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Diagnostic usefulness of denervation edema in the multifidus muscles using 3-Tesla magnetic resonance imaging in cervical radiculopathy

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Contributors: T.Y., Y. I., and H.N. designed the study. T.Y., S.S. examined the patients and conducted the electrophysiological study. T. S. conducted and read the magnetic resonance imaging. T. Y. performed the imaging analysis of the multifidus muscles. T.Y., S.S., Y.I, and H.N. analyzed the data. T. Y., and H. N. wrote the manuscript with input from all authors.

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position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

Abstract

Introduction/Aims: Diagnosing cervical radiculopathy (CR) can be difficult because of symptomatic overlap with peripheral neuropathies. In this retrospective observational study, we aimed to determine whether short-tau inversion recovery (STIR) magnetic resonance imaging (MRI) sequences are useful for detecting signs of denervation in the multifidus muscles in patients with CR.

Methods: We analyzed the data of 18 patients with CR who developed arm weakness within 1 year. We also included 10 patients with sensorimotor symptoms involving the upper extremities who did not have intervertebral foraminal stenosis on MRI as controls. For each patient with CR, the signal intensity (SI) of the affected multifidus muscles was measured and compared to that on the contralateral side (signal intensity ratio: SIR).

Results: Control patients without CR did not exhibit STIR signal abnormalities in the multifidus muscles. Most of the 18 patients with CR were male (83.3%), and the mean age was 59.4 years. Thirteen of 18 CR patients (72.2%) were determined to have STIR signal

abnormalities by a radiologist. The mean SIR in the 13 patients with increased SI was significantly higher than that in the five patients without signal abnormalities (1.23 vs. 0.97, p=0.004), supporting the radiologist's diagnosis. The distribution of signal abnormalities closely followed those identified via clinical and electrophysiological tests, especially severe weakness (p=0.044).

Discussion: Denervation edema of the multifidus muscles can be detected in CR and correlates with clinical/electrophysiological tests and weakness severity, which may aid in CR diagnostics.

Key words: cervical radiculopathy, magnetic resonance imaging, multifidus, denervated muscle

1 Introduction

The diagnosis of cervical radiculopathies (CR) can be difficult because brachial plexopathy and other peripheral nerve disorders can present with similar pain and neurological symptoms.[1-3] Examination of the multifidus muscle via needle electromyography (EMG) is shown to be sensitive and specific for the clinical diagnosis of lumbar spinal stenosis[4-5] and to also accurately differentiate radiculopathy from plexopathy.[6] However, needle EMG is invasive, and some patients have difficulty tolerating the examination or maintaining a fully relaxed state.[6] Previous studies have utilized magnetic resonance imaging (MRI) to detect acute denervation in skeletal muscles.[7-9] Short-tau inversion recovery (STIR) sequences can visualize denervation edema in affected muscles within 24 to 48 hours and are useful for determining the nerves involved as well as the levels of nerve entrapment or compression.[10] Therefore, we aimed to determine whether this imaging method is useful for detecting signs of denervation in the multifidus muscles in patients with CR.

2 Methods

2.1 Patients

We conducted a retrospective chart review in the National Hospital Organization Okinawa

Hospital, a referral center for neuromuscular diseases, from 2009 to 2014. The study consecutively included patients with suspected CR who underwent extensive clinical, electrophysiological, and radiological investigations, including 3 Tesla (3 T) MRI, in our institution for evaluation of unilateral arm pain and/or weakness. Patients with neurological symptoms that could not be explained by intervertebral foraminal stenosis were excluded from the current analysis. In addition, patients with CR without weakness, with coexistent cervical myelopathy, or with symptom duration more than 1 year were also excluded. We additionally included patients with peripheral neuropathies or other neurological disorders who presented with sensorimotor symptoms involving the upper extremities and underwent MRI but did not show cervical intervertebral foraminal stenosis, as disease controls. The present study was approved by the appropriate institutional review board of the National Hospital Organization Okinawa Hospital. Informed consent was obtained in the form of opt-out on the website of Okinawa National Hospital.

2.2 Clinical and Electrophysiological Data

The following data were evaluated for all patients: age, sex, presence of pain and sensorimotor symptoms, and muscle strength as determined using the modified Medical

Research Council (MRC) scale. Severe weakness was defined as the modified MRC scale = 3 or less. We also assessed the results of nerve conduction studies and needle EMG. Affected sides and nerve root levels were determined based on the distribution of weakness during the clinical examination and active denervation during needle EMG (fibrillation potentials or positive sharp waves). The myotome chart reported by Hakimi and Spanier[11] was used for this purpose. We also evaluated treatment response to short-course intravenous and/or oral corticosteroid therapy. An improvement of ≧1 point in the modified MRC scale within three months after initiation of the treatment was considered as positive treatment response.

2.3 MRI

We evaluated all patients using a 3 T MRI scanner (Achieva 3T, Release 2.6.3.4, PHILIPS MEDICAL SYSTEMS, Andover, MA). All MRI data were examined by a neuromuscular radiologist with 20 years of experience. Each multifidus muscle was evaluated for the presence of increased signal intensity (SI) on coronal STIR sections and muscle atrophy on T2-weighted images (T2WI; horizontal sections). We used coronal STIR images because of their advantages in depicting the multifidus muscles from initiation (articular processes) to termination (spinous process).

Affected nerve root levels were determined based on an anatomical study of the lumbar multifidus muscles, which revealed that each muscle was innervated by the dorsal rami of the corresponding nerve root,[12] although this muscle may be polysegmentally innervated.[13] We assumed that the same rule applied to the superior nerve root levels and that each cervical multifidus muscle was innervated by the dorsal rami of the nerve root one segment below (for example, the multifidus muscles attached to the C6 spinous process are innervated by the C7 nerve root).

Subsequently, we measured SI in the affected multifidus muscles. The level of the affected muscle was determined based on the results of clinical/electrophysiological tests. For each level, we selected the slice that showed the largest area of given multifidus muscle along its course. Using ImageJ (http://rsb.info.nih.gov/ij/), regions of interest (ROIs) were manually drawn along each multifidus muscle by the same person (T. Y.) blinded to the patient's name and clinical information. The mean SI of each muscle was measured and compared to that of the contralateral muscle. In addition, we created a circular ROI in the ipsilateral background area adjacent to the neck. Effort was made not to include soft tissue or artifacts within the region. An SI ratio (SIR) was calculated using the following formula: SIR = (SI of affected muscle – SI of background) / (SI of contralateral muscle – SI of background).[7] The mean SIR

was then calculated by averaging the SIR of the affected muscles in each patient.

2.4 Statistical Analysis

All statistical analyses were performed using EZR, a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria).[14] The Mann–Whitney U-test was used to compare the SIRs between patients with and without STIR abnormalities. The associations between STIR abnormalities and various clinical factors were analyzed using Fisher's exact tests. A p value of < 0.05 was determined as the cutoff for statistical significance.

3 Results

3.1 Clinical and Electrophysiological Data

After extensive review of the data of a total of 36 patients, 24 were classified as having CR based on the presence of significant intervertebral foraminal stenosis on MRI at appropriate cervical root levels. Eight patients had been diagnosed with intervertebral foraminal stenosis, but their clinical symptoms could not be explained by the MRI findings. Another four patients did not have intervertebral foraminal stenosis. Among 24 patients with CR, two did not show

weakness. One patient was excluded because of coexistent spinal cord compression. Three patients were excluded because of symptom duration of more than 1 year. The data of 18 of the 24 patients who showed clinical findings relevant for MRI study proceeded to the subsequent analysis. Table 1 and Figure 1 summarize the clinical data of these 18 patients.

Of the 10 patients included in the disease control group, six had various forms of peripheral neuropathy, including three with ulnar neuropathy, two with multiple mononeuropathy, and one with neurogenic thoracic outlet syndrome. Another four patients had persistent neurological symptoms such as neuropathic pain, ataxia, and fibromyalgia-like chronic pain. The mean age was 44.8 years, and the male-female ratio was 3:7. Among these patients, four showed various degrees of arm weakness.

Needle EMG was performed in all patients with CR (Figure 1). All muscles examined were located within the arm and shoulder girdle. At the time of study period, in our institution, EMG of the multifidus muscles was not routinely performed because of considerations of invasiveness and difficulty maintaining full relaxation in some patients. The sensitivity of denervation-related changes on needle EMG was 83.3%. The distribution of muscles with active denervation corresponded to that of muscle weakness, especially severe weakness.

3.2 Magnetic Resonance Imaging and Neurography

No patients in the disease control group or patients without intervertebral foraminal stenosis exhibited increased SI in the multifidus muscles. The radiologist determined 13 of the 18 patients (72.2%) with CR as having increased SI in the multifidus muscles (Figure 2). Three patients showed bilaterally increased SI, although clinical examination revealed unilateral weakness. The mean SIR of the affected muscles in these 13 patients was significantly higher than that in the five patients without apparent signal abnormalities (Figure 3A; 1.23 vs. 0.99, $p = 0.004$). However, two of three patients with bilaterally increased SI showed low SIR (patient 9 and patient 10). A threshold of mean SIR = 1.028 could best discriminate these two groups with an area under the curve of 0.92.

The distribution of STIR abnormalities closely followed those of weakness and/or active denervation (Figure 1). In particular, most STIR abnormalities were distributed in the muscles with severe weakness and active denervation on EMG. Among 120 muscles from 12 patients (five nerve root segments on each side), excluding patient 9 who presented 3 days after disease onset, 25 muscles were innervated at the cervical root levels that exhibited both severe weakness and active denervation. Notably, 14 of 20 muscles with increased SI were distributed within these 25 muscle segments ($p < 0.001$).

Subsequently, we analyzed the association of STIR abnormalities with various clinical factors and treatment response. The only statistically significant difference in clinical findings between patients with and without STIR abnormalities was the presence of a greater percentage with severe weakness in the group with STIR abnormalities (Figure 3B; p = 0.044).

In addition to STIR abnormalities, atrophy of the multifidus muscles was observed in most patients. However, it was frequently present on both sides and more widely distributed than were the STIR abnormalities.

4 Discussion

In the present study, STIR abnormalities in the multifidus muscles were frequently present in patients with CR who had weakness but not in patients without CR. In addition, our findings indicated that a radiologist was able to discriminate muscles with STIR abnormalities from those without. Moreover, the distribution of STIR abnormalities closely followed those of clinical weakness and EMG abnormalities. Patients with STIR abnormalities more often exhibited severe weakness. These preliminary findings suggest that MRI could be used to detect signal abnormalities of the multifidus muscles that could aid in

the clinical diagnosis of CR.

Compared to needle EMG, assessments of muscle STIR abnormalities may be more convenient and less invasive. The coronal STIR sequence we used in this study requires only 5 minutes and is easily translated into standard protocols. In this sequence, nerve roots and the brachial plexus can also be examined, adding diagnostic utility.[2] Conversely, this assessment may not be more accurate than EMG data in detecting denervation-related changes. Although we did not perform direct comparisons between MRI and needle EMG of multifidus muscles, MRI detected signs of muscle denervation in 72.2% of our cases, whereas needle EMG of limb muscles showed a detection rate of 83.3% despite lack of study of the cervical paraspinal muscles. However, as described above, the distribution of STIR abnormalities closely followed those of severe weakness and EMG signs of active denervation. Thus, STIR imaging of multifidus muscles might indicate the clinical severity of CR. Abnormal SI on STIR sequences reflects muscle denervation edema in the acute and subacute phases, beginning to appear within 24 to 48 hours after denervation episodes.[10] Thus, MRI exhibits good sensitivity for the detection of denervation-related changes and can detect the earliest changes associated with muscle denervation. In our patients with STIR abnormalities, disease duration ranged from a few days to several months, suggesting a

progressive or recurrent course of nerve injury beyond the first CR episode.[16] Although coronal STIR sequences of the cervical spine may be infrequently utilized in clinical practice, these sequences aided in visualization of the multifidus muscle from its attachment to the spinous process. Because of their small size, thinly sliced (3 mm in our study), gapless images are necessary for proper imaging of the multifidus muscles.

We used the SIR to determine the presence of increased muscle SI. This method was adapted from a study by McDonald et al., who assessed the usefulness of denervation edema on MRI relative to that of EMG.[7] Notably, the calculated values were well separated between patients with STIR abnormalities and those without, and in most cases, the results were consistent with the radiologist's opinion regarding the presence of STIR abnormalities. Although the results do not provide evidence for the usefulness of the SIR for the diagnosis of CR, they suggests that radiologists could reliably discriminate the multifidus muscles with STIR abnormality from those without, supporting the diagnostic utility of this method in daily clinical practice. Furthermore, the association with severe weakness and active denervation strongly suggests that STIR abnormalities in the multifidus muscles reflect ongoing axonal loss associated with CR.

The STIR imaging sequence might also be helpful in certain clinical situations, such as in

patients with presentations mimicking CR. For example, neuralgic amyotrophy (NA) can mimic CR. The paraspinal muscles are rarely involved in NA, while they are frequently involved in CR.[16] Additionally, because imaging of nerve roots per se may be difficult on conventional MRI sequence due to their small size, detection of STIR abnormalities in paraspinal muscles in non-compressive radiculopathies such as those caused by the varicella-zoster virus and sarcoidosis[17] may aid in confirming the presence of lesions involving the nerve roots.

The present study possesses certain limitations. First, most of our patients were referred from other hospitals. As such, their clinical presentation was more likely to be severe, and they were more likely to exhibit a protracted disease course. Thus, our patient group may not represent the entire population of patients with CR. Second, because we did not concurrently perform needle EMG of the paraspinal muscles, we could not directly compare the efficacy of MRI and needle EMG. Third, because of the study's retrospective nature and the small number of patients included in our study, associations between MRI abnormalities and various clinical factors could not be optimally assessed. A large prospective study incorporating the patients in the earlier phase of disease and structured clinical assessments with concurrent needle EMG and MRI is required to further elucidate these issues. Fourth,

the SIR measurement was time-consuming and difficult to perform routinely. In addition, because we used the SI of the contralateral muscles to calculate the SIR, patients with bilateral STIR hyperintensity showed a low SIR. Therefore, in clinical practice, simple measurement of the SIR may not be appropriate, and careful discussion with a radiologist regarding the MRI findings would be necessary. Finally, there were demographic differences between the case and control groups (for example, fewer women and older age in the CR population), which might have affected the MRI findings.

In conclusion, our findings showed that visualization of denervation edema in the multifidus muscles using STIR MRI sequences may aid in the diagnosis of CR. STIR abnormalities were also associated with clinical severity. Further large-scale studies involving direct comparisons of MRI and EMG findings and analyses of associated clinical factors are required to elucidate the nature of this radiological finding.

List of abbreviations

CR: cervical radiculopathy

EMG: electromyography

MRC: Medical Research Council

MRI: magnetic resonance imaging

NA: neuralgic amyotrophy

NCS: nerve conduction studies

ROI: region of interest

SI: signal intensity

SIR: SI ratio

STIR: short-tau inversion recovery

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Figure Legends

Figure 1. Summary of clinical, electromyographic, and magnetic resonance imaging findings.

Figure 2. Coronal short-tau inversion recovery images in patients with cervical radiculopathy. Increased signal intensity (SI) was observed in the multifidus muscles in each patient (arrows). The SI of the affected muscles was measured and compared to that in the contralateral muscles. A: Patient 9. B: Patient 5. C: Patient 12. D: Patient 4.

Figure 3. A. Comparison of signal intensity ratios (SIRs) between patients with cervical radiculopathy with and without short-tau inversion recovery (STIR) abnormalities. The calculated SIR values were well separated between the two groups. B. Association between severe weakness and STIR abnormalities. Patients with STIR abnormalities exhibited severe weakness more frequently than those without ($p = 0.044$).

Table 1. Clinical/laboratory findings and treatment responses.

Abbreviations. L: left, NS: not significant, R: right.

Table 1. Clinical and laboratory findings.

	Total	STIR abnormality (+)	STIR abnormality (-)	p value
Number	18	13	5	
Age (years, mean ± SD)	59.4 ± 12.4	59.8 ± 13.9	58.2 ± 8.2	NS
Male : Female ratio	15 : 3	11 : 2	4 : 1	NS
Affected side (%)	R 33.3 %, L 66.7 %	R 38.5 %, L 61.5 %	R 20 %, L 80 %	NS
Disease duration (median (IQR))	2.0 (1.8) months	2.0 (1.3) months	2.0 (2.0) months	NS
Diabetes mellitus (%)	27.8 %	28.6 %	25 %	NS
Manual labor (%)	50 %	53.8 %	40 %	NS
Pain (%)	94.4 %	92.3 %	100 %	NS
Weakness (%)	100 %	100 %	100 %	NS
Sensory loss (%)	38.9 %	38.5 %	40 %	NS
Severe weakness (%)	77.8 %	92.3 %	40 %	$p = 0.044$

Abbreviation. IQR: interquartile range, L: left, NS: not significant, R: right, SD: standard deviation.

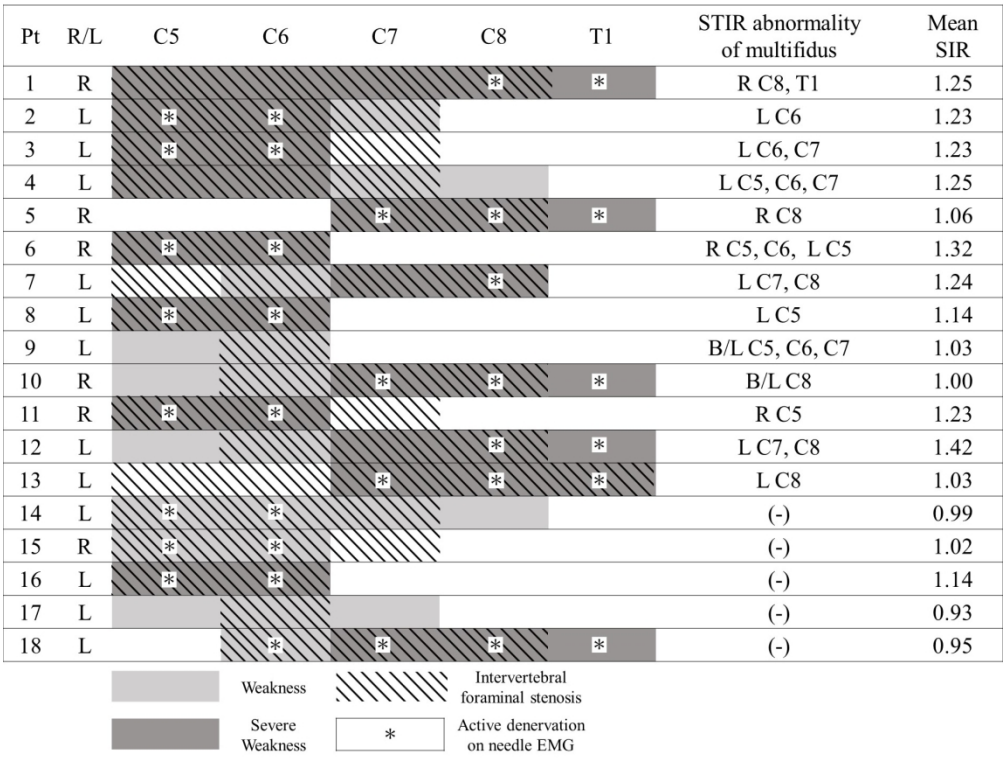

Figure 1. Summary of clinical, electromyographic, and magnetic resonance imaging findings.

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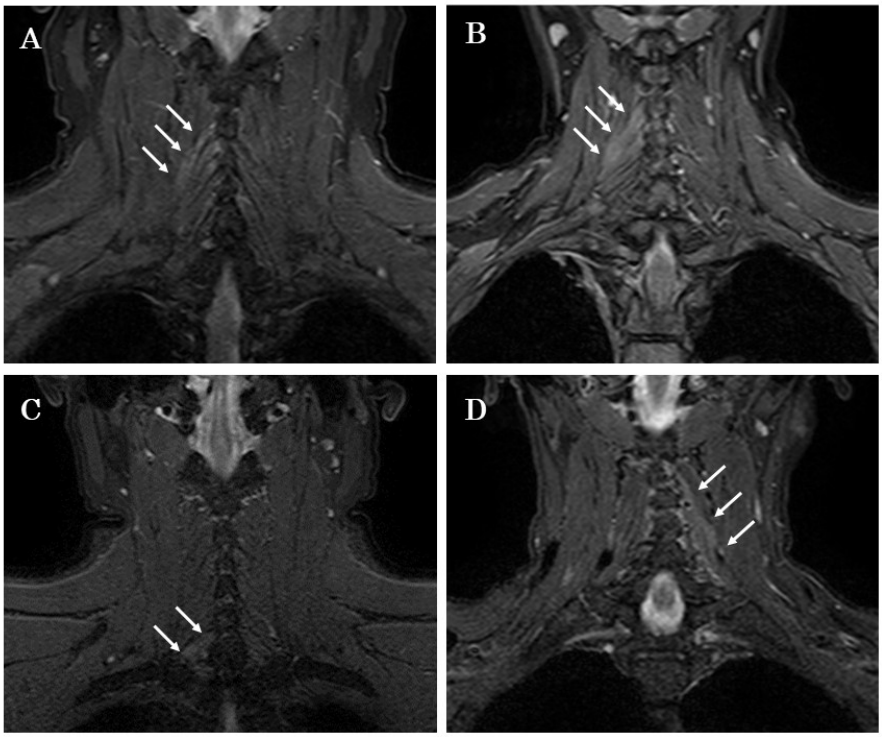

Figure 2. Coronal short-tau inversion recovery images in patients with cervical radiculopathy. Increased signal intensity (SI) was observed in the multifidus muscles in each patient. The SI of the affected muscles was measured and compared to that in the contralateral muscles. A: Patient 9. B: Patient 5. C: Patient 12. D: Patient 4.

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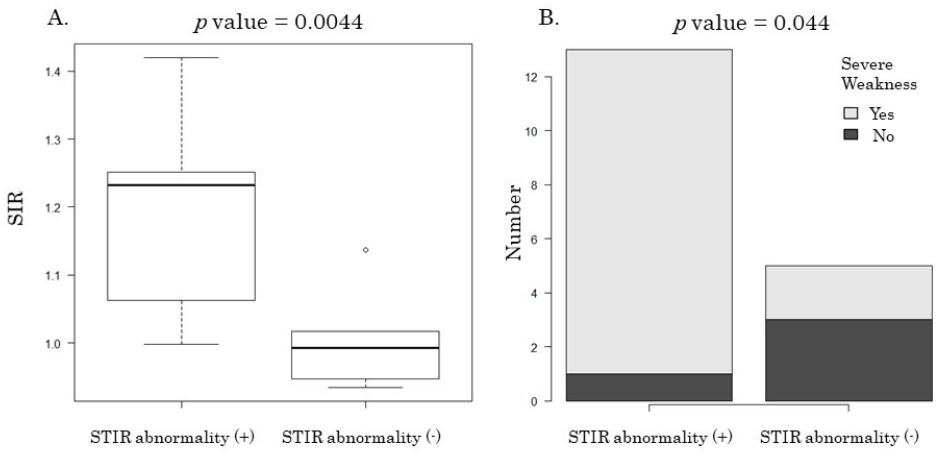

Figure 3. A. Comparison of signal intensity ratios (SIRs) between patients with cervical radiculopathy with and without short-tau inversion recovery (STIR) abnormalities. The calculated SIR values were well separated between the two groups. B. Association between severe weakness and STIR abnormalities. Patients with STIR abnormalities exhibited severe weakness more frequently than those without (p = 0.044).

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