

Refining prognosis in adult-onset multiple sclerosis: insights from a systematic review

Tommaso Guerra¹, Massimiliano Copetti², Mariacarla Achille^{1,3}, Caterina Ferri⁴, Marta Simone³, Sandra D'Alfonso⁵, Maura Pugliatti^{4,6}, Pietro Iaffaldano¹

1. Department of Translational Biomedicine and Neurosciences-DIBrain, University of Bari "Aldo Moro", Azienda Ospedaliero-Universitaria Consorziata Policlinico di Bari, Bari, Italy; 2. Unit of Biostatistics, Fondazione IRCCS "Casa Sollievo della Sofferenza", San Giovanni Rotondo, Italy; 3. Child Neuropsychiatry Unit, Department of Precision and Regenerative Medicine, Jonic Area University of Bari "Aldo Moro", Bari, Italy; 4. Department of Neurosciences, S. Anna University Hospital, Ferrara, Italy; 5. Department of Health Sciences, University of Piemonte Orientale, Novara, Italy; 6. Department of Neuroscience and Rehabilitation, University of Ferrara, Ferrara, Italy.



INTRODUCTION

Neurologists have long pursued the identification of robust prognostic factors to anticipate the variable course of multiple sclerosis (MS), both in clinical care and research contexts. To enable early diagnosis and accurately identify MS patients at elevated risk of progression, precise diagnostic criteria and prognostic markers are both essential, emphasizing the need for a comprehensive prognostic model incorporating imaging, molecular, clinical biomarkers.

AIM

To provide a comprehensive and up-to-date review of clinical and radiological prognostic factors in adult-onset MS. This study falls within the framework of the PROMISING study, which aims to predict MS disease progression through the development of a prognostic score.

METHOD

A systemic research was applied in the two primary academic databases, PubMed and Google Scholar. Our search strategy comprised pertinent keywords related to prognosis in MS. During the selection procedure, particular inclusion and exclusion criteria were applied to guarantee the high standard and applicability of this review. The main focus was about the prognostic role of different biomarkers in MS. Each identified published study was classified as high or low quality, depending on study design, population size, risk of bias, and assessment of outcomes. Following this search path, some papers were eliminated since they were either unpublished manuscripts or non-peer-reviewed materials. No restrictions were placed on publication dates, but we focused mainly on studies published in the last years.

RESULTS

Age consistently emerges as a strong determinant, with older patients exhibiting increased global disability and a heightened risk ($p < 0.001$) of progression independent of relapse activity (PIRA), while younger patients show greater responsiveness to disease modifying treatment (DMTs) and improved outcomes. Delayed DMT initiation is associated with higher risk ($p < 0.001$) of disability, dependent and independent of neuroinflammation. MRI parameters, particularly the burden and location of T2 lesions and spinal cord involvement, have been associated with long-term disability accumulation, often independently of relapse activity, and drove treatment changes. Secondary progressive conversion risk is higher in patients with multifocal symptoms, higher EDSS scores at onset, and with elevated relapse rates ($p < 0.001$). Fluid biomarkers are linked to immune-related pathways, predict future impairment and correlate with clinical and imaging outcomes of MS severity.

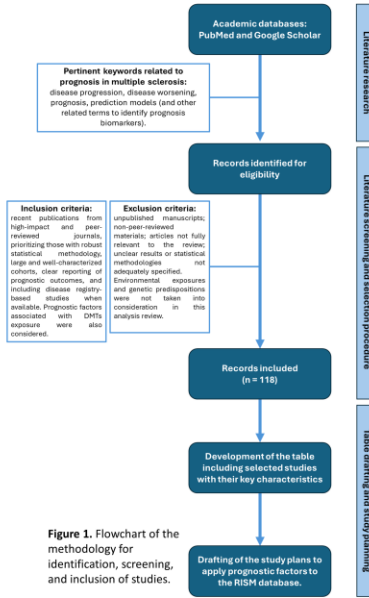


Figure 1. Flowchart of the methodology for the identification, screening, and inclusion of studies.

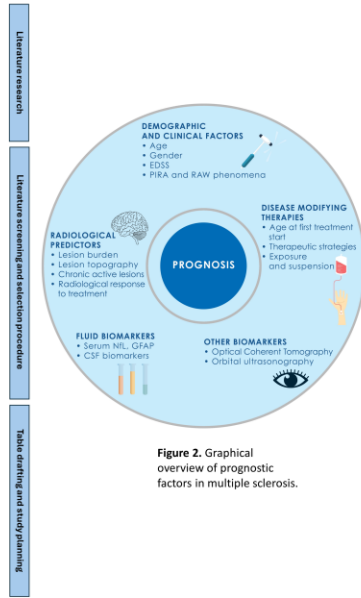


Figure 2. Graphical overview of prognostic factors in multiple sclerosis.

CONCLUSIONS

An up-to-date overview of the long-term prognostic value of different biomarkers could aid clinicians in better considering different aspects of clinical practice in MS. Expanding disease registries to incorporate as many biomarkers of disease progression as possible would promote the idea of merging datasets to provide a multifaceted picture of MS patients.

REFERENCES

- Calabrese M, Preziosa P, Scalfari A, et al. Determinants and Biomarkers of Progression Independent of Relapses in Multiple Sclerosis. *Ann Neurol.* 2024;96(1):1-20. doi:10.1002/ana.26913
- Filippi M, Amato MP, Avolio C, et al. Towards a biological view of multiple sclerosis from early subtle to clinical progression: an expert opinion. *J Neurol.* 2025;272(1):179. Published 2025 Feb 1. doi:10.1007/s00415-025-12917-4

FUNDINGS

This study falls into the framework of "PROMISING study" (Next Generation EU-NRRP M6C2-Investment 2.1 Enhancement and Strengthening of Biomedical Research in the NHS-PNRR-MAD-2022-12376868). The funds came from the Italian National Recovery and Resilience Plan, known as "Italia Domani", provided by the European Union (Next Generation EU) and the Ministry of Health of the Italian Republic. Soggetto Attuatore: Azienda Ospedaliero-Universitaria Policlinico di Bari.

CONTACT INFORMATION

pietro.iaffaldano@uniba.it; guerra.tommaso93@gmail.com

24-28 Ottobre 2025
Padova Congress

55° CONGRESSO
SOCIETÀ ITALIANA
DI NEUROLOGIA