Advances in Rheumatology

RESEARCH

Open Access

Could ultrasound and muscle elastography be associated with clinical assessment, laboratory and nailfold capillaroscopy in juvenile dermatomyositis patients?

Renata Lopes Francisco de Andrade[1*], José Alexandre Mendonça[2], Daniela Petry Piotto[1], Julio Brandão Guimarães[3] and Maria Teresa Terreri[1]

Abstract

Background Juvenile Dermatomyositis (JDM) is the most common idiopathic inflammatory myopathy in children. Imaging exams are useful for muscle assessment, with ultrasonography (US) being a promising tool in detecting disease activity and tissue damage. There are few studies about muscle elastography.

Objectives Our aim was to associate clinical, laboratory, and nailfold capillaroscopy (NC) assessments with US in JDM patients; and to compare the findings of US and Strain Elastography (SE) from patients and healthy controls.

Methods An analytic cross-sectional study was performed with JDM patients and healthy controls. Patients underwent clinical exam to access muscle strength and completed questionnaires about global assessment of the disease and functional capacity. Patients were submitted to NC and measurement of muscle enzymes. All subjects underwent US assessment, using gray scale, Power Doppler (PD), and SE.

Results Twenty-two JDM patients and fourteen controls, aged between 5 and 21 years, matched for age and sex were assessed. In qualitative and semi-quantitative gray scale, we observed a higher frequency of alterations in patients ($p < 0.001$), while in PD, there was a higher frequency of positivity in patients' deltoids and anterior tibialis ($p < 0.001$). Active disease was associated with an important change in the semi-quantitative gray scale in deltoids ($p = 0.007$), biceps brachii ($p = 0.001$) and quadriceps femoris ($p = 0.005$). The SE demonstrated a high negative predictive value of 87.2.

Conclusion US was able, through gray scale, to differentiate JDM patients from controls, while PD achieved such differentiation only for deltoids and anterior tibialis. The semi-quantitative gray scale showed disease activity in proximal muscles. SE was not able to differentiate patients from controls.

Keywords Dermatomyositis, Juvenile idiopathic myophaties, Ultrassonography, Muscle Elastrography

*Correspondence:
Renata Lopes Francisco de Andrade
drarenatalf@gmail.com
[1]Department of Pediatrics, Section of Rheumatology, Federal University of São Paulo – UNIFESP, Dr Bacelar, St, 173. Vila Clementino, São Paulo 01026-000, Brazil
[2] Department of Rheumatology, Pontifical Catholic University from Campinas - PUC/Campinas, John Boyd Dunlop, s/n, Avenue, Campinas 13034-685, Brazil
[3] Department of Radiology and Image Diagnosis, Federal University of São Paulo - UNIFESP, Napoleão de Barros, St, 800, São Paulo 04024-000, Brazil

Introduction

Juvenile Dermatomyositis (JDM) is the most prevalent form of Idiopathic Inflammatory Myopathies (IIM) in pediatrics, comprising up to 85% of cases [1–5]. While *Bohan & Peter* criteria are commonly used for JDM diagnosis, new ACR (American College of Rheumatology)/EULAR (European League Against Rheumatism) criteria were validated in 2017 [6–8]. However, measuring muscle enzymes may have limitations in evaluating disease activity in clinical practice [9].Electromyography (EMG) and muscle biopsy are important tools for the diagnosis of JDM, although they are not mandatory [8]. Indeed, due to the challenges of EMG and muscle biopsy, additional less invasive tools are necessary for diagnosis and assessing disease activity. Nailfold capillaroscopy (NC) is often altered at diagnosis, reflecting periungueal vasculopathy [2, 4, 10, 11]. Imaging assessments like Magnetic Resonance Imaging (MRI) and Ultrasonography (US) provide more objective muscle assessment, with MRI being capable of distinguishing active from inactive disease [2, 5, 9, 12]. Nevertheless, MRI is expensive, less accessible, and difficult to perform in children [2, 9, 13].US is a cost-effective and accessible tool for assessing myositis, particularly in pediatric populations [2, 9, 12, 14]. It can incorporate elastography, which can detect increased muscle stiffness similar to MRI findings in IIM [15]. However, for active myositis detection in children, elastography may not be as satisfactory, although it correlates with abnormal muscle echogenicity seen in US [16].

The study aimed to link clinical assessment (using validated tools), laboratory tests, NC, and US findings in JDM patients. Additionally, the study compared the US and SE results between JDM patients and healthy controls.

METHODS

This was an analytic cross-sectional study.

Patients

All patients diagnosed according to Bohan & Peter criteria [6, 7], aged between 5 and 21 years old at the assessment, regardless of disease activity and treatment, were eligible. This cross-sectional study included JDM patients in regular follow-up in a tertiary center, and 14 healthy volunteers, matched by age and sex. The exclusion criteria were: patients with other autoimmune diseases, chronic diseases or neoplasias, patients with extensive calcinosis that could difficult the visualization of the muscle at US, pregnant women, and presence of infectious diseases in the 15 days prior to data collection. Volunteers who had any chronic disease, needed continuous medication, had current infection, or who were pregnant, were also excluded.

Main outcome variable

Clinical and nailfold capillaroscopy assessments

All patients were assessed by three different examiners, each of whom was responsible for one area of assessment (clinical, ultrasonographic and capillaroscopic), had expertise in their area of assessment, and was -blinded in relation to the other assessments. The presence of disease activity was assessed through clinical parameters (active skin changes, signs of vasculopathy, muscle weakness, presence of calcinosis), and complementary tests (serum levels of muscle enzymes: lactic dehydrogenase – LDH, aspartate aminotransferase – AST, creatine kinase – CK, and aldolase).

The following questionnaires/scales were applied: Disease Activity Score (DAS), to assess the global disease activity, including cutaneous and muscular involvement [17]; Childhood Myositis Assessment Scale (CMAS), validated for assessing muscle strength in childhood [18]; Manual Muscle Testing (MMT), to assess muscle strength and function [18]; Visual Analogue Scale (VAS), for global assessment of the disease for physicians and for parents and patients [5]; and, Childhood Health Assessment Questionnaire (CHAQ), measurement of functional capacity in daily activities [5]. Patients were assessed for disease inactivity according to PRINTO criteria [19].

Conventional NC was performed with an Olympus stereomicroscope at 10 to 16x magnification, equipped with a graduated ruler (1 to 10 mm), as described in literature [20]. The NC was considered normal, if changes in number and morphology of capillaries were absent, or with scleroderma (SD) pattern, in the presence of capillaries with dilatations, giant capillaries, and avascular areas in more than half of the assessed fingers. In order to ensure the NC accuracy, patients were instructed not to undergo procedures that could traumatize their cuticles in the month prior to the exams, as well as not to use nail polish or other nail cosmetics on the day of the examination. The NC was performed at an interval of up to three months prior to the time of the other assessments, by the same examiner.

Ultrasonography exams

The US device used was the "MyLab Alpha", eHD Crystaline version −8.00.06, ESAOTE brand, with a high frequency linear transducer, from 6 to 19 MHz, for gray scale evaluation. The PD assessment in each muscle group was performed with a frequency of 8.3 MHz, ranging from 8.0 to 12.5 MHz, frequency repetition pulse was 730 MHz, ranging from 0.5 to 1.0 kHz, and filter ranging from 2 to 3. The following software were used: B-Mode, PD, Elaxto and Elaxto Advanced. All subjects were assessed following the same sequence, in muscle relaxation, with the probe positioned longitudinally and

transversely in relation to the assessed muscle, and with an abundant amount of gel in order to minimize anisotropies. They were initially assessed in the sitting position, for bilateral examination of the deltoids, biceps brachii, and forearm flexor muscles, always in the proximal third of the limb. Afterwards, the individuals were assessed in the supine position, for examination of the quadriceps femoris and anterior tibialis muscles, also in the proximal third of the limb. The exam was systematized by:

● Gray Scale (B-Mode): The examined area was classified as presenting preserved architecture (when its "feather pattern" aspect was preserved) or altered (when it presented any change to the normal pattern), as shown at the Fig. 1 [21]. A new classification was performed (semi-quantitative assessment), on a scale from 1 to 4, that represents the number of echoes displayed in the gray scale image, using the echogenicity of the cortical bone as a visual reference [21]. The musculature was graded as: Grade 1, when it presented an architectural pattern "in feather", that is, without invasion of the muscle by fat and/or connective tissue (normal for purposes of statistical analysis); Grade 2, when there was any invasion of the musculature by fat and/or connective tissue (moderate alteration); Grade 3, when the muscle presented more evident alterations, with some rupture of muscle fascicles (important alteration); and Grade 4, in the presence of severe alteration, with replacement of 50% or more of muscle by fat and/or connective tissue (important alteration).

● PD assessment: At the time of the examination, the PD technique was applied, and the area was assessed using a 0 to 4 scale, with higher PD scores indicating an increased degree of vascularization [22]. PD was classified as: Grade 0 if no vessels were seen in the captured image; Grade 1 if at least one intramuscular vessel was captured; Grade 2 in the presence of 5 or more vessels in a two-dimensional structure or a single large intramuscular vessel seen in cross-section > 5 mm or a segment length > 10 mm; Grade 3 when there was grade 2 vascularization plus small clusters of flow areas (≥3); and Grade 4 in the presence of diffuse flow through the muscle. PD ≥ 2 was considered positive, because in children, grade 1 is often represented by feeding vessels. Due to practical reasons, we classified the grades 0/1 as a single group. Feeding vessels were defined as those vessels found in normal anatomical distribution and in the absence of regional inflammatory signs [23]. All PD grades found in this study are shown at the Fig. 2.

Elastography assessment

The SE technique was used. This technology uses a color scale to assess the relative hardness of the tissue of each structure, through the muscle elasticity assessment by tissue deformation [15, 16, 24–26]. Images of all muscles were obtained and only those that reached the green spiral (which reflects the proper application of the technique), were considered. Two measurements were performed at different times for each muscle group. Two areas were selected that encompassed the largest transition area between soft and rigid musculature according to the examiner's assessment, and in these areas the predefined elliptical shape was applied. The most suitable areas were those that generated a histogram closer to zero, which indicates good homogeneity of the compression applied to the tissue [24–26].

Statistical analysis

Data was stored in an excel spreadsheet and analyzed using the R program, version 4.0.5. In descriptive analysis of the categorical variables of interest, absolute and relative frequencies were used, while in the numerical variablesmean and median were used according to parametrical or non-parametrical distribution. For the elastography values, the means and standard deviation were considered. To associate the results obtained by gray scale and PD in the 5 muscles between the right and left sides, the McNemar test was used, while for the association of the results obtained by SE between the right and

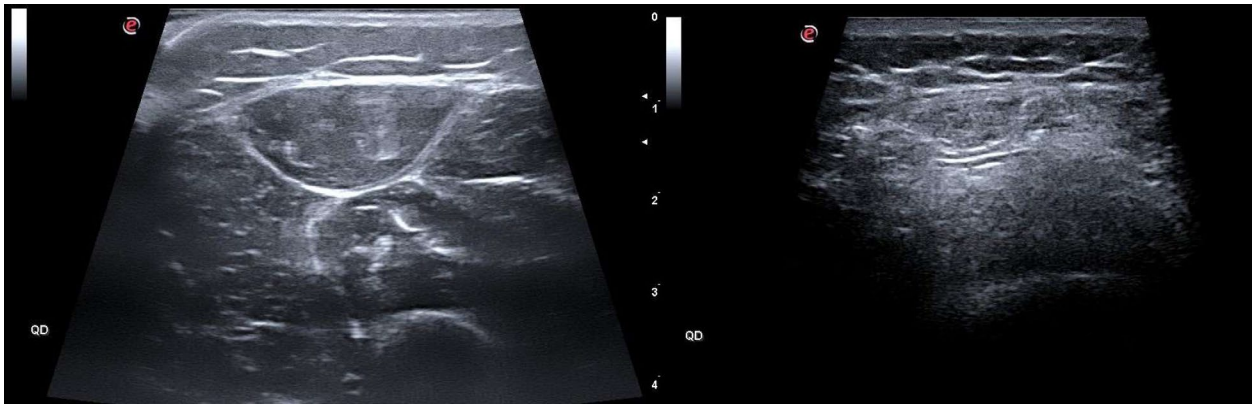

Fig. 1 B-mode. On the left - left quadriceps femoris from a healthy control. On the right - left quadriceps femoris from a JDM patient, with altered muscle

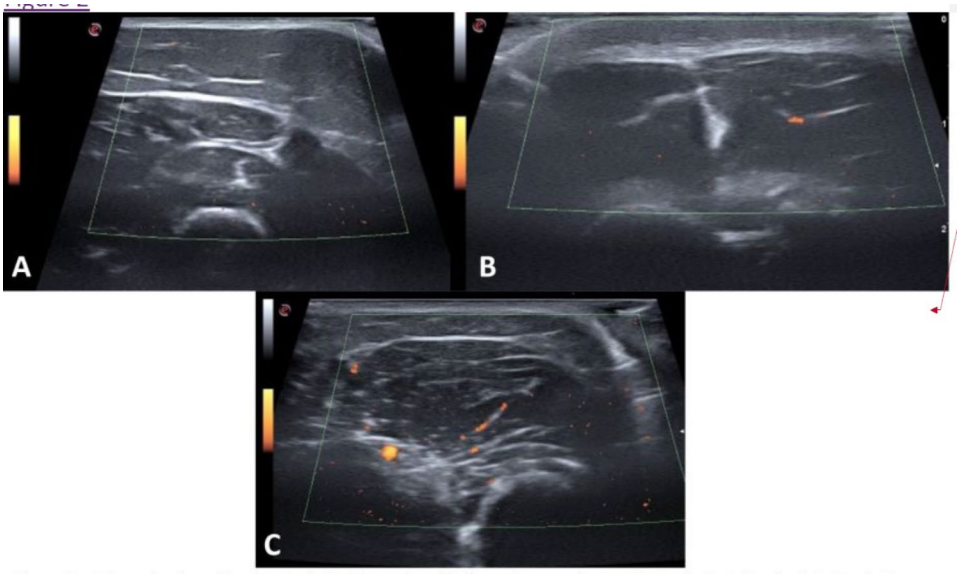

Fig. 2 PD grades found in the study, in biceps brachii, from three patients. **A**: Grade 0. **B**: Grade 1. **C**: Grade 2

left sides, the Wilcoxon test was used. Fisher's exact test was used to associate sex, the qualitative gray scale, semi-quantitative gray scale and PD variables between the groups, while the Mann-Whitney test was used to associate the elastography variables between the groups. The same tests were used to associate the US parameters with the other variables of interest (presence of disease activity, increase in muscle enzymes, NC, DAS, CMAS, MMT, physician's VAS, and parents' and patients' VAS). In addition, when both variables were numerical, Pearson's correlation was used.

. To compare the general elastography between the groups, the GEE (Generalized Equations Estimating) model was used, which is a way to account for the existing correlation between repeated measures. This model was also used in comparative analysis between the gray scale, semi-quantitative gray scale and PD assessments and the clinical and laboratory variables, regarding the presence or absence of disease activity. To propose a cut-off point for elastography according to the results obtained by gray scale, that is, to find the value that elastography should assume to maximize the quality of fit of the model, a Marginal Logistic Regression was adjusted. Values of $p<0.05$ were considered significant.

RESULTS

A convenience sample obtained from a total of 92 JDM patients in regular follow-up at our clinic, resulted in 54 eligible patients. From those, 12 lost follow-up, 17 refused to participate and 3 were excluded due to overlapping autoimmune disorders (neuromyelitis optica, juvenile idiopathic arthritis, and systemic lupus erythematosus).

We included 22 JDM patients (16 females, 6 males) and 14 healthy subjects (6 females, 8 males), with no statistical gender difference.

Clinical features.

Themean age at evaluation was 12.6 years for patients and 11.6 years for controls ($p=0.624$).At diagnosis, all patients had pathognomonic skin changes and increased muscle enzymes, while 21 had symmetrical proximal muscle weakness (95.5%). Six patients were in disease activity and had CMAS<48, with a mean of 47.05, five patients had MMT<78, with a mean of 77.45 ± 6.06. The median DAS was 2 (1–4.25), the median parents' and patients' VAS was 0.1 (0–0.53) and the median physician's VAS was 0 (0–0.33). Disease inactivity was present in 16 (72.7%) patients (Table 1).

Subsidiary exams.

Only 3 patients (13.6%) underwent EMG, which was altered. Two patients (9.1%) underwent muscle biopsy, with a normal result in one case, and findings of myopathy in one case. Six patients had an increase in CK, with a mean of 166.43 (units/L). In the NC assessment, nine patients presented a SD pattern (40.9% (Table 1).

Treatment.

all patients used corticosteroids and disease-modifying antirheumatic drugs (DMARDs) at some point during the disease. Pulse therapy with methylprednisolone followed by oral corticosteroid therapy was used in 20 patients (90.1%), and only two patients (9.1%) used oral prednisone only. At the time of the evaluations, four patients (18.2%) were on oral prednisone and 14 patients on DMARDs (8 on methotrexate).

Ultrasound findings.

A total of 360 Gy scale images, 360 PD images and 360 SE images were obtained among patients and controls.

Table 1 – Patients and control´s demographic data and patient´s clinical data

	Patients (N = 22)	Controls (N = 14)	p value
Female sex	16	9	0.59
Age at evaluation (years, mean)	12.6 ± 4.36	11.6 ± 5.71	0.624
Age at diagnosis (years, mean)	8.05 ± 4.52		
Diagnosis delay (months, median)	5 (1.88–9.0)		
Cumulative dose of corticosteroids (mg/kg, mean)	396.71 ± 256.67		
High CK	6 (27.3%)		
CK (units/L, mean)	166.43 ± 90		
Altered CMAS	6 (27.3%)		
CMAS (mean)	47.05 ± 7.07		
Altered MMT	5 (22.7%)		
MMT (mean)	77.45 ± 6.06		
DAS (median)	2 (1–4.25)		
Patients and parent´s VAS (median)	0.1 (0–0.53)		
Physician´s VAS (median)	0 (0–0.33)		
Absence of disease activity	16 (72.7%)		

Table 2 – Ultrasound evaluation at gray scale, qualitative and semiquantitative of patients and controls

Qualitative Gray Scale[1]	Patients (N = 22) N = 220 muscles	Controls (N = 14) N = 140 Muscles	p value
D	10 (22.7%)	0 (0%)	**< 0.001**
BB	9 (20.5%)	0 (0%)	**< 0.001**
FF	8 (18.2%)	0 (0%)	**< 0.001**
QF	14 (31.8%)	0 (0%)	**< 0.001**
AT	12 (27.3%)	0 (0%)	**< 0.001**
Semiquantitative Gray Scale[2]			
D moderate alteration important alteration	17 (38.6%) 24 (54.5%)	0 (0%) 0 (0%)	**< 0.001**
BB moderate alteration important alteration	16 (36.4%) 24 (54.5%)	2 (7.1%) 0 (0%)	**< 0.001**
FF moderate alteration important alteration	20 (45.6%) 19 (43.2%)	0 (0%) 0 (0%)	**< 0.001**
QF moderate alteration important alteration	4 (9.1%) 37 (84.1%)	5 (17.9%) 0 (0%)	**< 0.001**
AT moderate alteration important alteration	17 (38.6%) 25 (56.8%)	2 (7.1%) 0 (0%)	**< 0.001**

1Ultrasonography assessment altered when compared to normal muscle pattern

2Ultrasonography assessment with moderate alteration (grade 2) or important alteration (grades 3 and 4)

D: Deltoid; BB: Biceps brachii; FF: Forearm flexor; QF: Quadriceps femoris; AT: Anterior Tibialis

Among the SE images, 720 area measurements and 360 histogram measurements were generated.

Initially, the right musculature was compared to the left musculature, in a separate analysis of all examined muscles, in relation to the qualitative gray scale, PD and SE. There was no statistical difference in any of the three parameters assessed, in any muscle group, between the right and left sides. Therefore, the comparisons were performed with both sides of each muscle together.

Table 3 – Ultrasound evaluation by PD of patients and controls

PD assessment	Patients (N = 22) N = 220 muscles	Controls (N = 14) N = 140 muscles	p value
D	2 (4.5%)	0	**< 0.001**
BB	4 (9.0%)	1 (3.5%)	0.386
FF	0	0	1
QF	0	0	1
AT	4 (9.0%)	0	**< 0.001**

PD: Power-Doppler

D: Deltoid; BB: Biceps brachii; FF: Forearm flexors; QF: Quadriceps femoris; AT: Anterior Tibialis

In gray scale US assessment, the patients showed alterations in muscle pattern in: 10 deltoids muscles (5 patients), 9 biceps brachii (6 patients), 8 forearm flexors (4 patients), 14 quadriceps femoris (7 patients) and in 12 anterior tibialis (6 patients). No loss of muscle pattern was found in any control.

In semi-quantitative gray scale, the patients presented alterations: moderate in 17 and important in 24 of the deltoids muscles (22 patients), moderate in 16 and important in 24 of the biceps brachii (21 patients), moderate in 20 and important in 19 of the forearm flexors (21 patients), moderate in 4 and important in 37 of the quadriceps femoris (21 patients), and moderate in 17 and important in 25 of the anterior tibialis (21 patients). Controls showed only moderate changes in 2 biceps brachii muscles (2 subjects), 5 quadriceps femoris (3 subjects) and 2 anterior tibialis muscles (2 subjects). Table 2 shows qualitative and semi-quantitative gray scale US evaluations of patients and controls. Changes in qualitative and semi-quantitative gray scale were more frequent in patients than in controls, in all muscle groups ($p < 0.001$).

No patient or control presented PD grades 3 or 4 in any muscle group evaluated. The patients presented PD positivity more frequently than controls only in the deltoids and anterior tibialis ($p < 0.001$). Table 3 shows PD evaluation of patients and controls.

The elastography measurements were analyzed using the average obtained from the two measurements taken at the time of the exam. Considering the gray scale as the most appropriate US parameter for muscle assessment of patients with JDM, a cut-off point for SE was proposed, that is, a point from which there is greater reliability in the result considered to be altered. This point was 54.36, with an area under the curve of 0.514, with sensitivity of 45.3%, specificity of 64.4%, positive predictive value (PPV) of 18%, negative predictive value of 87.2% and accuracy of 61.6%. Using the SE tool, a higher muscle

stiffness was found in controls compared to patients, but only in the deltoids (mean 51.35±7.48 patients x 55.51±9.03 controls) (p=0.039). The comparative assessment between patients and controls of other muscle groups did not show statistical significance.

Associations between ultrasound findings and clinical features, nailfold capillaroscopy and corticosteroids use.

Associations between patients' disease activity and US changes were studied for qualitative gray scale, semiquantitative gray scale, PD, and SE. There was no association between disease activity and greater frequency of gray scale changes and greater muscle stiffness on SE. For the semi-quantitative gray scale, an association was observed between disease activity and important alterations in the deltoids (p=0.007), biceps brachii (p<0.001) and quadriceps femoris (p=0.005) (Table 4). For the assessment of PD, none important association was observed between disease activity and PD positivity.

SD pattern at NC was associated with important changes in semi-quantitative gray scale only in forearm flexors (p=0.033). Associations were also found between DAS score and qualitative gray scale changes in all muscle groups. In SE assessment, an association between lower elastography values in the anterior tibialis muscle and higher DAS values was found (p=0.009).

Considering the muscle assessment through the MMT and CMAS questionnaires, there was no association between changes in the qualitative gray scale and either of the questionnaires. Table 5 shows the associations found between gray scale US parameters and clinical-laboratory assessments, and Table 6 shows associations between PD and clinical-laboratory assessments.

Using the semiquantitative gray scale, we did not observe any association between changes, whether moderate or important, in any muscle group, with the mean cumulative dose of corticosteroids.

In patients with active disease (6 patients), there was an association between changes in qualitative gray scale in all muscle groups and SD pattern at NC, higher DAS scores, and higher parents' and patient´s VAS scores.

Patients with disease follow up of longer than 5 years presented greater mean values of SE in anterior tibialis muscles than the patients with up to 5 years of disease follow up (52.25%±12.47 vs. 45.29%±8.8, p=0.006). The other muscles were assessed but did not show statistical significance. Regarding the other US parameters (gray scale, semi-quantitative gray scale, and PD), there was no difference in frequency of changes in the exams related to long-term disease.

DISCUSSION

JDM is a chronic disease, where differentiation between activity and remission can be difficult, if evaluated only through clinical and laboratory manifestations. Other tests, such as invasive tests, are difficult to perform in children. For this reason, more accessible exams such as muscle US (cheaper) or MRI (more expensive but considered the gold standard), are potential and important tools, respectively, in determining disease activity. The use of more widely disseminated software, such as US B-Mode and PD, can be useful, both in the assessment of disease activity and in differentiating individuals with or without inflammatory muscle involvement.

This study observed that US was able to differentiate patients from controls, through qualitative and semi-quantitative gray scale, and only in the deltoid and anterior tibialis muscles through PD. We observed that the semi-quantitative gray scale US findings of the proximal musculature were associated with disease activity. Evaluation by SE was not able to differentiate patients from controls, nor to detect disease activity in patients.

Regarding the clinical-laboratory parameters, it was observed that the increase in muscle enzymes and VAS, did not present a strong association with US parameters. However, higher DAS scores were associated with loss of normal muscle architecture in all muscles on gray scale, with significant changes in the biceps brachii and forearm flexor muscles on semi-quantitative gray scale, and with greater PD positivity in the anterior tibialis. Regarding the strength and muscle function assessment questionnaires, it was observed that lower CMAS scores were associated with an important change in the semi quantitative gray scale of all muscles, with the exception of the anterior tibialis muscles, while for the MMT, such

Table 4 – Ultrasound evaluation by semiquantitative gray scale of patients in active disease and inactive disease

Semiquantitative Gray Scale[1] (IMPORTANT ALTERATION)	Active disease N=6 patients (60 muscles)	Inactive disease N=16 patients (160 muscles)	p value
D	9 (81.8%)	15 (46.9%)	0.007
BB	10 (90.9%)	15 (46.9%)	**<0.001**
FF	7 (63.6%)	12 (37.5%)	0.198
QF	11 (100%)	25 (78.1%)	**0.005**
AT	6 (54.5%)	17 (53.1%)	0.475

1Ultrasonography assessment with moderate alteration (grade 2) or important alteration (grades 3 and 4)

D: Deltoid; BB: Biceps brachii; FF: Forearm flexor; QF: Quadriceps femoris; AT: Anterior Tibialis

Table 5 – Association between clinical-laboratory variables and ultrasound findings (qualitative and semiquantitative gray scale)

	D	BB	FF	QF	AT
Qualitative Gray Scale (altered)					
Disease activity	4 (p = 0.241)	3 (p = 0.551)	2 (p = 0.967)	6 (p = 0.079)	4 (p = 0.471)
Muscle enzymes elevation	2 (p = 0.164)	2 (p = 0.244)	2 (p = 0.360)	2 **(p = 0.028)**	2 (p = 0.070)
Altered NC	6 (p = 0.334)	4 (p = 0.889)	4 (p = 0.827)	8 (p = 0.334)	6 (p = 0.776)
DAS	10 **(p = 0.002)**	9 **(p = 0.005)**	8 **(p = 0.007)**	14 **(p = 0.002)**	12 **(p = 0.013)**
MMT	10 (p = 0.533)	9 (p = 0.433)	8 (p = 0.340)	14 (p = 0.964)	12 (p = 0.747)
CMAS	10 (p = 0.170)	9 (p = 0.312)	8 (p = 0.315)	14 (p = 0.334)	12 (p = 0.360)
Physician´s VAS	10 (p = 0.110)	9 (p = 0.266)	8 (p = 0.340)	14 **(p = 0.05)**	12 (p = 0.307)
Patients and parent´s VAS	10 (p = 0.173)	9 (p = 0.327)	8 (p = 0.389)	14 (p = 0.194)	12 (p = 0.493)
Semi-quantitative Gray Scale (moderate alteration/ important alteration)					
Disease activity	2/9 **(p = 0.007)**	1/10 **(p < 0.001)**	3/7 (p = 0.198)	0/11 **(p = 0.005)**	5/6 (p = 0.475)
Muscle enzymes elevation	3/14 **(p < 0.001)**	6/11 (p = 0.157)	9/8 (p = 0.208)	3/13 (p = 0.563)	5/10 (p = 0.820)
Altered NC	7/13 (p = 0.094)	6/13 (p = 0.289)	5/13 **(p = 0.033)**	3/15 (p = 0.206)	9/11 (p = 0.296)
DAS	16/24 (p = 0.063)	14/25 **(p = 0.025)**	19/19 **(p = 0.037)**	4/36 (p = 0.138)	16/23 (p = 0.089)
MMT	16/24 **(p = 0.003)**	14/25 (p = 0.063)	19/19 **(p < 0.001)**	4/36 (p = 0.123)	16/23 (p = 0.813)
CMAS	16/24 **(p = 0.008)**	14/25 **(p = 0.006)**	19/19 **(p = 0.006)**	4/36 **(p = 0.015)**	16/23 (p = 0.929)
Physician´s VAS	16/24 (p = 0.092)	14/25 **(p = 0.015)**	19/19 (p = 0.088)	4/36 (p = 0,377)	16/23 (p = 0,081)
Patients and parent´s VAS	16/24 (p = 0.924)	14/25 (p = 0.140)	19/19 **(p = 0.017)**	4/36 (p = 0.165)	16/23 (p = 0.460)

D: Deltoid; BB: Biceps brachii; FF: Forearm flexors; QF: Quadriceps femoris; AT: Anterior Tibialis

NC: Nailfold capilaroscopy; DAS: Disease Activity Score; MMT: Manual Muscle Testing; CMAS: Childhood Myositis Assessment Scale; VAS: Visual analogic scale

Table 6 Association between clinical-laboratory variables and PD findings

	D	BB	FF	QF	AT
Disease activity	0 **(p < 0.001)**	1 (p = 0.978)	0 (p = 1)	0 (p = 1)	3 **(p < 0.001)**
Muscle enzymes elevation	0 **(p < 0.001)**	1 (p = 0.540)	0 (p = 1)	0 (p = 1)	3 **(p < 0.001)**
Altered NC	1 (p = 0.919)	1 (p = 0.382)	0 (p = 1)	0 (p = 1)	2 (p = 0.480)
DAS	2 **(p = 0.049)**	4 (p = 0.303)	0 (p = 1)	0 (p = 1)	3 **(p = 0.026)**
MMT	2 (-)	4 (p = 0.501)	0 (p = 1)	0 (p = 1)	3 **(p = 0.013)**
CMAS	2 (p = 0.422)	4 (p = 0.539)	0 (p = 1)	0 (p = 1)	3 **(p = 0.004)**
Physician´s VAS	2 (p = 0.131)	4 (p = 0.693)	0 (p = 1)	0 (p = 1)	3 **(p = 0.033)**
Patients and parent´s VAS	2 **(p = 0.045)**	4 (p = 0.699)	0 (p = 1)	0 (p = 1)	3 (p = 0.233)

D: Deltoid; BB: Biceps brachii; FF: Forearm flexors; QF: Quadriceps femoris; AT: Anterior Tibialis

NC: Nailfold capilaroscopy; DAS: *Disease Activity Score*; MMT: *Manual Muscle Testing*; CMAS: *Childhood Myositis Assessment Scale*; VAS: *Visual analogic scale*

association occurred only in the deltoid and forearm flexor muscles.

The most recent studies suggest the standardization of videocapillaroscopy due to its ability to provide more accurate results, as it does not require extensive training by the examiner [27]. However, the available device for this study was the conventional stereomicroscope, but its limitation can be considered overcome as the examiner is highly trained to perform this examination. NC can be considered a good marker for skin activity, but it is not always a good marker for muscle activity [11, 12]. In the present study, the SD pattern at NC was not associated with changes in US parameters.

In JDM, US proved to be useful in helping to define the degree of disease activity, and also in patients' follow-up, demonstrating severity and muscle damage associated with myopathy. Although there are currently no validated criteria for the use of gray scale and PD, recently, a study proposed validation for the use of US only in the rectus femoris muscles 28, 29]. Meng et al. assessed 37 patients with IIM, 17 with DM, and 6 controls, and observed an increase in the echogenicity of patients when compared to controls, suggesting muscle atrophy [22]. Another more recent validation study of US for JDM showed the same results [29]. This present study presented similar

results in the qualitative and semi-quantitative gray scale for all muscle groups assessed.

Regarding the evaluation of PD, the results are conflicting. In the study by Meng et al., patients presented higher PD scores, while in the one by Mamyrova et al., no similar results were found [22, 29]. Our study observed increased vascularity in PD only for the deltoid and anterior tibialis muscles. While in the study by Meng et al., it was concluded that the presence of pathological PD was more associated with short-term disease [22], it was not possible to confirm this fact in our study, since no association was found between PD positivity and presence of disease activity. Reimers et al. assessed muscle biopsies from adults with IIM and showed that in acute phase, US tends to show a reduction in echogenicity due to muscle edema, while in chronic phase an increase in echogenicity due to atrophy tends to occur [30]. However, Bhansing et al. [31] assessed 17 patients with JDM, 7 of whom were considered to have disease activity, and concluded that in acute phase there is an increase in muscle echogenicity and an even more significant increase when compared to patients in clinical remission. Habers et al. observed a slight increase in echogenicity at diagnosis, with a more significant increase during the course of the disease, particularly in a patient who developed a chronic course [9]. These findings were attributed to the presence of edema in the initial phase of the disease and to fatty infiltration in the follow up [9]. Although our study showed an increase in echogenicity [21] (through the semi-quantitative gray scale) in deltoids, biceps brachii and quadriceps femoris muscles of patients considered to have disease activity, we cannot infer at which stage of the disease they were. The qualitative gray scale, where the loss of normal muscle architecture was assessed, did not show significant differences between active and inactive disease. US proved to be even more useful in the examination of proximal muscles, where the prevalence of involvement is known.

The use of elastography in musculoskeletal assessment is still limited and the results are controversial. In this study, SE showed conflicting results when compared with the other clinical-laboratory parameters, and it was not possible to infer associations between increased muscle stiffness in the SE and any other parameter. The SE showed low sensitivity, specificity and PPV, so it was not possible to identify a cut-off from which we would consider the stiffness found to be pathological. However, its high negative predictive value shows that this test was able, in 87.2% of cases, to demonstrate the absence of inflammatory muscle involvement.

In a study that assessed patients with myopathies, one with JDM, another seven with other myopathies, and 20 healthy individuals, revealed that the patients with myopathies showed a reduction in muscle elasticity through a score that comparatively assessed the musculature with the fat around it, in addition to a significant increase in echogenicity only in the biceps brachii muscle [32]. Yet, another study evaluated 18 lesions seen in MRI in 17 patients with different myopathies and showed a reduction in muscle elasticity through a score calculated between the affected musculature and the adjacent musculature, which was more evident in patients with inflammatory myopathies than in other diagnoses (overlapping patients with systemic lupus erythematosus, rheumatoid arthritis and mixed connective tissue disease) [33]. Our study did not find similar results, but a different methodology was used by us.

While US is a valuable tool for muscle assessment, it may not always differentiate between inflammatory myophaties and muscular dystrophies. Muscular dystrophies typically exhibit a uniform increase in muscle echogenicity with significant attenuation of the US signal in deeper layers. In contrast, inflammatory myopathies also show a homogeneous increase in echogenicity without the attenuation seen in dystrophies. However, in advanced stages, inflammatory myopathies can show tissue destruction with fibrosis replacement, leading to severe muscle atrophy and signal attenuation, potentially causing confusion with muscular dystrophies [34].

The only study that assessed only JDM patients, included 18 children with 10 lesions considered active on MRI and used a pre-established score in biceps brachii and quadriceps femoris muscles of healthy children [16, 35]. This study concluded that SE did not correlate with disease activity, clinically or by MRI, and low sensitivity and specificity for detecting active myositis by SE was observed [35]. Our study found similar results for detection of active myositis (clinical and laboratory), however comparisons with MRI have not been made. The use of elastography is consolidated for more restricted lesions within an organ, such as nodular lesions of the breast and liver [26]. As the muscle can be heterogeneously and diffusely inflamed, we consider that this may have been an important factor that limited the detection of alteration using the SE technique. Other non-inflammatory, mechanical and exertion changes that may alter muscle fiber consistency may also have limited SE assessment [36, 37].

The study has some limitations, such as the small power of effect of the sample, due to the small number of patients in activity (27.3%). When analyzing active and inactive patients together, this may have resulted in underestimated cutoff values for quantitative and semi-quantitative changes. Another point was the inclusion of two patients older than 18 years old (although with JDM diagnosed before this age). Other limitations are the lack of standardization for assessment by SE, whose method of measurement varies greatly in the literature,

and, additionally, the absence of intra and inter-observer assessments. This was compromised by the difficulty of having another qualified professional in SE to perform dynamic and static measurements of the method, thus preventing the evaluation of the reproducibility index of this tool. An additional limitation is the lack of comparison with the gold standard imaging method, which is MRI. Although this is a limitation, it was not the aim of the study to compare US images with MRI, especially since previous studies have already demonstrated the US effectiveness in detecting muscular abnormalities [29, 38]. This study has strengths such as the quality of the methodology, citing the fact that all the examiners were blind to the other assessments, the execution of the assessments in very short timeframes or on the same day, with the assessment of several muscle groups, the assessment by professionals with expertise in their respective areas, and the use of a control group.

In conclusion, US was able, through qualitative and semi-quantitative gray scale assessment, to differentiate patients with JDM from healthy controls, while PD was able to perform such differentiation only for deltoids and anterior tibialis muscles. However, only a few muscle groups showed an association between the US findings, gray scale, PD and SE, with disease activity markers. SE was not able to differentiate patients from controls, nor to detect disease activity in patients.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s42358-023-00330-2.

Supplementary Material 1

Supplementary Material 2

Acknowledgements
Not applicable.
Authors' information (optional): Not applicable.

Authors' contributions
All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Renata Lopes Francisco de Andrade, Daniela Petry Piotto, José Alexandre Mendonça and Maria Teresa Terreri. The first draft of the manuscript was written by Renata Lopes Francisco de Andrade and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Funding
No funds to declare.

Data Availability
All data generated or analysed during this study are included in this published article.

Declarations

Ethics approval and consent to participate
This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of Federal University of São Paulo by the number 3.689.062.

Consent for publication
Informed consent was obtained from all individual participants included or their legal guardians (when applicable) in the study. Additional informed consent was obtained from all individual participants for whom identifying information is included in this article.

Competing interests
The authors declare that they have no competing interests.

Received: 30 May 2023 / Accepted: 28 September 2023
Published online: 06 October 2023

References

1. Bottai M, Tjärnlund A, Santoni G, Werth V, Pilkington C, de Visser M, et al. EULAR/ACR classification criteria for adult and juvenile idiopathic inflammatory myopathies and their major subgroups: a methodology report. RMD Open. 2017;12:1955–64.
2. Enders FB, Bader-Meunier B, Baildam E, Constantin T, Dolezalova P, Feldman B, et al. Consensus-based recommendations for the management of juvenile dermatomyositis. Ann Rheum Dis. 2017;76:329–40.
3. Papadopoulou C, Wedderburn L. Treatment of Juvenile Dermatomyositis: an update. Paediatr Drugs. 2017;19:423–34.
4. Mccann L, Pain C. A practical Approach to Juvenile Dermatomyositis and Juvenile Scleroderma. Indian J Pediatr. 2016;83:163–71.
5. Ruperto N, Ravelli A, Pistorio A, Ferriani V, Calvo I, Ganser G, et al. The Provisional Paediatric Rheumatology International trials Organisation/ American College of Rheumatology/European League against Rheumatism Disease Activity Core Set for the evaluation of response to Therapy in Juvenile Dermatomyositis: a prospective validation study. Arthritis Rheum. 2008;59:4–13.
6. Bohan A, Peter J. Polymyositis and dermatomyositis (first of two parts). N Engl J Med. 1975;292:344–7.
7. Bohan A, Peter J. Polymyositis and dermatomyositis (second of two parts). N Engl J Med. 1945;292:403–7.
8. Lundberg I, Tjärnlund A, Bottai M, Werth V, Pilkington C, de Visser M, et al. EULAR/ACR classification Criteria for Adult and Juvenile Idiopathic Inflammatory Myopathies and their major subgroups. Ann Rheum Dis. 2017;76:1955–64.
9. Habers GE, Van Brussel M, Bhansing KJ, Hoppenreijs EP, Janssen AJ, Van Royen-Kerkhof A. Quantitative muscle ultrasonography in the follow-up of juvenile dermatomyositis. Muscle Nerve. 2015;52:540–6.
10. Piotto D, Len C, Hilario M, Terreri M. Capilaroscopia periungueal em crianças e adolescentes com doenças reumáticas. (Nailfold capillaroscopy among children and adolescents with rheumatic diseases). Rev Bras Reumatol. 2012;52:727–32.
11. Barth Z, Witczak BN, Flatø B, Koller A, Sjaastad I, Sanner H. Assessment of Microvascular Abnormalities by Nailfold Capillaroscopy in Juvenile Dermatomyositis after Medium - to Long-Term follow- up. Arthritis Care Res (Hoboken). 2018;70:768–76.
12. Walker U. Imaging tools for the clinical assessment of idiopathic inflammatory myositis. Curr Opin Rheumatol. 2008;20:656–61.
13. Castro TC, Lederman H, Terreri MT, Caldana WI, Zatoneli E, Hilario MO. Whole-body magnetic resonance imaging in the assessment of muscular involvement in juvenile dermatomyositis/ polymyositis patients. Scand J Rheumatol. 2014;43:329–33.
14. Pillen S, Verrips A, van Alfen N, Arts IM, Sie LT, Zwarts MJ. Quantitative skeletal muscle ultrasound: diagnostic value in childhood neuromuscular disease. Neuromuscul Disord. 2007;17:509–16.
15. Ekşioğlu A, Çağlar A, Şahap S, Karacan C, Tuygun N. Value of strain-wave sonoelastography as an imaging modality in assessment of benign acute myositis in children. Turk J Med Sci. 2021;51:2951–8.
16. Berko N, Hay A, Sterba Y, Wahezi D, Levin T. Efficacy of ultrasound elastography in detecting active myositis in children: can it replace MRI? Pediatr Radiol. 2015;45:1522–8.
17. Bode R, Klein-Gitelman M, Miller M, Lechman T, Pachman L. Disease activity score for children with juvenile dermatomyositis: reliability and validity evidence. Arthritis Rheum. 2003;49:7–15.

18. Rider L, Werth V, Huber A, Alexanderson H, Rao A, Ruperto N, et al. Measures of adult and juvenile Dermatomyositis, Polymyositis, and inclusion body myositis. Arthritis Care Res (Hoboken). 2011;63:118–57.
19. Lazarevic D, Pistorio A, Palmisani E, Miettunen P, Ravelli A, Pilkington C, et al. The PRINTO criteria for clinically inactive disease in Juvenile Dermatomyositis. Ann Rheum Dis. 2013;72:686–93.
20. Andrade LE, Gabriel Júnior A, Assad RL, Ferrari AJ, Atra E. Panoramic nailfold capillaroscopy: a new reading method and normal range. Semin Arthritis Rheum. 1990;20:21–31.
21. Heckmatt JZ, Leeman S, Dubowitz V. Ultrasound imaging in the diagnosis of muscle disease. J Pediatr. 1982;101:656–60.
22. Meng C, Adler R, Peterson M, Kagen L. Combined use of Power Doppler and gray-scale sonography: a new technique for the assessment of inflammatory myopathy. J Rheumatol. 2001;28:1271–82.
23. Baksa G, Czeibert K, Sharp V, Handschuh S, Gyebnar J, Barany L, et al. Vascular supply of the metacarpophalangeal joint. Front Med. 2022;9:1015895.
24. Drakonaki E, Allen G, Wilson D. Ultrasound elastography for musculoskeletal applications. Br J Radiol. 2012;85:1435–45.
25. Conticini E, Falsetti P, Al Khayyat S, Baldi C, Bellisai F, Bardelli M, et al. A novel grey scale and power doppler ultrasonographic score for idiopathic inflammatory myopathies: Siena Myositis Ultrasound Grading Scale. Rheumatology (Oxford). 2021;61:185–94.
26. Dietrich CF, Barr RG, Farrokh A, Dighe M, Hocke M, Jenssenet C, et al. Strain Elastography - How to do it? Ultrasound Int Open. 2017;3(4):137–49.
27. Smith V, Vanhaecke A, Herrick A, Distler O, Guerra M, Denton C, et al. Fast track algorithm: how to differentiate a scleroderma pattern from a non-scleroderma pattern. Autoimmun rev. 2019;18:102394.
28. Paramalingam S, Needham M, Raymond W, Mastaglia F, Lightowler D, Morin N, et al. Muscle shear wave elastography, conventional B mode and power doppler ultrasonography in healthy adults and patients with autoimmune inflammatory myopathies: a pilot cross-sectional study. BMC Musculoskelet Disord. 2021;22:537.
29. Mamyrova G, McBride E, Yao L, Shrader J, Jain M, Yao J, et al. Preliminary validation of muscle ultrasound in juvenile dermatomyositis (JDM). Rheumatology (Oxford). 2022;61:I48–SI55.
30. Reimers CD, Fleckenstein JL, Witt TN, Müller-Felber W, Pongratz DE. Muscular ultrasound in idiopathic inflammatory myopathies of adults. J Neurol Sci. 1993;116:82–92.
31. Bhansing KJ, Hoppenreijs EP, Janssen AJ, van Royen-Kerkhof A, Nijhuis-Van der Sanden MW, van Riel PL, et al. Quantitative muscle ultrasound: a potential tool for assessment of disease activity in juvenile dermatomyositis. Scand J Rheumatol. 2014;43:339–41.
32. Teng P, Lo Y. A comparison study of Conventional Ultrasound and Ultrasound strain Elastography in the evaluation of Myopathy. Ultrasound Q. 2020;36:32–7.
33. Song Y, Lee S, Yoo DH, Jang K-S, Bae J. Strain sonoelastography of inflammatory myopathies: comparison with clinical examination, magnetic resonance imaging and pathologic findings. Br J Radiol. 2016;89:20160283.
34. Zaidman C, van Alfen V. Ultrasound in the Assessment of Myopathic Disorders. J Clin Neurophysiol. 2016;33:103–11.
35. Berko N, FitzGerald E, Amaral T, Payares M, Levin T. Ultrasound elastography in children: establishing the normal range of muscle elasticity. Pediatr Radiol. 2014;44:158–63.
36. Lacourpaille L, Nordez A, Hug F, Doguet V, Andrade R, Guilhem G. Early detection of exerciseinduced muscle damage using elastography. Eur J Appl Physiol. 2017;117:2047–56.
37. Zhou X, Wang C, Qiu S, Mao L, Chen F, Chen S. Non-invasive Assessment of Changes in muscle Injury by Ultrasound Shear Wave Elastography: na experimental study in Contusion Model. Ultras Med Bio. 2018;44:2759–67.
38. Guimaraes J, Cavalcante W, Cruz I, Nico M, Ormond Filho A, Silva A, et al. Musculoskeletal ultrasound in inclusion body myositis: a comparative study with magnetic resonance imaging. Ultrasound in Med & Bio. 2021;47:2186–92.

Publisher's Note