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Title: The Association Between Muscular Ultrasonographic Alterations and Clinical Symptoms in Patients With Inflammatory Myopathy

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Abstract

Purpose: We evaluated the ability of muscle ultrasound (MUS), a non-invasive and simple tool, to distinguish between healthy subjects and individuals with inflammatory myopathy.

Methods: This study was conducted on 17 patients with recently diagnosed biopsy-proven inflammatory myopathies (12 dermatomyositis, five polymyositis) compared with 17 age- and gender-matched healthy control adults. All patients underwent clinical assessments, including manual muscle testing (MMT) and hand-held dynamometry, as well as MUS evaluations, including thickness and echointensity (EI) in predefined muscle groups.

Results: The disease duration was seven months (interquartile range: 3-11). Except for biceps and gastrocnemius, the patients' muscles had significantly higher EI and lower thickness in comparison with the controls. The EI sum-score manifested the highest area under curve (AUC) in comparison with the sum-scores of other variables (EI vs. MMT: AUCs-difference = 0.18, $p < 0.01$; EI vs. dynamometry: AUCs-difference = 0.14, $p = 0.02$; EI vs. thickness: AUCs-difference = 0.25, $p < 0.01$).

Conclusion: EI of muscles differed significantly between healthy individuals and those with inflammatory myopathies and may potentially serve as a useful diagnostic biomarker.

Keywords: Case-control study, Inflammatory myopathy, Imaging, Muscle ultrasound

Highlights

- The patients with inflammatory myopathy had higher muscle echointensity than controls.
- The patients' muscles had lower thickness in comparison with the controls.
- Ultrasound may potentially serve as a useful diagnostic biomarker for IMs.

Plain Language Summary

Muscle Ultrasound (MUS) is a non-invasive and straightforward measurement tool in neuromuscular fields. The main goal of this study was to compare MUS parameters in inflammatory myopathies versus healthy subjects. We showed that MUS variables are considerably different between inflammatory myopathy patients and healthy individuals. Ultrasound is inexpensive, user-friendly, objective, and non-invasive, so further study of it is merited.

1.Introduction

Inflammatory myopathies (IMs) are a diverse group of muscular autoimmune disorders characterized by muscle weakness as the initial symptom. According to the new classification system for inflammatory myopathies, these disorders include inclusion body myositis (IBM), dermatomyositis (DM), polymyositis (PM), immune-mediated necrotizing myopathy, anti-synthetase syndrome, and overlap myositis (Selva-O'Callaghan et al., 2018). Except for IBM, most patients with inflammatory myopathy respond well to the immunosuppressive treatment. Nevertheless, it is essential to point out that many inflammatory myopathy patients continue to progress despite intense treatment (Schmidt, n.d.). The development of many outcome measures for myositis activity has brought standardization to the field, which has aided our understanding of these diseases' long-term outcomes and developing new therapies (Rider et al., 2018).

Currently, most clinicians use outcome measures such as manual muscle testing (MMT), hand-held dynamometry (HHD), electrodiagnostic tests, including electromyography (EMG), and serum markers [creatine kinase (CK)] for diagnosis and follow-up of the patients (Allenbach et al., 2012). Some clinical measures such as the MMT test may be affected by inter-observer differences (Miller et al., 2001); therefore, there is growing attention to the application of imaging modalities. Muscle MRI has been broadly used in inflammatory myopathies to assess the extent of muscle involvement and determine the best location for muscle biopsy and patients' follow-up; however, this modality is expensive, non-feasible, and time-consuming. Thus, the application of MUS has been increased due to its widespread availability, easier techniques, non-invasiveness, and cost-effectiveness for real-time imaging of the muscles (Pillen et al., 2006).

Both qualitative and quantitative methods are applied for muscle evaluations in MUS (Heckmatt et al., 1980, 1982). MUS benefits from an acceptable sensitivity to detect muscle changes even in the early stages of the disease, reflected by increased echo intensity (EI) due to acute inflammation and edema within the muscle tissue (Habers et al., 2015). EI, one of the main parameters of MUS, is an outcome of choice in patients with inflammatory myopathies (Pillen & Van Alfen, 2015), and the findings are less operator-dependent, with higher sensitivity than the subjective analysis (Pillen et al., 2006).

It has been well indicated that the muscles of patients with PM/DM have higher EI than healthy muscles (Mittal et al., 2003; Noto et al., 2014). However, there is limited data on the

diagnostic utility of MUS for differentiating PM/DM subjects from healthy ones. Besides, the association between MUS parameters and bedside clinical characteristics remains almost unknown. The main goal of this study was to compare MUS parameters in inflammatory myopathies versus healthy subjects and measure the associations between clinical scores and MUS scores in the patients.

2.Methods and Materials

2.1.Study design and participants

In this cross-sectional case-control study, we enrolled 17 adult patients (> 18 years old) with an established diagnosis of inflammatory myopathy, confirmed with a recent muscle biopsy, and 17 normal subjects in a neuromuscular referral center from September 2018 to January 2020. Inclusion criteria were defined as the presence of clinical evidence of inflammatory myopathies, including bilateral symmetric proximal muscles weakness, disease duration of fewer than five years, history of elevation in serum skeletal muscle enzymes (CK > 300 IU/L), or electromyography (EMG) results indicating myopathic pattern along with irritation on needle electromyography as well as definite evidence of inflammatory changes in muscle biopsy. Characteristic rashes on clinical examination and perifascicular atrophy in muscle biopsy were considered for the classification of dermatomyositis. We excluded the patients with possible evidence of inclusion-body myositis, muscular dystrophy, metabolic or endocrine myopathy, toxic myopathy, granulomatous and infectious myositis. Informed consent was obtained from participants. The study was approved by the local ethical committee (code: IR.TUMS.MEDICINE.REC.1398.367).

2.2.Functional measures

The manual muscle testing (MMT) was conducted by an expert neurologist using the medical research council (MRC) scale, scoring muscle groups that are responsible for the following activities from 0 to 5: arm abduction, elbow flexion/extension, wrist flexion, hip flexion, knee flexion/extension, and ankle dorsiflexion/plantar flexion. Moreover, the muscle forces were quantitatively measured by a calibrated hand-held dynamometer (microFET®2, Hoggan Scientific, USA). We calculated functional measures of MMT and dynamometry for each muscle separately. We defined the average sumscore of muscle groups for proximal and muscles of upper and lower extremities and the average total sumscore (Figure 1). For calculating each average sumscore, initially, we added the scores of all muscles or actions and then divided them by the number of muscles or actions.

2.3. Muscle Ultrasound

A standard ultrasound protocol was applied for MUS, using a Sonosite M-Turbo C machine with a 15-6 MHz linear probe (Sonosite, Fujifilm) by an expert in neuromuscular ultrasound. Ultrasound scans were made from the following muscles on both sides: Biceps Brachii (BB), Deltoid, Flexor Carpi Radialis (FCR), Vastus Lateralis (VL), gastrocnemius (GC), and Tibialis Anterior (TA). Before the ultrasound examination, dirt and debris were cleaned from the skin. The areas were prepped with alcohol, and a generous amount of contact gel was used to minimize the transducer's required pressure on the skin.

Each muscle underwent MUS three consecutive times, and the means of EI and thickness scores were calculated to minimize the variations. All scans were made in the transverse plane with a standard transducer location corresponding to the same investigator muscle belly, with three years of experience in neuromuscular ultrasound. To avoid oblique scanning, we adjusted the probe's angle until the best bone EI was acquired. For ultrasonographic evaluations, the ultrasound machine was set on musculoskeletal mode and autogain function. Furthermore, we considered the depth of 4 centimeters for BB, Deltoid, FCR, GC, TA muscles, and 6 centimeters for VL muscle. Afterward, images were imported to ImageJ software (Fiji version)(Schindelin et al., 2012), and the maximal thickness of individual muscles was measured at standardized locations (Figure 2). For each muscle, the region of interest (ROI) was determined as the region with the highest intensity of muscle tissue devoid of bone or surrounding tissue. The average gray-scale level was obtained for the EI using the ImageJ software histogram function (resolution: 32 bit, black = 0, white = 255) (Figure 2). We calculated EI and thickness for each muscle separately and defined the average sumscore of muscle groups by adding the EI and thickness of measured muscles.

2.4. Statistical analysis

Data analysis was performed using the RStudio (R version 3.2.2). We used the Shapiro-Wilk test to test the normality of data. Since the variables (MMT, Dynamometry, EI, and thickness) did not follow a normal distribution pattern, we used the non-parametric tests for analyses. For the comparison of scales between the patients and healthy subjects, we used the Mann-Whitney test. The data for the tools are presented as median [interquartile (IQR: 25th – 75th percentiles) range]. Diagnostic accuracy of MUS (EI and thickness), hand-held dynamometry, and MMT methods for distinguishing inflammatory myopathy patients and healthy controls were assessed using the receiver operating characteristic curve (ROC) analysis. The significance level of < 0.05 was regarded as significant.

3.Results

3.1.Demographic characteristics of the participants

We enrolled 17 patients with inflammatory myopathies and 17 healthy subjects. Inflammatory myopathies included dermatomyositis (12 patients) and polymyositis (5 patients). The median disease duration in the patients was 7 (IQR: 3 - 11) months. Patients and controls were matched in terms of age (patients: 45.8 ± 16.8 years, control: 41.7 ± 16.4 years; $p = 0.47$), and gender (patients: 13 females, control: 13 females; $p = 1.00$). All patients had received prednisolone [Median dose: 25 (IQR: 15-40) mg/day]; besides, two and three of the patients had received concurrent mycophenolate mofetil and methotrexate, respectively. At the visit, the mean CK level was 680 (250 - 1890) IU/L (Maximum = 8550 IU/L).

3.2.Functional measures

In terms of muscle strength, patients generally showed lower muscle strength than healthy subjects (Table 1). However, distal power, including wrist-flexion and foot plantar-flexion, and dorsiflexion were not different between the study groups.

3.3.MUS parameters

All patients' muscles showed significantly higher EI than the corresponding muscles of control subjects (Table 1). In terms of thickness, other than biceps and gastrocnemius muscles, all muscles and compartments demonstrated a lower thickness than the controls (Table 1). Average EI sumscore for patients was 54.4 (50.3 - 58.4) versus 35.8 (34.3 - 37.3) for healthy subjects ($p < 0.01$). Moreover, among patients, the EI sumscore of lower extremities muscles was higher than upper extremities muscles [57.5 (52.8 - 62.1) versus 51.3 (46.6 - 55.9), $p = 0.07$] and EI of proximal muscles was higher than distal muscles [55.9 (51.3 - 60.5) versus 52.8 (48.7 - 57.0), $p = 0.37$]; however, the differences were not significant.

3.4.The association between MUS and clinical parameters

The correlations between MUS parameters (EI and thickness) and clinical parameters (MMT and dynamometry) are indicated in Table 2. As shown, we found no significant correlation between MUS (EI and thickness) and clinical parameters (MMT and dynamometry), except for the correlation between distal dynamometry and EI. There was a significant negative correlation between distal dynamometry and EI ($r = -0.32$, $p = 0.01$).

3.5.Diagnostic utility of MUS

Diagnostic accuracy of MUS sumscores (average EI sumscore and average thickness sumscore) for distinguishing inflammatory myopathy from healthy status was assessed using the ROC curve analysis (Figure 3). Evaluating the average EI sumscore, scores of 39.7 or higher corresponded to a sensitivity of 100 and a specificity of 88.2 (LR+: 8.5, LR- = 0) to discriminate patients from control subjects, and the area under the ROC curve (AUC) was 0.97 (Figure 3). For the average thickness sumscore, scores of 13.6 mm or lesser corresponded to a sensitivity of 70.6 and a specificity of 88.2 (LR+: 6.0, LR- = 0.33) to discriminate patients from control subjects area under the ROC curve (AUC) was 0.75. The AUC was significantly different between EI and thickness (Difference between areas = 0.22, $p = 0.03$).

4.Discussion

In the present study, we evaluated the association between MUS variables (muscle EI and thickness) and clinical (MMT, dynamometry) measures in patients with inflammatory myopathy. Although both clinical and MUS variables were significantly different between the patients and healthy individuals, there was nearly no relationship between their scores. In this respect, we performed ROC analysis to better insight into MUS ability to distinguish IM patients from healthy subjects and observed good diagnostic utility for this ancillary method, especially for the echointensity parameter.

Although there is no trace of imaging methods in the current classification criteria of IMs, such modalities are useful in diagnosing and monitoring these disorders. MRI imaging is considered the gold standard in this regard, showing acceptable sensitivity and specificity (J. Day et al., 2017; Walker, 2008). However, MRI has significant disadvantages as it is expensive, difficult to tolerate for some patients, and contraindicated in those with ferromagnetic biomedical implants (Adler & Garofalo, 2009). On the other hand, ultrasonography is a simple, non-invasive, and cost-effective alternative that allows real-time analysis of the muscle condition with high spatial resolution and recently used in the neuromuscular field such as polyneuropathies and motor neuron disease as well as myopathies (Rajabkhah et al., 2020; Wijntjes & Alfen, 2021).

Healthy muscles are generally hypoechoic in MUS's cross-sectional view, probably due to the high abundance of blood in the muscle tissue (Campbell et al., 2005; Whittaker & Stokes, 2011). Reimers et al. showed that fat replacement constitutes the leading cause of increased

muscle echogenicity (Reimers et al., 1993). Also, It has been shown that PM/DM muscles exhibit higher echointensity than healthy muscles (Mittal et al., 2003; Noto et al., 2014). Meanwhile, there is evidence that muscle size is altered in patients with PM/DM (Bhansing et al., 2015; Mittal et al., 2003). In acute stages, muscles might be normal in size or might even represent slight edema. This finding stems from the fact that the deposition of fat tissue or edema could mask the muscles' reduced size in the early stages (Adler & Garofalo, 2009). In contrast, it has been observed that affected muscles experience a remarkable size reduction in chronic stages when atrophy turns out to be a prominent part. Our results support the previous literature, demonstrating higher EI and lower muscle thickness in patients with PM/DM.

There is evidence concerning the significant association between some clinical assessments and imaging modalities. For instance, Meng and colleagues indicated that abnormal gray-scale US scores were correlated with lower CPK levels and disease of longer duration (Meng et al., 2001). Meanwhile, the values obtained from the combination of MUS and elastography showed partial concordance with laboratory markers (Botar-Jid et al., 2010). However, the presence of an association between bedside disease activity assessments and muscle imaging parameters remains controversial. For instance, in a recent study of radiologic patterns in IM disorders, no significant correlation was found between MRI features and bedside measures, including MMT, myositis disease activity assessment tool (MDAAT-muscle), patient global visual analog scale, and physician global visual analog scale (J. A. Day et al., 2019). A similar result was observed in this study, finding an association merely between EI and dynamometry score of the distal compartment. Further investigations seem necessary to evaluate the association between clinical and imaging parameters.

This study has several limitations. First, the cross-sectional design of this investigation restricts the ability to discover the predictive ability of MUS in IMs. Second, our limited sample size questions the generalizability of the findings. Third, all patients were under treatment; this might provide variations in IM patients' clinical and paraclinical features compared to drug-naïve ones. Forth, patient selection was relatively heterogeneous. Fifth, muscle blood flow and elastography were not evaluated in our study.

5. Conclusion

In summary, we showed that MUS variables, including muscle thickness and echointensity, are considerably different between IM patients and healthy individuals and may potentially

serve as a useful diagnostic biomarker. The EI sumscore of lower extremities muscles was higher than upper extremities muscles, and EI of proximal muscles was higher than distal muscles. Moreover, we found no significant correlation between MUS (EI and thickness) and clinical parameters (MMT and dynamometry), except for the correlation between distal dynamometry and EI.

Declarations

Conflicts of interest

Authors have no conflict of interest to disclose.

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Ethics approval

The study was approved by the local ethical committee (code: IR.TUMS.MEDICINE.REC.1398.367).

Authors' contributions

Methodology: Farzad Fatehi, Shahriar Nafissi; Conceptualization and supervisor: Farzad Fatehi, Ali Asghar Okhovat, Shahriar Nafissi; Investigation: Parisa Khaghani, Mahsa Layegh, Akram Panahi; Writing – Original Draft: Kamyar Moradi, Farzad Teimouri, Mahsa Mortaja; Writing – Review & Editing, Ali Asghar Okhovat, Farzad Fatehi.

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TABLE 1. COMPARISON OF ULTRASOUND AND CLINICAL SCORES BETWEEN PATIENTS AND CONTROL SUBJECTS

		PATIENTS	CONTROLS	p
MUSCLES EI	Deltoid	51.0 (44.6-57.4)	27.0 (25.6-30.5)	<u>0.00</u>
	Biceps	57.0 (50.3-63.7)	41.5 (37.9-44.8)	<u>0.00</u>
	FCR	45.9 (39.8-51.9)	37.0 (35.1-40.0)	<u>0.00</u>
	Vastus lateralis	59.7 (54.0-65.5)	38.0 (36.6-41.5)	<u>0.00</u>
	Tibialis anterior	53.7 (48.2-59.2)	37.5 (35.5-39.1)	<u>0.00</u>
	Gastrocnemius	59.0 (53.2-64.8)	32.0 (28.8-33.9)	<u>0.00</u>
AVERAGE SUMSCORES EI	Upper muscles	51.3 (46.6-55.9)	35.7 (33.6-37.6)	<u>0.00</u>
	Lower muscles	57.5 (52.8-62.1)	35.9 (34.2-37.6)	<u>0.00</u>
	Proximal muscles	55.9 (51.3-60.5)	36.1 (34.3-38.0)	<u>0.00</u>
	Distal muscles	52.8 (48.7-57.0)	35.4 (33.7-37.1)	<u>0.00</u>
	Sumscore	54.4 (50.3-58.4)	35.8 (34.3-37.3)	<u>0.00</u>
MUSCLES THICKNESS (MM)	Deltoid	12.3 (11.5-13.0)	14.0 (13.4-14.4)	<u>0.00</u>
	Biceps	14.1 (12.7-15.5)	14.4 (13.3-14.8)	0.52
	FCR	8.5 (7.9-9.0)	9.2 (8.9-9.3)	<u>0.02</u>
	Vastus lateralis	7.6 (7.2-8.0)	8.7 (8.1-9.5)	<u>0.01</u>
	Tibialis anterior	24.4 (23.1-25.7)	27.5 (25.3-28.4)	<u>0.01</u>
	Gastrocnemius	15.5 (14.7-16.2)	15.2 (14.5-16.3)	0.87
AVERAGE THICKNESS SUMSCORES (MM)	Upper muscles	11.6 (11.0-12.2)	12.4 (12.0-12.7)	<u>0.01</u>
	Lower muscles	15.8 (15.1-16.5)	17.0 (16.1-17.9)	<u>0.02</u>
	Proximal	11.3 (10.6-12.0)	12.3 (11.8-12.7)	<u>0.01</u>

MUSCLES

DYNAMOMETRY (KG)

AVERAGE

DYNAMOMETRY

SUMSCORES (KG)

MUSCLES

SCORES

MMT

muscles			
Distal muscles	16.1 (15.5-16.7)	17.1 (16.4-17.9)	<u>0.03</u>
Sumscore	13.7 (13.1-14.3)	14.7 (14.1-15.2)	<u>0.01</u>
Arm abduction	5.4 (4.5-6.3)	6.8 (6.3-7.3)	<u>0.01</u>
Elbow flexion	6.2 (5.6-6.8)	7.3 (6.8-8.0)	<u>0.01</u>
Wrist flexion	4.6 (4.2-5.0)	5.2 (4.8-5.6)	<u>0.02</u>
Quadriceps	6.5 (5.8-7.3)	8.0 (7.7-8.7)	<u>0.00</u>
Foot dorsiflexion	6.6 (6.0-7.3)	7.8 (7.5-8.5)	<u>0.00</u>
Foot plantarflexion	6.8 (6.4-7.3)	8.0 (7.8-8.8)	<u>0.00</u>
Upper muscles	5.4 (4.8-6.0)	6.5 (6.0-6.9)	<u>0.01</u>
Lower muscles	6.7 (6.1-7.2)	8.1 (7.7-8.6)	<u>0.00</u>
Proximal muscles	6.0 (5.3-6.7)	7.5 (7.1-7.8)	<u>0.00</u>
Distal muscles	6.0 (5.6-6.5)	7.2 (6.8-7.5)	<u>0.00</u>
Sumscore	6.0 (5.5-6.6)	7.3 (7.0-7.6)	<u>0.00</u>
Arm Abduction	4.4 (4.0-4.8)	5.0 (5.0-5.0)	<u>0.00</u>
Elbow Flexion	4.4 (4.1-4.7)	5.0 (5.0-5.0)	<u>0.00</u>
Elbow Extension	4.4 (4.1-4.8)	5.0 (5.0-5.0)	<u>0.00</u>
Wrist Flexion	4.9 (4.7-5.0)	5.0 (5.0-5.0)	0.16
Hip			

**AVERAGE
SUMSCORES**

MMT

Flexion	4.2 (3.7-4.8)	5.0 (5.0-5.0)	<u>0.01</u>
Knee			
Flexion	4.6 (4.3-4.9)	5.0 (5.0-5.0)	<u>0.01</u>
Extension	4.5 (4.2-4.9)	5.0 (5.0-5.0)	<u>0.02</u>
Ankle			
Dorsiflexion	4.9 (4.8-5.0)	5.0 (5.0-5.0)	0.33
Plantar flexion	4.9 (4.8-5.0)	5.0 (5.0-5.0)	0.33
Upper muscles	4.5 (4.3-4.8)	5.0 (5.0-5.0)	<u>0.01</u>
Lower muscles	4.7 (4.4-4.9)	5.0 (5.0-5.0)	<u>0.00</u>
Proximal muscles	4.4 (4.1-4.8)	5.0 (5.0-5.0)	<u>0.00</u>
Distal muscles	4.9 (4.8-5.0)	5.0 (5.0-5.0)	0.56
Sumscore	4.6 (4.3-4.9)	5.0 (5.0-5.0)	<u>0.00</u>

Abbreviations: EI, Echo Intensity; MMT, Manual Muscle Testing; MUS, Muscle Ultrasonography.

Table 2. The correlation between MUS scores and clinical scores

MUS parameters		MMT		Dynamometry	
		r	p	r	p
Thickness	Upper	-0.13	0.63	0.03	0.63
	Lower	-0.04	0.89	0.30	0.89
	Proximal	-0.08	0.75	0.14	0.75
	Distal	-0.11	0.66	0.06	0.66
	Sumscore	-0.15	0.57	0.12	0.57
EI	Upper	-0.15	0.57	-0.58	0.21
	Lower	-0.08	0.76	-0.09	0.11
	Proximal	-0.07	0.80	-0.41	0.73
	Distal	-0.22	0.39	<u>-0.32</u>	<u>0.01</u>
	Sumscore	-0.10	0.69	-0.32	0.21

MMT: manual muscle testing; EI: Echo intensity

Table 3. Diagnostic utility of functional and ultrasonographic measurements in inflammatory myopathies

Abbreviations: AUC, Area Under Curve; EI, Echo Intensity; MMT, Manual Muscle Testing; MUS, Muscle Ultrasonography

Diagnostic variables	Muscles	cut-off value	AUC (95% CI)	Sensitivity (%)	Specificity (%)	likelihood ratio (+)	Likelihood ratio (-)
MUS							
Thickness							
	Sum-score	13.8	0.75 (0.58-0.93)	88.23	70.59	3.00	0.17
	Upper muscles	11.3	0.75 (0.57-0.92)	94.11	58.82	2.29	0.10
	Lower muscles	15.9	0.73 (0.56-0.91)	76.47	70.59	2.60	0.33
	Proximal muscles	12.0	0.77 (0.60-0.94)	70.59	82.35	4.00	0.36
	Distal muscles	16.2	0.71 (0.54-0.90)	82.35	70.59	2.80	0.25
EI							
	Sum-score	42	1.00 (1.00-1.00)	100	100	-	0
	Upper muscles	41.8	0.96 (0.91-1.00)	100	88.23	8.50	0
	Lower muscles	42.8	1.00 (1.00-1.00)	100	100	-	0
	Proximal muscles	41.2	0.99 (0.98-1.00)	94.12	100	-	0.06
	Distal muscles	42.1	0.99 (0.98-1.00)	100	94.12	17.01	0
Muscle Force Dynamometry							
	Sum-score	6.5	0.86 (0.74-0.98)	94.12	58.82	2.29	0.10
	Upper muscles	5.8	0.76 (0.59-0.92)	88.23	58.82	2.14	0.20
	Lower muscles	7.5	0.89 (0.78-0.99)	76.47	88.23	6.50	0.27
	Proximal muscles	6.7	0.79 (0.64-0.95)	94.11	58.82	2.29	0.10
	Distal muscles	6.4	0.86 (0.74-0.98)	94.11	64.70	2.67	0.09
MMT							
	Sum-score	4.94	0.82 (0.71-0.94)	100	64.71	2.83	0
	Upper muscles	4.75	0.76 (0.64-0.89)	100	52.94	2.12	0
	Lower muscles	4.9	0.79 (0.67-0.91)	100	58.82	2.43	0
	Proximal muscles	4.92	0.82 (0.71-0.94)	100	64.71	2.83	0
	Distal muscles	4.83	0.56 (0.48-0.64)	100	11.76	1.13	0

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Figures

Figure 1. Flowchart of the study

Tibialis Anterior

Figure 2. Ultrasound of Tibialis anterior muscle in a control subject (right side) and a patient with myositis (left side). The histogram, mean values, and echo-variance of the Tibialis anterior (in ROI) are indicated (bottom pictures). The histogram shows the echovariations of pixels. In the histogram of a healthy subject, pixel intensities are skewed to the left side, indicating darker pixels. In this control subject (right lower image) mean value was 20.04. In a myositis patient (left side image), the histogram is deviated to the right side with (left lower image), indicating brighter pixels in favor of more fibrosis/fat replacement or inflammation. In this patient, the mean value was 32.15.

Figure 3. Comparison of EI and thickness sumscores. AUC, Area Under Curve; EI, Echo Intensity.