CIDP Diagnostic Criteria and Response to Treatment

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ABSTRACT

Introduction. Diagnostic criteria for CIDP have been proven useful for clinical trials. However, use of these criteria in clinics has been limited by time constraints and unknown usefulness in predicting outcomes.

Methods. A retrospective chart review of CIDP patients at the University of Kansas seen between 2008 and 2014 was performed. We determined the diagnostic criteria fulfilled by each patient and assessed treatment responses. A positive response was defined by improvement sensory or motor examination as determined by a neuromuscular physician.

Results. There were 38 total patients included in the study. The response rate to IVIG in patients who fulfilled EFNS/PNS criteria was 20/22 (90.1%). Among patients who fulfilled AAN criteria, 8/9 (88.9%) responded positively to IVIG. Slightly lower response rates were seen in patients fulfilling INCAT criteria and Saperstein criteria at 10/15 (66.7%) and 12/17 (70.6%), respectively.

Discussion. EFNS/PNS and AAN criteria can similarly predict IVIG treatment response.

Keywords: *Chronic Inflammatory Demyelinating Polyneuropathy, Retrospective Chart Review, Diagnostic Criteria, Treatment Response, IVIG, EFNS/PNS.*

Introduction

Chronic Inflammatory Demyelinating Polyneuropathy is known to be an immune-mediated peripheral neuropathy, but the precise pathogenesis has yet to be fully elucidated.[1] It is a relatively rare disease with an estimated prevalence of 4.7 per 100,000 adults.[2] Although the "typical" form of CIDP presents clinically with symmetric, proximal and distal weakness, hypo- or areflexia, and mainly large fiber sensory loss, there is a large range of clinical heterogeneity in the disease.[3] Various diagnostic criteria have been developed to help diagnose this condition in clinical and research settings including AAN, Saperstein, INCAT, and EFNS/PNS. Currently, the most commonly used, especially in research settings, is the EFNS/PNS criteria that was developed in 2010.

The major highlights of the diagnostic criteria that were used in this study are reviewed in Table 1. Generally speaking, all of the criteria rely on clinical, electrophysiological, and supportive studies to make the diagnosis of CIDP. Additionally, disorders that may appear similarly to CIDP

Table 1: Major clinical and diagnostic features of various criteria.

	Clinical	Nerve Conduction Studies	Other
EFNS/PNS	>2 mo, hypo/areflexia, proximal and distal weakness, sensory deficits	Must fulfill at least **1 out of 7** parameters to be considered "definite" CIDP	LP results, MRI, Abnormal sensory electrophysiology, objective improvement following immunomodulatory therapy, sural nerve biopsy
AAN	>2 mo, hypo/areflexia, motor dysfunction, sensory dysfunction of >1 limb or both	Must fulfill at least **3 out of 4** parameters, more stringent than other criteria.	LP results, Nerve Biopsy (supportive)
Saperstein	>2 mo, hypo/areflexia, **symmetric** proximal and distal weakness, or exclusively distal weakness, sensory loss	Must fulfill at least **2 out of 4** of the AAN parameters	LP results, Nerve Biopsy (supportive)
INCAT	> 2 mo, hypo/areflexia, progressive or relapsing motor or sensory dysfunction in more than 1 limb	Must fulfill at least **2 out of 4** parameters or **1 out of 3** of slightly different parameters	LP results, Nerve Biopsy (can be used if electrodiagnostic testing is not conclusive)

must be excluded. The major differences between the criteria are in the electrophysiological parameters. For example, the AAN criteria tends to be more conservative in defining parameters of demyelination such as abnormal conduction velocity and prolonged distal latency compared to the other criteria. Furthermore, some criteria such as EFNS/PNS only require 1 out of 7 electrophysiological parameters be fulfilled to meet diagnostic standards while AAN requires 3 out of 4.

At the present time, it is unclear whether or not these criteria have clinical applications beyond assisting in diagnosis. The goals of this study were to identify patients with a clinical diagnosis of CIDP who fulfilled the diagnostic criteria under investigation and also determine whether fulfilling certain criteria had any implications in treatment response.

Methods

Using the Neuromuscular database at the University of Kansas Hospital, we searched for ICD-9 and PNS codes specific for CIDP. Using this method, we identified 53 potential patients for the study. Following identification, we collected patient data from the clinical record including date of diagnosis, clinical presentation, nerve conduction study data, initial treatment, and clinical response to the initial treatment. Data was collected from the initial patient visit at the time of diagnosis and the initial follow-up after therapy. Using this information, we were able to determine which patients fulfilled EFNS/PNS, INCAT, Saperstein, or AAN diagnostic criteria. We subsequently determined whether or not these patients responded to the initial treatment that was given. Treatment response was defined by improvement in sensory or motor examination as determined during initial follow-up by the examining neuromuscular physician.

Patient Characteristics

There were a total of 53 patients identified for potential inclusion in the study based on our data search. After initial data collection, 15 patients were excluded leaving 38 who were ultimately included in the study. Of those excluded, 10 patients did not have a formal diagnosis of CIDP by a neuromuscular physician and five had insufficient data in the records to assess which diagnostic criteria they fulfilled (Figure 1).

The male to female ratio of those included in the study was 22 to 16. The age range at diagnosis was 17 to 81 years (mean 51.5, SD ± 12.9). Of the 23 patients who had CSF
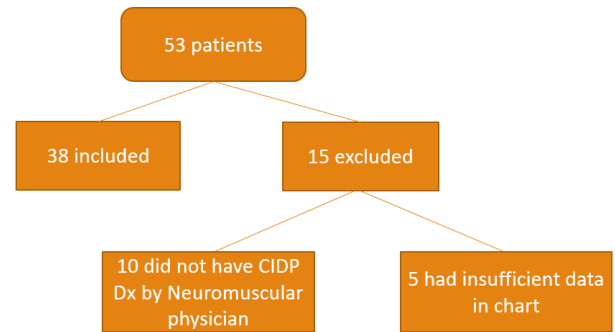

Figure 1: Patient Entry Criteria

data available, 78% had elevated CSF protein without pleocytosis.

Diagnostic Criteria

A basic overview of the requirements for each diagnostic criteria we assessed is provided in Table 1. A total of 28 of our patients fulfilled the "Definite" EFNS/PNS criteria (73.68%) and another five fulfilled the "Probable" EFNS/PNS criteria (13.16%). Saperstein and INCAT criteria were fulfilled by 20 patients each (52.6%), and ten patients fulfilled the criteria proposed by AAN (26.3%). Of the 25 patients who fulfilled multiple criteria, seven fulfilled all of the diagnostic criteria under investigation. All of the patients that fulfilled either the AAN, Saperstein, or INCAT criteria also fulfilled the EFNS/PNS criteria, and eight patients fulfilled the EFNS/PNS criteria alone. All but five patients fulfilled at least one of the diagnostic criteria. (Figure 2)

Treatment Response

A complete representation of response rates to various therapies in our study is provided in Table 2. A positive treatment response was defined by improvement in motor or sensory examination as determined during initial follow-up by a neuromuscular physician. The median time to follow-up at which treatment response was assessed was 6 months. A total of 29 patients in our study received IVIG as an initial therapy. Of those patients, 22 responded positively (75.9%). Of those who met EFNS/PNS criteria, 20 out of 22 patients had a positive response (90.1%), and patients who fulfilled AAN criteria responded at a similar rate of 88.9%. Patients fulfilling Saperstein criteria responded at a rate of 70.6%, and 66.7% of the INCAT patients responded favorably. Response rates for those receiving steroids were slightly lower overall when compared to IVIG. A total of 9 patients received steroids and 6 of those patients had a
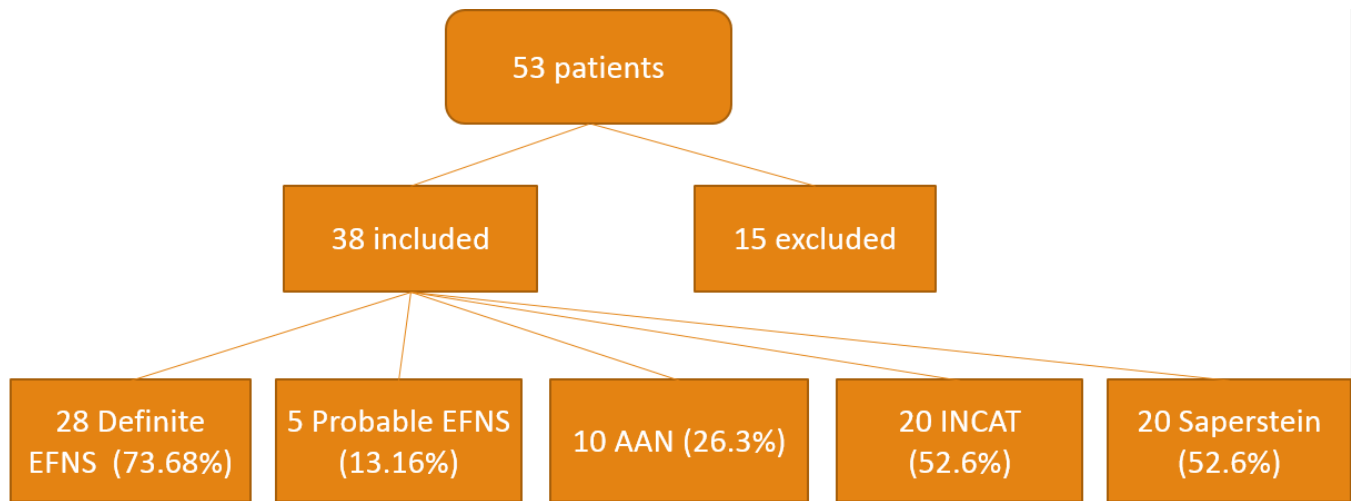
Figure 2: Number of patients fulfilling each criterion.

positive response. Of those meeting EFNS/PNS criteria, five out of 8 responded favorably (62.5%). Similar numbers were seen for those meeting AAN (66.7%), INCAT (71.4%) and Saperstein (50%) criteria. The time to follow-up at which treatment response was measured ranged from one to 29 months (mean 7.5 months, SD ± 6.8).

Discussion

The diagnostic criteria under investigation in this study have varying sensitivities and specificities[4]. A retrospective study by Breiner in 2014 showed that the 2010 EFNS/PNS definite criteria had a sensitivity of 73.2% and a specificity of 88.2% which is favorable compared to other diagnostic criteria for CIDP[4]. The relatively high sensitivity of the EFNS/PNS criteria is consistent with the findings of this

study as the majority of our patients fulfilled this criteria. Conversely, the AAN criteria has a specificity of 100%, but the sensitivity for possible CIDP is only 25%.[4] This is also consistent with our findings as a much smaller percentage of our patients fulfilled the AAN criteria.

The ICE trial, a randomized placebo controlled study, demonstrated the efficacy of IVIG in patients with CIDP.[5] This trial used the INCAT diagnostic criteria for inclusion in the study and found that 54% had functional improvement in the INCAT disability score during the first 24 weeks of treatment IVIG.[5] A more recent phase III trial published in 2017 by Kuwabara et al. found that 77.8% of patients had improvement in INCAT disability scores when treated with IVIG after 28 weeks of therapy.[6] In contrast to the ICE trial, patients in the Kuwabara et al. study fulfill the EFNS/

Table 2: Comparison of treatment responses of patients fulfilling various CIDP criteria.

Therapy	Number Responded Overall	Number Responded EFNS/PNS	Number Responded AAN	Number Responded INCAT	Number Responded Saperstein
IVIG	22/29 (75.9%)	20/22 (90.1%)	8/9 (88.9%)	10/15 (66.7%)	12/17 (70.6%)
Steroids	6/9 (66.7%)	5/8 (62.5%)	2/3 (66.7%)	5/7 (71.4%)	2/4 (50%)
PLEX	2/4 (50%)	2/4 (50%)	0 (0%)	2/3 (66.7%)	1/2 (50%)
Mycophenolate Mofetil	2/3 (66.7%)	2/3 (66.7%)	1/1 (100%)	1/2 (50%)	1/2 (50%)
Azathioprine	0/1 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

PNS definite or probable criteria prior to enrollment. Our findings were consistent with the data in these trials in that patients fulfilling the EFNS/PNS criteria in our study responded at a higher rate (90.1%) than those fulfilling the INCAT criteria (66.7%). The slightly higher response rates seen in our study compared to previous trials may be related to differences in outcome measures.

Prior to this study, there was limited data comparing the treatment responses of patients fulfilling different diagnostic criteria for CIDP. This information has clinical significance in that it may help predict outcomes in patients with this condition. Using the results of this study in conjunction with previous studies on the sensitivity and specificity data of these criteria, it could be argued that neurologists should use the EFNS/PNS criteria when predicting treatment response for patients with CIDP. The high sensitivity and specificity of the EFNS/PNS criteria along with the relatively high treatment response rates seen in this study suggest that it may be favorable to other diagnostic criteria in clinical settings. Patients who fulfill the EFNS/PNS criteria appear to have equal or superior treatment response rates compared to patients fulfilling more specific criteria, such as those proposed by the AAN, suggesting little clinical benefit when using the most specific diagnostic criteria.

Limitations of this study include its retrospective nature and the descriptive statistical analysis used to compare treatment responses. In addition to this limitation, it should be noted that data was only obtained from two time points, and although the median time to follow-up was 6 months, there was considerable variation between patients. Future studies should include long-term follow-up data to determine whether or not initial response rates predict clinical stability or future response to therapy. Furthermore, our study used an "all-or-none" approach when determining patient response to therapy, so there may be significant variability in functional outcomes even between patients with a positive response. Using tools utilized in other studies such as the INCAT disability score would be helpful in assessment of the degree of improvement between patient subsets and would allow for easier comparison with previous studies.

In conclusion, this study provides information on some of the diagnostic criteria used for CIDP and a possible relationship with these criteria to treatment responsiveness. Despite differences in sensitivities and specificities, the response rates to IVIG appear to be similar for those meeting AAN and EFNS/PNS criteria. Additional studies that have longer follow-up and that use a functional outcome measures to stratify treatment responsiveness are needed to support these findings.

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