Arthritis & Rheumatism (Arthritis Care & Research)
Vol. 57, No. 7, October 15, 2007, pp 1202–1210
DOI 10.1002/art.23008

ORIGINAL ARTICLE

The Effects of Vigorous Exercise Training on Physical Function in Children With Arthritis: A Randomized, Controlled, Single-Blinded Trial

DAVINDER SINGH-GREWAL,[1] JANE SCHNEIDERMAN-WALKER,[2] VIRGINIA WRIGHT,[3] ODED BAR-OR,[†] JOSEPH BEYENE,[2] HIRAN SELVADURAI,[4] BONNIE CAMERON,[2] RONALD M. LAXER,[2] RAYFEL SCHNEIDER,[2] EARL D. SILVERMAN,[2] LYNN SPIEGEL,[2] SHIRLEY TSE,[2] CLAIRE LEBLANC,[5] JANICE WONG,[6] SAMANTHA STEPHENS,[2] AND BRIAN M. FELDMAN[7]

Objective. **To examine the effectiveness of high-intensity aerobic training compared with low-intensity training in terms of energy cost of locomotion, peak oxygen uptake, peak power, and self-reported physical function in children with juvenile idiopathic arthritis (JIA).**
Methods. **Eighty children with JIA, ages 8–16 years, were enrolled in a randomized, single-blind controlled trial. Both groups participated in a 12-week, 3-times–weekly training program consisting of high-intensity aerobics in the experimental group and qigong in the control group. Subjects underwent exercise testing measuring submaximal oxygen uptake at 3 km/hour ($VO_{2submax}$) as the primary outcome, maximal oxygen uptake, and peak power at the beginning and end of the program. Physical function was measured using the Child Health Assessment Questionnaire (C-HAQ).**
Results. **The exercise program was well tolerated in both groups. There was no difference in $VO_{2submax}$ or any other exercise testing measures between the groups through the study period and no indication of improvement. Both groups showed significant improvements in C-HAQ with no difference between the groups. Adherence was higher in the control group than the experimental group.**
Conclusion. **Our findings suggest that activity programs with or without an aerobic training component are safe and may result in an important improvement in physical function. The intensity of aerobic training did not seem to provide any additional benefits, but higher adherence in the qigong program may suggest that less intensive regimens are easier for children with JIA to comply with, and provide a degree of benefit equivalent to more intensive programs.**

KEY WORDS. Juvenile idiopathic arthritis; Exercise training; Randomized controlled trial.

INTRODUCTION

Juvenile idiopathic arthritis (JIA) affects ~1 in 1,000 children (1). These children participate in less physical activity and have more sleep hours than their peers (2). A meta-analysis of studies examining peak oxygen consumption (VO_{2peak}) showed a 22% reduction in children with arthritis compared with their peers (3). Other studies have shown a reduction in muscular endurance in children with JIA (4,5). These factors may lead to a spiral of decon-

ClinicalTrials.gov identifier: NCT00213187. ISRCTN 12040055.
Supported by the Arthritis Society of Canada and by an operating grant from the Canadian Institutes of Health Research. Dr. Feldman holds the Canada Arthritis Chair in Childhood Arthritis.
[1]Davinder Singh-Grewal, MBBS: The Hospital for Sick Children, Toronto, Ontario, Canada, and Children's Hospital at Westmead, Sydney, New South Wales, Australia; [2]Jane Schneiderman-Walker, MSc, Joseph Beyene, PhD, Bonnie Cameron, MD, Ronald M. Laxer, MD, Rayfel Schneider, MD, Earl D. Silverman, MD, Lynn Spiegel, MD, Shirley Tse, MD, Samantha Stephens, MSc: The Hospital for Sick Children, Toronto, Ontario, Canada; [3]Virginia Wright, MD: Bloorview Kids Rehab, Toronto, Ontario, Canada; [4]Hiran Selvadurai, MD: Children's Hospital at Westmead, Sydney, New South Wales, Australia; [5]Claire LeBlanc, MD: Children's Hospital of Eastern Ontario, Ottawa, Canada; [6]Janice Wong, BSc: University of Toronto, Toronto, Ontario, Canada; [7]Brian M. Feldman, MD, MSc, FRCPC: The Hospital for Sick Children, Bloorview Kids Rehab, and the University of Toronto, Toronto, Ontario, Canada.
†Dr. Bar-Or is deceased.
Address correspondence to Brian M. Feldman, MD, MSc, FRCPC, Division of Rheumatology, The Hospital for Sick Children, 555 University Avenue, Toronto, Ontario, M5G 1X8 Canada. E-mail: brian.feldman@sickkids.ca.
Submitted for publication October 20, 2006; accepted in revised form February 26, 2007.

ditioning and inactivity resulting in further deconditioning and limited participation, culminating in prolonged disability (6).

Traditionally, physical therapy for JIA has aimed to manage pain, preserve range of motion, and limit the strain on arthritic joints (7,8). More active forms of therapy have been recently instituted (9), and guidelines have included recommendations for fitness and strengthening exercise to improve function and promote lifetime physical activity (10).

Systematic reviews examining aerobic training in adults with rheumatoid arthritis (RA) found improvements in aerobic capacity, muscle strength, and disease activity, with possible beneficial effects on pain, function, and quality of life (11,12). Early studies in children suggested that exercise was well tolerated and might improve function (13–15). However, these studies were small, uncontrolled, and relied on field testing rather than laboratory measurements. Subsequently, Oberg et al (16) reported that children with arthritis achieved improvements in muscular strength and endurance after a 3-month training program and that electromyographic abnormalities improved with training. An uncontrolled study of 25 children with polyarticular JIA demonstrated improvements in aerobic capacity and flexibility after an 8-week, low-impact aerobic and resistance program (17). A recent randomized controlled study of aerobic pool exercise involving 54 children suggested (nonsignificant) improvements in quality of life, joint status, and submaximal endurance (18).

Maximal oxygen uptake (VO_{2max}) protocols used to assess fitness in adults are rigorous and have proven difficult to apply in pediatrics. Less intensive peak VO_2 (VO_{2peak}) protocols have been used in children (19). However, VO_{2peak} may be an inappropriate outcome measure in groups with significant limitations. Instead, submaximal VO_2 ($VO_{2submax}$) may be used as a predictor of VO_{2max} or as an independent measure of performance in standardized activities (18,20–23). Giannini and Protas (24) reported that children with JIA had higher submaximal heart rate (HR) and tended towards higher $VO_{2submax}$ (higher oxygen requirement) as compared with matched controls during a bicycle task. Children with JIA may also have an exaggerated energy cost of locomotion (higher $VO_{2submax}$) that manifests as early fatigue during normal activity. Thus $VO_{2submax}$ may provide a means of measuring disability in JIA and provide a well-tolerated measure of aerobic fitness and response to therapy.

The goals of this study were to examine the effectiveness of a high-intensity 12-week program in terms of $VO_{2submax}$ in children with inflammatory arthritis and to determine the effectiveness of this program in terms of self-reported physical function, VO_{2peak}, and peak power.

PATIENTS AND METHODS

Patients. Eighty patients with JIA, ages 8–16 years, who were considered stable by their rheumatologist and unlikely to require modification of therapy during the study were recruited from The Hospital for Sick Children. No restrictions were placed on medication use, but every effort was made to maintain stable dosage through the study.

Patients were excluded if they had significant cardiac, pulmonary, or metabolic comorbidity; if they had moderate or severe hip pain while walking (judged by the patient as $\geq$3 on a 4-point scale) because hip pain was identified as a major limitation to participation in our pilot study (25); if they were engaged in $\geq$3 hours per week of extracurricular physical activity, excluding physiotherapy pool programs because these children might not show additional gains from fitness training; or if they were unable to cooperate with training or testing.

Block randomization balanced for pubertal stage (less than or equal to Tanner stage 2 versus greater than or equal to Tanner stage 3) and degree of disability as measured by the Childhood Health Assessment Questionnaire (C-HAQ) (26) (score $\geq$0.125 versus score $<$0.125) was undertaken, as these factors might independently influence fitness measures. The concealed allocation scheme involved sequential opaque envelopes in blocks of 2–4. Although it was impossible to blind the subjects because the programs were obviously different, study personnel responsible for administering the fitness testing, statistical analysis, and manuscript preparation were blinded to patient allocation.

Interventions. Groups undertook a 12-week exercise program consisting of 1 supervised session and 2 unsupervised sessions per week. The supervised sessions, held in 6 locations, were led by an exercise therapist with a 1:4 instructor to subject ratio.

Experimental sessions commenced with a 10-minute warm-up mimicking the exercise routine, followed by light stretching. The aerobic training program, drawn from dance and martial arts (cardio-karate), was designed to avoid activities that might be unsafe (details of the exercise programs are available from the authors). The 30-minute sessions increased progressively in intensity from low to moderate/high as tolerated. Sessions concluded with 5–10 minutes of passive stretching. HR was measured either as a manual 15-second count at the carotid artery or by HR monitor (Polar 650i, Polar Instruments, Kempele, Finland). Target HR range was >75% of the maximal HR (MHR) determined from VO_{2peak} testing conducted at enrollment. Instructors encouraged subjects to exercise in this range. Rating of perceived exertion (RPE) using the children's OMNI scale (27) was used to determine exercise intensity.

Control sessions were held at the same locations as the experimental group session, but at different times. The program was based on qigong (28), a gentle relaxation program similar to tai chi. Tai chi has been reported as a safe and feasible activity for adults with RA (29). Sessions were based on an 18-posture program designed to avoid aerobic training or elevating HR. Each posture was repeated 8 times. A cool down of gentle stretching concluded the session. Subjects recorded HR and RPE to ensure that it was below 75% of MHR.

Unsupervised sessions for both groups followed the same program as in-class sessions, but used videotaped instruction. Subjects were asked to complete 2 at-home video sessions per week, and if a class session was missed, the subject was instructed to make up that session at home.

Outcomes. Subjects underwent 3 testing sessions: the first at enrollment, during which subjects were familiarized with the testing equipment and the data collected was used in balancing the randomization process; the second planned 2 weeks later at the time of group allocation and just prior to commencement of the program; and the third within 2 weeks of completion of the training program.

At each session, height (Harpenden Stadiometer, London, UK) and weight (SR555 Stand-on Scale System, SR Instruments, Tonawanda, NY) measurements were obtained to the nearest 0.1 cm and 0.1 kg, respectively, with the subjects wearing light clothes, but not shoes. Percent body fat was calculated from skin-fold measurements of the bicep, tricep, subscapular, and suprailiac crest regions using the average of 3 trials and entered into the Slaughter equation (30).

The $VO_{2submax}$ was measured while treadmill walking at 1.5 km/hour and 3.0 km/hour for 5 minutes (8,31). Absolute $VO_{2submax}$ at 3 km/hour was the primary outcome measure. During all treadmill testing expired gases were collected continuously, with ventilatory equivalent ratio for oxygen (VE/VO_2), ventilatory equivalent ratio for carbon dioxide (VE/VCO_2), respiratory exchange ratio (RER), and HR recorded at 20-second intervals (Physiodyne Max-II metabolic cart, Quogue, NY) using a 4-lead electrocardiogram system (GE Case 8000, General Electric Medical Systems, Milwaukee, WI) and RPE was assessed using the Children's OMNI scale (27). Steady state for each stage was recorded as the average of the last minute of VO_2 measurements.

The VO_{2peak} was measured through an incremental, continuous walking task on a treadmill with speed or incline increased every minute until volitional fatigue. No preselected increments were used due to low and heterogeneous fitness common in children with chronic disease (8). Increments were selected by an experienced exercise tester according to the child's HR, RER, RPE, and overall appearance. Test duration was targeted at 6–10 minutes. Criteria for VO_{2peak} were attaining RER $>$1.0 and reaching age-predicted MHR.

After 10–15 minutes of rest, subjects performed a modified Wingate test via 10-second and 30-second all-out cycling tasks on an isokinetic cycle ergometer (Biodex lower body cycle, Biodex Medical Systems, Shirley, NY). The isokinetic cycle fixes the speed of pedaling to measure the force output and is a highly reproducible and safe method of assessing anaerobic power (32,33). Peak power was measured over 10 seconds at 90 revolutions per minute, and then over 30 seconds (after a 2-minute recovery period) to estimate total work output in watts.

The C-HAQ was used to assess physical function. Items are scored on a 4-point scale with scores of 0 denoting no disability and 3 denoting severe disability. It is validated for use in JIA (26). We chose to use the C-HAQ in preference to the modified $C\text{-}HAQ_{38}$ as the latter instrument has not yet been validated for longitudinal studies (34). Physical activity levels outside the study were measured using the Habitual Activity Estimation Scale (HAES), a validated tool for measuring activity levels in both healthy and chronically ill children (35,36). It asks children to recall an average weekday and a weekend day with regard to the proportion of time spent inactive (e.g., sleeping), somewhat inactive (e.g., sitting), somewhat active (e.g., walking), and active (e.g., running), and provides a summary score of these activity levels. Overall quality of life (QOL) and health-related quality of life (HRQOL) were measured on 10-cm visual analog scales (VAS) previously validated for children with JIA, with higher scores indicating better QOL or HRQOL (37).

Adherence and safety. The study coordinator and fitness instructors maintained frequent contact with the subjects to maintain adherence, and the instructors met together on a monthly basis to review each individual's progress. Subjects measured and recorded RPE, HR (pulse point or monitor), and pain on a 10-cm VAS in a diary for each session they completed. HR monitors were loaned intermittently to check adherence. Children were rewarded with stickers for completed sessions and were able to trade these for small gifts to further encourage adherence. These strategies had enhanced adherence in our pilot study (25).

Safety was monitored in diary records of pain and through joint examination at testing sessions. A joint was considered active if it was swollen or had 2 of the following features: limited range of movement, pain on movement/tenderness, and/or warmth. Range of motion was assessed at testing sessions using the Pediatric Escola Paulista de Medicina Range of Motion scale (38).

Statistical analysis. A sample size of 35 subjects per group was calculated to detect a meaningful difference between the groups in absolute $VO_{2submax}$ at 3 km/hour, with an α (false-positive) error of 0.05, β (false-negative) error of 0.20, and δ (the size of a clinically important difference) of 10% (39). Based on an anticipated 10% dropout rate, the intended recruitment number was 80 subjects.

The change in $VO_{2submax}$ between the 2 groups was compared using a linear mixed-effects model with compound symmetry covariance structure. Potential confounders (sex, pubertal stage, C-HAQ score, and HAES activity level outside the study) were entered into the model. Differences between the groups for secondary outcomes were tested similarly. Analyses were completed using SAS software version 9.1 (SAS Institute, Cary, NC) and SPSS version 12.0 (SPSS, Chicago, IL).

The primary analysis was intent-to-treat, with the subjects analyzed per their original group assignment regardless of adherence. The exercise dosage used in this study was considered a minimum to improve aerobic capacity. However, exercising less often has been shown to have benefit for adults with arthritis (11,12). In an attempt to see whether adherence significantly influenced the results, we analyzed data from experimental subjects and controls who participated in $>$70% of sessions and also those experimental group subjects who attended $>$70% of sessions

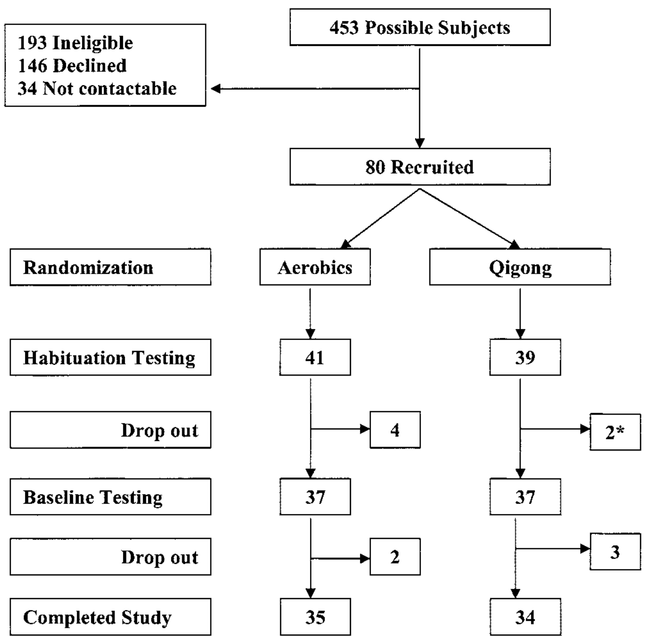

Figure 1. Flowchart of recruitment and completion of the trial. * = includes 1 ineligible subject.

and also achieved >75% of MHR in >50% of sessions attended compared with controls. Missing primary outcome data was analyzed through a sensitivity analysis using imputation with the mean and median of nearby points replacing missing values. Post hoc subgroup analyses of Tanner stage (≤ Tanner stage 2 versus ≥ Tanner stage 3), sex (boys versus girls), and baseline activity (HAES <2 active weekday hours versus ≥2 active weekday hours) were also completed.

This study was approved by the Research Ethics Boards at The Hospital for Sick Children and Bloorview Kids Rehab. All subjects were enrolled only after fully-informed written consent was obtained from the parent and the child.

RESULTS

Patients and adverse events. Of 453 potential subjects, 80 were recruited (Figure 1). Ten patients dropped out after randomization and 1 patient was ineligible (6 from the experimental group and 5 from the control group). All dropouts reported lack of time as the reason.

Patient characteristics at enrollment are shown in Table 1. Differences are evident in the distribution of JIA subgroups between the groups. The blocking factors, Tanner stage, and C-HAQ used in randomization were equally distributed.

No adverse events were reported during testing or training sessions. There was no worsening of active joint count, Pediatric Escola Paulista de Medicina Range of Motion scale, C-HAQ, QOL, or HRQOL in either group during the study (Table 2). Low levels of pain were recorded on a 10-cm VAS during training sessions. These were not different between the 2 groups (median 0; range 0–10 in both groups; $P = 0.09$ Mann-Whitney U test).

Adherence. Patient adherence is outlined in Table 3. Completion of training sessions was 78% in the control arm and 56% in the experimental arm. An average of 2 sessions per week were completed by the experimental subjects and 1.7 sessions per week by the control subjects. The difference was most apparent in the number of home-based sessions. As expected, RPE was significantly different between interventions with a median (range) of 5.0 (0.0–10.0) and 1.0 (0.0–9.0), respectively, for the experimental and control groups ($P < 0.0001$). Only 51% of the completed experimental sessions succeeded in achieving the target HR. The RPE correlated moderately with HR in the experimental group ($r = 0.41$; $P < 0.0001$) and less so in the control group ($r = 0.32$; $P < 0.0001$).

Exercise testing outcomes. Subjects' baseline fitness measured by VO_{2peak} and compared with published age and body surface area matched norms (40) demonstrated a

Table 1. Patient characteristics at enrollment*

Characteristic	Control group (n = 39)	Experimental group (n = 41)
Female, n (%)	29 (74.4)	35 (85.4)
Age, mean ± SD (range) years	11.5 ± 2.4 (8–16)	11.7 ± 2.5 (8–16)
Postpubertal, n (%)	22 (56.4)	23 (56.1)
C-HAQ score, mean ± SD (range)	0.34 ± 0.43 (0–2.0)	0.31 ± 0.48 (0–2.13)
JIA subtype, n		
Polyarticular	15†	19
Persistent oligoarticular	2	5
Extended oligoarticular	5	6
Systemic	6	1
Enthesitis-related	4	7
Psoriatic	6	2
Other	1	1

* C-HAQ = Childhood Health Assessment Questionnaire; JIA = juvenile idiopathic arthritis.
† Including 2 patients with rheumatoid factor-positive polyarticular disease.

Table 2. Exercise testing and questionnaire results at enrollment and completion of the trial for patients that completed the trial*

Outcome variable	Control group (n = 34) Commencement	Control group (n = 34) Completion	Experimental group (n = 35) Commencement	Experimental group (n = 35) Completion	Estimate†	P†
$VO_{2submax}$ 1.5 km/hour						
Absolute, liter/minute	0.4 ± 0.1	0.4 ± 0.1	0.4 ± 0.1	0.4 ± 0.1	0.03	0.07
Relative, ml/kg/minute	9.4 ± 1.6	9.3 ± 1.8	9.5 ± 1.7	8.7 ± 1.4	0.7	0.051
$VO_{2submax}$ 3.0 km/hour						
Absolute, liter/minute	0.5 ± 0.1	0.5 ± 0.1	0.5 ± 0.1	0.5 ± 0.1	0.02	0.31
Relative, ml/kg/minute	11.5 ± 1.9	11.6 ± 1.8	11.4 ± 1.9	11.0 ± 1.5	0.5	0.23
VO_{2peak}						
Absolute, liter/minute	1.5 ± 0.5	1.6 ± 0.5	1.4 ± 0.4	1.5 ± 0.5	−0.04	0.43
Relative, ml/kg/minute	35.7 ± 7.8	36.2 ± 8.0	33.3 ± 6.8	34.8 ± 8.8	−0.01	0.80
Peak power, watts						
10 seconds	211 ± 136	216 ± 137	204 ± 120	233 ± 125	−12.6	0.40
30 seconds	218 ± 133	225 ± 134	209 ± 103	236 ± 114	−9.7	0.40
Active joints, mean ± SD (range)	2.5 ± 5.1 (0–21)	2.1 ± 5.1 (0–21)	3.5 ± 6.8 (0–28)	2.2 ± 6.5 (0–15)	0.93	0.41
EPM score	0 ± 0.1	0.1 ± 0.4	0.1 ± 0.1	0.1 ± 0.2	0.03	0.35
Body fat percentage	23.1 ± 7.5	23.3 ± 8.1	24.0 ± 8.8	22.9 ± 7.3	0.58	0.43
C-HAQ score	0.32 ± 0.45	0.21 ± 0.35	0.34 ± 0.49	0.22 ± 0.37	−0.01	0.80
QOL	8.5 ± 1.6	8.7 ± 1.4	7.9 ± 1.8	8.4 ± 2.0	−0.3	0.55
HRQOL	8.3 ± 1.9	8.5 ± 1.7	7.7 ± 1.8	7.8 ± 1.9	0.2	0.55

* Values are the mean ± SD unless otherwise indicated. $VO_{2submax}$ = submaximal oxygen consumption; VO_{2peak} = peak oxygen uptake; EPM = Pediatric Escola Paulista de Medicina Range of Motion scale; C-HAQ = Childhood Health Assessment Questionnaire; QOL = quality of life; HRQOL = health-related quality of life.
† Estimates and P values are presented for the β-term for the interaction of (group allocation × testing session) in the repeated measures, auto-regressive model, and represent the difference of the paired differences in response seen in each of the 2 groups.

significantly lower VO_{2peak} in our patients (Table 4). Results of exercise testing and questionnaires are also shown in Table 2.

No difference was found in the change in the absolute $VO_{2submax}$ at 3 km/hour between the groups from baseline to completion of the study (Figure 2). Nor were any significant differences seen in the change in other fitness parameters between the groups. When missing data was accounted for through imputation analysis, there was still no difference in the primary outcome between the groups.

Analysis of those with >70% completion of training sessions showed no significant difference in any of the fitness parameters between the 2 groups over time. We examined subjects in the experimental arm who attended >70% of training sessions and achieved HRs >75% of MHR in >50% of sessions. This subgroup contained only 8 patients and, when compared with the control group, showed no significant benefit in $VO_{2submax}$.

Subgroup analyses for sex, pubertal stage, and baseline activity did not show any difference between the subgroups in $VO_{2submax}$ in response to training. The amount of improvement in self-reported physical function as measured by the C-HAQ was similar between groups (Figure 2), although the within-group change was statistically significant (mean difference −0.12, $P < 0.0001$) and clinically meaningful in magnitude (41).

DISCUSSION

This study is the first well-powered, randomized controlled trial of land-based aerobic training in children with JIA. We found that participating in a 12-week exercise program did result in improved physical function as measured by the C-HAQ, but did not result in improved economy of locomotion, and that there was no extra improve-

Table 3. Adherence measures in both groups*

Adherence measure	Control group	Experimental group
Training sessions completed		
Supervised in class, 12 possible sessions	7.8 ± 2.8	7.3 ± 2.9
Home-based sessions, 24 possible sessions	20.4 ± 7.1	14.9 ± 7.1
Total sessions completed of 36 possible session, n (%)	28.6 (79.4)	20.5 (56.9)
HR during sessions	95 ± 26	136 ± 33
Sessions in which HR >75% MHR, %	7.4	51.0
Total minutes of training per session	32.2 ± 8.2	34.3 ± 10.0

* Values are the mean ± SD unless otherwise indicated. HR = heart rate; MHR = maximal heart rate.

Table 4. Comparison of maximum oxygen consumption values according to body surface area, between subjects at study start and published values for healthy untrained children*

Body surface area	Washington study (ref. 40)	Current study
<1.0 m^2		
Boys	47 ± 6	49.6†
Girls	42 ± 5	35.8 ± 5.3
≥1.0 m^2 and <1.2 m^2		
Boys	46 ± 5	39.6, 42.8, 38.1†
Girls	43 ± 7	35.8 ± 6.7
≥1.2 m^2		
Boys	47 ± 10	39.3 ± 9.4
Girls	41 ± 6	31.9 ± 7.3

* Values are the mean ± SD in ml/minutes/m^2.
† Subgroup had <7 patients, therefore all results are listed.

ment conferred by high-intensity aerobic training. The benefits observed in the C-HAQ might be a result of being involved in a trial and the added attention received from trainers and study personnel (Hawthorne effect), or it may reflect a true benefit of training.

When considering the role of vigorous physical training in childhood arthritis, we must consider that the failure to demonstrate improvements in this study may have been a result of patient selection, the training program instituted, adherence with the program, or a general poor response of fitness training in young children.

It is possible that subjects were too mildly affected as measured by their C-HAQ scores to have benefited from the training program. Previous studies have shown that children with arthritis have reduced fitness when compared with their healthy peers (3), and while many of our subjects had mild disease, they were deconditioned when compared with available normal values for healthy untrained children (40). In adults, treadmill protocols attain 6–10% higher VO_{2max} than bicycle protocols (42,43). Thus, as the comparison data from Washington et al (40) were obtained using a cycle ergometer and ours were obtained from treadmill testing, it is likely that subjects in this study were even more deconditioned than these data suggest. Nonetheless, even though it might be expected that the deconditioned subjects included in this study would be more likely to benefit from an exercise program, no benefit in fitness parameters was seen.

Submaximal exercise testing has been reported as a safe, simple, and well-tolerated estimate of VO_{2max} and functional ability in children with chronic disease (20,22–25). Giannini and Protas (24) showed that children with arthritis had higher submaximal HR and trended towards higher $VO_{2submax}$ than healthy peers, suggesting significantly lower submaximal efficiency. The failure of our study to show significant changes after training may be because disease activity of patients in the Giannini and Protas study (24) was significantly greater than in our study, with a mean joint count of 13 compared with <3 in our study. However, we feel that the subjects included represent a realistic cross section of JIA patients in our clinic and that the results are generalizable to clinic populations in most developed countries.

Training programs should involve an exercise prescription of adequate frequency, intensity, and duration to achieve the desired results. A minimum of twice-weekly training is required to achieve significant improvements in physical fitness (12,44). An 8-week study by Klepper (17)

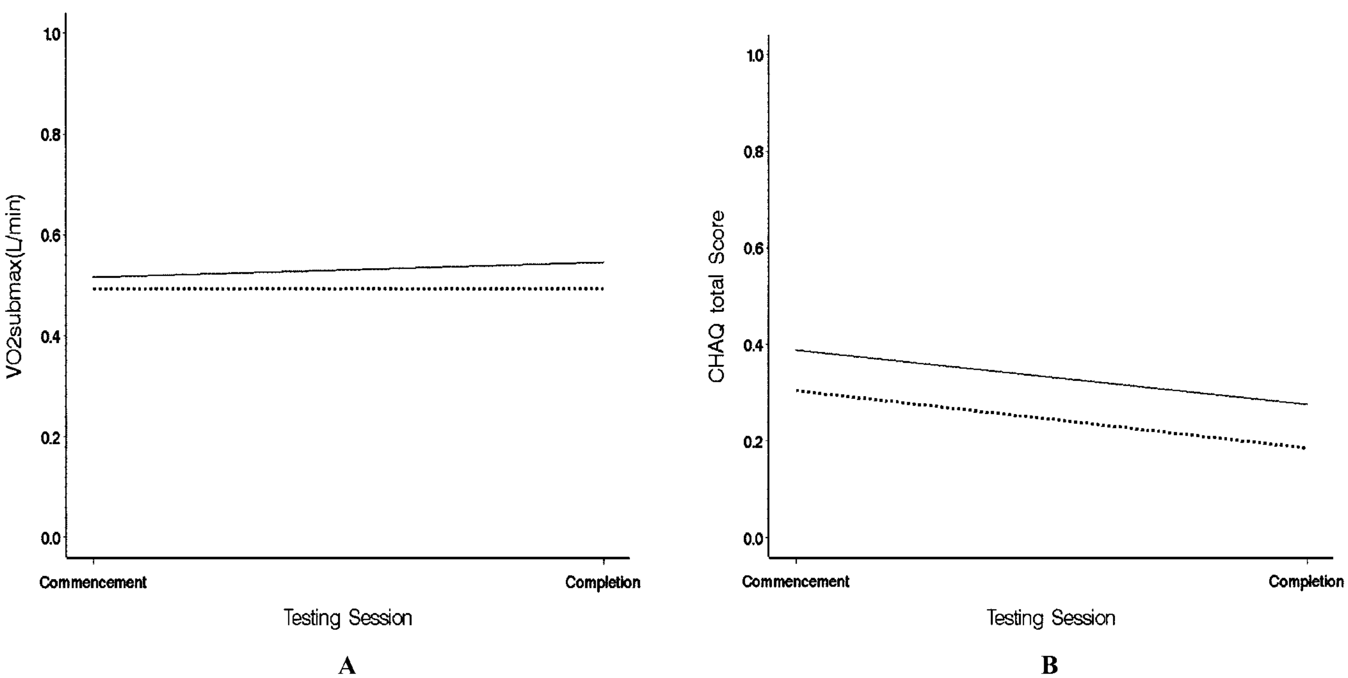

Figure 2. A, Plot of predicted absolute submaximal oxygen uptake ($VO_{2submax}$) at 3 km/hour, and **B,** Childhood Health Assessment Questionnaire (C-HAQ) by treatment group using a mixed model procedure. Solid line = control group; dotted line = experimental group. L = liter; min = minute.

involved training twice weekly in class format and once weekly at home. Studies of aquatic training (18,45) and the pilot study undertaken prior to this trial (25) used once-weekly class-based training for 15, 20, and 12 weeks, respectively. Feedback from our pilot study highlighted difficulties in attending frequent formal training sessions and suggested that a partially home-based program would help adherence (25). The program used in our present study was designed to provide adequate frequency (3 sessions per week), intensity (≥75% MHR), and duration (30 minutes) of aerobic training based on existing recommendations and the findings of earlier studies.

Failure to achieve target HR may have been due to the training program not being strenuous enough to achieve the desired range. While RPE measured in training sessions was significantly higher in the experimental group than in the control group, which suggests at least moderate exertion in the experimental group, HR and RPE were only moderately correlated. It is possible that the more complicated exercise maneuvers in the experimental program, compared with treadmill walking or running, added complexity which translated as a higher RPE without concurrent increase in HR. Also, the novelty of the vigorous program may have resulted in earlier exertion in the subjects with a tailing off towards the end of the session when RPE was measured. Furthermore, the OMNI scale was validated using treadmill or cycling protocols that were continuous in nature, but our program was intermittent, possibly resulting in a lower correlation (27).

Differences in the modality of training and testing may have affected our results. Patients were trained in floor-based programs but tested on treadmill and cycle ergometers. In the pilot study, subjects were trained in a circuit format incorporating treadmill and stationary cycle and then tested on these 2 apparatus (25). Thus there may be an issue with the specificity of the testing method to detect changes resulting from the training modality.

Adherence in this study was higher in the control group than in the experimental group. Takken et al (18) showed good adherence with once-weekly aquatic training, whereas our own pilot study achieved only fair adherence with a once-weekly program (25). A home exercise intervention in cystic fibrosis from Schneiderman-Walker et al (46) reported good long-term adherence with a 3-times–weekly program out to 3 years, while Greenan-Fowler et al (47) were unable to maintain adherence in children with hemophilia in home exercises. Munneke et al (48) found that adult patients with RA maintained good adherence in a 2-year, twice-weekly training program. Our results highlight the difficulties in obtaining adequate and sustained adherence with intensive exercise programs from children with arthritis.

The training HR was only achieved in half of all sessions in the experimental arm, reducing the effective training frequency to once a week when adherence with sessions was taken into account. This may have significantly reduced the training effect, and may explain the lack of efficacy. Post hoc analyses of compliant subjects showed no differences, but these subanalyses may not have been adequately powered to show a difference if one did exist.

Our results are not consistent with studies of fitness training in adults with RA that have shown significant benefits in fitness and functional outcomes (11,12). They are, however, consistent with existing studies of exercise interventions in children with arthritis that have shown slight or no significant improvement in fitness or functional outcomes (15,18,25,45).

Studies of exercise training in healthy children suggest that prepubertal children experience only modest improvements (<11%) in VO_{2max} after training (49). Pubertal children are capable of achieving 20–25% increases in VO_{2max} with training, which is similar to adults (49). Furthermore, it has been suggested that aerobic training of healthy prepubescent children may require training intensities of up to 90% MHR (50), which are significantly higher than those used in this study. Half of the subjects in this study were postpubertal, and post hoc analysis failed to show a response in VO_{2max} or $VO_{2submax}$ in either the prepubertal or postpubertal groups, which does not support the idea that a differential training effect in these 2 groups could explain our results.

Our findings suggest that activity programs with or without aerobic training are safe and may result in improved physical function. This is supported by other studies of exercise programs in childhood arthritis (17,18,25,45). A higher intensity of aerobic training did not provide any additional benefits in this study to functional outcome. This may be a result of the experimental program not being intensive enough to show a response; however, it would require additional studies of different training protocols to determine whether measurable benefits are achievable in this population. A high adherence rate of 80% in the qigong program may suggest that less intensive regimens are easier for children with JIA to comply with and seem to produce an equivalent degree of benefit as more intensive programs.

ACKNOWLEDGMENTS

The authors wish to acknowledge the assistance of Helen Wu in developing the qigong program, and Marie Hennings and Kristen Bustamante, who developed the aerobic training program.

AUTHOR CONTRIBUTIONS

Dr. Feldman had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study design. Singh-Grewal, Schneiderman-Walker, Wright, Selvadurai, Laxer, Schneider, Tse, Wong, Stephens, Feldman.

Acquisition of data. Singh-Grewal, Selvadurai, Cameron, Laxer, Silverman, Spiegel, Tse, LeBlanc, Wong, Stephens, Feldman.

Analysis and interpretation of data. Singh-Grewal, Schneiderman-Walker, Wright, Beyene, Selvadurai, Cameron, Laxer, Schneider, Silverman, Spiegel, LeBlanc, Stephens, Feldman.

Manuscript preparation. Singh-Grewal, Schneiderman-Walker, Wright, Beyene, Cameron, Laxer, Schneider, Silverman, Spiegel, Tse, LeBlanc, Wong, Stephens, Feldman.

Statistical analysis. Singh-Grewal, Beyene, Stephens, Feldman.

Program instructor training. Wright.

REFERENCES

1. Manners P, Bower C. Worldwide prevalence of juvenile arthritis why does it vary so much? J Rheumatol 2002;29:1520–30.
2. Henderson CJ, Lovell DJ, Specker BL, Campaigne BN. Physical activity in children with juvenile rheumatoid arthritis: quantification and evaluation. Arthritis Care Res 1995;8:114–9.
3. Takken T, Hemel A, van der Net J, Helders PJ. Aerobic fitness in children with juvenile idiopathic arthritis: a systematic review. J Rheumatol 2002;29:2643–7.
4. Golebiowska M, Brozik H, Bujnowski T. Aerobic and anaerobic metabolism in children with juvenile chronic arthritis in relation to some clinical data. In: Coudert J, editor. Pediatric work physiology. Paris: Masson; 1992. p. 175–7.
5. Klepper SE, Darbee J, Effgen SK, Singsen BH. Physical fitness levels in children with juvenile rheumatoid arthritis. Arthritis Care Res 1992;5:93–100.
6. Bar-Or O. Pediatric sports medicine for the practitioner. In: Katz M, Stiehm ER, editors. Comprehensive manuals in pediatrics. New York: Springer-Verlag; 1983. p. 68.
7. Alexander GJ, Hortas C, Bacon PA. Bed rest, activity and the inflammation of rheumatoid arthritis. Br J Rheumatol 1983; 22:134–40.
8. Wright V, Smith E. Physical therapy management of children with juvenile rheumatoid arthritis. In: Walker J, Helewa A, editors. Physical therapy in arthritis. New Jersey: W. Saunders Publishers; 1996. p. 211–63.
9. Minor MA. Arthritis and exercise: the times they are a-changin' [letter]. Arthritis Care Res 1996;9:79–81.
10. Minor MA. 2002 Exercise and Physical Activity Conference, St Louis, Missouri: exercise and arthritis "we know a little bit about a lot of things. . ." [editorial]. Arthritis Rheum 2003;49: 1–2.
11. Stenstrom CH, Minor MA. Evidence for the benefit of aerobic and strengthening exercise in rheumatoid arthritis. Arthritis Rheum 2003;49:428–34.
12. Van den Ende CH, Vliet Vlieland TP, Munneke M, Hazes JM. Dynamic exercise therapy in rheumatoid arthritis: a systematic review. Br J Rheumatol 1998;37:677–87.
13. Baldwin J. Pool therapy compared with individual home exercise therapy for juvenile rheumatoid arthritic patients. Physiotherapy 1972;58:230–1.
14. Brennan GP. Objective documentation of increased walking tolerance. Phys Ther 1978;58:697–9.
15. Moncur C, Marcus RC, Johnson S. Pilot project of aerobic conditioning of subjects with juvenile arthritis [abstract]. Arthritis Care Res 1991;3:S16.
16. Oberg T, Karsznia A, Gare BA, Lagerstrand A. Physical training of children with juvenile chronic arthritis: effects on force, endurance and EMG response to localized muscle fatigue. Scand J Rheumatol 1994;23:92–5.
17. Klepper SE. Effects of an eight-week physical conditioning program on disease signs and symptoms in children with chronic arthritis. Arthritis Care Res 1999;12:52–60.
18. Takken T, van der Net J, Kuis W, Helders PJ. Aquatic fitness training for children with juvenile idiopathic arthritis. Rheumatology (Oxford) 2003;42:1408–14.
19. Washington RL, Bricker JT, Alpert BS, Daniels SR, Deckelbaum RJ, Fisher EA, et al. Guidelines for exercise testing in the pediatric age group: from the Committee on Atherosclerosis and Hypertension in Children, Council on Cardiovascular Disease in the Young, the American Heart Association. Circulation 1994;90:2166–79.
20. Noonan V, Dean E. Submaximal exercise testing: clinical application and interpretation [review]. Phys Ther 2000;80:782–807.
21. Bar-Or O. Role of exercise in the assessment and management of neuromuscular disease in children [review]. Med Sci Sports Exerc 1996;28:421–7.
22. Waters RL, Mulroy S. The energy expenditure of normal and pathologic gait. Gait Posture 1999;9:207–31.
23. Paap E, van der Net J, Helders PJ, Takken T. Physiologic response of the six-minute walk test in children with juvenile idiopathic arthritis. Arthritis Rheum 2005;53:351–6.
24. Giannini MJ, Protas EJ. Exercise response in children with and without juvenile rheumatoid arthritis: a case-comparison study. Phys Ther 1992;72:365–72.
25. Singh-Grewal D, Wright V, Bar-Or O, Feldman BM. Pilot study of fitness training and exercise testing in polyarticular childhood arthritis. Arthritis Rheum 2006;55:364–72.
26. Singh G, Athreya BH, Fries JF, Goldsmith DP. Measurement of health status in children with juvenile rheumatoid arthritis. Arthritis Rheum 1994;37:1761–9.
27. Robertson RJ, Goss FL, Boer NF, Peoples JA, Foreman AJ, Dabayebeh IM, et al. Children's OMNI scale of perceived exertion: mixed gender and race validation. Med Sci Sports Exerc 2000;32:452–8.
28. Farrell SJ, Ross AD, Sehgal KV. Eastern movement therapies [review]. Phys Med Rehabil Clin N Am 1999;10:617–29.
29. Wang C, Roubenoff R, Lau J, Kalish R, Scmid CH, Tighiouart H, et al. Effect of Tai Chi in adults with rheumatoid arthritis. Rheumatology (Oxford) 2005;44:685–7.
30. Slaughter MH, Lohman TG, Boileau RA, Horswill CA, Stillman RJ, van Loan MD, et al. Skinfold equations for estimation of body fatness in children and youth. Hum Biol 1988;60: 709–23.
31. Hoofwijk M, Unnithan V, Bar-Or O. Maximal treadmill performance in children with cerebral palsy. Pediatr Exerc Sci 1995;7:305–13.
32. Bar-Or O. The Wingate anaerobic test: an update on methodology, reliability and validity. Sports Med 1987;4:381–94.
33. Tirosh E, Bar-Or O, Rosenbaum P. New muscle power test in neuromuscular disease: feasibility and reliability. Am J Dis Child 1990;144:1083–7.
34. Lam C, Young N, Marwaha J, McLimont M, Feldman BM. Revised versions of the Childhood Health Assessment Questionnaire (C-HAQ) are more sensitive and suffer less from a ceiling effect. Arthritis Rheum 2004:51:881–9.
35. Hay JA. Development and testing of the Habitual Activity Estimation Scale. Proceedings of the XIXth International Symposium of the European Group of Pediatric Work Physiology; 1997. p. 125–9.
36. Molgaard C. Bone mineralisation during growth: the influence of growth, puberty, and calcium intake [PhD thesis]. Fredenksberg (Denmark): Research Department of Human Nutrition, The Royal Veterinary and Agricultural University; 1996. In Danish.
37. Feldman BM, Grundland B, McCullough L, Wright V. Distinction of quality of life, health related quality of life, and health status in children referred for rheumatologic care. J Rheumatol 2000;27:226–33.
38. Len C, Ferraz MB, Goldenberg J, Oliveria LM, Araujo PP, Quaresma MR, et al. Pediatric Escola Paulista de Medicina Range of Motion scale: a reduced joint count scale for general use in juvenile rheumatoid arthritis. J Rheumatol 1999;26: 909–13.
39. Dupont WD, Plummer WD Jr. Power and sample size calculations: a review and computer program. Control Clin Trials 1990;11:116–28.
40. Washington RL, van Gundy JC, Cohen C, Sondheimer HM, Wolfe RR. Normal aerobic and anaerobic exercise data for North American school-age children. J Pediatr 1988;112:223–33.
41. Dempster H, Porepa M, Young N, Feldman BM. The clinical meaning of functional outcome scores in children with juvenile arthritis. Arthritis Rheum 2001;44:1768–74.
42. Maeder M, Wolber T, Atefy R, Gadza M, Ammann P, Myers J, et al. Impact of the exercise mode on exercise capacity: bicycle testing revisited. Chest 2005;128:2804–11.
43. Hermansen L, Saltin B. Oxygen uptake during maximal treadmill and bicycle exercise. J Appl Physiol 1969;26:31–7.
44. American College of Sports Medicine. American College of Sports Medicine Position Stand: the recommended quantity and quality of exercise for developing and maintaining cardiorespiratory and muscular fitness, and flexibility in healthy adults. Med Sci Sports Exerc 1998;30:975–91.

45. Takken T, van der Net J, Helders PJ. Do juvenile idiopathic arthritis patients benefit from an exercise program? A pilot study. Arthritis Rheum 2001;45:81–5.
46. Schneiderman-Walker J, Pollock SL, Corey M, Wilkes DD, Canny GJ, Pedder L, et al. A randomized controlled trial of a 3-year home exercise program in cystic fibrosis. J Pediatr 2000;136:304–10.
47. Greenan-Fowler E, Powell C, Varni JW. Behavioral treatment of adherence to therapeutic exercise by children with hemophilia. Arch Phys Med Rehabil 1987;68:846–9.
48. Munneke M, de Jong Z, Zwinderman AH, Jansen A, Ronday HK, Peter WF, et al. Adherence and satisfaction of rheumatoid arthritis patients with a long-term intensive dynamic exercise program (RAPIT program). Arthritis Rheum 2003;49:665–72.
49. Braden DS, Carroll JF. Normative cardiovascular responses to exercise in children [review]. Pediatr Cardiol 1999;20:4–11.
50. Obert P, Mandigouts S, Nottin S, Vinet A, N'Guyen LD, Lecoq AM. Cardiovascular responses to endurance training in children: effect of gender. Eur J Clin Invest 2003;33:199–208.