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Analysis of long-term disability trajectories in patients with primary progressive multiple sclerosis

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Background: Several primary progressive multiple sclerosis (PPMS) natural history studies have demonstrated a large degree of heterogeneity in time from disease onset to high levels of disability.

Objective: We aimed to investigate the heterogeneity of long-term disability accumulation in a cohort of PPMS patients and to determine if there are differences between the trajectories of PPMS adjusting for sex.

Methods: All PPMS patients enrolled in RelevEM registry who had ≥ 2 Expanded Disability Status Scale (EDSS) score, were included in the analysis. A linear mixed model was used to model longitudinal EDSS scores. The best model (lower values better fit) was selected according to both Akaike Information Criterion and Bayesian Information Criterion fit indices and also to parsimony and clinical interpretability of the data. The same indices were used to determine which time function (linear, quadratic, square root, logarithm) best fit the EDSS trajectories over time. Fractional polynomials were used to obtain the best longitudinal fit of the dependent variable (EDSS). The root mean square errors were also calculated.

Results: A total of 125 patients with longitudinal data were included (median observations/patients was 3 (2-5)). Mean age at onset of PPMS was 41 years (± 11), and mean PPMS duration was 11 years ± 5.9 . The male/female ratio was 1.4. Baseline EDSS was 2.97 (± 1.16) in women and 3.11 (± 1.20) in men, ($p = 0.50$); last EDSS was 5.66 (± 1.56) in women and 6.06 (± 1.56) in men ($p = 0.155$). The mean follow-up time was 10 years (± 5.11) in women and 12.8 (± 6.49) in men ($p < 0.001$). We found high heterogeneity between individuals (intraclass coefficient 43%), suggesting the usual clinical and radiologic variables are not enough to explain the variability in disability accumulation trajectories. We did not observe differences in disability trajectories stratified by sex, adjusted for potential confounders.

Conclusion: A high heterogeneity was found in the trajectory between individuals regarding disability accumulation. We have not found differences stratified by sex. As previously reported, there is a high variability between individuals that cannot be explained by the prognostic markers that we currently have.

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