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The physiological and physical determinants of functional ability measures in children with juvenile dermatomyositis

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Objective. **To study the relationships of muscle strength and maximal oxygen consumption (Vo_{2peak}) with Childhood Health Assessment Questionnaire (CHAQ) score, Childhood Myositis Assessment Score (CMAS) and Child Health Questionnaire [physical summary (CHQ-PhS) and psychosocial summary (CHQ-PsS)] scores in juvenile dermatomyositis.**
Method. **Fifteen patients (age 5–14 yr) participated. CMAS, CHAQ, CHQ, muscle strength and Vo_{2peak} were measured.**
Results. **Correlations revealed significant relationships between CHAQ and (i) muscle strength ($r = -0.72$) and (ii) absolute Vo_{2peak} ($r = -0.68$); between CMAS and relative Vo_{2peak} ($r = 0.73$); and between CHQ-PhS and (i) muscle strength ($r = 0.57$) and (ii) relative Vo_{2peak} ($r = 0.58$). Backward regression analysis showed that muscle strength was the best indicator of variation in CHAQ. Age and relative Vo_{2peak} were the best indicators for CMAS. Body mass and age were the best indicators for CHQ-PsS. Body mass and muscle strength were the best indicators for CHQ-PhS.**
Conclusion. **CMAS, CHAQ and CHQ correlate with muscle strength and Vo_{2peak}. CMAS, CHAQ and CHQ depend on different physical and physiological variables.**

KEY WORDS: Physical fitness, Physical activity, Activities of daily living, Quality of life, Functional ability, Maximal oxygen consumption, Muscle strength, Exercise tolerance, Endurance.

Juvenile dermatomyositis (JDM) is one of the rheumatic diseases of childhood. JDM is an inflammatory myopathy in which the immune system targets the microvasculature of the skeletal muscle and skin, leading to muscle weakness and a typical skin rash [1]. Generally, symptoms of weakness, muscle tenderness and stiffness follow the skin manifestations [2]. The main pathological changes found in muscle biopsies are muscle fibre degeneration and necrosis, with inflammatory infiltration in perivascular, perimysial and endomysial areas. Atrophied fibres, particularly in perifascicular areas, and fibres with an abnormal architecture may also be found [3].

In general, the age of onset has two peaks, between 5 and 9 yr and between 11 and 14 yr. In all age groups there is a predominance of females [4]. Since the introduction of corticosteroids there has been a marked decrease in mortality, and as a result attention has shifted towards functional limitations and ability to perform activities of daily living [4–6].

In exercise physiology, two non-invasive indicators of muscle function can be distinguished: muscle strength and maximal muscular oxygen uptake (Vo_{2peak}). [Maximal exercise tests with children and adolescents are usually terminated when the young person, despite strong verbal

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encouragement from the experimenters, is unwilling or unable to continue. The appropriate term to use is therefore 'peak oxygen consumption' ($V_{O_{2peak}}$), which represents the greatest oxygen uptake during an exercise test to volitional exhaustion.] Hicks *et al.* [7] and Takken *et al.* (Takken T, Spermon N, Helders PJM, Prakken ABJ, Van der Net J, submitted for publication) recently reported that children with JDM showed a decreased $V_{O_{2peak}}$ during aerobic exercise testing. Also, muscle strength is often diminished due to chronic inflammation, which induces muscle atrophy [1, 8].

Currently, the Childhood Health Assessment Questionnaire (CHAQ) and the Childhood Myositis Assessment Score (CMAS) are generally accepted tests to measure functional ability in patients with JDM [6, 9, 10]. The CMAS is specifically designed to assess the functional consequences of proximal muscle strength and endurance. The CHAQ is a questionnaire which measures the grade of disability in performing activities of daily living [10, 11]. Besides these specific outcome measures, Miller *et al.* [12] proposed the use of the Child Health Questionnaire (CHQ) as a generic tool to measure disease outcome in inflammatory myopathies, such as JDM. The CHQ measures the physical and psychosocial well-being of children. As the CHAQ, CMAS and CHQ are used more frequently in clinical practice, it is important to examine their relationships with exercise physiological indicators, as these are directly linked with the underlying muscular changes. The CHAQ, CMAS and CHQ are especially important in clinical practice, as all of them are non-invasive and easy to administer.

Our objective was to study the relationships of two non-invasive indicators of muscle function with CMAS, CHAQ and CHQ as distinct indicators of functioning in order to gain better understanding of the content validity of these functional outcome tools.

Methods

Fifteen patients (age 5–14 yr) participated in this study. JDM was diagnosed by a paediatric rheumatologist according to the criteria of Bohan and Peter [13]. The characteristics of the patients at baseline are presented in Table 1. Each patient was classified as monocyclic, chronic polycyclic or chronic continuous, as defined by Spencer *et al.* [14]. 'Monocyclic' is defined as full recovery within 2 yr without relapse, 'chronic polycyclic' as having a prolonged relapsing course with at least one relapse occurring while not receiving any medication, and 'chronic continuous' as persistent disease for longer than 2 yr despite daily glucocorticoid therapy, all relapses occurring during the period of therapy. A cross-sectional design was used to explore the applicability of the functional assessment tools in a wide range of clinical presentations of the disease.

Table 1. Subject characteristics

	Mean	S.D.	Range
Age at onset (yr)	5.67	2.21	3.4–11.4
Height (m)	1.36	0.18	1.1–1.60
Body mass (kg)	36.64	14.56	20.2–71.7
Σ skinfolds (mm)	93.79	46.53	44.3–208.7
CHAQ	0.68	0.50	0–1.4
CMAS	44.6	5.9	33–53
CHQ-PhS	41.67	12.6	17.17–57.2
CHQ-PsS	46.92	6.1	35.1–58.9
Muscle strength (N)	91.94	35.2	42.25–154.6
Absolute $V_{O_{2peak}}$ (l/min)	1.72	2.3	0.45–2.1
Relative $V_{O_{2peak}}$ (ml/kg/min)	30.4	9.4	15.6–45.4

Five subjects had active disease, five were in clinical remission (remission while taking medication) and five were in remission without taking medication.

All subjects were recruited from the paediatric rheumatology out-patient clinic of the Wilhelmina Children's Hospital, University Medical Center Utrecht, The Netherlands. Parents gave their informed consent for participation in the study. All procedures were approved by the Medical Ethics Committee of the University Medical Center Utrecht, The Netherlands.

The patient's body mass and height were determined using an electronic scale and a wall-mounted stadiometer. Body composition was assessed using the sum of skinfolds method (Σ skinfolds) according Pollock *et al.* [15]. The measurements were taken at seven sites (on the right side of the body: triceps, biceps, subscapular, suprailiac, mid-abdominal, medial calf and thigh) by the test leader (TT) in accordance with the American College of Sports Medicine guidelines [16]. It was not possible to assess the medial thigh site in four patients because of the involvement of the skin in the inflammation process. Therefore, this site was omitted from the analysis.

The cross-culturally adapted and validated Dutch translation of the CHAQ was used as a self-administered pencil and paper questionnaire for the parents (as proxies) as an index of functional ability [10, 11]. The CHAQ [17] has been adapted from the Stanford Health Assessment Questionnaire so that at least one question in each domain is relevant to children aged 0.6–19 yr. The CHAQ was recently validated for patients with juvenile idiopathic inflammatory myopathies [10].

The question with the highest score within each domain (range 0–3; 0 = able to do with no difficulty, 1 = able to do with some difficulty, 2 = able to do with much difficulty, 3 = unable to do; the time frame was last week) determined the score for that domain, unless aids or assistance were required (raising the score for that domain to a minimum of 2). The mean of the scores on the eight domains provided the CHAQ disability scale (range 0–3).

The CMAS is specifically designed to assess the functional consequences of proximal muscle strength and endurance in patients with myositis across a wide age range (2 yr to adult) [9]. The primary purpose of the CMAS is to serve as a longitudinal assessment tool for an individual patient to see if muscle function changes over time. The CMAS consists of 14 ordinal items of motor performance (e.g. head elevation, sit-ups and arm-raising) [9]. These items were chosen to assess primarily the proximal and axial muscle groups, and are ranked by means of standard performance and scoring methods. The sum of the scores on all items provided the CMAS score (range 0–53), higher scores indicating better muscle function.

The CHQ is a generic health instrument designed to assess the physical and psychosocial well-being of children independently of the underlying disease. The Dutch version of the CHQ (parent form 50) [11] was used in this study. The paper-and-pencil version of this questionnaire was administered to the parents of the JDM patients. The questionnaire consists of 50 items and nine domains: (1) general health (one item); (2) physical activities of the child (six items); (3) daily activities of the child/limitations (two items); (4) pain (two items); (5) behaviour (six items); (6) well-being (five items); (7) self-worth

(six items); (8) health of your child (six items); (9) you and your family (three items). from these domains a physical (CHQ-PhS) and psychosocial (CHQ-PsS) summary was calculated according to the user manual [18].

A hand-held dynamometer (Citec dynamometer type CT 3001; C.I.T. Technics, Groningen, The Netherlands) was used to test the isometric muscle strength (in Newtons). Isometric strength is the torque generated by a muscle group when it is not allowed to shorten during contraction, the muscle being made to contract against an immovable load. Maximum muscle strength was tested using the 'break' method, in which the examiner gradually overcomes the muscle strength of the patient and stops at the moment the extremity gives way. We used a protocol in which six muscle groups were tested: shoulder abductors, elbow flexors, wrist dorsal flexor, hip flexors, knee extensors and ankle dorsal flexor; all on both sides. This test was performed according to Backman [19, 20], with a minor adaptation for the position in which the elbow flexor was tested. During the test, the examiner manually stabilized the body parts proximal to the tested limb segment. Each muscle group was tested three times consecutively and the highest score was recorded. The scores of the six muscle groups were summed and used as an index of total muscle strength. Hand-held dynamometry was used because this method distinguished better between the muscle strength levels of our patients, all of whom were able to overcome moderate to maximum resistance (manual muscle testing, MRC scale 4 and 5). Moreover, hand-held dynamometry provided a continuous variable, and this enabled us to make use of a multiple linear regression model for our statistical analysis. Using the MRC scale would have resulted in ordinal data, which were not suited to our statistics.

Subjects performed a maximal exercise test using a motor-driven treadmill (Jaeger, Breda, The Netherlands) as described previously (Takken T, Spermon N, Helders PJM, Prakken ABJ, Van der Net J, submitted for publication). Every 3 min the workload was increased according to the protocol of Bruce *et al.* [21]. This protocol continued until the patient stopped because of volitional exhaustion, despite strong verbal encouragement from the experimenters. During the maximal exercise test, subjects breathed through a facemask (Hans Rudolph, Kansas City, Missouri, USA) connected to a calibrated metabolic cart (Oxycon Champion; Jaeger, Mijnhart, Bunnik, The Netherlands). Expired gas was passed through a flowmeter, an oxygen (O_2) analyser and a carbon dioxide (CO_2) analyser. The flow meter and gas analysers were connected to a computer, which calculated breath-by-breath minute ventilation (V_E), oxygen consumption (V_{O_2}), carbon dioxide production (V_{CO_2}) and respiratory exchange ratio from conventional equations. Heart rate was measured continuously during the maximal exercise test, using a bipolar electrocardiogram. Absolute peak oxygen consumption was taken as the average value over the last 30 s during the maximal exercise test. Relative $V_{O_{2peak}}$ was calculated as absolute $V_{O_{2peak}}$ divided by body mass. Usually only relative $V_{O_{2peak}}$ is reported in order to remove the influence of body size on $V_{O_{2peak}}$ [22]. However, as some of our patients had an increased body mass due to their glucosteroid medication, this would have resulted in a lower $V_{O_{2peak}}$ because of the higher body mass rather than reduced capacity of the muscles to consume oxygen. Therefore $V_{O_{2peak}}$ was reported as both absolute and relative $V_{O_{2peak}}$ values.

All data were entered and analysed in SPSS 9.0 for Windows (SPSS Inc., Chicago, IL, USA). Descriptive statistics were used to describe the characteristics of the patients. Partial correlation coefficients (controlled for age) were calculated to find the relationship between the functional outcome measures and other physiological parameters. Predictors of CHAQ, CMAS and CHQ were determined using multiple linear regression analysis. Backward elimination was used to identify variables significantly related to the functional outcome measures. The independent variables entered in the regression model included age, height, body mass, Σ skinfolds, isometric muscle strength, absolute $V_{O_{2peak}}$ and relative $V_{O_{2peak}}$.

Results

In this cross-sectional study, 15 JDM patients were examined (10 girls and five boys). The average age was 9.56 ± 2.7 yr. Their characteristics are displayed in Table 1. There were nine patients with a monocyclic course, two with a polycyclic course and four with a chronic course. The mean disease duration was 2.9 yr (S.D. 2.1, range 0.8–5 yr). The mean creatine phosphokinase (CPK), lactic dehydrogenase (LDH) and alanine aminotransferase (ALAT) at onset were 3281.5, 1235.5 and 83.15 U/l respectively. The mean initial dose of prednisone was 1.23 mg/kg/day (S.D. 0.62, range 0.61–1.85 mg/kg/day). At the time of this study the mean dose of prednisone was 0.18 mg/kg/day (S.D. 0.27, range 0.00–0.44 mg/kg/day).

In Table 2 the partial correlation coefficients are displayed. The correlations between CHAQ and physical and physiological indicators ranged from 0.05 to 0.72, showing that the CHAQ had a strong correlation ($r > 0.5$) with absolute $V_{O_{2peak}}$ and height, and a very strong correlation ($r > 0.7$) with muscle strength.

The correlations between CMAS and physical and physiological indicators ranged from 0.24 to 0.74, showing that the CMAS had a strong correlation ($r > 0.5$) with absolute $V_{O_{2peak}}$ and muscle strength, and a very strong correlation ($r > 0.7$) with relative $V_{O_{2peak}}$.

The correlations between CHQ-PhS and physical and physiological indicators ranged from 0.22 to 0.61, showing that CHQ-PhS had a strong correlation ($r > 0.5$) with muscle strength and relative $V_{O_{2peak}}$.

The correlations between CHQ-PsS and physical and physiological indicators ranged from 0.22 to 0.61, showing that the CHQ-PsS had a strong correlation ($r > 0.5$) with body mass and both absolute and relative $V_{O_{2peak}}$.

In Table 3 the results of the backward regression analysis are shown. Muscle strength, which accounted for 48% of the total variance, was the best indicator of variation in CHAQ. Age and relative $V_{O_{2peak}}$, which accounted for 73.5% of the total variance, were the best indicators of variation in CMAS. Body mass and muscle strength were the best indicators of variation in CHQ-PhS, and accounted for 49% of the total variance in

TABLE 2. Partial correlation coefficients (controlled for age) of functional outcome instruments with physical and physiological variables

	CHAQ	CMAS	CHQ-PhS	CHQ-PsS
Height	−0.5510	0.2742	0.2941	−0.2156
Body mass	−0.2517	−0.2906	−0.3396	−0.6051*
Σ skinfolds	0.0534	−0.2437	−0.2991	−0.3929
Muscle strength	−0.7165**	0.5337	0.5747*	0.2970
Relative $V_{O_{2peak}}$	−0.3784	0.7356**	0.5759*	0.5281
Absolute $V_{O_{2peak}}$	−0.6806*	0.6010*	0.4946	0.2281

*$P < 0.05$; **$P < 0.01$.

TABLE 3. Results of backward regression analysis

Value	Coefficient ± S.E.	*P*
CHAQ		
Intercept	1.60 ± 0.30	<0.001
Muscle strength	−0.01 ± 0.003	<0.01
R^2	0.479	
CMAS		
Intercept	21.19 ± 4.34	<0.001
Relative Vo_{2peak}	0.37 ± 0.10	<0.01
Age	1.26 ± 0.35	<0.01
R^2	0.735	
CHQ-PhS		
Intercept	30.36 ± 8.55	<0.001
Body mass	−0.51 ± 0.25	>0.05
Muscle strength	0.33 ± 0.10	<0.01
R^2	0.487	
CHQ-PsS		
Intercept	35.60 ± 4.14	<0.001
Body mass	−0.34 ± 0.14	>0.05
Age	2.39 ± 0.71	<0.01
R^2	0.509	

CHQ-PhS score. Body mass and age, which accounted for 51% of the total variance, were the best indicators of variation in CHQ-PsS.

Discussion

Our objective was to study the relationships of muscle strength, Vo_{2peak} with CMAS, CHAQ and CHQ to obtain a better understanding of changes in these functional outcome assessment tools in a disease that directly affects muscle tissue. The patient group involved in this study represented a wide range of all facets of the disease course, enabling us to test the outcome measures in different clinical conditions. Our study showed that CMAS, CHAQ and CHQ were associated with physical and physiological parameters. The very large correlation between CHAQ and muscle strength found in this study exceeded those reported by Feldman *et al.* [6], who found moderate to high correlations between CHAQ and muscle strength in the hip ($r = 0.57$) and shoulder ($r = 0.51$) of JDM patients. Huber *et al.* [10] also found a large correlation ($r = 0.64$) between CHAQ and manual muscle testing in JDM patients.

The moderate correlation between CHAQ and relative Vo_{2peak} was confirmed in the study of Hicks *et al.* [7], who found a correlation of 0.46 between CHAQ and relative Vo_{2peak}.

The large correlation between CMAS and muscle strength was not as high as that found in the study of Lovell *et al.* [9], who found a nearly perfect correlation ($r = 0.93$) between manually tested muscle strength and performance on the CMAS in JDM patients ($n = 10$). In our study the correlation was not significant, however. This discrepancy might be explained by the different methods of muscle strength measurement (manual muscle testing *vs* use of a hand-held dynamometer).

The very large correlations between CMAS and both absolute and relative Vo_{2peak} were somewhat higher than the correlations found by Hicks *et al.* [7], who reported a moderate relationship ($r = 0.52$) between relative Vo_{2peak} and CMAS score. Hicks *et al.* [7] used a bicycle protocol and different statistics (Spearman correlations).

The relationship between CHQ scores and exercise physiological parameters have not been determined previously in JDM patients. The CHQ-PhS was significantly correlated with muscle strength and relative Vo_{2peak}. Our results suggest that the CHQ-PsS is, as expected, not significantly correlated with Vo_{2peak} and muscle strength, as it measures domains such as behaviour, well-being and self worth, which are not expected to depend solely on physical performance.

The results of our backward regression analysis show that the CMAS, CHAQ and CHQ are complementary instruments as they are dependent on other physical and physiological variables. The CHAQ seems more dependent on muscle strength than on Vo_{2peak}. Recently, Takken *et al.* [23] showed that CHAQ scores in juvenile idiopathic arthritis patients were more dependent on anaerobic power (speed × strength) than on Vo_{2peak}, indicating a similar relationship. Muscle strength is dependent on the cross-sectional area of the muscle fibres and neuromuscular coordination [3]. Muscular atrophy will be reflected in diminished muscle strength. Improvements in CHAQ scores might thus indicate better muscle strength and muscle performance.

The backward regression analysis showed that age and relative Vo_{2peak} were the best predictors of performance in the CMAS. Although CMAS consists predominantly of items assessing muscle strength, it was more dependent on Vo_{2peak} compared with muscle strength. Some of the items take up to 2 min or six repetitions to obtain a maximum score [9]. These items might be more dominant in the final score than the items dependent on strength. Vo_{2peak} is dependent on both muscle mass and muscle quality [3]. Changes in CMAS score might thus reflect improvements in muscle mass and muscle oxidative capacity. It was also surprising that age was also a predictive factor for CMAS score. Lovell *et al.* [9] reported no correlation between the age of the subjects and performance in the CMAS and stated that the CMAS is an age-independent instrument. However, the present data indicate that there might be an influence of age on the CMAS score. The influence of age might also be explained by the fact that the younger subjects in the current study were also the children with active disease.

CHQ-PhS score was predicted best by body mass and muscle strength. The regression coefficient for body mass was negative (higher body mass was associated with a decrease in physical functioning). The regression coefficient for muscle strength was positive, indicating that muscle strength has a positive effect on the CHQ physical summary. A higher body mass is often the result of side-effects of glucosteroid medication, resulting in a cushingoid appearance; not only might this account for the effects on psychosocial functioning, but an increased body mass (overweight) might restrict patients in the performance of activities of daily living. Moreover, it is known that glucosteroid medication results in muscular atrophy, which can be reversed by physical training [24]. The

positive relationship between muscle strength and the PhS domain of CHQ might be explained by improved physical functioning that is the result of increased muscle strength in these patients with JDM, just as we found in the relationship with CHAQ and muscle strength.

The backward regression analysis indicated that body mass and age were the best predictors of CHQ-PsS score. There was a negative regression coefficient for body mass, indicating that a higher body mass was related to lower psychosocial functioning. A higher body mass is often the result of side-effects of glucosteroid medication, resulting in a cushingoid appearance. This might account for the negative self-worth assessment in these children and explain the association found in this study. The regression coefficient for age was positive, indicating that psychosocial functioning improved with age. This might have been caused by the fact that the children with active disease were younger than the children with disease in clinical remission or in remission.

The clinical relevance of the results from the backward regression is that CMAS, CHAQ and CHQ each depend on different physical and physiological measures. Therefore, they have to be regarded as distinctive functional outcome instruments. We strongly advise the use of the instruments, as they are complementary in both clinical practice and trials.

Future studies are necessary to establish these results also in a longitudinal setting. Such studies should reveal the nature of response of these outcome measures with respect to the disease course and the interventions that have been or will be developed for these patients.

Conclusion

The results of this study show that the CMAS, CHAQ and CHQ correlate with muscle strength and $V_{O_{2peak}}$. This is supported only partly by the previous evidence. The backward regression analysis showed that the CMAS, CHAQ and CHQ are complementary functional outcome instruments as they are dependent on different physical and physiological variables.

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