Cardiopulmonary Exercise Testing in Juvenile Idiopathic Arthritis

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ABSTRACT. ***Objective***. To assess aerobic fitness and exercise capacity in patients with juvenile idiopathic arthritis (JIA) and to determine subgroup differences.

Methods. Thirty-four patients diagnosed with JIA and 21 healthy sedentary volunteers were studied. Aerobic fitness was determined by measuring peak power and peak oxygen uptake (VO_{2peak}) during an incremental cycling test. The patient group consisted of systemic JIA (n = 8), polyarticular JIA (n = 13), oligoarticular JIA (n = 7), and enthesitis-related arthritis (ERA, n = 6). Results from different subgroups of JIA were compared to determine subgroup differences.

Results. All subjects tolerated maximal exercise testing well. The JIA group had lower aerobic fitness than controls. In our comparison of JIA subgroups, we found no significant differences in cardiopulmonary measures. The ERA group had higher aerobic capacity than other subgroups. There was no difference in exercise capacity between patients with active disease (n = 10) and those in remission (n = 24).

Conclusion. We suggest that heterogeneity in VO_{2peak} levels among JIA patients is due to subgroup differences. Exercise programs for improvement of aerobic fitness should be individualized or at least be modified according to different subgroups. (J Rheumatol 2004;31:1834–9)

Key Indexing Terms:
JUVENILE IDIOPATHIC ARTHRITIS
EXERCISE TESTING
OXYGEN UPTAKE
AEROBIC FITNESS

Children with rheumatic disease are believed to be less physically fit and are deconditioned compared to healthy peers. A number of recent studies report moderate to heavy impairment in aerobic exercise capacity of children with dermatomyositis[1], juvenile idiopathic arthritis (JIA)[2], or juvenile spondyloarthropathy[3]. A low aerobic capacity is an important indicator for comorbidity[4]. Together with chronic joint pain, stiffness, and deformity, it may lead to impaired physical activity and unsatisfactory lifestyle. JIA presents with a complex pattern of signs and symptoms that can compromise a child's performance in a range of activities, disadvantaging the child in many areas of life[5]. Patients with JIA have weaker and thinner leg muscles than normal. Muscle function declines rapidly when arthritis develops[6]. On the basis of these considerations, a training program that will prevent joint stiffness and deformity, muscle atrophy, and development of contractures is crucial to maximize function. Thus, the inactive lifestyle of children with JIA may improve. Several studies introduced different training programs that improved physical capacity of JIA patients[7,8]. However, exercise testing is relatively less employed in formulating a convenient exercise prescription or training program.

Maximal oxygen uptake (VO_{2max}) is accepted as the most accurate measure of cardiopulmonary physical fitness. It integrates evaluation of the state of the oxygen transport system and includes functions of the pulmonary, cardiovascular, and muscular systems. In adults, during a maximal exercise testing (MET), VO_2 reaches a plateau at VO_{2max}, and no further increase is observed with further increases in the rate of work. This plateau is infrequently found when testing children, and VO_{2max} cannot be precisely determined in many pediatric studies; thus, VO_{2peak} is used instead[9]. It is also suggested that peak VO_2 values reflect true VO_{2max} in children, although a VO_2 plateau is not observed[10].

JIA patients are known to have some degree of impairment in physical activity and aerobic fitness[11-13], which may be moderate to heavy, as shown by measurement of VO_{2peak}. In a recent metaanalysis, significant heterogeneity was observed between studies that reported lower VO_{2peak} levels in patients with JIA[2]. An important reason for this heterogeneity in results may be differences in subgroup distributions in different studies. It is obvious that the more severe subgroups [systemic JIA (SJIA), polyarticular JIA (PJIA)] will have more pronounced impairment. JIA consists of 7 distinct subgroups[14], and the data on the exercise characteristics of individual subgroups are very limited.

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Our main objective was to determine aerobic fitness and exercise capacity differences between subgroups of JIA in order to provide strategies for optimizing exercise challenge and/or prescription and for establishing the range of activities that are likely to be successfully undertaken by these patients.

MATERIALS AND METHODS

Subjects. Thirty-four patients (21 F, 13 M) ages 7–16 years with a diagnosis of JIA were included in the study. Twenty-one healthy (13 F, 8 M) children ages 11–15 years served as a control group. Control subjects were recruited from a primary school close to the hospital, using a posted written announcement. Volunteers were given a complete physical examination by a general pediatrician. Healthy volunteers with a sedentary lifestyle were included in the study. Patients were diagnosed and divided into subgroups by a pediatric rheumatologist (ÖK) according to the criteria of the International League of Associations for Rheumatology[14]. Patients with no limitation in range of motion in the ankle, knee, or hip joints were included in the study in a nonrandomized manner. Disease activity was determined according to Giannini, *et al*[15]. The patient group had systemic JIA (SJIA, n = 8), polyarticular JIA (PJIA, n = 13), oligoarticular JIA (OJIA, n = 7), and enthesitis-related arthritis (ERA, n = 6). Mean disease duration of patients with JIA was 5.9 years (SD ± 2.7, range 2–12). Medications were as follows: methotrexate (23 patients), nonsteroid antiinflammatory drugs and sulfasalazine (11 patients). The median Childhood Health Assessment Questionnaire (CHAQ) disability score was 0.40 (range 0–2) in patients with JIA. The median number of active joints was 2 (range 0–8). Prior to testing, parents of subjects read and signed a consent form that was approved by the university's Policy and Review Committee on Human Research.

Anthropometry. Body mass was measured on a balance beam medical scale (Fairbanks) to the nearest 0.1 kg. Stature was measured on a portable stadiometer to an accuracy of ± 0.5 cm with the subject barefoot, feet together, and head level. Body mass index was calculated as weight in kilograms divided by square of height in meters.

Experimental protocol. The peak oxygen uptake (VO_{2peak}) of all subjects was measured during MET. Each patient first underwent a comprehensive physical examination that included a 12 lead electrocardiogram (ECG) recording and blood pressure measurement at rest. They performed pulmonary function tests before exercise testing. All tests were performed in an air-conditioned laboratory room at 20–22°C and 40% relative air humidity, to minimize thermal stress. Subjects had a light breakfast 2 h before exercise and abstained from strenuous exercise for a week prior to MET.

Exercise testing. The subjects exercised on a cycle ergometer with electronic braking (ercometrics 800, Ergoline, Germany) at an initial work-rate of 10 W, which was increased by 10 W at the end of each 1 minute segment. Peak power (W_{peak}) was calculated as follows:

$$W_{peak} = W_f + (t / 60\ s \times 10\ W)$$

where W_f = power output (W) of last complete stage; t = duration (s) of final non-complete stage; 60 s = workload duration, and 10 W = workload increment. Prior to testing, the subjects were acclimatized to the cycle ergometer with a 2-min warmup period. The pedal rate was kept constant at 70 rpm throughout the test. Each test was terminated by subject fatigue or maximal exercise level. A subject was considered to have reached maximal level by achieving one of 2 test criteria: (1) a respiratory exchange ratio (RER) ≥ 1.00, (2) heart rate reaching 85% of age-predicted maximal heart rate. Maximal heart rate (HR_{max}) was calculated by using the formula [HR_{max} = 210 – (0.65*age)][16]. Age and sex-specific maximal predicted values of remaining exercise variables were calculated according to American Thoracic Society and American College of Chest Physicians statement on cardiopulmonary exercise testing[16]. A full 4-electrode, 6-lead ECG was monitored. Heart rate was monitored by ECG. Blood pressure was measured every 2 minutes using cuff manometry for children (ERKA, Germany).

Direct measurements of maximal oxygen uptake. Peak VO_2 was determined from expired gas measurements during testing. Expired gases (O_2 and CO_2) were analyzed breath by breath on a SensorMedics Vmax 29c Metabolic Measurement Cart (Sensormedics Corporation, Anaheim, CA, USA). Samples were analyzed for O_2 and CO_2 content by fast paramagnetic and nondispersive infrared analyzers, respectively. The system was calibrated before each test with standard gases of known O_2 and CO_2 concentrations. The most elevated VO_2 measured over 10 seconds during the last minute of exercise was considered the VO_{2peak}.

Statistical analysis. All data were analyzed using SPSS 11.0 for Windows. Values are given as means ± standard deviation (SD). Results from healthy controls and patients were compared using the independent samples t test. To detect sex differences between patient and control groups, the chi-square test was used by cross-tabulation. Comparisons between subgroups were performed using the Kruskal-Wallis test. Post hoc pairwise comparisons were by Mann-Whitney U test. A comparison was also performed between the JIA patients with active disease and those in remission using Mann-Whitney U test. A probability value of 0.05 was accepted as statistically significant.

RESULTS

All patients showed good tolerance of the maximal exercise test on the bicycle ergometer. We encountered no complications during 55 tests. Four patients and one control ended the MET session before meeting one of the maximal exercise criteria (HR > 85% of age-predicted HR, RER > 1.00). There was no difference between patients and controls in regard to percentage of predicted maximal heart rate and maximal RER. Therefore, we are confident that patients and controls in this study exerted an equally maximal effort during MET. Results of the healthy control group and patient group are given in Table 1 and 2. We found no significant difference between the mean ages of the patient and

Table 1. Comparison of physical characteristics and exercise performance between patients with JIA and controls. Age and sex-specific maximal predicted values were calculated according to the ATS/ACCP statement on cardiopulmonary exercise testing[16].

	JIA, n = 34	Healthy Controls, n = 21	p
Age, yrs	11.5 ± 2.8	12.6 ± 1.5	NS
Height, cm	142.3 ± 14.2	147.0 ± 8.9	NS
Weight, kg	37.0 ± 11.9	42.2 ± 6.9	NS
BMI, kg/m^2	17.9 ± 3.1	19.4 ± 1.7	< 0.05
Exercise load			
Exercise time, s	480 ± 146	614 ± 172	< 0.01
Peak power, % predicted	70.8 ± 15.3	76.7 ± 19.1	NS
Metabolic analysis			
VO_{2peak}, ml/kg/min	29.1 ± 5.2	33.9 ± 5.4	< 0.01
VO_{2peak}, % predicted	61 ± 13	76 ± 10	< 0.001
RER	1.09 ± 0.04	1.08 ± 0.04	NS

BMI: body mass index, RER: respiratory exchange ratio. % predicted: Percentage of age-predicted maximal value.

Table 2. Comparisons of the cardiovascular and respiratory measurements of patients with JIA versus healthy controls during maximal level of exercise testing.

	JIA, n = 34	Healthy Controls, n = 21	p
Cardiovascular			
HR, bpm	185 ± 11	185 ± 5	NS
HR, % predicted	91 ± 5	92 ± 2	NS
SBP, mm Hg	116 ± 10	129 ± 7	< 0.001
DBP, mm Hg	52 ± 6	58 ± 7	< 0.01
O_2 pulse, % predicted	69 ± 12	82 ± 9	< 0.001
Pulmonary			
V_{Epeak}/MVV	68 ± 13	67 ± 11	NS
V_{Epeak}, % predicted	57 ± 11	56 ± 11	NS
Peak V_E/VO_2	44.2 ± 7.3	40.1 ± 5.0	< 0.05
V_D/V_T, estimated	0.28 ± 0.05	0.26 ± 0.05	NS
V_T/IC	61.2 ± 12.6	64.3 ± 6.3	NS

HR: heart rate; % predicted: Percentage of age-predicted maximal value; SBP: systolic blood pressure; DBP: diastolic blood pressure; V_{Epeak}/MVV: Mean dyspnea index; V_{Epeak}: peak minute ventilation; Peak V_E/VO_2: Peak ventilatory equivalent; V_D/V_T: ratio of dead space to tidal volume; V_T/IC: Ratio of tidal volume to inspiratory capacity. NS: nonsignificant.

the control groups. Chi-square test of sex distribution showed no difference between the patient and the control groups (62% female, 38% male vs 62% female, 38% male, respectively; $p > 0.05$). VO_{2peak} measurement and exercise time indicated that JIA patients have impaired aerobic capacity and exercise tolerance. Both relative VO_{2peak} and percentage of predicted VO_{2peak} values were lower in JIA patients (Table 1). In addition, exercise time was also lower in the JIA group (Table 1).

Systolic blood pressure, diastolic blood pressure, and percentage of predicted O_2 pulse values during exercise were found to be significantly lower in the JIA group than in the control group (Table 2). Among pulmonary variables, only ventilatory equivalent was significantly higher in the JIA group than in controls (Table 2).

An enrollment of 34 JIA patients enabled us to analyze the group as 4 distinct subgroups: SJIA, PJIA, OJIA, and ERA. When results from subgroups of JIA were compared, we found no difference in exercise characteristics between SJIA, PJIA, and OJIA subgroups (Table 3). Peak oxygen uptake of ERA patients was higher than the remaining 3 groups (Figure 1). They also continued exercise longer than the other subgroups (Figure 2). These findings suggested that the ERA subgroup was less deconditioned in terms of aerobic fitness. Results of cardiopulmonary measurements during exercise are given in Table 4. Measured variables showed the same characteristics in all our JIA subgroups.

We also divided the patient group into 2 subgroups: patients with active disease (n = 10) and patients in remission (n = 24). When we compared the results of the 2 groups, no significant difference was found in terms of aerobic fitness and exercise capacity (Table 5).

DISCUSSION

We found lower peak oxygen uptake (VO_{2peak}) values in the JIA group. VO_{2peak} in our JIA group was somewhat lower compared to other JIA populations of previous studies[2,12,13]. This may be explained by the number of SJIA patients. Our study group included more SJIA patients than previous studies. Another factor may be the study protocol, which included higher increments during each stage. Thus, before reaching the cardiopulmonary limit, local muscular fatigue can undermine exercise testing. The mean exercise time value was also lower in the JIA group compared to controls. These findings indicated that our JIA group was deconditioned and had impaired aerobic fitness. Oxygen pulse, defined as the volume of O_2 consumed per single heartbeat,

Table 3. Physical characteristics and exercise performance of JIA subgroups.

	SJIA, n = 8	PJIA, n = 13	OJIA, n = 7	ERA, n = 6
Age, yrs	11.5 ± 3.0	11.6 ± 3.1	10.0 ± 2.1	13.3 ± 1.7
Height, cm	136 ± 8	141 ± 16	139 ± 10	155 ± 10*
Weight, kg	33.5 ± 7.1	36.0 ± 14.2	34.3 ± 8.7	46.9 ± 11.6
BMI, kg/m^2	18.2 ± 4.0	17.4 ± 2.9	17.4 ± 2.6	19.1 ± 3.5
Exercise load				
Exercise time, s	386 ± 74	462 ± 119	450 ± 121	680 ± 133†
Peak power, % predicted	66.2 ± 18.6	69.6 ± 13.6	75.0 ± 16.9	74.8 ± 14.0
Metabolic analysis				
VO_{2peak}, ml/kg/min	26.1 ± 2.8	28.2 ± 4.7	30.6 ± 4.2	33.3 ± 7.3
VO_{2peak}, % predicted	58.6 ± 13.8	57.5 ± 10.0	60.4 ± 10.7	77.6 ± 14.2‡
RER	1.08 ± 0.04	1.10 ± 0.06	1.06 ± 0.03	1.10 ± 0.03

BMI: body mass index, RER: respiratory exchange ratio. % predicted: Percentage of age-predicted maximal value. * ERA subgroup was higher than SJIA and OJIA subgroups ($p < 0.01$ and $p < 0.02$, respectively). † ERA subgroup continued exercise longer than SJIA, PJIA, and OJIA subgroups ($p < 0.01$, $p < 0.01$, and $p < 0.02$, respectively). ‡ ERA subgroup also reached VO_{2peak} levels significantly higher than SJIA, PJIA, and OJIA subgroups ($p < 0.05$, $p < 0.01$, and $p < 0.05$, respectively).

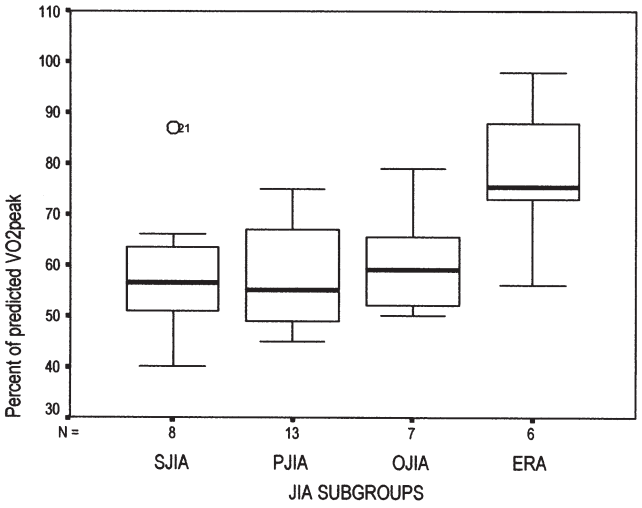

Figure 1. Box plot of VO_{2peak} measurements of 4 JIA subgroups. The enthesitis-related arthritis (ERA) group showed significantly higher VO_{2peak} levels than the systemic (SJIA), polyarticular (PJIA), and oligoarticular (OJIA) JIA subgroups. Circle indicates an outlier between 1.5 and 3 times the interquartile range (IQR) from the box. Whiskers represent highest and lowest values within 1.5 times the IQR. Lower and upper horizontal lines of the box indicate 25th and 75th percentiles, respectively. Horizontal bar shows the median.

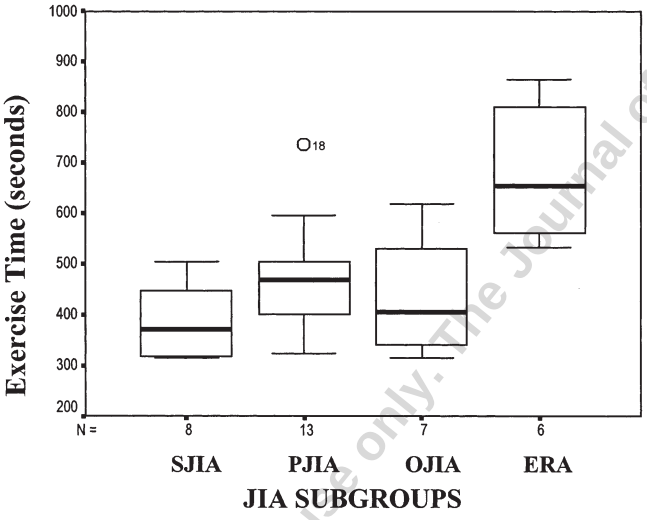

Figure 2. Box plot of exercise duration in JIA subgroups. The enthesitis-related arthritis (ERA) group continued exercise significantly longer than systemic (SJIA), polyarticular, and oligoarticular (OJIA) subgroups. Circle indicates an outlier between 1.5 and 3 times the interquartile range (IQR) from the box. Whiskers represent highest and lowest values within 1.5 times the IQR. Lower and upper horizontal lines indicate 25th and 75th percentiles, respectively. Horizontal bar shows the median.

is also used as an index of fitness[17]. JIA patients showed lower O_2 pulse than controls in our study. This finding further supports that JIA patients exhibited impaired aerobic fitness.

Maximal systolic and diastolic blood pressures were lower in the JIA group during exercise. This may be due to decreased stroke volume, which is a determinant of blood pressure, and which is reportedly the result of sedentary lifestyle[18]. Our results revealed that maximal HR in both groups were similar. Thus, it can be concluded that lower O_2 pulse levels may be a result of lower stroke volume in our JIA group.

Ventilatory equivalent for oxygen (VE/VO_2) is a measure of efficiency of the ventilatory pump at various workloads. This useful variable to evaluate the level of total ventilation required for a particular exercise allows assessment of the role of the lungs in exercise limitation[17]. Peak VE/VO_2 in the JIA group was significantly higher than in the control group. Many subjects hyperventilate during the resting phase at the beginning of an exercise evaluation. The result is an increased VE/VO_2 that usually returns to the normal range during exercise[17]. In our JIA patients, higher peak VE/VO_2 values indicate that they have to exert a higher respiratory workload to match their O_2 consumption during exercise. This suggests that the lungs also should be taken into account when considering exercise limitation in JIA patients.

Impaired aerobic capacity in patients with JIA may be attributed to muscle weakness, psychological factors, or parental factors, etc. Lindehammar, *et al*[6,19] found that normal muscle strength and bulk were rapidly lost near an inflamed joint in patients with JIA. Eventually, leg muscles become weaker and thinner than normal; muscle weakness is in part caused by muscle atrophy.

Parental factors may force a child to have an inactive lifestyle. Parents may impose inactivity on their child for protective reasons by not allowing sports activities[3]. Unfounded fear of exercise has also been shown to negatively affect children whose parents thought something was wrong with their child's heart[20]. In our patient group, exercise limitation and/or termination resulted from lower extremity fatigue rather than cardiac or pulmonary reasons.

Subgroup analysis showed that maximal oxygen uptake and exercise duration of the ERA group were higher than those of the remaining 3 subgroups (Figures 1 and 2). Cardiopulmonary measures during MET showed similar characteristics among the JIA subgroups. Hence, it is unlikely that the difference in aerobic fitness was due to cardiac or pulmonary functions. Higher aerobic condition in the ERA subgroup may be explained by better adaptation of muscles to physical activities. We think that this subgroup was not limited in their daily and creative activities. Eventually, muscle atrophy was prevented in these patients. Another possible factor may be previous severity of joint pain. It can be expected that the patients with more severe pain previously (i.e., SJIA, PJIA) will be more discouraged from physical activity even during symptom-free periods. Hebestreit, *et al*[3] reported that some patients with juvenile spondyloarthropathy had impaired aerobic fitness long after

Table 4. Cardiovascular and respiratory measurements during maximal level of exercise testing in JIA patients.

	SJIA, n = 8	PJIA, n = 13	OJIA, n = 7	ERA, n = 6
Cardiovascular				
HR, bpm	182 ± 11	186 ± 11	184 ± 10	189 ± 13
HR, % predicted	90 ± 5	92 ± 5	90 ± 4	93 ± 5
SBP, mm Hg	109 ± 7	115 ± 10	121 ± 7	122 ± 9
DBP, mm Hg	50 ± 1	50 ± 6	55 ± 3	55 ± 9
O_2 pulse, % predicted	69.7 ± 15.3	63.7 ± 9.1	68.7 ± 14.2	79.8 ± 11.1
Pulmonary				
V_{Epeak}/MVV	64 ± 10	67 ± 15	69 ± 11	72 ± 17
V_{Epeak}, % predicted	53.2 ± 10.4	56.6 ± 11.1	56.5 ± 11.2	63.1 ± 11.6
Peak V_E/VO_2	45.3 ± 7.8	45.3 ± 5.9	43.7 ± 7.8	41.1 ± 9.6
V_D/V_T, estimated	0.28 ± 0.03	0.30 ± 0.06	0.29 ± 0.05	0.22 ± 0.03
V_T/IC	64.2 ± 16.2	62.0 ± 13.5	55.7 ± 9.0	62.0 ± 9.4

Differences between groups were not statistically significant. HR: Heart rate; % predicted: Percentage of age-predicted maximal value; SBP: systolic blood pressure; DBP: diastolic blood pressure; V_{Epeak}/MVV: Mean dyspnea index; V_{Epeak}: peak minute ventilation; Peak V_E/VO_{2peak}: Peak ventilatory equivalent; V_D/V_T: ratio of dead space to tidal volume; V_T/IC: Ratio of tidal volume to inspiratory capacity.

Table 5. Exercise characteristics of JIA patients in active disease state and remission.

	Patients with Active Disease, n = 10	Patients in Remission, n = 24	p
Exercise time, s	517 ± 189	465 ± 126	NS
Peak power, % predicted	75.2 ± 19.7	69.0 ± 13.1	NS
VO_{2peak}, % predicted	61.3 ± 13.9	62.2 ± 13.7	NS
HR, % predicted	91 ± 6	92 ± 5	NS
O_2 pulse, % predicted	68.8 ± 13.5	69.1 ± 13.0	NS
V_{Epeak}, % predicted	59.3 ± 10.2	56.0 ± 11.4	NS

% predicted: Percentage of predicted maximal value; HR: heart rate; V_{Epeak}: peak minute ventilation.

arthritis had ceased that was attributable to psychological factors. To our knowledge, no study has addressed the longterm effects of pain in JIA patients after entering remission. As a result, it is critical to encourage and prescribe exercise in SJIA, PJIA, and OJIA subgroups to improve aerobic capacity. Such an approach will increase health-related quality of life and activities of daily life in these subgroups.

An important finding of our study is that patients with active disease and those in remission both tolerated MET well. We failed to find any difference in cardiopulmonary variables of these 2 disease states. Previous studies suggested that exercise programs can be started soon after diagnosis[8] and can be continued during episodes of active disease[21]. These latter findings are in accord with our finding that all JIA patients irrespective of disease state tolerated MET well.

Several potential limitations of the study deserve comment. First, there is little information on reference values for healthy children in Turkey. Thus, we could not compare our VO_{2peak} values with standardized reference values for Turkish children. We added a healthy control group to overcome that disadvantage. Second, we did not use the Borg scale, a subjective rating of perceived exertion by the person exercising, which is a good indicator of relative fatigue. This scale is used for quantifying effort during exercise[22]. Borg scale measurements would have increased the validity of our study; however, a Turkish version has not been validated. A Turkish language version of the Childhood Health Assessment Questionnaire was recently validated[23], which allowed us to measure the CHAQ disability scores of our patients. However, adding other outcome measures to assess health-related quality of life and function such as the Juvenile Arthritis Functional Assessment Report would have been beneficial.

In addition, a study of a log-linear scaling model[24] identified a significant influence of maturation on peak VO_2 that indicated exercise testing results can be influenced by pubertal stage. Taking into account the pubertal stage would increase the validity of our study. We did not investigate the pubertal stages of our subjects; however, we think that this limitation is debatable for several reasons. Most previous studies on exercise capacity in JIA patients[1-3] did not report or take into account the pubertal stage of their subjects. Thus, lack of pubertal information in our study does not limit comparability or preclude performing, for example, a metaanalysis. Pubertal stage may be important for achieving a VO_2 plateau during exercise testing. In published studies, only about one-third of prepubescent children were reported to achieve a VO_2 plateau; for others, a peak VO_2 is reported[25-27]. Armstrong, *et al*[25] and Rowland[10] demonstrated that in children, a peak VO_2 taken over several seconds is an index of maximal exercise, even in the absence of a plateau. Lastly, the peak attainable lactate

levels during exercise are higher for adults than for children[9]. The ability to tolerate increased serum lactate levels and to persist with exercise in the anaerobic state may depend on the degree of the subject's sexual maturity. We think that pubertal stage is important when studying anaerobic rather than aerobic capacity.

Our results allow us to conclude that (1) there is an impairment of aerobic capacity in patients with JIA compared to healthy controls; (2) the ERA subgroup exerted better aerobic fitness than the remaining subgroups; (3) both patients with active disease and those in remission tolerated MET well and should be encouraged to exercise; and (4) we suggest that heterogeneity in VO_{2peak} levels among JIA patients is due to subgroup differences. Thus, exercise programs for improvement of aerobic fitness should be individualized or at least be modified according to different subgroups.

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