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The ulnar ratio as a sensitive and specific marker of acute inflammatory demyelinating polyneuropathy

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HIGHLIGHTS

- Ulnar ratio definition: SNAP amplitude of palmar cutaneous over that of dorsal branch of ulnar nerve.
- Ulnar ratio $\geq$ 0.78 can rule out diagnosis of Acute Inflammatory Demyelinating Polyneuropathy (AIDP), with high specificity (100%) and sensitivity (87%).
- Incorporating specific sensory abnormalities in AIDP criteria may enhance their reliability.

ABSTRACT

Objectives: To explore the value of a novel sensory criterion, the ulnar ratio – defined as the SNAP amplitude of the palmar cutaneous (pUN) over that of the dorsal branch (dUN) of the ulnar nerve – as a predictor of Acute Inflammatory Demyelinating Polyneuropathy (AIDP).
Methods: We prospectively included 22 patients with AIDP, 20 patients with diabetic peripheral neuropathy (DPN), and 18 controls. Eligible subjects underwent nerve conduction studies including, among others, the dUN, pUN, and sural nerve.
Results: A sural sparing pattern was found in 72% of AIDP cases. The ulnar ratio was significantly lower in patients with AIDP compared to those with DPN or controls. The ROC curve area to discriminate AIDP (versus controls and diabetics together) was higher with the ulnar ratio and pUN compared to dUN. An ulnar ratio $\geq$ 0.78 seems to be the best threshold to rule out the diagnosis of AIDP, with a specificity of 100% and a sensitivity of 87%. The ulnar ratio was equally reliable in the subgroup of patients presenting within a week of symptoms onset.
Conclusion: The ulnar ratio is a highly sensitive and specific marker of AIDP and can help confirm the diagnosis when direct signs of demyelination are lacking.
Significance: Incorporating specific sensory abnormalities, such as the ulnar ratio, in the electrodiagnostic criteria of AIDP could enhance their reliability.

1. Introduction

Acute inflammatory demyelinating polyneuropathy (AIDP) is an acute demyelinating neuropathy classically defined as ascending paralysis associated with areflexia (Guillain et al., 1916). Sensory symptoms are common and occur early in the course of the

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disease, often before the onset of significant motor weakness. Diagnosis is based on a typical clinical picture, characteristic cerebrospinal fluid findings, and evidence of widespread demyelination on nerve conduction studies (NCS). The commonly used electrodiagnostic (EDX) criteria rely exclusively on the motor NCS findings (Ho et al., 1995; Hadden et al., 1998; Van Den Bergh and Piéret, 2004) despite the widely recognized value of sensory abnormalities in the diagnosis of GBS (Albers et al., 1985; Gordon and Wilbourn, 2001; Kuwabara et al., 2004; Al-Shekhlee et al., 2005, 2007). Abnormal sensory nerve action potentials (SNAP) occur in nearly all patients (Albers et al., 1985; Kuwabara et al., 2004; Ahdab et al., 2017) and are often observed early in the course of the disease (Gordon and Wilbourn, 2001). Furthermore, the pattern of sensory loss can be highly suggestive of GBS, although not directly reflecting demyelination (Bromberg and Albers, 1993; Bansal et al., 2001; Wee and Abernathy, 2003, Al-Shekhlee et al., 2005). A sural sparing pattern has been widely accepted as a specific marker of AIDP (Bromberg and Albers, 1993; Bansal et al., 2001; Wee et al., 2003; Al-Shekhlee et al., 2005, 2007). The sensory ratio (amplitude ratio of sural plus radial SNAPs/median plus ulnar SNAPs) has also been proposed as a marker of this disease (Al-Shekhlee et al., 2007).

We undertook this study to explore the value of a novel sensory criterion, the ulnar ratio as a predictor of AIDP, with the hypothesis that relative sparing of the dorsal branch of the ulnar nerve could be a sensitive and specific marker of this illness.

2. Materials and methods

We prospectively included patients referred to our neurophysiology department at Henri Mondor Hospital (Creteil, France) with the clinical diagnosis of GBS according to the clinical criteria of Asbury and Cornblath (1990). The inclusion period was between 2008 and 2013. All patients presented with rapidly progressive limb weakness and decreased or absent deep tendon reflexes, with or without distal paresthesia. Patients underwent motor NCS (Keypoint®, Dantec™, Denmark; Natus Neurology Hand-held Bipolar Stimulating electrode) and were included if findings fulfilled the EDX criteria for AIDP (Hadden et al., 1998). We excluded patients presenting after 6 weeks of symptoms' onset, those with GBS variants such as Miller Fisher syndrome and acute motor axonal neuropathy, and those with medical conditions that could affect nerve conduction parameters such as diabetes mellitus, alcohol abuse, thyroid disorder, family history of polyneuropathy, and neurotoxic drug intake. Eligible patients underwent sensory NCS of the sural nerve, the dorsal (dUN) and palmar cutaneous branches (pUN) of the ulnar nerve and the median nerve. Motor NCS of the peroneal and tibial nerves were performed on both sides, whereas those of the median and ulnar nerves were tested on the left side only. Skin temperature was kept above 34°. Sensory NCS were performed using orthodromic techniques on the pUN (stimulating the palm and recording over the medial aspect of the wrist) (Fig. 1). Antidromic techniques were used for the dUN (stimulating the lateral aspect of the wrist and recording over the dorso-medial aspect of the hand) (Fig. 1) and the sural nerve (recording lateral to the lateral malleolus and stimulating 8 cm proximal to the recording site and 2 cm lateral to the Achilles tendon).

A sural sparing pattern was defined as a normal sural and abnormal pUN amplitude. The ulnar ratio was defined as the pUN/dUN amplitude ratio. NCS findings were compared to those obtained in a group of age-matched patients with diabetic peripheral neuropathy (DPN) and a group of healthy volunteers. The diagnostic value of the ulnar ratio was determined for the entire GBS group and then separately, for the subgroup of patients presenting within one week of symptom onset.

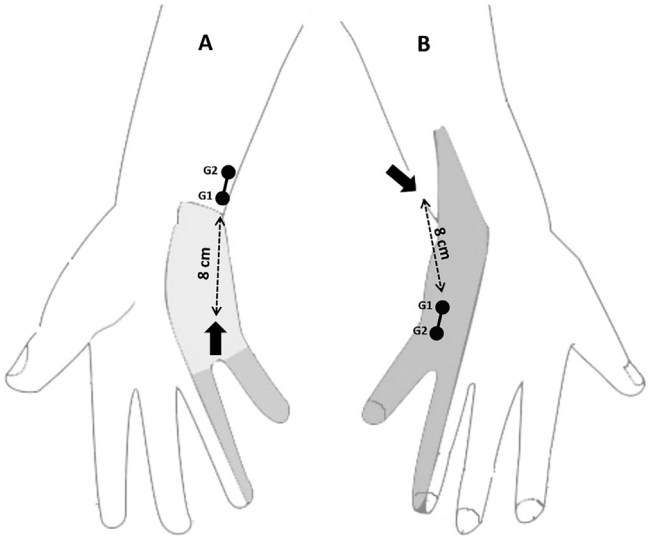

Fig. 1. Nerve conduction studies of the dorsal (dUN) and the palmar cutaneous branches of the ulnar nerve (pUN). Stimulation sites (arrows) and recording sites are represented for the pUN (A) and dUN (B). The pUN and dUN sensory supplies are shaded in grey.

2.1. Statistical analysis

Categorical variables were presented as the number of patients with the corresponding percentage. Continuous variables were expressed as mean (standard deviation (SD)), or median (interquartile range (IQR)) for those with a skewed distribution. dUN and pUN SNAP amplitudes and the ulnar ratio were compared according to the neurological status (AIDP, DPN, or controls) using Kruskal–Wallis test (Kruskal and Wallis, 1952). These comparisons were also performed using the ANCOVA test after adjustment for age and sex. The receiver operating characteristic (ROC) curves were used to compare the effect of dUN and pUN SNAP amplitudes and the ulnar ratio in AIDP discrimination. Sensitivity and specificity were computed to detect the best discrimination threshold for AIDP. Statistics were performed using JMP Pro 13 software (SAS Institute Inc., Cary, NC) and Stata software version 13 (StataCorp, Texas, USA; www.stata.com). Two-sided p-values less than 0.05 were considered significant.

2.2. Consent

This research abides by the ethical bylaws stated in the Declaration of Helsinki and all its applicable amendments and has been approved by the Institutional Review Board of the institutions in which it was conducted. All patients consented to the participation in this project prior to enrollment.

3. Results

In the AIDP group, 22 patients (63.6% males) were included, with a mean (SD) age of 54 (13) years. NCSs were performed within 3–39 days of symptom onset (median (IQR) 10 (5 – 19) days). In the DPN group, 20 patients were included (65% males), with a mean (SD) age of 60 (12) years. Seven patients in this group were found to have EDX evidence of a superimposed carpal tunnel syndrome. Eighteen subjects were included in the control group (16.7% males) with a mean (SD) age of 49 (12) years.

The mean (range) sural SNAP amplitude was 36.1 (0–85), 15.9 (5–44), and 52.9 (30–85) microvolts for the AIDP, DPN and healthy control groups, respectively. The sural SNAP amplitude in the GBS