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Motor unit number index (MUNIX): Is it relevant in chronic inflammatory demyelinating polyradiculoneuropathy (CIDP)?

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HIGHLIGHTS

- In CIDP, the MUNIX technique estimates the axonal loss and the number of functional motor units.
- The MUNIX technique has a good intra and inter-rater reproducibility in CIDP.
- The MUNIX sumscore is related to patients' disability.

ABSTRACT

Objective: To determine the test–retest reliability of motor unit number index (MUNIX) technique and to explore if the MUNIX sumscore could be related with disability in chronic inflammatory demyelinating polyradiculoneuropathy (CIDP).
Methods: The MUNIX technique was unilaterally assessed in the abductor digiti mini (ADM), the abductor pollicis brevi (APB) and the tibialis anterior (TA) muscles two different times by two blinded examiners. The MUNIX sumscore was calculated by adding the results of the ADM, APB and TA muscles.
Results: 14 CIDP patients were enrolled. The intraclass correlation coefficient (ICC) was great for inter and intra variability for ADM muscles (0.8 and 0.81), TA muscles (0.86 and 0.89) and MUNIX sumscore (0.76 and 0.83). The MUNIX sumscores from the first and second evaluations were strongly correlated ($r = 0.83$, $p < 0.001$). The MUNIX sumscore was significantly correlated with MRC testing ($r = 0.71$, $p < 0.01$), overall neuropathy limitation scale (ONLS) ($r = -0.70$, $p < 0.001$), rasch-built overall disability scale (R-ODS) ($r = 0.71$, $p < 0.001$).
Conclusions: The MUNIX technique has a good reproducibility and the MUNIX sumscore is related to the disability.
Significance: The MUNIX technique estimates the axonal loss and the number of functional motor units. The MUNIX sumscore may be a good instrument to evaluate the CIDP patients during their follow-up.

1. Introduction

Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is a treatable immune-mediated peripheral nerve disorder (Joint Task Force of the EFNS and the PNS, 2010). Patients are usually treated for long period of time. There is a need to properly evaluate these patients to avoid over treatment (Hughes et al., 2008; Group RMCT, 2009; Allen and Lewis, 2015). Objective evaluation usually rely on scales evaluating the impairment level or the activities and participation levels (Vanhoutte et al., 2013). The nerve conduction studies are necessary for the diagnosis and are objective measures. They are rarely used as endpoint in the follow-up of CIDP patients, because they may be considered as less sensitive and less relevant than clinical evaluation. In multi-central trials, electrophysiological data may be used as secondary outcome

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measures, but a central core lab is recommended to improve quality control (Vanhoutte et al., 2013).

Techniques which count the motor units estimates the number of functional motor units and the axonal loss (Paramanathan et al., 2016). These electrophysiological assessments have been widely used in amyotrophic lateral sclerosis (ALS) where they have been correlated with functional outcome measurements (Neuwirth et al., 2015). Motor unit number index (MUNIX) (Nandedkar et al., 2004) is a novel electrophysiological measure that provides an index of the number of functional motor unit in a given muscle. In comparison to others motor unit number estimation (MUNE) techniques, MUNIX is a faster non-invasive technique that can be applied to any distal or proximal muscles in which a compound muscle action potential (CMAP) can be elected by nerve stimulation. Correlation between MUNIX and MUNE and good reproducibility of MUNIX have been established in ALS and healthy volunteers (Ahn et al., 2010; Nandedkar et al., 2010; Neuwirth et al., 2011; Boekestein et al., 2012; Furtula et al., 2013). MUNIX has been poorly studied in CIDP, where only one published study showed correlation between multiple point stimulation MUNE and MUNIX techniques in the thenar muscle group (Paramanathan et al., 2016).

The objective of this study was to determine the test–retest reliability of MUNIX in CIDP and to explore if the MUNIX sumscore could be related with functional scales currently used in CIDP.

2. Methods

14 patients, fulfilling the CIDP EFNS/PNS criteria (Joint Task Force of the EFNS and the PNS, 2010), were included in this study. These patients were currently treated with intravenous immunoglobulin (IVIg) infusions in the referral center for neuromuscular diseases and ALS of Marseille, France. Results were compared with 28 healthy controls. Informed consent was obtained from all the subjects and controls according to the Helsinki Declaration.

Age, gender, duration of the disease, overall neuropathy limitations scale (ONLS) score (Graham, 2006) and rasch-built overall disability scale (R-ODS) score (Van Nes et al., 2011) were collected. Muscle strength measurement and MUNIX protocol were assessed in the abductor pollicis brevis muscle (APB), abductor digiti mini muscle (ADM) and tibialis anterior muscle (TA) of the right side. If symptoms were asymmetrical, the weaker side was studied. Muscle strength was measured through manual testing using the MRC (medical research council) scale and through quantitative muscle testing (QMT) using a standardized dynamometer (Micro-FET 2™, Hoggan health industry, Salt Lake City, UT, USA). MRC sumscore, QMT sumscore and MUNIX sumscore were calculated by adding the corresponding results of the APB, ADM and TA muscles.

Two investigators (observers A and B) performed the MUNIX studies. They were blinded to each other's results. Electrodes and marks were totally removed so that any traces of electrodes placement was erased. Inter-rater variability study was performed on the 14 subjects included in this study. To estimate the intra-rater variability, the MUNIX study was assessed twice in 9 patients, stable under IVIg treatment. These patients had MRC and ONLS score unchanged between the MUNIX studies. The measures were performed the first day of two consecutive IVIg infusions (4–6 weeks interval).

The MUNIX protocol was carried out as previously reported (Nandedkar et al., 2004, 2010; Ahn et al., 2010; Neuwirth et al., 2011, 2015; Furtula et al., 2013) in the APB, ADM and TA muscles. Supramaximal distal stimulations of the corresponding nerves were performed to achieve maximal CMAP amplitude with minimum rise time and sharp negative take-off. The recordings were assessed on a 300 ms window with filter setting of 3–3000 Hz. Ten isometric contractions were recorded as surface interference pattern (SIP) ranging from 10% to 100% of contraction. The degree of the force increment was estimated by the resistance given by the examiner and by the amplitude and the fullness of the SIP. The data were exported from a keypoint.net device to an excel file designed to calculate MUNIX and motor unit size index (MUSIX). SIP epochs were accepted if SIP area > 20 mV/ms, ideal case motor unit count (ICMUC) < 100 and SIP area/CMAP area > 1 (Nandedkar et al., 2010).

Quantitative data were expressed in median with interquartile range, and were compared using the nonparametric Wilcoxon–Mann–Whitney test. The two-way random, single measure intraclass correlation coefficient (ICC) was calculated to assess the intra-rater and the inter-rater variability of the MUNIX. The ICC values range from 0 to 1, where 1 is a perfect reproducibility and ICC > 0.75 is interpreted as a good reproducibility of the measures (Furtula et al., 2013). Statistical analysis, including Spearman's correlation analysis, linear regression, Bland–Altman plots, coefficient of variation and ICC, were performed using Graph Pad Prism 5 and IBM SPSS statistics (version 20). A two-sided p value < 0.05 was considered as significant.

3. Results

9 male and 5 female CIDP patients were enrolled in this study. Median age was 66 years old (inter quartile 57–70 years). Median duration of the disease was 8 years (3–14 years). Median MRC sumscore was 12 (10–13) and median QMT sumscore 14.3 kPa (12.4–17.1). Median ONLS score was 4 (4–6), median R-ODS score was 57/100 (55–63).

Table 1
Results of MUNIX protocols in CIDP patients and healthy controls. Data are expressed in median with inter quartile ranges.

		CIDP (n = 14)	Healthy controls (n = 28)	p value
ADM	MUNIX	82 (60–126)	134 (90–155)	**p < 0.05**
	MUSIX (μV)	72.4 (55–80)	68 (60–94)	p > 0.05
	CMAP (mV)	7.6 (4.4–8.1)	8.7 (7.7–10.1)	**p = 0.01**
APB	MUNIX	69 (35–98)	133 (96–178)	**p = 0.01**
	MUSIX (μV)	94 (62–97)	61.9 (52–73)	**p < 0.05**
	CMAP (mV)	5.7 (3–7.3)	8.8 (6.3–11.1)	**p < 0.01**
TA	MUNIX	63 (31–97)	102 (81–118)	**p < 0.05**
	MUSIX (μV)	61.9 (51–64)	51 (45–56)	**p < 0.05**
	CMAP (mV)	3.2 (1.7–5)	4.9 (3.9–5.9)	p > 0.05
ADM + APB + TA Sumscore	MUNIX	240 (169–299)	379 (279–430)	**p = 0.001**
	MUSIX (μV)	223 (181–245)	184 (165–222)	p = 0.05
	CMAP (mV)	14.5 (11–21)	22.2 (19–25.8)	**p < 0.01**

Sumscores are obtained by adding the corresponding results of ADM, APB and TA muscles. MUNIX motor unit number index, MUSIX motor unit size index, CMAP compound muscle action potential amplitude, ADM abductor digiti mini, APB abductor pollicis brevis, TA tibialis anterior.