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FULL PAPER

The diagnostic value of T_2 maps and rs-EPI DWI in dermatomyositis

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Objective: To explore and confirm feasibility the T_2 maps and readout-segmented echoplanar imaging (rs-EPI) diffusion-weighted imaging (DWI) characteristics of the thigh muscles for dermatomyositis (DM) patients.

Methods: This study was approved by the University Institutional Review and written informed consent was obtained from all subjects before enrollment (trial registration number: TJ-C20121221). 28 patients with DM proven by diagnostic criteria were enrolled in the study along with 9 healthy control subjects. Conventional MR, T_2 maps and rs-EPI DWI were obtained for all subjects. Both of T_2 and apparent diffusion coefficient (ADC) values for thigh muscles were compared between the DM and healthy control groups. The amount of inflammation and fatty infiltration were respectively assigned a score of 0 to 5 for all thigh muscles. The Kruskal-Wallis tests were utilized and the Spearman correlation coefficients models were used to correlate both of the T_2 and ADC value with non-quantitative MRI. P -values <0.05 reflected statistical significance.

Results: Both of the T_2 and ADC values among all affected muscles, unaffected muscles and the control groups were respectively statistical difference ($p < 0.05$ respectively), the T_2 value of affected muscles was greater than that of unaffected muscles in DM patients ($p < 0.05$). Differences of the T_2 value in DM patients among the combination the edematous with fatty infiltration score groups were statistically significant ($p < 0.001$). The T_2 value showed a significant correlation with the non-quantitative MRI score for edema and fatty infiltration.

Conclusions: T_2 maps may have a specialized ability for the detection severity of damaged muscles in comparison to the rs-EPI DWI sequence.

Advances in knowledge: A new application of rs-EPI DWI is proposed for DM patients. First, comparison of T_2 maps and rs-EPI DWI technology are applied for DM. The results demonstrate that T_2 maps may be more potential value in determining the severity of diseased muscles for DM patients.

INTRODUCTION

Dermatomyositis (DM) is an autoimmune myositis (AIM), which is a group of heterogeneous systemic connective tissue diseases, DM is a rare disease but affects both children and adults with an overall female/ male ratio of about 2:1.^{1,2} The precise etiology is still unknown, and the hallmark histopathological criterion is the infiltrate with inflammatory cells of perivascular or the interfascicular and fascicles.³ Conventional and primary procedures for diagnosis and therapeutic evaluation are limited by subjectivity and low specificity.⁴

MRI has become a non-invasive tool and widely used for patients with inflammatory myopathies.⁵ Non-quantitative MRI has been used to characterize the pattern of edema and fatty infiltration within muscles for AIM patients by using T_1 weighted and T_2 weighted with fat suppression, which

is considered to be a subjective method to assess disease severity. Given the diffuse extent and variable intensity of characteristic muscles signal changes, the conventional MRI of muscles may be challenging. MR further enables assessment of changes in degree of muscles inflammation and provides a detailed anatomic view of disease activity.⁶ T_2 maps is considered to be a quantitative MRI technique, which could measure altered water binding related to tissue physiologic or pathologic macromolecular environmental change.⁷ Diffusion-weighted imaging (DWI) as a specialized MRI technique, could provide molecular information regarding fluid motion in tissues. Readout-segmented echo-planar imaging (rs-EPI) diffusion weighted imaging with either sensitivity-encoding or generalized autocalibrating partial parallel acquisition (GRAPPA) could contribute to reducing artifacts in comparison to single-shot EPI (ss-EPI).^{8,9} This parallel imaging technique has been used

to detect tumors in brain, breast and prostate, particularly, the smaller focal tumors.^{10,11} Therefore, our study was to analyze T_2 maps and rs-EPI DWI of thigh muscles, to try to confirm a characteristic disease and to identify the most appropriate technique for disease severity in DM.

METHODS AND MATERIALS

Study population

This study was approved by the University Institutional Review. Written informed consent was obtained from all subjects before enrollment. 9 healthy subjects (four males, five females, mean age, 35 years, range 15–38 years), 28 patients with DM (nine males, 19 females, mean age, 46 years, range 6–67 years) were evaluated in this study. The International Myositis Assessment and Clinical Studies Group criteria were utilized to establish the diagnosis of DM.¹²

MRI protocol

Imaging was performed for all participants on a 3.0 T MR system (Magnetom Skyra, Siemens Healthcare, Germany). The subjects were placed in foot-first supine position on the MRI scanner table with an 18-element body matrix coil and in-built 32-element spinal matrix coil covering both thighs. All participants were asked to limit activity and have a rest for 30 min before the MRI examination. Total combined scan time of the non-quantitative MRI, T_2 maps and rs-EPI DWI sequences was around 20 min.

The conventional MRI study included a fast spin-echo T_2 weighted with spectral fat suppression sequence in the axial plane (repetition time/echo time (TR/TE), 2400/84 ms; matrix, 240×320 ; section thickness, 8 mm; section gap, 2.4 mm) and a short TI inversion recovery magnitude weighted sequence in the coronal plane (TR/TE, 3160/38 ms; inversion time, 230 ms; section thickness, 7 mm; section gap, 1.4 mm, section number, 30). Conventional axial T_1 weighted images were obtained without fat suppression (TR/TE, 530/11 ms, matrix, 176×384 ; section thickness, 8 mm; section gap, 2.4 mm, section number, 30). The field of view (FOV) ranged from 36 to 40 cm was determined according to the patient's size.

Axial T_2 maps were obtained using a T_2 weighted multisection multiecho sequence¹³ with an echo train length of eight and the following parameters: TE/TR, 1370/10.7, 21.4, 32.1, 42.8, 53.5, 64.2, 74.9, 85.6 ms; matrix, 160×320 ; section thickness, 8 mm; section gap, 2.4 mm; and FOV, 36–40 cm.

Axial rs-EPI DWI of thigh was performed on the same center slice positions to the axial T_2 maps. The total number of slices was 50 with a slice thickness of 5 mm and a slice gap of 1 mm. The FOV was 36–40 cm; matrix, 96×192 ; TR/TE, 5000/53 ms. DWI with b -value of 500 s mm^{-2} was acquired, a GRAPPA of two and five readout segments were used.

Imaging data analysis

All imaging were presented at a digital workstation (Syngo Multi-Modality Workplace VE40B, Siemens Healthcare) and reviewed in consensus by two musculoskeletal radiologists with more than 10 years' experience. The radiologists were blinded to clinical data and

pathology information, and evaluated non-quantitative MR, T_2 maps and rs-EPI DWI imaging characteristics. With use of the axial T_1 weighted and T_2 weighted with fat suppression images, edema and fatty infiltration of the thigh musculature were respectively subjectively graded by using a version of the scale described by Stramare¹⁴ and Mercuri et al.¹⁵ The degree of muscles edema was assessed from 0 to 4 scale (total score 5), namely from unaffected to moderate intrafascicular global edema changes: 0, unaffected (score 0); 1, mild, interfascicular (score 1); 2A, mild, intrafascicular, segmented (score 2); 2B, mild, intrafascicular, global (score 3); 3, moderate, intrafascicular, segmented (score 4); 4, moderate, intrafascicular, global (score 5). And the fatty infiltration and distribution within muscles of thigh were stage by 4 (total score 5), as follows: Stage 0, unaffected appearance (score 0); Stage 1, mildly-predominantly homogeneous muscle signal intensity with minimal scattered fatty infiltration (score 1); Stage 2A, moderate moth-eaten appearance with numerous scattered T_1 hyperintense areas (score 2); Stage 2B, severely moth-eaten appearance with numerous confluent areas of T_1 hyperintensity (score 3); Stage 3, confluent areas of signal hyperintensity (score 4) and Stage 4, complete fatty degeneration with replacement of muscle by connective tissue and fat (score 5).

Circular regions of interest ranged from 70 to 100 mm^2 was semiautomatically drawn according to the axial T_1 weighted and T_2 weighted with fat suppression imaging in an affected and unaffected area within 11 muscles (vastus lateralis, vastus intermedius, vastus medialis, rectus femoris, sartorius, long head of biceps femoris, semitendinosus, semimembranosus, adductor longus, adductor magnus and gracilis) in both thighs and copied to the corresponding T_2 maps and rs-EPI DWI, thus yielding an average T_2 relaxation time and apparent diffusion coefficient (ADC) value for affected muscles, unaffected muscles and healthy muscles.

Statistical analysis

Commercial statistics software package (SPSS21.0, Chicago, IL) was used to analyze all data. The T_2 values of thigh muscles are demonstrated as medians and a range of percentiles from 25 to 75% (Md, P_{25} – P_{75}). The Kruskal–Wallis tests were applied to analyze parameters of T_2 and ADC value differences among the three groups (including the affected muscle group, the unaffected muscle group, and the normal muscle group) and the score groups (score 0–10 groups) of edema and fatty infiltration within muscle. The correlation between T_2 relaxation times and ADC values are respectively to non-quantitative MRI by using the Spearman correlation coefficients model. Positive and negative correlations were evaluated. P -values < 0.05 were considered statistically significant.

RESULTS

There were no statistically significant differences in age and gender distribution between the healthy control group and the DM group. 1 of 28 DM patients was juvenile, it is reported that up to 40% juvenile dermatomyositis patients have long-term dystrophic calcification and functional disability.¹⁶ The typical DM affected and healthy muscles have been demonstrated in Figure 1.

Figure 1. Images in a 36-year-old male with DM and a 25-year-old healthy female. (A, B) show T_1 weighted and T_2 weighted with fat suppression of normal skeletal muscles from the healthy female. (C, D) show T_1 weighted and T_2 weighted with fat suppression of edema, fatty infiltration and atrophy within skeletal muscles from the DM patient. DM, dermatomyositis.

In the DM group, 360 of 616 muscles were affected and 256 of 616 muscles were unaffected on conventional MR images. Comparisons of the T_2 relaxation time and ADC values between the affected muscles, unaffected muscles and healthy muscles were shown in Table 1. The T_2 relaxation times and ADC values of all affected muscles and the unaffected muscles in DM patients were respectively higher than those of the healthy muscles group ($p < 0.05$), the T_2 value of the affected muscles was also greater than the unaffected muscles in DM patients ($p < 0.05$) (Figure 2), but the ADC value was not statistical difference between the affected and unaffected muscles groups ($p > 0.05$) (Figure 3).

The thigh muscles were assessed from 0 to 10 score groups according to the edema and fatty infiltration within thigh musculature. The score of thigh muscles in DM patients were as follows: score 0, namely unaffected muscles, 50 muscles; score 1, 70 muscles; score 2, 100 muscles; score 3, 84 muscles; score 4, 105 muscles; score 5, 133 muscles; score 6, 51 muscles, score 7, 23 muscles, and score 8–10 was respectively 0 muscle. The T_2 relaxation time and ADC value of score 0 were respectively (41.75, 40.00~45.25) ms and (1.81, 1.67~1.88) ($\times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$); score 1 were respectively (47.80, 41.70~56.10) ms and (1.75, 1.62~1.86) ($\times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$); score 2 were (47.30, 42.625~52.675) ms and (1.75, 1.62~1.85) ($\times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$); score 3 were (46.90, 42.20~56.08) ms and (1.75, 1.64~1.89) ($\times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$); score 4 were (54.30, 44.55~65.65) ms and (1.76, 1.65~1.87) ($\times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$); score 5 were (63.50, 48.85~77.80) ms and (1.77, 1.65~1.86) ($\times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$); score 6 were (78.20, 59.80~89.80) ms and (1.76, 1.64~1.87) ($\times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$), and score 7 were (85.80, 66.80~93.70) ms and (1.71, 1.59~1.77) ($\times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$). There was a significant difference for the T_2 relaxation time among these score groups, and ordinal non-quantitative MRI score of edema and fatty infiltration ($r = 0.519$, $p < 0.001$) (Figure 4), this

suggests that the T_2 relaxation time correlates with an increase in disease severity. The ADC values were not statistical different among these score groups ($p < 0.05$) (Figure 5).

DISCUSSION

MR T_2 maps has been shown to be reproducible across institutions, different MR systems, and field strengths.¹⁷ DWI has been widely used in the field of neuroradiology,¹⁸ and ss-EPI with susceptibility artifacts and a low signal-to-noise ratio was commonly used in clinical, which has not an ability to achieve good spatial resolution, particularly at high field strengths or tissue-air boundaries, as a result, the smaller focal disease might not be detected.¹⁹ GRAPPA-accelerated rs-EPI DWI has been reported²⁰ as an alternative approach to high-resolution DWI with the best balance of imaging speed and quality.

In the present study, female patients were more than male, which is similar to epidemiology studies.³ Statistically differences both of the MRI T_2 and ADC values between the affected muscles, unaffected muscles in DM patients and control muscles in healthy volunteers were confirmed, and the MRI T_2 relaxation times and ADC values both of the affected muscles and unaffected were respectively higher on average than those of the control muscles group. These results confirmed that T_2 relaxation time and ADC value measurements may be as markers of musculature active inflammation for DM patients. Intramuscular edema is may be due to increased intra- or extracellular free water. A spatial compartmentation of water into intra- and extracellular spaces may be result in the change of the origin of T_2 value of tissue, and the T_2 transverse relaxation times of inflamed or edematous muscles are longer than those of normal muscle have been convincingly demonstrated by some studies.^{21–23} ADC represents the combined effects of dephasing from random water

Table 1. Medians with a range of percentiles from 25 to 75% and the statistical parameters both of T_2 relaxation time and ADC value in affected muscles, unaffected muscles and healthy muscles groups

Parameters	Groups			<i>p</i>
	Affected muscles	Unaffected muscles	Healthy muscles	
T_2 relaxation time (ms)	62.90 49.00~77.98	44.80 40.80~49.50	40.90 36.58~48.00	<0.001
ADC value($\times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$)	1.7 1.71.65~1.90	1.7 51.64~1.83	1.6 91.62~1.78	<0.001

ADC, apparent diffusion coefficient.

ADC value 1.77 1.75 1.69 24.327 < 0.001

($\times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$) 1.65 1.90 1.64 1.83 1.62 1.78

Figure 2. Graph illustrating the comparison of the T_2 relaxation time among edematous muscles, unaffected muscles and normal muscles. ★★: indicates the T_2 value both of affected and unaffected muscles were significantly higher than that of normal muscles ($p < 0.05$). ★: indicates the T_2 value was significantly higher in unaffected muscles than in normal muscles ($p < 0.05$).

Figure 3. Graph illustrating the comparison of the ADC value among affected muscles, unaffected muscles and normal muscles. ★: indicates the ADC value both of affected and unaffected muscles were significantly higher than that of normal muscles ($p < 0.05$). The ADC value was no statistical difference between affected muscles and unaffected muscles ($p > 0.05$). ADC,apparent diffusion coefficient.

diffusion within both of intra- and extracellular, which is also related to water content in tissue.^{24,25} Inflamed myopathies for AIM are a group of muscle diseases characterized histologically by the presence of inflammatory cells surrounding and invading

Figure 4. Graph shows correlation between T_2 value and non-quantitative MRI score for 28 DM patients. DM, dermatomyositis.

non-necrotic muscle fibers, which pathologic state may increase sarcolemma permeability, and resulting in increased intracellular free water, with increased T_2 relaxation times and ADC value of muscle tissue. Finding on muscle biopsy have showed that deposition of membrane attack complex on endomysial capillaries with a subsequent reduction in capillary density, leading to muscle tissue ischemia and infarcts nearby. In early stages of disease, this ischemic microangiopathy may induce tissue hyperperfusion, increasing extracellular water content. Resulting low ATP levels lead to dysfunction of the sodium/potassium pump, with a consequent shift of water from the interstitial to the intracellular space may be increasing the content of water from the interstitial to the intracellular space, increasing the content of free water within muscle fibers.¹³ Intracellular water is thought to combine with cytoplasmic proteins resulting in a gel-like state, altering T_2 relaxation times of edematous muscle tissue. Gambarota et al²⁷ concluded that a two-phase system of free and

Figure 5. Graph shows correlation between ADC value and non-quantitative MRI score for 28 DM patients. ADC, apparent diffusion coefficient; DM, dermatomyositis.

bound water explained the sensitivity of T_2 weighted images to intramuscular inflammation.

Interestingly, both of the MRI T_2 relaxation times and ADC value of the unaffected muscles in DM patients were also respectively higher in comparison to control muscles of healthy subjects, indicating that grossly unaffected muscles on conventional MRI are still affected in DM, namely, MRI with T_2 maps and rs-EPI DWI could detect abnormalities in muscle groups that appear to be uninvolved by conventional MRI. The potentially ongoing pathologically inflammatory penetration may be in the early stage and invisible in conventional MRI, but could be quantitatively detected by measuring T_2 relaxation time and ADC values. By this way, the specialized MR techniques including T_2 maps and DWI sequences may differentiate diagnosis the affected and control muscles in the early disease.

The T_2 relaxation times of the affected muscles in DM patients in our study was lower than that reported by S. M. Maillard, who²¹ demonstrated that the MRI T_2 relaxation time of more than 86 ms is highly likely to have active inflammation within their muscles for juvenile dermatomyositis. These slight differences may result from differences in imaging parameters or sampling error. One intriguing aspect of this study is that the T_2 relaxation times of the affected muscle demonstrated higher than that of the unaffected, but the ADC value has no statistical difference for DM patients. The reason may be that T_2 relaxation times are not only related to edema but also other changes within skeletal muscle,²⁸ including fatty infiltration and fiber necrosis. In fact, nearly all pathophysiological changes in muscle could alter T_2 relaxation times, and thus T_2 maps could be used not only to evaluate muscle inflammation, but also potentially fatty infiltration and fiber necrosis. During the progression of myopathy, edema and inflammation can coexist with fatty infiltration and necrosis in myopathic tissue also resulting in longer T_2 relaxation times. The rs-EPI DWI may be a marker of the water motion within the muscle fibers, while the ADC value may be changed in the condition that edema coexists with fatty infiltration within muscles for DM patients. Qi et al²⁹ reported that the pathological changes of myopathies with fat infiltration could reduce water content and restrict diffusion and that greater fat infiltration is associated with lower ADC values, because fat cells are densely packed with low free water content. On the other hand, histological analysis of myopathic tissue reveals both degenerating and regenerating muscle fibers as well as inflammatory infiltrates and fibrosis in a diffuse distribution, no difference ADC values between edematous muscles and non-edematous based upon the type of myopathies may indicate the extent of muscle tissue disorganization with degenerating and regenerating myofibers, and ADC values of muscles may be also associated with the directionality of muscle fibers.

The scales of combination edema and fatty infiltration changes on non-quantitative MR images in DM may be affected by observer variance, but these are widely used in clinical practice. The grading score both of edema and fatty infiltration by using non-quantitative MRI showed a negative correlation with serum CK level for inflammation myositis,³⁰ suggesting that

the non-quantitative MRI may be useful to assess the severity of patients, particularly for the juvenile dermatomyositis. There was a significant correlation between T_2 values and the non-quantitative MRI score of combination edema with fatty infiltration changes, demonstrating that the T_2 relaxation time measurement of muscles is a quantitative and objective method to measure edema, fatty and atrophy changes within muscles for DM patients, and could provide crucial diagnostic information in the initial assessment of patients with early AIM. The absence of correlation between ADC value and non-quantitative MRI score was not surprising, DWI is sensitive to water motion within muscle fiber, and may be reduced with progressive stages of muscle necrosis and fatty infiltration.

In our study, the b -value of 500 s mm^{-2} was used, which came from our preliminary experience,³¹ and this value was not consistent with Schwenzer's study,³² in which b -value of 700 s mm^{-2} was chosen to reveal significant changes in diffusion characteristics

induced by passive muscle shortening and stretching. In the future study, we may have an optimal choice of b -value for the imaging evaluation of the inflammatory myopathies.

The major limitation of the current study is the small sample size. Li et al²⁰ proposed the approach imaging with rs-EPI could produce high-resolution DW images with robust correction of motion-induced phase artifacts, and the ss-EPI DWI sequence has been not compared with rs-EPI in this study.

CONCLUSION

The T_2 maps may have a specialized ability for the detection severity of damaged muscles in comparison to rs-EPI DWI.

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