

Cardiopulmonary Exercise Capacity, Muscle Strength, and Physical Activity in Children and Adolescents with Achondroplasia

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Objective To study in children with achondroplasia the response to exercise and muscle strength compared with healthy peers and to describe the relation between exercise capacity, anthropometric factors, and physical activity.

Study design Patients (7 boys and 10 girls; mean age, 11.8 ± 3.3 years) with achondroplasia performed a maximal treadmill exercise test. Anthropometric variables and muscle strength were measured and compared with the general population. The level of everyday physical activity was measured by using a diary. Functional ability was measured by using the Activity Scale for Kids.

Results The exercise capacity of the children with achondroplasia was significantly reduced compared with reference values. All anthropometrical measurements differed significantly from reference values. There was a decrease in muscle strength in almost all muscle groups. We found a reduced physical activity level and impairments in functional ability.

Conclusions Cardiopulmonary exercise capacity and muscle strength in children with achondroplasia was reduced compared with reference values. Children with achondroplasia have a unique response to exercise. Clinicians should take these characteristic differences into account when the exercise capacity of subjects with achondroplasia is being tested. (*J Pediatr* 2007;150:26-30)

Skeletal dysplasias consist of a large group of different, rare skeletal disorders, which often express themselves in disproportionately short stature. Classification is not always possible.¹ The most commonly found and well-known skeletal dysplasia is achondroplasia, with an incidence of 1 in 25,000 to 40,000 births.¹ This type of dwarfism is characterized by rhizomelic shortening of the limbs in combination with an almost normal trunk length.

The disturbed growth related to achondroplasia may influence functional ability and exercise capacity. Little research has been performed concerning the functional ability of achondroplastic dwarfs. Exercise intolerance and exercise-induced fatigue is an often-heard complaint in children with achondroplasia. Fatigue may limit patients in their activities of daily living. On the other hand, children with achondroplasia may have reduced exercise capacity as the result of hypoactivity as a result of their complaints. Bar-Or² described that besides hypoactivity resulting in deconditioning, deficient exercise capacity can also be caused by restricted exercise-related functions due to specific pathophysiological factors in pediatric patients.

To our knowledge, exercise capacity of children with achondroplasia has never been described in the literature. Previous research found that patients with achondroplasia have normal lung functions, even though their vital capacity was smaller, because of their smaller thorax.³⁻⁵ The aim of the current study was to study the response to exercise and the muscle strength in children and adolescents with achondroplasia compared with healthy peers and to describe the relation between exercise capacity and anthropometric factors and physical activity.

METHODS

Thirty-two children diagnosed with achondroplasia older than 6.9 years of age were asked to participate in the study; 17 patients agreed (7 boys and 10 girls). The major reason for not participating in the study was the travel distance to our hospital. The mean age of the subjects was 11.8 ± 3.3 years (range, 6.9 to 19.4). The participants were

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ASK	Activity Scale for Kids	HR	Heart rate
FFM	Fat-free mass	PAL	Physical activity level

referred from the pediatric orthopedic and general pediatrics outpatient clinic to our department. Two boys were Asian; the other subjects were Caucasian. One boy had lumbar spondylolysis because of symptomatic myelin compression. All participants and parents gave informed consent before participation. This study was approved by the Medical Ethics Committee of the University Medical Center Utrecht.

Standing height, sitting height, arm span, and head circumference were measured in a standardized manner, to the nearest centimeter; the children wore no shoes while the measurements were taken. Weight was determined to the nearest 100 g, using an electronic scale. From the values of weight and height, the body mass index ($\text{kg}\cdot\text{m}^{-2}$) was calculated. The ratio between arm span and height was also calculated. The values of height, sitting height, weight, and body mass index were compared with reference values for healthy subjects matched for age and sex, and Z-scores were calculated.⁶ The measured values were also compared with reference values for achondroplastic patients.⁷⁻⁹ Body composition was assessed by using the sum of 7 skin folds ($\Sigma\text{skin folds}$), according to the method of Pollack et al.¹⁰ The measurements were taken at 7 sites at the right side of the body, in accordance with the American College of Sports Medicine guidelines.¹¹ The sites were biceps, triceps, suprailiac, midabdominal, subscapular, medial thigh, and calf.

Leg volume was measured by using the anthropometric method described by Jones and Pearson.¹² Volume was calculated from leg circumferences measurements and skinfold measurements. All anthropometric measurements were carried out by the same experienced senior pediatric physical therapist to reduce interobserver variability.

The fat-free mass (FFM) of the body was estimated by using a bioelectric impedance measurement with the Xitron-Hydra bioelectric measurements system (Xitron Technologies Inc, San Diego, Calif). Multifrequency Bioelectric Impedance Analysis (BIA) measurements were performed while the child was lying quietly supine with arms and legs slightly abducted from the trunk. Two pairs of pregelled electrodes were placed on the right hand and foot. The two current introduction electrodes were placed on the dorsal surface of the right hand, over the distal end of the second and third metacarpals and on the dorsal surface of the foot, over the distal end of the second and third metatarsals. The recording electrodes were placed on the dorsal surface of the wrist on a line bisecting the styloid processes of the radius and the ulna and on the dorsal surface of the ankle, on a line bisecting the medial and lateral malleoli. From the measured volumes of extracellular and intracellular water, the FFM and the fat mass were calculated according to the manufacturer's manual.

The subject's maximal exercise capacity was determined by treadmill (Enmill, Enraf, Delft, The Netherlands) exercise testing. The test started with a 1-minute rest period. A modified Bruce protocol was used.¹³ The original protocol was modified with two 1.5-minute steps at 1.4 km/h with 0% gradient and 2.1 km/h with 5% gradient before the original

protocol started because of adaptation toward the decreased step length in achondroplasia. The protocol continued until the patient stopped because of voluntary exhaustion, despite verbal encouragement of the test leader. During the test, heart rate (HR) and gas exchange variables were measured by using a heart-rate monitor (Polar heart rate monitor, Polar Electro Oy, Kempele, Finland) and a calibrated mobile gas analysis system (Cortex Metamax B³, Cortex Medical GmbH, Leipzig, Germany). The Cortex Metamax is a valid and reliable system for measuring ventilatory parameters during exercise.^{14,15}

Metabolic stress test software (Metasoft, Version 2.6, Cortex Medical GmbH, Leipzig, Germany) was used to measure and calculate breath-by-breath minute ventilation (\dot{V}_E), oxygen consumption (\dot{V}_{O_2}), carbon dioxide production (\dot{V}_{CO_2}), respiratory exchange ratio ($\text{RER} = \dot{V}_{CO_2}/\dot{V}_{O_2}$), and HR.

Absolute peak oxygen uptake ($\dot{V}_{O_{2\text{peak}}}$) was taken as the average value over the last 30 seconds during the maximal exercise test. Relative $\dot{V}_{O_{2\text{peak}}}$ ($\dot{V}_{O_{2\text{peak}}}/\text{kg}$) was calculated as absolute $\dot{V}_{O_{2\text{peak}}}$ divided by body mass. Predicted $\dot{V}_{O_{2\text{peak}}}$ values were obtained from established values from age- and sex-matched historical Dutch control subjects.¹⁶

The strength of the proximal and distal muscles in lower and upper extremities was measured by using a hand-held Dynameter (Citec dynamometer type CT 3001, CIT Technics, Groningen, The Netherlands) in Newtons. Measurements were sequentially performed 3 times by an experienced pediatric physical therapist, and the highest value was used for analysis. Maximum isometric contraction values were measured in by using the "break" technique, in which the examiner gradually overcomes the muscle force and stops at the moment the extremity gives way. The following six muscles were measured at both extremities: shoulder abductors, grip strength, dorsal extensors of the wrist, hip flexors, knee extensors, and dorsal flexors of the foot. Mean values of the muscle strength of the left and the right extremity were used to prevent the influence of left-right differences. Reference values for muscle strength were obtained from a study of healthy Dutch children.¹⁷

A 3-day activity record was used to estimate energy expenditure, as has been described by Bouchard et al.¹⁸ On two weekdays and one weekend day, the patients had to fill out the activity record every 15 minutes. For each 15-minute period, energy expenditure was qualified on a scale from 1 to 9, depending on exercise intensity. Daily energy expenditure for each individual was estimated from the summation of all 15-minute periods. The activity record was shown to be reliable and valid in children and adolescents.^{18,19}

Perceived functional ability was measured by using the Activity Scale for Kids (ASK).²⁰ The ASK was designed for children with neuromuscular and musculoskeletal conditions between the ages of 5 and 15 years. It contains 30 items representing 9 domains, and scores are reported as a percentage of the highest score (a score of 100% means no problems in activities of daily living). In this study, a Dutch translation

Table I. Anthropometric Measurements Compared With Age-Matched Reference Values

	Achondroplasia mean \pm SD (range)	Z-Score mean \pm SD	Reference values mean \pm SD (range)
Height (m)	118.0 \pm 9.93 (90.0–125.5)	-5.77 \pm 0.98	150.70 \pm 14.19† (126.71–172.07)
Sitting height (cm)	72.29 \pm 7.50 (51.50–82.0)	-2.18 \pm 1.49	79.50 \pm 6.84† (69.84–90.88)
Arm span (cm)	104.0 \pm 10.78 (86.0–121.0)	-6.39 \pm 1.02	150.73 \pm 14.64† (126.95–173.60)
Head circumference (cm)	56.68 \pm 1.90 (52.0–59.5)	1.88 \pm 1.13	54.05 \pm 0.99† (52.19–55.41)
Weight (kg)	31.19 \pm 10.48 (19.10–55.60)	-1.53 \pm 0.89	40.01 \pm 11.58† (24.34–59.82)
BMI ($\text{kg}\cdot\text{m}^{-2}$)	24.41 \pm 5.44 (17.75–40.27)	4.24 \pm 2.49	17.26 \pm 1.87† (15.17–21.15)
Sum of 7 skin folds (mm)	108.51 \pm 40.92 (60.0–217.30)	0.78 \pm 1.31	86.29 \pm 24.95* (58.62–137.65)
Fat percentage (%)	23.98 \pm 10.09 (4.62–39.63)	1.30 \pm 2.27	17.45 \pm 5.65* (9.80–24.60)

BMI, Body mass index.

* $P < .05$.

† $P < .0001$.

Table II. Exercise Capacity in Subjects With Achondroplasia Compared With Reference Values

	Achondroplasia mean \pm SD (range)	Z-Score mean \pm SD	Reference values mean \pm SD (range)
$\dot{V}O_{2\text{peak}}$ ($\text{L}\cdot\text{min}^{-1}$)	1.04 \pm 0.30 (0.67–1.61)	-3.23 \pm 0.66	1.86 \pm 0.43* (1.20–2.50)
$\dot{V}O_{2\text{peak/kg}}$ ($\text{mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$)	32.83 \pm 5.07 (22.30–39.70)	-2.59 \pm 0.70	46.65 \pm 3.91* (41.0–52.30)
VE_{peak} ($\text{L}\cdot\text{min}^{-1}$)	46.75 \pm 13.33 (27.70–81.50)	-2.20 \pm 0.73	69.82 \pm 12.02* (50.0–86.10)

$\dot{V}O_{2\text{peak}}$, Maximal oxygen uptake; VE_{peak} , peak ventilatory exchange.

* $P < .0001$.

of the ASK was used. The ASK consists of two versions, each covering the same activities but with different response options. The ASK-capability (ASKc) measures what the child “could do,” whereas the ASK-performance (ASKp) measures what the child usually “does do.” The two versions appear to provide different and complementary information. ASKc assesses the difficulty a child experienced during an activity in the last week, and the ASKp assesses how often the child performed an activity during the last week. Both versions were scored on a 5-point scale (ASKc: 4 = with no problem, 3 = with a little problem, 2 = with a moderate problem, 1 = with a big problem, 0 = “I could not.” ASKp: 4 = all of the time, 3 = most of the time, 2 = sometimes, 1 = once in a while, 0 = none of the time). This instrument has been shown to be reliable and valid in children and adolescents with musculoskeletal disorders.^{20,21}

Statistical analyses were performed with the use of the Statistical Package for the Social Sciences for Windows (version 12.0, SPSS Inc, Chicago, Ill). Independent-samples t tests were used to test differences between patients and reference values. Correlations were calculated by using the Pearson correlation coefficient for parametric values. Non-parametric statistics were used when variables were not normally distributed according to the Shapiro-Wilk test. The α -level was set at $P < .05$ for all analyses.

RESULTS

The anthropometric measurements are presented in Table I. As expected, all anthropometric measurements differed significantly from the general population. The mean

height of the patients was almost 6 standard deviations lower compared with the general population. Sitting height was less affected and was about 2 standard deviations below normal, which showed the reduced leg length in these patients. The mean sitting height/height ratio in the patients was 22.3% higher compared with reference values. The arm span of the subjects was more than 6 standard deviations below normal but was not significantly different from height-matched reference values. The head circumference was almost 2 standard deviations higher compared with normal values ($P < .001$). Moreover, the skinfold measurements and body fat percentage was higher in children with achondroplasia. Anthropometrical parameters could be considered as normal compared with growth diagrams for children with achondroplasia.

All patients were able to perform the maximal exercise test without complications. One patient terminated the exercise test prematurely because of back pain secondary to lumbar spondylolysis. Therefore, we excluded this patient’s exercise testing data from the analysis. The HR_{peak} of the patients was 178.6 ± 14.9 (range, 151 to 201) $\text{beats}\cdot\text{min}^{-1}$. The RER_{peak} of the patients was 1.15 ± 0.1 (range, 1.0 to 1.41). The data on $\dot{V}O_{2\text{peak}}$ and $\dot{V}O_{2\text{peak/kg}}$ and VE are presented in Table II and were significantly reduced compared with reference values for age and sex. The Z-score for $\dot{V}O_{2\text{peak}}$ for estimated age for height was $+1.77 \pm 2.0$. The mean oxygen pulse ($\dot{V}O_{2\text{peak}}/HR_{\text{peak}}$) was 5.86 ± 1.9 (range, 3.7 to 10.7) $\text{mL}\cdot\text{beat}^{-1}$, which was $63\% \pm 10.73\%$ (46.8% to 92.7%) of predicted for age and sex. There was a significant difference between the mean Z-score for $\dot{V}O_{2\text{peak}}$ and the mean Z-score for $\dot{V}O_{2\text{peak/kg}}$ ($P < .01$). A significant difference between the

Table III. Muscle Strength in Children With Achondroplasia Compared With Reference Values

Muscle group	Achondroplasia mean \pm SD (range)	Z-Score mean \pm SD	Reference values mean \pm SD
Shoulder abductors (Newton)	140.26 \pm 50.24 (76.50–222.50)	0.36 \pm 1.17	134.60 \pm 38.48 (NS)
Hip flexors (Newton)	130.41 \pm 36.86 (85.0–195.50)	-2.23 \pm 0.60	247.06 \pm 50.19*
Dorsal extensors of the wrist (Newton)	74.88 \pm 32.50 (39.0–158.50)	-3.55 \pm 3.33	119.0 \pm 34.42*
Knee extensors (Newton)	129.12 \pm 39.67 (65.50–204.0)	-2.47 \pm 0.92	255.12 \pm 69.43*
Dorsal flexors of the foot (Newton)	141.82 \pm 35.47 (84.0–196.0)	-1.13 \pm 0.70	174.29 \pm 42.69*

NS, Not significant.

* $P < .01$.

mean Z-score for $\dot{V}O_{2peak}$ and the mean Z-score for $\dot{V}E_{peak}$ was found as well ($P < .01$), which was not the case between the mean $\dot{V}E_{peak}$ and the mean $\dot{V}O_{2peak/kg}$. The peak ventilatory equivalent for $\dot{V}O_2$ ($\dot{V}E_{peak}/\dot{V}O_{2peak}$) was higher in subjects with achondroplasia compared with reference values (45.25 ± 5.9 and 37.9 ± 2.8 , $P < .001$, for subjects with achondroplasia and healthy children, respectively), which was $119.9\% \pm 18.9\%$ (98% to 154%) of predicted. The peak ventilatory equivalent for $\dot{V}CO_2$ ($\dot{V}E_{peak}/\dot{V}CO_{2peak}$) was also higher in subjects with achondroplasia compared with reference values (39.25 ± 3.8 , and 31.9 ± 2.7 , $P < .001$, for subjects with achondroplasia and healthy children respectively), which was $123.72\% \pm 14.0\%$ (100% to 154%) of predicted).

$\dot{V}O_{2peak}$ was significantly correlated with leg volume ($r = 0.73$, $P = .002$) and with FFM ($r = 0.71$, $P = .004$). $\dot{V}O_{2peak/kg}$ was only related to Z-score of sitting height ($r = 0.59$, $P = .02$).

Because of short fingers in children with achondroplasia, the grip strength could not be performed and was excluded from the analysis. The children with achondroplasia showed abnormal muscle strength in almost all muscle groups (Table III). The dorsal extensors of the wrist, hip flexors, knee extensors, and dorsal flexors of the foot were significantly reduced compared with reference values matched for age and sex. The strength of the shoulder abductors was normal. No associations were found between muscle strength measurements and exercise capacity. A strong correlation was found between knee extensor strength and leg volume ($r = 0.71$, $P < .002$) and also between total muscle strength and FFM ($r = 0.92$, $P < .0001$).

The mean \pm SD energy expenditure in the subjects was 41.69 ± 3.5 (range, 37.26 to 50.74) kcal/day per kilogram, which was only significantly correlated with Z-score for $\dot{V}O_{2peak}$ ($r = 0.591$, $P < .05$). The calculated physical activity level from the activity record (PAL; total energy expenditure/estimated basal metabolic rate²⁶) was 1.67 ± 0.14 .

The ASKp and ASKc scores of children with achondroplasia showed a significant decrease in functional ability in both versions ($73.1\% \pm 12.6\%$ and $77.7\% \pm 16.3\%$, respectively). The ASKp was unrelated to anthropometric and exercise capacity parameters. The ASKc was correlated with arm span ($r = -0.68$, $P = .02$), Z-score $\dot{V}O_{2peak}$ for height ($r = 0.70$, $P = .02$), and strength of the hip muscles ($r = 0.57$, $P = .04$).

DISCUSSION

The exercise capacity of the subjects with achondroplasia was significantly reduced compared with age- and sex-matched reference values for the general population. Because of a lower weight for age, the mean Z-score of $\dot{V}O_{2peak/kg}$ was less pronounced than $\dot{V}O_{2peak}$. Their reduced exercise capacity cannot be explained by their smaller height because no significant correlation was found between these two variables. In fact, these children showed a significantly increased exercise capacity, with a mean Z-score of +1.77 when compared with height-matched reference values, which is a result of a higher muscle mass for a given height compared with healthy subjects. The $\dot{V}O_{2peak}$ and $\dot{V}O_{2peak/kg}$ in our subjects was 56% and 70% of predicted for age, which is lower compared with children other growth disturbances. Hinkel et al²² found a $\dot{V}O_{2peak}$ and $\dot{V}O_{2peak/kg}$ between 57% to 77% and 79% to 108% of predicted, respectively, in a heterogeneous group of 139 patients with growth disturbances. They found a normalization of $\dot{V}O_{2peak/kg}$ in their patients,²² which was not observed in the current study because of the higher weight for height in subjects with achondroplasia.

The increased ventilatory equivalent for oxygen uptake showed that subjects with achondroplasia have to ventilate more (higher breathing frequency) for the uptake of 1 liter of oxygen compared with age- and sex-matched reference values. This might be caused by the reduced vital capacity.^{4,5} A lower tidal volume is thus compensated with a higher breathing frequency and a higher ventilation of alveolar death space and thus a lower ventilatory efficiency.

Moreover, the reduced oxygen pulse of the patients showed that they have a higher heart rate for a given oxygen uptake compared with age- and sex-matched reference values. This implies that they have a reduced cardiac stroke volume during exercise as a result of their smaller thoracic volume.

Children with achondroplasia showed reduced muscle strength in almost all muscle groups compared with age- and sex-matched reference values. Lower muscle strength may be caused by a decrease in muscle mass, by reduced neuromuscular coordination, or by altered biomechanics. Because of the comparison with age- and sex-matched reference values, a lower muscle mass for their age could be an explanation for these results. Indeed, there was a strong correlation between knee extensor strength and leg volume ($r = 0.71$, $P < .002$) and also between total muscle strength and FFM ($r = 0.92$,

$P < .0001$), suggesting the first hypothesis. However, we did not study coordination and biomechanics in the subjects.

Another possible explanation for reduced muscle strength could be that their muscle tone is not optimal because of the relatively short bones in combination with relatively normal length of the muscles and other tissues in the extremities, causing relative muscle hypotonia and decreased muscle strength.²³ However, shoulder abductor muscle strength was normal compared with reference values. The shoulder muscles might be less affected by the short posture in comparison with the other muscle groups.

The physical activity record showed that the achondroplastic children had a lower energy expenditure compared with the normative values for healthy children provided by Bouchard et al.¹⁸ Moreover, the calculated energy expenditure was also lower compared with other studies from our country. Emons et al²⁴ found a mean energy expenditure by using double-labeled water in healthy children of 8 and 9 mega-Joules per day for girls and boys, respectively. The subjects with achondroplasia had a mean energy expenditure of 5.3 mega-Joules per day. However, because of their unique physique, the validity of the physical activity record is uncertain. The activity record is based on the ratio of work metabolic rate to a standard resting metabolic rate (MET) values.²⁵ The same physical activity (for example, walking 15 minutes at 5 km/h) might use more energy in subjects with achondroplasia compared with healthy subjects. Therefore, the energy use of physical activities of subjects with achondroplasia should be addressed in a future study. When energy expenditure was expressed as PAL,²⁶ the value found in the subjects was not different from healthy children. van Mil et al²⁷ reported in their meta-analysis a mean PAL of 1.73 ± 0.21 for healthy adolescents and 1.64 ± 0.19 for obese adolescents. The PAL value found in the current study was between these two groups. However, these studies were performed by using double-labeled water, the gold standard; the current study used a physical activity questionnaire.

One of the challenges we faced during this study was the choice of an appropriate comparison group. In this study, age- and sex-matched reference values were used. Hinkel et al²² used length-related reference values for their growth-retarded patients. However, because of the disproportion in patients with achondroplasia, matching is very difficult. Length-matched subjects will have a lower body mass, and weight-matched subjects will be larger. This means that patients with achondroplasia are a population with a unique physique and provides a challenge for scaling outcomes in relation to body size.²⁸

Clinicians should review the energy balance of subjects with achondroplasia regularly because obesity is prevalent in this patient group.^{8,29} An appropriate activity program with acceptable physical activities should be developed to increase energy expenditure³⁰ and improve exercise capacity. A future study should determine the effects of a lifestyle intervention (eating and exercise habits) in subjects with achondroplasia.²⁹⁻³⁰

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