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Exercise Tolerance in Children and Adolescents With Musculoskeletal Pain in Joint Hypermobility and Joint Hypomobility Syndrome

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ABSTRACT

OBJECTIVES. Musculoskeletal pain is a common complaint in a pediatric health care practice, but exercise tolerance has never been described in detail in these children. Our objectives for this study were to evaluate the maximal exercise capacity, including peak heart rate and oxygen consumption, of children with pain-related musculoskeletal problems, particularly in children with (symptomatic) generalized joint hypermobility and hypomobility, during a bicycle ergometry test to exhaustion; to evaluate muscle strength, bone mineral density, and sports activities in these children and to associate these observations with exercise capacity; and to compare these results with reference values.

METHODS. Thirty-two children (mean age: 12.1 years; SD: 3.4 years; range: 6.2–20.1 years; 62% male) with musculoskeletal pain-related syndromes (joint hypermobility syndrome [$n = 13$] and joint hypomobility syndrome [$n = 19$]) participated. The reference group consisted of 117 healthy primary school prepubertal children, 167 healthy secondary school adolescents, and 98 young adults (249 girls and 133 boys; mean age total reference group: 14.5 ± 4.0 years; range: 8–20.8 years). Anthropometry, range of joint motion, muscle strength, bone mineral density (speed of sound and broadband ultrasound attenuation), sports activities, and a maximal exercise test using an electronically braked cycle ergometer were performed, and the patient stopped because of volitional exhaustion. Expired gas analysis and heart rate and transcutaneous oxygen saturation by pulse oximetry measurements also were performed.

RESULTS. Children with joint hypomobility syndrome as well as children with joint hypermobility syndrome had a higher mean z score (SD) of weight and BMI compared with the reference group. A significantly decreased absolute peak oxygen consumption and relative peak oxygen consumption in both patient groups was found compared with control subjects. In 14 of 32 children with a z score relative peak oxygen consumption of less than -2 , maximal heart rate was significantly decreased compared with 18 children with a z score relative peak

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Key Words

symptomatic joint hypermobility, symptomatic joint hypomobility, exercise tolerance, musculoskeletal-pain, bone density, sports activities

Abbreviations

JHyperS—joint hypermobility syndrome

JHypoS—joint hypomobility syndrome

HR—heart rate

$\dot{V}O_2$ —oxygen consumption

BMD—speed of sound

QUS—quantitative ultrasound

BUA—broadband ultrasound attenuation

SOS—speed of sound

$\dot{V}O_{2\text{ peak}}$ —peak oxygen consumption

$\dot{V}O_{2\text{ peak}}/\text{kg}$ —relative $\dot{V}O_{2\text{ peak}}$

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oxygen consumption of -2 or more (mean [SD] z score speed of sound: -1.3 [0.8] vs -0.5 [1.0] and mean [SD] heart rate: 175.9 [11.5] vs 187.5 [10.9], respectively). In the total group, a high significant correlation between the z score of relative peak oxygen consumption and the z score of the speed of sound was found as well as with z score of BMI. Sixteen (50%) of 32 participated in sports activities with (mean: 0.9 hours/week; SD: 1.4 hours/week), whereas in the control group, 12% of did not participate in sports activities (mean: 2.8 hours/week; SD: 2.2 hours/week). Children who participated in sports activities had a (borderline) significant increased mean (SD) z score of absolute peak oxygen consumption and mean (SD) z score of broadband ultrasound attenuation compared with children who did not participate in sports activities (-0.3 [1.1] vs -1.2 [1.3] and -0.45 [0.8] vs -0.9 [0.5], respectively).

CONCLUSIONS. In children with musculoskeletal pain-related syndromes, particular in children with (symptomatic) generalized joint hypermobility and hypomobility, maximal exercise capacity is significantly decreased compared with age- and gender-matched control subjects. The most probable explanation for the reduced exercise tolerance in our patients is deconditioning.

MUSCULOSKELETAL PAIN IS a common complaint in a pediatric health care practice. In a Dutch study of 5336 children between 0 and 18 years of age, 25% of the children reported chronic or recurrent pain.¹ In this study, chronic pain was reported most frequently in the age group 12 to 15 years. More than one third of this age group reported having chronic pain, more reported by girls than by boys.¹

Other population-based studies reported prevalence estimates from 9.4% to 32% for musculoskeletal pain in children.^{2,3} A short-term follow-up study on musculoskeletal pain among school children showed that musculoskeletal pain still was present after 1 year of follow-up in approximately one third of the sample.²

Joint hypermobility is known to induce musculoskeletal pain. In children with symptomatic generalized joint hypermobility, the major presenting complaint was arthralgia in 64% of 125 cases.⁴

Joint hypermobility, or ligamental laxity, at 1 end of the Gaussian distribution of joint mobility, has been described as a separate entity with characteristic pathophysiology.⁵ Most patients with loose joints experience no ill effects and may be an advantage in certain professions, such as musicians.⁶ When generalized hypermobility becomes symptomatic, joint hypermobility syndrome (JHyperS) is diagnosed, provided that the patient does not show signs of any rheumatic, neurologic, skeletal, or metabolic disease.^{7,8} The prevalence of generalized joint hypermobility in children and adults varies

between 2.3% and 30% and is related to age, gender, and race, whereas symptomatic generalized joint hypermobility is seen in adults: $\sim 3.3\%$ among women and 0.6% among men.^{4,9}

JHyperS has a favorable prognosis by comparison with other, more serious, connective tissue disorders that are associated with hypermobility, such as Ehlers-Danlos syndrome, Marfan syndrome, and osteogenesis imperfecta.⁵ Although children with JHyperS frequently complain of fatigue and musculoskeletal pain, exercise tolerance has never been described in detail. In serious connective tissue disorders such as osteogenesis imperfecta, exercise tolerance and muscle strength were found to be significantly impaired, which might account for the increased levels of fatigue during activities of daily living.¹⁰

Generalized joint hypomobility with musculoskeletal complaints (joint hypomobility syndrome [JHypoS]), at the other end of the Gaussian distribution of range of joint motion, was described recently as a possible new entity, probably caused by an increased stiffness of the joint ligaments.¹¹ Until now, JHypoS had not been clarified as a distinct clinical or pathologic entity by other investigators. As the biomechanical properties of ligaments are determined mainly by the collagen network, the molecular defect that is involved in the pathogenesis of symptomatic generalized joint hypomobility may reside within these proteins (higher amounts of collagen with increased cross-linking).¹¹

When generalized hypomobility becomes symptomatic, JHypoS is diagnosed, provided that the patient does not show signs of any rheumatic, neurologic, skeletal, or metabolic disease. Clinical characteristics of JHypoS are decreased ranges of joint motion and pain in soft periarticular tissues for >12 weeks, particularly exercise-induced pain in calf, knee, and/or hip muscles. Although familial hypomobility has been reported, data regarding prevalence of JHypoS are not yet available.¹¹

In this group of patients, it is believed that they have low fitness levels because of their inactivity as a result of pain. This deconditioning also might result in higher fatigue levels. Exercise tolerance, measured using a treadmill protocol according to Bruce,¹¹ was reported to be normal in 78% of the patients, whereas 22% of these patients terminated the test prematurely because of pain in calf, knee, and/or hip muscles. On the basis of these findings, a bicycle ergometry test to evaluate maximal exercise tolerance might be more appropriate in this patient group. Moreover, the exercise capacity of the patients was evaluated on the basis of measuring just the endurance time. Neither heart rate (HR) nor oxygen consumption ($\dot{V}O_2$) was monitored during that study.

It is widely known from the literature that physical inactivity leads to a deterioration of exercise capacity in children¹² and that increased physical activity influences muscle strength and bone density positively.¹³ Because

only a few studies have investigated the level of exercise tolerance in patients with musculoskeletal pain-related syndromes, it is unclear how exercise tolerance in these patients compares with matched reference values. Therefore, our aim for this study was to evaluate the maximal exercise capacity, including peak HR and $\dot{V}O_2$, of children with pain-related musculoskeletal problems during a bicycle ergometry test to exhaustion and to compare these results with age- and gender-matched reference values. A second aim was to evaluate muscle strength, bone mineral density (BMD), and sports activities and to associate these observations with exercise capacity.

METHODS

Participants

Thirty-two children (mean age: 12.1 years; SD: 3.4 years; range: 6.2–20.1 years; 62% male) with JHyperS ($n = 13$) and JHypoS ($n = 19$) were referred from the pediatric orthopedic and general pediatric outpatient clinic to our department. Children with JHyperS were included when generalized hypermobility of the joints and musculoskeletal symptoms (arthralgia in >2 joints for >12 weeks) and exercise-induced pain and exercise intolerance were present in the absence of signs of any rheumatic, neurologic, skeletal, or metabolic disease.

Children with JHypoS were included when generalized hypomobility of the joints and musculoskeletal symptoms (pain in extra-articular soft tissues in >2 joints for >12 weeks, exercise-induced pain, and/or exercise intolerance) were present in the absence of signs of any rheumatic, neurologic, skeletal, or metabolic disease. All children were assessed by an experienced pediatric physical therapist (R.H.H.E.) and an experienced pediatric exercise physiologist (T.T.). All patients also were examined clinically by a senior clinical geneticist and senior orthopedic surgeon to exclude signs or symptoms indicating (known) collagen disorders or other syndromes involving joint laxity and joint stiffness.

The reference group consisted of 117 healthy primary school prepubertal children, 167 healthy secondary school adolescents, and 98 young adults (249 girls and 133 boys; mean age total reference group: 14.5 ± 4.0 years; range: 8–20.8 years). Data were obtained between 2002 and 2004 and served as a reference group for studies regarding (symptomatic) generalized joint hypermobility and hypomobility.^{11,14} Children and adolescents with known diseases or disorders involving skin, joints, bone density, or vessels were not included.

A team of 8 examiners (physiotherapists) conducted all measurements under supervision of the principal investigator (R.H.H.E.). Before assessments took place, all physiotherapists participated in a reliability study regarding range of joint motion and muscle strength. The study was started when intra- and intertester reli-

ability was high.^{11,14} All measurement procedures described herein were applied similarly to both patients and healthy control subjects.

In this reference group, no children with past or present signs of any rheumatic, neurologic, skeletal, metabolic, or collagen disease were included. The Medical Ethics Committee of the Wilhelmina Children's Hospital (University Medical Center Utrecht) approved this study, and informed consent was obtained from all children and parents, as well as adolescents and adults who were older than 16 years.

Anthropometry

Standing height and weight were measured in a standardized manner without wearing shoes and heavy clothing to the nearest centimeter and 100 g, respectively. From these values, the BMI (kg/m^2) was calculated. The values of height, weight, and BMI were compared with the reference values for healthy subjects matched for age and gender, and z scores were calculated.¹⁵

Range of Joint Motion

The active range of joint motion of the shoulder (ante-flexion), elbow (flexion and extension), wrist (palmar and dorsal extension), hip (flexion and extension), knee (flexion and extension), and ankle joints (plantar and dorsal extension) was measured bilaterally to the nearest 5° with a standard 2-legged 360° goniometer, using the anatomic landmark method.¹⁶ Children were asked to actively stretch or bend the joint maximally without interference by the investigator. Children were not allowed to help the ipsilateral muscles by the use of contralateral limbs. No significant differences were found between the left and right extremities; therefore, the mean range of joint motion was calculated. Total range of joint motion was a summing-up of all of the measurements and was compared with the reference group. z scores of total joint motion were calculated. Inter- and intrarater reliability of goniometry in hypermobile and hypomobile children, as well as in the reference group, was high.¹¹

Muscle Strength

Data that were collected of the proximal and distal muscles in the lower and upper extremities were measured reliably with a handheld myometer.¹⁷ Measurements were performed consecutively 3 times, and the highest value was registered. In the upper extremity, shoulder abductors and grip strength were measured; in the lower extremity, hip flexors and dorsal extensors of the foot were measured. Because of the inability of the investigator to use the "break method" of measuring the muscle strength of the dorsal extensors of the foot, especially in older adolescents and adults, data could not be collected in all participants and therefore were

excluded from analysis. Therefore, total muscle strength was analyzed as a summation of the measurements of shoulder abductors, grip strength, and hip flexors, and *z* scores were calculated.

BMD

Quantitative ultrasound (QUS) measurement was performed as a noninvasive method of bone quantity assessment and provides information of bone structure.¹⁸ Measurements of the right os calcis were performed with a Sahara ultrasound device (Hologic QDR 4500, Hologic Inc, Waltham, MA) measuring broadband ultrasound attenuation (BUA; dB/MHz) and speed of sound (SOS; m/second) as indicators of bone quantity and bone stiffness, respectively. Both measures were compared with reference values matched for gender and age, and *z* scores were calculated. Acoustic phantoms that were provided by the manufacturer were scanned daily and showed no drift during the study period.

A limitation of QUS measurement is that it focuses on bone quantity of just the calcaneus, which might not be representative for BMD of the entire body. However, QUS measurement in healthy children provided good precision and discrimination of normal from osteopenic patients,¹⁹ also correlating significantly with dual-energy x-ray absorptiometry ($r = 0.67-0.83$ ¹⁹; $r = 0.58-0.72$ ²⁰).

Maximal Exercise Test

Participants performed a maximal exercise test using an electronically braked cycle ergometer (Lode Examiner; Lode BV, Groningen, Netherlands). The work rate was increased with 20 Wt/minute to bring the patient to his or her limit between 6 and 10 minutes of exercise.²¹ This protocol continued until the patient stopped because of volitional exhaustion, despite strong verbal encouragement of the investigators. During the maximal exercise test, participants breathed through a face mask (Hans Rudolph Inc, Kansas City, MO) connected to a calibrated expired gas analysis system (Oxycon Champion; Viasys, Bilthoven, Netherlands). Expired gas was passed through a flow meter and an oxygen and a carbon dioxide analyzer. The flow meter and gas analyzers were connected to a computer, which calculated breath-by-breath minute ventilation, \dot{V}_{O_2} , carbon dioxide production, and respiratory exchange ratio (carbon dioxide production/oxygen consumption [\dot{V}_{O_2}]) from conventional equations. During the maximal exercise test, HR was monitored continuously by a 3-lead electrocardiogram (Hewlett-Packard, Amstelveen, Netherlands), and transcutaneous oxygen saturation was measured by pulse oximetry (Nellcor 200 E, Breda, Netherlands). Absolute peak \dot{V}_{O_2} ($\dot{V}_{O_2 \text{ peak}}$) was taken as the average value during the last 30 seconds of 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. W_{peak} was the highest achieved work rate. The oxygen cost of exercise

was calculated as the difference in \dot{V}_{O_2} between unloaded cycling and $\dot{V}_{O_2 \text{ peak}}$ divided by the peak work rate ($\Delta\dot{V}_{O_2}/\Delta WR$). Predicted $\dot{V}_{O_2 \text{ peak}}$ and W_{peak} values were obtained from established values from age- and gender-matched historical Dutch controls.²²

Physical Activity

Because the amount of daily activities might influence exercise tolerance and BMD, we asked anamnesticly for sports activities (yes/no) and the amount of hours spent on sports activities per week.²³ No distinction was made in the amount of weight bearing and intensity of sports activities.

Statistics

Variables were expressed as means, SD, and range. Statistical comparisons between measurements were made by using the Student's *t* test. The data also were expressed as percentage of the total group or as *z* scores [$z \text{ score} = (\text{observed value} - \text{mean value})/\text{SD}$]. Associations between measurements and $\dot{V}_{O_2 \text{ peak}}$ were calculated using Pearson's correlations. The α level was set at $P < .05$ for all analyses. All statistical analyses were performed by using SPSS 11.0 for Windows (SPSS, Inc, Chicago, IL). Because we studied a convenient sample, a sample-size calculation was not performed.

RESULTS

Patient characteristics are presented in Tables 1 and 2. Children with JHyperS were significantly younger than the reference group. Children with JHypoS as well as children with JHyperS had a higher mean *z* score \pm SD of weight and BMI compared with the reference group (JHypoS: 1.0 ± 1.9 , 1.1 ± 1.9 ; JHyperS: 1.0 ± 0.9 , 1.1 ± 1.4). As expected, the mean total joint mobility of children with JHyperS was $3.0 (\pm 0.9)$ SD higher and of children with JHypoS $2.4 (\pm 1.3)$ SD lower compared with the reference values. The total muscle strength (SD) was 1.0 ± 1.1 higher in children with JHypoS as compared with the reference values, whereas in JHyperS, there was no significant difference.

All exercise tests were performed without complications. No desaturation was observed during exercise. The average peak HR of the children with JHypoS was 181 ± 9.7 and for children with JHyperS was 184 ± 16.0 beats per minute without a significant difference. The average peak respiratory exchange ratio of the children with JHypoS was 1.16 ± 0.08 and for children with JHyperS was 1.2 ± 0.06 without a significant difference.

The $\dot{V}_{O_2 \text{ peak}}$ and $\dot{V}_{O_2 \text{ peak}}/\text{kg}$ and W_{peak} can be appreciated from Table 3 and showed a significantly decreased $\dot{V}_{O_2 \text{ peak}}$ and $\dot{V}_{O_2 \text{ peak}}/\text{kg}$ in both patient groups. However, the magnitude of the impairment was not very large. $\dot{V}_{O_2 \text{ peak}}$ was within -2 SD from normal in 27 of 32 patients.

In 3 (23%) of 13 children with JHyperS, a *z* score

TABLE 1 Clinical Characteristics in Symptomatic Generalized Joint Hypermobility (n = 13) Compared With Reference Values (n = 382)

	Joint Hypermobility (n = 13), Mean ± SD (Range)	z Score, Mean ± SD	Reference Values (n = 382), Mean ± SD (Range)	P
Age, y	10.7 ± 2.7 (6.2–14.9)		14.5 ± 4.0 (8.0–20.8)	<.01
Boys, %	46.2		34.6	
Sports activities, h/wk	1.4 ± 1.3 (0.0–5.0)		2.8 ± 2.2 (0.0–18.0)	<.05
Height, cm	150.0 ± 19.8 (121.0–78.8)	0.4 ± 1.0	162.0 ± 18.1 (118.0–196.0)	.2 (NS)
Weight, kg	43.4 ± 16.8 (22.7–78.8)	1.0 ± 0.9	52.9 ± 16.8 (21.0–103.0)	<.05
BMI, kg/m ²	18.6 ± 3.7 (15.0–29.7)	1.1 ± 1.4	19.5 ± 3.3 (14.0–31.9)	<.05
BUA, dB/MHz	49.6 ± 9.8 (41.5–77.5)	−0.7 ± 0.7	66.1 ± 16.3 (18.5–150.7)	<.05
SOS, m/s	1540.5 ± 21.9 (1511.3–1574.9)	−1.0 ± 0.9	1567.4 ± 28.9 (1430.7–1685.9)	<.05
Total muscle strength, n	757.8 ± 317.5 (364.0–1355.0)	0.3 ± 1.8	826.9 ± 290.1 (365.0–1999.0)	.5 (NS)
Total range of joint motion, degrees	1715.4 ± 57.6 (1600.0–1790.0)	3.0 ± 0.9	1562.0 ± 68.4 (1365.0–1749.0)	<.05

NS indicates not significant.

TABLE 2 Clinical Characteristics in Symptomatic Generalized Joint Hypomobility (n = 19) Compared With Reference Values (n = 382)

	Joint Hypomobility (n = 19), Mean ± SD (Range)	z Score, Mean ± SD	Reference Values (n = 382), Mean ± SD (Range)	P
Age, y	13.1 ± 3.6 (7.9–20.2)		14.5 ± 4.0 (8.0–20.8)	.1 (NS)
Boys, %	73.7		34.6	
Sports activities, h/wk	1.4 ± 1.3 (0.0–5.0)		2.8 ± 2.2 (0.0–18.0)	<.05
Height, cm	159.5 ± 19.7 (127.0–193.0)	0.3 ± 1.5	162.0 ± 18.1 (118.0–196.0)	.1 (NS)
Weight, kg	50.7 ± 16.4 (23.8–81.1)	1.0 ± 1.9	52.9 ± 16.8 (21.0–103.0)	<.05
BMI, kg/m ²	19.4 ± 3.0 (14.5–26.5)	1.1 ± 1.9	19.5 ± 3.3 (14.0–31.9)	<.05
BUA, dB/MHz	55.1 ± 8.7 (37.5–75.0)	−0.7 ± 0.7	66.1 ± 16.3 (18.5–150.7)	<.05
SOS, m/s	1544.2 ± 21.9 (1506.0–1581.5)	−0.8 ± 1.0	1567.4 ± 28.9 (1430.7–1685.9)	<.05
Total muscle strength, n	992.6 ± 268.2 (555.0–1524.0)	1.0 ± 1.1	826.9 ± 290.1 (365.0–1999.0)	<.05
Total range of joint motion, degrees	1417.9 ± 73.6 (1275.0–1570.0)	−2.4 ± 1.3	1562.0 ± 68.4 (1365.0–1749.0)	<.05

TABLE 3 Exercise Capacity in Symptomatic Generalized Joint Hypermobility (n = 13) and Symptomatic Generalized Joint Hypomobility (n = 19) Compared With Age- and Gender-Matched Control Subjects

	Joint Hypomobility (n = 19), Mean ± SD (Range)	z Score, Mean ± SD	P	Joint Hypermobility (n = 13), Mean ± SD (Range)	z Score, Mean ± SD	P	Reference Values
Absolute $\dot{V}O_{2\text{peak}}$ L/min	1.96 ± 0.59 (1.0–3.2)	−0.66 ± 1.1	<.05	1.52 ± 0.66 (1.0–3.0)	−0.87 ± 1.6	<.05	1.98 ± 0.62
Relative $\dot{V}O_{2\text{peak}}$ mL/kg per min	40.61 ± 8.43 (27.0–57.0)	−1.33 ± 1.6	<.05	37.57 ± 8.94 (22.0–52.0)	−1.65 ± 1.6	<.05	46.87 ± 4.34
W_{peak} W	163.1 ± 52.1 (90.0–280.0)	−1.2 ± 1.15	<.05	134.9 ± 69.0 (70.0–260.0)	−0.7 ± 1.43	.1	150.0 ± 48.8

$\dot{V}O_{2\text{peak}}$ of less than -2 , indicating a severe decrease in exercise capacity, was present, whereas this was found in 2 (10%) of 19 children with JHypoS. In these 5 children, with a z score $\dot{V}O_{2\text{peak}}$ of less than -2 , maximal HR was (borderline) significantly decreased, as compared with 27 children with a z score $\dot{V}O_{2\text{peak}}$ of -2 or more (mean [SD] z score SOS: -1.6 [0.6] vs -0.7 [0.9]; $P = 0.04$; mean [SD] heartbeat: 174.0 [10.0] vs 184.0 [12.4]; $P = 0.07$). In children with JHyperS, a z score $\dot{V}O_{2\text{peak}}$ /kg of less than -2 , indicating a severe decrease in exercise capacity, was present in 6 (46%) of 13, whereas in JHypoS, this was present in 8 (42%) of 19 children. In these 14 children with a z score $\dot{V}O_{2\text{peak}}$ /kg of less than -2 , maximal HR was significantly decreased compared with 18 children with a z score $\dot{V}O_{2\text{peak}}$ /kg of -2 or more (mean [SD] z score SOS: -1.3 [0.8] vs -0.5 [1.0]; $P = 0.02$; mean [SD] heartbeat: 175.9 [11.5] vs 187.5 [10.9]; $P = 0.07$). The mean oxygen pulse was 10.9 ± 3.4 mL/beat and 8.3 ± 3.3 mL/beat in JHyperS

and JHypoS, respectively ($90 \pm 16\%$ of predicted), without significant difference when compared with reference values, indicating normal hemodynamics during peak exercise. Moreover, the average $\Delta\dot{V}O_2/\Delta WR$ of the children with JHypoS was 8.6 ± 1.1 mL O_2/W and for children with JHyperS was 8.4 ± 0.9 O_2/W , without a significant difference between the groups.

In the total group, a high significant correlation between the z score of $\dot{V}O_{2\text{peak}}$ /kg and the z score of the SOS was found ($r = 0.5$; $P = .01$) as well as with z score of BMI ($r = -0.43$; $P = 0.02$). The z score of total muscle strength was high significantly correlated with the z score of BMI ($r = 0.52$; $P = 0.002$) as well as BMD (z score BUA: 0.52; $P = 0.002$) and borderline significantly correlated with SOS (z score SOS: 0.33; $P = 0.06$). As can be expected, children with JHyperS and JHypoS differed significantly only in range of joint motion (mean [SD] z score total range of joint motion JHyperS versus JHypoS: 3.0 [0.9] and -2.4 [1.3], respectively).

Sixteen (50%) of 32 participated in sports activities with a mean of 1.4 hours/week (SD: 1.3). The control group participated in sports activities a mean of 2.8 hours/week (SD: 2.2; $P = 0.002$); 12% of the control subjects did not participate on sports activities. Children who participated in sports activities had a (borderline) significant increased mean (SD) $\dot{V}O_{2\text{ peak}}$ and mean (SD) z score of BUA compared with children who did not participate in sports activities (-0.3 [1.1] vs -1.2 [1.3; $P = 0.056$] and -0.45 [0.8] vs -0.9 [0.5; $P = 0.059$], respectively). In the total group with musculoskeletal pain, the hours of sports per week correlated moderately with mean z score of $\dot{V}O_{2\text{ peak}}$ (Pearson correlation coefficient: .32; $P = 0.07$) and mean z score of BUA (Pearson correlation coefficient: .35; $P = 0.05$).

DISCUSSION

In children with musculoskeletal pain-related syndromes, maximal exercise capacity was significantly decreased compared with age- and gender-matched control subjects. Moreover, the patients had an increased BMI. As expected, the total joint mobility of children with JHyperS was significantly higher compared with the reference group, whereas children with JHypoS showed significantly lower ranges of joint motion. When comparing JHyperS and JHypoS children, we found no significant differences except for range of joint motion, so reduced physical fitness may be related to other aspects than range of joint motion.

$\dot{V}O_{2\text{ peak}}$ was within the reference range (z score more than -2 SD) in the majority of the patients. However, corrected for body mass ($\dot{V}O_{2\text{ peak}}/\text{kg}$), the impairment became more significantly decreased because of a higher body mass in this patient group. In a study of children with a recently diagnosed chronic fatigue syndrome, we found a comparable exercise tolerance. Children with chronic fatigue syndrome had an average $\dot{V}O_{2\text{ peak}}$ z score of -0.33 ± 1.0 and an average z score for $\dot{V}O_{2\text{ peak}}/\text{kg}$ of -1.13 ± 1.41 .²⁴

The most probable explanation for the reduced exercise tolerance in our patients is deconditioning. Adult patients with low back pain had comparable $\dot{V}O_{2\text{ peak}}$ compared with sedentary control subjects.²⁵ However, in healthy children, sedentary control subjects should never be the reference norm, because a sedentary lifestyle imposes a significant health risk for children as well as adults.²⁶ We found a strong association only between all measurements and cardiopulmonary fitness. SOS was positively correlated with the $\dot{V}O_{2\text{ peak}}$ ($r = 0.4$; $P < .05$) and with the $\dot{V}O_{2\text{ peak}}/\text{kg}$ ($r = 0.5$; $P < .01$). The BMD of our patients was significantly lower compared with that of healthy subjects. In a recent study, Roberto et al²⁷ concluded that BMD may be lower in children with joint hypermobility (independent of musculoskeletal pain) as well. In their opinion, it was possible that structural alterations to the collagen of children with joint hyper-

mobility were responsible for these results. In children with symptomatic generalized joint hypermobility, besides lower QUS measurements, significantly higher degradation products in urine were reported.¹⁴

We found indications for another explanation. We found that patients with a higher cardiopulmonary fitness had a higher BMD. Physical activity has a beneficial effect on the bone development in circumpubertal children. Janz et al²³ concluded that more active children will have greater bone mass. Because the SOS is the only association with cardiopulmonary fitness, the implication is that the low exercise intolerance in hypermobile and hypomobile children is attributable to inactivity. In our study population, symptomatic children participated significantly less in sports activities, whereas in the patient group, children who participated in sports activities had a higher exercise capacity and BMD compared with the patients who did not participate in sports. Moreover, hours of sports activities were correlated with exercise capacity and BMD, suggesting a dose-response relationship. In future studies, more detailed information about the amount of weight bearing and intensity of sports activities should be gathered.

Several studies have indicated that $\dot{V}O_{2\text{ peak}}$ depends on physical activity and inactivity on the one hand and on genetic factors on the other hand,²⁸ even in children.^{29,30} The increase in $\dot{V}O_{2\text{ peak}}$ as a result of physical training is well documented and also is genetically heritable. Data from the HERITAGE Family study indicate that familial factors underlying $\dot{V}O_{2\text{ peak}}$ in sedentary families are quantitatively similar to those underlying its response to physical training.³¹

The strong association of the $\dot{V}O_{2\text{ peak}}/\text{kg}$ and the SOS compared with the absolute values also can be explained by the higher weight. We found a positive relationship between the total muscle strength and the $\dot{V}O_{2\text{ peak}}$ ($r = 0.5$; $P < .05$). An explanation for this association may be that reduced physical activity results in reduced muscle mass. Reduced muscle mass will result in decreased muscle strength. Therefore, the relationship between these 2 variables depended on physical activity as well. Remarkable is the significant higher total muscle strength in children with JHypoS compared with the reference group. An explanation for this increase is currently unknown.

El-Metwally et al³² reported recently in a population-based study on the prognosis of nonspecific pain in preadolescents. They used a shuttle-run test, which measures maximal performance and provides a surrogate index for $\dot{V}O_{2\text{ peak}}$ in healthy individuals. They found no significant difference in endurance at adolescence between the group with and without musculoskeletal pain. In population-based studies, it often is not possible to measure $\dot{V}O_{2\text{ peak}}$ directly, as can be performed in clinical studies. However, a maximal exercise test with expiratory gas analysis is more sensitive than a field test to detect differences in exercise capacity between patient groups.

CONCLUSIONS

Children and adolescents with musculoskeletal pain-related syndromes, in particular with (symptomatic) generalized joint hypermobility and hypomobility, maximal exercise capacity is significantly decreased compared with age- and gender-matched control subjects. We assume that inactivity, possibly related to musculoskeletal pain, is involved in the occurrence of exercise intolerance in this patient group. An intervention study to influence pain and inactivity therefore seems indicated.

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