


RESEARCH REPORT

Diagnosis and treatment of chronic inflammatory demyelinating polyradiculoneuropathy in clinical practice: A survey among Dutch neurologists

Merel C. Broers¹  | Pieter A. van Doorn¹ | Krista Kuitwaard² | Filip Eftimov³ | Paul W. Wirtz⁴ | Stephan Goedee⁵ | Hester F. Lingsma⁶ | Bart C. Jacobs^{1,7}

¹Department of Neurology, Erasmus MC, University Medical Center Rotterdam, Rotterdam, The Netherlands

²Department of Neurology, Albert Schweitzer Hospital, Dordrecht, The Netherlands

³Department of Neurology, Amsterdam UMC, University of Amsterdam, Amsterdam, The Netherlands

⁴Department of Neurology, Haga Teaching Hospital, The Hague, The Netherlands

⁵Department of Neurology, Brain Centre Rudolf Magnus, UMC Utrecht, Utrecht, The Netherlands

⁶Department of Public Health, Erasmus MC, University Medical Center Rotterdam, Rotterdam, The Netherlands

⁷Department of Immunology, Erasmus MC, University Medical Center Rotterdam, Rotterdam, The Netherlands

Correspondence

Merel C. Broers, Department of Neurology, Erasmus MC, University Medical Center Rotterdam, Rotterdam, The Netherlands.
Email: m.broers@erasmusmc.nl

Funding information

Prinses Beatrix Spierfonds, Grant/Award Number: W.OR16-18

Abstract

The diagnosis and treatment of chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is often a challenge. The clinical presentation is diverse, accurate biomarkers are lacking, and the best strategy to initiate and maintain treatment is unclear. The aim of this study was to determine how neurologists diagnose and treat CIDP. We conducted a cross-sectional survey on diagnostic and treatment practices among Dutch neurologists involved in the clinical care of CIDP patients. Forty-four neurologists completed the survey (44/71; 62%). The respondents indicated to use the European Federation of Neurological Societies/Peripheral Nerve Society (EFNS/PNS) 2010 CIDP guideline for the diagnosis in 77% and for treatment in 50%. Only 57% of respondents indicated that the presence of demyelinating electrophysiological findings was mandatory to confirm the diagnosis of CIDP. Most neurologists used intravenous immunoglobulins (IVIg) as first choice treatment, but the indications to start, optimize, or withdraw IVIg, and the use of other immune-modulatory therapies varied. University-affiliated respondents used the EFNS/PNS 2010 diagnostic criteria, nerve imaging tools, and immunosuppressive drugs more often. Despite the existence of an international guideline, there is considerable variation among neurologists in the strategies employed to diagnose and treat CIDP. More specific recommendations regarding: (a) the minimal set of electrophysiological requirements to diagnose CIDP, (b) the possible added value of nerve imaging, especially in patients not meeting the electrodiagnostic criteria, (c) the most relevant serological examinations, and (d) the clear treatment advice, in the new EFNS/PNS guideline, would likely support its implementation in clinical practice.

KEYWORDS

chronic inflammatory demyelinating polyradiculoneuropathy, corticosteroid, guideline, immunoglobulin, survey

1 | INTRODUCTION

Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is a rare, treatable immune-mediated neuropathy that typically presents as a symmetric chronic progressive or relapsing sensorimotor polyneuropathy of all extremities, often with clear involvement of proximal muscles.^{1,2} Despite the published European Federation of Neurological Societies/Peripheral Nerve Society (EFNS/PNS) 2010 diagnostic criteria for CIDP, the diagnosis can be challenging, leading to both over- and underdiagnosis.³⁻⁸ The extent to which patients can differ in clinical presentation has become more visible in the last decade, resulting in an extended group of atypical CIDP variants, such as distal predominant and asymmetric, for which clear definitions are lacking.^{1,9} In addition, not all patients with a clinical suspicion of CIDP completely fulfil the EFNS/PNS 2010 (electro) diagnostic criteria for CIDP.¹ Moreover, there is a broad differential diagnosis where accurate diagnostic biomarkers for CIDP are lacking.^{1,10} Intravenous (IVIg) and subcutaneous (SCIg) immunoglobulins, corticosteroids, and plasma-exchange (PE) are all proven effective treatments for CIDP.¹¹⁻¹⁵ The best strategy to initiate and maintain treatment, however, is not known, largely due to a lack of head to head and long-term treatment comparisons.¹⁵ Furthermore, the best approach to manage wear-off signs and withdrawal of IVIg is unclear.^{16,17} Because of these challenges, we expect that both the diagnostic workup and treatment strategies for CIDP patients are highly variable.

Insight in current clinical practice and potential diagnostic and therapeutic pitfalls is needed to improve current CIDP guidelines and could help for educational purposes. Therefore, the aim of this study is to determine how Dutch neurologists diagnose and treat patients with CIDP, and their use of existing CIDP guidelines.

2 | MATERIALS AND METHODS

2.1 | Study design

A cross-sectional questionnaire study was conducted among neurologists who diagnose and/or treat CIDP patients. We approached all university hospitals in The Netherlands ($n = 7$), and all non-university hospitals in South Holland ($n = 14$), the province where the Erasmus MC is located, to participate. We included non-university hospitals in only one Dutch province due to logistic reasons and because we expected that, our regional network would maximize the participation rate of the neurologists. We approached: (a) neurologists who had referred patients with CIDP to the Erasmus MC, (b) neurologists who indicated on their hospital website that they had expertise in neuromuscular diseases, (c) neurologists that were part of our (CIDP) network, and (d) neurologists who were participating in our ongoing research projects on Guillain-Barré syndrome (GBS) or CIDP. This study was approved by the medical ethical

committee of the Erasmus University Medical Center in Rotterdam (MEC-2018-1569).

2.2 | Development survey

Based on the current literature and clinical experience, M. C. B. and B. C. J. developed an online survey with multiple-choice (multi-select and single-select) and open-ended questions. The full set of questions could be filled out in 20 minutes, and included the following topics: (a) diagnostic workup of CIDP, (b) treatment of CIDP, and (c) profile of the neurologist. In several questions, we asked for quantitative estimations. The respondents could indicate how often they used a particular diagnostic or treatment strategy (never = 0%, rarely = 1-10%, sometimes = 10-50%, most of the time = 50-90%, and always = 90-100%). We defined 'most of the time' and 'always' as essential in the diagnostic workup or representative of the general policy of the responding neurologist. The survey was reviewed by an expert in medical decision-making (H. F. L.) and four neurologists from both university (P. A. D., F. E.) and non-university hospitals (K. K., P. W. W.) who regularly diagnose and/or treat CIDP patients. A pilot version of the survey was tested by the GBS/CIDP research team at Erasmus MC to ensure that all questions were clear. Several strategies were used to increase the response rate.¹⁸⁻²⁰ The survey was developed in English, with the aim of facilitating and extending its use and to enable future comparison in an international setting. The survey is available on request.

2.3 | Data collection

We used the GemsTracker Software for web-based data collection.²¹ Neurologists were invited by email with a personal link to access the online survey. Neurologists were asked to provide information based on their own individual strategy of preference (eg, not necessarily according to their local departmental policies) regarding the diagnosis and treatment of CIDP. No specific information regarding individual patients was collected.

2.4 | Statistical analyses

We presented continuous data as means and SD or medians with full ranges. Frequencies and proportions were calculated for dichotomized and categorical variables related to the number of respondents for that variable. We examined factors associated with diagnostic and treatment practice, including (a) university affiliation, (b) expertise in neuromuscular diseases, (c) more than 5 CIDP diagnosed patients per year, and (d) more than 10 CIDP patients in follow-up, with the χ^2 test and Fisher's exact test. A two-sided P -value $< .05$ was considered significant. We used Statistical Package for Social Sciences (SPSS) version 25 for data analysis.

TABLE 1 Profile of participating neurologists (n = 44)

Age, y, n (%)	
≤40	12 (27)
41-50	17 (39)
51-60	11 (25)
>60	4 (9)
Hospital type, n (%)	
University	25 (57)
Non-university	19 (43)
Years practicing as neurologist, median (range)	11 (1-36)
Field of interest or expertise in neuromuscular diseases ^a , n (%)	31 (71)
Completion fellowship neuromuscular diseases, n (%)	15 (34)
CIDP patients diagnosed per year, n (%)	
<1	16 (36)
1-5	18 (41)
6-10	6 (14)
11-20	4 (9)
CIDP patients currently treated or under follow-up, n (%)	
0	10 (23)
1-10	26 (60)
11-25	5 (11)
26-50	1 (2)
>50	2 (5)

Abbreviation: CIDP, chronic inflammatory demyelinating polyradiculoneuropathy.

^aExpertise in neuromuscular diseases (64%), immune-mediated diseases of the peripheral nervous system (32%), and/or clinical neurophysiology (16%).

3 | RESULTS

3.1 | Participating neurologists

The survey was sent to 81 neurologists between June 2018 and September 2018. Ten neurologists were excluded, because they no longer diagnosed or treated CIDP patients (n = 7) or were no longer employed at one of the included centers (n = 3). Forty-four neurologists completed the survey (response rate 62%). The respondents varied regarding age and experience as a neurologist (Table 1). Twenty-five respondents worked in a university hospital and 19 respondents in a non-university hospital. The majority of respondents (71%) reported neuromuscular diseases as field of interest or expertise. Ten respondents (23%) diagnosed more than 5 CIDP patients yearly and eight (18%) had more than 10 CIDP patients under follow-up.

3.2 | Diagnosis of CIDP

Most respondents (77%) indicated that they used the EFNS/PNS 2010 diagnostic criteria for CIDP (Table 2). Various laboratory tests were performed in the diagnostic workup of CIDP to exclude other diagnoses

TABLE 2 Diagnostic workup of CIDP (n = 44)

Diagnostic criteria used	
EFNS/PNS 2010 ³	34 (77)
(Local) guideline based on EFNS/PNS 2010 ³ , n (%)	40 (91)
Lumbar puncture	
CSF testing essential, n (%)	24 (55)
Reason to testing CSF, n (%)	
Support or confirm CIDP diagnosis	28 (64)
Exclude other diseases	39 (89)
How CSF results are used, n (%)	
Elevated CSF protein level without pleiocytosis support (but is not mandatory) CIDP diagnosis	39 (89)
Normal CSF protein level will raise doubt about CIDP diagnosis	3 (7)
Pleiocytosis will raise doubt about CIDP diagnosis	27 (61)
Pleiocytosis is not compatible with CIDP	2 (5)
NCS	
NCS essential, n (%)	43 (98)
Reason to perform NCS, n (%)	
Demyelinating features are mandatory to confirm CIDP diagnosis	25 (57)
Demyelinating features support CIDP diagnosis, but are not mandatory to confirm the diagnosis	18 (41)
To exclude other diseases	6 (14)
NUS	
NUS used to support or to confirm CIDP diagnosis, n (%)	
Never	11 (25)
Most of the time/always	15 (34)
Contribution findings nerve ultrasound to confirm CIDP diagnosis, n (%)	
Positive findings support CIDP diagnosis. However, positive findings are not specific and negative findings do not exclude the diagnosis.	40 (91)
MRI nerve root and/or plexus	
MRI nerve root or plexus used to support or to confirm CIDP diagnosis, n (%)	
Never	8 (18)
Most of the time/always	3 (7)
Contribution findings MRI nerve root or plexus to confirm CIDP diagnosis, n (%)	
Positive findings support CIDP diagnosis. However, positive findings are not specific and negative findings do not exclude the diagnosis.	37 (84)

Abbreviations: CIDP, chronic inflammatory demyelinating polyradiculoneuropathy; CSF, cerebrospinal fluid; EFNS, European Federation of Neurological Societies; MRI, magnetic resonance imaging; NCS, nerve conduction studies; NUS, nerve ultrasound; PNS, Peripheral Nerve Society.

(Figure A1). Of all respondents, 91% screened for the presence of paraproteinemia. Almost all respondents indicated that nerve conduction studies (NCS) were essential in the diagnostic workup of CIDP; however, only 57% indicated that demyelinating findings on NCS were mandatory

TABLE 3 Treatment of CIDP (n = 34)

Guideline used	
EFNS/PNS 2010 ³ , n (%)	17 (50)
(Local) guideline based on EFNS/PNS 2010 ³ , n/N (%)	31/33 (94)
Hospital facilities of respondents	
Hospital day care available for IVIg treatment, n (%)	30 (88)
Plasma exchange facility available in hospital, n (%)	29 (85)
Initial therapy	
Fulfillment of diagnostic criteria for CIDP required to start initial therapy, n (%)	
Yes	1 (3)
Yes, with the exception of patients who not completely fulfilling the diagnostic criteria but are highly suspected for CIDP	31 (91)
No	2 (6)
When do you start (induction) therapy? n (%)	
In all cases of CIDP irrespective of the signs or symptoms and the interference with daily life activities	11 (32)
Only in cases of CIDP with severe signs or symptoms that interfere with daily life activities	23 (68)
Long-term and maintenance treatment with IVIg	
When do you start IVIg maintenance therapy? n/N (%)	
Improvement after first IVIg induction course not followed by deterioration	8/28 (29)
Improvement after first IVIg induction course followed by deterioration	7/28 (25)
Improvement after second IVIg induction course not followed by deterioration	4/28 (14)
Improvement after second IVIg induction course followed by deterioration	8/28 (29)
Other	1/28 (4)
First choice in case of clinical deterioration while on IVIg treatment, n/N (%)	
Increase IVIg dosage	14/31 (45)
Increase IVIg frequency	6/31 (19)
Give an extra IVIg course	6/31 (19)
Other	5/31 (16)
First choice in case of occurring wear-off symptoms on IVIg treatment, n/N (%)	
Increase IVIg dosage	2/31 (7)
Increase IVIg frequency	28/31 (90)
Other	1/31 (3)
Treatment strategy in clinically stable patients on IVIg treatment, n/N (%)	
Reduce IVIg dosage	13/31 (42)
Reduce IVIg frequency	12/31 (39)
Stop IVIg	3/31 (10)
Other	3/31 (10)
How many months does the patient need to be stable before you try to reduce (or stop) maintenance therapy with IVIg? n/N (%)	
3	6/31 (19)
6	19/31 (61)
12	3/31 (10)
Other	3/31 (10)

Abbreviations: CIDP, chronic inflammatory demyelinating polyradiculoneuropathy; EFNS, European Federation of Neurological Societies; IVIg, intravenous immunoglobulins; PNS, Peripheral Nerve Society.

to confirm a CIDP diagnosis. Cerebrospinal fluid (CSF) testing was considered mandatory for the diagnostic workup of CIDP in only 55% of respondents. This may be explained by the fact that majority of respondents considered an elevated CSF protein level not a prerequisite to confirm CIDP diagnosis. Thirty-four percent of respondents indicated

that nerve ultrasound (NUS) was generally used to support or confirm CIDP diagnosis, while only 7% indicated using magnetic resonance imaging (MRI) as diagnostic tool. The minority of respondents with a non-university affiliation (42%) indicated that their general policy was to refer patients to a center of expertise to confirm CIDP diagnosis.

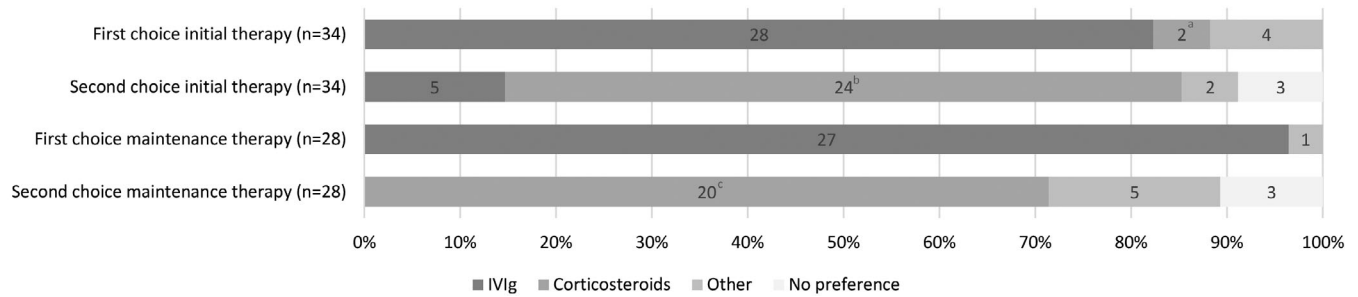


FIGURE 1 First and second choice initial and maintenance treatment of CIPD (n = 34). CIPD, chronic inflammatory demyelinating polyradiculoneuropathy; IVIg, intravenous immunoglobulins. Superscript alphabets a, b, and c represent methylprednisolone (n = 1) and dexamethasone (n = 1); prednisone/prednisolone (n = 14), dexamethasone (n = 6), methylprednisolone (n = 2), and other (n = 2); and prednisone/prednisolone (n = 16), dexamethasone (n = 3), and other (n = 1), respectively

3.2.1 | Factors associated with diagnostic practice

The EFNS/PNS 2010 diagnostic criteria was used more often by university-affiliated respondents ($P = .07$), neuromuscular experts ($P < .01$), and respondents diagnosing more than five CIPD patients yearly ($P = .09$). Respondents who indicated that electrophysiological demyelinating features support a CIPD diagnosis but were not mandatory to confirm the diagnosis of CIPD performed NUS more often (44% vs 24%; $P = .16$), although this was not significantly associated. NUS was more often performed by university-affiliated respondents ($P < .01$), neuromuscular experts ($P < .01$), and respondents who diagnose more CIPD patients (>5) yearly ($P = .02$). A similar correlation was seen for MRI and university-affiliated respondents (3 vs 0 respondents; $P = .25$) and neuromuscular experts (3 vs 0 respondents; $P = 0.54$), although this was not significantly associated.

3.3 | Treatment of CIPD

3.3.1 | General

Thirty-four (77%) respondents indicated that they were treating CIPD patients, and half of them indicated that they used the EFNS/PNS 2010 treatment guideline (Table 3). Almost all respondents indicated that fulfilment of diagnostic criteria was required to start therapy, with the exception of patients with a high clinical suspicion that did not completely fulfil these diagnostic criteria. Thirteen (68%) respondents with a non-university affiliation treated CIPD patients, of which the minority (31%) indicated that their general policy was to refer patients to a center of expertise for a treatment-related second opinion.

3.3.2 | Initial therapy

The majority of respondents (68%) indicated that they only started (induction) therapy in patients with severe signs or symptoms that interfered with daily life activities, while 32% of respondents indicated that they started therapy in all diagnosed CIPD cases. Most respondents

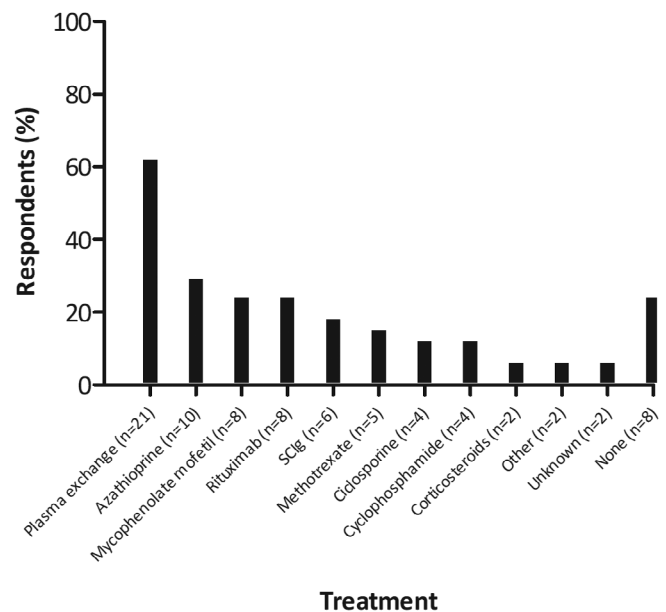


FIGURE 2 Other types of treatment used besides first and second choice of treatment of chronic inflammatory demyelinating polyradiculoneuropathy (n = 34). SClg, subcutaneous immunoglobulins

reported IVIg as first treatment choice (82%) and corticosteroids as second choice (71%) (Figure 1), with the rapid improvement following IVIg treatment as the most important reason (54%). Of the 28 respondents who started with IVIg as initial treatment, 25 reported to start with an IVIg loading dose of 2 g/kg over two to five consecutive days.

3.3.3 | Long-term therapy

Three respondents did not divide CIPD treatment into induction and maintenance therapy and three respondents referred all patients who required maintenance treatment, leaving 28 respondents with data for specific analysis on maintenance treatment. The majority of respondents reported IVIg as first choice of maintenance treatment (96%) and corticosteroids as second choice (71%) (Figure 1), with the low risk of side effects related with IVIg treatment as the most

important reason (67%). Fifty-two percent of the respondents (14/27) reported giving a dosage of 0.4 g/kg varying between once every 2 and 4 weeks, while four respondents reported giving a dosage of 1 g/kg varying between once every 3 and 4 weeks. Timing of initiation and optimizing of maintenance therapy varied. In the case of clinical deterioration, most respondents (45%) would increase the IVIg dose, whereas almost all respondents (90%) would increase the frequency in the case of wear-off signs. If a patient was clinically stable on IVIg treatment, most respondents would reduce IVIg dosage or frequency, while 10% would stop IVIg immediately. IVIg maintenance treatment was reported as given at home most of the time/always by 71% of respondents. The majority of respondents used one or more second line treatment options of which 14 respondents (11 university affiliated vs 3 non-university affiliated) reported using immunosuppressive treatments, including azathioprine, mycophenolate mofetil, rituximab, methotrexate, ciclosporine, and cyclophosphamide (Figure 2).

3.3.4 | Factors associated with treatment practice

Non-university-affiliated respondents were more likely to prefer IVIg as initial therapy compared to university-affiliated respondents (71% university- vs 100% non-university-affiliated; $P = .06$), although this was not significantly different. Immunosuppressive drugs were more often used by university-affiliated respondents (55% university- vs 25% non-university-affiliated; $P = .10$) and neuromuscular experts (52% neuromuscular vs 14% non-neuromuscular experts; $P = 0.10$), although this was not significantly different.

4 | DISCUSSION

Although the majority of Dutch neurologists used the EFNS/PNS 2010 guideline, we found considerable variation in the strategy to diagnose and treat CIDP. While most neurologists consider NCS essential in the diagnostic workup of CIDP, only 57% indicated that the presence of demyelinating electrophysiological findings was mandatory to confirm the diagnosis of CIDP. IVIg was most often used as first choice therapy and corticosteroids as second choice in the treatment of CIDP. Variation in treatment of CIDP was found when considering when to start treatment, when and how to withdraw IVIg, what to do in case of clinical deterioration during treatment, and the use of immunosuppressive treatment options. University-affiliated respondents used the EFNS/PNS 2010 diagnostic criteria, nerve ultrasound, and immunosuppressive drugs more often compared to non-university-affiliated respondents.

A cross-sectional survey was conducted recently to evaluate how neurologists from the United States diagnosed and treated CIDP.²² Corresponding with our findings, these authors reported IVIg as first choice treatment and corticosteroids as second choice in CIDP but also found variation in the neurologists' strategy of when and how to withdraw IVIg treatment. In contrast to our study, the US study showed that the respondents were less familiar with the EFNS/PNS

diagnostic criteria and only 55% of respondents reported using the EFNS/PNS recommended loading dose of 2.0 g/kg, possibly due to the lower percentage (22%) of neuromuscular experts.³

Two studies were performed to investigate adherence of the EFNS/PNS guideline for CIDP and multifocal motor neuropathy (MMN).^{23,24} The European study group on guidelines for neuropathy conducted a survey on compliance with the EFNS/PNS 2010 guidelines on CIDP and MMN in eight European countries and the state of Kerala in India. This study found that nearly 60% of non-neuromuscular neurologists use the EFNS/PNS guidelines to treat CIDP and MMN.²³ However, the response rate of this study was low (4.2%) and a selection bias is likely to have occurred. A survey conducted among French neurologists studied the daily practice of IVIg treatment for CIDP and MMN in relation to the EFNS/PNS 2010 guideline.²⁴ The authors of this French study concluded that these guidelines were followed. However, several discrepancies concerning IVIg treatment compared to the EFNS/PNS 2010 guideline were observed, specifically the number of induction courses without dose modification (approximately 45% >3 courses of 2 g/kg), maximum frequency of long-term treatment (76% >6 weeks), and the use of immunosuppressive drugs (40%). Furthermore, the response rate of this French study was low (17%).

In the current study, the minority of respondents diagnosed more than five patients per year. Some respondents did not screen for the presence of paraproteinemia, despite the consensus that the diagnosis CIDP cannot be made in patients with IgM anti-MAG antibodies.³ Surprisingly most respondents otherwise excluded various rare causes of a (axonal) polyneuropathy, such as beriberi or syphilis. Although the frequency of examining CSF in patients varied among neurologists, there was consensus on the interpretation of the CSF protein level. The majority of neurologists indicated that an elevated CSF protein level without pleiocytosis supported, but was not mandatory to confirm the diagnosis of CIDP, and only a few respondents mentioned diagnostic doubts in the case of a normal CSF protein level. These results may suggest that neurologists examine CSF in particular in cases of diagnostic doubts. Although demyelinating findings on NCS are considered essential for a CIDP diagnosis,³ surprisingly only 57% indicated that the presence of demyelinating findings on NCS were mandatory for a CIDP diagnosis. Apparently, many neurologists considered that the EFNS/PNS 2010 electrodiagnostic criteria are not sensitive enough to identify all CIDP patients. We did not collect information regarding the outcome measures and the definition of treatment response used in practice. Such information is important as the diagnosis of CIDP needs to be reconsidered in absence of a treatment response, especially if the electrodiagnostic requirement is not fulfilled. It would be helpful if the new EFNS/PNS guideline could specify a definition of treatment response. The availability of NUS as additional diagnostic tool in CIDP patients may also play a role. Although NUS is not considered supportive according to the current EFNS/PNS guideline, this diagnostic tool was often used, while the use of MRI was limited in our study. Results of NUS and MRI can support the diagnosis and might be particularly useful in patients with a strong clinical suspicion of CIDP that do not fulfil the full EFNS/PNS

2010 electrodiagnostic criteria.^{1,3,25} However, interpretation of NUS and MRI findings both require neurophysiological and radiological expertise and standardized protocols with specified reference and cutoff values are scarce.^{1,26-28} These limitations may explain why these modalities are less often used in non-university hospitals. Importantly, specificity of NUS and especially MRI are not optimal, thus reliance on these tools without other supportive evidence might lead to false positive CIDP diagnosis and overtreatment of patients.²⁸

We found variation in treatment practices that are not specifically addressed in the EFNS/PNS 2010 guideline. This guideline states that an IVIg maintenance dose of 1.0 g/kg over 1 to 2 days every 3 weeks has been shown to be efficacious, but the appropriate dose needs to be individualized (usually 0.4-1.2 g/kg every 2-6 weeks). Furthermore, it is advised to reduce the dose or frequency of IVIg if a patient becomes stable on a regimen of intermittent IVIg. However, the EFNS/PNS 2010 guideline is not fully clear about the indications to start maintenance therapy, how to optimize and reduce IVIg, and how to manage wear-off symptoms. The lack of these specific recommendations might explain some of the variation in treatment practices. A few studies on how to dose maintenance treatment for CIDP have recently been published or are currently ongoing, and may be helpful in the next version of the EFNS/PNS guideline on treatment.^{16,17,29-32}

About one-third of respondents indicated that they would start initial therapy in all CIDP patients irrespective of the severity of symptoms and the interference with daily life activities, while the EFNS/PNS 2010 guideline recommends only to treat patients with moderate or severe disability. Although 5% to 30% of CIDP patients only needs one IVIg course (2 g/kg) to induce remission, almost one-third of the respondents indicated starting maintenance therapy after improvement on the first IVIg induction course without subsequent deterioration.^{3,33} All non-university-affiliated respondents preferred IVIg as treatment. This may be biased by the fact that these centers are located in the area near the Erasmus MC and therefore may have consulted this center, where IVIg usually is preferred as a first choice treatment for CIDP. Nevertheless, most respondents indicated that their IVIg preference is due to the rapid improvement following IVIg and the low risk of side effects. Despite the absence of evidence that immunomodulatory drugs than IVIg, SClg, corticosteroids, and PE work in CIDP, nearly half of the respondents indicated that they also use second line therapy, such as mycophenolate mofetil and rituximab.¹¹⁻¹⁵

Our study has several strengths. First, the survey was developed by experts in the field. Second, data were collected from both university and non-university affiliated neurologists to optimize generalizability of our findings. A limitation of our study was the relatively small number of respondents, although the response rate was 62%. Our study probably underestimates the variation in clinical practice as we included all non-university hospitals from a single province only, as these centers likely collaborate with one or a few neuromuscular expertise centers. Nevertheless, we think that this effect is limited, because the majority of non-university affiliated neurologists do not refer to a center of expertise. Furthermore, experienced neurologists are probably more likely to respond. In addition, we asked for general policies. However, in clinical practice, diagnostic and treatment

strategies could be different and might depend on patient characteristics or CIDP variants. Finally, we realize that the use of SClg is likely increasing since the publication of the PATH trial and that our results could be an underestimation of the current use of SClg.¹²

Despite the fact that the majority of respondents indicated to use the EFNS/PNS 2010 CIDP guideline, we found substantial variation in the diagnostic and treatment practice of CIDP among Dutch neurologists. Our findings suggest that it would be helpful if the EFNS/PNS guideline, which is currently undergoing revision, could be more specific about: (a) the minimal set of electrophysiological requirements to diagnose CIDP, (b) the possible added value of NUS and MRI in the diagnostic workup of CIDP, especially in patients not meeting the electrodiagnostic criteria, (c) the most relevant serological examinations, and (d) a clear treatment advice. In addition, strategies for implementing the guideline should be considered. We encourage to refer patients to CIDP expertise centers if they do not fulfil the diagnostic criteria, or respond poorly or not at all to proven effective treatments for CIDP, in order to reevaluate the diagnosis before further treatment options may be tried.

ACKNOWLEDGEMENTS

This study is funded by the Dutch Prinses Beatrix Spierfonds (grant application number: W.OR16-18). We thank all the neurologists who participated in this study. We also thank Maryse C. Cnossen for sharing her expertise in conducting survey studies regarding clinical-decision making. We thank Carina Bunschoten, Sonja E. Leonhard, and Melissa R. Mandarakas (Erasmus University Medical Center, Rotterdam, The Netherlands) for their feedback on the draft version of the questionnaire.

ORCID

Meryl C. Broers  <https://orcid.org/0000-0002-7770-8475>

REFERENCES

- Bunschoten C, Jacobs BC, van den Bergh PYK, Cornblath DR, van Doorn PA. Progress in diagnosis and treatment of chronic inflammatory demyelinating polyradiculoneuropathy. *Lancet Neurol.* 2019;18(8):784-794.
- Broers MC, Bunschoten C, Nieboer D, Lingsma HF, Jacobs BC. Incidence and prevalence of chronic inflammatory demyelinating polyradiculoneuropathy: a systematic review and meta-analysis. *Neuroepidemiology.* 2019;52(3-4):161-172.
- van den Bergh PY, Hadden RD, Bouche P, et al. European Federation of Neurological Societies/peripheral nerve society guideline on management of chronic inflammatory demyelinating polyradiculoneuropathy: report of a joint task force of the European Federation of Neurological Societies and the peripheral nerve society—first revision. *Eur J Neurol.* 2010;17:356-363.
- Allen JA, Gorson KC, Gelinas D. Challenges in the diagnosis of chronic inflammatory demyelinating polyneuropathy. *Brain Behav.* 2018;8(3):e00932.
- Allen JA, Lewis RA. CIDP diagnostic pitfalls and perception of treatment benefit. *Neurology.* 2015;85(6):498-504.
- Allen JA, Ney J, Lewis RA. Electrodiagnostic errors contribute to chronic inflammatory demyelinating polyneuropathy misdiagnosis. *Muscle Nerve.* 2018;57(4):542-549.

7. Kaplan A, Brannagan TH 3rd. Evaluation of patients with refractory chronic inflammatory demyelinating polyneuropathy. *Muscle Nerve*. 2017;55(4):476-482.
8. Bunschoten C, Blomkwist-Markens PH, Horemans A, van Doorn PA, Jacobs BC. Clinical factors, diagnostic delay, and residual deficits in chronic inflammatory demyelinating polyradiculoneuropathy. *J Peripher Nerv Syst*. 2019;24(3):253-259.
9. van den Bergh PYK, van Doorn PA, Jacobs BC, Querol L, Bunschoten C, Cornblath DR. Boundaries of chronic inflammatory demyelinating polyradiculoneuropathy. *J Peripher Nerv Syst*. 2020;25(1):4-8.
10. Neligan A, Reilly MM, Lunn MP. CIDP: mimics and chameleons. *Pract Neurol*. 2014;14(6):399-408.
11. Hughes RA, Mehndiratta MM, Rajabally YA. Corticosteroids for chronic inflammatory demyelinating polyradiculoneuropathy. *Cochrane Database Syst Rev*. 2017;11:CD002062.
12. van Schaik IN, Brill V, van Geloven N, et al. Subcutaneous immunoglobulin for maintenance treatment in chronic inflammatory demyelinating polyneuropathy (PATH): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet Neurol*. 2018;17(1):35-46.
13. Eftimov F, Winer JB, Vermeulen M, de Haan R, van Schaik IN. Intravenous immunoglobulin for chronic inflammatory demyelinating polyradiculoneuropathy. *Cochrane Database Syst Rev*. 2013;12:CD001797.
14. Mehndiratta MM, Hughes RA, Pritchard J. Plasma exchange for chronic inflammatory demyelinating polyradiculoneuropathy. *Cochrane Database Syst Rev*. 2015;8:CD003906.
15. Oaklander AL, Lunn MP, Hughes RA, van Schaik IN, Frost C, Chalk CH. Treatments for chronic inflammatory demyelinating polyradiculoneuropathy (CIDP): an overview of systematic reviews. *Cochrane Database Syst Rev*. 2017;1:CD010369.
16. Allen JA, Berger M, Querol L, Kuitwaard K, Hadden RD. Individualized immunoglobulin therapy in chronic immune-mediated peripheral neuropathies. *J Peripher Nerv Syst*. 2018;23(2):78-87.
17. Kuitwaard K, Fokkink WR, Brusse E, et al. Maintenance IV immunoglobulin treatment in chronic inflammatory demyelinating polyradiculoneuropathy. *J Peripher Nerv Syst*. 2017;22(4):425-432.
18. Edwards PJ, Roberts I, Clarke MJ, et al. Methods to increase response to postal and electronic questionnaires. *Cochrane Database Syst Rev*. 2009;3:MR000008.
19. Barclay S, Todd C, Finlay I, Grande G, Wyatt P. Not another questionnaire! Maximizing the response rate, predicting non-response and assessing non-response bias in postal questionnaire studies of GPs. *Fam Pract*. 2002;19(1):105-111.
20. Edwards P, Roberts I, Clarke M, et al. Increasing response rates to postal questionnaires: systematic review. *BMJ*. 2002;324(7347):1183.
21. GemsTracker (GEneric Medical Survey Tracker) software package: <https://gemstracker.org/>.
22. Gelinas D, Katz J, Nisbet P, England JD. Current practice patterns in CIDP: a cross-sectional survey of neurologists in the United States. *J Neurol Sci*. 2019;397:84-91.
23. Rajabally YA, van den Bergh P, European Study Group on Guidelines for Neuropathy. Compliance with international guidelines for chronic inflammatory neuropathies. *Eur J Neurol*. 2019;26(4):557-558.
24. Rosier C, Graveline N, Lacour A, Antoine JC, Camdessanche JP. Intravenous immunoglobulin for treatment of chronic inflammatory demyelinating polyneuropathy and multifocal motor neuropathy in France: are daily practices in accordance with guidelines? *Eur J Neurol*. 2019;26(4):575-580.
25. Pitarokoili K, Kronlage M, Baumer P, et al. High-resolution nerve ultrasound and magnetic resonance neurography as complementary neuroimaging tools for chronic inflammatory demyelinating polyneuropathy. *Ther Adv Neurol Disord*. 2018;11:1756286418759974.
26. Goedee HS, van der Pol WL, van Asseldonk JH, et al. Diagnostic value of sonography in treatment-naive chronic inflammatory neuropathies. *Neurology*. 2017;88(2):143-151.
27. Goedee HS, Brekelmans GJ, Visser LH. Multifocal enlargement and increased vascularization of peripheral nerves detected by sonography in CIDP: a pilot study. *Clin Neurophysiol*. 2014;125(1):154-159.
28. Oudeman J, Eftimov F, Strijkers GJ, et al. Diagnostic accuracy of MRI and ultrasound in chronic immune-mediated neuropathies. *Neurology*. 2020;94(1):e62-e74.
29. Lunn MP, Ellis L, Hadden RD, Rajabally YA, Winer JB, Reilly MM. A proposed dosing algorithm for the individualized dosing of human immunoglobulin in chronic inflammatory neuropathies. *J Peripher Nerv Syst*. 2016;21(1):33-37.
30. Eftimov F, Adrichem ME, de Haan RJ, Dijkgraaf MGW, Merkies IS, Vrancken AFJ, et al. Intravenous immunoglobulin overtreatment in chronic inflammatory demyelinating polyneuropathy: a double-blind, randomized controlled non-inferiority trial (IOC trial). *J Peripher Nerv Syst*. 2015;20(2):88-253.
31. Cornblath DR, Hartung HP, Katzberg HD, Merkies ISJ, van Doorn PA. A randomised, multi-Centre phase III study of 3 different doses of intravenous immunoglobulin 10% in patients with chronic inflammatory demyelinating polyradiculoneuropathy (ProCID trial): study design and protocol. *J Peripher Nerv Syst*. 2018;23(2):108-114.
32. Kuitwaard K, Fokkink WR, Brusse E, et al. Protocol of a dose response trial of IV immunoglobulin in chronic inflammatory demyelinating polyradiculoneuropathy (DRIP study). *J Peripher Nerv Syst*. 2018;23(1):5-10.
33. Kuitwaard K, Hahn AF, Vermeulen M, Venance SL, van Doorn PA. Intravenous immunoglobulin response in treatment-naive chronic inflammatory demyelinating polyradiculoneuropathy. *J Neurol Neurosurg Psychiatry*. 2015;86(12):1331-1336.

How to cite this article: Broers MC, van Doorn PA, Kuitwaard K, et al. Diagnosis and treatment of chronic inflammatory demyelinating polyradiculoneuropathy in clinical practice: A survey among Dutch neurologists. *J Peripher Nerv Syst*. 2020;25:247-255. <https://doi.org/10.1111/jns.12399>

APPENDIX

FIGURE A1 Laboratory tests generally performed in the diagnostic work-up of CIDP to exclude other disorders (n = 44). ANA, antinuclear antibodies; CK, creatine kinase; ESR, erythrocyte sedimentation rate; Hb, hemoglobin; LDH, lactate dehydrogenase; TSH, thyroid-stimulating hormone

