

MRI of the cervical nerve roots in the diagnosis of chronic inflammatory demyelinating polyradiculoneuropathy: a single-institution, retrospective case-control study

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ABSTRACT

Objective: To systematically evaluate the usefulness of assessing the cervical nerve roots by MRI for the diagnosis of chronic inflammatory demyelinating polyradiculoneuropathy (CIDP).

Design: Single-institution, retrospective case-control study.

Setting: A regional referral hospital.

Participants: We retrospectively enrolled 15 consecutive patients with CIDP who satisfied the European Federation of Neurological Societies/Peripheral Nerve Society (EFNS/PNS) typical and definite criteria and underwent cervical MRI. 30 control patients who had also undergone cervical MRI were included, matched with regard to sex, age and MRI system. The diagnoses of the control patients included cervical spondylosis (n=19), cervical spine trauma (n=2), infection (n=1), malignancies (n=4), demyelinating disorders (n=2) and neurodegenerative disorders (n=2).

Measurement: A radiologist determined the C5–C8 root diameters on the coronal short tau inversion recovery (STIR) images. Signal intensities of these roots were quantified as nerve-to-muscle contrast-to-noise ratios (CNRs), which were calculated using mean signal intensities of the roots and sternocleidomastoid muscle as well as SD of background noise. Statistical analyses were performed to determine the diagnostic accuracy of the diameters and nerve-to-muscle CNRs. Another radiologist reviewed MRI for ensuring reproducibility.

Results: The root diameters showed no significant differences between the patients with CIDP and control patients. The nerve-to-muscle CNRs were significantly higher in the patients with CIDP. We defined the sum of nerve-to-muscle CNRs of C5–C8 roots as the CNR score to serve as an index of overall signal intensity. The area under the receiver operating characteristic curve of CNR scores was 0.731. The reproducibility of the assessment procedure was satisfactory.

Conclusions: Our results suggest that assessment of the cervical nerve roots by MRI is useful for CIDP diagnosis when the signal intensities, rather than the diameters, are paid more attention on STIR images.

ARTICLE SUMMARY

Article focus

- Thus far, few studies have systematically evaluated the accuracy of MRI for the diagnosis of chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) with appropriately selected control participants.
- The primary objective of this study was to systematically evaluate the usefulness of assessing the cervical nerve roots by MRI for the diagnosis of CIDP.

Key message

- Assessment of the cervical nerve roots by MRI will be useful for the diagnosis of CIDP when the signal intensities, rather than diameters, are paid more attention on STIR images.

Strengths and limitations of this study

- This is the first study that systematically measured the usefulness of MRI for the diagnosis of CIDP, with appropriately selected control patients/participants.
- The study design embraces sampling bias. However, we selected patients with CIDP and control patients from the same institution and matched these groups with regard to sex, age and MRI system. Thus, such bias was adequately controlled.

INTRODUCTION

Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is a clinically heterogeneous, grossly symmetric, sensory and motor neuropathy evolving as a monophasic, relapsing or progressive disorder.¹ CIDP is regarded as an autoimmune disease and is treatable with immunotherapy.² To aid recognition of this treatable condition, the American Academy of Neurology (AAN) proposed research diagnostic criteria.³ However, these criteria have since then been proven as

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insufficiently sensitive for clinical practice⁴ and several new criteria sets have been proposed.^{5–8} For instance, the sensitivity of European Federation of Neurological Societies/Peripheral Nerve Society (EFNS/PNS) criteria is greater than that of the AAN criteria. Rajabally *et al*⁹ reported that more than 80% of the AAN criteria-negative but EFNS/PNS criteria-positive patients were responsive to treatment. Therefore, improving the accuracy for the diagnosis of CIDP will help to prevent underdiagnosis.

Although EFNS/PNS supportive criteria assist the diagnosis by probably increasing the accuracy, which include MRI findings such as hypertrophy of the cervical nerve roots or brachial plexus,⁸ only a few studies have evaluated such MRI abnormalities in patients with CIDP. Duggins *et al*¹⁰ studied 14 consecutive patients with CIDP and reported that MRI revealed hypertrophy of the cervical nerve roots and brachial plexus in 8 patients. Tazawa *et al*¹¹ reported that the cervical nerve root diameters on the short tau inversion recovery (STIR) images had higher values in 14 consecutive patients with CIDP than in 10 control patients. Adachi *et al*¹² reported that high intensity of the brachial plexus on the STIR images was shown in 9 of 13 patients with CIDP and that all plexuses with high intensity appeared swollen. Thus far, however, few studies have systematically evaluated the accuracy of MRI for the diagnosis of CIDP with appropriately selected control participants.¹³

The primary objective of this study was to systematically evaluate the usefulness of assessing the cervical nerve roots by MRI for the diagnosis of CIDP. In our experience, similar to the report by Adachi *et al*,¹² the cervical nerve roots of patients with CIDP tend to appear with high intensity on STIR images (figure 1).¹⁴ We, therefore, quantified signal intensities as well as diameters of the cervical nerve roots on STIR images, and then determined the diagnostic accuracy of these

parameters. The secondary objective was to investigate the reproducibility of the assessment procedure.

PATIENTS AND METHODS

Study design and setting

We conducted a retrospective case–control study in a regional referral hospital. We considered a case–control study to be appropriate because CIDP is a relatively rare disease.¹⁵ The need for informed consent was waived because this study did not impose any additional invasive procedure or cost on the study participants and the information was sufficiently anonymised.

Study subjects

We enrolled 15 consecutive patients with CIDP who satisfied the EFNS/PNS typical and definite CIDP criteria,⁸ and who had undergone cervical MRI from October 2005 to April 2011. We used only clinical and electrodiagnostic criteria.⁸ The EFNS/PNS supportive criteria were not used because it included MRI findings.⁸ When the time from disease onset to MRI did not exceed 8 weeks, we judged whether the disease course was compatible with CIDP over the following 6 months for each patient.¹⁶ In one patient, a sural nerve biopsy was performed with pathological confirmation of the CIDP diagnosis. There were four male and 11 female patients; mean age \pm SD was 56.8 \pm 16.6. The mean disease duration \pm SD was 430.9 \pm 693.3 weeks. Upper limb involvement was observed in all patients with CIDP. The median of functional disability scale (0, healthy; 1, minor symptoms or signs and able to run; 2, able to walk 5 m without assistance but unable to run; 3, able to walk 5 m with assistance; 4, chair bound or bed bound; 5, requiring assisted ventilation for at least part of the day or night; and 6, dead) at the time of MRI among the patients with CIDP was 2 (range 1–4).^{17 18} The

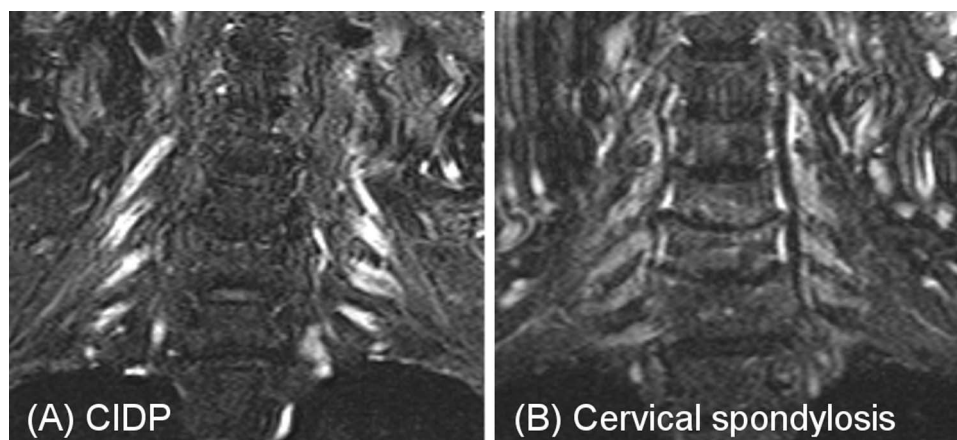


Figure 1 Coronal STIR cervical MRI. (A) A patient with CIDP: TR/TE/TI=6600/72/180 ms. (B) A patient with cervical spondylosis matched for sex and age: TR/TE/TI=7000/72/180 ms. The signal intensities of the cervical nerve roots are higher in the patient with CIDP, although the diameters do not show significant difference between the patients. CIDP, chronic inflammatory demyelinating polyradiculoneuropathy; STIR, short tau inversion recovery; TE, echo time; TI, inversion time; TR, repetition time.

mean cerebrospinal fluid (CSF) protein level, which had been analysed at the time of MRI, was 2.033 ± 3.018 g/L. Nine patients with CIDP have undergone MRI before treatment. The remaining six patients with CIDP have received treatment with steroid, intravenous immunoglobulin and/or immunoadsorption before MRI.

The control participants were patients who were required to undergo cervical MRI from October 2005 to April 2011 and who did not satisfy the EFNS/PNS criteria. We sampled the candidate patients matched with respect to sex, age (± 2 years) and MRI system for each enrolled patient with CIDP, using the MRI reporting system at our institution. Then, we randomly sampled the final control patients from the candidate patients without replacement, in which two control patients were sampled for each patient with CIDP. Eventually, 30 control patients were enrolled. There were 8 male and 22 female control patients; mean age \pm SD was 56.9 ± 16.1 . The diagnoses of the control patients included cervical spondylosis ($n=19$), cervical spine trauma ($n=2$), infection ($n=1$), malignancies ($n=4$), demyelinating disorders ($n=2$) and neurodegenerative disorders ($n=2$). The patients with cervical spondylosis presented neck or arm pain with or without limb paraesthesia, numbness or weakness. The diagnoses were made through clinical and radiological findings. The MRI findings showed radiculopathy in 4 patients, myelopathy in 3 patients and both in 12 patients.

MRI technique and image interpretation

Cervical MRI examination of all participants was performed using 1.5-T MRI systems (MAGNETOM Avanto or MAGNETOM Vision, Siemens, Erlangen, Germany). The MRI of each enrolled participant was reviewed in a random order on a workstation (Centricity Radiology RA 1000, GE Healthcare, Illinois, USA) by a radiologist (YY, 1 year of experience in radiology), without prior knowledge of the patient diagnoses. Coronal STIR images were used to measure the diameters and signal intensities of the cervical nerve roots (C5–C8; figure 2). The parameters of the coronal STIR sequence were as follows: repetition time/echo time/inversion time, 5500–7000/60–73/150–180 ms; section thickness, 3–5 mm; section gap, 0.2–1.2 mm; fields of view, 239–350 \times 239–350 cm; imaging matrix, 192–230 \times 256–384 matrix; and number of excitations, 1. Axial and sagittal MRI were also used, when required, to enable accurate setting of the sight on the targeted nerve root.

The diameter of the cervical nerve root was defined as the vertical length of the root at the outlet of the intervertebral foramen.¹¹ The diameter of the larger side was employed.

Signal intensity of the cervical nerve root was quantified as a nerve-to-muscle contrast-to-noise ratio (CNR).¹⁹ To compute the nerve-to-muscle CNRs, mean signal intensity (SI) in the C5–C8 roots and the sternocleidomastoid muscle as well as SD of the background noise, were measured on coronal STIR images using an operator-defined region of interest (ROI). The ROI

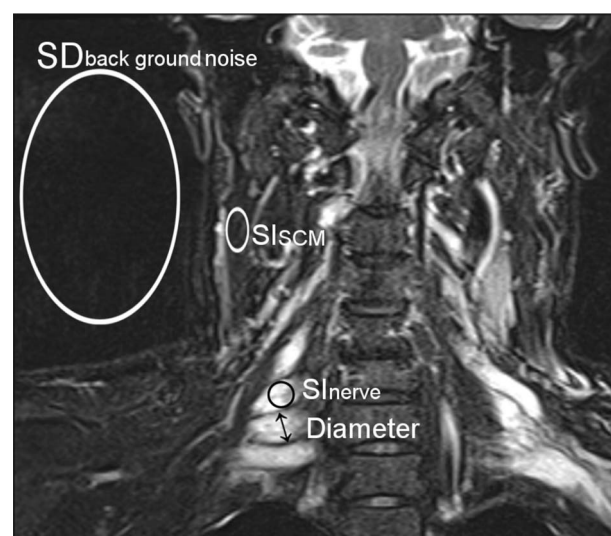


Figure 2 Coronal STIR cervical MRI of a patient with CIDP showing the way in which diameters and nerve-to-muscle CNRs of the cervical nerve roots were measured: TR/TE/TI, 6600/72/180 ms. Diameter was measured as the vertical length of the root at the outlet of the intervertebral foramen. SIs in the C5–C8 roots and SCM, as well as SD of the background noise, were measured using an operator-defined ROI. Nerve-to-muscle $CNR = \frac{SI_{nerve} - SI_{SCM}}{SD_{background\ noise}}$. Notably, this patient showed obvious thickening of the cervical nerve roots. CIDP, chronic inflammatory demyelinating polyradiculoneuropathy; CNR, contrast-to-noise ratio; ROI, region of interest; SCM, sternocleidomastoid muscle; SI, mean signal intensity; STIR, short tau inversion recovery; TE, echo time; TI, inversion time; TR, repetition time.

cursors were located on the side employed during diameter measurement. ROIs were drawn to avoid vessels, prominent artefacts and focal differences in SI in the corresponding areas. ROI for measuring SD of the background noise was positioned outside the patient's body region. The nerve-to-muscle CNR was calculated as follows: nerve-to-muscle $CNR = \frac{SI_{nerve} - SI_{sternocleidomastoid\ muscle}}{SD_{background\ noise}}$.

To investigate the reproducibility, another radiologist (NM, 12 years of experience in radiology) reviewed MRI in the same way as described above, also without prior knowledge of the patients' diagnoses.

Both radiologists reviewed these images in December 2011.

Outcome measures

The primary outcome of our study was the diagnostic accuracy of diameters and nerve-to-muscle CNRs of the C5–C8 roots on coronal STIR images for CIDP diagnosis, with the EFNS/PNS clinical and electrodiagnostic criteria used as the reference standard. Our secondary outcome was the reproducibility of the assessment procedure.

Statistical analysis

Stata statistical software V.12.1 (Stata Corp LP, College Station, Texas, USA) was used to perform the statistical

analyses. Measurements of continuous variables were reported as means and SDs, and those of categorical variables were reported as frequencies and proportions. The functional disability scale of patients with CIDP was reported as medians and ranges. A significance level of 0.05 was used throughout. The Wilcoxon rank-sum test was used to compare continuous variable measurements among the patient groups and the Fisher's exact test was used for categorical variable measurements.

We performed receiver operating characteristic (ROC) analysis to assess the diagnostic accuracy of C5–C8 diameters and/or nerve-to-muscle CNRs.^{20–21} Correlations of these values with disease duration, functional disability scale and CSF protein level were checked among patients with CIDP using the Spearman's rank test.

The reproducibility of the assessment procedure was first evaluated through observation of similarity of the obtained results between the two radiologists. Thereafter, interobserver agreement was evaluated using the Bland-Altman analysis.^{22–23} Furthermore, the ROC curves generated from the two radiologists' results were compared.²⁴

95% CIs were calculated for all measures that required statistical uncertainty to be reported.

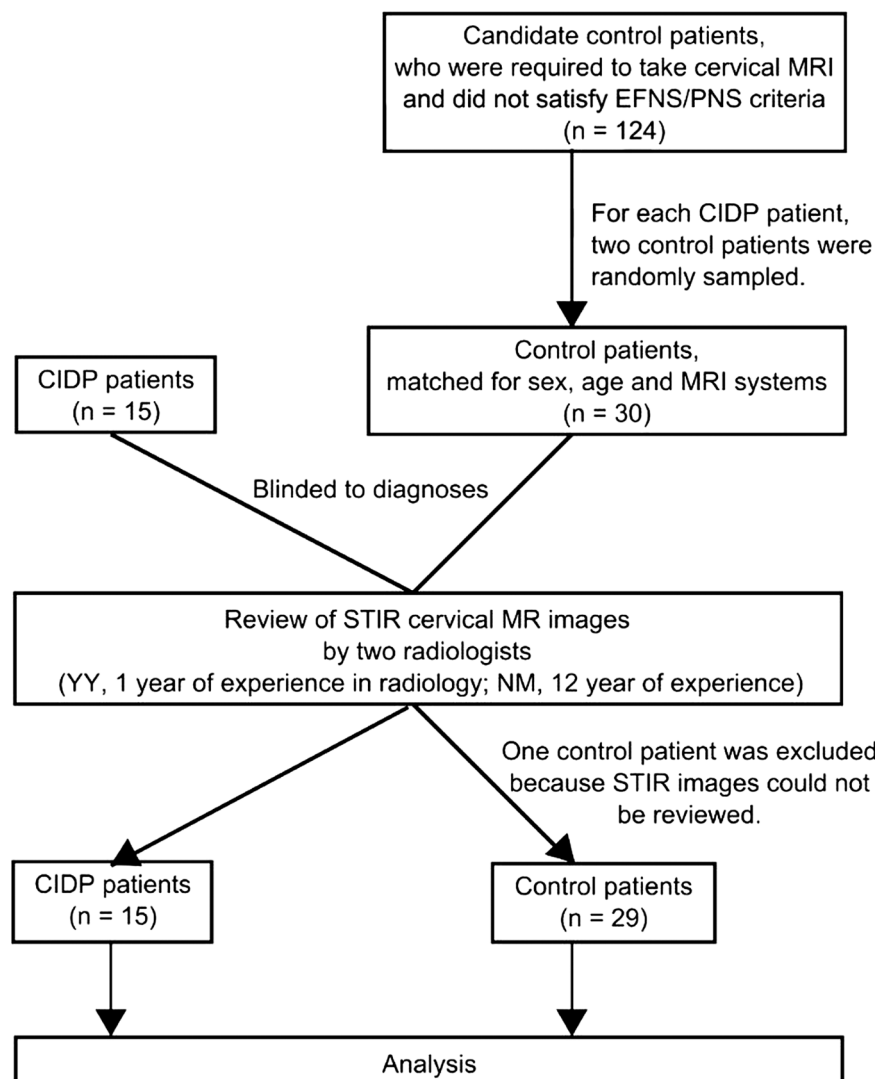
RESULTS

Characteristics of study subjects

One control patient (cervical spondylosis with radiculopathy) was excluded before analysis because of lack of coronal STIR images. Ultimately, the data for the 15 patients with CIDP and 29 control patients were analysed. The study flow chart is presented in figure 3. There were no statistically significant differences among the patient groups with respect to sex, age or MRI system (sex, $p=1.00$; age, $p=0.95$; and MRI system, $p=1.00$).

The mean \pm SD areas of ROI located in the C5, C6, C7 and C8 nerve roots and sternocleidomastoid muscle were 5.05 ± 3.65 , 7.80 ± 4.52 , 8.67 ± 5.45 , 7.85 ± 5.14 and 34.07 ± 17.56 cm², respectively, and were not significantly different among the patient groups (C5, $p=0.92$; C6, $p=0.95$; C7, $p=0.25$; C8, $p=0.77$; and sternocleidomastoid muscle, $p=0.49$). ROI for measuring SD of the background noise was 157.97 ± 150.47 cm². They were significantly higher in those patients with CIDP (patients with CIDP, 201.17 ± 127.66 cm²; control patients, 135.62 ± 158.44 cm²; $p=0.02$). However, the ROI areas were sufficiently large to prevent significant variability of SD of the background noise.

Figure 3 The study flow chart. CIDP, chronic inflammatory demyelinating polyradiculoneuropathy; EFNS/PNS, European Federation of Neurological Societies/Peripheral Nerve Society; STIR, short tau inversion recovery.



Main results

The results obtained from one radiologist (YY) are presented here. The diameters and nerve-to-muscle CNRs of the C5–C8 roots are shown in table 1. For the diameters, there were no statistically significant differences between patients with CIDP and control patients (C5, $p=0.92$; C6, $p=0.32$; C7, $p=0.16$; and C8, $p=0.36$). However, two patients with CIDP (see also figure 2) showed obvious thickening of the cervical nerve roots with a similar extent. The nerve-to-muscle CNRs of the C5, C6, C7 and C8 roots were significantly higher in patients with CIDP than in control patients (C5, $p=0.03$; C6, $p=0.02$; C7, $p=0.01$; and C8, $p=0.04$).

We defined the sum of nerve-to-muscle CNRs of the C5–C8 roots as the CNR score, which was considered to represent overall signal intensity (table 1). The means±SDs of CNR scores in patients with CIDP and control patients were 134.29 ± 93.79 and 71.10 ± 42.85 , respectively ($p=0.01$). ROC analysis of the CNR score for the diagnosis of CIDP revealed the area under the curve of 0.731 (95% CI 0.568 to 0.894).

In patients with CIDP, there were no statistically significant correlation between the CNR score and disease duration (Spearman's rho -0.14 ; $p=0.18$), functional disability scale (Spearman's rho -0.09 ; $p=0.73$) or CSF protein level (Spearman's rho 0.36 ; $p=0.18$). Moreover, there were no statistically significant difference in the CNR score between patients with CIDP with and without treatments before MRI ($p=0.29$).

Reproducibility of the assessment procedure

To determine the reproducibility of the assessment procedure, another radiologist (NM) reviewed STIR cervical MRI. There were no statistically significant differences in root diameter between patients with CIDP and control patients (C5, $p=0.38$; C6, $p=0.12$; C7, $p=0.96$; and C8, $p=0.35$). However, nerve-to-muscle CNRs were significantly higher in patients with CIDP, except for root C5 (C5, $p=0.12$; C6,

$p=0.003$; C7, $p=0.03$; and C8, $p=0.04$). The means±SDs for CNR scores in patients with CIDP and control patients were 148.08 ± 111.89 and 76.74 ± 35.29 , respectively ($p=0.03$). The area under the ROC curve for CNR score was 0.699 (95% CI 0.521 to 0.877). These results were similar to those described in the Main results section.

The Bland-Altman analysis of CNR scores yielded a mean interobserver bias of -8.42 (95% CI -115.79 to 98.96). Comparison of the ROC curves of CNR scores for the diagnosis of CIDP between the two radiologists revealed no statistically significant difference (0.731 vs 0.699, $p=0.73$).

DISCUSSION

In our study, diameters of the C5–C8 roots showed no significant differences between patients with CIDP and control patients, whereas the nerve-to-muscle CNRs were significantly higher in patients with CIDP on coronal STIR images. The area under the ROC curve for CNR scores was 0.731, with the EFNS/PNS clinical and electrodiagnostic criteria used as the reference standard. Between the two radiologists, the results obtained were similar and the ROC curves of CNR score did not show significant differences.

Our study did not find any significant difference in cervical nerve root diameter between patients with CIDP and control patients, although 2 of the 15 patients with CIDP showed obvious thickening of the cervical nerve roots. This is different from the report by Tazawa *et al*,¹¹ in which the root diameters on STIR images were significantly larger in patients with CIDP than in control participants. Those control participants, however, were not necessarily individuals who required cervical MRI examination; their cervical nerve roots might have lacked pathological changes.¹¹ To evaluate the usefulness of cervical MRI in clinical settings, control participants should be sampled from patients who have disorders requiring cervical MRI examination.¹⁵ In our study, the control patients were selected from individuals who required cervical MRI examination. Many of the control patients had cervical spondylosis, which may clinically mimic CIDP.²⁵ In patients with cervical spondylosis, in which fibrous thickening of the dural root sleeves occurs,²⁶ the cervical nerve root diameter measured on STIR images may increase. This is because the high signal representing the root could actually include the thickened dural sleeve.¹¹ Furthermore, hypertrophy of the cervical nerve root does not necessarily occur in patients with CIDP.^{10 12} Therefore, our study did not demonstrate any significant difference in root diameter between the study groups. This result could be considered to be in accordance with genuine clinical settings.

In our study, the nerve-to-muscle CNR of the cervical nerve roots on STIR images was significantly higher in patients with CIDP. Signal intensity of the oedematous tissue increases on STIR images,²⁷ whereas the histological abnormalities typical of CIDP include

Table 1 Diameters, nerve-to-muscle CNRs, and CNR score in patients with CIDP and control patients

	CIDP (n=15)	Control (n=29)	p Value*
Diameter (mm)			
C5	3.89±1.36	3.75±1.09	0.92
C6	5.31±1.52	4.80±1.16	0.32
C7	5.70±1.73	4.93±1.14	0.16
C8	4.91±1.72	4.30±0.75	0.36
Nerve-to-muscle CNR			
C5	32.68±24.76	16.63±11.21	0.03
C6	36.76±24.26	20.06±15.03	0.02
C7	34.75±24.75	15.92±8.40	0.01
C8	30.09±22.87	18.49±17.51	0.04
CNR score	134.29±93.79	71.10±42.85	0.01

*Wilcoxon rank-sum test.

CIDP, chronic inflammatory demyelinating polyradiculoneuropathy; CNR, contrast-to-noise ratio; CNR score, the sum of nerve-to-muscle CNRs for C5–C8 nerve roots on the employed side.

perivascular mononuclear cells, diffuse mononuclear cells in the endoneurium, onion-bulb formations and oedema in the endoneurium as well as between the endoneurium and perineurium.¹ The increased nerve-to-muscle CNR in patients with CIDP demonstrated in our study may reflect the inflammatory process, including oedematous changes, in the cervical nerve roots. Of note, we used signal intensity of the sternocleidomastoid muscle to compute nerve-to-muscle CNR. Cranial nerve involvement is observed in approximately 15% of patients with CIDP.²⁸ Thus, signal intensity of the sternocleidomastoid muscle might have been higher among patients with CIDP than in control patients in our study, because the denervated muscles display higher signal intensity on STIR images.²⁹ This effect would make nerve-to-muscle CNR in patients with CIDP smaller than expected; hence our result that nerve-to-muscle CNR in the patients with CIDP had higher value seems valid.

CNR score, calculated to represent the overall signal intensity of the cervical nerve roots, showed adequate diagnostic accuracy for the diagnosis of CIDP, with the EFNS/PNS clinical and electrodiagnostic criteria used as the reference standard.⁸ The specificity of the EFNS/PNS criteria has been reported as approximately 96% when definite or probable criteria were met.^{30–31} In addition, we included only those patients who satisfied the EFNS/PNS typical and definite criteria. Therefore, the reference standard used in our study can be considered appropriate for evaluating the diagnostic accuracy of MRI assessment for the cervical nerve roots. Moreover, the reproducibility of the assessment procedure in our study was satisfactory. Consequently, our results suggest that assessment of the cervical nerve roots by MRI will be useful for the diagnosis of CIDP when signal intensities, rather than the diameters, are paid more attention on STIR images.

The limitations of our study are as follows. First, the study design embraces sampling bias. The small number of participants may have caused the biased enrolment of the patients with CIDP without cervical nerve root thickening. However, we selected patients with CIDP and control patients from the same institution and matched these groups with regard to sex, age and MRI system. Thus, such bias was adequately controlled.¹⁵ Second, the parameters of coronal STIR sequences showed some variability. This may have affected measurement of the cervical nerve root diameters. Nonetheless, the root boundary could be defined, even if a partial volume effect attenuated signal intensity of the root. This variability may also have affected signal intensity. However, we matched the MRI systems between patients with CIDP and control patients to assure equality of the condition to the extent possible. Therefore, we do not consider this limitation to have significantly affected the results. Third, the diagnoses of control patients did not include peripheral neuropathies. Therefore, our results could not show the usefulness of MRI in differentiating CIDP from other peripheral neuropathies.

In conclusion, assessment of the cervical nerve roots by MRI will be useful for the diagnosis of CIDP when signal intensities, rather than diameters, are paid more attention on STIR images. This is the first study that systematically measured the usefulness of MRI for the diagnosis of CIDP, with appropriately selected control patients.

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Contributors KT, NM and YY conceived the study and designed the protocol. TS supervised the conduct of the study and data collection, and provided statistical advice on study design and data analysis. KT enrolled the study participants, managed the data, drafted the manuscript and took responsibility for the manuscript as a whole. NM and YY performed interpretation of MRI. All authors contributed substantially to its revision.

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Competing interests None.

Ethics approval This study was approved by the Institutional Review Board of Tenri Hospital in Japan.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement No additional data are available.

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