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FULL PAPER

Diffusion tensor imaging in evaluation of thigh muscles in patients with polymyositis and dermatomyositis

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Objective: To explore the diffusion tensor imaging (DTI) characteristics of thigh muscles in patients with polymyositis (PM) and dermatomyositis (DM).

Methods: 12 patients with known PM/DM and 10 healthy volunteers were enrolled in this study. Both DTI and conventional MR sequences were performed on both thighs of all subjects. Apparent diffusion coefficient (ADC), fractional anisotropy (FA) and three eigenvalues were compared between the PM/DM group and the healthy group. One-way analysis of variance and Student's *t*-test were used for statistical analyses with a significance of $p < 0.05$.

Results: In the healthy group, the vastus intermedius muscle showed the highest ADC value and the gracilis (GA) muscle showed the lowest ADC value. These results were statistically significant when compared with other muscles ($p < 0.05$). The GA, semi-tendinosus and semi-membranosus muscles showed higher FA values than the other three thigh muscles ($p < 0.05$). The mean ADC

value and three eigenvalues of oedematous muscles in the PM/DM group were higher on average and showed a statistically significant difference when compared with unaffected (non-oedematous muscles in patients) and normal muscles ($p < 0.05$). There was no statistical difference in the mean FA value between oedematous and normal muscles. The mean ADC, FA and three eigenvalues in unaffected muscles (in patients) showed no statistical differences from those in normal muscles ($p > 0.05$).

Conclusion: DTI can be used to quantitatively evaluate the anisotropic diffusion characteristics of muscles in patients with PM/DM.

Advances in knowledge: A new application of DTI is proposed for inflammatory myopathies. The results show that ADC and the three eigenvalues were significantly different between diseased and normal muscles, a finding of potential value in both diagnosis and treatment monitoring of myopathies.

Polymyositis (PM) and dermatomyositis (DM) are two common idiopathic inflammatory myopathies. In the past, the diagnosis of PM/DM depended primarily on clinical features, enzyme levels within the blood, electromyogram and muscle biopsies.¹⁻³ Recently, MRI has been proven to be valuable in evaluating patients with PM/DM.⁴⁻⁶ Using traditional sequences, MRI is able to detect muscle oedema and fat infiltration/fatty replacement in muscles, with high spatial resolution and superior soft-tissue contrast compared with other imaging modalities.⁷⁻⁹

However, conventional MR techniques, such as T_2 weighted imaging and short tau inversion recovery, are limited to providing qualitative information, as opposed to quantitative information, which is important for the early detection of

inflammatory changes in these diseases. The findings of PM/DM on traditional MRI images are non-specific, making it difficult to distinguish PM/DM from other myopathies on MRI. In addition, the muscular microstructure needs to be evaluated for staging and therapy monitoring in clinical practice.

Diffusion tensor imaging (DTI) is an advanced functional MRI technique that has been used to evaluate the anisotropic diffusion characteristics of tissues, such as fibre bundles of white matter and peripheral nerves. Skeletal muscle fibres are cylindrical and well ordered along a specific direction, with the longitudinal axis significantly longer than the transverse axis. Therefore, the diffusion of water molecules in the muscle fibres is faster along the longitudinal

axis than along the transverse axis because of the restrictions from the muscle cell membrane (sarcolemma) laterally. Based on these theories, DTI has also been successfully applied in the evaluation of skeletal muscles with quantitative measurements of muscular microstructure and physical function.^{10,11}

In PM/DM, muscle degeneration and inflammatory cell infiltration in the muscle fibres are typical pathological changes that could affect the diffusion of water molecules within muscles. In this study, we aimed to investigate the anisotropic diffusion characteristics of thigh muscles in patients with PM/DM using DTI and to compare it with DTI in healthy volunteers.

METHODS AND MATERIALS

Patients and healthy controls

This study was approved by the institutional review board. Written informed consent was obtained from all subjects. The PM/DM group consisted of 12 consecutive patients who were referred to Tongji Hospital, Wuhan, China from 2011 to 2012. The patients were seven females and five males, ranging in age from 15 to 63 years with an average age of 38 years. Muscle biopsies of all 12 patients were used to verify the pathology of either PM or DM (7 patients were found to have PM and 5 DM). MR examinations were performed within 6 months of diagnosis of each patient. All patients demonstrated increased serum level enzymes consistent with the active stage of PM/DM disease. In addition, ten healthy volunteers without PM/DM (six females and four males) were enrolled as a healthy group with ages ranging from 24 to 60 years and an average age of 32 years. There were no significant differences in age and sex between the two groups.

MRI technique

Both DTI and conventional MR were performed on a 3-T MR system (Signa® HDxt; GE Healthcare, Milwaukee, WI) utilizing an eight-channel TORso body coil. The thighs, bilaterally, were scanned for each subject. First, conventional axial T_1 weighted MR images [repetition time (TR)/echo time (TE), 440/10.8 ms] and T_2 weighted MR images (TR/TE, 3800/70 ms) with fat suppression were acquired using a fast spin echo sequence in order to depict the anatomical structures and detect muscle oedema. Then, DTI MR images were acquired using an echo planar imaging (EPI) sequence with 15 gradient directions. The acquisition parameters for DTI were as follows: b -value, 500 s cm^{-2} ; TR/TE, 6000/62.2 ms; field of view, $38 \times 38 \text{ cm}^2$; number of excitations, two; matrix, 192×160 ; slice thickness, 6 mm; and no slice gap. Each DTI acquisition had an imaging time of about 4 min, and the total scan time for each subject was around 20 min.

Image analysis

The thigh muscles mainly consist three groups, the anterior group, posterior group and medial group. Two muscles from each group were selected to be evaluated: vastus medialis (VM), vastus intermedius (VI), adductor magnus (AD), gracilis (GA), semi-tendinosus (ST) and semi-membranosus (SM). In total, 144 muscles in the PM/DM group and 120 muscles in the healthy group were evaluated.

The measurement of DTI parameters was completed using a function tool on an off-line workstation (ADW4.4; GE Healthcare).

The reader was blinded to clinical information and group when measuring the DTI parameters. Circular regions of interest (ROIs; 70 mm^2) were placed on the selected muscles according to the following rules:

- (1) In PM/DM patients with diffuse muscle oedema, the middle slice, which contained the largest area of the selected muscles, was chosen to place the ROIs.
- (2) In PM/DM patients with focal muscle oedema, the slice that contained the largest area of muscle oedema was selected, and the ROIs were placed at the centre of the oedematous area.
- (3) In both healthy volunteers and PM/DM patients with unaffected muscles, the middle slice was chosen to place the ROIs.

After ROI placement, the following parameters were measured for selected muscles in the DTI images: apparent diffusion coefficient (ADC), three eigenvalues (λ_1 , λ_2 and λ_3) and fractional anisotropy (FA). The differences of these parameters within the healthy volunteer group and between the PM/DM and healthy volunteer group were compared separately.

Statistical analysis

The results were presented as mean $\pm$ standard deviation. A one-way analysis of variance was used to compare the ADC and FA among the six muscles in the healthy volunteer group. The comparisons of ADC, FA and three eigenvalues between the patient group and the controls were conducted using Student's t -test. The statistical significance was set to $p < 0.05$ for all analyses.

RESULTS

In the healthy volunteer group, the mean ADC, FA and three eigenvalues (λ_1 , λ_2 and λ_3) were 1.71 ± 0.12 , 0.29 ± 0.05 , 2.26 ± 0.29 , 1.63 ± 0.21 and 1.24 ± 0.17 , respectively, for all evaluated thigh muscles. The detailed results for each muscle are shown in Table 1. The mean ADC value of the VI muscle was higher, and the difference was statistically significant when compared with other muscles, with the exception of the ST muscle ($p < 0.05$). The GA muscle had a lower average mean ADC value than do the other muscles, and the difference was statistically significant ($p < 0.05$). The GA, ST and SM muscles had higher FA values than the VM, VI and AD muscles, and this difference was found to be statistically significant ($p < 0.05$).

In the PM/DM group, there were 7 (of 12, or 58.3%) patients with diffuse muscle oedema and 5 (of 12, or 41.7%) patients with multifocal muscle oedema. In total, there were 102 (of 144, or 70.8%) oedematous muscles and 42 (of 144, or 29.2%) unaffected (non-oedematous) muscles detected with conventional MR images (Figure 1). The average ADC values were 1.97 ± 0.19 for all oedematous muscles and 1.72 ± 0.11 for all unaffected muscles. The GA had a lower mean ADC than do the other muscles, and this was significant to the other muscles except SM. The average FA values were 0.29 ± 0.05 for all oedematous muscles and 0.28 ± 0.05 for all unaffected muscles, respectively. The three measured eigenvalues (λ_1 , λ_2 and λ_3) were 2.56 ± 0.30 , 1.90 ± 0.21 , 1.44 ± 0.17 for all oedematous muscles and 2.25 ± 0.25 , 1.65 ± 0.10 , 1.24 ± 0.12 for all unaffected muscles. The

Table 1. Mean and standard deviation values of apparent diffusion coefficient (ADC), fractional anisotropy (FA) and three eigenvalues in normal muscles (control group)

DTI parameters	VM	VI	AD	GA	ST	SM	Average
ADC ($10^{-3} \text{ mm}^2 \text{ s}^{-1}$)	1.69 ± 0.06	1.85 ± 0.08^a	1.74 ± 0.06	1.54 ± 0.09^b	1.76 ± 0.06	1.67 ± 0.12	1.71 ± 0.12
FA	0.26 ± 0.01	0.25 ± 0.03	0.25 ± 0.01	0.33 ± 0.03^c	0.35 ± 0.05^c	0.33 ± 0.05^c	0.29 ± 0.05
λ_1 ($10^{-3} \text{ mm}^2 \text{ s}^{-1}$)	2.15 ± 0.10	2.35 ± 0.14	2.20 ± 0.08	2.09 ± 0.29	2.39 ± 0.25	2.29 ± 0.21	2.26 ± 0.29
λ_2 ($10^{-3} \text{ mm}^2 \text{ s}^{-1}$)	1.63 ± 0.08	1.81 ± 0.09	1.69 ± 0.04	1.48 ± 0.18	1.63 ± 0.10	1.54 ± 0.12	1.63 ± 0.21
λ_3 ($10^{-3} \text{ mm}^2 \text{ s}^{-1}$)	1.27 ± 0.09	1.38 ± 0.08	1.31 ± 0.11	1.05 ± 0.10	1.20 ± 0.06	1.18 ± 0.11	1.24 ± 0.17

AD, adductor magnus; DTI, diffusion tensor imaging; GA, gracilis; SM, semi-membranosus; ST, semi-tendinosus; VI, vastus intermedius; VM, vastus medialis.

^aThe mean ADC value for VI muscles was significantly greater than those of the other muscles, except ST muscles ($p < 0.05$).

^bThe mean ADC value for GA muscles was significantly lower than those of the other muscles, except SM muscles ($p < 0.05$).

^cThe mean FA values of GA, ST and SM muscles were significantly greater than those of VM, VT and AD muscles ($p < 0.05$).

detailed results for each muscle can be seen in Table 2. The mean ADC values and three eigenvalues (λ_1 , λ_2 and λ_3) of all oedematous muscles were higher on average than those of all unaffected muscles and all normal muscles, with this difference also statistically significant (Figure 2). Compared with normal muscles, the oedematous muscles showed a 15.8% increase in ADC value and 12.8%, 15.9% and 16.9% increase in λ_1 , λ_2 and λ_3 , respectively. The statistical results for the pairwise comparisons between oedematous muscles and normal muscles are given in Table 3.

There was no statistical difference in the mean FA values among oedematous (0.29 ± 0.05), unaffected (0.28 ± 0.05) and normal (0.29 ± 0.05 ; $p = 0.10$) muscles. Additionally, there were no statistical difference in the ADC, FA and the three eigenvalues between unaffected and normal muscles.

DISCUSSION

DTI in skeletal muscles is feasible owing to the orientation of their fibres, which run lengthwise, within these muscles. Recently, DTI has been used to determine the characteristics of normal and abnormal muscles in both humans and animals.^{12–18} In this study, DTI as an imaging tool was used to evaluate human inflammatory myopathies, which to our knowledge has not been reported before.

In this study, two muscles from each group of thigh muscles were selected to be assessed for each subject. These muscles included the VM, VI, AD, GA, ST and SM. There are three additional muscles in the thigh (vastus lateralis, rectus femoris and biceps femoris) that were not included because of the difficulty associated with imaging them. The primary difficulty in

Figure 1. A 28-year-old female patient with dermatomyositis. T_1 weighted (WI) (a), fat-suppression T_2 WI (b) and diffusion tensor imaging (c) images reveal multiple focal lesions with both muscle oedema and subcutaneous tissue oedema, and thickening and oedema of muscular fasciae. Using a colour scale, depiction of apparent diffusion coefficient (d) and the three eigenvalues (λ_1 , λ_2 and λ_3 corresponding to f–h) demonstrated that the diffusion of oedematous muscle was significantly higher than that of the unaffected muscle [regions of interest (ROIs) 1 vs ROI 2]. Fractional anisotropy mapping (e) showed no significant difference between oedematous muscle and unaffected muscle. An overlay of the muscle fibres (j) are viewed in a three-dimensional sagittal image. The fibres were tracked from an elliptical ROI of oedematous muscle (i, arrow).

Table 2. Mean and standard deviation values of apparent diffusion coefficient (ADC), fractional anisotropy (FA) and three eigenvalues in diseased muscles and unaffected muscles (patient group)

Parameters	Vastus medialis	Vastus intermedius	Adductor magnus	Gracilis	Semi-tendinosus	Semi-membranosus	Average
ADC							
Oedematous	1.97 ± 0.18	2.14 ± 0.17	1.94 ± 0.16	1.90 ± 0.17	1.97 ± 0.17	1.87 ± 0.15	1.97 ± 0.19
Unaffected	1.69 ± 0.10	1.81 ± 0.07	1.74 ± 0.06	1.63 ± 0.15	1.76 ± 0.07	1.72 ± 0.05	1.72 ± 0.11
<i>p</i> -value	<0.001	<0.001	<0.001	<0.001	<0.001	0.005	<0.001
FA							
Oedematous	0.25 ± 0.03	0.25 ± 0.03	0.25 ± 0.04	0.31 ± 0.05	0.34 ± 0.08	0.30 ± 0.06	0.29 ± 0.05
Unaffected	0.24 ± 0.02	0.26 ± 0.08	0.25 ± 0.03	0.32 ± 0.08	0.34 ± 0.07	0.28 ± 0.03	0.28 ± 0.05
<i>p</i> -value	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05
λ_1							
Oedematous	2.51 ± 0.23	2.68 ± 0.24	2.46 ± 0.23	2.50 ± 0.25	2.72 ± 0.36	2.50 ± 0.24	2.56 ± 0.30
Unaffected	2.24 ± 0.10	2.41 ± 0.14	2.19 ± 0.10	2.20 ± 0.34	2.39 ± 0.25	2.25 ± 0.14	2.25 ± 0.25
<i>p</i> -value	0.002	0.005	0.002	<0.05	0.02	0.005	0.02
λ_2							
Oedematous	1.97 ± 0.16	2.10 ± 0.27	1.87 ± 0.14	1.81 ± 0.18	1.87 ± 0.12	1.76 ± 0.12	1.90 ± 0.21
Unaffected	1.62 ± 0.11	1.73 ± 0.09	1.68 ± 0.07	1.56 ± 0.12	1.68 ± 0.09	1.62 ± 0.06	1.65 ± 0.10
<i>p</i> -value	<0.001	<0.001	<0.001	<0.001	<0.001	0.002	0.002
λ_3							
Oedematous	1.43 ± 0.15	1.63 ± 0.19	1.49 ± 0.09	1.37 ± 0.14	1.33 ± 0.11	1.36 ± 0.12	1.44 ± 0.17
Unaffected	1.22 ± 0.11	1.29 ± 0.08	1.34 ± 0.07	1.13 ± 0.11	1.19 ± 0.09	1.28 ± 0.07	1.24 ± 0.12
<i>p</i> -value	<0.001	<0.001	<0.001	<0.001	0.005	<0.05	0.005

Figure 2. Comparisons of the mean apparent diffusion coefficient (ADC) value and three eigenvalues (λ_1 , λ_2 and λ_3) among oedematous muscles, unaffected muscles and normal muscles. The mean ADC value and three eigenvalues were significantly higher in oedematous muscles than in unaffected muscles and normal muscles ($p < 0.05$). There were no statistical differences in the mean ADC values and three eigenvalues between unaffected muscles and normal muscles. *indicates statistically significant differences ($p < 0.05$). DTI, diffusion tensor imaging.

imaging these muscles is that the fat signal cannot be fully suppressed when an EPI sequence with fat suppression is used to obtain DTI images, in particular, at the edges of the radio-frequency coil. Additionally, chemical shift artefacts are more pronounced in the three excluded muscles, making their evaluation difficult.

The mean ADC value of all selected muscles was $1.71 \pm 0.12 \text{ mm}^2 \text{ s}^{-1}$ in the healthy volunteer group. Kermarrec et al¹⁴ reported that the mean ADC value of all thigh muscles was $1.83 \text{ mm}^2 \text{ s}^{-1}$ in healthy volunteers. Our result is slightly lower than that reported by Kermarrec et al,¹⁴ but the mean FA value in our study is slightly higher than what was reported (0.29 vs 0.26). These subtle differences in ADC and FA values may result from the differences in imaging parameters and sampling error. In this

study, the GA, ST and SM muscles showed higher FA values than those of the other three muscles (VM, VI and AD). These results are similar to those obtained in the Kermarrec's study.¹⁴ It is well known that the uniformity of muscle fibres results in a higher degree of anisotropy and consequently a higher FA value. Thus, the arrangement of the muscle fibres in the GA, ST and SM muscles are assumed to have a more defined fibre track with higher uniformity than do the other three muscles. A reason for the lower FA values in the VM, VI and AD muscles could be owing to their pennate structure.

For oedematous muscles, ADC values and three eigenvalues were significantly different and were larger than those of normal and unaffected muscles. The increased diffusion of water molecules in oedematous muscles reflects active inflammation. The pathological changes in PM/DM are characterized by degeneration and regeneration of muscle fibres, necrosis, inflammatory cell infiltration and fibrous hyperplasia.^{1,19} In this study, compared with normal muscles, oedematous muscles showed a 15.8% increase in ADC. This result is similar to a previous study, in which the authors reported that ADC in inflamed muscles was increased by 15% compared with that in unaffected muscles.²⁰ The eigenvalues of oedematous muscles compared with normal muscles were also larger suggesting that water diffusion increased in all three directions owing to active inflammation within the muscles. The eigenvalues in our study represent those of typical eigenvalues as seen in other studies. As defined in previous studies, our eigenvalues represent the following. λ_1 is defined as the diffusivity along the longitudinal orientation parallel to the muscle fibres.²¹ Meanwhile, λ_2 and λ_3 are assumed to represent the diffusivity within the endomysium along the perpendicular orientation to the muscle fibres, and λ_3 is associated with the diameter of a single muscle fibre.¹³

Inflammation can result in an increase in water content and an increase in the transmembrane movement of water molecules across endomysium and sarcolemma within muscles. Thus, the increase of λ_2 (15.9%) and λ_3 (16.1%) is most likely in response to the inflammatory infiltration within muscles. In addition, inflammatory degeneration can cause cellular swelling and increased extracellular space in the early stages of PM/DM, this likely further increases λ_3 . The increase in λ_1 (13.8%) values was

Table 3. The statistical results of the Student's *t*-test between oedematous muscles and normal muscles

Muscles	Apparent diffusion coefficient		Fractional anisotropy		λ_1		λ_2		λ_3	
	<i>t</i>	<i>p</i> -value	<i>t</i>	<i>p</i> -value	<i>T</i>	<i>p</i> -value	<i>t</i>	<i>p</i> -value	<i>T</i>	<i>p</i> -value
Vastus medialis	5.94	<0.001	0.560	0.583	4.72	<0.001	6.350	<0.001	4.96	<0.001
Vastus intermedius	5.30	<0.001	-0.098	0.923	3.82	0.001	3.340	0.003	4.41	<0.001
Gracilis	4.23	<0.001	-0.110	0.917	3.45	0.004	4.010	0.002	3.96	0.001
Adductor magnus	3.76	0.002	-1.580	0.132	2.63	0.018	3.380	0.004	5.27	<0.001
Semi-tendinosus	4.86	<0.001	-0.190	0.854	2.16	0.044	5.140	<0.001	3.59	0.002
Semi-membranosus	3.56	0.002	-1.140	0.268	2.22	0.038	4.340	<0.001	3.72	0.001
Average	9.88	<0.001	-1.660	0.100	6.52	<0.001	7.920	<0.001	7.56	<0.001

lower than in λ_2 and λ_3 values. A potential reason for this smaller increase is the length of the muscle fibres are far greater than the diffusion distance of water molecules; therefore, the increase in water content is the primary contributor to the increase in λ_1 . A more detailed explanation of the mechanisms of the increase in the third eigenvalue is beyond the scope of this article and would require further studies.

The FA value showed no statistical significance in terms of a difference between the oedematous muscles and normal muscles evaluated. DTI in muscles relies on the presence of uniformly ordered muscle fibres; the FA value is one of the parameters that reflects the degree of anisotropy within these muscle fibres. Thus, the results in our study indicated that the structure and orientation of muscle fibres in PM/DM were not destroyed despite the occurrence of denaturation, necrosis and regeneration within the PM/DM-affected muscles.

The major limitation of this study is a relatively small patient population. In addition, only b -value = 500 s cm⁻² was used for

the measurement of ADC parameters, which comes from our preliminary experience and may not be the optimal choice for the imaging evaluation of the varying inflammatory myopathies. Currently, an ongoing project is underway to expand the applications of biexponential ADCs involving a wide range of inflammatory myopathies.

In conclusion, the increase in eigenvalues related to DTI images of PM/DM vs normal thigh muscles can be explained at the molecular level providing a new perspective in relation to PM/DM disease. By measuring the anisotropic diffusion characteristics, the diseased muscles in PM/DM can be distinguished from the unaffected and normal muscles. Further studies could potentially use DTI to show distinction between PM/DM and other causes of muscle myopathies.

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