

Aerobic and anaerobic capacity in Juvenile Idiopathic Arthritis: evaluation of the cardiorespiratory response

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Citation

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Abstract

Objectives: To compare the cardiac response during maximal aerobic exercise in JIA with healthy children.

Methods: Thirteen children aged 10 to 17 years with JIA and 9 controls (CON) participated. All performed maximal VO_2 and Wingate tests on a cycle ergometer. Cardiac output (CO) was measured during exercise with Doppler echocardiography. Arterial – mixed venous oxygen index (A- VO_2) and systemic vascular resistance (SVR) were calculated.

Results: JIA subjects had decreased aerobic fitness (VO_2 31.3, CON 47.9 ml/kg/min $p = 0.013$). There was no significant difference in CO, A- VO_2 or SVR but we observed trends towards lower CO and higher SVR in JIA. During anaerobic exercise JIA subjects completed less total work.

Conclusions: Children with JIA have moderate impairment in aerobic fitness. CO and A- VO_2 during aerobic exercise did not differ between JIA subjects and CON. Further research with is required to determine factors contributing to limited fitness in JIA.

CONTRIBUTING INSTITUTIONS

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INTRODUCTION

As a group, children with chronic disease or physical disability are less active than their healthy peers and studies show children with juvenile idiopathic arthritis (JIA) have reduced vigorous physical activity levels, sports participation and decreased fitness compared to healthy children. (1,2,3)

Children with JIA have moderate impairments (21.8% in meta-analysis) in aerobic fitness as measured by $\text{VO}_{2\text{ peak}}$ (4,5,6,7). $\text{VO}_{2\text{ peak}}$ is the gold standard for aerobic fitness and is equal to the product of cardiac output (CO, maximal heart rate multiplied by maximal stroke volume), and arterial venous oxygen (A- VO_2) difference as defined by Fick equation. Suboptimal $\text{VO}_{2\text{ peak}}$ may be due to central limitations, characterized by suboptimal heart rate response,

CO or oxygen saturation; or peripheral limitations, characterized by high mixed venous oxygen content (low A- VO_2).

Peripheral limitations due to muscle atrophy and weakness are hypothesized to largely account for diminished aerobic fitness in children with JIA. Children with JIA have generalized muscle weakness and muscle atrophy, most pronounced in muscles surrounding inflamed joints and often persisting even after clinical resolution of inflammation. (8,9,10,11) Muscle atrophy may lead to decreased oxygen extraction from the exercising muscle, resulting in high mixed venous oxygen content and a low $\text{VO}_{2\text{ peak}}$. Central and peripheral measures of aerobic fitness in children with JIA have not been reported.

There is limited data on anaerobic fitness in JIA with recent studies describing significant anaerobic impairment in children and adolescents. (7, 12,13,14,15) Most childhood play and activities of daily living are anaerobic in nature. Impaired anaerobic fitness may make activities difficult or impossible for children to perform. An association between anaerobic fitness and functional capacity has been described.

(₁₆)

The purpose of this study is to examine the cardiorespiratory response during aerobic exercise and the anaerobic to aerobic ratio (metabolic index) in children with JIA compared to healthy children.

METHODS

Participants: Patients between 8 and 18 years of age followed at British Columbia's Children's Hospital arthritis clinic with a definite diagnosis of JIA and history of lower extremity joint involvement were invited to participate. (₁₇) Patients were excluded if they had active systemic disease manifest by fever, pericarditis or pleuritis; disease remission greater than one year; primary cardio-respiratory disease with the exception of mild asthma; were unable to cycle due to pain or decreased range of motion of lower extremity joints or were unable to tolerate the mouthpiece for $\text{VO}_{2\text{peak}}$ testing due to temporomandibular joint disease. Controls (CON) were physically healthy age and sex matched peers, friends or relatives of patients with JIA. Study assessments occurred between January and September 2007. All participants and caregivers provided assent and consent prior to participation. Ethical approval was obtained from the University of British Columbia's Clinical Research Ethics Board and the Hospital's Research Review Committee.

Materials and Methods: Study participants with JIA underwent a clinical assessment by a rheumatologist (KH) the same day as the exercise testing. Assessment included a complete physical examination including active joint count, calculation of the articular severity index (ASI), and data collection for age, sex, disease duration, history of previous cardiac or respiratory disease, recent hemoglobin level and current medications. Subjects underwent all testing in the afternoon to negate morning stiffness as a potential confounding factor.

ANTHROPOMETRIC DATA

Height (Harpenden Stadiometer, London) and body mass (SECA electronics, Hamburg, Germany) were measured to the nearest 0.1cm and 0.1kg respectively. Body mass index (BMI) was calculated (kg/m^2). Obesity was defined as BMI or greater than the 95th percentile according to reference data. (₁₈)

FITNESS

A Wingate test was done first followed by a modified stress echocardiogram with VO_2 measurement. Both exercise tests

were done on an upright cycle ergometer. Anaerobic fitness: Subjects initially warmed up for a few minutes with easy pedaling interposed with 5 to 7 second sprints. Subjects then performed the Wingate test; a 30 second maximal test on an upright cycle ergometer against a high constant resistance (0.070 Newton / kg). (₁₉) Leg peak power (Watts, W) in any 5 second period, peak power expressed per kg body mass (W/kg) and total work (Joules, J) completed were calculated by a computer software package (Wingate for Windows). Aerobic fitness: Subjects completed a maximal graded cycle ergometer exercise test to volitional fatigue. After a 3 minute warm-up period, the initial workload of 0 watts was increased by 20 to 40 watts (dependent on the age and fitness of the subject) every 3 minutes using a staged protocol. Open circuit spirometry was used to determine gas exchange variables during exercise and averaged over 15-second intervals. Subjects breathed through a Hans Rudolph valve (Hans Rudolph, Inc., Kansas City, MO.) Using a MOXUS Modulator VO_2 system (AEI Technologies, Inc, Pittsburgh, PA), expired gases were analyzed by oxygen and carbon dioxide analyzers (Model S-3A and CD-3A, respectively, AEI Technologies, Inc, Pittsburgh, PA). The system was calibrated before each test with standard gases of known oxygen (20.93% and 15.00%) and carbon dioxide (0.03% and 5.02%) concentrations. Volume was calibrated and verified using a 3-litre syringe (Hans-Rudolph, INC, Kansas City, MO). Measurements included total test duration, $\text{VO}_{2\text{ peak}}$ (defined as highest VO_2 achieved in any 15 second period), maximal ventilation and peak respiratory exchange ratio (RER). Doppler echocardiogram images (parasternal long axis at base of sternum) were taken prior to exercise, 150 seconds into each 3 minute stage of exercise, immediately post exercise and 3 minutes post exercise. Two lead electrocardiogram (ECG) recorded continuous heart rate (HR) measurements. Blood pressure was measured manually prior to exercise, 120 seconds into each 3 minute stage of exercise, immediately post exercise and 3 minutes post exercise. Mean arterial blood pressure (MAP) was calculated [$\text{Pressure}_{\text{Diastolic}} + 1/3 (\text{Pressure}_{\text{Systolic}} - \text{Pressure}_{\text{Diastolic}})$]. A maximal test was defined as achieving an RER > 1.0 or reaching MHR greater than 195. (₂₀)

CARDIAC OUTPUT (CO)

CO was measured with Doppler echocardiography by a single echocardiographer (AH). Parasternal long-axis view was used to measure the left ventricular outflow tract (LVOT) diameter at the aortic valve hinge-point during systole. The LVOT area was calculated from this diameter.

From an apical 4-chamber view with the transducer tilted anteriorly towards the LVOT, a pulsed wave Doppler sample volume was taken from the centre of the LVOT. The velocity-time integral (VTI) was calculated. The frequency of the transducer (7, 5S, M3S MHz) varied depending on the size of the child. Stroke volume (SV) was calculated as the product of the VTI and LVOT area. Both SV and CO were indexed to body surface area (BSA). CO was calculated as the product of SV and HR. Measurements were taken at rest, 150 seconds into each stage of exercise, immediately post exercise and 3 minutes post exercise.

ARTERIAL-MIXED VENOUS O₂ DIFFERENCE (A-VO₂) AND SYSTEMIC VASCULAR RESISTANCE (SVR)

A-VO₂ was calculated as the absolute oxygen uptake divided by the absolute CO ($A-VO_2 = VO_{2peak}/CO$). A-VO₂ is equal to arterial O₂ content minus the mixed venous O₂ content. SVR was calculated from CO and MAP ($SVR = MAP / CO$).

JOINT PAIN

Subjects with JIA completed a visual analogue scale (VAS) for joint pain on the day of testing, over the previous week and immediately after testing using a 10 point validated VAS scale from the Pediatric Pain Questionnaire. ^(21, 22) Control subjects completed the VAS after completion of the exercise test.

DISEASE ACTIVITY ASSESSMENT

Subjects with JIA were assessed on the day of testing prior to performing any exercise. ASI was calculated as the sum of scores for joint swelling, pain on motion, tenderness, and limitation of motion. ⁽²³⁾ Active joint count was determined as the number of joints with either swelling or painful, limited range of motion.

FUNCTIONAL DISABILITY

Subjects with JIA or their proxy (parent or guardian) completed the childhood health assessment questionnaire (CHAQ), a valid and reliable measure of function in children with JIA. ⁽²⁴⁾

PHYSICAL ACTIVITY

A questionnaire was completed by patients and controls to determine habitual physical activity and general health. (Adapted from the Children's Exercise and Nutrition Centre at McMaster University. Developed by Oded Bar-Or, MD, FACSM.)

Statistical Analysis: Baseline characteristics were compared with Student's T-test. Descriptive statistics were calculated for fitness measures. Median values and ranges are presented for non-normally distributed data. Z-scores are presented for individual subjects. Differences in fitness measures between subjects with JIA and controls were determined using wilcoxin mann-whitney test for non-normally distributed data. The association between continuous variables was assessed using Pearson and Spearman correlation coefficients. Linear regression models were used to explore the relationships between aerobic fitness, anaerobic fitness, disease activity and function in subjects with JIA. Correlation coefficients of 0.3 to 0.5 were set as low, 0.5 to 0.7 moderate and 0.7 to 1.0 as high correlation. Significance level for all tests was set at $P < 0.05$. Statistics were performed using SPSS 15.0 (SPSS Inc, Chicago, IL).

RESULTS

Thirteen children and adolescents aged 10 to 17 years with JIA and 9 CON participated in the study. Table 1 shows patient and CON demographics. There was no difference between the two groups. JIA subjects median age was 13.9 (10.5-17.7) and the control subjects was 12.8 (11.3-16.5). Two of the JIA subjects met the operational definition of obesity. ⁽¹⁸⁾

Figure 1

Table 1: Patient and Control Demographics

Patient	Age	Sex	BMI (kg/m ²)	PA	CON	Age	Sex	BMI (kg/m ²)	PA
1	12.4	F	21.9	A	1	14.3	M	19.6	A
2	14.9	M	19.0	NA	2	11.9	M	17.9	A
3	12.8	F	21.6	A	3	11.9	M	18.4	A
4	11.7	F	16.9	A	4	14.1	F	17.1	A
5	16.8	F	32.7	NA	5	12.8	M	16.1	A
6	16.9	F	34.6	A	6	14.5	F	19.2	A
7	10.5	F	19.2	A	7	12.2	F	20.8	A
8	14.7	M	19.2	A	8	11.3	F	17.0	A
9	17.7	M	27.6	A	9	16.5	F	21.4	A
10	12.8	M	16.5	A					
11	16.4	F	19.1	A					
12	13.5	M	18.1	A					
13	13.9	M	21.4	A					
Median (Range)	13.9 (10.5-17.7)	6M:7F	19.2 (16.5-34.6)	11 active		12.8 (11.3-16.5)	4M:5F	18.4 (17.0-21.4)	9 active

F = Female, M = Male, BMI = Body Mass Index, PA = physical activity, NA = not active, A= active

JIA subject disease characteristics are shown in Table 2. Median disease duration was 24 (5-166) months. All JIA

subjects were on at least one medication for their arthritis. Eleven (85%) were on a non-steroidal anti-inflammatory medication (NSAID), 9 (69%) on disease modifying anti-rheumatic disease therapy (DMARD), 2 (15%) on corticosteroids and 1 (8%) on biologic anti-cytokine therapy. Disease activity was variable with median active joint count=1 (0-22) and ASI=6 (0-64). Function and pain was also variable with a median CHAQ score=0 (0-1.4); 5 patients had mild-to-moderate disability. (25)

Figure 2

Table 2: Patient Disease Characteristics

Patient	JIA subtype	Disease duration (months)	Active joint count	ASI	Hgb (g/L)	Meas	CHAQ, VAS pain (0-100)
1	Poly RF-	5	10	28	124	MTX, Naproxen, Prednisone	1.4, 64
2	ERA	21	2	7	129	MTX, SSZ, Naproxen	0.3, 17
3	Poly RF-	8	2	8	133	MTX, Naproxen	0, 13
4	EOJIA	98	1	7	129	MTX, Naproxen	0.4, 86
5	Ps A	166	0	3	117	MTX, Naproxen, Prednisone	0, 43
6	ERA	23	1	6	117	MTX	0,18
7	Poly RF-	24	0	0	142	None	0, 0
8	Poly RF +	32	22	64	108	Infliximab, MTX, Naproxen	0, 20
9	SJIA	44	7	11	120	MTX, Naproxen, Prednisone	0,0
10	E-OJIA	103	0	0	139	MTX	0,5
11	ERA	79	0	0	129	Naproxen, SSZ	0,11
12	O JIA	23	0	0	142	MTX, Ibuprofen	0.25,10
13	ERA	22	0	3	139	Ibuprofen	0.5,70
Median (Range)		24 (5-166)	1 (0-22)	6 (0-64)	132 (108-142)		22 (0-1.4) 17 (0-86)

JIA = juvenile idiopathic arthritis, Poly RF- =polyarticular JIA rheumatoid factor negative, Poly

RF+ =polyarticular JIA rheumatoid factor positive, ERA =Enthesitis related arthritis, O JIA

=oligoarticular JIA, EOJIA =extended oligoarticular JIA, Ps A =psoriatic arthritis, SJIA

=systemic JIA, ASI =articular severity index, Hgb = Hemoglobin, MTX = methotrexate, SSZ

=sulfasalazine

Fitness: Summary fitness measures are shown in Table 3. All subjects were able to complete the exercise tests without any adverse events. There was a large range in aerobic fitness measures for JIA subjects. $VO_{2\text{ peak}}$ was 31.3 ml/min/kg (20.2-49.9) corresponding to 67.7% (50.4-101.0) predicted and a Z score of -1.4 (-.06--2.4). Five (38%) JIA subjects had Z scores of -2 or lower. CON subjects $VO_{2\text{ peak}}$ was 47.9 ml/min/kg (32.7-54.1) corresponding to 97.0% (77.4-126.6) predicted and a Z score of -.17 (-1.6-.87). The difference between JIA subjects and CON subjects was significant ($P = .013$ for $VO_{2\text{ peak}}$, $P=.012$ for % predicted and $P=.011$ for Z score).

Figure 3

Table 3: JIA subjects and control subjects fitness measures

	JIA Subjects Median (Range)	CON Subjects Median (Range)	Wilcoxin-Mann-Whitney (P value)
$VO_{2\text{ peak}}$ (ml/min/kg)	31.3 (20.2-49.9)	47.9 (32.7-54.1)	0.013*
$VO_{2\text{ peak}}$ (% predicted)	67.7 (50.4-101.0)	97.0 (77.4-126.6)	0.012*
$VO_{2\text{ peak}}$ (Z-score)	-1.4 (-.06--2.4)	-.17 (-1.6-1.28)	0.011*
Max CO (L/min)	7.4 (5.6-13.1)	9.0 (6.7-11.5)	0.11
AVO_2	4.4 (2.5-6.4)	4.7 (3.6-6.4)	0.29
Systemic Vascular Resistance (SVR)	13.3 (8.5-20.2)	10.8 (9.4-14.4)	0.12
Peak power (watts/kg)	9.7 (5.6-13.7)	11.3 (9.8-14.5)	0.095
Total work (joules/kg)	168.5 (107-252)	224 (180-248)	0.036*
Metabolic index (anaerobic: aerobic power)	3.5 (2.1-5.9)	3.6 (3.2-4.4)	0.57

CO = cardiac output, A- VO_2 = Arterial-mixed venous O_2 difference, SVR = systemic vascular resistance.

Anaerobic fitness measures were variable for JIA subjects. Peak power was 9.7 W/kg (5.6-13.7) and total work completed 168.5 j/kg (107-252) compared to CON subject values of 11.3 W/kg (9.8-14.5) and 224 j/kg (180-248). There was no significant difference between the two groups for peak power ($P=.095$) but there was for total work completed ($P=.036$). The metabolic index did not differ between the two groups. Two subjects with JIA had a metabolic index less than 2.5, suggesting greater impairment of the anaerobic than aerobic system. (26)

Cardiac output: Maximal CO for JIA subjects was 7.4 L/min (5.6-13.1) and for CON subjects 9.0 (6.7-11.5). There was a trend towards lower CO in JIA subjects but no significant difference between the two groups ($P=0.11$).

A- VO_2 and SVR: A- VO_2 did not differ between JIA subjects and CON subjects ($P=0.29$) but there was a trend towards higher SVR in subjects with JIA. ($P=0.12$)

Physical activity: All CON subjects and 11 (85%) of JIA subjects were physically active.

Correlations: Correlations between aerobic and anaerobic fitness measures for JIA subjects are shown in Table 4. VO_2

$VO_{2\text{ peak}}$ showed moderate positive correlation with CO (.615, $P=.025$) and A- VO_2 (.637, $P=.019$) consistent with the Fick principle. $VO_{2\text{ peak}}$ and CO showed low and high negative correlation, respectively, with SVR which is consistent with basic physiology principles. Aerobic and anaerobic fitness showed moderate positive correlation: $VO_{2\text{ peak}}$ and peak power (0.664, $P=.019$) and $VO_{2\text{ peak}}$ and total work (.619, $P=.032$). In JIA subjects, there was no significant correlation between disease activity, function and fitness measures.

Figure 4

Table 4 : Correlations between aerobic and anaerobic fitness measures in children with JIA

	Max CO (L/min)	A- VO_2	Systemic Vascular Resistance (SVR)	Peak power (watts/kg)	Total work (joules/kg)
$VO_{2\text{ peak}}$ (ml/min/kg)	.615 * $P=.025$.637 * $P=.019$	-.366 $P=.218$.664 * $P=.019$.619 * $P=.032$
Max CO (L/min)		-.204 $P=.503$	-.800 * $P=.001$.353 $P=.260$.325 $P=.302$
Peak power (watts/kg)					.786 * $P=.002$

* P less than 0.05

CO = cardiac output, A- VO_2 = Arterial-mixed venous O_2 difference, SVR = systemic vascular resistance.

DISCUSSION

Children with JIA have moderate impairments (21.8% in meta-analysis) in aerobic fitness as measured by $VO_{2\text{ peak}}$ (5,6,7, 27). Our patients' aerobic fitness is similar to previous reports with $VO_{2\text{ peak}}$ 67.7% (50.4-101.0) predicted and a Z score of -1.4 (-.06--2.4). $VO_{2\text{ peak}}$ is the gold standard for aerobic fitness and is equal to the product of cardiac output (maximal heart rate multiplied by maximal stroke volume), and A- VO_2 (arterial oxygen content – mixed venous oxygen content) as defined by the Fick equation. Suboptimal $VO_{2\text{ peak}}$ may be due to central limitations, characterized by suboptimal heart rate response, CO or arterial oxygen content; or peripheral limitations, characterized by high mixed venous oxygen content (low A- VO_2).

Maximal CO in healthy children reaches three to four times the resting value. Most of the increase is due to HR with only 20-25% due to an increase in stroke volume. (28) $VO_{2\text{ peak}}$ in children with JIA may be limited centrally by low stroke volume (deconditioning) or low maximal heart rate (cessation of exercise due to fatigue or pain prior to reaching peak heart rate). (26) Children with JIA also have high sub-maximal energy expenditures suggesting increased metabolic demands for routine physical activity. (6) Doppler

echocardiography measures of CO at a given VO_2 did not differ between our JIA subjects and controls. This finding supports our original hypothesis that children with JIA have normal cardiac response to exercise and suboptimal $VO_{2\text{ peak}}$ is due to peripheral limitations.

$VO_{2\text{ peak}}$ may be limited peripherally by low arterial oxygen content or high mixed venous oxygen content. Low red cell mass leads to decreased arterial oxygen content, a reduction in maximal A- VO_2 and limitation of $VO_{2\text{ peak}}$. A moderate positive relationship between $VO_{2\text{ peak}}$ and total body hemoglobin is well described. (29) Anemia is common in children with poorly controlled polyarticular disease and systemic JIA. Only one of our JIA subjects had anemia and this subject had a $VO_{2\text{ peak}}$ of 91.5% predicted, making reduced arterial oxygen carrying capacity an unlikely contributor to suboptimal $VO_{2\text{ peak}}$ in our study population. Therefore, in our population high mixed venous oxygen content likely accounts for low A- VO_2 and low $VO_{2\text{ peak}}$. High mixed venous oxygen content is present when there is suboptimal blood flow to exercising muscles or deficient oxygen extraction from exercising muscles. During aerobic exercise, arterial systolic blood pressure increases in proportion to exercise intensity. Changes (increase or decrease) in diastolic pressure are smaller and reflect changes in peripheral vascular resistance. Mean arterial pressure (MAP), defined as the average arterial pressure during a single cardiac cycle, is considered the perfusion pressure seen by organs in the body. MAP and CO both increase during exercise. Lower SVR results in greater blood flow to exercising muscles.

Children with JIA have generalized muscle weakness and muscle atrophy, most pronounced in muscles surrounding inflamed joints and often persisting even after clinical resolution of inflammation. (8,9,10,11, 30, 31) Children with JIA likely have a combination of peripheral limitations to their aerobic capacity including: increased SVR which may limit blood flow to exercising muscles; muscle atrophy may lead to decreased oxygen extraction from the exercising muscle; and low muscle endurance may lead to decreased oxygen extraction at some stage during an exercise task. We found trends towards higher SVR and lower muscle endurance (lower total work completed during the anaerobic Wingate Test) in our subjects with JIA. We did not specifically measure muscle atrophy or muscle strength. We attempted to non-invasively measure of tissue oxygenation using near infrared spectrophotometer (NIRS) technology but were

unable to obtain reliable data in our subjects (data not published). (32, 33) There are no data on A-VO₂ in children with JIA or other chronic musculoskeletal conditions.

Anaerobic exercise is high intensity exercise that can't be sustained for more than 30 to 60 seconds. Anaerobic fitness depends predominantly on non-oxidative energy turnover and is related to local characteristics of working muscle groups. There is recognition that children's play activities are anaerobic in nature with short, intense bursts of high energy activity. Anaerobic fitness improves during childhood and adolescence concomitant with increased muscle mass, increased glycolytic capability and improved neuromuscular coordination. Until very recently, there was limited data on anaerobic fitness in JIA. (7, 12, 13) Two recent Dutch studies describe significant anaerobic impairment in children and adolescents with JIA. (14, 15) They performed Wingate exercise tests on 62 children with JIA and found impairment of mean power (66.7% predicted) and peak power (65.5% predicted) compared to healthy children. (14) A similar study of 22 adolescents with JIA found lower mean power for adolescent girls (74%) and boys (88%) and lower peak power for girls (67%). (15)

Anaerobic fitness may be lower in children with JIA due to muscle atrophy. In adults with rheumatoid arthritis, neuromuscular complications are not uncommon. Both neuropathy and a selective reduction in type II muscle fibres have been described. (34-36) A single study of muscle biopsies in children with JIA demonstrated the presence of inflammatory changes in the muscle but no evidence of type II muscle fibre hypotrophy or neuropathy. (37)

In our study, we found children with JIA had mild impairments in anaerobic fitness with less total work completed and a trend towards lower peak power. There are several possible reasons that our subjects with JIA did not have significant impairments. Our clinic's philosophy is to encourage activity and most of our patients participate in regular physical activity. There was also a study selection bias; the patients who volunteered to participate were generally quite fit and interested in sport. Impaired total work during maximal anaerobic exercise suggests poor muscle endurance. Poor muscle endurance may translate to muscular fatigue in daily activities. Given the anaerobic nature of children's activities they may be limited by low muscular endurance rather than suboptimal oxygen consumption. Children with significant anaerobic impairment may be unable to perform all their activities of

daily living. In support of this hypothesis, a recent study described a positive relationship between functional ability and anaerobic fitness in children with JIA. (16)

The anaerobic: aerobic ratio or metabolic index is usually greater than 2.5 in healthy children. A lower ratio implies that anaerobic power is compromised more than aerobic power. Children with advanced neuromuscular disease have a low metabolic index. (26) The metabolic index in our patients did not differ from our control population or referenced normative data.

Most studies show aerobic fitness is not significantly related to disease severity or activity but may be related to disease duration. (5,6,7, 16, 27) Increased physical activity levels and self efficacy for exercise correlate with improved aerobic capacity but a causal effect has not been established. (7) There is suggestion that anaerobic fitness is positively related to function. (16) We did not find any significant correlation between fitness measures, disease activity and function in this study.

This study has several limitations. Small subject numbers, a heterogeneous JIA population, and enrollment bias of fitter patients and controls limits generalization of our results. Age and gender differences for VO_{2 peak} are captured by normative data and calculation of Z scores. There are no gender differences in cardiac output and A-VO₂ in children so measures amongst JIA subjects and controls were grouped. (38, 39) We did not subdivide participants based on pubertal status due to small numbers. This may limit generalization of our findings as prepubertal children have lower maximal CO and higher A-VO₂ at a given VO_{2 peak}. (40) Future studies with larger numbers, subgroups of pubertal status and disease subtype may allow greater power to determine differences in aerobic and anaerobic fitness for children and teenagers with JIA.

In summary, we found moderate impairments in aerobic fitness in a cohort of children with JIA. Cardiac output and A-VO₂ during aerobic exercise did not significantly differ from healthy controls. According to Fick principle VO_{2 peak} is dependent on CO and A-VO₂. Redistribution of CO and / or a combination of peripheral limitations such as increased systemic vascular resistance, decreased oxygen extraction from exercising muscles due to muscle atrophy or poor muscle endurance may account for the lower VO_{2 peak} seen in our cohort of children with JIA. Anaerobic fitness was

mildly impaired with less total work completed in children with JIA. This may translate to fatigue in daily activities. Further research with larger numbers is required to determine factors contributing to limited aerobic and anaerobic fitness in children with JIA and to guide exercise therapies. Exercise capacity is increasingly recognized as an important predictor of mortality. (₄₁, ₄₂) Fitness as measured by $\text{VO}_{2\text{ peak}}$ may emerge as an important outcome measure for children with JIA.

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