Long-term follow-up study of chronic pain in a cohort of patients with Multiple Sclerosis: preliminary results

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INTRODUCTION

A previous study on the assessment and characterization of chronic pain in Multiple Sclerosis patients [1], conducted in 2015 on 374 patients, showed that approximately one half of patients suffered from chronic pain, the most frequent type being neuropathic pain (NP), which was present in 23.7% of the whole cohort, and was associated with a sensory functional system involvement.

METHODS

Patients enrolled at baseline (T1) in the previous study were assessed, during routine follow-up clinical visits (T2) for the presence of chronic pain and, in particular, for the presence of neuropathic pain (NP) using the DN4 questionnaire. Based on the presence of NP at both time-points, we defined four mutually exclusive trajectories: 1) NEVER: no NP at any time-point, 2) RECEDED: NP present at T1 but not at T2, 3) NEWONSET: NP absent at T1 but present at T2, and 4) PERSISTENT: NP pain present at both time-points.

We performed a multinomial logistic regression to identify baseline clinical and demographic predictors of NP trajectories with the NEVER group as the reference category. Results are reported as Relative Risk Ratios (RRR) with 95% confidence intervals.

To examine the association between individual EDSS Functional System (FS) scores at T1 and NP trajectories we performed an additional multinomial logistic regression including the following covariates: pyramidal, cerebellar, brainstem, sensory, bowel and bladder, visual and mental FS scores. For FS domains that showed a statistically significant association, we further assessed the presence of a dose–response relationship by estimating adjusted probabilities of belonging to each NP trajectory across the range of FS scores, while holding other covariates constant.

RESULTS

To date, 240 patients have been reassessed (169F, 71M). Of these, 51 (21.3%) had NP pain at follow-up. **Table 1** shows patients' clinical characteristics at baseline and at follow-up.

Multinomial logistic regression including age at disease onset, sex, disease phenotype, disease duration, overall disability (EDSS), use of high-efficacy disease-modifying therapy (HET), use of NP treatment at baseline as covariates (and the NEVER group as reference group) showed that a progressive disease phenotype was associated with lower odds of being in the RECEDED group (RRR = 0.09, 95% CI [0.015 – 0.540], p = 0.008), while a higher EDSS increased this risk compared to the reference category (RRR = 1.70, 95% CI [1.27 – 2.29], p < 0.001). A longer disease duration at baseline decreased the risk of being in the NEWONSET NP group (RRR = 0.89, 95% CI [0.82 – 0.97], p = 0.011) and a higher baseline EDSS was associated with increased risk of PERSISTENT NP (RRR = 1.34, 95% CI [1.01 – 1.78], p = 0.043).

Multinomial logistic regression including the different EDSS FS as covariates (and the NEVER group as reference group) showed that patients in the RECEDED group were more likely to have visual (RRR = 3.17, 95% CI [1.24 – 8.06], p = 0.016) and sensory (RRR = 2.05, 95% CI [1.19 – 3.52], p = 0.009) involvement. The only significant association with a PERSISTENT NP trajectory was a sensory system involvement at baseline (RRR = 2.08, 95% CI [1.28 – 3.37], p = 0.003).

Post-estimation margins analysis (**Figure 1**) shows that the probability of belonging to the NEVER trajectory decreases steadily as sensory scores increases (from 77% for a sensory FS score of 0 to 13% for a FS score of 5). The predicted probability of belonging to the PERSISTENT NP group increases steadily with higher sensory scores (from 8% for a sensory FS score of 0 to 46% for a FS score of 5).

CONCLUSIONS

Disease severity and phenotype are associated with NP trajectories in MS: patients with progressive MS are significantly less likely to experience receding NP. Higher disability at baseline (EDSS) increases the likelihood of both transient and persistent NP. A longer disease duration at baseline is associated with lower risk of developing new-onset NP. Furthermore, specific EDSS FS impairments are linked to NP trajectories with clear dose-response relationships between sensory FS score and NP trajectory: the probability of remaining NP-free (NEVER) declines steadily with increasing sensory dysfunction. Conversely, the probability of PERSISTENT NP increases with sensory score.

OBJECTIVES/AIMS

The main aim of the study was to reassess the previously enrolled cohort, after a minimum follow-up of 8 years, in order to identify distinct trajectories of NP and to investigate their potential predictors.

Figure 1 Predicted probabilities of each NP trajectory across increasing levels of sensory dysfunction.

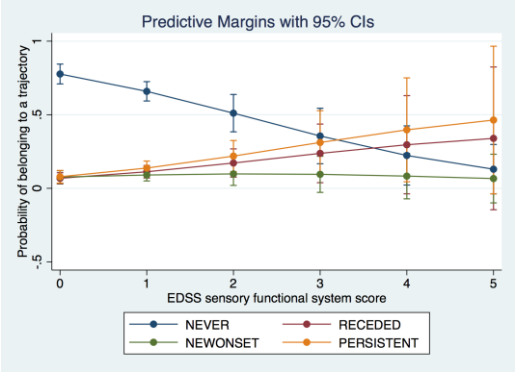

Table 1 Clinical characteristics of patients (nr=240) at baseline and at last follow-up.

	T1	T2	p-value
Age in years, mean (SD)	45 (12)	-	-
Sex, n (%)	M 71 (30) F 169 (70)	.	-
Disease duration in years, mean (SD)	22 (9)	-	-
EDSS, mean (SD)	2.3 (2.1)	3.2 (2.4)	<0.001
Clinical phenotype, n (%)	Prog 35 (15) RR 205 (85)	Prog 58 (24) RR 182 (76)	0.008
DMT, n (%)	HET 53 (22) NHET 187 (78)	HET 97 (40) NHET 143 (60)	<0.001
Neuropathic pain Y/N, n (%)	Y 56 (23) N 184 (77)	Y 51(21) N 189 (79)	0.583
Use of neuropathic pain treatment Y/N, n (%)*	Y 49 (20) N 191 (80)	Y 68 (28) N 172 (72)	0.043

SD: standard deviation; M: males; F: females; Prog: Primary and Secondary Progressive Multiple Sclerosis; RR: Relapsing-Remitting Multiple Sclerosis; DMT: Disease Modifying Treatments; HET: High Efficacy Therapies (Anti-CD20 monoclonal antibodies, Cladribine, Natalizumab, S1P-modulators, Mitoxantrone); NHET: non-High Efficacy Therapies (Teriflunomide, Dimethyl fumarate, Glatiramer acetate, Interferon, no DMT); Y: yes; N: no; *NP pain treatment (Gabapentin, Pregabalin, Duloxetine, Cannabidiol, Valproate, Amitriptyline, Baclofen, Lamotrigine, Paracetamol/FANS, Carbamazepine, Oxcarbazepine, Clonazepam, Tapentadol, Tramadol, multiple treatments).

References:

[1] Ferraro D, Plantone D, Morselli F, Dallari G, Simone AM, Vitetta F, Sola P, Primiano G, Nociti V, Pardini M, Mirabella M, Vollono C. Systematic assessment and characterization of chronic pain in multiple sclerosis patients. Neurol Sci. 2018 Mar;39(3):445-453. doi: 10.1007/s10072-017-3217-x. Epub 2017 Dec 9. PMID: 29224058.

Disclosures: The authors have nothing to disclose in relation to the study.