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Review

Derivation and validation of diagnostic criteria for chronic inflammatory demyelinating polyneuropathy ☆

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ABSTRACT

To develop diagnostic criteria for chronic inflammatory demyelinating polyneuropathy (CIDP), a retrospective series of patients' records diagnosed by sexpert consensus as CIDP or other chronic polyneuropathies were analyzed. Classification and regression tree analysis was applied to 150 patients to derive a classification rule. According to the rule, diagnosis of CIDP required that a patient have a chronic non-genetic polyneuropathy, progressive for at least eight weeks, without a serum paraprotein and either 1) recordable compound muscle action potentials in ≥75% of motor nerves and either abnormal distal latency in >50% of nerves or abnormal motor conduction velocity in >50% of nerves or abnormal F wave latency in >50% of nerves; or 2) symmetrical onset of motor symptoms, symmetrical weakness of four limbs, and proximal weakness in ≥1 limb. When validated in 117 patients, the rule had 83% sensitivity (95% confidence interval 69%–93%) and 97% specificity (95% confidence interval 89%–99%) and performed better than published criteria.

Contents

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1. Introduction

The diagnosis of chronic inflammatory demyelinating polyneuropathy (CIDP) is based on the recognition of a characteristic history and examination and supported by evidence of peripheral nerve demyelination from nerve conduction studies or nerve biopsy, albumino-cytological dissociation in the cerebrospinal fluid (CSF), and laboratory tests to exclude other potential etiologies of peripheral nerve disease. There is no diagnostic biological marker or laboratory test for CIDP.

The clinical phenotype of CIDP distinguishes it from other chronic acquired demyelinating polyneuropathies (CADP) such as multifocal motor neuropathy (MMN) and the anti-myelin associated glycoprotein (MAG) neuropathy syndrome which are also distinct from CIDP in their prognosis and response to therapy. Other disorders under the rubric of CADP including the Lewis–Sumner syndrome, pure demyelinating sensory neuropathy and CIDP associated with a monoclonal gammopathy of unknown significance (MGUS), other than that associated with antibodies to MAG are believed by some investigators to represent subtypes of CIDP because the response of these disorders to immunomodulatory treatments is similar to that of CIDP.

Since there is no biological marker for CIDP, the diagnostic criteria developed by expert consensus panels included clinical, pathological, electrophysiological, and laboratory studies. At least nine sets of diagnostic criteria for CIDP have been proposed [1–9]. These criteria differ in several ways, including the extent of symmetry required on the motor examination, the extent and distribution of demyelination present on electrodiagnostic studies, and whether CSF analysis and nerve biopsy are required for a definite diagnosis. None of these sets of diagnostic criteria has been evaluated empirically using rigorous epidemiologic and statistical methods. Furthermore, most existing sets of criteria were developed for clinical research and, therefore, were designed to maximize specificity, possibly at the expense of sensitivity [2,10–12]. Thus, use of these criteria in clinical practice may result in under-diagnosis and delayed treatment [12].

In the current study, the clinical, electrodiagnostic and laboratory variables of patients diagnosed by expert consensus as having CIDP, CADP or other polyneuropathies were analyzed with predictive modeling methods to establish a set of criteria that would distinguish CIDP from non-CIDP. The goal was to derive empirically a set of criteria that would be useful in clinical practice and have excellent sensitivity and specificity relative to the expert consensus diagnosis.

2. Methods

The CIDP Criteria Working Group included 13 neurologists from the United States, Canada, and Europe, an epidemiologist (MB) and a biostatistician (LSM).

The first step involved generating a set of candidate variables to be evaluated as potential diagnostic criteria (Fig. 1, Appendix A). The Working Group used the published literature and clinical expertise to select candidate variables that could plausibly be expected to distinguish between CIDP and other polyneuropathies. The selected candidate variables included aspects of the history, neurologic examination, electrodiagnostic data, and ancillary laboratory studies. This inclusive set of characteristics was developed into a medical record abstraction form.

In the second step, we assembled a set of detailed case descriptions of patients with a chronic polyneuropathy. To be included, a case had to have progressive neuropathy for eight weeks or more, had to have been seen by one of the Working Group neurologists (or at their institution), and had to have clinical and laboratory data of sufficient quality to establish a diagnosis. All EMG-NCV studies were performed in the centers of the participating neurologists. Patients with primarily focal, compressive or traumatic conditions were excluded. Each participating neurologist was to contribute information on approximately equal numbers of patients diagnosed with CIDP, with CADP, and with other chronic neuropathies. The CADP category included diagnoses of Lewis–Sumner syndrome, MMN and neuropathies associated with paraprotein. In each disease category, the cases submitted from each practice represented a consecutive series of patients with that particular diagnosis most recently evaluated in that clinic. The case description had three parts: 1) a structured patient profile completed by the submitting neurologist; 2) copies of the clinical notes and selected ancillary studies; and 3) electrodiagnostic reports including the primary data. Patient identifiers were deleted from the case descriptions.

The next step involved generating a consensus diagnosis for each of the cases (the "gold standard"). The case descriptions were posted on a password protected interactive web site. Cases were reviewed by the participating neurologists who submitted their diagnostic ratings (CIDP, CADP, or Other) and their degree of diagnostic certainty (rated

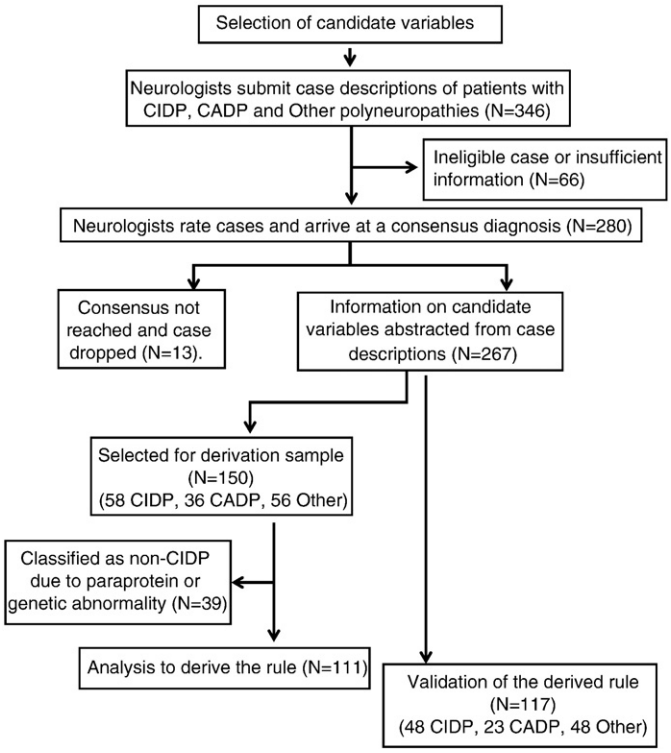

Fig. 1. Overview of Study.