Magnetic resonance imaging of the cervical nerve roots in the diagnosis of chronic inflammatory demyelinating polyradiculoneuropathy: A single-institution, retrospective case-control study

<table>
<thead>
<tr>
<th>Journal:</th>
<th>BMJ Open</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manuscript ID:</td>
<td>bmjopen-2013-003443</td>
</tr>
<tr>
<td>Article Type:</td>
<td>Research</td>
</tr>
<tr>
<td>Date Submitted by the Author:</td>
<td>19-Jun-2013</td>
</tr>
</tbody>
</table>
| Complete List of Authors: | Tanaka, Kanta; Tenri Hospital, Department of Neurology
Mori, Nobuyuki; Tenri Hospital, Department of Radiology
Yokota, Yusuke; Tenri Hospital, Department of Radiology
Suenaga, Toshihiko; Tenri Hospital, Department of Neurology |
| Primary Subject Heading: | Neurology |
| Secondary Subject Heading: | Radiology and imaging |
| Keywords: | chronic inflammatory demyelinating polyradiculoneuropathy, Magnetic resonance imaging < RADIOLOGY & IMAGING, short tau inversion recovery, diagnostic accuracy, cervical nerve roots |
Magnetic resonance imaging of the cervical nerve roots in the diagnosis of chronic inflammatory demyelinating polyradiculoneuropathy: A single-institution, retrospective case-control study

Kanta Tanaka¹, Nobuyuki Mori², Yusuke Yokota², Toshihiko Suenaga¹

¹Department of Neurology, Tenri Hospital, Tenri, Japan
²Department of Radiology, Tenri Hospital, Tenri, Japan

Correspondence to

Dr Kanta Tanaka, Department of Neurology, Tenri Hospital, 200 Mishima, Tenri, Nara 632-8552, Japan
Tel: (+81)743-63-5611
Fax: (+81)743-63-1530
E-mail: ktanaka@tenriyorozu.jp

Keywords: chronic inflammatory demyelinating polyradiculoneuropathy, magnetic resonance imaging, short tau inversion recovery, diagnostic accuracy, cervical nerve roots

Research paper, 2981 words (INTRODUCTION through DISCUSSION)

Reference number, 31
ABSTRACT

Objective: To systematically evaluate the usefulness of assessing the cervical nerve roots by magnetic resonance imaging (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 CIDP patients who satisfied the European Federation of Neurological Societies/Peripheral Nerve Society (EFNS/PNS) typical and definite criteria and underwent cervical MRI. Thirty 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 the standard deviation of background noise. Statistical analyses were performed to determine the
diagnostic accuracy of the diameters and nerve-to-muscle CNRs. Another radiologist reviewed the MR images for ensuring reproducibility.

**Results:** The root diameters showed no significant differences between the CIDP and control patients. The nerve-to-muscle CNRs were significantly higher in the CIDP patients. 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

1) Thus far, few studies have systematically evaluated the accuracy of magnetic resonance imaging (MRI) for the diagnosis of chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) with appropriately selected control subjects.

2) 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 messages

1) 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

1) This is the first study that systematically measured the usefulness of MRI for the diagnosis of CIDP, with appropriately selected control patients enrolled.

2) The study design embraces sampling bias. However, we selected 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 proven as insufficiently sensitive for clinical practice,[4] and new several 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. reported that more than 80% of the AAN criteria-negative but EFNS/PNS criteria-positive patients were responsive to treatment.[9] Therefore, improving the accuracy for the diagnosis of CIDP will help to prevent underdiagnosis.

Although EFNS/PNS supportive criteria, which assist the diagnosis by probably increasing the accuracy, 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. studied 14 consecutive patients with CIDP and reported that MRI revealed hypertrophy of the cervical nerve roots and
brachial plexus in eight patients.[10] Tazawa et al. reported that the cervical nerve root diameters on the short tau inversion recovery (STIR) images had higher values in 14 consecutive CIDP patients than in 10 control patients.[11] Adachi et al. reported that high intensity of the brachial plexus on STIR images was shown in nine out of 13 CIDP patients and that all plexuses with high intensity appeared swollen.[12] Thus far, however, few studies have systematically evaluated the accuracy of MRI for the diagnosis of CIDP with appropriately selected control subjects.[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 institutional review board of Tenri Hospital (200 Mishima, Tenri, Nara 632-8552, Japan) approved the research protocol. The need for informed consent was waived because this study did not impose any additional invasive procedure or cost on the study subjects and the information was sufficiently anonymised.

**Study subjects**

We enrolled 15 consecutive CIDP patients 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 includes MRI findings.[8] When the time from disease onset to MR imaging did not exceed 8 weeks, we judged if 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 ± standard deviation (SD) was 56.8 ± 16.6. The mean disease duration ± SD was 430.9 ± 693.3 weeks. Upper limb involvement was observed in all of the CIDP patients. 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- or bed-bound; 5, requiring assisted ventilation for at least part of the day or night; 6, dead) at the time of MR imaging among the CIDP patients was 2 (range, 1–4).[17, 18] The mean cerebrospinal fluid (CSF) protein level, which had been analysed most recently at the time of MR imaging, was 2.033 ± 3.018 g/l. Nine CIDP patients have undergone MR imaging before treatment. The remaining 6 CIDP patients have received treatment with steroid, intravenous immunoglobulin and/or immunoabsorption before MR imaging.

The control subjects 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 CIDP patient, 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 CIDP patient. Eventually, 30 control patients were enrolled. There were eight male and 22 female control patients; mean age ± 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 paresthesia, 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 examinations of all subjects were performed using 1.5-T MRI systems (MAGNETOM Avanto or MAGNETOM Vision, Siemens, Erlangen, Germany). The MRI image of each enrolled subject was reviewed in a random order on a workstation (Centricity Radiology RA 1000, GE Healthcare, IL, 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 (TR/TE/TI), 5500–7000/60–73/150–180 ms; section thickness, 3–5 mm; section gap, 0.2–1.2 mm; fields of view, 239–350 × 239–350 cm; imaging matrix, 192–230 × 256–384 matrix; number of excitations, 1. Axial and sagittal MR images 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.

The 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 intensities (SIs) in the C5–C8 roots and the sternocleidomastoid muscle, as well as the SD of background noise, were measured on coronal STIR images using an operator-defined region-of-interest (ROI). The ROI cursors were located on the side employed during diameter measurement. The ROIs were drawn to avoid vessels, prominent artefacts and focal differences in signal intensity in the corresponding areas. ROI for measuring the SD of background noise was positioned outside the patient’s body region. The nerve-to-muscle CNR was calculated as follows: nerve-to-muscle CNR = \([S_{\text{nerve}} - S_{\text{sternocleidomastoid muscle}}]/S_{\text{background noise}}\).

To investigate the reproducibility, another radiologist (NM, 12 years of experience in radiology) reviewed the MR images in the same way described above, also without prior knowledge of the patient 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 version 12.1 (Stata Corp. LP, College Station, TX, 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 CIDP patients 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 between 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 the CIDP patients 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]

Ninety-five percent confidence intervals (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 a lack of coronal STIR images. Ultimately, the data for the 15 CIDP patients and 29 control patients were analysed. The study flow chart is presented in figure 3. There were no statistically significant differences between the patient groups with respect to sex, age or MRI system (sex, p = 1.00; age, p = 0.95; MRI system, p =
The mean ± SD areas of the ROI located in the C5, C6, C7 and C8 nerve roots and sternocleidomastoid muscle were 5.05 ± 3.65 cm$^2$, 7.80 ± 4.52 cm$^2$, 8.67 ± 5.45 cm$^2$, 7.85 ± 5.14 cm$^2$, and 34.07 ± 17.56 cm$^2$, respectively, and were not significantly different between the patients groups (C5, p = 0.92; C6, p = 0.95; C7, p = 0.25; C8, p = 0.77; sternocleidomastoid muscle, p = 0.49). ROI for measuring the SD of background noise was 157.97 ± 150.47 cm$^2$. They were significantly higher in the CIDP patients (CIDP patients, 201.17 ± 127.66 cm$^2$; control patients, 135.62 ± 158.44 cm$^2$; p = 0.02). However, the ROI areas were large enough to prevent significant variability of the SD of background noise.

**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 the CIDP and control patients (C5, p = 0.92; C6, p = 0.32; C7, p = 0.16; C8, p = 0.36). However, two CIDP patients (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 the CIDP patients than in the control patients (C5, p = 0.03; C6, p = 0.02; C7, p = 0.01; 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 the 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, 0.568–0.894).
Table 1  Diameters, nerve-to-muscle CNRs, and CNR score in CIDP and control patients

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

CNR, contrast-to-noise ratio; CIDP, chronic inflammatory demyelinating polyradiculoneuropathy.
CNR score: the sum of nerve-to-muscle CNRs for C5-C8 nerve roots on the employed side.
*Wilcoxon rank sum test
In the CIDP patients, 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 the CIDP patients with and without treatments before MR imaging (p = 0.29).

**Reproducibility of the assessment procedure**

To determine the reproducibility of the assessment procedure, another radiologist (NM) reviewed the STIR cervical MR images. There were no statistically significant differences in root diameter between the CIDP and control patients (C5, p = 0.38; C6, p = 0.12; C7, p = 0.96; C8, p = 0.35). However, nerve-to-muscle CNRs were significantly higher in the CIDP patients, except for root C5 (C5, p = 0.12; C6, p= 0.003; C7, p= 0.03; C8, p = 0.04). The means ± SDs for CNR scores in the 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, 0.521–0.877). These results were similar to those described in the Main results section.

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

**DISCUSSION**

In our study, diameters of the C5–C8 roots showed no significant differences between the CIDP and control patients, whereas the nerve-to-muscle CNRs were significantly higher in the CIDP patients 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 obtained results 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 the CIDP and control patients, although two out of the 15 CIDP patients showed obvious thickening of the cervical nerve roots. This is different from the report by Tazawa et al., in which the root diameters on STIR images were significantly larger in the CIDP patients than in the control subjects.[11] Those control subjects, 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 subjects 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 the 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 CIDP patients.[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 the CIDP patients. Signal intensity of the oedematous
tissue increases on STIR images,[27] whereas the histological abnormalities typical of
CIDP include 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
CIDP patients demonstrated in our study may reflect the inflammatory process, including oedematous changes, in the cervical nerve roots. Of note, we used the signal intensity of the sternocleidomastoid muscle to compute nerve-to-muscle CNR. Cranial nerve involvement is observed in approximately 15% of CIDP patients.[28] Thus, signal intensity of the sternocleidomastoid muscle might have been higher among the CIDP patients than in the 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 the CIDP patients smaller than expected, hence our result that nerve-to-muscle CNR in the CIDP patients 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 96.0% when definite or probable criteria were met.[30, 31] In addition, we included only the 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 the 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 CIDP patients without cervical nerve root thickening. However, we selected 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 CIDP and control patients in order 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 the 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 enrolled.
Acknowledgements We thank Dr Takashi Kageyama, Dr Akiyo Shinde, Dr Daisuke Kambe and Dr Taro Okunomiya for their academic support and Yukikazu Hiura for his technical support.

Contributors KT, NM and YY conceived the study and designed the protocol. TS supervised the conduct of the study and data collection. KT enrolled the study subjects. NM and YY performed interpretation of the magnetic resonance images. KT managed the data. TS provided statistical advice on study design and data analysis. KT drafted the manuscript, and all authors contributed substantially to its revision. KT takes responsibility for the paper as a whole.

Funding This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None.

Ethics approval This study was approved by the institutional review board of Tenri Hospital in Japan.
Data sharing statement No additional data are available.
REFERENCES


18 Matsuoka N, Kohriyama T, Ochi K, et al. Detection of cervical nerve root...


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

Figure 2 Coronal STIR cervical MR image of a CIDP patient, 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 the sternocleidomastoid muscle (SCM), as well as SD of background noise, were measured using an operator-defined ROI. Nerve-to-muscle CNR = \([S_{\text{nerve}} - S_{\text{SCM}}]/SD_{\text{background noise}}\). Notably, this patient showed obvious thickening of the cervical nerve roots. STIR, short tau inversion recovery; MR, magnetic resonance; CIDP, chronic inflammatory demyelinating polyradiculoneuropathy; CNR, contrast-to-noise ratio; TR, repetition time; TE, echo time; TI, inversion time.
time; SI, mean signal intensity; SD, standard deviation; ROI, region-of-interest.

**Figure 3** Study flow chart. MRI, magnetic resonance imaging; EFNS/PNS, European Federation of Neurological Societies/Peripheral Nerve Society; CIDP, chronic inflammatory demyelinating polyradiculoneuropathy; STIR, short tau inversion recovery.
Figure 1 Coronal STIR cervical MR images. (A) A CIDP patient: TR/TE/TI = 6600/72/180 ms. (B) A cervical spondylosis patient matched for sex and age: TR/TE/TI = 7000/72/180 ms. The signal intensities of the cervical nerve roots are higher in the CIDP patient, although the diameters do not show significant difference between the patients. STIR, short tau inversion recovery; MR, magnetic resonance; CIDP, chronic inflammatory demyelinating polyradiculoneuropathy; TR, repetition time; TE, echo time; TI, inversion time.

90x40mm (300 x 300 DPI)
Figure 2 Coronal STIR cervical MR image of a CIDP patient, 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 the sternocleidomastoid muscle (SCM), as well as SD of background noise, were measured using an operator-defined ROI. Nerve-to-muscle CNR = [(SI_{nerve} - SI_{SCM})/SD_{background noise}]. Notably, this patient showed obvious thickening of the cervical nerve roots. STIR, short tau inversion recovery; MR, magnetic resonance; CIDP, chronic inflammatory demyelinating polyradiculoneuropathy; CNR, contrast-to-noise ratio; TR, repetition time; TE, echo time; TI, inversion time; SI, mean signal intensity; SD, standard deviation; ROI, region-of-interest.

90x78mm (300 x 300 DPI)
Figure 3 Study flow chart. MRI, magnetic resonance imaging; EFNS/PNS, European Federation of Neurological Societies/Peripheral Nerve Society; CIDP, chronic inflammatory demyelinating polyradiculoneuropathy; STIR, short tau inversion recovery.
<table>
<thead>
<tr>
<th>Section and Topic</th>
<th>Item #</th>
<th>Item</th>
</tr>
</thead>
<tbody>
<tr>
<td>TITLE/ABSTRACT/KEYWORDS</td>
<td>1</td>
<td>Identify the article as a study of diagnostic accuracy (recommend MeSH heading 'sensitivity and specificity').</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>State the research questions or study aims, such as estimating diagnostic accuracy or comparing accuracy between tests or across participant groups.</td>
</tr>
<tr>
<td>INTRODUCTION</td>
<td>3</td>
<td>The study population: The inclusion and exclusion criteria, setting and locations where data were collected.</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>Participant recruitment: Was recruitment based on presenting symptoms, results from previous tests, or the fact that the participants had received the index tests or the reference standard?</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>Participant sampling: Was the study population a consecutive series of participants defined by the selection criteria in item 3 and 4? If not, specify how participants were further selected.</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>Data collection: Was data collection planned before the index test and reference standard were performed (prospective study) or after (retrospective study)?</td>
</tr>
<tr>
<td>METHODS</td>
<td>7</td>
<td>The reference standard and its rationale.</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>Technical specifications of material and methods involved including how and when measurements were taken, and/or cite references for index tests and reference standard.</td>
</tr>
<tr>
<td></td>
<td>9</td>
<td>Definition of and rationale for the units, cut-offs and/or categories of the results of the index tests and the reference standard.</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>The number, training and expertise of the persons executing and reading the index tests and the reference standard.</td>
</tr>
<tr>
<td></td>
<td>11</td>
<td>Whether or not the readers of the index tests and reference standard were blind (masked) to the results of the other test and describe any other clinical information available to the readers.</td>
</tr>
<tr>
<td>Test methods</td>
<td>12</td>
<td>Methods for calculating or comparing measures of diagnostic accuracy, and the statistical methods used to quantify uncertainty (e.g. 95% confidence intervals).</td>
</tr>
<tr>
<td></td>
<td>13</td>
<td>Methods for calculating test reproducibility, if done.</td>
</tr>
<tr>
<td>RESULTS</td>
<td>14</td>
<td>When study was performed, including beginning and end dates of recruitment.</td>
</tr>
<tr>
<td></td>
<td>15</td>
<td>Clinical and demographic characteristics of the study population (at least information on age, gender, spectrum of presenting symptoms).</td>
</tr>
<tr>
<td></td>
<td>16</td>
<td>The number of participants satisfying the criteria for inclusion who did or did not undergo the index tests and/or the reference standard; describe why participants failed to undergo either test (a flow diagram is strongly recommended).</td>
</tr>
<tr>
<td></td>
<td>17</td>
<td>Time-interval between the index tests and the reference standard, and any treatment administered in between.</td>
</tr>
<tr>
<td></td>
<td>18</td>
<td>Distribution of severity of disease (define criteria) in those with the target condition; other diagnoses in participants without the target condition.</td>
</tr>
<tr>
<td></td>
<td>19</td>
<td>A cross tabulation of the results of the index tests (including indeterminate and missing results) by the results of the reference standard; for continuous results, the distribution of the test results by the results of the reference standard.</td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>Any adverse events from performing the index tests or the reference standard.</td>
</tr>
<tr>
<td>Estimates</td>
<td>21</td>
<td>Estimates of diagnostic accuracy and measures of statistical uncertainty (e.g. 95% confidence intervals).</td>
</tr>
<tr>
<td></td>
<td>22</td>
<td>How indeterminate results, missing data and outliers of the index tests were handled.</td>
</tr>
<tr>
<td></td>
<td>23</td>
<td>Estimates of variability of diagnostic accuracy between subgroups of participants, readers or centers, if done.</td>
</tr>
<tr>
<td></td>
<td>24</td>
<td>Estimates of test reproducibility, if done.</td>
</tr>
<tr>
<td>DISCUSSION</td>
<td>25</td>
<td>Discuss the clinical applicability of the study findings.</td>
</tr>
</tbody>
</table>
Magnetic resonance imaging of the cervical nerve roots in the diagnosis of chronic inflammatory demyelinating polyradiculoneuropathy: A single-institution, retrospective case-control study

Kanta Tanaka¹, Nobuyuki Mori², Yusuke Yokota², Toshihiko Suenaga¹

¹Department of Neurology, Tenri Hospital, Tenri, Japan

²Department of Radiology, Tenri Hospital, Tenri, Japan

Correspondence to

Dr Kanta Tanaka, Department of Neurology, Tenri Hospital, 200 Mishima, Tenri, Nara 632-8552, Japan

Tel: (+81)743-63-5611

Fax: (+81)743-63-1530

E-mail: ktanaka@tenriyorozu.jp

Keywords: chronic inflammatory demyelinating polyradiculoneuropathy, magnetic resonance imaging, short tau inversion recovery, diagnostic accuracy, cervical nerve roots

Research paper, 298104 words (INTRODUCTION through DISCUSSION)
ABSTRACT

Objective: The aim of this study was to systematically evaluate the usefulness of assessing the cervical nerve roots by magnetic resonance imaging (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 CIDP patients who satisfied the European Federation of Neurological Societies/Peripheral Nerve Society (EFNS/PNS) typical and definite criteria and underwent cervical MRI. Thirty 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 the standard deviation of background noise. Statistical analyses were performed to determine the
diagnostic accuracy of the diameters and nerve-to-muscle CNRs. Another radiologist
reviewed the MR images for ensuring reproducibility.

**Results:** The root diameters showed no significant differences between the CIDP and
control patients. The nerve-to-muscle CNRs were significantly higher in the CIDP
patients. 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

1) Thus far, few studies have systematically evaluated the accuracy of magnetic resonance imaging (MRI) for the diagnosis of chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) with appropriately selected control subjects.

2) 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 messages

1) 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

1) This is the first study that systematically measured the usefulness of MRI for the diagnosis of CIDP, with appropriately selected control patients enrolled.
2) The study design embraces sampling bias. However, we selected 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 proven as insufficiently sensitive for clinical practice.[4] and new several 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. reported that more than 80% of the AAN criteria-negative but EFNS/PNS criteria-positive patients were responsive to treatment.[9] Therefore, improving the accuracy for the diagnosis of CIDP will help to prevent underdiagnosis.

Although EFNS/PNS supportive criteria, which assist the diagnosis by probably increasing the accuracy, 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. studied 14 consecutive patients with CIDP and reported that MRI revealed hypertrophy of the cervical nerve roots and brachial plexus in eight patients.[10] Tazawa et al. reported that the cervical nerve root diameters on the short tau inversion recovery (STIR) images had higher values in 14 consecutive CIDP patients than in 10 control patients.[11] Adachi et al. reported that high intensity of the brachial plexus on STIR images was shown in nine out of 13 CIDP patients and that all plexuses with high intensity appeared swollen.[12] Thus far, however, few studies have systematically evaluated the accuracy of MRI for the diagnosis of CIDP with appropriately selected control subjects.[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 institutional review board of Tenri Hospital (200 Mishima, Tenri, Nara 632-8552, Japan) approved the research protocol. The need for informed consent was waived because this study did not impose any additional invasive procedure or cost on the study subjects and the information was sufficiently anonymised.

Study subjects

We enrolled 15 consecutive CIDP patients 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 includes MRI findings.[8] When the time from disease onset to MR imaging did not exceed 8 weeks, we judged if 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 ± standard
deviation (SD) was 56.8 ± 16.6. The mean disease duration ± SD was 430.9 ± 693.3 weeks. Upper limb involvement was observed in all of the CIDP patients. The functional disability of patients at the time of MR imaging was assessed on the scale adopted by Hughes (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- or bed-bound; 5, requiring assisted ventilation for at least part of the day or night; 6, dead).[17, 18] 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- or bed-bound; 5, requiring assisted ventilation for at least part of the day or night; 6, dead) at the time of MR imaging among the CIDP patients was 2 (range, 1–4).[17, 18] The total protein level of cerebrospinal fluid (CSF), which had been analysed most recently at the time of MR imaging, was recorded for each CIDP patient. The mean cerebrospinal fluid (CSF) protein level, which had been analysed most recently at the time of MR imaging, was 2.033 ± 3.018 g/l. Nine CIDP patients have undergone MR imaging before any treatment was administered. The remaining 6 CIDP patients have received treatment with steroid, intravenous immunoglobulin and/or immunoabsorption before MR imaging.
The control subjects were patients who were required to undergo cervical MRI from October 2005 to April 2011 and who did not satisfy the EFNS/PNS criteria. The enrolment procedure was as follows. We sampled the candidate patients matched with respect to sex, age (± 2 years), and MRI system for each enrolled CIDP patient, using the MRI reporting system at our institution. None of the 124 candidate patients that we examined satisfied the EFNS/PNS criteria [8]. Then, we randomly sampled the final control patients from the candidate patients without replacement, in which two control patients were sampled for each CIDP patient. Eventually, 30 control patients were enrolled. There were eight male and 22 female control patients; mean age ± 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 paresthesia, 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 examinations of all subjects were performed using 1.5-T MRI systems (MAGNETOM Avanto or MAGNETOM Vision, Siemens, Erlangen, Germany). The MRI image of each enrolled subject was reviewed retrospectively in a random order on a picture-archiving and communication system workstation (Centricity Radiology RA 1000, GE Healthcare, IL, USA) by a radiologist (YY, 1 year of experience in radiology), who had 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 (TR/TE/TI), 5500–7000/60–73/150–180 ms; section thickness, 3–5 mm; section gap, 0.2–1.2 mm; fields of view, 239–350 × 239–350 cm; imaging matrix, 192–230 × 256–384 matrix; number of excitations, 1. Axial and sagittal MR images 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] Although root diameters were measured on both sides, the diameter of the larger side was employed as the root diameter of that vertebral level.

The signal intensity of the cervical nerve root was quantified as a
nerve-to-muscle contrast-to-noise ratio (CNR). To compute the nerve-to-muscle CNRs, mean signal intensities (SIs) in the C5–C8 roots and the sternocleidomastoid muscle, as well as the SD of background noise, were measured on coronal STIR images using an operator-defined region-of-interest (ROI). The ROI cursors were located on the side employed during diameter measurement. The ROIs were drawn to avoid vessels, prominent artefacts and focal differences in signal intensity in the corresponding areas. ROI for measuring the SD of background noise was positioned outside the patient’s body region, i.e. in the air. The nerve-to-muscle CNR was calculated as follows:

\[
\text{nerve-to-muscle CNR} = \frac{\text{SI}_{\text{nerve}} - \text{SI}_{\text{sternocleidomastoid muscle}}}{\text{SD}_{\text{background noise}}}.
\]

To investigate the reproducibility of the assessment procedure, another radiologist (NM, 12 years of experience in radiology) reviewed the cervical MR images in the same way described above, also without prior knowledge of the patient 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 version 12.1 (Stata Corp. LP, College Station, TX, 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 CIDP patients 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 between 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 the CIDP patients 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]

Ninety-five percent confidence intervals (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 a lack of coronal STIR images. Ultimately, the data for the 15 CIDP patients and 29 control patients were analysed. The study flow chart is presented in figure 3. The characteristics of the study subjects in the CIDP and control patient groups are shown in table 1. There were no statistically significant differences between the patient groups with respect to sex, age or MRI system (sex, p = 1.00; age, p = 0.95; MRI system, p = 1.00).

The mean ± SD areas of the ROI located in the C5, C6, C7 and C8 nerve roots and sternocleidomastoid muscle were 5.05 ± 3.65 cm², 7.80 ± 4.52 cm², 8.67 ± 5.45 cm², 7.85 ± 5.14 cm², and 34.07 ± 17.56 cm², respectively, and were not significantly...
different between the patients groups (C5, p = 0.92; C6, p = 0.95; C7, p = 0.25; C8, p = 0.77; sternocleidomastoid muscle, p = 0.49). ROI for measuring the SD of background noise was $157.97 \pm 150.47 \text{ cm}^2$. They were significantly higher in the CIDP patients (CIDP patients, $201.17 \pm 127.66 \text{ cm}^2$; control patients, $135.62 \pm 158.44 \text{ cm}^2$; p = 0.02). However, the ROI areas were large enough to prevent significant variability of the SD of background noise.
<table>
<thead>
<tr>
<th>Table 1</th>
<th>Characteristics of study subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CIDP patients</td>
</tr>
<tr>
<td></td>
<td>(n = 15)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>4</td>
</tr>
<tr>
<td>Female</td>
<td>11</td>
</tr>
<tr>
<td>Age (years)</td>
<td>56.8 ± 16.6</td>
</tr>
<tr>
<td>MRI systems: n</td>
<td></td>
</tr>
<tr>
<td>Avanto</td>
<td>9</td>
</tr>
<tr>
<td>Vision</td>
<td>6</td>
</tr>
</tbody>
</table>

CIDP, chronic inflammatory demyelinating polyradiculoneuropathy; MRI, magnetic resonance imaging.

*Fisher’s exact test

**Wilcoxon rank sum test
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 21. For the diameters, there were no statistically significant differences between the CIDP and control patients (C5, p = 0.92; C6, p = 0.32; C7, p = 0.16; C8, p = 0.36). However, two CIDP patients (see also figure 2) showed obvious thickening of the cervical nerve roots with a similar extent, and the diameters tended to be larger in the CIDP patients than in the control patients. The nerve-to-muscle CNRs of the C5, C6, C7 and C8 roots were significantly higher in the CIDP patients than in the control patients (C5, p = 0.03; C6, p = 0.02; C7, p = 0.01; 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 21). The means ± SDs of CNR scores in the 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, 0.568–0.894) (figure 4).
<table>
<thead>
<tr>
<th>Table 21</th>
<th>Diameters, nerve-to-muscle CNRs, and CNR score in CIDP and control patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CIDP (n = 15)</td>
</tr>
<tr>
<td>Diameter (mm)</td>
<td></td>
</tr>
<tr>
<td>C5</td>
<td>3.89 ± 1.36</td>
</tr>
<tr>
<td>C6</td>
<td>5.31 ± 1.52</td>
</tr>
<tr>
<td>C7</td>
<td>5.70 ± 1.73</td>
</tr>
<tr>
<td>C8</td>
<td>4.91 ± 1.72</td>
</tr>
<tr>
<td>Nerve-to-muscle CNR</td>
<td></td>
</tr>
<tr>
<td>C5</td>
<td>32.68 ± 24.76</td>
</tr>
<tr>
<td>C6</td>
<td>36.76 ± 24.26</td>
</tr>
<tr>
<td>C7</td>
<td>34.75 ± 24.75</td>
</tr>
<tr>
<td>C8</td>
<td>30.09 ± 22.87</td>
</tr>
<tr>
<td>CNR score</td>
<td>134.29 ± 93.79</td>
</tr>
</tbody>
</table>

CNR, contrast-to-noise ratio; CIDP, chronic inflammatory demyelinating polyradiculoneuropathy.

CNR score: the sum of nerve-to-muscle CNRs for C5-C8 nerve roots on the employed side.

*Wilcoxon rank sum test
In the CIDP patients, 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 the CIDP patients with and without treatments before MR imaging (p = 0.29).

Reproducibility of the assessment procedure

To determine the reproducibility of the assessment procedure, another radiologist (NM) reviewed the STIR cervical MR images. There were no statistically significant differences in root diameter between the CIDP and control patients (C5, p = 0.38; C6, p = 0.12; C7, p = 0.96; C8, p = 0.35). However, nerve-to-muscle CNRs were significantly higher in the CIDP patients, except for root C5 (C5, p = 0.12; C6, p = 0.003; C7, p = 0.03; C8, p = 0.04). The means ± SDs for CNR scores in the 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, 0.521–0.877). These results were similar to those described in the Main results section.

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

**DISCUSSION**

In our study, diameters of the C5–C8 roots showed no significant differences between
the CIDP and control patients, whereas the nerve-to-muscle CNRs were significantly
higher in the CIDP patients on coronal STIR images. We defined the sum of
nerve-to-muscle CNRs of the C5–C8 roots as the CNR score to represent the overall
signal intensity of those roots. 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 obtained results 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 the CIDP and control patients, although two out of the 15 CIDP patients
showed obvious thickening of the cervical nerve roots. This is different from the report
by Tazawa et al., in which the root diameters as depicted on STIR images were
significantly larger in the CIDP patients than in the control subjects.[11] Those control subjects, 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 subjects 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 the 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] Tazawa et al.’s abovementioned study did not include patients with cervical spondylosis as control subjects.[11] Furthermore, hypertrophy of the cervical nerve root does not necessarily occur in CIDP patients.[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, which was used to quantify signal intensity of the cervical nerve root on STIR
images, was significantly higher in the CIDP patients. Signal intensity of the oedematous tissue increases on STIR images,[27] whereas the histological abnormalities typical of CIDP include 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 CIDP patients demonstrated in our study may reflect the inflammatory process, including oedematous changes, in the cervical nerve roots. Of note, we used the signal intensity of the sternocleidomastoid muscle to compute nerve-to-muscle CNR. Cranial nerve involvement is observed in approximately 15% of CIDP patients.[28] A previous study has reported neck muscle weakness in four out of 53 patients.[1] Thus, signal intensity of the sternocleidomastoid muscle might have been higher among the CIDP patients than in the 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 the CIDP patients smaller than expected, hence our result that nerve-to-muscle CNR in the CIDP patients 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. (Figure
The specificity of the EFNS/PNS criteria has been reported as approximately 96.0% when definite or probable criteria were met. In addition, we included only the 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, including CNR score. Moreover, the reproducibility of the assessment procedure in our study was satisfactory, with respect to the diameters, nerve-to-muscle CNRs, and diagnostic accuracy. Consequently, our results suggest that assessment of the cervical nerve roots by MRI will be useful for the diagnosis of CIDP when the 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 CIDP patients without cervical nerve root thickening. However, we selected 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. Moreover, this is the first study where appropriately sampled control patients were enrolled.

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 CIDP and control patients in order 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 the 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 enrolled.
Acknowledgements We thank Dr Takashi Kageyama, Dr Akiyo Shinde, Dr Daisuke Kambe and Dr Taro Okunomiya for their academic support and Yukikazu Hiura for his technical support.

Contributors KT, NM and YY conceived the study and designed the protocol. TS supervised the conduct of the study and data collection. KT enrolled the study subjects. NM and YY performed interpretation of the magnetic resonance images. KT managed the data. TS provided statistical advice on study design and data analysis. KT drafted the manuscript, and all authors contributed substantially to its revision. KT takes responsibility for the paper as a whole.

Funding This research received no specific grant from any funding agency in the public,
commercial or not-for-profit sectors.

**Competing interests** None.

**Ethics approval** This study was approved by the institutional review board of Tenri Hospital in Japan.

**Data sharing statement** No additional data are available.
REFERENCES


5 Hughes R, Bensa S, Willison H, et al. Randomized controlled trial of intravenous


23 Steichen TJ, Cox NJ. A note on the concordance correlation coefficient. The Stata


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

Figure 2 Coronal STIR cervical MR image of a CIDP patient, 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 the sternocleidomastoid muscle (SCM), as well as SD of background noise, were measured using an operator-defined ROI. Nerve-to-muscle CNR = \[\frac{S_{\text{nerve}} - S_{\text{SCM}}}{\text{SD}_{\text{background noise}}}\]. Notably, this patient showed obvious thickening of the cervical nerve roots. STIR, short tau inversion recovery; MR, magnetic resonance; CIDP, chronic inflammatory demyelinating polyradiculoneuropathy; CNR, contrast-to-noise ratio; TR, repetition time; TE, echo time; TI, inversion time; SI, mean signal intensity; SD, standard deviation; ROI, region-of-interest.

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

Figure 4 An ROC curve depicting the accuracy of the CNR score of the cervical nerve roots on coronal STIR images for the diagnosis of chronic inflammatory demyelinating polyradiculoneuropathy. The CNR score is the sum of nerve-to-muscle CNRs for nerve roots C5–C8 and was considered to represent overall signal intensity. The area under the ROC curve was 0.731 (95% CI,
0.569–0.894). The dashed line represents the curve for a test that is no better than chance. ROC, receiver operating characteristic; CNR, contrast-to-noise ratio; STIR, short tau inversion recovery.