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Quantitative MRI in myositis patients: comparison with healthy volunteers and radiological visual assessment

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AIM: To assess whether magnetic resonance imaging (MRI)-based measurements of T2, fat fraction, diffusion tensor imaging, and muscle volume can detect differences between the muscles of myositis patients and healthy controls, and to identify how they compare with semi-quantitative MRI diagnosis.

MATERIALS AND METHODS: Sixteen myositis patients and 16 age- and gender-matched healthy controls underwent MRI of their thigh. Quantitative MRI measurements and radiologists' semi-quantitative scores were assessed. Strength was assessed using an isokinetic dynamometer.

RESULTS: Fat fraction and T2 values were higher in myositis patients whereas muscle volume was lower compared to healthy controls. There was no difference in diffusion. Muscle strength was lower in myositis patients compared to healthy controls. In a subgroup of eight patients, scored as unaffected by radiologists, T2 values were still significantly higher in myositis patients.

CONCLUSIONS: Quantitative MRI measurements can detect differences between myositis patients and healthy controls. Changes in the muscles of myositis patients, undetected by visual, semi-quantitative scoring, can be detected using quantitative T2 measurements. This suggests that MRI T2 values may be useful for the management of myositis patients.

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Introduction

Idiopathic inflammatory myopathies (IIM), representing forms of myositis, are a heterogeneous group of diseases affecting approximately 5,000–6,000 people in the UK.[1] Dermatomyositis (DM) and polymyositis (PM) are two common types of myositis. They are characterised by muscle pain and weakness, with overlapping features and often present with the same autoantibodies.[2] Myositis predominantly manifests in skeletal muscle, with features of inflammation, fatty infiltration, muscle atrophy, and alterations in muscle microstructure.[3] The symptoms of myositis often result in a severe impairment in quality of life,[4,5] and are associated with increased mortality.[6] The diagnosis and monitoring of myositis is reliant on clinical examination, invasive muscle biopsies, blood tests, and subjective muscle tests.

Imaging is frequently used to aid in the diagnosis and monitoring of myositis,[7] with visual scoring based on magnetic resonance imaging (MRI) playing a key role in the assessment of muscle oedema, fatty infiltration, and atrophy.[8] An important role of imaging is the identification of sites of muscle inflammation, which can then be targeted for muscle biopsy.[9] Currently, this is usually done by subjective visual assessment of the muscle, a technique that may be relatively insensitive to systemic muscle changes. As an alternative, there are a range of quantitative MRI techniques that can detect subtle muscle changes in muscle diseases and may have a role in the future clinical management of DM and PM, and the identification of sites for biopsy and the monitoring of response to treatment.[10–14]

Quantitative T2 measurements are sensitive to fluid related to physiological or pathological changes at the macromolecular level[15] and may have a role in the long-term follow-up of muscle oedema and inflammation.[16] MRI-based fat fraction (FF) measurements in the muscle are useful for identifying fatty infiltration.[17,18] Recently, interest has grown regarding diffusion tensor imaging (DTI) techniques in the muscle, which are sensitive to changes in muscle microstructure.[11,19,20] All of these measurements have been shown to have excellent intra- and inter-rater variability.[21]

There are few studies investigating these measurements in myositis and, to the authors' knowledge, this is the first study to apply all these MRI techniques to a group of myositis patients and to compare with current semi-quantitative radiologist scoring. The aims of this study were to compare FF, T2, muscle volume, and DTI diffusion measurements in the muscle between myositis patients and a directly matched healthy population, and to compare quantitative MRI measurements with radiologist's scores and muscle strength.

Materials and Methods

Study design

This observational, case–control study was approved by the local research ethics committee (17/EM/0079). All participants were 18 years of age and above with no contraindications to MRI and provided informed written consent. Recruitment began in May 2017 and ended in July 2018.1:1 matching was used (matching the patient with a healthy control of the same gender and within a 5-year age range). The inclusion criteria for patients were based on the Bohan and Peter criteria for myositis.[3,22] Patients also fulfilled the 2017 EULAR/ACR criteria for IIM for DM or PM, which was published after the start of the study.[23] Myositis patients were included in the study if they were clinically suspected of being active at the time of recruitment, with muscle weakness and elevated creatinine kinase (CK; >200 IU/l in females and >320 IU/l in males), or had clinically diagnosed muscle weakness, antibody positive, on treatment for myositis, and had a patient global visual analogue score (VAS) of >20/100 mm. These eligibility criteria have been used in previous studies.[24,25] Healthy controls were included if they were asymptomatic with no history of muscle disease. Clinical information was collected, including CK, antibody status, and medication.

MRI measurements

MRI data were acquired using a MAGNETOM Verio 3T MRI machine (Siemens Healthcare, Erlangen, Germany; Table 1). The imaging protocol has been described previously.[26] Images of the dominant thigh (the right if the participant was unsure) were acquired using two small four-channel flex coils.

All quantitative images were aligned to each other and acquired with the same field of view to enable cross-propagation of regions of interest (ROIs). For fat quantitation a 40-section, volume-interpolated breath-hold examination (VIBE), two-point Dixon sequence was used.[21] Diffusion-weighted images were acquired using a STEAM prototype sequence, with an echo-planar imaging (EPI) readout[27] and SPAIR (spectral adiabatic inversion recovery) fat suppression.[21]

For T2 measurements, axial images were obtained using a T2-weighted, multi-echo, spin-echo (MESE) sequence with SPAIR fat suppression with an echo train length of 16. FF values were calculated from the fat and water images generated from the VIBE Dixon images for each ROI. To calculate T2 values the signal intensity versus echo time decay curves from each ROI were fitted using a mono-exponential decay function. To reduce the effect of additional signal from stimulated echoes the signal from the earliest time point was excluded from the fit.[28] Diffusion-weighted images (DWI; Fig 1) were converted to MD, FA, and eigenvalue maps using the vendor's software.

Muscle volume estimates were obtained using a semi-automated algorithm.[26] The algorithm segmented muscle from the FF maps generated by the VIBE Dixon analysis using a FF threshold of <50%.

ROIs were contoured using Osirix imaging software (version 4.0; open-source DICOM viewer, www.osirix-viewer.com). Regions depicting the individual hamstring muscles (semitendinosus, semimembranosus, and biceps femoris) and quadriceps muscles (rectus femoris, vastus

Table 1
Magnetic resonance imaging sequence methodology.

	Fat quantification	T1 weighted	T2	Diffusion
Imaging sequence	Two-point VIBE Dixon	Turbo spin-echo (TSE)	Multi-echo, multi-section (MESE)	STEAM-EPI
Repetition time	11	697	1,500	6,300
Echo time (ms)	2.45 and 3.675	9.1	9.6, 9.4, 153.6 (16 echoes)	42.4
Field of view (mm)	300×300	300×300	300×300	300×300
Section thickness (mm)	5	5	5	5
Fat suppression	N/A	STIR	SPAIR	SPAIR
Acquisition matrix	256×256	256×256	256×256	128×128
Number of sections	40	60	4	4
Number of averages	1	1	1	8
Receiver bandwidth (Hz/pixel)	510	222	510	1,502
Flip angle (degrees)	15	90	15	-
Generalised auto calibrating partial parallel acquisition (GRAPPA)		-	-	2 (24 reference lines)
Partial Fourier		-	-	6/8
B values (s/mm^2)		-	-	0, 500
Directions		-	-	6
Mixing time (T_m) (ms)		-	-	981
Diffusion time (Δ; ms)		-	-	1,000
Acquisition time (min:s)		2:19	2:05	6:12

lateralis, vastus medialis, and vastus intermedius) were drawn on the middle section of the in-phase VIBE Dixon volume for each participant, avoiding fascial tissue and subcutaneous fat (Fig 1). ROIs were copied to the corresponding FF, T2, and diffusion parameter maps, accounting for differences in image resolution, and the mean value within each ROI was measured. The quantitative MRI section analysed corresponded to the central section (section20) of the VIBE Dixon muscle volume.

As ROIs depicting the whole muscle cross-section were used in this study, both fatty infiltration and oedema may be present within the same ROI. These two pathologies may have opposite influences on DTI measures, so that if both oedema and fat are present in the same ROI, the effects can oppose each other and reduce the sensitivity of the measure to disease.[11] Therefore, in a subgroup analysis, nine patients were identified: three with fatty-infiltrated regions, three with oedematous regions, and three with unaffected regions. One identical 5 mm circular ROI was placed within either a fatty infiltrated, oedematous, or unaffected muscle region respectively. DTI measurements in these three separate regions were then compared (Electronic Supplementary Material Fig. S1).

Muscle strength analysis

Knee extension (quadriceps) and flexion (hamstrings) isokinetic assessment of the dominant thigh were performed following MRI. The muscle strength testing protocol has been described previously.[26] Participants performed three maximum effort repetitions for three sets, separated by a 30-second rest interval. Power (Watts) was the assessed variable. Handgrip strength, of their dominant hand, was also measured using a Jamar plus isokinetic dynamometer.

Radiologist semi-quantitative scoring

To compare with semi-quantitative radiologist scoring, the muscles of the hamstrings and quadriceps were scored on a four-point visual scale as either unaffected (0), mild[1]:

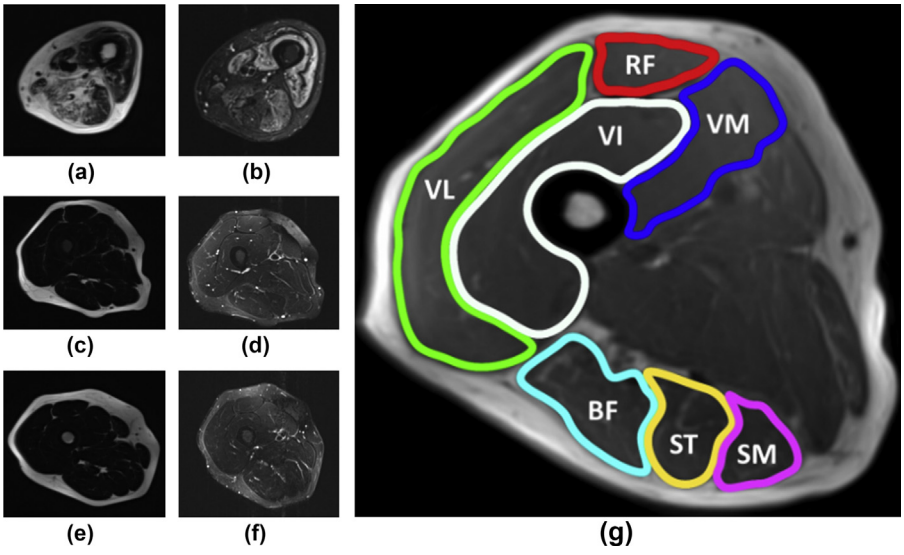

Figure 1 (a) Dixon fat and (b) T2-STIR MRI images as reported by radiologists in a myositis patient with affected muscle (left thigh). (c) Dixon fat and (d) T2-STIR iamges of a myositis patient with scored unaffected muscle (but elevated quantitative T2; right thigh). (e) Dixon fat and (f) T2-STIR image in a healthy participant (right thigh). (g) ROIs: RF, rectus femoris; VL, vastus lateralis; VM, vastus medialis; VI, vastus intermedius; BF, biceps femoris; ST, semitendinosus; SM, semimembranosus.

up to 33% of muscle involved, moderate[2]: 33–66% of muscle involved, or severe[3]: >66% of muscle involved. Two radiologists scored the muscles across the entire thigh using the T2-weighted short tau inversion recovery (STIR) images (3 minutes 18 seconds acquisition time [TA], 6,550 ms, 87 ms echo time [TE]) to identify muscle oedema and T1-weighted images (1 minute 21 seconds TA, 658 ms repetition time [TR], 8.8 ms TE) to identify fatty infiltration. If there was disagreement between scores, these were resolved on consensus following joint review.

Hamstrings and quadriceps scores were derived from the mean of the individual muscle scores and rounded to the nearest integer. The radiologists were blinded to other clinical, laboratory, quantitative MRI, and muscle function results. Patients who were scored as unaffected by the radiologists (n=8) were then compared with a matched subgroup of healthy controls as a separate sub-study.

Statistical analyses

Offline image analysis was performed using MATLAB software (R2018b, Mathworks, Natick, MA, USA). Statistical analyses were performed using SPSS (Version 25.0. IBM, Armonk, NY, USA). Paired samples t-tests were used to test for differences in MRI measurements between patients and healthy controls. Spearman's rank correlation was used to measure correlation; r_s values $\geq$0.3 were considered indicative of potential association, and p-values reported to identify significance. Receiver operator characteristic (ROC) curves were generated to assess diagnostic performance. Cohen's delta (d) has been provided for key comparisons, with effect sizes interpreted as small (d=0.2), medium (d=0.5), or large (d=0.8).

Results

Sixteen myositis patients were recruited (10/16 female, 10 polymyositis, six dermatomyositis, mean age 50±26, mean height 165±10 cm, mean weight 77.1±8 kg, mean body mass index [BMI] 25±4), median CK of 1,000 IU/l (range 70–12,802). The mean disease duration for the myositis patients was 5 years (range 1 month–22 years). Five of the 16 (31%) myositis patients were positive for the anti-Jo-1 antibody. The following myositis associated antibodies were recorded as anti-PM-Scl 75 (2/16, 13%), anti-PM-Scl 100 (2/16, 13%), anti-PL 12 (1/16, 6%). Other connective tissue disease associated antibodies included anti-Ro (5/16, 31%), anti-La (1/16, 6%), anti-Sm/RNP (3/16, 19%), anti-chromatin (3/16, 19%), anti-centromere (1/16, 6%). Four patients tested negative for antibodies. At the time of the study, the patients were on the following therapies: prednisolone: 9/16 (56%), hydroxychloroquine: 4/16 (25%), methotrexate: 3/16 (19%), rituximab: 2/16 (13%), intravenous immunoglobulins: 2/16 (13%), cyclophosphamide: 2/16 (13%), mycophenolate mofetil: 2/16 (13%), azathioprine: 1/16 (6%). Most of the patients were receiving a combination of some of the above therapies, one patient was newly diagnosed and yet to receive any therapy at the time of the MRI. Sixteen age- and gender-matched healthy controls were recruited (mean height 167±9 cm, mean weight 74±11 kg, mean BMI 26±2).

Within the hamstrings, the mean peak torque in the myositis patients was lower than healthy controls by −24.4 Nm (95% confidence interval [CI]: −42.4, 6.4 Nm; p=0.01). Within the quadriceps, the mean peak torque in the patients was lower by −48.2 Nm (95% CI: −79.9, −22.2 Nm; p<0.001). Descriptive data for quantitative MRI and muscle strength is reported in Table 2.

The ROC curves and area under the ROC curve (AUC) values for the quantitative measures are shown in Fig 2. Considering the individual muscles that make up the hamstrings and quadriceps (semitendinosus, semimembranosus, biceps femoris, rectus femoris, vastus lateralis, vastus medialis, vastus intermedius), there were significant difference between myositis and healthy groups, consistent with those seen in the hamstrings and quadriceps (Electronic Supplementary Material Table S1).

Muscle T2

Within the hamstrings, there was a difference of 7.9 ms (95% CI: 3.9, 11.9 ms; p<0.001) between the myositis patients and healthy controls, representing a large effect size (Cohen's d=0.80). Within the quadriceps, there was a difference of 11.7 ms (95% CI: 5.4, 17.9 ms; d=0.88; p<0.001; Fig 3).

T2 was inversely correlated with muscle strength measurements in myositis and healthy controls in both the quadriceps and the hamstrings (Fig 4).

Muscle FF

FF was higher in myositis patients compared to healthy controls with a difference in the hamstrings of 6.6% (95% CI:

Table 2
Quantitative MRI and strength measurements of scanned muscles for dermatomyositis and polymyositis patients and healthy controls.

		Mean (SD)	
		Hamstrings	Quadriceps
T2 (ms)	Myositis	47.8 (7.7)	53.8 (12.1)
	Healthy	39.9 (1.5)	42.1 (2.1)
Fat fraction (%)	Myositis	10.7 (9.4)	11.1 (13.1)
	Healthy	4.1 (1.2)	2.7 (1.1)
Muscle volume (cm^3)	Myositis	1152 (594)	
	Healthy	1468 (331.4)	
Mean diffusivity ($\times10^{-3}$ mm^2/s)	Myositis	1.29 (0.1)	1.31 (0.1)
	Healthy	1.32 (0.1)	1.34 (0.1)
Fractional anisotropy	Myositis	0.41 (0.004)	0.36 (0.03)
	Healthy	0.39 (0.1)	0.34 (0.1)
Eigenvalue 1 ($\times10^{-3}$ mm^2/s)	Myositis	1.93 (0.1)	1.86 (0.1)
	Healthy	1.91 (0.1)	1.84 (0.1)
Eigenvalue 2 ($\times10^{-3}$ mm^2/s)	Myositis	1.09 (0.1)	1.16 (0.1)
	Healthy	1.13 (0.2)	1.18 (0.2)
Eigenvalue 3 ($\times10^{-3}$ mm^2/s)	Myositis	0.86 (0.1)	0.94 (0.1)
	Healthy	0.89 (0.1)	0.98 (0.1)
Peak torque flexion (Nm)	Myositis	32.8 (23)	N/A
	Healthy	57.2 (26)	N/A
Peak torque extension (Nm)	Myositis	N/A	53.4 (46)
	Healthy	N/A	101.6 (45)

N/A, not applicable.

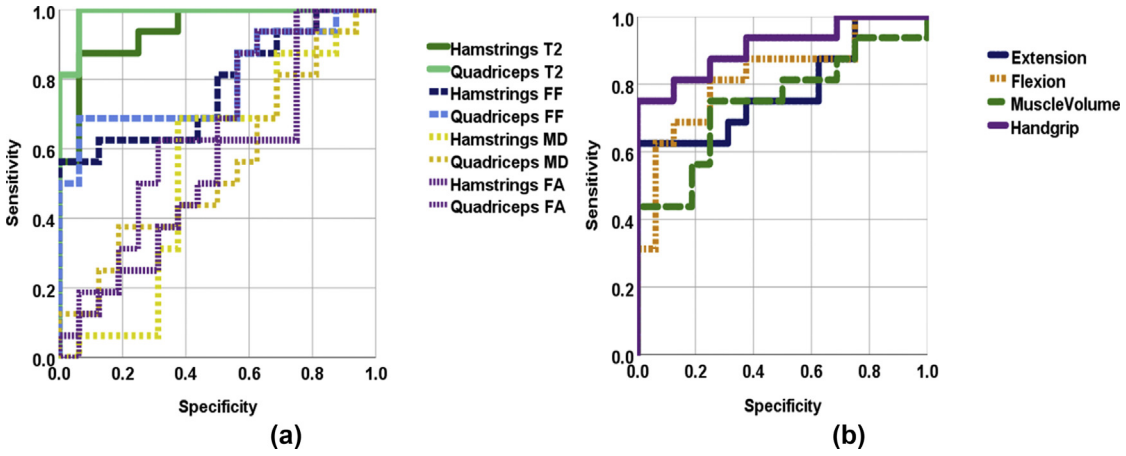

Figure 2 (a) ROC curve for quantitative MRI performance in discriminating myositis and healthy muscle. AUC hamstrings: T2 = 0.941, MD = 0.535, FF = 0.773; FA = 0.543 Quadriceps: T2 = 0.84, MD = 0.547, FF = 0.789; FA = 0.652. (b) ROC curve for muscle volume and muscle strength performance in discriminating myositis and healthy muscle. AUC: knee extension = 0.785; knee flexion = 0.824; muscle volume = 0.746; handgrip = 0.910.

1.9%, 11.4%; d=0.68; p=0.006) and in quadriceps of 8.4% (95% CI: 1.6%, 15.1%; d=0.64; p=0.01), representing medium-to-large effect sizes (Fig 3). FF correlated with muscle strength in the quadriceps with a correlation coefficient of r_s= −0.5 (p=0.001) and weakly correlated in the hamstrings r_s=0.3 (p=0.08).

Muscle DTI

There was no significant difference in mean diffusivity (MD) between the myositis patients and healthy controls in the hamstrings (Fig 2), with a difference of 0.03×10^{-3} mm^2/s (95% CI: −0.05, 0.06; d=0.17; p=0.5) or the quadriceps,

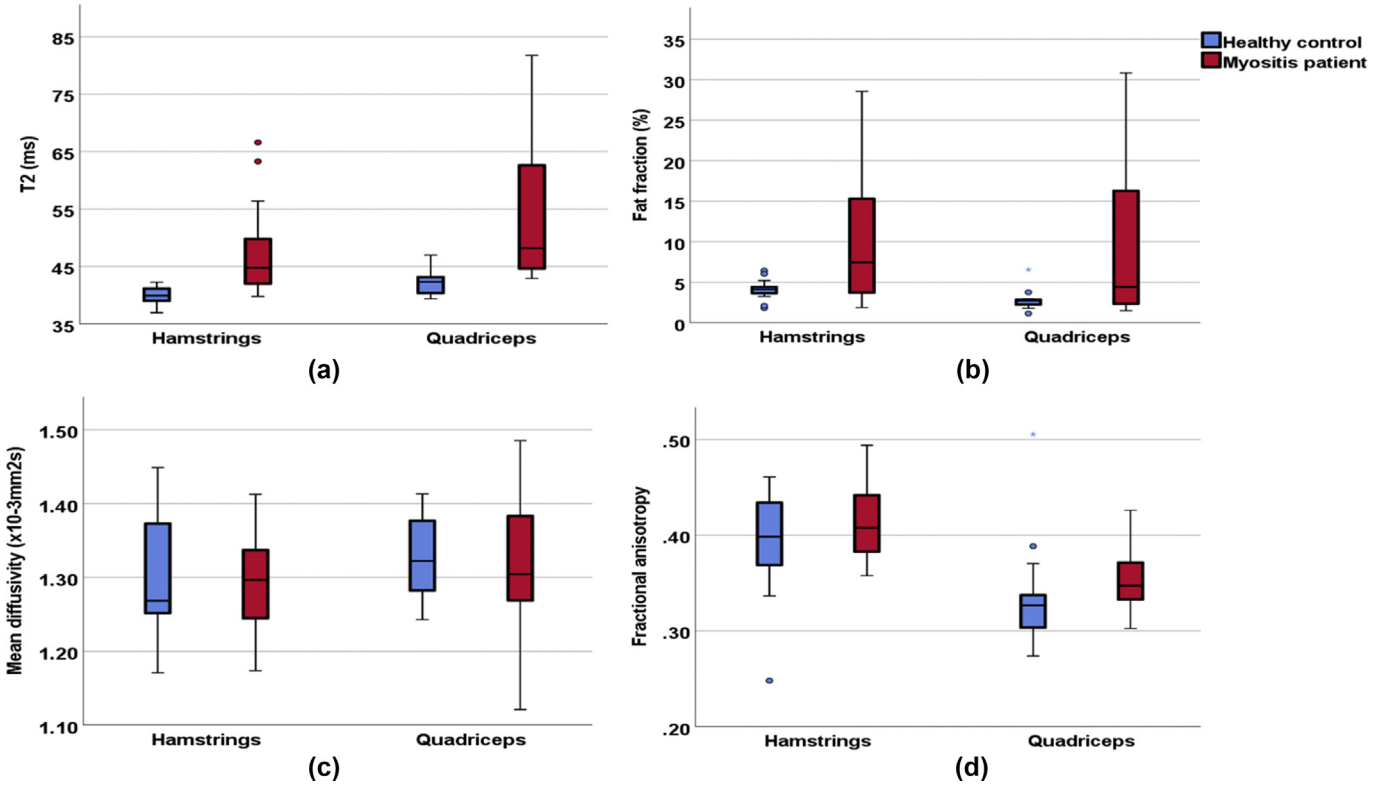

Figure 3 Quantitative MRI measurements in 16 myositis patients compared to 16 healthy controls: (a) quantitative T2; (b) quantitative FF; (c) quantitative mean diffusivity; (d) quantitative FA.

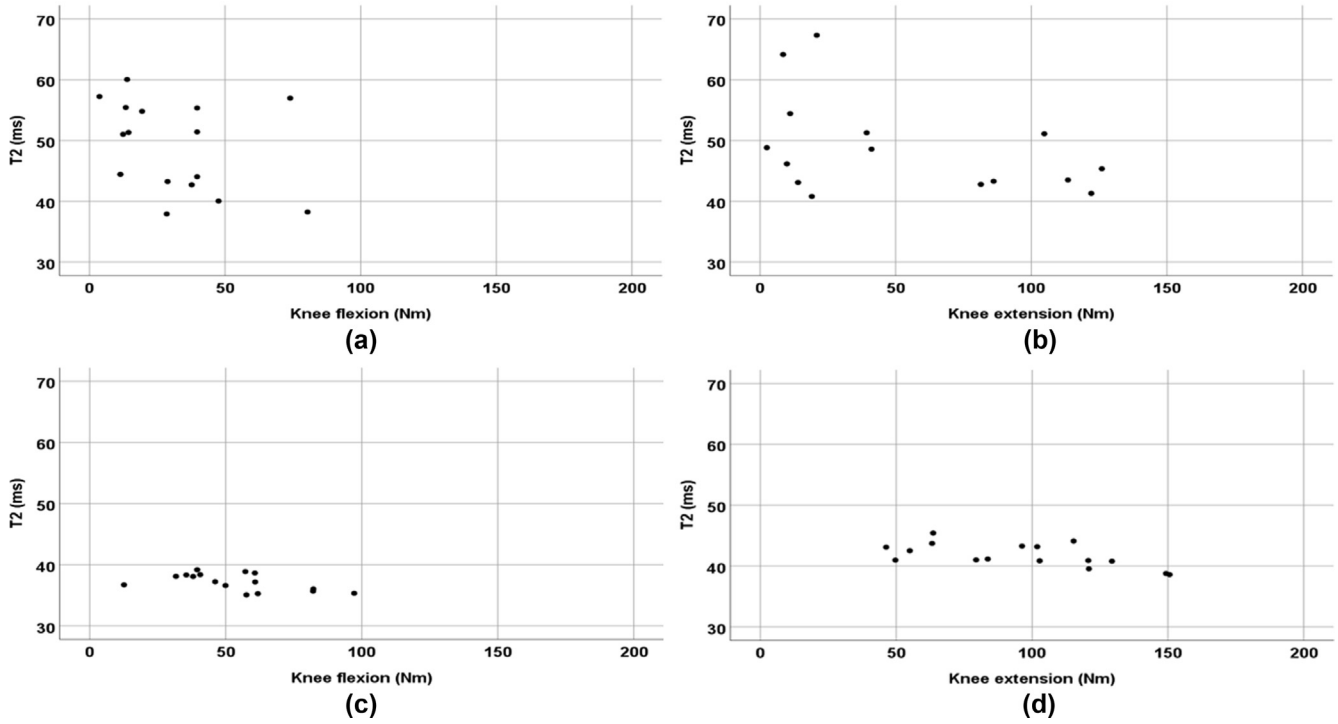

Figure 4 Quantitative T2 measurements show substantive correlation with peak torque flexion (hamstrings) and extension (quadriceps) in 16 myositis patients and healthy controls in the (a) myositis patients hamstrings (r_s=−0.4; p=0.1); (b) myositis patients quadriceps (r_s=−0.7; p=0.001); (c) healthy control hamstrings (r_s=−0.9; p<0.001); (d) healthy control quadriceps (r_s=−0.6; p=0.02).

with a difference of 0.03×10^{-3} mm^2/s (95% CI: −0.09, 0.06; d=0.14; p=0.6). There were no significant differences between myositis and healthy controls in fractional anisotropy (FA) in the hamstrings with a difference of 0.02 (95% CI: −0.01, 0.06; d=0.2; p=0.2) or quadriceps, with a difference of 0.02 (95% CI: −0.01, 0.06; d=0.1; p=0.6).

In the small sub-analysis that investigated the contradictory effects of fat and oedema on DTI measurements, diffusion was found to be higher in the oedematous regions and lower in the fatty regions.

Muscle volume

Patients had smaller muscle volumes than age- and gender-matched healthy controls (Fig 5) with a difference of −316 cm^3 (95% CI −648 and −62 cm^3; p=0.01). Muscle volume correlated with knee flexion torque (r_s=0.47) and knee extension torque (r_s=0.63) in patients and healthy controls combined (both p<0.001).

Comparison with radiologist scoring

Quantitative T2 correlated with the radiologists' oedema scores with r_s=0.7 in the hamstrings (p<0.001) and r_s=0.6 in the quadriceps (p<0.001), with an upward trend in T2 as radiologist scored visible oedema increased (Fig 6). In a separate comparison between the muscles in the myositis patients who had been classified as unaffected by the radiologists (n=8), T2 values for patients were still higher than those for age- and gender-matched healthy controls. In this subgroup analysis, the mean T2 in the hamstrings in patients was 42.2 ms while healthy controls had a mean T2 of 38.7 ms, a difference of 3.5 ms (95% CI: 1.4, 5.5; p=0.004). In the quadriceps, the mean T2 in unaffected muscles of the myositis patients (n=8) was 43.9 ms and healthy controls had a T2 of 40.1 ms, a difference of 3.8 ms (95% CI: 1.9, 5.6; p=0.001; Fig 7).

Within both the hamstrings and quadriceps, quantitative FF correlated with radiologists' scores for fatty infiltration at r_s=0.79 in the hamstrings (p<0.001) and r_s=0.93 in the quadriceps (p<0.001) with an upward trend in FF as radiologist scored visible fatty infiltration increased (Fig 8). FF values for patients with normal muscles according to radiologists scoring were not substantively different to those for healthy controls. In this subgroup analysis, the mean FF in the hamstrings in patients was 3.4%, while healthy controls had a mean FF of 2.9%, a difference of 0.5% (95% CI: −1.6, 0.9; p=0.5). In the quadriceps, the mean FF in patients was 2.5% and 2% in healthy controls, a difference of 0.5% (95% CI: −0.9, 0.1; p=0.1).

Discussion

The present study investigated the utility of quantitative MRI as an indicator of active disease and muscle damage in DM and PM patients compared with healthy controls. As expected, there were significant differences in T2, FF, and muscle volume between myositis patients and healthy controls; however, differences in T2 remained significant even when myositis patients who had been classed as

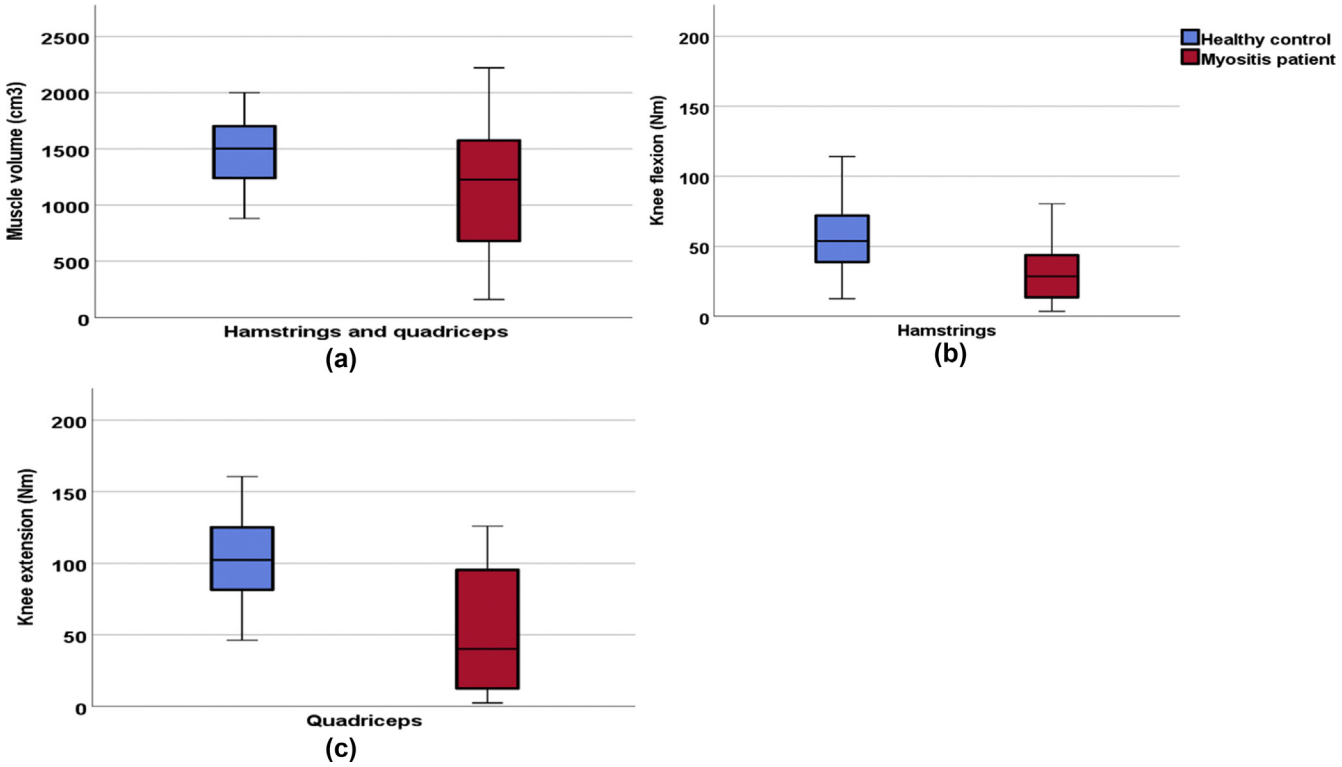

Figure 5 Quantitative muscle volume measurements, knee flexion and extension in 16 myositis patients compared to 16 healthy controls: (a) muscle volume; (b) knee flexion; (c) knee extension.

"unaffected" by a radiologist were compared with healthy controls. This suggests that these measures may be a useful non-invasive measure in the diagnosis and monitoring of myositis. This is corroborated by the ROC analysis area AUC values which, despite not being adequately powered, demonstrate that T2 and FF could be useful in the diagnosis of myositis, in particular T2, which is sensitive to both oedema and fatty infiltration, supporting previous work by Ran *et al.*[12]

T2 was higher in myositis patients compared to healthy controls, which is consistent with previous studies.[10,29] This may be due to the combined effects of increased fat (10,43), inadequately suppressed by the SPAIR fat suppression, and increased fluid due to inflammation.[12] Although the

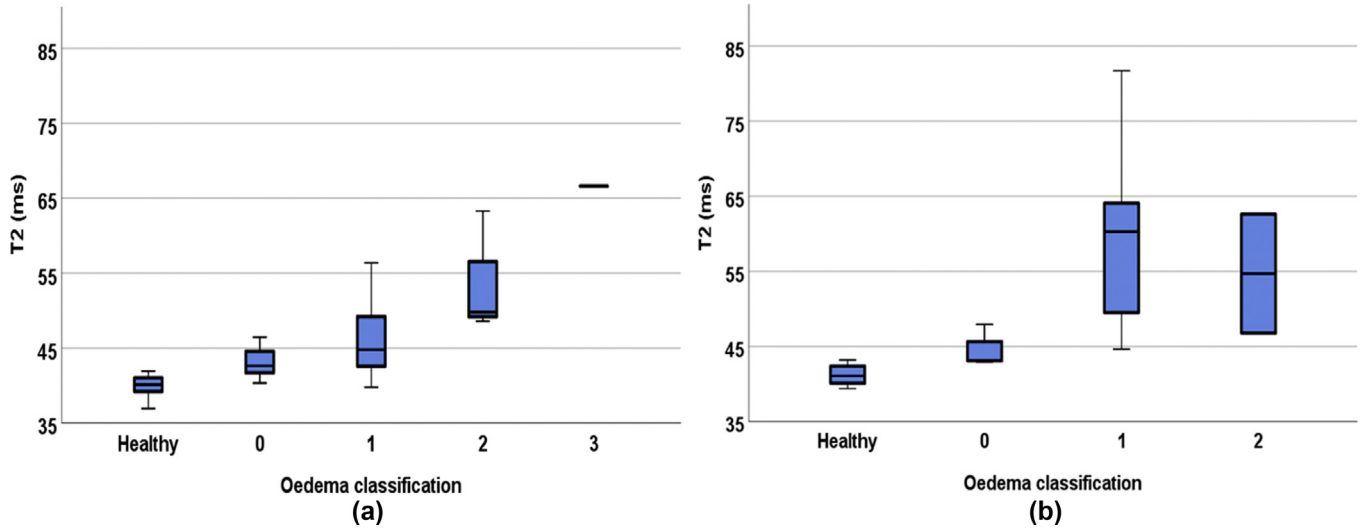

Figure 6 T2 values grouped by radiologists' oedema score compared with values in myositis patients (0, no oedema; 1, mild oedema; 2, moderate oedema; 3, severe oedema) and healthy controls: (a) hamstrings; (b) quadriceps. *Quadriceps had no grade 3 (severe oedema) scored.

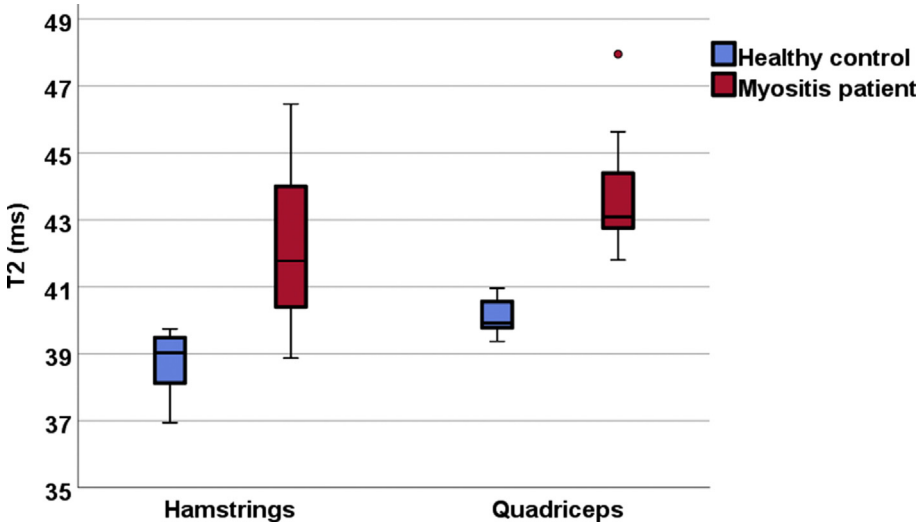

Figure 7 T2 values of patients scored as having unaffected muscles matched with age, and gender-matched healthy controls.

contribution of fat in diseased muscle is clear, the presence of increased fluid is contested. Although most papers, using fat corrected T2 measurements, show increased T2 in myositis.[10,30] Schlaeger *et al.*[31] found that T2 can decrease in neuromuscular disease patients; however, their study sample was heterogeneous including a range of muscular diseases along with myositis.

In the present study, patient T2 values correlated with radiologists' visual scoring of muscle pathology, showing, for the first time, that the changes in T2 agreed with radiological assessment of active disease. The fact that the eight myositis patients, classified as unaffected by radiologists, showed raised T2 compared to healthy controls suggests that there is a certain threshold of muscle pathology that is required before myositis can be detected visually on conventional MRI sequences. This suggests that quantitative T2 measurements could be used in conjunction with the visual assessment of muscle to improve diagnostic sensitivity. In particular, it suggests that relying on subjective assessment of sites of muscle inflammation by radiologists may fail to identify lower-grade inflammation in the muscle and subtle changes in disease activity. It also means that muscles classed as normal by the radiologist may still be a useful target for diagnostic biopsy. Indeed, use of quantitative measures may increase the number of sites available for biopsy and identify sites that are technically less challenging and safer for biopsy.

This study demonstrated for the first time that muscle strength correlated with MRI T2, demonstrating that T2 relaxation times correlate with the severity of the disease as assessed by patient muscle strength; however, the relationship in the present study appears to be bimodal, rather than a gradual linear degrading, giving the plots a characteristic "L-shape". This suggests that after a certain threshold of T2, muscle strength deteriorates at a substantive rate. Further work is needed to better characterise this

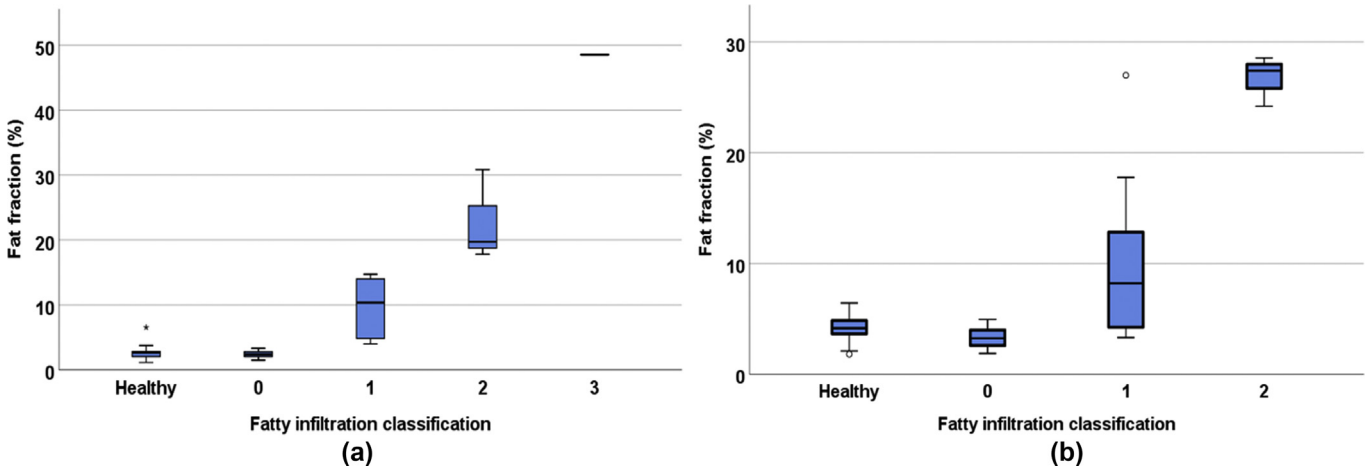

Figure 8 FF values grouped by radiologist's oedema score compared with values in myositis patients (0, no fatty infiltration; 1, mild fatty infiltration; 2, moderate fatty infiltration; 3, severe fatty infiltration): (a) hamstrings; (b) quadriceps. *Quadriceps had no grade 3 (severe fatty infiltration) scored.

relationship. In healthy individuals, T2 had a linear correlation with muscle strength, and lower T2 values were associated with increased strength.

The correlation between FF values and radiologists' scores of fatty infiltration agrees with the literature.[14] Patients' FF values were higher in both the hamstrings and the quadriceps compared to healthy controls, which is consistent with the known fatty infiltration that occurs due to myositis. This study showed for the first time that FF correlated with muscle strength within the quadriceps and the hamstrings in myositis patients. This supports previous studies that have found an inverse relationship between muscle strength and fatty infiltration in Duchenne muscular dystrophy.[32] This suggests that when fatty infiltration increases due to myositis, muscle strength decreases, and this can be identified by MRI FF.

There was a difference in muscle volume between myositis patients and healthy controls and muscle volume correlated with both knee extension and flexion torque in both patients and healthy controls. This confirms that muscle volume and muscle strength are related, and that muscle loss is apparent in myositis. This agrees with previous studies that suggest that muscle volume is an important measure in terms of muscle function, and that interventions such as exercise to increase muscle mass might be beneficial for function and to improve quality of life.[33]

DTI measurements showed no meaningful differences in FA, eigenvalues, or MD between patients and healthy controls, which is in disagreement with previously published work by Ai *et al.*[34] Given that T2 was higher in patients, one might expect to see raised MD due to increased fluid; however, increased cellularity and fatty infiltration, which is known to occur in myositis, have been demonstrated to restrict diffusion[11]

Ai *et al.*[34] used small ROIs over diseased areas as opposed to the ROIs in the present study depicting the entire muscle (Fig 1). The differences in the present results could be due to the competing influences of fat and water across the whole muscle in the large ROIs whereas the measurements by Ai *et al.* would be mainly dominated by reduced MD due to fat in the small ROI focussed on the diseased area. The results from the present sub-study, which utilised small ROIs, support this theory, with an increase in MD in oedematous regions, and a decrease in MD in fatty infiltrated regions,[11,34] This study suggests that diffusion measurements can be useful in the management of myositis, but should be used with small ROIs due to the competing influence of fat and oedema on the measurements.

The present study is subject to some limitations. This study used SPAIR fat suppression, which only achieves robust suppression with the main methylene and methyl peaks. The olefinic fat peak ($\sim$10% of fat signal, T2 $\sim$ 120 ms) will still contribute to the signal. Therefore, it is important to understand that the present T2 measurements will be affected by changes in both fluid and fat levels, resulting in increased T2 values in heavily fat infiltrated muscle.[35,36] Advanced methods for separating fat from T2 measurements have been published in the literature[33,34]; however, these are not widely available clinically. Conversely, the T2 measurements in the present study could be carried out on any clinical MRI system without advanced imaging or post-processing. Analysis of the FF, T2, and diffusion measurements were only made on a single section, raising the possibility of sampling variation if the muscle changes were not homogeneous. Multi-echo sequences are known to overestimate T2 due to the formation of stimulated echoes,[28,37] but are widely used in practice to keep scan times tolerably short for participants. The present study only utilised six diffusion directions to decrease the scan times, whereas 12 directions have been recommended to reduce bias between the encoding and underlying tissue. This could have limited the sensitivity of the present measurements to changes in diffusion.[38] More elegant analysis methods that take the full extended phase graph into account have been used[36,39,40]; however, these methods are complex and not easily available to clinical imaging. The two-point Dixon imaging technique did not correct for T2* effects, eddy currents, noise-related bias, or the spectral complexity of fat. The muscle volume measurements did not consider differences in shape and length of thigh muscles between patients, although an attempt was made to control for these differences by positioning relative to an anatomical reference marker, similar to previous studies[41]; however, work has also been published demonstrating the validity of measuring total muscle volume using one section as frequently reported.[42] As T2, FF, and diffusion were only measured on one section, some differences may be due to differences in relative section position, rather than due to disease induced differences alone.

In conclusion, the present study has demonstrated differences in MRI T2, FF, and muscle volume between patients with DM and PM and matched healthy controls. The present results suggest that these measurements, in particular T2 and FF, could be used as an objective method to monitor muscles. Furthermore, T2, FF, and muscle volume correlated with muscle function, demonstrating for the first time a decrease in muscle function due to inflammation, myosteatosis, and muscle atrophy. In addition, it was shown that T2 measurements are sensitive to differences that may not be detected by radiologists, potentially offering an improvement in the ability of MRI to detect changes in disease activity compared to reliance on subjective assessment. The use of quantitative techniques may also identify additional sites of muscle inflammation to target for diagnostic biopsy. This work will inform future efforts to validate quantitative MRI measurements as a diagnostic and management tool in myositis.

Conflict of interest

The authors declare no conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.crad.2020.08.022.

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