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Metabolic Abnormalities and Cardiovascular Risk Factors in Children with Myositis

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Abstract

Objective—We studied children with myositis to characterize their metabolic abnormalities and risk factors for future cardiovascular disease.

Methods—Seventeen patients with severe juvenile myositis, primarily referred because of refractory disease, were assessed using standardized disease activity and damage measures. Body mass index (BMI), fasting insulin and lipids, 2-hour oral glucose tolerance test (OGTT), and cytokine levels were obtained.

Results—The majority (71%) had blood pressures > 75th percentile, 23.5% had hypertension, and BMI was > 85th percentile in 47%. Metabolic abnormalities were also frequent: 41.2% had an elevated fasting insulin level, 47.1% had hypertriglyceridemia and 25% met criteria for the metabolic syndrome. While insulin resistance was common (based on homeostasis model assessment (HOMA), and glucose: insulin (G:I) ratio), insulin secretion appeared to be unaffected. Thigh muscle damage assessed by magnetic resonance imaging (MRI) significantly correlated with fasting insulin, glucose and G:I ratio. Glucose indices also correlated with the pro-inflammatory cytokines IL-2 and IL-12 and inversely with anti-inflammatory cytokines IL-1RA and IL-10.

Conclusions—In this referral cohort of children with severe juvenile myositis, metabolic abnormalities and predictors of cardiovascular disease were common, suggesting an increased risk of future cardiovascular disease. Indicators of insulin resistance correlated with muscle damage on MRI and pro-inflammatory cytokines and inversely with anti-inflammatory cytokines.

Keywords

juvenile dermatomyositis; insulin resistance; hyperlipidemia; metabolic syndrome

Introduction

Juvenile dermatomyositis (JDM) and polymyositis (JPM) are childhood-onset immune-mediated disorders characterized by proximal weakness and, in the case of JDM, distinguishing rashes. Metabolic abnormalities, including insulin resistance and hyperlipidemia, are frequent sequelae of pediatric rheumatic diseases like juvenile rheumatoid arthritis and systemic lupus erythematosus (SLE) (1). Insulin resistance and hyperlipidemia, in the presence or absence of lipodystrophy (LD), has been observed in up to 66% and 46%, respectively, of patients with JDM screened (2–5). These findings in JDM may in part be confounded by corticosteroid usage and deconditioning.

Increased risk of atherosclerosis has been established in multiple rheumatic diseases in adults, with relative risks varying from approximately 1.6 – 6.0 in SLE, rheumatoid and psoriatic arthritis, and ankylosing spondylitis (6). Conclusive evidence of a similarly increased cardiovascular risk does not exist in patients with myositis. We speculated that increased cardiovascular risk would be evident in patients with juvenile myositis.

We systematically examined metabolic variables in a cohort of children with severe, treatment-refractory myositis to characterize the frequency of metabolic abnormalities and to identify risk factors for cardiovascular disease.

Patients and Methods

Seventeen consecutive patients with probable or definite juvenile myositis by modified Bohan and Peter criteria (7) enrolled within a 1.5 year period and underwent evaluation by a pediatric rheumatologist (LR) and endocrinologist (KR) at the National Institutes of Health Clinical Center, Bethesda MD. Patients were primarily referred for an evaluation of their myositis disease activity, often because of chronic disease or non-reponsiveness to therapy. Patients were assessed at a baseline evaluation, with median disease duration of 38 months. Sixteen patients had JDM and one had JPM. The research protocol was approved by the NIDDK/NIAMS/NIEHS Institutional Review Board and informed consent was provided by parents or legal guardians, and assent by patients when appropriate.

Disease course was defined as monocyclic if myositis was in remission within two years of diagnosis, polycyclic if the course was relapsing remitting, with periods of inactivity, chronic continuous if the illness was persistently active for more than two years, and undefined if there was < 2 years follow-up from diagnosis (3). Patients were categorized as having partial LD if they demonstrated loss of upper and/or lower extremity fat with relative sparing of abdominal and trunk fat, whereas those with generalized fat loss in the face, trunk, abdomen and all extremities were classified as having generalized LD (3).

Blood pressure was assessed with the patient seated; the measurement was repeated if the initial reading was elevated. Patients were characterized as hypertensive if systolic and/or diastolic blood pressure results were greater than 95th percentile for age, gender and height (8).

Myositis disease activity and damage were assessed using several standardized measures, including physician and parent global activity and damage assessments on a 5 point Likert scale, the Childhood Myositis Assessment Scale (CMAS, range 0– 52 with a score of 52 equivalent to normal physical function and strength) and the Childhood Health Assessment Questionnaire (CHAQ, range 0 – 3, with a score of 0 meaning no detectable physical disability) as measures of physical function, a skin global activity assessment and serum levels of muscle enzymes, including creatine phosphokinase (CK), aldolase, lactate dehydrogenase (LDH), alanine transaminase (ALT) and aspartate aminotransferase (AST)(9). A pediatric physical therapist tested the strength of 26 muscle groups by manual muscle testing (MMT) on a 0–10

point scale, with a range of 0–260 for the total MMT score, with a score of 260 equal to normal strength (9). Bilateral thigh magnetic resonance imaging (MRI) was performed on a 1.5 Tesla scanner (General Electric Medical Systems, Milwaukee, WI). Short tau inversion recovery (STIR) sequences, which detect edema, were used to assess active muscle disease and T1 MRI was used to evaluate muscle damage (muscle atrophy and fatty replacement), using a 5 point Likert scale (10).

Family histories of diabetes mellitus (DM) and hyperlipidemia were obtained. Body mass index (BMI) was calculated according to sex and age-specific guidelines (11).

Serum lipids and leptin were measured following an overnight fast before taking morning medications. Elevated triglyceride, total cholesterol and low density lipoprotein (LDL) levels were defined as greater than the 95th percentile and low high density lipoprotein (HDL) as less than the 5th percentile based on age and sex established normal limits (12). Serum glucose and insulin were measured at baseline in all patients and every thirty minutes for 2 hours following a 1.75 g/kg (maximum 75g) oral glucose load (OGTT) in thirteen patients. A fasting plasma glucose of 100–125 mg/dL was considered impaired, and a level ≥ 126 mg/dL was consistent with diabetes mellitus (13). Plasma glucose values at 2 hours were considered impaired when ≥ 140 mg/dL and diabetic if > 200 mg/dL (13). A fasting insulin of ≥ 15 uU/mL was considered elevated in prepubertal patients and ≥ 30 uU/mL in pubertal patients, to account for the physiologic insulin resistance associated with puberty (14). Area under the curve (AUC) for insulin and glucose was calculated using the trapezoidal method (15).

Insulin sensitivity was determined via three validated measures. A homeostasis model assessment (HOMA) of ≥ 4 was indicative of insulin resistance, and a value of > 8 was consistent with diabetes (16). A glucose to insulin (G:I) ratio of < 4.5 was considered abnormal (17). Insulin Sensitivity Index ($ISI_{0,120}$) was calculated based on glucose and insulin values obtained at 0 and 120 minutes of the OGTT (18). Insulin secretion was quantified as the ratio of the incremental insulin to glucose responses over the first 30 minutes during the OGTT ($\Delta I_{30}/\Delta G_{30}$) (19). This measure was also adjusted for insulin sensitivity as it modulates beta-cell function ($\Delta I_{30}/\Delta G_{30}/HOMA-IR$) (19). There are no established norms for the $ISI_{0,120}$, $\Delta I_{30}/\Delta G_{30}$ or $\Delta I_{30}/\Delta G_{30}/HOMA-IR$.

Leptin values < 2.0 ng/ml were low in pre-pubertal children (20). For post-pubertal girls, leptin levels below the 5th percentile for healthy women were considered abnormal (21).

Patients who had at least three of the following criteria were classified as having the metabolic syndrome: (1) Obesity: BMI $\geq 95^{\text{th}}$ percentile for age and sex; (2) Abnormal glucose homeostasis: fasting hyperinsulinemia or impaired fasting glucose or impaired glucose tolerance; (3) Hypertension: systolic blood pressure $> 95^{\text{th}}$ percentile for age and sex; and (4) Dyslipidemia: triglycerides ≥ 150 mg/dL or HDL < 35 mg/dL or total cholesterol > 200 mg/dL (14).

Double antibody radioimmunoassay was used to measure insulin (Diagnostic Product Corporation, Los Angeles CA); the assay's range was 3.75–600 pmol/L. Serum leptin levels were determined by radioimmunoassay (Human Leptin RIA Kit, Linco Research, Inc., St. Charles, MO). Serum cytokines and receptor antagonists were measured by Enzyme-Linked Immunosorbent Assay (R&D Systems, Minneapolis, MN; Endogen, Woburn, MA).

Sigma Stat version 3.0.1 (Systat Software, Inc., Richmond CA) was used for analysis. Data were expressed as median and interquartile (IQ) ranges and p values were obtained by the Mann-Whitney test. When comparing proportions between groups, p values were calculated by Fisher's exact test. Spearman rank correlation (r_s) was used to assess the relationship

between variables. A p value ≤ 0.05 was considered significant. As this was an exploratory study, correction for multiple comparisons was not performed.

Results

The demographic and clinical characteristics of the population are summarized in Table 1. The majority of this cohort was female (82%) and ages ranged from 4.6 to 16.4 years. Median disease duration was 38 months, and the majority had a chronic continuous or polycyclic illness course. All patients were receiving prednisone; the median dose was 0.56 mg/kg/day (range 0.08–1.10 mg/kg/day). Five patients were receiving hydroxychloroquine, six were receiving methotrexate with a median dose of 0.4 mg/kg/week (IQ range 0.4 – 0.6 mg/kg/week), and two were taking both. The median physician global disease activity was mildly active and median CMAS score was in a mild range of physical dysfunction. The median CHAQ score was 0.50 [IQ range 0.0 – 1.6].

Based on age and gender norms, BMI was $\geq 85^{\text{th}}$ percentile in 47% and $>95^{\text{th}}$ percentile in 23.5% of patients (Table 1). The systolic blood pressures of 52.3% of these patients were $>90^{\text{th}}$ percentile, with diastolic blood pressure $>90^{\text{th}}$ percentile in 11.7% (Table 1). Neither systolic nor diastolic blood pressures correlated with disease activity measures, BMI or prednisone dose.

The most common lipid abnormality was hypertriglyceridemia, present in 47.1% of patients, and 17.1% had elevated cholesterol, elevated LDL or decreased HDL (Table 2). Despite normal fasting glucose levels in all but one patient, a high frequency of abnormalities in multiple other measures of glucose metabolism was found: 35.2% had an impaired 2-hour OGTT, 41.2% had elevations in fasting insulin, 47.1% had abnormal G:I ratio and 47.1% had an elevated HOMA (Table 2). Beta cell function appeared unaffected (Table 2), supporting the notion that insulin resistance was the predominant abnormality, not insulin secretion.

Patients with a family history of diabetes mellitus ($n=8$) had significantly higher HOMA values than those without ($n=9$) (median HOMA 7.0 [IQ range 4.1 – 9.1] versus 2.9 [IQ range 2.1 – 4.2]) and lower G:I ratios (median G:I ratio 2.9 [IQ range 2.2 – 4.0] versus median 5.8 [IQ range 4.6 – 7.9]; $p=0.04$ for each). A family history of hyperlipidemia ($n=3$) had no influence on lipid/metabolic variables in this cohort.

Four patients (24%) met Viner criteria for the metabolic syndrome (14); all had hypertension. Fifty-three percent had at least two criteria for the metabolic syndrome.

The above findings were examined after exclusion of patients with LD. There were no significant differences in median values of the glucose, lipid or metabolic variables regardless of the inclusion of LD patients. Also, the presence of calcinosis did not impact glucose metabolism, lipid or metabolic indices. While prednisone dose did not correlate with any metabolic variables ($r_s = -0.46 - 0.50$, $p = 0.06 - 0.98$), duration of prednisone use correlated inversely only with BMI-SDS ($r_s = -0.51$, $p = 0.04$) and HDL ($r_s = -0.50$, $p = 0.03$). There were no differences in the effects of prednisone dose or duration in lipid or glucose indices in patients receiving hydroxychloroquine versus those not receiving hydroxychloroquine.

T1 MRI assessment of muscle damage significantly correlated with several metabolic measures (Table 3). The MRI thigh muscle fatty infiltration score inversely correlated with G:I Ratio and $ISI_{0,120}$ (lower values indicating higher insulin resistance) and positively correlated with fasting insulin levels and HOMA. The thigh muscle atrophy MRI score correlated inversely with $\Delta\text{ins30}/\Delta\text{gluc30}/\text{HOMA-IR}$. A combined T1 MRI fatty infiltration and muscle atrophy score correlated with fasting glucose. Additional significant correlations between metabolic variables and myositis disease activity measures included a direct correlation of CMAS with

HDL, as well as an inverse correlation of AST with HDL and leptin. Other myositis disease activity and damage measures, including physician and patient global activity and damage assessments, MMT, CHAQ, skin global activity, and other enzymes, did not correlate with the glucose or metabolic parameters.

Glucose metabolism measures correlated positively with several pro-inflammatory cytokines and inversely with anti-inflammatory cytokines. Fasting glucose correlated with interleukin-2 (IL-2) ($r_s = 0.70$, $p = 0.001$) and IL-12 ($r_s = 0.73$ respectively, $p = 0.001$). Inverse correlations were observed between IL-1 α with G:I ratio ($r_s = -0.62$, $p = 0.04$), as well as with IL-10 and G:I ratio ($r_s = -0.58$, $p = 0.05$), 120 minute glucose ($r_s = -0.69$, $p = 0.02$), insulin AUC ($r_s = -0.81$, $p = 0.004$) and glucose AUC ($r_s = -0.79$, $p = 0.01$). Inverse correlations were also found between IL-1Ra and fasting glucose ($r_s = -0.89$, $p = 0.04$), insulin AUC ($r_s = -0.94$, $p = 0.02$) and glucose AUC ($r_s = -0.94$, $p = 0.02$). No significant correlations were found between tumor necrosis factor alpha (TNF- α), type I TNF receptor (sTNF-R1), type II TNF receptor (sTNF-R2), IL-6, interleukin-6 receptor (sIL-6R), interferon gamma (IFN- γ) or intracellular adhesion molecule (ICAM) and glucose or lipid parameters (range: $r_s = -0.51 - 0.80$, $p = 0.10 - 0.92$).

Discussion

Juvenile myositis is frequently associated with insulin resistance and hyperlipidemia(2,4,5). Similar to previous reports, we showed that these metabolic abnormalities, although characteristic of LD, are present in patients with JDM even in the absence of LD (2,5). This study also highlights the increased prevalence of the metabolic syndrome in JDM. However, this finding needs to be placed in perspective. The usefulness of metabolic syndrome definitions in childhood for the prediction of future cardiovascular disease remains controversial (22). In addition, our relatively small sample size and the fact that this is a referral population may contribute to an overestimate of the prevalence of the metabolic syndrome in this disorder. The patients included in this study, for example, had a chronic or polycyclic course of illness and these findings may not be relevant to patients with milder disease, such as those who achieve remission and are able to discontinue medications.

Half of the patients studied had hyperlipidemia, which is consistent with reports of dyslipoproteinemias in JDM, as well as in adult and pediatric SLE (1). Longitudinal studies in SLE show two lipid patterns. The first pattern, associated with active disease, is characterized by low HDL and Apo A-1 and high VLDL and triglyceride levels, similar to that seen in the metabolic syndrome (23). The second, thought to be corticosteroid induced, is associated with high total cholesterol, VLDL and triglycerides (24). HDL levels are thought to represent a balance between active disease (which depresses HDL) and corticosteroid use (which elevates HDL). Thus, our findings of a significant correlation of HDL with CMAS and a significant inverse correlation with AST are consistent with an inverse relationship of HDL with active myositis. Our results are similar to those of Huemer et al. who also found inverse correlations of HDL with transaminases and von Willebrand factor VIII related antigen and a direct correlation of triglycerides with ALT (2). It is possible that the trend in our cohort toward low HDL, high total cholesterol and triglycerides and LDL is the result of a complex interplay of disease activity, insulin resistance and chronic prednisone usage. Consideration should also be given to the potential contribution of hydroxychloroquine use, as it may decrease total cholesterol, LDL, and triglycerides in patients receiving corticosteroids. Longitudinal evaluation of a larger cohort would enable greater clarification of these factors.

Multiple separate validated measures (HOMA, G:I ratio, ISI_{0,120}, $\Delta I_{30}/\Delta G_{30}$, $\Delta I_{30}/\Delta G_{30}/$ HOMA-IR) demonstrated that this cohort had impaired glucose regulation. These measures have well-established limitations, including their inability to account for hepatic glucose

production (25). Although our study lacked a control group, our results are consistent with the increased prevalence of insulin resistance seen in JDM (2,5), rheumatoid arthritis, and adult (26) and pediatric SLE (1). Also, a hereditary component appears to contribute to alterations in glucose metabolism as evidenced by the greater fasting insulin and HOMA values in patients with a family history of diabetes.

In addition to glucocorticoids, which can induce insulin resistance (27,28), the chronic inflammation present in rheumatic diseases may have resulted in findings of heightened insulin resistance (29). This concept of inflammation causing insulin resistance is also supported in our study by the strong correlations of glucose with the pro-inflammatory cytokines IL-2 and IL-12, and inverse correlations with the anti-inflammatory cytokines IL-10 and IL-1RA (35). Our finding of a positive correlation of IL-2 with markers of insulin resistance is mirrored by similar findings in patients with rheumatoid arthritis (30). We did not find significant correlations between these indicators and IL-6 or TNF- α ; however, these cytokines have been reported to be elevated in diabetic and insulin resistant states and in patients with JDM with a chronic illness course (29,31). The inverse correlation of glucose metabolism indices with cytokines with anti-inflammatory effects such as IL-1 RA and IL-10 is consistent with current literature on cytokines in insulin resistance (32). It should be noted that cytokine levels were not analyzed in all patients and although our results are consistent with previous findings, the small sample size limits their interpretability.

We also found correlations of glucose/insulin variables with MRI muscle atrophy and fatty infiltration. Since insulin mediated glucose disposal occurs principally in skeletal muscle and fatty acid in muscle modulates insulin action (33), it is feasible that skeletal muscle inflammation and/or fibrosis may contribute further to glucose and insulin dysregulation. A potential mechanism may include an insulin receptor metabolic defect in affected muscle, as seen in myotonic dystrophy, which is also associated with insulin resistance (34).

Medications are potential confounders of our results. We likely did not find significant correlations of glucose abnormalities with prednisone dose or duration due to the overall low dose (range 0.08–1.10 mg/kg/day). These doses in children have the potential to contribute to the underlying insulin resistance. Despite previous work suggesting that hydroxychloroquine may be protective against abnormal glucose metabolism and hyperlipidemia in SLE, type II diabetes and RA (35,36), we did not find differences in these measures based on administration of hydroxychloroquine. However, our study was underpowered to detect such differences.

Our study and others (2,5,37) indicate that metabolic abnormalities are frequent in patients with juvenile myositis, with a high frequency of the metabolic syndrome that could predispose to early cardiovascular disease. Our study, however, is limited primarily to a population of patients with severe, chronically active disease. The chronic inflammatory state of juvenile myositis, muscle damage, as well as long term high dose corticosteroid therapy, appear to contribute to an increased cardiovascular risk. Importantly, although atherosclerotic complications generally do not emerge until adulthood, the atherosclerotic process begins in childhood. Thus, interventions directed at reducing or preventing atherosclerosis should also begin in childhood. There are only four reports characterizing asymptomatic atherosclerosis in pediatric patients with rheumatic disease. Pachman reported premature carotid artery disease in young adults with JDM (37). Reports in pediatric SLE revealed significantly increased carotid artery intima-media thickness (38) and significant myocardial perfusion abnormalities on thallium scanning (39), while a third report failed to show abnormalities in endothelial function (40).

Limitations of this study include potential confounding of prednisone dosage and duration, use of a single blood pressure measurement rather than the average of two readings, and the study

population, which is a small referral population that may be biased towards more severe underlying disease. We did not use the euglycemic insulin clamp study to determine insulin resistance. We did not include measurements of the waist: hip ratio for several reasons, including the confounding effects of corticosteroid therapy which can increase central obesity and the controversial utility of waist: hip ratio in childhood (22).

Close attention should be paid to monitoring blood pressure according to age and sex norms. The systolic blood pressure was >90th percentile in half of the cohort. It is important to note that a cursory review of the blood pressure readings appear normal (the mean systolic blood pressure was 117 mm Hg, while mean diastolic blood pressure was 66 mm Hg), whereas quite a few were abnormal based on age-, height- and sex defined normal limits. Blood pressure elevation in juvenile myositis may be related to small vessel vasculopathy, corticosteroid use with consequent weight gain, as well as sodium and water retention.

Metabolic abnormalities and cardiovascular risk factors were common in this juvenile myositis cohort. These appear to be related to underlying myositis disease activity, muscle damage and cytokine release. Our findings point to a need for risk factor evaluation and modification in this population.

Abbreviations

JDM	juvenile dermatomyositis
JPM	juvenile polymyositis
SLE	systemic lupus erythematosus
LD	lipodystrophy
CMAS	Childhood Myositis Assessment Scale
CHAQ	Childhood Health Assessment Questionnaire
CK	creatinine kinase
LDH	lactate dehydrogenase
ALT	alanine transaminases
AST	aspartate aminotransferase
MMT	manual muscle testing
MRI	magnetic resonance imaging
STIR	short tau inversion recovery
DM	diabetes mellitus
BMI	body mass index
LDL	low density lipoprotein
HDL	high density lipoprotein
OGTT	oral glucose tolerance test
AUC	area under the curve
HOMA	homeostasis model assessment
G:I	glucose to insulin ratio
ISI _{0,120}	Insulin Sensitivity Index

$\Delta I_{30}/\Delta G_{30}$	ratio of the incremental insulin to glucose responses over the first 30 minutes during the oral glucose tolerance test
Hgb A1c	glycosylated hemoglobin
IQ	interquartile
r_s	Spearman rank correlation
IL	interleukin
TNF- α	tumor necrosis factor alpha
sTNF-R1	type I TNF receptor
sTNF-R2	type II TNF receptor
sIL-6R	interleukin-6 receptor
IFN- γ	interferon gamma
ICAM	intracellular adhesion molecule

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Table 1

Demographic and Clinical Characteristics of 17 Patients with Juvenile Dermatomyositis at Baseline Evaluation.

Variable	Median [25%, 75%] Or Number (%)
Female, <i>n</i> (%)	14 (82%)
Duration of active disease (months)	38.0 [5.8, 66.3]
Disease course, <i>n</i> (%)	
Chronic continuous	6 (35%)
Polycyclic	6 (35%)
Undefined	5 (30%)
Calcinosis, <i>n</i> (%)	9 (53%)
Lipodystrophy, <i>n</i> (%)	3 (17.6%)
Prednisone dose (mg/kg/day)	0.56 [0.14, 0.88]
Physician Global Disease Activity (0 – 4) *	1 [0, 2]
CMAS (0–52)	45 [41, 49]
BMI actual	19.7 [18.4, 23.9]
(% tile) kg/m ²	80.0 [52.8, 92.5]
Systolic BP (% tile)	117 [109, 122]
Diastolic BP (% tile)	66 [61, 74]

* 0=inactive, 4=extremely severe.

Abbreviations: CMAS, Childhood Myositis Assessment Scale; BMI, body mass index; BP, blood pressure.

Table 2

Baseline Metabolic Evaluations in Seventeen Patients with Juvenile Myositis*

Variable	Median [25%, 75%]	% Abnormal
LDL (mg/dL)	106 [84.3, 128.3]	17.6
Triglycerides (mg/dL)	115 [86, 197]	47.1
HDL (mg/dL)	39 [26, 53]	17.6
Total cholesterol (mg/dL)	165 [156, 194]	17.6
Fasting glucose (mg/dL)	85 [82, 93]	5.9
Glucose 120 min (mg/dL/2h)	125 [89, 159]	35.2
Fasting insulin (uU/mL)	18.9 [12.3, 35.3]	41.2
Metabolic syndrome criteria	2 [0.8, 2.3]	23.5
HOMA	3.7 [2.8, 7.3]	47.1
G:I ratio (mg/10 ⁻⁴)	4.1 [2.3, 6.4]	47.1
ISI _{0,120} (mg·l ² /mmol·mU·min)	41.7 [30.2, 57.7]	NA
$\Delta\text{ins}_{30}/\Delta\text{gluc}_{30}/\text{HOMA-IR}$ (1/mmol ²)*	8.7 [5.4, 10.2]	NA
Leptin (ng/mL)	10.3 [3.5, 16.0]	5.8

* 9 pubertal and 8 prepubertal.

Abbreviations: LDL, low-density lipoprotein; HDL, high-density lipoprotein; min, minutes; HOMA, homeostatic model assessment; G:I, glucose to insulin ratio; ISI_{0,120}, insulin sensitivity index; $\Delta\text{G}_{30}/\Delta\text{I}_{30}$, 30-minute change in insulin divided by 0- to 30-minute change in glucose; HOMA-IR, homeostatic model assessment–insulin resistance; NA, not available.

Table 3

Significant Correlations Between Myositis Assessment Measures and Metabolic Parameters.

Myositis Assessment Measure Median [25%, 75%]	Endocrine Measure	Spearman Rank Correlation coefficient, r_s	p value
CMAS 45 [41,49]	HDL	0.54	0.04
Serum Aspartate Aminotransferase (AST), U/L 26 [17, 38]	HDL Leptin	-0.66 -0.60	0.004 0.03
T1 MRI Fatty Infiltration Score 1.0 [0.0, 1.0]	G:I ratio ISI _{0,120} HOMA Fasting insulin	-0.56 -0.70 0.56 0.56	0.02 0.01 0.02 0.02
T1 MRI Muscle Atrophy Score [0.0,2.0]	$\Delta G_{30}/\Delta I_{30}/HOMA-IR$	-0.68	0.01
T1 MRI Combined Atrophy/Fatty Infiltration Score [0.0, 2.3]	Fasting glucose	0.48	0.03

The number of patients ranged from 14 – 17.

Abbreviations: r_s , spearman rank correlation coefficient; CMAS, Childhood Myositis Assessment Scale; MRI, magnetic resonance imaging; G:I, glucose: insulin; HDL high density lipoprotein; ISI_{0,120}, Insulin Sensitivity Index; HOMA, Homeostatic Model Assessment; $\Delta G_{30}/\Delta I_{30}/HOMA-IR$ 0 to 30 minute change in glucose divided by 0 to 30 minute change in insulin divided by Homeostatic Model Assessment-Insulin Resistance.