Stiles TC, Vogel PA. Effects of aerobic exercise versus stress management treatment in fibromyalgia: a 4.5 year prospective study. Scand J Rheumatol 1996;25:77-86.
6. Buckelew SP, Conway R, Parker J, et al. Biofeedback/relaxation training and exercise interventions for fibromyalgia: a prospective trial. Arthritis Care Res 1998;11:196-209.
7. Gowans SE, deHueck A, Voss S, Richardson M. A randomized controlled trial of exercise and education for individuals with fibromyalgia. Arthritis Care Res 1999;12:120-9.
8. Meiworm L, Jakob E, Walker UA, Peter HH, Keul J. Patients with fibromyalgia benefit from aerobic endurance exercise. Clin Rheumatol 2000;19:253-7.
9. Meyer BB, Lemley KL. Utilising exercise to affect the symptomatology of fibromyalgia: a pilot study. Med Sci Exerc 2000;32:1691-7.
10. Mannerkorpi K, Nyberg B, Ahlmen M, Ekdahl C. Pool exercise combined with an education program for patients with fibromyalgia syndrome. A prospective, randomized study. J Rheumatol 2000;27:2473-81.
11. van Santen M, Bolwijn P, Verstappen F, et al. A randomized clinical trial comparing fitness and biofeedback training versus basic treatment in patients with fibromyalgia. J Rheumatol 2002; 29:575-81.
12. Astrande P, Rodahl K. Textbook of work physiology. New York: McGraw Hill; 1986:423-27, 453.
13. Wolfe F, Smythe HA, Yunus MB, et al. The American College of Rheumatology 1990 criteria for the classification of fibromyalgia. Report of the Multicenter Criteria Committee. Arthritis Rheum 1990;33:160-72.
14. American College of Sports Medicine. Guidelines for exercise testing and prescription. Philadelphia: Lea & Febiger; 1991:93-4.
15. Borg G. Subjective effort in relation to physical performance and working capacity: from research to practice. New York: Plenum Publishing; 1978.
16. Taal E, Jacobs JW, Seydel ER, Wiegman O, Rasker JJ. Evaluation of the Dutch Arthritis Impact Measurement Scales (Dutch-Aims) in patients with rheumatoid arthritis. Br J Rheumatol 1989;28:487-91.
17. Derogatis LR. SCL-90: Administration, scoring and procedures manual-I for the revised version. Baltimore: Johns Hopkins University School of Medicine, Clinical Psychometrics Research Unit; 1977.
18. Häkkinen A, Häkkinen K, Hannonen P, Alen M. Strength training induced adaptations in neuromuscular function of premenopausal women with fibromyalgia: comparison with healthy women. Ann Rheum Dis 2001;60:21-6.
19. Moses J, Steptoe A, Mathews A, Edwards S. The effects of exercise training on mental well-being in the normal population: a controlled trial. J Psychosom Res 1989;33:47-61.
20. Weinberg RS, Gould D. Foundations of sports and exercise psychology. Champaign, IL: Human Kinetics; 1995:362-6.
21. Holmes DS, Rother DL. Effects of aerobic exercise training and relaxation training on cardiovascular activity during psychological stress. J Psychosom Res 1988;32:469-74.
22. North TX, McCullagh P, Tran ZV. Effect of exercise on depression. In: Pandolf KB, Holloszy JO, editors. Exercise and sport sciences review. Vol. 18. Baltimore: Williams & Wilkins; 1990:379-416.
23. Culos-Reed SN, Brawley LR. Fibromyalgia, physical activity, and daily functioning: the importance of efficacy and health-related quality of life. Arthritis Care Res 2000;13:343-51.