

Machine learning analysis applied to prediction of early progression independent of relapse activity in multiple sclerosis patients

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ABSTRACT

Background. Predicting prognosis in people with multiple sclerosis (pwMS) at early disease stages still remains an unmet need. Machine learning (ML) strategies demonstrated good reliability when applied for prediction in medicine. This study aimed at developing a predictive algorithm comparing different ML approaches, by using routine demographic, clinical and radiological data from a large multicentric cohort of newly-diagnosed pwMS.

Methods. Demographic, clinical, radiological and biochemical data were retrospectively collected at three Italian MS centers at baseline and four timepoints thereafter (6, 12, 24, 36 months). Data from first evaluation and subsequent 2-year follow-up were analysed, comparing different ML models (Random Forest, Extra Trees, XGBoost, Logistic Regression and Support Vector Classifier) to predict progression independent-of-relapse activity (PIRA) at year 3. To understand how features impacted the selected model's output, a ML explainability analysis was performed on the whole

cohort and on specific subsets of patients, those aged under 45 and those NEDA-3 at 2- year follow-up.

Results. Data from 719 pwMS (age $34,6 \pm 11,2$ years; female sex 501(70%)) were analysed. Ninety-two pwMS (13%) developed PIRA at year 3. Random Forest achieved the highest score, with a test set area under the ROC curve (AUC) of 0.75 ± 0.06 . Features with highest predictive impact were Expanded Disability Status Scale at 24 months, age at symptoms onset and disease duration at baseline.

Conclusion. Our results showed feasibility of applying ML techniques to predict short term PIRA in newly-diagnosed pwMS by using routine clinical practice data, paving the way for tailored and personalized approaches.