Arthritis & Rheumatism (Arthritis Care & Research)
Vol. 53, No. 3, June 15, 2005, pp 351–356
DOI 10.1002/art.21175


ORIGINAL ARTICLE

# Physiologic Response of the Six-Minute Walk Test in Children With Juvenile Idiopathic Arthritis

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***Objective.*** **To determine the physiologic response of the 6-minute walk test (6-mwt) in children with juvenile idiopathic arthritis (JIA).**
***Methods.*** **Eighteen children with JIA (age 7–17 years; 6 boys, 12 girls) performed a 6-mwt and a maximal exercise test.**
***Results.*** **The physiologic response of the 6-mwt was on average between 80% and 85% of the peak values of heart rate and oxygen uptake ($\dot{V}O_{2peak}$) during the maximal exercise test, except for the minute ventilation, which had a mean percentage of 68.5%. Backward regression analysis showed that height and distance walked were the best predictors of $\dot{V}O_{2peak}$ during cycling ($R^2 = 0.883$, $P < 0.001$). During the 6-mwt, the difference between the first and second minute was significant in every variable, except for heart rate. The range of walking distance of children with JIA was comparable with that of healthy elderly people.**
***Conclusion.*** **The physiologic response of the 6-mwt is at a submaximal, intense level of exercise. The course of the responses during the 6-mwt was normal. The 6-mwt can be regarded as a good test for measuring functional exercise capacity.**

**KEY WORDS.** 6-minute walk test; Physiologic response; JIA; Exercise test; Physiology; Children.

## INTRODUCTION

Children with juvenile idiopathic arthritis (JIA) are believed to be less physically fit compared with healthy children (1). They also have a lower functional ability, which means that they have more problems in performing daily activities compared with healthy children (2). Pain, joint swelling, and limited range of motion can also aggravate an inactive lifestyle. To determine aerobic fitness in pediatric patients, a maximal exercise test is commonly employed (3). There is some evidence that the outcome of the maximal exercise test is not a precise predictor of functional ability (2). For children with JIA, the ability to perform daily activities is just as important as aerobic fitness. For this reason, performing a test that predicts functional ability might be of clinical relevance.

The 6-minute walk test (6-mwt) is a well standardized, simple, safe, and inexpensive test (4,5). It is a self-paced, submaximal endurance test. Therefore, the 6-mwt might be a good test for measuring functional ability (4,6,7). The test has been used previously in several studies in children with JIA (8,9), patients with fibromyalgia (10,11), and patients with other rheumatic conditions (12,13). However, to our knowledge the physiologic response and exercise intensity of the 6-mwt in children with JIA have never been studied.

Studies of the physiologic response of the 6-mwt in patients with a cardiac or pulmonary disease indicated that the 6-mwt was at a high intensity of submaximal level (14–17). We therefore hypothesized that the 6-mwt would be at an intensive level (>80% of maximal heart rate and maximal oxygen uptake [$\dot{V}O_{2peak}$]) in children with JIA. Moreover, we tried to assess the predictive value of the 6-minute walk test for $\dot{V}O_{2peak}$.

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**Submitted for publication September 6, 2004; accepted in revised form February 6, 2005.**

## PATIENTS AND METHODS

**Patients.** In this study, 18 patients with JIA (6 boys and 12 girls) with an age range of 7–17 years (mean ± SD 13.3 ± 3.1) participated. JIA was diagnosed by a pediatric rheumatologist. The subjects were recruited from the pediatric rheumatology outpatient clinic of the Wilhelmina Children's Hospital of the University Medical Center Utrecht. The patients were divided into different JIA sub-

**Table 1. Patient characteristics (n = 18)***

| Variable | |
|---|---|
| Sex, no. M/F | 6/12 |
| Age, years | 13.3 ± 3.1 |
| Weight, kg | 51.8 ± 18.0 |
| Height, meters | 1.6 ± 0.2 |
| Body mass index, kg/m$^2$ | 19.8 ± 3.9 |
| Σ7-skinfolds, mm | 106.5 ± 55.7 |
| Disease subclass, no. | |
| OJIA | 7 |
| PJIA | 7 |
| SJIA | 3 |
| PsA | 1 |

* Data presented as mean ± SD unless otherwise noted. OJIA = oligoarticular juvenile idiopathic arthritis; PJIA = polyarticular juvenile idiopathic arthritis; SJIA = systemic juvenile idiopathic arthritis; PsA = psoriatic arthritis.

types according to the International League of Associations for Rheumatology criteria (18): oligoarthritis, polyarthritis, systemic arthritis, and psoriatic arthritis. The characteristics of the patients are presented in Table 1.

Twelve patients were receiving a local or systemic arthritis-related therapy consisting of nonsteroidal antiinflammatory drugs, disease-modifying antirheumatic drugs, or immunosuppressive drugs. One patient underwent autologous stem cell transplantation 7 years prior to the study. Five patients were in remission and were not receiving any medication.

Patients were excluded if they had minor surgery <14 days prior to inclusion or major surgery <6 weeks prior to inclusion. The parents signed an informed consent for the participating children in this study. All procedures were approved by the local medical ethics committee.

**Anthropometry.** The patients' body mass and height were determined using an electronic scale and a wall-assembled stadiometer. Subcutaneous adiposity was measured from the skinfold using Harpenden skinfold calipers. Body composition was assessed using the sum of 7 skinfolds according to the method of Pollack et al (19). The measurements were taken at 7 sites at the right side of the body by the test leader in accordance with the American College of Sports Medicine guidelines (20). The sites were biceps, triceps, suprailiac, midabdominal, subscapular, medial thigh, and calf. Body mass index was calculated as body mass/height$^2$.

**Six-minute walk test.** Submaximal endurance was measured during the 6-mwt. The test was performed on an 8-meter track in a straight corridor as described by Gulmans et al (21). Patients were instructed to cover the largest possible distance in 6 minutes at a self-chosen walking speed. Turns were made on both ends of the 8-meter track. The distance walked was recorded with a lap counter. Each time the patient returned to the starting line, the lap counter was clicked once. Every minute the patients were encouraged in a standardized way (5) and time, recorded with a stopwatch, was called every minute. At the end of the test, the patient was asked to stand still and the distance covered in the final partial lap was measured. This was done with measuring tape. The total distance covered was calculated by multiplying the number of laps by 16 meters and adding the additional meters in the final partial lap. The total distance walked was rounded to the nearest meter. Physiologic responses during the test were measured using a heart-rate monitor (Polar) and a calibrated mobile gas analysis system (Cortex Metamax B$^3$, Cortex Medical GmbH, Leipzig, Germany). The Cortex Metamax is a valid and reliable system for measuring ventilatory parameters during exercise (22–24). The mobile gas analysis system consisted of a facemask, a transmitting unit (containing different $O_2$ and $CO_2$ gas analyzers), and a receiving unit. The transmitting unit and facemask with tubing (total weight 0.57 kg) were attached to the patient with a harness, and the receiving unit was connected to a laptop located within 500 meters of the transmitting unit. Metabolic stress test software (Metasoft, Version 2.6, Cortex Medical GmbH) was used to measure and calculate breath-by-breath minute ventilation (VE), oxygen consumption ($VO_2$), carbon dioxide production ($VCO_2$), respiratory exchange ratio (RER = $VCO_2/VO_2$), and heart rate (HR).

**Maximal exercise test.** After the 6-mwt, subjects performed a maximal exercise test using an electronically braked cycle ergometer (Lode Examiner, Lode BV, Groningen, the Netherlands). This test was used to standardize the response of the 6-mwt and to account for differences in fitness levels, age, and sex (25).

The seat height of the ergometer was adjusted to the patient's leg length (comfortable cycling height). Between the 6-mwt and the maximal exercise test, there was a rest period of at least 15 minutes. After this period, the patients were rested enough to start the cycling test without tiredness. The test started with 1 minute of unloaded cycling. After this minute, workload was increased with a constant increment of 20 Watts every minute. This protocol continued until the patient stopped because of voluntary exhaustion, despite verbal encouragement of the test leader. During the maximal exercise test, subjects breathed through a facemask (Hans Rudolph Inc, Kansas City, MO) connected to a calibrated metabolic cart (Oxycon Champion, Jaeger, Viasys, Bilthoven, the Netherlands). Expired gas was passed through a flowmeter (Triple V volume transducer), an oxygen analyzer, and a carbon dioxide analyzer. The flowmeter and gas analyzers were connected to a computer, which calculated breath-by-breath VE, $VO_2$, $VCO_2$, and the RER from conventional equations. Heart rate was measured continuously during the maximal exercise test through a bipolar electrocardiogram. Maximal effort occurred when 1 of the 2 criteria were met: HR > 180 beats/minute or RER > 1.0. Peak oxygen consumption ($VO_{2peak}$) was taken as the average value over the last 30 seconds during the maximal exercise test. Relative $VO_{2peak}$ was calculated as absolute $VO_{2peak}$ divided by body mass.

**Statistical analysis.** All data were entered and analyzed in SPSS 12.0 for Windows (SPSS, Chicago, IL). Pearson correlation coefficients were calculated to describe the

**Table 2. Physiologic measurements during the maximal exercise test and the percentages achieved during the 6-minute walk test (6-mwt)**

| Variable | Maximal exercise test | | 6-mwt percentages | |
|---|---|---|---|---|
| | Mean ± SD | Range | Mean ± SD | Range |
| Absolute $Vo_{2peak}$, liter/min | 1.85 ± 0.61 | 0.8–2.9 | 81.2 ± 18.5 | 51–113 |
| Relative $Vo_{2peak}$, ml/kg/min | 36.58 ± 6.84 | 24.1–51.7 | 80.8 ± 18.9 | 50–114 |
| Peak heart rate | 187 ± 15.73 | 142–213 | 85.4 ± 9.9 | 63–100 |
| Peak respiratory exchange ratio | 1.15 ± 0.10 | 0.89–1.34 | 86.2 ± 9.2 | 75–108 |
| Peak minute ventilation, liter/min | 62.49 ± 20.98 | 28.4–104.6 | 68.5 ± 16.3 | 45–108 |

relationship between the distance walked and $Vo_{2peak}$. Exercise intensity was calculated using the exercise parameters obtained during the 6-mwt and expressed in percentages of the maximal values obtained during the maximal exercise test. Error bars were computed to show the course of the physiologic response to the 6-mwt. The nonparametric Friedman test (26) and Wilcoxon's signed rank test were used to test for differences between exercise parameters every minute during the 6-mwt. Predictors of $Vo_{2peak}$ from the variables of the 6-mwt were determined using multiple linear regression analysis. Backward elimination procedure was used to identify variables significantly related to $Vo_{2peak}$. The independent variables entered in the regression model included age, height, body mass, and 6-mwt distance. Results of all analyses were considered to be significant when $P < 0.05$.

## RESULTS

Descriptive statistics for the 6-mwt and the maximal exercise test are displayed in Table 2. Variables of the 6-mwt are expressed as a percentage of the maximal value of the variables of the maximal exercise test.

The mean ± SD distance walked in the 6-mwt was 545 ± 20.7 meters (range 392–688). The results from Table 2 show the response of the 6-mwt. This response was between 80% and 85% of maximal exercise, except for the variable VE, which had a mean percentage of 68.5%. Figures 1–4 show the course of the different physiologic variables during the 6-mwt every minute, expressed as a percentage of the maximal value during the maximal exercise test.

$Vo_{2peak}$ during the 6-mwt increased significantly during the first 2 minutes of exercise and stabilized thereafter. The RER decreased significantly between the first and second minute of exercise and increased thereafter, and stabilized after 3 minutes. An initial drop with an increase thereafter is a normal response to exercise (27). The heart rate increased during the 6-mwt from 75% to 85% of the maximal heart rate. Minute-to-minute differences were statistically significant except for the differences between minutes 2 and 3. Minute ventilation during the 6-mwt showed a significant increase from the first minute toward the sixth minute. The range of the measured variables was quite large. One patient even performed at 100% of $Vo_{2peak}$ during the 6-mwt. The correlation between distance walked and $Vo_{2peak}$ was large ($r = 0.53$, $P = 0.02$), however with a low explained variance ($R^2 = 28\%$).

Backward regression analysis showed that height and distance walked were the best predictors of $Vo_{2peak}$ during cycling ($R^2 = 0.883$, $P < 0.001$). Regression equation: $Vo_{2peak}$ (liters/minute) = 0.002 × distance walked (meters) + 3.156 × height (meters) – 4.397 (standard error of the estimate [SEE] = 0.22).

## DISCUSSION

The purpose of this study was to determine the demand of the 6-mwt in patients with JIA. Patients' physiologic response to the 6-mwt was compared with their physiologic response to the maximal exercise test.

The results show that the highest achieved values of the variables absolute $Vo_{2peak}$, HR, and RER were between 80% and 85% of the physiologic response during the maximal exercise test. Exercise activities are considered mild to moderate from 30% to 74% of $Vo_{2peak}$ and from 35% to 79% of the maximal HR. Above these levels, exercise activities are considered to be intense (27). Compared with these levels, our results on the 6-mwt in children with JIA indicate an intense level of exercise. These results are comparable with results obtained in elderly patients

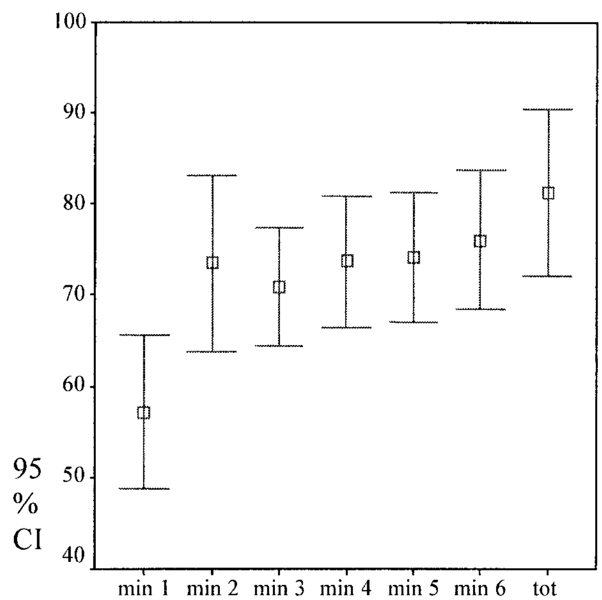


**Figure 1.** Course of $Vo_2$ expressed as a percentage of $Vo_{2peak}$ during the 6-minute walk test. Minute-to-minute increases in $Vo_2$ were only statistically significantly between minutes 1 and 2. 95% CI = 95% confidence interval; min = minute; tot = total.

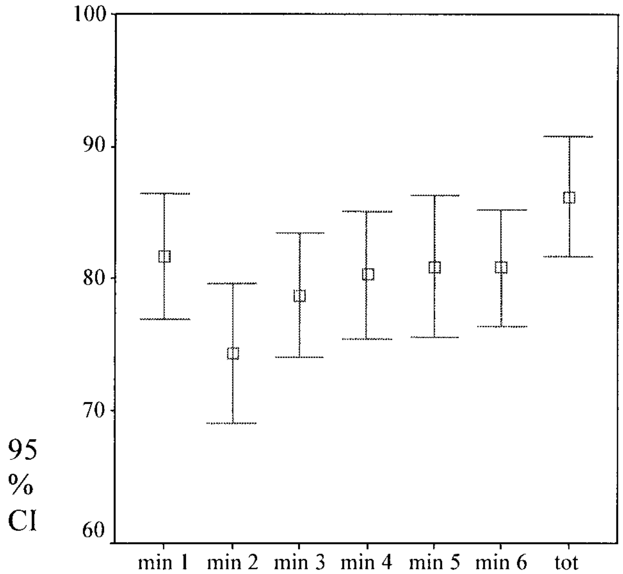


**Figure 2.** Course of the respiratory exchange ratio (RER) expressed as a percentage of maximum RER (RERmax) during the 6-minute walk test. Minute-to-minute increases in RER were statistically significantly between minutes 1 and 2 and between minutes 2 and 3. 95% CI = 95% confidence interval; min = minute; tot = total.

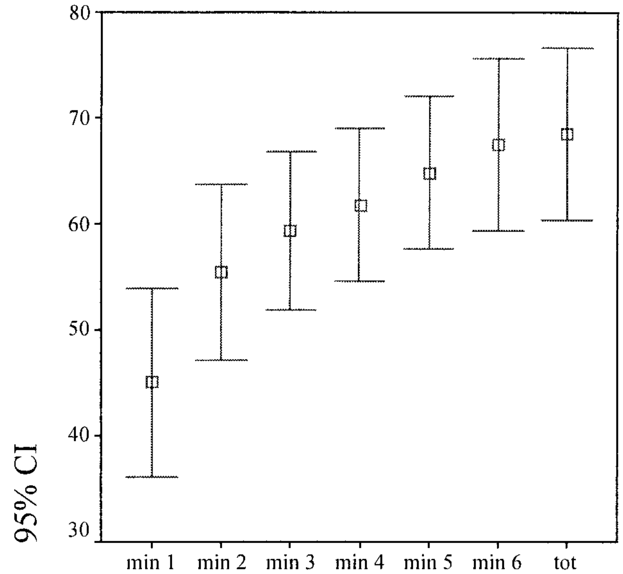


**Figure 4.** Course of minute ventilatory exchange (VE) expressed as a percentage of maximum VE (VEmax) during the 6-minute walk test. Minute-to-minute increase were statistically significantly throughout the test. 95% CI = 95% confidence interval; min = minute; tot = total.

with cardiac or pulmonary diseases (14–17). In research done in healthy elderly people, the 6-mwt shows comparable physiologic response. In healthy elderly, Kervio et al found values of 80% of $VO_{2peak}$ and 86% of the maximal HR (28). Troosters et al found a value of 77% of the maximal heart rate (29). These results indicate that the 6-mwt is a test of equal intensity for healthy elderly as well as for patients.

In our patients, the walking distance ranged from 392 to 688 meters, with a mean value of 545 meters. The normal range for a walking distance by healthy adults is from 400 to 700 meters (30); a range for healthy children has not yet been established. The patients in the current study fit within the range for healthy adults. We found in a previous study in JIA patients (31) a mean walking distance of 468 meters, which is lower than in the current study (545 meters). This difference can be explained by differences in age. In the study of Lelieveld et al (31), the mean ± SD age was 8.6 ± 2.0 years, whereas in the current study the mean age was 13.3 years. Because both exercise capacity and walking distance improve with age in children, it is not surprising that 5-year-older subjects walked 77 meters more.

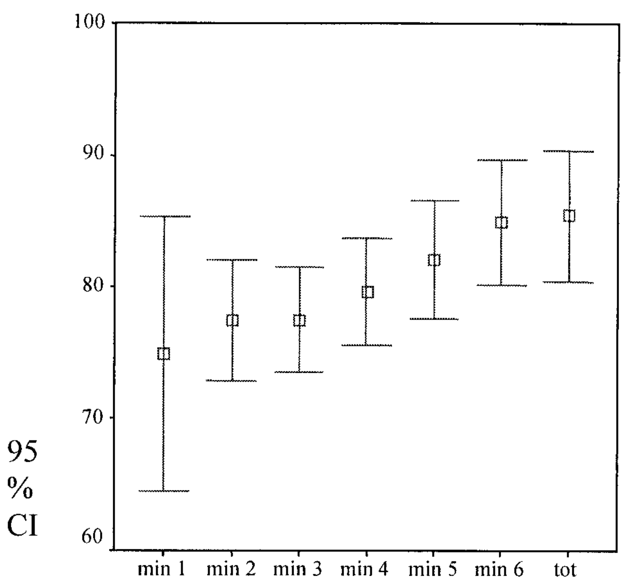


**Figure 3.** Course of heart rate (HR) expressed as a percentage of maximum HR (HRmax) during the 6-minute walk test. Minute-to-minute increases in HR were statistically significantly throughout the test except for the difference between minutes 2 and minute 3. 95% CI = 95% confidence interval; min = minute; tot = total.

The 6-mwt distance of our patients was higher compared with children with severe cardiopulmonary disease. Nixon et al (32) found a mean ± SD walking distance of 407 ± 143 meters in children of comparable age who were possible candidates for heart, lung, or combined heart and lung transplantation.

Regression analysis showed that the $VO_{2peak}$ could be predicted from the walking distance and the height of a patient. However, the SEE of the regression equation was 0.22. The SEE is a statistic indicator of the accuracy of a prediction equation. According to Gore, an SEE >0.20 is too high to give an accurate prediction of $VO_{2peak}$ (33). Moreover, the SEE is a half SD in a population of healthy children (34), which is quite large. This is indicating that the accuracy of the prediction is not very high. Including a larger number of children with JIA in the prediction might reduce the SEE of the prediction; the current equation is only based on 18 observations. The prediction equation needs the be cross-validated in another sample of JIA patients.

The error bars showed a significant change between minutes 1 and 2 for every variable except for heart rate. The HR had a wide confidence interval during the first minute. In this interval, patients had to choose their walking speed. Moreover, in the first minute during the walking test, the cardiopulmonary system has to adapt to the exercise. This is a normal adaptive reaction of the body to exercise. Physiologic responses are not an on/off process, many physiologic processes reach a steady state after 2–3 minutes of constant exercise (27). Psychophysical factors might account for the differences in exercise intensity between patients. We found a large range in ventilatory parameters and heart rate during the 6-mwt. VE was the factor with the lowest calculated percentages. This can be explained by the fact that patients stayed below their respiratory compensation point and did not hyperventilate during walking.

Comparing the 6-mwt with the maximal exercise test has some limitations. During both exercises there are differences in muscle mass and types of fibers recruited. During cycling, the external work is performed by a smaller muscle mass (35). This could lead to a difference in physiologic response during the 6-mwt and the maximal exercise test. During walking, the $Vo_{2peak}$ and the RER are higher compared with cycling. Besides this, the 6-mwt is a self-paced test. The children were told to walk as fast as possible. The motivation of each child during a self-paced test is of more importance than during an externally paced test, such as the maximal exercise test. During the maximal exercise test, the resistance increases every minute and there are criteria that indicate that the child has performed a maximal exercise (36). The motivational aspects during the 6-mwt are difficult to assess and no criteria are defined to qualify a 6-mwt.

The exercise tests were performed using different gas analysis systems. This could have resulted in a small variation in the measured physiologic parameters. To reduce this bias, we calibrated both systems before each measurement according to the manufacturer's instructions. Recently, various studies from independent laboratories showed that the used portable gas analysis system was a valid instrument to determine ventilatory parameters during submaximal exercise (24) and maximal exercise (22,23).

In conclusion, the physiologic response of the 6-mwt is at a submaximal, intense level of exercise. The range of walking distance of children with JIA was comparable with that of healthy elderly. The course of the responses during the 6-mwt in JIA was normal. The 6-mwt can be regarded as a good test for measuring functional exercise capacity. Yet it is necessary to establish normative values for children, enabling clinicians to set goals for interventions.

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