RESEARCH ASSOCIATION

ABSTRACT BOOK

2025

Multiple Sclerosis Study Group Research Abstracts

77 abstracts · 11 thematic sections

Contents

I	Cognitive Function and Cognitive Reserve	9 abstracts	3
II	Motor Function, Mobility and Falls	19 abstracts	13
III	Pain, Personality and Quality of Life	5 abstracts	33
IV	Disease Course, Prognosis and Disability Assessment	6 abstracts	39
V	Cerebrospinal Fluid and Immunological Markers	4 abstracts	46
VI	Age at Onset, Ageing, Sex and Menopause	5 abstracts	51
VII	Pregnancy, Breastfeeding and Offspring	4 abstracts	57
VIII	Disease-Modifying Therapies: Long-Term Real-World Outcomes	10 abstracts	62
IX	Treatment Safety, Infections and Wearing-Off	7 abstracts	73
X	COVID-19 Pandemic	3 abstracts	81
XI	Neuromyelitis Optica Spectrum Disorder and MOGAD	5 abstracts	85

SECTION I

Cognitive Function and Cognitive Reserve

9 ABSTRACTS

001

Whose Perspective Reflects Reality? Informant-Based Versus Patient-Reported Cognitive Status in Multiple Sclerosis

Ela Zengin, Gözde Deniz Ünal, İrem Kara, Can Caliskan, Serkan Ozakbas

INTRODUCTION Multiple sclerosis is a chronic neurological disorder involving both physical and cognitive impairments. Cognitive deficits are often overlooked, especially in patients with low self-awareness. Thus, self-reports may not accurately reflect cognitive status. The patient version of the Multiple Sclerosis Neuropsychological Questionnaire (MSNQ-P) assesses perceived cognitive issues, while the informant version (MSNQ-I) reflects caregiver observations.

OBJECTIVES This study aimed to compare the associations of both tools with objective cognitive performance and physical disability in individuals with multiple sclerosis.

METHODS Participants completed the MSNQ-P and MSNQ-I. Cognitive performance was measured using the SDMT, CVLT-II, and BVMT-R. Physical disability was assessed via EDSS and PDDS. Pearson correlations were used to examine associations between all measures.

RESULTS A total of 222 patients with multiple sclerosis were included in the study. The mean age was 37.75 years (SD = 10.34), the mean disease onset age was 29.75 years (SD = 9.52), and the mean disease duration was 7.99 years (SD = 6.96). Of the participants, 73.9% were women, and 96.8% were diagnosed with relapsing-remitting multiple sclerosis. There was a significant moderate positive correlation between MSNQ-P and MSNQ-I scores ($r = 0.540$, $p < 0.001$). The MSNQ-I score showed a significant negative correlation with all three objective cognitive tests: SDMT (mean = 51.19, SD = 12.53; $r = -0.387$, $p < 0.001$), CVLT-II (mean = 52.02, SD = 12.89; $r = -0.293$, $p < 0.001$), and BVMT-R (mean = 26.91, SD = 6.79; $r = -0.358$, $p < 0.001$). In contrast, the MSNQ-P score was not significantly associated with any of these cognitive measures (SDMT: $r = 0.015$, $p = 0.820$; CVLT-II: $r = -0.097$, $p = 0.149$; BVMT-R: $r = -0.056$, $p = 0.404$). Regarding physical disability, the mean EDSS score was 0.81 (SD = 1.30), and the mean PDDS score was 0.58 (SD = 1.17). MSNQ-I was positively correlated with both EDSS ($r = 0.352$, $p < 0.001$) and PDDS ($r = 0.317$, $p < 0.001$), whereas MSNQ-P did not show any significant relationship with either measure ($p > 0.05$).

CONCLUSION The results show that MSNQ-I correlates more strongly with cognitive performance and physical disability than the self-reported MSNQ-P. This suggests that individuals with MS may lack insight into their cognitive issues, and self-reports may underestimate impairment. Using informant-based tools can improve cognitive assessment accuracy, support earlier interventions, and aid in personalized care planning

002

Tracking Verbal Memory in Multiple Sclerosis: Predictors of One-Year Change in California Verbal Learning Test-II Performance

İrem Kara, Gözde Deniz Ünal, Ela Zengin, Serkan Ozakbas

INTRODUCTION The California Verbal Learning Test-Second Edition (CVLT-II) is a widely recognized neuropsychological tool for evaluating verbal learning and memory. In people with multiple sclerosis (pwMS), monitoring changes in CVLT-II performance over time may offer insights into cognitive trajectories and disease burden. However, the clinical and behavioral correlates of these changes are still not fully understood.

OBJECTIVES To examine the clinical, cognitive, and behavioral predictors of one-year changes in CVLT-II scores in pwMS, and to evaluate the prognostic value of such changes.

METHODS This study retrospectively analyzed a cohort of pwMS who underwent cognitive and clinical assessments at baseline and at one-year follow-up. The primary outcome was the change in CVLT-II score. Predictor variables included changes in Symbol Digit Modalities Test (SDMT), Brief Visuospatial Memory Test-Revised (BVMT-R), Timed 25-Foot Walk (T25-FW), and 9-Hole Peg Test (9-HPT), as well as EDSS scores, relapse frequency, and lifestyle behaviors (smoking and alcohol use). Statistical analyses included Pearson correlations, ANOVA, and multiple linear regression. For group comparisons, patients were categorized according to the percentage change in CVLT-II scores: ≥20% improvement, ≥20% worsening, or stable.

RESULTS A total of 393 pwMS were included in the study. Of these, 54 patients demonstrated ≥20% improvement in CVLT-II performance, 85 experienced ≥20% worsening, and 254 showed no significant change. The three groups were matched for age and disease duration. The mean CVLT-II change over one year was 0.96 (SD = 0.23). Change in CVLT-II scores was negatively correlated with change in SDMT ($r = -0.205$, $p < 0.01$) and positively correlated with change in T25-FW ($r = 0.164$, $p < 0.01$). ANOVA revealed significant between-group differences for EDSS at follow-up ($F(2, 390) = 3.741$, $p = 0.025$) and relapse count at follow-up ($F(2, 390) = 3.810$, $p = 0.023$), but not for other variables. Multiple linear regression analysis indicated that the model was statistically significant ($F(12, 322) = 2.452$, $p = 0.005$), though it explained a modest proportion of the variance ($R2 = 0.084$). The change in SDMT ($\beta = -0.143$, $p = 0.009$) and T25-FW ($\beta = 0.155$, $p = 0.006$) emerged as significant independent predictors of CVLT-II change.

CONCLUSION Over a one-year period, changes in verbal memory were significantly associated with both cognitive and physical performance metrics. Reductions in information processing speed and increased gait time were linked to poorer verbal learning outcomes. Although the explained variance was limited, these findings emphasize the multifactorial nature of cognitive change in MS and support the integration of both cognitive and motor assessments into routine clinical follow-up. Monitoring subtle shifts in verbal learning may facilitate early identification of cognitive decline and inform timely, individualized intervention strategies.

003

What Drives Change in Cognitive Speed? Predictors of One-Year Symbol Digit Modalities Test Performance in Multiple Sclerosis

İrem Kara, Gözde Deniz Ünal, Ulvi Samadzade, Serkan Ozakbas

INTRODUCTION The Symbol Digit Modalities Test (SDMT) is a sensitive measure of information processing speed and attention, widely used in the cognitive assessment of people with multiple sclerosis (pwMS). Longitudinal tracking of SDMT performance can help uncover the clinical and behavioral factors that contribute to cognitive decline or improvement over time.

OBJECTIVES To identify the clinical, cognitive, and behavioral predictors of one-year changes in SDMT performance in pwMS.

METHODS This retrospective analysis examined one-year changes in SDMT scores as the primary outcome. Predictor variables included changes in California Verbal Learning Test-II (CVLT-II), Brief Visuospatial Memory Test-Revised (BVMT-R), Timed 25-Foot Walk (T25-FW), and 9-Hole Peg Test (9-HPT), as well as baseline and follow-up EDSS scores, annual relapse count, and lifestyle behaviors (smoking and alcohol use). Statistical analyses involved Pearson correlations, ANOVA, and multiple linear regression. For group comparisons, participants were categorized into three subgroups based on the percentage change in SDMT performance over one year: ≥20% improvement, ≥20% worsening, and stable performance. Age and disease duration were matched across groups.

RESULTS The analysis included 399 pwMS. Among them, 95 showed ≥20% improvement in SDMT scores, 43 experienced ≥20% worsening, and 261 remained stable. The three groups were matched for age and disease duration. The mean SDMT change over one year was 1.07 (SD = 0.22). SDMT improvement was positively correlated with changes in CVLT-II ($r = 0.294$, $p < 0.01$), BVMT-R ($r = 0.218$, $p < 0.01$), and 9-HPT ($r = 0.141$, $p < 0.01$), and negatively correlated with changes in T25-FW ($r = -0.168$, $p < 0.01$) and EDSS at follow-up ($r = -0.080$, $p < 0.05$). ANOVA indicated significant group differences based on EDSS scores ($F(2, 396) = 4.804$, $p = 0.009$) and relapse count at follow-up ($F(2, 396) = 3.944$, $p = 0.020$), but no differences in other clinical variables. Multiple linear regression showed a statistically significant model ($F(14, 323) = 4.132$, $p < 0.001$), explaining 15.2% of the variance in SDMT change ($R2 = 0.152$). The most significant predictors were change in CVLT-II ($\beta = 0.319$, $p < 0.001$) and change in T25-FW ($\beta = -0.121$, $p = 0.023$).

CONCLUSION One-year changes in information processing speed, as measured by the SDMT, are shaped by both cognitive and motor performance. Improvements in verbal learning strongly align with gains in SDMT, whereas deteriorations in gait function are associated with slower cognitive speed. These findings underscore the need to monitor both cognitive and physical domains when evaluating cognitive trajectories in MS. A multidimensional follow-up approach may improve the early detection of decline and guide targeted interventions to preserve cognitive health.

004

Cognitive Reserve at Diagnosis Predicts Nine-Year Cognitive Outcomes in Multiple Sclerosis

İrem Kara, Ela Zengin, Gözde Deniz Ünal, Serkan Ozakbas

INTRODUCTION Cognitive impairment is a common and often disabling feature of multiple sclerosis (MS), occurring even in patients with minimal physical disability. Among the proposed protective factors against cognitive decline, cognitive reserve has received growing attention. Cognitive reserve reflects the brain's resilience to neuropathological damage and is thought to modulate the relationship between disease burden and cognitive performance. Although cross-sectional studies have supported the role of cognitive reserve in MS, longitudinal data examining its predictive value remain limited.

OBJECTIVES This study aimed to investigate whether cognitive reserve at the time of diagnosis predicts long-term cognitive outcomes in people with MS (pwMs) over a nine-year follow-up period.

METHODS In this prospective longitudinal study, cognitive reserve was assessed at baseline using the Cognitive Reserve Index questionnaire (CRIq). Cognitive performance was evaluated both at baseline and at nine-year follow-up using the Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS). A clinically meaningful cognitive decline was defined as a 20% or greater reduction in performance in at least one of the BICAMS tests. Statistical analyses included group comparisons and logistic regression models to assess the predictive value of baseline CRIq scores on long-term cognitive status, while controlling for age, sex, and baseline disability.

RESULTS A total of 148 pwMs (68% female, EDSS score≤3.5) were followed for nine years. At baseline, the mean age was 34.7 (SD: 7.9). At follow-up, 46 participants (31.1%) showed clinically significant cognitive decline as defined by the criteria. Those who experienced decline had significantly lower CRIq scores at baseline compared to individuals who remained cognitively stable or improved. Logistic regression analysis revealed that higher baseline CRIq scores were independently associated with a lower risk of future cognitive decline, even after adjusting for age, sex, and baseline disability.

CONCLUSION The findings from this nine-year prospective study demonstrate that cognitive reserve at diagnosis, as measured by the CRIq, is a strong and independent predictor of long-term cognitive outcomes in pMs. Individuals with lower cognitive reserve were significantly more likely to experience deterioration in processing speed and visual memory. These results underscore the clinical value of assessing cognitive reserve at the earliest stages of the disease and suggest that strategies aimed at enhancing cognitive reserve - such as educational, occupational, and cognitively stimulating activities - may have long-term protective effects on cognitive health in MS.

005

Social Cognition Impairments in Individuals with Multiple Sclerosis: Evidence from Emotion Recognition and Theory of Mind Tasks

İrem Kara, Gözde Deniz Ünal, Serkan Ozakbas

INTRODUCTION Cognitive dysfunction is a recognized feature of multiple sclerosis (MS), yet social cognition - defined as the ability to perceive, interpret, and respond appropriately to social cues - remains a relatively underexplored domain. While impairments in information processing speed, memory, and executive function have been widely documented, deficits in understanding others' emotions and mental states may emerge early in the disease course and contribute significantly to interpersonal difficulties and reduced quality of life.

OBJECTIVES This study aimed to investigate social cognition impairments in individuals with MS by comparing their performance to healthy controls (HC) on two well-established tasks: the Reading the Mind in the Eyes Test (RMET), and the Ekman Facial Emotion Recognition Test (EFERT).

METHODS In this cross-sectional design, people with relapsing-remitting MS (pwRRMS) and HC, matched for age and education level, were administered two tests of social cognition. RMET was used to evaluate the capacity to infer mental states from subtle visual cues, while EFERT assessed participants' ability to identify six basic emotions from facial expressions. Mood-related factors were assessed using the Hospital Anxiety and Depression Scale. Between-group comparisons were conducted using independent samples t-tests and ANCOVA, controlling depression scores.

RESULTS 70 pwRRMS (mean age: 36.2 ± 7.8; EDSS <4.0) and 48 HC (mean age: 35.4 ± 6.9) were included. The MS group demonstrated significantly lower performance on RMET, with a mean score of 21.4 ± 4.1, compared to a mean of 25.6 ± 3.2 in HC group ($p < 0.001$). Similarly, total accuracy EFERT was reduced in the MS group (71.2% ± 9.8) relative to HC (82.3% ± 7.1), with the difference again reaching statistical significance ($p < 0.001$). Emotion-specific analyses revealed that pwRRMS were particularly impaired in recognizing anger and fear (both $p < 0.001$), while performance in identifying happiness was comparable between groups and remained near the ceiling in both samples. These findings persisted even after adjusting for mood-related symptoms, indicating that the observed deficits are not solely attributable to depression or anxiety.

CONCLUSION PwRRMS exhibited marked impairments in both theory of mind and facial emotion recognition when compared to matched HC. Notably, the ability to recognize negative emotions such as anger and fear was disproportionately affected, whereas recognition of positive emotions such as happiness remained intact. The persistence of these deficits after controlling depressive symptoms supports the view that social cognition represents a distinct and vulnerable cognitive domain in MS. Early identification of such impairments is crucial, as they may negatively impact social functioning, adherence to treatment, and quality of life.

006

Cognitive Profiles of Relapsing Multiple Sclerosis Patients with Progression Independent of Relapse Activity Versus Non-NEDA-3 Status

Said Alizada, Asiye Tuba Ozdogar, Ulvi Samadzade, Can Caliskan, Serkan Ozakbas

INTRODUCTION NEDA-3 (No Evidence of Disease Activity) is considered a primary treatment goal in RRMS (Relapsing-Remitting Multiple Sclerosis). However, some patients do not meet this goal, and others experience Progression Independent of Relapse Activity (PIRA). The cognitive consequences of PIRA in these patients remain uncertain.

OBJECTIVES Our hypothesis is that cognitive impairment might distinguish those with disease activity despite meeting the PIRA criteria from those without any disease activity (NEDA-3).

METHODS We followed 180 RRMS patients (mean age 38.62 ± 9.63; 77.2% female) over a five-year period. Cognitive performance was assessed using the BICAMS battery. Patients were categorized based on their NEDA-3 status. Among the 109 patients who did not achieve NEDA-3, we further identified two subgroups: those with PIRA (n=19; 10.6%) and those with Relapse-Associated Worsening (RAW) (n=16; 8.9%). Changes in SDMT, CVLT, and BVMTR scores were analyzed across these subgroups.

RESULTS Of the 180 patients, 71 (39.4%) achieved NEDA-3. In the non-NEDA-3 group, the mean changes in SDMT, CVLT, and BVMTR scores were 3.06 (±9.07), 8.07 (±11.05), and 3.05 (±5.77), respectively. In the PIRA subgroup, the changes were 3.84 (±9.08), 9.00 (±11.61), and 2.53 (±4.56), showing no significant differences compared to the broader non-NEDA-3 group ($p > 0.05$).

CONCLUSION The findings from this study suggest that, despite disease progression in the absence of relapses (PIRA), cognitive decline does not necessarily accompany clinical worsening over the long term in RRMS patients. This highlights the need for a deeper understanding of the mechanisms underlying PIRA and its potential dissociation from cognitive impairment. It also suggests that cognitive outcomes in RRMS patients may not always align with clinical progression, pointing to the necessity of tailored approaches in monitoring and treating cognitive dysfunction, especially in patients exhibiting disease activity without relapse.

007

Cognitive Decline as the First Sign of Progression in Multiple Sclerosis: A Comparative Analysis of Cognitive and Physical Decline

Serkan Ozakbas, Said Alizada, Ulvi Samadzade, Can Caliskan

INTRODUCTION Multiple Sclerosis (MS) is a chronic, progressive neurological disease that affects both physical and cognitive functioning. While clinical assessments typically focus on physical disability, cognitive decline - particularly in processing speed, verbal memory, and visual memory - can occur early and significantly impair daily functioning. This study investigates whether cognitive decline precedes physical decline in MS patients over time.

OBJECTIVES The primary aim of this study was to determine whether cognitive deterioration occurs before physical decline by comparing the onset of cognitive and physical impairments in MS patients.

METHODS Physical function was assessed using the 9-Hole Peg Test (9HPT) and the T25-Foot Walk (T25FW). Cognitive function was measured using the Symbol Digit Modalities Test (SDMT), the California Verbal Learning Test (CVLT), and the Brief Visuospatial Memory Test (BVMT). A total of 235 MS patients, drawn from a cohort of 4,191 individuals, were included in the analysis, all of whom exhibited either cognitive or physical decline during a five-year follow-up period. A cut-off of 20% deterioration was used to define significant decline. Statistical analyses were conducted using Wilcoxon Signed Rank Tests for related samples and Friedman's Two-Way Analysis of Variance by Ranks, with a significance threshold of $p < .001$.

RESULTS Among the participants, cognitive decline preceded physical decline across all tested domains. In the comparison of SDMT and 9HPT, 97 participants exhibited earlier cognitive decline (mean ranks: SDMT = 1.13, 9HPT = 1.88; $p < .001$). Similar results were observed for the CVLT and 9HPT comparison, with 94 participants showing earlier cognitive deterioration (mean ranks: CVLT = 1.15, 9HPT = 1.85; $p < .001$). A consistent pattern emerged in the BVMT-R and 9HPT comparison, where 98 participants showed earlier decline in cognitive performance (mean ranks: BVMT-R = 1.16, 9HPT = 1.84; $p < .001$). This trend was also found in comparisons with the T25FW: 92 participants showed earlier cognitive deterioration in the SDMT-T25FW comparison (mean ranks: SDMT = 1.16, T25FW = 1.84; $p < .001$), and 91 participants in the CVLT-T25FW comparison (mean ranks: CVLT = 1.19, T25FW = 1.81; $p < .001$). Cognitive decline occurred at an average of 2.7 to 2.72 years, while physical decline was observed after 3.85 to 3.95 years on the 9HPT and T25FW tests.

CONCLUSION These findings indicate that cognitive decline, particularly in processing speed, verbal memory, and visual memory, occurs prior to physical decline in MS patients. This emphasizes the importance of routine cognitive assessments, even in the absence of significant physical disability, and underscores the need for early cognitive intervention to improve long-term outcomes for MS patients.

008

Age at Symptom Onset and its Impact on Cognitive and Physical Outcomes in Multiple Sclerosis

Gözde Deniz Ünal, Can Caliskan, İrem Kara, Ulvi Samadzade, Serkan Ozakbas

INTRODUCTION Multiple Sclerosis (MS) is a chronic neurological disease that affects both cognitive and physical functioning. While previous research has explored cognitive and motor deficits in MS, less is known about the influence of age at symptom onset on these outcomes. This study investigates whether the age at which MS symptoms first appear - either between 18- 30 years or 31-50 years - affects long-term cognitive performance and disability.

OBJECTIVES The aim of this study was to explore the relationship between age at symptom onset and cognitive, physical, and disability profiles in individuals with MS. Specifically, we compared the outcomes between those whose first symptoms appeared at 18-30 years and those whose symptoms began at 31-50 years.

METHODS This cross-sectional study included 2,621 participants diagnosed with MS. Participants were grouped based on the age at symptom onset: 18-30 years and 31-50 years. Key outcome measures included physical tests (Timed 25-Foot Walk [T25FW], Nine-Hole Peg Test [9HPT]), cognitive assessments (California Verbal Learning Test [CVLT-II], Symbol Digit Modalities Test [SDMT], Brief Visuospatial Memory Test [BVMT-R]), and disability levels measured using the Expanded Disability Status Scale (EDSS). Independent samples t-tests were conducted to compare means between the groups, with effect sizes calculated using Cohen's d.

RESULTS There were no significant differences in physical performance between the two groups (T25FW: $p = 0.479$, 9HPT: $p = 0.204$), indicating that age at symptom onset does not significantly affect motor function. However, individuals with earlier onset (18-30 years) performed significantly better in all cognitive domains: verbal learning (CVLT-II: $M = 53.69$ vs. $M = 49.47$, $p < 0.001$, $d = 0.332$), information processing speed (SDMT: $M = 49.41$ vs. $M = 41.69$, $p < 0.001$, $d = 0.563$), and visuospatial memory (BVMT-R: $M = 26.67$ vs. $M = 23.18$, $p < 0.001$, $d = 0.512$). The SDMT demonstrated the largest effect size. Additionally, individuals with later onset (31-50 years) exhibited higher EDSS scores ($p < 0.001$, $d = -0.226$), indicating a greater degree of disability.

CONCLUSION This study underscores the significant influence of age at symptom onset on cognitive and physical outcomes in MS. While physical performance appears to be relatively independent of age at symptom onset, individuals with earlier onset (18-30 years) show superior cognitive performance, especially in areas like processing speed, verbal learning, and visuospatial memory. In contrast, later onset (31-50 years) is associated with a higher degree of disability. These findings suggest that earlier onset may offer a protective advantage in cognitive function and lower disability, highlighting the importance of early identification and monitoring for more effective MS management. Regular cognitive assessments are critical in developing tailored interventions for MS patients across different age groups.

009

Verbal Memory as a Leading Indicator of Cognitive Decline in Multiple Sclerosis with Stable Physical Function

Gözde Deniz Ünal, Can Caliskan, Ulvi Samadzade, Esra Aydın

INTRODUCTION Multiple sclerosis (MS) is a chronic disease of the central nervous system that affects both physical and cognitive domains. While motor disability often receives primary clinical attention, cognitive impairment may develop silently - even in patients whose physical function appears stable. Early identification of cognitive decline is essential for timely therapeutic intervention, yet the most sensitive cognitive tests for detecting such early changes remain unclear.

OBJECTIVES This study aimed to determine which of three commonly used neuropsychological tests - the California Verbal Learning Test-II (CVLT-II), Brief Visuospatial Memory Test-Revised (BVMT-R), or Symbol Digit Modalities Test (SDMT) - most frequently and most rapidly identifies cognitive deterioration in MS patients with stable motor performance over a five-year period.

METHODS Patients with MS who showed no progression in physical disability over five years were included. Each participant completed annual assessments using CVLT-II, BVMT-R, and SDMT. Cognitive decline was defined as a significant performance drop in any of the tests. Descriptive statistics, one-sample proportion tests (Agresti-Coull, Jeffreys, Wilson), paired-samples t-tests, effect size calculations (Cohen's d), and Pearson correlation coefficients were used for statistical analysis.

RESULTS Of the 190 patients followed, the first cognitive decline was detected by CVLT-II in 52 patients, by BVMT-R in 40, and by SDMT in 22. No decline was observed in 76 patients over five years. Proportion tests confirmed that all three distributions differed significantly from chance ($p < .001$ for each). CVLT-II decline occurred significantly earlier than BVMT-R ($t = -3.665$, $p < .001$, $d = -0.291$) and SDMT ($t = -4.405$, $p < .001$, $d = -0.349$), whereas no significant difference was found between BVMT-R and SDMT ($p = 0.406$). Test results were moderately intercorrelated (r range = .207-.250, all $p < .01$).

CONCLUSION In MS patients with stable physical function over five years, verbal memory - assessed via CVLT-II - was the most frequent and earliest domain to exhibit cognitive decline. These findings suggest that verbal learning and memory may serve as a sentinel marker for cognitive progression independent of motor worsening, reflecting an early form of cognitive progression independent of relapse activity (cognitive PIRA). Incorporating verbal memory assessments into routine follow-up could enhance early detection of cognitive impairment and support timely intervention strategies to preserve long-term cognitive health in MS.

SECTION II

Motor Function, Mobility and Falls

19 ABSTRACTS

010

The Role of Upper Extremity Fatigability in Multiple Sclerosis: Correlations with Function and Quality of Life

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INTRODUCTION Fatigue is one of the most debilitating symptoms in people with multiple sclerosis (MS, pwMS), influencing their ability to carry out everyday activities and negatively affecting their quality of life. While much attention has been given to general fatigue, its specific impact on upper extremity function, and its relationship with both fatigue perception and functional capacity, remains insufficiently understood.

OBJECTIVES The objective of this study was to investigate the relationships between self-reported levels of fatigue, measured fatigability, and functional capacity in pwMS, focusing particularly on the upper extremities.

METHODS A total of 246 pwMS participated in the study. Fatigability was assessed using the Dynamic Fatigue Index (DFI) and the Static Fatigue Index (SFI) for measuring gross grip strength. Manual dexterity was evaluated with the Nine Hole Peg Test (N-HPT). Patient-reported outcomes, including upper extremity ability, fatigue levels, and health-related quality of life, were assessed using the Manual Ability Measure (MAM-36), the Modified Fatigue Impact Scale (MFIS), and the Preference-Based Multiple Sclerosis Index (PBMSI).

RESULTS The participants had a mean age of 37.99±11.04 years, a mean disease duration of 11.20±8.16 years, and an average EDSS score of 1.33±1.72. The study identified significant correlations between various measures of fatigability and self-reported fatigue levels, manual dexterity, and overall health-related quality of life. Specifically, the DFI-right correlated with the PBMSI subscales for mood ($p=0.048$, rho=−0.126) and concentration ($p=0.026$, rho=−0.141). The DFI-left was significantly associated with the MAM-36 ($p=0.007$, rho=0.173), and several MFIS subscales, including physical ($p<0.001$, rho=−0.350), cognitive ($p<0.001$, rho=−0.334), and physiological ($p<0.001$, rho=−0.228). Moreover, the SFI-right showed significant relationships with MFIS-physical ($p=0.002$, rho=0.200), MFIS-cognitive ($p=0.001$, rho=0.208), and PBMSI-walking ($p=0.038$, rho=0.132), while SFI-left was closely linked with the MAM-36 ($p<0.001$, rho=−0.300) and the N-HPT scores for both dominant ($p<0.001$, rho=0.260) and non-dominant hands ($p<0.001$, rho=0.365).

CONCLUSION The study demonstrates that both dynamic and static fatigability are significantly correlated with fatigue perception, manual dexterity, and quality of life in individuals with MS. These results highlight the importance of measuring fatigability as a key determinant of functional ability, suggesting that tailored interventions targeting fatigability could improve both daily functioning and overall well-being in pwMS.

011

Patient-Reported Disability Accurately Reflects Motor Performance: The Association Between the Patient Determined Disease Steps and One-Leg Stance Test in People with Multiple Sclerosis

Ela Zengin, Gözde Deniz Ünal, Can Caliskan, Esra Aydın, Serkan Ozakbas

INTRODUCTION Accurate assessment of motor function is essential in managing multiple sclerosis (MS), a condition marked by progressive disability. While clinician-rated tools like the Expanded Disability Status Scale (EDSS) are widely used, patient-reported measures such as the Patient Determined Disease Steps (PDDS) offer a quick, accessible alternative. However, the extent to which PDDS reflects actual motor capacity remains underexplored. Balance tasks, particularly the one-leg stance test, provide objective insight into lower-limb control and functional stability, making them suitable for evaluating the validity of PDDS in clinical contexts.

OBJECTIVES This study aimed to examine the relationship between PDDS and objective balance performance measured via the one-leg stance test in individuals with MS. It also compared the motor correlates of PDDS with EDSS and explored differences between dominant and nondominant leg performance

METHODS This cross-sectional study included individuals diagnosed with MS. Disability levels were assessed using both PDDS and EDSS. Balance performance was measured by the duration of one-leg stance on dominant and nondominant legs; the mean of both was recorded as average stance time. Pearson correlation was used to assess relationships between variables. Paired samples t-tests and the Friedman test examined group differences, with Bonferroni correction applied to pairwise comparisons. Cohen's d was used for effect size calculation.

RESULTS PDDS showed a strong negative correlation with average stance time ($r = -0.645$, $p < .001$), indicating that higher perceived disability is associated with poorer balance. PDDS also correlated with stance duration on the dominant ($r = -0.200$, $p = .008$) and nondominant legs ($r = -0.218$, $p = .004$). EDSS showed a moderate correlation with average stance time ($r = -0.480$, $p < .001$). PDDS and EDSS were strongly correlated ($r = 0.690$, $p < .001$). Mean balance time differed significantly across variables ($p < .001$), but no significant difference was found between legs ($p = .813$). Effect sizes exceeded 45 seconds on average ($p < .001$).

CONCLUSION PDDS is a reliable patient-reported measure that correlates well with objective balance performance in MS, outperforming EDSS in this context. Given its ease of use, low cost, and alignment with physical performance, PDDS may serve as a practical alternative or complement to clinician-rated tools, particularly when clinical resources are limited.

012

Reliability and Validity of the Turkish Version of the Arm Function in Multiple Sclerosis Questionnaire (AMSQ)

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INTRODUCTION Upper extremity dysfunction is common in persons with multiple sclerosis (pwMS) and significantly impacts daily activities such as dressing and eating. However, it is often under-assessed, as clinical attention tends to focus on mobility issues. The Arm Function in Multiple Sclerosis Questionnaire (AMSQ) is a disease-specific patient-reported outcome measure (PROM) that captures patients' perceptions of upper limb function. Validating the Turkish version of the AMSQ allows its use in clinical and research settings in Türkiye, providing a patient-centred tool to complement objective assessments.

OBJECTIVES This study aimed to examine the reliability and validity of the Turkish version of the AMSQ in pwMS.

METHODS The AMSQ was translated and culturally adapted into Turkish under the supervision of an expert committee to ensure linguistic accuracy and cultural relevance. A total of 230 pwMS were included. To assess reliability, internal consistency was measured using Cronbach's alpha, and test-retest reliability was evaluated with intraclass correlation coefficients (ICCs). Construct validity was examined using exploratory factor analysis. For convergent and known-group validity, the AMSQ was compared with the Manual Ability Measure-36 (MAM-36), Multiple Sclerosis International Quality of Life Questionnaire (MusiQoL) and its activities of daily living (ADL) subscale, 9-Hole Peg Test (9HPT), Coin Rotation Task (CRT), Jamar handgrip dynamometer, Patient-Determined Disease Steps (PDSS), Expanded Disability Status Scale (EDSS), and Modified Ashworth Scale (MAS).

RESULTS The mean age of participants was 40.3 years (SD=11.3), and 70% were female. Most had relapsing-remitting MS (80%), with a mean EDSS score of 2.9 (SD=2.3). Internal consistency of the AMSQ was excellent (α=0.98), and test-retest reliability was high (ICC=0.96). Factor analysis supported a single-factor structure explaining 62.4% of the variance. High correlations were found with MAM-36 (ρ = -0.91) and the MusiQoL ADL subscale (ρ = -0.72), and moderate correlations with 9HPT, CRT, handgrip strength, and the MusiQoL. Known-group validity was supported by significantly higher AMSQ scores in participants with upper limb spasticity ($p<0.001$).

CONCLUSION The Turkish version of the AMSQ is a reliable and valid tool for evaluating upper extremity function in pwMS. It helps identify patient-reported upper limb limitations. Its use in rehabilitation can support personalised treatment planning, improve patient engagement, and track therapy outcomes. It also holds potential as an outcome measure in clinical trials targeting upper limb function in pwMS.

013

Fine Motor Impairment in Early-Phase Multiple Sclerosis Without Disability: A Comparison with Matched Healthy Controls

Turhan Kahraman, Gözde Deniz Ünal, Ozge Ertekin, Serkan Ozakbas

INTRODUCTION Early detection of functional impairments in multiple sclerosis (MS) is essential for timely intervention. While previous research has identified significant physical, cognitive, and patient-reported deficits in early-phase MS, the extent of upper limb dysfunction in patients with no measurable disability [Expanded Disability Status Scale (EDSS) 0] remains unclear.

OBJECTIVES This study aimed to assess upper limb function in people with early-phase MS (≤2 years from diagnosis) with no disability (EDSS = 0) compared to age- and sex-matched healthy controls (HC).

METHODS A cross-sectional study was conducted with 50 persons with MS and 50 HC. Upper limb function was evaluated using the Nine-Hole Peg Test (9HPT) for both dominant and non-dominant hands and handgrip strength using a Jamar dynamometer. The Mann-Whitney U test with rank biserial correlation was used to assess group differences.

RESULTS Persons with MS exhibited significantly slower performance on the dominant-hand 9HPT compared to HC, with people with MS being approximately 8% slower ($p = 0.019$, rank biserial correlation = 0.2736). No significant differences were observed in non-dominant 9HPT, total 9HPT time, or grip strength measurements ($p > 0.05$).

CONCLUSION Despite the absence of measurable disability, individuals with early-phase MS show subtle fine motor impairments in the dominant hand. These findings underscore the need for sensitive functional assessments in early MS, as upper limb dysfunction may develop before overt disability emerges.

014

Sex-Specific Challenges and Associated Factors in Upper Extremity Function in Persons with Multiple Sclerosis

Turhan Kahraman, Gözde Deniz Ünal, Ozge Ertekin, Serkan Ozakbas

INTRODUCTION Upper extremity dysfunction is common in persons with multiple sclerosis (pwMS), often leading to significant limitations in daily activities and reduced quality of life. Understanding the most challenging tasks, particularly with consideration of sex-specific differences, may guide the development of tailored rehabilitation strategies.

OBJECTIVES This study aimed to identify the most challenging upper extremity activities in persons with multiple sclerosis (pwMS) using the Manual Ability Measure-36 (MAM-36) and to explore the factors associated with these difficulties.

METHODS A total of 463 pwMS (333 females and 130 males) with an EDSS range from 0 to 7.5 participated in this study. Upper extremity function was evaluated using the MAM-36. Grip strength was measured with a Jamar Hydraulic Hand Dynamometer, and dexterity was assessed using the Nine-Hole Peg Test (NHPT). Frequencies of reported difficulty for each MAM-36 item were analysed, with scores of 0, 1, or 3 considered indicative of limitations in that activity. The three most challenging activities were identified based on response frequency. Sex-specific analyses explored differences in task difficulty and correlations with objective measures.

RESULTS In the overall cohort, the three most challenging upper extremity activities were carrying a shopping bag with a hand loop (11.1%), tying shoelaces (9.7%), and using a hammer or screwdriver (9.2%). When analysed by sex, different patterns emerged. Among males, the most difficult tasks were writing 3 to 4 sentences legibly (13.0%), tying shoelaces (11.6%), and cutting nails with a nail clipper (11.5%). In contrast, females most frequently reported difficulties with carrying a shopping bag with a hand loop (11.7%), wringing out a towel (9.3%), and using a hammer or screwdriver (9.0%). Chi-square analysis revealed that males experienced significantly greater impairments than females in five activities, particularly those involving fine motor skills. Correlation analyses further supported these differences, showing that in males, 13 activities demonstrated strong correlations with NHPT performance, whereas no strong correlations were identified in females. Similarly, most upper extremity activities in males were moderately correlated with grip strength, while such relationships were not observed in females.

CONCLUSION This study identifies the most challenging upper extremity activities in pwMS and underscores notable sex-specific differences. In males, difficulties were closely linked to impairments in fine motor control and grip strength, whereas in females, these factors played a less prominent role, suggesting that other mechanisms contribute to upper extremity limitations. These findings highlight the need for personalised, sex-specific rehabilitation strategies to optimise functional outcomes in pwMS. Future research should further investigate targeted interventions to address these distinct challenges.

015

Determinants of Walking Capacity in People With MS: The Role of Balance Confidence and Cognitive Function

Zuhal Abasiyanik, Gözde Deniz Ünal, İrem Kara, Serkan Ozakbas

INTRODUCTION Walking impairment is a common and disabling symptom in people with multiple sclerosis (pwMS), often influenced by a combination of physical, psychological, and cognitive factors. Understanding the relative contribution of these factors may guide targeted interventions to improve mobility outcomes.

OBJECTIVES To investigate the contribution of balance confidence, fatigue, depression, and cognitive function to walking capacity in pwMS with different levels of disability.

METHODS Walking capacity was assessed using the 6-Minute Walk Test (6MWT). Balance confidence was measured with the Activities-Specific Balance Confidence (ABC) Scale, fatigue with the Modified Fatigue Impact Scale (MFIS), and depression with the Beck Depression Inventory. Cognitive function was evaluated using the Symbol Digit Modalities Test (SDMT) for cognitive processing speed and the Brief Visuospatial Memory Test-Revised (BVMT-R) for visuospatial memory. Stepwise linear regression was conducted to examine the contribution of these factors to walking capacity.

RESULTS A total of 440 pwMS participated in the study, including 340 individuals with mild disability and 100 with moderate-to-severe disability. In the mild disability group, balance confidence (β = 0.44-0.51), cognitive processing speed (β = 0.14-0.21), and visuospatial memory (β = 0.12) together explained 30% of the variance in 6MWT performance, with balance confidence showing the strongest effect. In the moderate-to-severe group, balance confidence also significantly predicted walking performance (β = 0.35, $p < .001$), though it accounted for only 11% of the variance.

CONCLUSION Balance confidence was the strongest and most consistent predictor of walking capacity in pwMS, especially among those with mild disability. Cognitive processing speed and visuospatial memory added modest predictive value in the mild group but had limited influence in more disabled individuals, suggesting that physical limitations may play a larger role in walking performance in the later stages of the disease.

016

Validation of the Spinal Cord Injury-Falls Concern Scale in Wheelchair Users with Multiple Sclerosis

Zuhal Abasiyanik, Gözde Deniz Ünal, Turhan Kahraman, Ozge Ertekin, Serkan Ozakbas

INTRODUCTION Falls and fear of falling are significant concerns among people with multiple sclerosis (pwMS), particularly those with severe disability requiring wheelchair use. Despite the high relevance of fall-related concerns in this population, there is currently no validated tool specifically designed to assess these concerns in wheelchair users with MS. The Spinal Cord Injury-Falls Concern Scale (SCI-FCS), a validated instrument in individuals with spinal cord injury, may offer a promising option, but its applicability and psychometric properties in pwMS remain unexplored.

OBJECTIVES To adapt the SCI-FCS for use in pwMS who dependent on wheelchair and evaluate its psychometric properties.

METHODS Test-retest reliability was assessed using the intraclass correlation coefficient (ICC). The standard error of measurement (SEM) and smallest detectable change (SDC) were calculated. Convergent validity was evaluated through predefined hypotheses by correlating SCI-FCS scores with the number of falls, Barthel Index (BI), EuroQol (EQ-5D-5L), Modified Fatigue Impact Scale (MFIS), Beck Depression Inventory (BDI), and functional reach tests (forward and lateral).

RESULTS Thirty-one pwMS (mean age±SD: 54.5±11.2 years; 58% female) who were wheelchair-dependent participated. The SCI-FCS demonstrated excellent test-retest reliability (ICC=0.98; 95%CI: 0.96-0.99), with an SEM of 0.27 and an SDC of 0.75. As hypothesized, SCI-FCS scores showed strong correlations with number of falls (rho = 0.597), forward and side reach distance (rho=-0.757 and -0.743), BI (r=-0.750), and BDI (rho=0.561). Correlations with EQ-5D-5L subscales ranged from low to moderate (rho = -0.227 to -0.478). No significant correlation was found with MFIS.

CONCLUSION The Turkish version of the SCI-FCS is a valid and reliable instrument for assessing fall-related concerns in wheelchair users with MS. It demonstrates strong psychometric properties and can support clinical decision-making and fall-risk monitoring in this population.

017

Tracking Walking Capacity in People With Multiple Sclerosis Without Disability: 3-Year Follow-Up of Objective and Subjective Gait Measures

Zuhal Abasiyanik, Cavid Baba, Pinar Yigit, Ulvi Samadzade, Turhan Kahraman, Serkan Ozakbas

INTRODUCTION This study aimed to investigate longitudinal changes in walking performance over a three-year period in individuals with multiple sclerosis (pwMS) exhibiting no or mild disability.

OBJECTIVES A cohort of 321 pwMS (32.3 ± 9.8 years, 75% females, median EDSS 1.0) was followed for three years. Walking performance was assessed using the Timed 25-Foot Walk Test (T25FW), Six-Spot Step Test (SSST), 2-Minute Walk Test (2MWT), Timed Up and Go (TUG) test, and the Multiple Sclerosis Walking Scale-12 (MSWS-12). Leisure-time exercise behaviour was assessed using the Godin Leisure-time Exercise Questionnaire.

METHODS A cohort of 321 pwMS (32.3 ± 9.8 years, 75% females, median EDSS 1.0) was followed for three years. Walking performance was assessed using the Timed 25-Foot Walk Test (T25FW), Six-Spot Step Test (SSST), 2-Minute Walk Test (2MWT), Timed Up and Go (TUG) test, and the Multiple Sclerosis Walking Scale-12 (MSWS-12). Leisure-time exercise behaviour was assessed using the Godin Leisure-time Exercise Questionnaire.

RESULTS No significant changes in walking performance were observed over the three-year period. The median T25FW duration remained stable (4.8 s to 4.7 s, $p = 0.3$), and similarly, the SSST time did not show significant change (7.7 s to 7.2 s, $p = 0.517$). No significant change was observed in the 2MWT distance (171 m to 174 m, $p = 0.178$) or TUG time (6.8 s to 6.9 s, $p = 0.831$). Self-reported walking disability (MSWS-12) and leisure-time physical activity also remained unchanged ($p = 0.692$ and $p = 0.394$, respectively).

CONCLUSION This study demonstrated that pwMS with no or minimal disability maintain stable walking performance over a three-year period. This stability may reflect functional reserve and lifestyle factors, allowing preservation of mobility despite disease progression. Future research should include more complex gait analyses and consider additional lifestyle factors.

018

High Prevalence of Falls and Near-Falls in Mild Multiple Sclerosis: A Hidden Clinical Concern

Zuhal Abasiyanik, Gözde Deniz Ünal, Ela Zengin, Serkan Ozakbas

INTRODUCTION Falls are a well-recognized concern in persons with multiple sclerosis (pwMS), with prevalence and risk factors studied across various disability levels. However, near-falls have received comparatively little attention, especially among pwMS with mild disability who are often not considered at high risk for falling.

OBJECTIVES To investigate the prevalence and characteristics of both falls and near-falls in pwMS with mild disability and to identify potential contributing factors.

METHODS This cross-sectional study included pwMS with mild disability, defined as having an Expanded Disability Status Scale (EDSS) score of 3.0 or below. Participants were asked to report any falls and near-falls in the past six months, including associated injuries and contextual details such as location and activity during the event. Clinical assessments included static balance measured by the One Leg StanceTest, balance confidence assessed via the Activities-specific Balance Confidence (ABC) Scale, walking speed and endurance using the Timed 25-Foot Walk (T25FW) and 2-Minute Walk Test (2MWT), and cognitive processing speed via the Symbol Digit Modalities Test (SDMT).

RESULTS A total of 212 individuals with mild MS were included in the study. Over the previous six months, 26% reported at least one fall and 42% reported experiencing at least one near-fall. Most incidents occurred during ordinary daily activities such as walking indoors or outdoors, cleaning, or going up or down stairs. The primary self-reported causes of falls were loss of balance while walking (41%), tripping (41%), and slipping (18%). Near-falls were similarly attributed to balance loss (45%), tripping (38%), and slipping (17%). Fallers demonstrated significantly lower performance in walking speed, SDMT, and the 2MWT. However, there were no significant differences between non-fallers and near-fallers on these same measures. Likewise, balance confidence and static balance performance were comparable across all groups.

CONCLUSION Falls and near-falls are surprisingly common even among pwMS with mild disability, a group traditionally viewed as low risk. Importantly, while fallers showed measurable impairments in motor and cognitive functions, near-fallers performed similarly to non-fallers in clinical assessments. This suggests that near-falls may precede detectable functional decline and serve as an early warning sign of instability. Given their frequency and their occurrence during ordinary activities, routine screening for near-falls - alongside traditional fall assessments - may enable earlier identification of individuals at risk. In this cohort, where one in four had fallen and nearly half had experienced a near-fall, these seemingly subtle events may represent the first signal of a shift in dynamic stability, calling for proactive prevention even in patients with only mild clinical disability.

019

Cognitive Stability Over Three Years Despite Loss of Ambulation in Progressive Multiple Sclerosis with Preserved Upper Limb Function

Ulvi Samadzade, Gözde Deniz Ünal, Can Caliskan, Esra Aydın, Serkan Ozakbas

INTRODUCTION Progressive forms of multiple sclerosis (MS) are frequently associated with accumulating physical disability, particularly loss of ambulation. However, the relationship between advanced motor impairment and cognitive decline remains incompletely understood.

OBJECTIVES This study aimed to examine longitudinal changes in cognitive performance over a three-year period in patients with progressive MS who had lost ambulatory function but retained upper extremity capabilities.

METHODS Sixty-six patients with either primary progressive (PPMS) or secondary progressive MS (SPMS), all of whom were non-ambulant yet had preserved upper limb function, were included in this longitudinal study. Cognitive function was assessed at baseline and after three years using the Symbol Digit Modalities Test (SDMT), the California Verbal Learning Test (CVLT), and the Brief Visuospatial Memory Test (BVMT). Paired comparisons were used to evaluate changes over time, and subgroup analyses were conducted between PPMS and SPMS patients.

RESULTS Cognitive performance remained stable or improved across all domains. Mean SDMT scores increased from 29.09 (±14.70) to 30.95 (±14.27), CVLT scores from 37.17 (±15.18) to 54.33 (±45.70), and BVMT scores from 16.34 (±8.65) to 19.84 (±7.73). Only a small proportion of patients showed cognitive decline: 8.1% in SDMT, 7.5% in CVLT, and 16.7% in BVMT. SPMS patients demonstrated significantly better SDMT performance at follow-up compared to those with PPMS ($p = 0.043$).

CONCLUSION In patients with progressive MS who are no longer ambulant but retain upper limb function, cognitive abilities - particularly processing speed, attention, and verbal memory - were largely preserved over a three-year period. These findings suggest that severe motor impairment does not inevitably lead to cognitive decline. Notably, patients with secondary progressive MS performed better than those with primary progressive MS in cognitive assessments, which may reflect underlying differences in disease mechanisms. The greater cognitive involvement observed in PPMS may be related to cortical pathology, which remains less well characterized in this MS subtype. This highlights the need for more advanced imaging and biomarker studies in PPMS to better understand the neurobiological basis of cognitive decline. Overall, the results support the routine assessment of cognition in non-ambulant patients and underscore the value of preserving upper limb function to enable cognitive rehabilitation and engagement strategies aimed at maintaining quality of life.

020

Enhancing Fine Motor Assessment: The 9HPT-Extended as a Superior Alternative to the Standard 9HPT

Gözde Deniz Ünal, Esra Aydın, Can Caliskan, Ulvi Samadzade, Asiye Tuba Ozdogar, Turhan Kahraman, Serkan Ozakbas

INTRODUCTION The 9-Hole Peg Test (9HPT) is a standard tool for assessing fine motor function, especially in neurological conditions like multiple sclerosis (MS). Despite its widespread use, concerns exist regarding its sensitivity and reliability in detecting subtle impairments. To overcome these limitations, the 9HPT-Extended was developed, aiming to improve measurement precision, consistency, and clinical utility. This study investigates whether the 9HPT-Extended outperforms the standard 9HPT and supports its adoption in clinical and research contexts.

OBJECTIVES This study compares the 9HPT-Extended with the standard 9HPT to evaluate improvements in reliability, sensitivity, and clinical relevance. It further explores the tool's ability to reflect disease progression and differentiate between patient groups more effectively.

METHODS A total of 500 individuals with MS and 66 healthy controls completed both the standard and extended versions of the 9HPT. While the standard version includes two trials per hand (four total), the 9HPT-Extended comprises three trials per hand (six total), with the average time used as the final score. Standardized conditions minimized external influences. Statistical analyses included t-tests, Levene's test, effect size calculations (Cohen's d), and Pearson's correlations with clinical measures such as EDSS and MAM-36. Analyses were conducted in SPSS 26.0, with significance set at $p < 0.05$.

RESULTS The 9HPT-Extended demonstrated significantly superior reliability, sensitivity, and clinical relevance compared to the standard 9HPT. It yielded lower variance (22.941 vs. 25.676) and standard deviation (4.79 vs. 5.07), indicating enhanced measurement stability. It was more effective in distinguishing between groups, as evidenced by a higher t-value ($t = 5.432$, $p < 0.001$) and a greater effect size ($d = 0.52$ vs. $d = 0.50$). Furthermore, the 9HPT-Extended showed stronger correlations with key clinical variables, including disease duration ($r = 0.394$) and functional ability as measured by the MAM-36 ($r = 0.374$), indicating its superior capacity to capture disease progression and real-life motor impairment. Levene's test further confirmed its greater stability in variance. Importantly, these advantages were consistent even among healthy controls, reinforcing the test's robustness across populations.

CONCLUSION The 9HPT-Extended shows superior reliability, reduced variability, and stronger correlations with clinical markers compared to the standard 9HPT. Its enhanced performance in detecting motor impairments and reflecting disease status supports its use as a new standard in neurological assessment, promising better patient evaluation and treatment guidance.

021

Fine Motor Function as a Potential Indicator of Cognitive Status in Multiple Sclerosis: A Cross-Sectional Study

Gözde Deniz Ünal, Can Caliskan, İrem Kara, Esra Aydın, Nurbanu Yapıcı, Serkan Ozakbas

INTRODUCTION Cognitive dysfunction in MS is often assessed with the BICAMS battery. The 9-Hole Peg Test (9HPT) is a measurement tool that assesses fine motor function and coordination in MS. The 9-Hole Peg Test (9HPT) is a well-established measure of fine motor function and coordination in MS. Slower performance on the 9HPT is associated with increased disability and disease progression.

OBJECTIVES The aim of this study was to investigate the relationship between motor skills and cognitive performance in patients with Multiple Sclerosis (MS). Specifically, it examined how motor function assessed with the 9-Hole Peg Test (9HPT) relates to cognitive performance measured with the BICAMS battery.

METHODS A total of 1,077 MS patients participated in the study. They were divided into two groups based on their 9HPT performance: those who completed the test in less than 18 seconds (n = 191) and those who completed the test in 18 seconds or more (n = 886). Cognitive performance was assessed using the SDMT, CVLT-II, and BVMT-R. Additionally, disability was assessed using the Expanded Disability Status Scale (EDSS), and disease duration was recorded. Independent samples t-tests were used to compare cognitive test scores, EDSS scores, and disease duration between the two groups.

RESULTS SDMT scores were significantly higher in the faster motor performance group ($t(316.52) = 9.203$, $p < .001$). The mean SDMT score in the faster group was 58.32 ± 12.07 and in the slower group was 49.15 ± 14.32, representing a medium effect size (Cohen's $d = 0.658$). CVLT-II scores were also significantly higher in the faster group ($t(321.26) = 3.571$, $p < .001$), with mean scores of 60.40 ± 10.92 and 57.17 ± 13.18, respectively, representing a small effect size (Cohen's $d = 0.253$). BVMT-R scores followed a similar pattern ($t(317.98) = 3.998$, $p < .001$), with mean scores of 29.23 ± 6.22 and 27.17 ± 7.42, respectively, and a small effect size (Cohen's $d = 0.285$). EDSS scores were significantly lower in the faster motor performance group ($t(769.31) = -12.08$, $p < .001$), indicating a lower level of disability (mean EDSS = 0.31 ± 0.72 vs. 1.29 ± 1.82) and a moderate negative effect size (Cohen's $d = -0.581$). In addition, illness duration was significantly shorter in the faster group ($t(476.49) = -5.471$, $p < .001$).

CONCLUSION MS patients with better motor performance exhibit higher cognitive performance on attention, verbal memory, and visuospatial memory tasks. In addition, longer disease duration and higher disability levels (EDSS scores) were associated with poorer motor and cognitive performance. These findings highlight the importance of a comprehensive assessment of both motor and cognitive functions in MS patients, as motor function impairments may be an indicator of cognitive decline. Future research should investigate potential rehabilitation strategies that target both motor and cognitive functions to improve overall patient outcomes.

022

Nine-Hole Peg Test-Extended as a Predictor of Cognitive Performance in Multiple Sclerosis: Uncovering the Link Between Motor and Cognitive Function

Gözde Deniz Ünal, Can Caliskan, İrem Kara, Esra Aydın, Nurbanu Yapıcı, Serkan Ozakbas

INTRODUCTION Cognitive impairment is a common problem in multiple sclerosis (MS). The Nine-Hole Peg Test (9HPT) is a widely used tool to assess fine motor skills and manual dexterity in MS patients. A modified version, the Nine-Hole Peg Test-Extended (9HPT-Extended), includes three repetitions per hand and has been proposed as a more comprehensive measure of motor function. Given that motor performance may be related to cognitive performance, this study aimed to investigate whether the 9HPT-Extended may serve as a predictor of cognitive function in MS patients.

OBJECTIVES The objective of this study is to assess the relationship between motor performance, as measured by the Nine-Hole Peg Test-Extended, and cognitive performance in individuals with MS. The study investigates whether 9HPT-Extended scores can provide valuable insights into cognitive function, potentially enhancing the understanding of motor-cognitive relationships in MS.

METHODS This study analyzed data from 482 MS patients with a mean age of 38.86 years (±12.22) and a mean disease duration of 8.44 years (±7.27). Participants completed various motor and cognitive assessments, including the Nine-Hole Peg Test, Nine-Hole Peg Test-Extended, Jamar dynamometry, MAM-36, and BICAMS battery. Patients were divided into two groups according to their 9HPT-Extended performance: those with better motor performance and those with poorer motor performance. Cognitive scores were compared between these groups, and Pearson correlation analysis was performed to investigate relationships between motor and cognitive measures. Logistic regression analysis was used for cognitive performance.

RESULTS The results showed significant differences between the “good” and “poor” cognitive performance groups, with the former showing younger age, shorter disease duration, earlier disease onset, and lower EDSS scores ($p < 0.001$). Nine-Hole Peg Test-Extended scores were significantly higher in the “good” cognitive performance group ($p < 0.001$), suggesting that motor performance may be linked to better cognitive outcomes. BICAMS scores were significantly higher in the “good” group ($p < 0.01$). In particular, the correlation between the 9HPT-Extended and cognitive scores was strong, with the 9HPT-Extended showing significant negative correlations with measures such as the BICAMS battery and the MAM-36 ($p < 0.05$). An almost perfect correlation was observed between the original 9HPT and the 9HPT-Extended ($p < 0.01$).

CONCLUSION This study highlights the potential of the Nine-Hole Peg Test-Extended as a predictor of cognitive performance in MS patients. The strong association between motor performance and cognitive function emphasizes the importance of considering both domains in MS assessment. These findings suggest that the 9HPT-Extended could be an important tool in identifying cognitive impairment in MS and may serve as a useful measure for future clinical and research applications.

023

Turning-Based Gait Assessment Better Predicts Self-Perceived Mobility and Balance Confidence Than Traditional Straight-Line Walk Tests in Individuals with Multiple Sclerosis

Gözde Deniz Ünal, Can Caliskan, Esra Aydın, Asiye Tuba Ozdogar, Turhan Kahraman, Serkan Ozakbas

INTRODUCTION Walking impairment is among the most disabling symptoms in individuals with multiple sclerosis (MS). Although widely used, conventional walking assessments such as the Timed 25-Foot Walk Test (T25FW-T) focus primarily on straight-line walking and may not reflect the complexities of everyday mobility. Real-world ambulation typically involves frequent changes in direction, turns, and continuous dynamic movement. To better capture this complexity, this study introduces a turning-based walking metric that reflects the average time needed to walk continuously back and forth over a 7.62-meter course, incorporating directional transitions that mimic daily activities.

OBJECTIVES This study aimed to compare the clinical utility of turning performance versus T25FW-T in predicting perceived mobility limitations and balance confidence in people with MS. Self-reported outcomes were measured using the Modified Multiple Sclerosis Walking Scale (MSWS) and the Activities-specific Balance Confidence (ABC) scale. It was hypothesized that turning performance would show stronger associations with both self-reported outcomes due to its greater ecological validity

METHODS This cross-sectional study included individuals with MS who underwent standardized assessments of gait and completed self-report questionnaires. Two objective walking measures were evaluated: T25FW-T (a straight-line walking test) and turning performance (continuous back-and-forth walking over 7.62 meters). Pearson correlations and multiple linear regression analyses were conducted to examine associations between gait metrics and perceived mobility (MSWS) and balance confidence (ABC).

RESULTS The final sample included 381 individuals with MS; 346 completed the MSWS, and 343 completed the ABC scale. Turning performance was significantly associated with both outcome measures - positively with MSWS (indicating greater perceived disability) and negatively with ABC (indicating lower balance confidence). Regression analyses revealed that turning performance was a significant predictor of both perceived mobility and balance confidence, whereas T25FW-T was not. Effect size calculations supported the superior predictive utility of turning performance over T25FW-T.

CONCLUSION These findings highlight turning performance as a stronger and more ecologically valid indicator of functional mobility and balance confidence in individuals with MS than traditional straight-line walking tests. Unlike T25FW-T, turning-based assessments better approximate real-world ambulation, where directional changes and dynamic movement are constant. Integrating turning metrics into clinical gait evaluations may enhance the sensitivity of assessments and guide more individualized rehabilitation strategies that reflect the everyday functional challenges faced by people with MS.

024

The 6-Minute Threshold: Tracking Three-Year Disability and Cognition in Multiple Sclerosis

Gözde Deniz Ünal, Can Caliskan, Ela Zengin, Serkan Ozakbas

INTRODUCTION This study examined whether baseline performance on the 6-Minute Walk Test (6MWT) can predict long-term motor and cognitive outcomes in people with multiple sclerosis (PwMS). By using a 446-meter threshold, we aimed to assess the clinical utility of this cutoff through a three-year follow-up of physical and cognitive tests.

OBJECTIVES To investigate whether the 6-Minute Walk Test (6MWT) threshold of 446 meters can serve as a predictive marker for long-term motor and cognitive outcomes in PwMS, and to determine the clinical relevance of this cutoff by comparing demographic, clinical, and functional characteristics between stratified groups over a three-year follow-up period

METHODS A total of 402 PwMS were classified into two groups based on their 6MWT performance: above (n = 282) and below (n = 120) the 446-meter cutoff. This threshold was derived from associations with PDDS, EDSS, and MSWS-12 scores. Assessments included EDSS, T25FW, 9HPT, SDMT, CVLT-II, and BVMT-R at baseline and three years later. General Linear Model (GLM) and correlation analyses were performed

RESULTS The above-446 group predominantly included RRMS (99.3%), whereas the below-446 group had a higher frequency of SPMS (22.8%) and PPMS (6.9%). Baseline EDSS scores were significantly lower in the above-446 group (1.13 ± 0.97) than in the below-446 group (3.15 ± 2.00). Motor and cognitive test scores were significantly higher in the above-446 group at both timepoints ($p < 0.001$). Over time, greater declines in 9HPT, T25FW, SDMT, CVLT-II, and BVMT-R were observed in the below-446 group. GLM showed significant time effects and group differences in all outcome measures. Baseline EDSS positively correlated with age ($r = 0.493$), disease duration ($r = 0.461$), and MS subtype ($r = 0.624$), while cognitive scores negatively correlated with age. Initial test performance was predictive of subsequent deterioration

CONCLUSION The 446-meter threshold on the 6MWT serves as a practical marker for disease stratification in MS. Walking less than 446 meters at baseline was linked to worse physical and cognitive profiles and greater decline over three years. These results support the integration of functional thresholds like the 6MWT into clinical decision-making to better predict disease trajectory, personalize care, and optimize long-term monitoring in PwMS

025

Earlier Decline in Upper Limb Function Than Gait in Multiple Sclerosis: A Five-Year Longitudinal Study

Gözde Deniz Ünal, Ulvi Samadzade, Esra Aydın, Can Caliskan, Serkan Ozakbas

INTRODUCTION This study aimed to compare the timing of functional decline in two commonly used performance tests in individuals with multiple sclerosis (MS): the Nine-Hole Peg Test (9HPT) for upper extremity function and the Timed 25-Foot Walk Test (T25FW) for lower extremity function. Using five-year longitudinal data, we investigated which domain tends to show earlier deterioration.

OBJECTIVES The aim of this study was to determine which functional domain - upper or lower extremity - exhibits earlier deterioration in individuals with multiple sclerosis (MS) over a five-year period. Specifically, the study sought to compare the timing of clinically meaningful decline between the Nine-Hole Peg Test (9HPT) and the Timed 25-Foot Walk Test (T25FW), and to assess the relationship between the progression of impairments in these two motor domains.

METHODS This retrospective study included annual clinical assessments over a five-year period. Upper extremity function was measured using the 9HPT, and lower extremity function with the T25FW. The “year of deterioration” was defined as the first year a clinically meaningful decline was observed in test performance. Pearson correlation analysis was used to assess the association between deterioration timings in both tests. A paired-samples t-test compared the mean years of decline, and effect sizes were calculated using Cohen’s d and Hedges’ g.

RESULTS A total of 232 MS patients (mean age: 44.00 ± 11.00; mean EDSS: 1.54 ± 1.74) were included, of whom 63% were female. The majority (87%) had relapsing-remitting MS (RRMS), while the remaining 13% had either secondary progressive (SPMS) or primary progressive MS (PPMS). The mean year of functional decline was 2.31 for the 9HPT and 2.89 for the T25FW, indicating that upper extremity function deteriorated earlier. This difference was statistically significant ($t = -2.14$, $p = 0.037$). A moderate and significant positive correlation was observed between the deterioration years of the two tests ($r = 0.512$, $p < 0.001$). Effect sizes were small (Cohen’s $d = 0.091$; Hedges’ $g = 0.091$).

CONCLUSION This five-year longitudinal study suggests that upper extremity function, as assessed by the 9HPT, tends to decline earlier than lower extremity function in individuals with MS. These findings highlight the need for routine monitoring of hand and arm performance - not just ambulation - in clinical practice. Earlier identification of upper limb dysfunction may provide an opportunity for timely interventions aimed at preserving fine motor skills and promoting independence in daily activities.

026

Earlier Decline in Upper Limb Function Than Gait in Multiple Sclerosis: A Five-Year Longitudinal Study

Gözde Deniz Ünal, Can Caliskan, Ulvi Samadzade, Serkan Ozakbas

INTRODUCTION Accurate assessment of motor function is essential in the management of multiple sclerosis (MS). While clinician-administered scales such as the Expanded Disability Status Scale (EDSS) are widely used, patient-reported outcome measures like the Patient Determined Disease Steps (PDDS) offer advantages in terms of speed and accessibility. However, the degree to which PDDS correlates with objective performance-based tests, such as the Timed Up and Go (TUG), remains to be fully elucidated.

OBJECTIVES This study explores the extent of agreement between these instruments and investigates whether PDDS can reliably reflect motor performance.

METHODS A cohort of individuals diagnosed with MS participated in this cross-sectional study. Each participant's disability level was assessed using the PDDS and EDSS. Motor performance was evaluated using the TUG test. Pearson correlation analysis was used to examine associations between PDDS, EDSS, and TUG scores. Paired samples t-tests were applied to assess mean differences, and effect sizes were calculated using Cohen's d. Friedman's test followed by Bonferroni-adjusted pairwise comparisons was conducted to evaluate overall differences among the three metrics.

RESULTS A total of 207 pwMS (151 females, 56 males) were included in the study, with EDSS scores ranging from 0 to 6.5. The mean age of the participants was 45.00 ± 12.00 years and 91% of this group had Relapsing-Remitting MS (RRMS) subtype. A statistically significant, moderate positive correlation was observed between PDDS and TUG duration ($r = 0.241$, $p = .005$). The mean difference in TUG scores associated with PDDS levels was -8.08 seconds ($t = -62.144$, $p < .001$), corresponding to a large effect size (Cohen's $d = -5.309$). A stronger correlation was found between EDSS and TUG ($r = 0.442$, $p < .001$), with a mean difference of -7.82 seconds ($p < .001$, $d = -5.458$). Friedman's test indicated significant differences among PDDS, EDSS, and TUG measures ($\chi 2 = 702.938$, $p < .001$). Pairwise comparisons revealed a significant difference between PDDS and TUG, but not between PDDS and EDSS ($p = 1.000$).

CONCLUSION The PDDS scale demonstrates a high degree of concordance with motor performance as measured by the TUG test, supporting its validity as a rapid and user-friendly tool for assessing physical function in MS patients. Its alignment with both objective and clinician-rated measures underscores its potential utility in both clinical and research contexts.

027

When Perceived Disability Reflects Real-World Performance: A Walking Function Comparison in People with Multiple Sclerosis

Gözde Deniz Ünal, Can Caliskan, Esra Aydın, Ulvi Samadzade, Serkan Ozakbas

INTRODUCTION Multiple sclerosis (MS) is a chronic, progressive neurological disease that often leads to impairments in mobility and walking ability. Evaluating functional status in MS requires both objective assessments and self-reported measures to capture the full impact of the disease on daily life. The Patient-Determined Disease Steps (PDDS) is a simple, self-rated scale that strongly correlates with clinician-rated disability and has been widely used in research and clinical settings. However, the extent to which PDDS reflects actual walking performance has not been fully explored. This study investigates whether higher self-perceived disability, as indicated by PDDS scores, is aligned with real-world reductions in walking function.

OBJECTIVES To compare objective walking performance in individuals with MS grouped by their PDDS scores, and to evaluate whether self-reported disability levels predict measurable mobility limitations.

METHODS A total of 222 individuals with MS participated in this cross-sectional study. Participants were classified into two groups based on their PDDS scores: minimal disability (PDDS ≤ 2, n = 191) and higher perceived disability (PDDS > 2, n = 31). Walking ability was evaluated using three validated clinical tools: the Multiple Sclerosis Walking Scale (MSWS), the Two-Minute Walk Test (2MWT), and the Six-Minute Walk Test (6MWT). Group comparisons were conducted using independent samples t-tests. Descriptive statistics were also calculated for EDSS, MSWS, 2MWT, and 6MWT

RESULTS Participants with higher PDDS scores showed significantly worse outcomes on all walking assessments. The MSWS score was significantly elevated in the higher-disability group (mean = 23.71, SD = 13.90) compared to the minimal-disability group (mean = 14.74, SD = 4.28), $t(220) = -7.132$, $p < .001$. In the 2MWT, participants with minimal disability walked 179.64 meters (SD = 22.10), while those with greater disability walked 126.35 meters (SD = 68.56), $t(220) = 8.442$, $p < .001$. Similarly, 6MWT results showed significantly shorter distances in the higher PDDS group (298.10 meters, SD = 175.92) compared to the minimal group (446.47 meters, SD = 99.12), $t(208) = 6.722$, $p < .001$. The overall sample had a mean EDSS of 0.81 (SD = 1.30) and PDDS of 0.58 (SD = 1.17). No missing data were reported

CONCLUSION This study demonstrates a strong concordance between self-perceived disability (PDDS) and objectively measured walking performance. Even slight increases in PDDS scores were associated with substantial reductions in walking capacity. These findings support the clinical utility of PDDS as a meaningful indicator of real-world functional limitations and highlight the value of combining self-reported and performance-based measures in the routine monitoring of MS patients.

028

The Relationship Between Motor and Cognitive Performance in Multiple Sclerosis Patients

Gözde Deniz Ünal, Can Caliskan, Esra Aydın, Nurbanu Yapıcı, Ulvi Samadzade, Serkan Ozakbas

INTRODUCTION Cognitive impairment in Multiple Sclerosis (MS) frequently affects processing speed, attention, executive functions, and memory. The Symbol Digit Modalities Test (SDMT) is a validated measure of cognitive processing speed, while the California Verbal Learning Test - Second Edition-II (CVLT-II) and Brief Visuospatial Memory Test (BVMT) assess verbal and visuospatial memory. The 9-Hole Peg Test (9HPT) is a sensitive tool for evaluating fine motor function and upper limb coordination. Slower performance on the 9HPT is associated with increased disability and disease progression.

OBJECTIVES To examine the relationship between motor performance and cognitive functioning in MS patients using objective neuropsychological and motor assessment tools.

METHODS Participants were grouped based on their 9HPT performance: fast group (<18 seconds) and slow group (≥18 seconds). Cognitive function was assessed via SDMT (processing speed and attention), CVLT-II (verbal memory), and BVMT (visuospatial memory). Disability was measured using the Expanded Disability Status Scale (EDSS), and disease duration was recorded. Between-group comparisons were conducted using independent samples t-tests.

RESULTS A total of 1,077 MS patients were included. SDMT scores were significantly higher in the fast motor performance group (58.32 ± 12.07 vs. 49.15 ± 14.32; p<.001, Cohen's d=0.658). CVLT-II scores (60.40 ± 10.92 vs. 57.17 ± 13.18; p<.001, d=0.253) and BVMT scores (29.23 ± 6.22 vs. 27.17 ± 7.42; p<.001, d=0.285) were also significantly higher, although with smaller effect sizes. EDSS scores were significantly lower in the fast group (0.31 ± 0.72 vs. 1.29 ± 1.82; p<.001, d=−0.581), indicating lower disability. Disease duration was shorter in the fast group (6.38 ± 4.45 vs. 8.65 ± 7.75 years; p<.001, d=−0.311).

CONCLUSION Better motor performance is associated with better cognitive outcomes in MS, particularly in processing speed, verbal memory, and visuospatial memory. Furthermore, higher EDSS scores and longer disease duration are linked to poorer cognitive and motor performance. These results suggest that motor assessments like the 9HPT may be useful indicators of cognitive decline in MS. Comprehensive monitoring and rehabilitation strategies targeting both motor and cognitive domains may enhance clinical outcomes in this population.

SECTION III

Pain, Personality and Quality of Life

5 ABSTRACTS

029

Impact of Chronic Pain on Cognitive Reserve in Multiple Sclerosis

Asiye Tuba Özdoğar, Turhan Kahraman, Said Alizada, Pervin, Serkan Ozakbas

INTRODUCTION Chronic pain in people with multiple sclerosis is associated with worse mental health and cognitive impairment, which can be both a cause and a consequence of brain structure and function alterations, such as maladaptive plasticity and dysregulation of the antinociceptive system. Cognitive reserve, which reflects the efficiency of internal brain connections, is a protective factor in multiple sclerosis (MS), potentially mitigating cognitive decline and reducing the risk of mental health disorders.

OBJECTIVES The current study explored the impact of chronic pain on psychosocial factors, mental health, and cognition in people with MS (pwMS).

METHODS This cross-sectional study involved a total of 131 pwMS. The PainDETECT Questionnaire (PD-Q) was used to differentiate between nociceptive and neuropathic pain. The scores ≤ 12 were considered as the presence of musculoskeletal pain,>12 as neuropathic pain, and zero as non-presence of pain. The Brief International Cognitive Assessment in Multiple Sclerosis (BICAMS) battery includes three subtests: Symbol Digit Modalities Test (SDMT), California Verbal Learning Test-II (CVLT-II), and Brief Visuospatial Memory Test-Revised (BVMT-R) was used to assess cognitive functions. Cognitive reserve level was assessed using the Cognitive Reserve Index Questionnaire (CRIq). Information such as Expanded Disability Status Scale (EDSS), disease duration and age of the participants were also recorded.

RESULTS The 131 participants included in the study were divided into three groups: 49 without pain (NP), 60 with Musculoskeletal Pain (MSP) and 22 with Neuropathic Pain (NP). There was no difference between the groups regarding age, disease duration and EDSS scores ($p>0.05$). There were no significant differences between groups regarding CRIq-education, CRIq-leisure time activities, CRIq-total score, and all three subtests of the BICAMS battery ($p>0.05$). However, there was a significant difference regarding CRIq-working activity. As a result of post-hoc analysis, there was a difference between MSP (95.73±8.56) and without pain (100.24±12.17) groups for CRIq-working activity.

CONCLUSION This study suggests that while chronic pain in pwMS does not significantly impact overall cognitive reserve or cognitive performance as measured by the BICAMS battery, it may influence specific aspects of cognitive reserve, particularly work-related cognitive activities. The observed differences in CRIq-working activity between pwMS with musculoskeletal pain and those without pain highlight the potential role of pain in shaping cognitive engagement in occupational settings. Further research is needed to explore the mechanisms underlying this association and to develop targeted interventions to support cognitive function in pwMS experiencing chronic pain.

030

The Role of Personality Traits in Disease Course, Cognition, and Mental Health in Multiple Sclerosis

Özge Sağıcı, Asiye Tuba Özdoğar, Taha Aslan, Serkan Ozakbas

INTRODUCTION Personality plays a crucial role in explaining individual differences in disease acceptance, coping strategies, and psychological well-being. It also influences the functional outcomes of brain diseases. Personality is commonly defined as a stable set of thoughts, feelings, and behaviors that differentiate individuals and persist over time and across situations. The term "personality trait" refers to enduring personal characteristics that predict behavior. Many studies have used personality traits to understand patients' responses to illness-related challenges. Since personality changes and personality disorders are frequently observed in multiple sclerosis (MS), personality may play a role in disease progression and outcomes.

OBJECTIVES The aim of this study is to investigate the relationship between personality traits, disease characteristics, and their effects on cognitive, physical, and psychosocial factors in people with MS (pwMS).

METHODS One hundred two pwMS were enrolled in this study. Demographic and clinical characteristics were recorded. The Revised Eysenck Personality Questionnaire-Abbreviated Form (EPQR-A) was used to measure personality dimensions, including four subscales: extraversion, neuroticism, psychoticism, and the lie scale. Anxiety and depression levels, quality of life, and neuropsychological symptoms were measured using the Hospital Anxiety and Depression Scale (HADS), the EuroQol-5D Quality of Life Scale (EQ-5D), and the Multiple Sclerosis Neuropsychological Questionnaire (MSNQ), respectively.

RESULTS There was no significant correlation between the extraversion, psychoticism, and lie subscales of the EPQR-A and EDSS, number of relapses, disease duration, HADS, EQ-5D, and MSNQ ($p>0.05$). While there was no relationship between the neuroticism subscale of the EPQR-A and disease-related measures such as EDSS, disease duration, and number of relapses, neuroticism was found to be associated with EQ-5D mobility ($r=-.273$, $p=0.007$), usual activity ($r=-.286$, $p=0.005$), pain ($r=-.556$, $p<0.001$) and health subscales ($r=-.287$, $p=0.005$), MSNQ ($r=.478$, $p<0.001$), HADS-anxiety ($r=-.577$, $p<0.001$), and HADS-depression ($r=.414$, $p<0.001$).

CONCLUSION This study highlights the significant relationship between personality traits, particularly neuroticism, and various aspects of disease impact in pwMS. While no strong associations were found between extraversion, psychoticism, and lie subscales and clinical and psychological factors, neuroticism showed a clear connection with reduced quality of life, increased neuropsychological symptoms, and higher anxiety and depression levels. These findings emphasize the role of personality traits in shaping the experiences and outcomes of individuals with MS, suggesting that psychological interventions targeting neuroticism-related vulnerabilities may improve overall well-being and disease management.

031

Personality Traits Shape Emotional Well-being, Quality of Life, and Treatment Persistence in Multiple Sclerosis

İrem Kara, Gözde Deniz Ünal, Serkan Ozakbas

INTRODUCTION Personality traits have been increasingly recognized as factors influencing quality of life, mood, and treatment adherence in people with multiple sclerosis (pwMS). However, few studies have comprehensively examined how Big Five personality dimensions, as assessed by the NEO Five-Factor Inventory (NEO-FFI), relate to patient-reported outcomes and medication discontinuation in MS.

OBJECTIVES To investigate the relationship between personality traits and clinical-relevant outcomes such as health-related quality of life, anxiety and depression, and reasons for treatment discontinuation in a sample of patients with MS.

METHODS This cross-sectional study evaluated five personality traits - Neuroticism, Extraversion, Openness, Agreeableness, and Conscientiousness - using the NEO Five-Factor Inventory. Participants also completed the EQ-5D and Hospital Anxiety and Depression Scale (HADS). Medication discontinuation history and reasons were retrospectively assessed. Relationships between personality traits and clinical variables were analyzed using correlation analyses and hierarchical regression models. Associations between personality profiles and reported discontinuation reasons were explored via chi-square tests.

RESULTS Seventy pwMS (mean age: 37.1 ± 8.2 years; 74.3% female; EDSS < 4.5) completed all assessments. Higher neuroticism scores were significantly associated with greater anxiety ($r = 0.54$, $p < 0.001$), greater depression ($r = 0.48$, $p < 0.001$), and lower EQ-5D index scores ($r = -0.41$, $p = 0.002$). Conscientiousness was positively correlated with EQ-5D scores ($r = 0.36$, $p = 0.004$) and negatively with HADS-depression scores ($r = -0.32$, $p = 0.01$). The most frequently reported reason for treatment discontinuation among patients with higher neuroticism, lower conscientiousness, and lower agreeableness was “patient choice/convenience” ($\chi 2 = 8.2$, $p = 0.017$).

CONCLUSION This study demonstrates that specific personality traits, particularly higher neuroticism and lower conscientiousness and agreeableness, are significantly associated with increased emotional distress, lower quality of life, and a greater likelihood of treatment discontinuation based on patient-driven factors. These findings suggest that personality dimensions, as assessed by the NEO-FFI, may serve as clinically relevant indicators of psychological vulnerability and medication persistence in people with multiple sclerosis. The consistent associations between neuroticism and elevated anxiety and depression, as well as between conscientiousness and both better mood and health-related quality of life, emphasize the importance of early psychosocial profiling.

032

Prevalence and Impact of Pain on Quality of Life in a Large Multiple Sclerosis Cohort: A Cross-Sectional Study

Said Alizada, Asiye Tuba Ozdogar, İrem Kara, Turhan Kahraman, Serkan Ozakbas

INTRODUCTION Pain is a common but often underrecognized and undertreated symptom in people with multiple sclerosis (pwMS).

OBJECTIVES This study aimed to evaluate the prevalence, distribution, and impact of different types of pain on quality of life in a large cohort of pwMS.

METHODS This cross-sectional study included pwMS categorized into three groups based on their pain experience: no pain, musculoskeletal pain (MSP), and neuropathic pain (NP). Sociodemographic and clinical characteristics were recorded. Pain types and distribution were assessed through structured interviews, and quality of life was evaluated using the EQ-5D questionnaire. Comparative analyses were adjusted for disease severity and duration.

RESULTS A total of 1503 pwMS were evaluated. Among them, 478 had no pain, 759 reported musculoskeletal pain, and 266 had neuropathic pain. Although age did not differ significantly between groups, both disease duration and EDSS scores were significantly higher in the NP group ($p < 0.05$). The most frequently reported pain locations over the past year were the lower back (33.4%), neck (31.3%), and knees (31.0%). Pain that most commonly interfered with work and daily functioning was localized in the lower back (15.6%), foot-ankle (14.4%), and knees (12.9%). Pain locations over the previous seven days mirrored these findings, with lower back (19.6%), neck (19.2%), and knee pain (18.0%) remaining most common. Quality of life scores differed markedly among the groups. Even after adjusting for EDSS and disease duration, the NP group had significantly lower scores across mobility, self-care, and usual activities domains compared to those with MSP and those without pain ($p < 0.05$). EQ-5D pain/discomfort scores showed a progressive decline in quality of life from the no-pain group (65.46±25.38), to MSP (43.10±31.25), and NP (22.57±24.06).

CONCLUSION This study highlights the high prevalence and substantial impact of pain, particularly neuropathic pain, in pwMS. Neuropathic pain was associated with greater disability and more severe quality of life impairment than musculoskeletal pain or the absence of pain. These findings emphasize the need for routine pain assessment as part of standard MS care. Integrating pain management strategies - especially for neuropathic pain - into multidisciplinary MS care models may significantly enhance quality of life and functional independence. Greater clinical awareness and targeted interventions could help address this often-overlooked but critical dimension of MS care

033

The Migraine Screen Questionnaire (MS-Q): A Valid Tool for Identifying Migraine in Persons with Multiple Sclerosis

Said Alizada, Can Caliskan, Turhan Kahraman, Serkan Ozakbas

INTRODUCTION Despite the high prevalence of migraine in persons with multiple sclerosis (pwMS) and its impact on quality of life, there is a lack of validated screening tools tailored for this population. This study addresses this gap by validating the Migraine Screen Questionnaire (MS-Q) as a brief and practical tool for migraine identification in clinical and research settings.

OBJECTIVES The objective of this study is to evaluate the diagnostic accuracy and reliability of MS-Q in pwMS.

METHODS A total of 210 pwMS (EDSS ranged from 0 to 7.5) were included in the study. The MS-Q was compared to clinical judgment and the International Headache Society (IHS) diagnostic criteria for identifying migraine. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive probability ratio (PPR), and negative probability ratio (NPR) were calculated for the overall cohort and stratified by sex. Additionally, the internal consistency of the MS-Q was assessed using the Kuder-Richardson 20 (KR-20) coefficient.

RESULTS According to clinical judgment and IHS criteria, there were 63 pwMS (30%) with migraine, while the MS-Q identified 61 pwMS (29%) as having migraine. The MS-Q demonstrated a Kappa of 0.68 ($p < 0.001$) for overall agreement with clinical diagnosis. For the overall cohort (n=210), the sensitivity was 0.76 (95%CI 0.64-0.86), specificity was 0.91 (95%CI 0.85-0.95), PPV was 0.79 (95%CI 0.66-0.88), NPV was 0.90 (95%CI 0.84-0.94), PPR was 8.62 (95% CI 5.04-14.74), and NPR was 0.26 (95%CI 0.17-0.41). When stratified by sex, males (n=46) showed a sensitivity of 0.80 (95%CI 0.30-0.99) and specificity of 0.93 (95%CI 0.79-0.98), whereas females (n=164) had a sensitivity of 0.76 (95%CI 0.63-0.86) and specificity of 0.91 (95%CI 0.83-0.95). The KR-20 for internal consistency was 0.67, suggesting questionable reliability.

CONCLUSION The MS-Q shows good diagnostic accuracy in identifying migraine in pwMS, particularly in females. While the internal consistency is questionable, the tool demonstrates promising potential as a screening instrument for migraine in pwMS. Further validation studies are needed to confirm its reliability and clinical utility.

SECTION IV

Disease Course, Prognosis and Disability Assessment

6 ABSTRACTS

034

How Much Damage Is Too Much? Early Predictors of Physical and Cognitive Decline After Treatment Switch in Multiple Sclerosis

Asiye Tuba Özdoğar, Ulvi Samadzade, Serkan Ozakbas

INTRODUCTION Treatment switching is common in multiple sclerosis (MS), yet the short-term outcomes following such changes remain unpredictable for many patients.

OBJECTIVES To identify the clinical predictors of physical, cognitive, and combined worsening over one year in people with MS (pwMS) undergoing a disease-modifying therapy (DMT) switch.

METHODS PwMS who had undergone a DMT change were retrospectively included in the study. Baseline variables included Expanded Disability Status Scale (EDSS), total relapse count from disease onset to the time of switch, age, sex, disease duration, MS subtype, DMT category, and regular exercise status. Physical function was assessed using the Timed 25-Foot Walk (T25FW) and the 9-Hole Peg Test (N-HPT), while cognitive performance was evaluated using the Brief International Cognitive Assessment for MS (BICAMS), which includes the Symbol Digit Modalities Test (SDMT), California Verbal Learning Test II (CVLT-II), and Brief Visuospatial Memory Test-Revised (BVMTR). Physical worsening was defined as at least 20% decline on either the T25FW or N-HPT. Cognitive worsening was defined as at least 20% decline on one or more BICAMS subtests. Combined worsening referred to deterioration in either or both domains.

RESULTS A total of 778 pwMS met the inclusion criteria. At the one-year follow-up, 17 participants (2.2%) exhibited physical worsening, 17 (2.2%) showed cognitive worsening, and 33 (4.2%) experienced combined worsening. A higher baseline EDSS was significantly associated with increased risk of both physical (OR = 2.133, p = 0.001) and combined worsening (OR = 1.516, p = 0.009). In contrast, the total number of relapses was the only factor significantly associated with cognitive worsening (OR = 1.422, p = 0.009).

CONCLUSION Although only a small proportion of patients showed physical or cognitive decline one year after switching therapy, the identified predictors offer meaningful insights. Higher baseline disability independently predicted further physical decline, which aligns with the expected clinical trajectory. However, the association between cumulative relapse burden and persistent cognitive worsening is particularly striking. This finding reinforces the concept that cognition reflects an integrated brain function sensitive to diffuse injury. In essence, the more inflammatory episodes the brain endures, the greater the risk of lasting cognitive impairment - even in the short term.

035

Pseudorelapse in Multiple Sclerosis: Clinical Features and Potential Implications

Ergi Kaya, Yasemin Şimşek, Can Caliskan, Serkan Ozakbas

INTRODUCTION Pseudorelapse is a common phenomenon that clinicians frequently encounter in the management of Multiple Sclerosis (MS). Although it does not reflect new inflammatory activity, it can significantly impair the quality of life of people with MS (pwMS). Despite its prevalence, the impact of pseudorelapse on long-term disease prognosis and the patient profiles in which it is more frequently observed remain unclear.

OBJECTIVES To compare people with MS who experienced a pseudorelapse (MS-P) with those who did not (MS-N), focusing on clinical and demographic characteristics.

METHODS This retrospective study included participants with relapsing-remitting MS and an Expanded Disability Status Scale (EDSS) score below 5.5. Participants were categorised into two groups based on the presence or absence of pseudorelapse. An experienced MS clinician determined the presence and type of pseudorelapse, which was categorized as motor, cerebellar, fatigue, cognitive, optic, or bladder-related. Sensorial pseudorelapses were excluded. Clinical and demographic variables - including relapse count, gender, age, EDSS score, first symptom localisation, and the interval between first symptom onset and diagnosis - were recorded and analysed.

RESULTS A total of 90 MS-P and 156 MS-N participants were included in the study. Motor, cerebellar, and optic symptoms were the most commonly observed pseudorelapse types, reported in 55, 15, and 13 patients, respectively. No significant differences were found between the two groups in terms of gender, age, or first symptom localisation (MS-P vs. MS-N, age [years], median, min-max: 40.5, 26-64 vs. 41, 35-55; $p > 0.05$). Similarly, current EDSS scores and the time from the first symptom to diagnosis did not differ significantly between groups (EDSS, median, min-max: 1.0, 0-5.0 vs. 0.5, 0-5.0; $p > 0.05$; time to diagnosis [months], median, min-max: 9.5, 0-372 vs. 6.5, 0-224; $p > 0.05$). However, the total number of relapses was significantly higher in the MS-P group compared to the MS-N group (median relapses: 3, range 1-15 vs. 2, range 1-14; $p = 0.03$).

CONCLUSION Previous relapses in pwMS may be associated with the development of subsequent pseudorelapses, which could further impact quality of life. These findings suggest that effective relapse prevention strategies may also reduce the frequency of pseudorelapse. Nevertheless, prospective studies are needed to determine the prognostic significance of pseudorelapses and their potential role as a clinical marker in the disease course.

036

Do Multiple Sclerosis Patients Perceive the Effectiveness of Relapse Treatment? A Comprehensive Evaluation Through the Expanded Disability Status Scale and Patient Determined Disease Steps Correlation

Can Caliskan, Gözde Deniz Ünal, Ela Zengin, Serkan Ozakbas

INTRODUCTION Multiple sclerosis (MS) is a chronic demyelinating disease marked by relapses and remissions, affecting motor, sensory, and cognitive functions. Relapse treatment aims to reduce inflammation and promote recovery. This study compares clinician-based (EDSS) and patient-reported (PDDS) measures to evaluate the effectiveness of relapse treatment.

OBJECTIVES To evaluate the effectiveness of relapse treatment in MS patients by comparing clinician-assessed (EDSS) and patient-reported (PDDS) disability scores, and to assess accompanying changes in cognitive and motor functions.

METHODS This study retrospectively analyzed clinical data from MS patients who were given steroids in 2025 due to relapse. Neurological disability was assessed using both the Expanded Disability Status Scale and the Patient Determined Disease Steps.

RESULTS A total of 25 patients included in the study. The cohort consisted of 64% females, with a mean age of 38 years and a mean disease duration of 11.04 years. Among these patients, 72% had relapsing-remitting MS, and 28% had secondary progressive MS. Following relapse treatment, both objective and patient-reported disability scores showed significant improvement. The Expanded Disability Status Scale score decreased from a mean of 2.96 to 2.00 ($p<0.001$), while the Patient Determined Disease Steps score decreased from 1.44 to 1.28 ($p=0.043$). These findings indicate that patients not only experienced clinical improvement but also perceived functional recovery in their daily lives. Cognitive test scores showed numerical improvement, but they did not reach statistical significance. The Symbol Digit Modalities Test scores rose from 45.36 to 49.88 ($p=0.197$), the California Verbal Learning Test scores increased from 47.12 to 53.04 ($p=0.081$), and the Brief Visuospatial Memory Test scores increased from 27.64 to 28.56 ($p=0.355$). These modest changes suggest that cognitive functions may recover more slowly or may require different intervention strategies. In terms of motor function, a significant improvement was observed in the 9-Hole Peg Test, with a decrease in time from 22.89 seconds to 22.07 seconds ($p=0.017$), indicating enhanced fine motor coordination. However, no significant changes were observed in the Timed 25-Foot Walk (from 5.71 to 5.58 seconds, $p=0.752$) or the 2-Minute Walk Test (from 161.85 meters to 164.04 meters, $p=0.654$).

CONCLUSION The improvements observed in both the Expanded Disability Status Scale and the Patient Determined Disease Steps suggest that patients' perceptions of functional recovery align with the clinical assessments conducted by neurologists. Although cognitive and motor improvements were limited in this short-term analysis, the significant improvement in fine motor skills points to a positive impact of relapse treatment. Long-term, larger-scale studies are necessary to further investigate the durability and scope of these functional improvements.

037

Evaluation of Disability in Individuals with Multiple Sclerosis Using Clinician-Rated and Patient-Reported Measures: A Cross-Sectional and Retrospective Study

Can Caliskan, Yasemin Şimşek, Ulvi Samadzade, Serkan Ozakbas

INTRODUCTION The Expanded Disability Status Scale (EDSS) and the Patient Determined Disease Steps (PDDS) are widely recognized and commonly used tools in both clinical practice and research to assess and monitor disability in individuals with multiple sclerosis. The EDSS is a neurologist-rated scale that emphasizes ambulation and functional system scores, while the PDDS is a simpler, patient-reported measure that reflects the individual's perceived level of disability.

OBJECTIVES This study aims to comprehensively evaluate demographic and clinical characteristics in a cohort of individuals with multiple sclerosis and analyze the relationships among key clinical variables.

METHODS This cross-sectional and retrospective analysis included individuals with multiple sclerosis who were under follow-up in our cohort. Demographic variables (age, sex, age at disease onset, disease duration, time to diagnosis) and clinical variables (multiple sclerosis subtype, clinician-rated and patient-reported disability scores, total number of relapses, and annualized relapse rate) were collected and analyzed.

RESULTS The cohort comprised 527 females (73.3%) and 192 males (26.7%). Distribution of multiple sclerosis subtypes was as follows: relapsing-remitting (n = 619, 88.6%), secondary progressive (n = 32, 4.6%), primary progressive (n = 29, 4.1%), progressive-relapsing (n = 1, 0.1%), and clinically isolated syndrome (n = 18, 2.6%). The mean baseline EDSS was 2.41 (SD = 1.68), while the mean final EDSS was 1.26 (SD = 1.81). The mean baseline PDDS was 1.42 (SD = 1.63), and the mean final PDDS was 0.97 (SD = 1.68). The average total number of relapses was 3.03 (SD = 2.66), and the mean ARR was 1.39 (SD = 2.34). The mean participant age was 39.28 years (SD = 12.14), mean age at disease onset was 28.41 years (SD = 9.70), mean disease duration was 10.87 years (SD = 8.81), and mean time to diagnosis was 2.66 years (SD = 4.83). The mean difference between baseline and final EDSS scores was 1.15 (SD = 1.51), which was statistically significant ($p < .001$). The mean difference between baseline and final PDDS scores was 0.45 (SD = 1.12), also statistically significant ($p < .001$). Strong correlations were observed between baseline EDSS and baseline PDDS ($r = .690$, $p < .001$) as well as between final EDSS and final PDDS ($r = .886$, $p < .001$).

CONCLUSION This study highlights the consistent and complementary nature of clinician-rated and patient-reported tools for assessing disability in multiple sclerosis. The strong correlations observed between these measures underscore their reliability in capturing both objective neurological findings and patients' subjective experiences. Future prospective, multicenter studies with longer follow-up periods are warranted to further validate these tools, explore their prognostic value, and examine their responsiveness to treatment-related changes in real-world practice.

038

A Generation Apart: Long-Term Outcomes of People with Multiple Sclerosis Diagnosed in the 1990s vs. 2010s

Serkan Ozakbas, Ulvi Samadzade, Yasemin Şimşek, Can Caliskan

INTRODUCTION Over the last three decades, the landscape of multiple sclerosis (MS) has changed dramatically due to earlier recognition of disease symptoms, advances in neuroimaging and diagnostic criteria, and the availability of increasingly effective disease-modifying therapies (DMTs).

OBJECTIVES This study aimed to compare the clinical trajectories of patients diagnosed with MS in two distinct periods - 1990-1996 and 2008-2014 - to evaluate the real-world impact of evolving clinical practice on long-term disease outcomes.

METHODS A retrospective cohort design was used to compare patients diagnosed in two eras: Group 1 (1990-1996, n=133) and Group 2 (2008-2014, n=579). Demographic data, time from symptom onset to diagnosis, Expanded Disability Status Scale (EDSS) scores at diagnosis and 10-year follow-up, annualized relapse rates (ARR), and the rate of conversion to secondary progressive MS (SPMS) were recorded. Statistical analyses included independent and paired sample t-tests, chi-square tests, and Mann-Whitney U tests as appropriate.

RESULTS The total cohort included 712 patients (mean age: 50.7 ± 12.2 years; mean disease duration: 20.7 ± 8.8 years; 70.4% female). Time from symptom onset to diagnosis was significantly shorter in Group 2 (3.2 ± 4.6 years) compared to Group 1 (4.2 ± 4.7 years, $p<0.005$). The initial EDSS scores were lower in Group 2 (2.32 ± 1.52) than in Group 1 (2.95 ± 1.63; $p<0.001$). After 10 years, patients in Group 2 had significantly better disability outcomes (mean EDSS: 1.85 ± 2.02) compared to Group 1 (3.97 ± 2.23; $p<0.001$). ARR was also lower in Group 2 (0.18 ± 0.20) than in Group 1 (0.23 ± 0.20; $p<0.05$). While 52.6% of Group 1 patients had progressed to SPMS after 10 years, this figure was only 5.4% in Group 2.

CONCLUSION This comparative analysis provides compelling evidence that major advances in MS diagnosis and treatment have substantially improved long-term outcomes. Patients diagnosed in more recent years benefited from earlier detection, more rapid initiation of therapy, and access to higher efficacy DMTs. These factors likely contributed to the significantly lower levels of disability, reduced relapse rates, and markedly lower rates of SPMS conversion observed in Group 2. Our findings highlight the importance of continued refinement in diagnostic strategies, early therapeutic intervention, and widespread access to potent DMTs in shaping the disease trajectory. Looking ahead, real-world data such as this not only validate.

039

Higher Body Mass Index Is Associated with Greater Physical Disability in Multiple Sclerosis: A Five-Year Prospective Study

Ulvi Samadzade, İrem Kara, Serkan Ozakbas

INTRODUCTION Body mass index (BMI) has emerged as a potentially modifiable factor that may influence the clinical course of multiple sclerosis (MS). While its association with disease activity and progression has been the subject of prior research, findings remain inconclusive, particularly with respect to cognitive and functional outcomes.

OBJECTIVES This study aims to investigate the relationship between baseline BMI and five-year changes in clinical disability and cognitive performance in persons with MS (pwMS).

METHODS In this prospective observational study, pwMS were grouped based on their BMI at baseline: Group 1 (BMI < 25), Group 2 (BMI 25-30), and Group 3 (BMI > 30). Clinical and cognitive assessments were performed at baseline and at five years, including the Expanded Disability Status Scale (EDSS), Timed 25-Foot Walk (T25-FW), 9-Hole Peg Test (9-HPT), Symbol Digit Modalities Test (SDMT), California Verbal Learning Test-II (CVLT-II), Brief Visuospatial Memory Test-Revised (BVMT-R), Godin Leisure-Time Exercise Questionnaire, and the Hospital Anxiety and Depression Scale (HADS). Statistical analyses included one-way ANOVA for relapse rate comparisons and repeated-measures ANOVA for time, group, and interaction effects.

RESULTS A total of 103 patients were included in the study, with 57 individuals in the normal BMI group. There were no significant differences in five-year relapse rates across BMI categories. Although the interaction between time and BMI was not significant for EDSS progression, individuals in the higher BMI group had significantly higher EDSS scores at year five compared to the lower BMI groups ($p < 0.05$). Similarly, despite the absence of a significant interaction effect for walking speed, the high BMI group demonstrated significantly longer T25-FW times ($p < 0.001$). No group differences were found in 9-HPT performance. Regarding cognitive outcomes, participants with higher BMI scores performed worse on the SDMT ($p < 0.05$), while no significant differences were detected in CVLT-II or BVMT-R scores. Physical activity levels, as measured by the Godin scale, improved over time across all groups without significant between-group differences. Anxiety and depression scores increased over time ($p < 0.001$), though no significant differences were observed between BMI groups.

CONCLUSION While BMI did not influence relapse rates or most cognitive measures, higher BMI was associated with greater physical disability and slower walking performance over a five-year period in pwMS. These findings emphasize the relevance of addressing lifestyle and metabolic factors in the long-term management of MS. This highlights the need for routine monitoring of BMI and implementation of targeted lifestyle interventions as part of comprehensive MS care, particularly in individuals at risk for mobility impairment.

SECTION V

Cerebrospinal Fluid and Immunological Markers

4 ABSTRACTS

040

The Prognostic Role of Type 2 and Type 3 Oligoclonal Bands in Multiple Sclerosis: A Five-Year Clinical Outcome Comparison

Sumeyye Cevik, Said Alizada, Ela Zengin, Ulvi Samadzade, Nurbanu Yapıcı, Cavid Baba, Serkan Ozakbas

INTRODUCTION Oligoclonal bands (OCBs) in the cerebrospinal fluid are key biomarkers in multiple sclerosis (MS), reflecting intrathecal immunoglobulin synthesis. Although their diagnostic utility is well established, the prognostic significance of different OCB patterns - particularly Type 2 and Type 3 - remains unclear. While both patterns indicate central nervous system immune activation, it is uncertain whether they differ in their association with long-term clinical outcomes. This study aimed to compare the five-year clinical trajectories of patients with Type 2 versus Type 3 OCBs, focusing on disability progression, relapse activity, and conversion to secondary-progressive MS (SPMS).

OBJECTIVES This study aimed to investigate whether different oligoclonal band (OCB) patterns - specifically Type 2 and Type 3 - are associated with distinct long-term clinical trajectories in patients with multiple sclerosis. By comparing five-year outcomes related to disability progression, relapse activity, and conversion to secondary-progressive MS (SPMS), the study sought to determine the potential prognostic relevance of OCB subtypes beyond their established diagnostic role.

METHODS This cross-sectional study evaluated the five-year clinical outcomes of MS patients with either Type 2 or Type 3 OCB positivity. Demographic and clinical parameters - including age at onset, sex, Expanded Disability Status Scale (EDSS) scores, annualized relapse rate, and conversion to secondary-progressive MS - were analyzed at two distinct time points: year two and year five following diagnosis.

RESULTS The study included a total of 1,270 patients, with 1,090 patients positive for Type 2 OCBs and 180 patients positive for Type 3 OCBs. At year two, patients with Type 3 OCBs exhibited significantly lower mean EDSS scores compared to those with Type 2 OCBs, suggesting a milder early disease course. However, by year five, the EDSS scores had increased in both groups, and the difference between them was no longer statistically significant. There were no notable differences between the groups in terms of relapse rates or conversion to SPMS during the five-year follow-up.

CONCLUSION Type 3 OCB positivity appears to be associated with lower disability in the early stages of MS; however, this benefit does not persist in the long term. By year five, disability progression, relapse rates, and conversion to SPMS were similar between Type 2 and Type 3 OCB groups. These findings suggest that OCB subtype alone may have limited prognostic value when assessed with standard clinical measures.

041

Elevated IgM Index Is Linked to More Severe Cognitive Impairment in Multiple Sclerosis

Ulvi Samadzade, Can Caliskan, Gözde Deniz Ünal, İrem Kara, Esra Aydın, Serkan Ozakbas

INTRODUCTION Multiple sclerosis (MS) is a chronic inflammatory and neurodegenerative disease of the central nervous system. Beyond physical disability, cognitive impairments - particularly in attention, memory, and processing speed - are frequently observed and have a profound impact on daily life and quality of life. While the IgM index has been proposed as a biomarker of intrathecal immune activity, its association with cognitive functioning remains unclear.

OBJECTIVES To compare the severity of cognitive impairment between MS patients with high and normal IgM index values and to evaluate whether this association is statistically significant.

METHODS This cross-sectional study categorized patients into two groups based on their IgM index levels: a high IgM index group and a normal IgM index group. Cognitive performance was evaluated using the Symbol Digit Modalities Test (SDMT), the California Verbal Learning Test-II (CVLT-II), and the Brief Visuospatial Memory Test-Revised (BVMT-R). Impairment thresholds were defined as 1.5 standard deviations below normative scores. Based on the number of impaired domains, cognitive impairment was classified as moderate (one test), severe (two tests), or very severe (three tests). Statistical analyses included chi-square and ordinal correlation tests.

RESULTS A total of 300 patients diagnosed with MS were included in the study. The high IgM index group (n = 150) exhibited more severe levels of cognitive impairment compared to the normal IgM index group (n = 150). Moderate cognitive impairment was more frequently observed in the normal IgM group (n = 127) than in the high IgM group (n = 89). In contrast, severe (n = 37) and very severe (n = 19) cognitive impairment were more prevalent among patients with high IgM index values, while these numbers were lower in the normal IgM group (n = 17 and n = 6, respectively). These differences were statistically significant ($\chi 2 = 21.709$, $p < .001$). Ordinal correlation coefficients also revealed a significant negative association between IgM index and severity of cognitive impairment: Gamma = -0.533 ($p < .001$), Spearman rho = -0.267 ($p < .001$), and Somers' d = -0.280 ($p < .001$).

CONCLUSION This study shows that an elevated IgM index is associated with more severe cognitive impairment in MS patients. Those with high IgM index values were more likely to show deficits in multiple cognitive domains, especially in processing speed and memory. Although the IgM index is primarily a laboratory marker of immune activity, these findings underline its clinical relevance in identifying patients at greater risk for cognitive decline. Longitudinal studies are needed to confirm whether the IgM index may serve as a prognostic marker for neuropsychological deterioration in MS.

042

Serum IgM Index and Functional Performance in Multiple Sclerosis: A Biomarker Beyond Inflammation?

Ulvi Samadzade, Can Caliskan, Gözde Deniz Ünal, İrem Kara, Esra Aydın, Serkan Ozakbas

INTRODUCTION The immunoglobulin M (IgM) index, a laboratory marker indicating intrathecal IgM synthesis, has been proposed as a potential biomarker reflecting disease activity and progression in multiple sclerosis (MS). However, its clinical relevance in long-term motor and cognitive performance has not been fully elucidated. This study investigates functional differences in MS patients grouped according to their serum IgM index levels.

OBJECTIVES To evaluate motor and cognitive performance differences between MS patients with persistently high IgM index values and those with normal IgM index, and to explore the potential prognostic implications of this laboratory biomarker.

METHODS This retrospective observational study included MS patients with elevated IgM index values and long-term clinical follow-up. A control group with normal IgM index levels was selected from a larger MS cohort of 4,191 patients, matched based on disease duration and baseline Expanded Disability Status Scale (EDSS) scores. Motor performance was assessed using the Timed 25-Foot Walk (T25FW) and the Nine-Hole Peg Test (9HPT). Cognitive performance was evaluated using the Symbol Digit Modalities Test (SDMT), Brief Visuospatial Memory Test (BVMT-R), and California Verbal Learning Test (CVLT-II).

RESULTS The study included 268 MS patients with high IgM index and 150 patients with normal IgM index. In terms of motor performance, the high IgM index group showed significantly poorer results in the T25FW ($p = .040$) and 9HPT ($p = .001$). Regarding cognitive performance, the normal IgM index group scored significantly higher on the SDMT ($p = .022$) and the BVMT-R ($p = .011$), indicating better information processing speed and visual memory. No significant difference was observed in CVLT-II scores ($p = .173$). These findings suggest that patients with elevated IgM index may experience subtle yet functionally meaningful impairments.

CONCLUSION MS patients with a high IgM index - a laboratory indicator of intrathecal immune activity - demonstrated poorer performance in both motor and selected cognitive domains compared to those with a normal IgM index. Particularly, deficits in processing speed and visuospatial memory were more pronounced. These findings support the potential utility of the IgM index as a prognostic biomarker in MS and highlight the need to integrate laboratory parameters into long-term functional assessments. Future longitudinal studies may clarify whether sustained IgM elevation can predict disability progression or cognitive decline over time.

043

Prognostic Significance of Intrathecal IgM Index in Multiple Sclerosis: A Three-Year Comparative Study of Physical and Cognitive Outcomes

Serkan Ozakbas, Gözde Deniz Ünal, Can Caliskan, Esra Aydın, Ulvi Samadzade

INTRODUCTION Multiple sclerosis (MS) is a chronic inflammatory disease of the central nervous system characterized by cognitive courses. IgM index, a marker of humoral immune activation, has been proposed as a prognostic biomarker for disease progression. This study evaluates clinical and cognitive changes over a three-year period in MS patients with high and normal IgM index values to investigate the predictive value of this biomarker in long-term outcomes.

OBJECTIVES To compare the three-year clinical and cognitive trajectories of MS patients with elevated versus normal intrathecal IgM index levels and assess the potential of the IgM index as a prognostic tool in MS management.

METHODS This retrospective longitudinal study included patients with MS at baseline and at 3-year follow-up. Patients were divided into two groups, high and normal, according to intrathecal IgM index levels. Clinical disability was assessed using the Expanded Disability Status Scale (EDSS), Timed 25-Foot Walk (T25FW), and Nine-Hole Peg Test (9HPT). Cognitive performance was assessed using the Symbol Digit Modalities Test (SDMT), California Verbal Learning Test-Second Edition (CVLT-II), and Brief Visual-Spatial Memory Test-Revised (BVMT-R).

RESULTS A total of 210 patients were included in the analysis, of whom 89 had an elevated IgM index and 121 had a normal IgM index. The groups were compared in terms of demographic characteristics, and the high IgM group had slightly higher EDSS scores. Over 3 years, patients in the normal IgM group showed significant improvements: CVLT-II scores increased from 57.20 to 60.54 and EDSS scores decreased from 0.89 to 0.67, with the greatest effect observed in EDSS ($p<0.001$). In contrast, the high IgM group showed deterioration in cognitive and clinical domains: CVLT-II scores decreased from 56.26 to 51.53 and EDSS scores increased from 1.26 to 1.36 ($p<0.001$). No significant changes were observed in T25FW, 9HPT, or SDMT in either group. Subgroup analysis in the high IgM group showed that patients with worsening EDSS (n=17) were significantly older ($p=0.029$), had later disease onset (35.94 vs. 30.08 years; $p=0.044$), and had higher follow-up EDSS scores. Intergroup comparisons at both time points revealed significant differences in CVLT-II, BVMT-R, and EDSS scores ($p<0.05$). More importantly, the rate of EDSS worsening was significantly higher in the high IgM group than in the normal group ($p<0.001$).

CONCLUSION This study shows that MS patients with high IgM index levels are more likely to experience both cognitive decline and clinical progression over a three-year period compared to those with normal IgM levels. These findings highlight the prognostic potential of the IgM index in early disease monitoring and long-term care strategies. Incorporating this biomarker into routine clinical practice may support more accurate risk stratification and help personalize therapeutic decision-making.

SECTION VI

Age at Onset, Ageing, Sex and Menopause

5 ABSTRACTS

044

Motivations and Treatment Shifts in Older Multiple Sclerosis Patients: Understanding Treatment Changes After Age 50

Ergi Kaya, Yasemin Şimşek, Can Caliskan, Ela Zengin, Serkan Ozakbas

INTRODUCTION Managing disease progression and adjusting treatment strategies becomes more complex in people with Multiple Sclerosis (pwMs) over 50. Understanding the motivations behind treatment changes in this group, especially in the context of comorbidities, is essential for guiding clinical practice and improving long-term outcomes.

OBJECTIVES The main objective of this study was to investigate the motivations behind treatment changes in pwMS over the age of 50 and to examine the impact of these changes on disability progression. Secondary objectives include evaluating the role of comorbidities in treatment decisions and understanding how disease-modifying therapies (DMTs) influence patient outcomes.

METHODS This retrospective analysis included pwMS diagnosed before age 50 but underwent DMT changes after that age. The patients were categorized based on their treatment modifications: those who remained on first-line therapies and those who transitioned to higher-efficacy DMTs. Comorbidities were categorized into cardiovascular, neurological, endocrine, and hematological conditions. The Expanded Disability Status Scale (EDSS) was used to assess disability level.

RESULTS A total of 158 (65.8% female) pwMS who were diagnosed before age 50 but underwent DMT changes after age 50 were included in the study. The mean age was 65.9 ± 4.6 years, with a mean disease duration of 24.7 ± 7.3 years. The baseline EDSS score was 3.44 ± 1.92 and 4.31 ± 2.44 at the recent visit. The most common comorbidities observed were cardiovascular/metabolic diseases (26.6% of the total cohort). Infections were the leading causes of death (12 patients, 7.6%). Regarding treatment shifts, 45 patients (28.5%) continued with first-line DMTs, while 113 (71.5%) transitioned to higher efficacy DMTs. The most common higher-efficacy DMTs were 52 (33%) fingolimod and 34 (21.5%) ocrelizumab. The analysis showed a statistically significant association between treatment type and EDSS progression ($p < 0.001$), with those on higher efficacy DMTs demonstrating slower progression than those who remained on first-line treatments.

CONCLUSION In older pwMS who underwent treatment changes after the age of 50, transitioning to higher efficacy DMTs, such as ocrelizumab and fingolimod, was associated with a slower progression of disability compared to those who continued with first-line therapies. Although comorbidities were prevalent in this group, they did not directly influence treatment decisions or disease progression in this cohort.

045

Age Matters: Distinct Disability Patterns in Multiple Sclerosis Patients Initiating Therapy After the Age of 50

Ela Zengin, Can Caliskan, Yasemin Şimşek, Gözde Deniz Ünal, Serkan Ozakbas

INTRODUCTION While late-onset and adult-onset multiple sclerosis (MS) have been frequently studied, less attention has been given to patients who initiate disease-modifying therapy (DMT) after the age of 50, regardless of their age at disease onset.

OBJECTIVES This study compares clinical features and disease course between those starting DMT after versus before age 50, with focus on immunosenescence.

METHODS This retrospective study analyzed medical records of 732 MS patients followed at a single center. Patients were categorized into two groups based on their age at DMT initiation: post-50 and pre-50. Clinical variables included MS subtype, Expanded Disability Status Scale (EDSS) scores at diagnosis and last follow-up, total relapse count, annualized relapse rate (ARR), and time from disease onset to DMT initiation. Group comparisons were conducted using appropriate statistical tests, with a significance level set at $p < 0.05$.

RESULTS Of the 365 patients in the post-50 group, 59.5% had relapsing-remitting MS (RRMS), 21.4% had secondary progressive MS (SPMS), and 19.2% had primary progressive MS (PPMS). In contrast, the 367 patients in the pre-50 group included 83.7% RRMS, 16.1% SPMS, and 0.3% PPMS. The mean EDSS score at diagnosis was higher in the post-50 group (3.70) than in the pre-50 group (2.95), and this difference persisted at last follow-up (3.76 vs. 2.58). EDSS progression occurred in 35.8% of the post-50 group versus 27.5% of the pre-50 group ($p < 0.05$). Relapse burden was significantly lower in the post-50 group, both in terms of total relapse count (2.93 vs. 4.90) and ARR (0.186 vs. 0.229; $p < 0.05$). Additionally, the time from disease onset to DMT initiation was significantly longer in the post-50 group (4.96 years) compared to the pre-50 group (3.60 years; $p < 0.001$).

CONCLUSION MS patients who initiate disease-modifying therapy after the age of 50 demonstrate a distinct clinical profile characterized by a higher proportion of progressive MS subtypes, greater disability at presentation and follow-up, and more frequent EDSS progression - despite experiencing fewer relapses. The significant treatment delay in this group may reflect diagnostic challenges or clinical inertia and appears to contribute to a more unfavorable disease course. These findings underscore the importance of early treatment initiation in older patients and highlight immunosenescence as a potential driver of accelerated disability, warranting further investigation in this age group.

046

Impact of Menopause on Initial Clinical Presentation and Comorbidities in Women with Multiple Sclerosis: A Comparative Study with Age-Matched Men

Yasemin Şimşek, Can Caliskan, Said Alizada, Serkan Ozakbas

INTRODUCTION Hormonal transitions such as menopause may influence how multiple sclerosis (MS) initially manifests and progresses. While female sex is a known prognostic factor, the impact of menopause on the anatomical localization of first MS symptoms remains underexplored. This study compares premenopausal and postmenopausal women with MS in terms of their initial clinical presentation, using age-matched men as a contextual reference group.

OBJECTIVES To investigate the influence of menopausal status on the anatomical localization of initial MS symptoms, comorbidity burden, and disability outcomes in women, with age-matched men serving as a contextual control group.

METHODS A total of 864 MS patients were selected from a larger cohort of 4191 individuals. Men were selected as an age-matched control group corresponding to the postmenopausal women. Clinical characteristics such as initial symptom localization, MS subtype, comorbidities, malignancy status, and mortality were examined across groups.

RESULTS Out of an initial cohort of 4,191 individuals with MS, a total of 864 patients were included in the analysis. These comprised 298 premenopausal women, 300 postmenopausal women, and 265 age-matched men. Initial symptoms of localization differed significantly between groups. The optic nerve was the most frequent site of first involvement in premenopausal women (n = 65, 21.8%), followed by postmenopausal women (n = 45, 15.0%) and men (n = 31, 11.7%) (p = .004). In contrast, spinal cord was the initial site in 82 premenopausal women (27.5%), 132 postmenopausal women (44.0%), and 128 men (48.3%) (p <0 .001). Comorbidities were notably more prevalent in postmenopausal women (n = 123, 41.0%) and men (n = 97, 36.6%) compared to premenopausal women (n = 45, 15.1%) (p < .001). Among postmenopausal women, the most common comorbid category was cardiovascular disease (n = 74, 24.7%), including hypertension, arrhythmia, and coronary artery disease. Endocrine/metabolic disorders such as type 2 diabetes, hypothyroidism, and dyslipidemia were also frequent (n = 31, 10.3%). Psychiatric comorbidities, although less common overall, were more frequently observed in premenopausal women (e.g., depression, anxiety) than in postmenopausal women. Men had a comorbidity profile resembling that of postmenopausal women, particularly with respect to cardiovascular risk. Mortality occurred in 15 men (5.7%) and 9 postmenopausal women (3.0%), while no deaths were reported among premenopausal women.

CONCLUSION Postmenopausal women exhibited higher rates of cardiovascular and endocrine/metabolic comorbidities compared to premenopausal women, who showed a lower overall comorbidity burden. Age-matched men displayed a comorbidity profile like that of postmenopausal women. Further research is needed to better understand the underlying mechanisms and to guide evidence-based care and treatment approaches for different patient groups.

047

Impact of Menopausal Status and Gender on Disease Progression and Clinical Outcomes in Multiple Sclerosis

Yasemin Şimşek, Can Caliskan, Ela Zengin, Serkan Ozakbas

INTRODUCTION Sex and hormonal status are increasingly recognized as important modifiers of disease course in multiple sclerosis (MS). Hormonal fluctuations, particularly those associated with menopause, may impact both disease activity and long-term disability. Clarifying these differences may contribute to more personalized and effective management strategies in MS.

OBJECTIVES To investigate clinical characteristics and EDSS progression in MS patients stratified by menopausal status and gender.

METHODS MS patients were stratified into three groups according to menopausal status and gender. Men were selected to match the age distribution of postmenopausal women. Demographic and clinical characteristics were compared across groups.

RESULTS The study included 864 individuals with MS, drawn from a larger cohort. Of these, 300 (34.7%) were postmenopausal women, 298 (34.5%) were premenopausal women, and 265 (30.7%) were men. The mean age was 64.77 ± 6.87 years in postmenopausal women, 40.86 ± 4.15 years in premenopausal women, and 61.01 ± 8.25 years in men. Disease duration was 24.17 ± 10.84 years in postmenopausal women, 19.49 ± 3.65 years in premenopausal women, and 21.09 ± 9.78 years in men. Age at disease onset was 40.60 ± 10.88 years in postmenopausal women and 39.91 ± 10.52 years in men. In the total cohort, 592 patients (68.5%) had relapsing-remitting MS (RRMS), 181 (21.0%) had secondary progressive MS (SPMS), and 90 (10.4%) had primary progressive MS (PPMS). At first clinical assessment, EDSS scores were significantly higher in men (3.79 ± 1.92) than in postmenopausal women ($p<.001$), while no significant difference was found between the two female groups ($p=0.671$). At the time corresponding to menopause, EDSS scores were similar between postmenopausal women (3.60 ± 2.32) and premenopausal women ($p=0.555$). Premenopausal women reported using a significantly higher number of disease-modifying therapies (2.27 ± 1.22) compared to postmenopausal women ($p=0.024$), while medication use in men (2.20 ± 0.98) was similar to both female groups ($p>0.05$). The annualized relapse rate (ARR) was highest in premenopausal women (0.25 ± 0.15), followed by men (0.20 ± 0.16) and postmenopausal women ($p<0.001$). EDSS progression was observed most frequently in men (n=96, 36.8%), followed by premenopausal women (n=83, 28.6%) and postmenopausal women (n=78, 27.5%, $p=0.039$). Although premenopausal women had greater relapse activity and treatment intensity, disability worsening over time was more pronounced in the male group.

CONCLUSION Men demonstrated the highest rate of EDSS worsening despite comparable disease duration and age at onset with postmenopausal women. Premenopausal women showed greater relapse activity and treatment intensity, while men exhibited more pronounced disability progression.

048

Clinical Characteristics and Disease Progression in Multiple Sclerosis: A Comparison of Late Middle-Age Onset vs. Late Adulthood Onset

Serkan Ozakbas, Yasemin Şimşek, Can Caliskan, Asiye Tuba Ozdogar

INTRODUCTION The age at which multiple sclerosis (MS) presents can impact the disease's progression and long-term outcomes. Late middle age onset MS (LMOMS) and late adulthood onset MS (LAOMS) are considered distinct subgroups within the MS spectrum, but the rationale for selecting specific age thresholds for comparison remains underexplored.

OBJECTIVES This study aimed to investigate clinical differences, including disability level, relapse frequency, and MS type, between patients diagnosed with LMOMS and LAOMS.

METHODS Patients with MS were grouped into two categories based on the age of onset: LMOMS (onset between 50 and 60 years) and LAOMS (onset after 60 years). Data regarding the Expanded Disability Status Scale (EDSS) scores, demographic information, disease duration, and relapse frequency were retrospectively collected and analyzed.

RESULTS A total of 89 patients with MS were included: 12 in the LMOMS group and 77 in the LAOMS group. The mean age at diagnosis was significantly higher in the LAOMS group compared to the LMOMS group (68.25 ± 3.77 vs. 57.34 ± 4.20, $p<0.001$), and the mean age of patients was also higher in LAOMS (78.00 ± 7.19 vs. 68.32 ± 4.78, $p<0.001$). However, no significant differences were observed between the groups regarding disease duration, EDSS scores at the first and last visit, total number of relapses, or relapses per year. MS subtypes were similarly distributed across both groups: LMOMS (RRMS: 44, SPMS: 12, PPMS: 21), and LAOMS (RRMS: 5, SPMS: 1, PPMS: 6).

CONCLUSION Although patients with LAOMS were older and diagnosed later than those with LMOMS, there were no significant differences in disability progression, relapse frequency, or MS subtype distribution. These findings suggest that the age of onset beyond 50 years does not substantially alter the clinical course of MS, underscoring the importance of individualized care regardless of onset age.

SECTION VII

Pregnancy, Breastfeeding and Offspring

4 ABSTRACTS

049

Pregnancy and Future Disability in MS: Can Machine Learning Help Predict the Trajectory?

Murat Emec, Ergi Kaya, Yasemin Şimşek, Mehmet Hilal Ozcanhan, Serkan Ozakbas

INTRODUCTION Artificial Intelligence (AI) techniques, particularly Machine Learning (ML), have demonstrated considerable promise in various healthcare domains. In multiple sclerosis (MS), the Expanded Disability Status Scale (EDSS) serves as a gold standard for quantifying disability. This study focuses on women with MS (wwMS) who have experienced pregnancy, aiming to integrate ML models into clinical workflows to support accurate EDSS prediction by incorporating pregnancy-related variables.

OBJECTIVES The study aims to develop and evaluate ML-based models for predicting disability status in wwMS following pregnancy using clinical, demographic, and pregnancy-related data. It also aims to compare the performance of different ML algorithms in predicting post-pregnancy disability.

METHODS This retrospective study included pwMS with a history of a single pregnancy. A dataset comprising clinical, demographic, and pregnancy-related variables was prepared. Feature selection was conducted through correlation analysis to identify variables most relevant to EDSS prediction. Four ML algorithms - CatBoost (with hyperparameter tuning), XGBoost, Random Forest, and Decision Tree - were trained to classify patients into three EDSS categories: Mild (EDSS 0-3.5), Moderate (EDSS 4-6.5), and Severe (EDSS ≥7). Model performance was evaluated using standard classification metrics, including accuracy, F1 score, recall, and precision.

RESULTS A total of 636 wwMS with a history of pregnancy were included (66 mild, 532 moderate, and 38 severe EDSS scores). The CatBoost model with hyperparameter tuning achieved the highest accuracy and F1 score among all models tested. Correlation analysis revealed that disease course, age, breastfeeding status, and EDSS scores before and after pregnancy were the most predictive features of post-pregnancy disability level.

CONCLUSION This study's findings hold significant promise for the future of MS care. By demonstrating the effectiveness of ML techniques - particularly the CatBoost algorithm with hyperparameter tuning - in predicting EDSS scores in pwMS who have experienced one pregnancy, the study highlights the potential of incorporating pregnancy-related factors into predictive models. The results suggest that pregnancy and associated variables such as pre- and post-pregnancy EDSS, age, disease course, and breastfeeding status may contribute meaningfully to the prediction of long-term disability.

050

Timing Matters: Early Initiation of Fingolimod Before Pregnancy Improves Postpartum Outcomes in Women with Multiple Sclerosis

Ela Zengin, Can Caliskan, Yasemin Şimşek, Gözde Deniz Ünal, Serkan Ozakbas

INTRODUCTION Fingolimod, an effective oral disease-modifying therapy (DMT) for relapsing-remitting MS (RRMS), is generally avoided in this population due to its potential teratogenic risks, making it a less preferred treatment option during the reproductive period. Differences in relapse frequency, disability progression, and perinatal factors such as birth weight and breastfeeding duration may reflect the impact of treatment timing on maternal and disease outcomes.

OBJECTIVES This study aims to compare the clinical and demographic characteristics of MS patients who initiated fingolimod therapy before pregnancy with those who began treatment postpartum. The primary objective is to evaluate how treatment timing influences relapse activity, disability status, birth outcomes, and breastfeeding patterns, thereby informing evidence-based decisions in reproductive-age MS management.

METHODS Participants were categorized into two groups based on the timing of fingolimod initiation: those who started treatment before pregnancy and those who began after childbirth .Clinical and demographic data collected included age, age at disease onset, disease duration, time to diagnosis, birth weight, breastfeeding duration, relapse counts, and Expanded Disability Status Scale (EDSS) scores. Independent samples t-tests were conducted to compare the groups. A significance level of $p < 0.05$ was adopted for all statistical analyses.

RESULTS Age at disease onset was significantly lower in the pre-pregnancy group (21.80 ± 5.01 years) compared to the postpartum group (29.73 ± 8.11 years, $p < 0.001$). Relapse activity also differed significantly between groups: the mean number of relapses before pregnancy was higher in patients who initiated fingolimod pre-pregnancy (4.02 ± 2.47) than in those starting postpartum (0.73 ± 1.21, $p < 0.001$). Conversely, postpartum relapse rates were significantly lower in the pre-pregnancy group (0.49 ± 0.77) than in the postpartum initiation group (2.80 ± 2.54, $p < 0.001$). EDSS scores before pregnancy were lower in the pre-pregnancy group (1.26 ± 1.54) versus postpartum group (2.39 ± 1.70, $p < 0.001$), and postpartum EDSS scores followed the same pattern (1.61 ± 1.77 vs. 2.39 ± 1.74, $p = 0.006$). Regarding birth outcomes, birth weight was slightly lower in the pre-pregnancy group (2975.10 ± 307.28 g) compared to postpartum group (3084.01 ± 297.25 g, $p = 0.025$). Breastfeeding duration did not differ significantly between groups ($p = 0.120$).

CONCLUSION Initiating fingolimod therapy before pregnancy is associated with better post-pregnancy clinical outcomes, including lower relapse rates and reduced disability progression. Despite its teratogenic risks, appropriately managed fingolimod use may provide protective benefits in the context of reproductive health planning.

051

Children of Parents with Multiple Sclerosis: A Health and Psychosocial Profile

Yasemin Şimşek, Can Caliskan, Said Alizada, Serkan Ozakbas

INTRODUCTION Multiple sclerosis (MS) is a chronic neurological disorder that often affects individuals during their reproductive years. This raises questions regarding the long-term well-being of their children. Understanding the demographic, health, and psychosocial characteristics of children born to individuals with MS may help identify both potential vulnerabilities and areas of resilience within this population.

OBJECTIVES This study aimed to assess the demographic, perinatal, health, and psychosocial characteristics of children of individuals with MS, with particular attention to mental health outcomes such as depression and anxiety in the children themselves.

METHODS This study included children of individuals with MS, based on parental reports and clinical records. Variables examined included demographic data, perinatal outcomes, breastfeeding history, health status, academic performance, and parental mental health.

RESULTS A total of 247 children born to 161 individuals with MS (13.7% male, 86.3% female) were evaluated. The mean age of the children was 16.04 years, and their mean body mass index (BMI) was 21.9. Cesarean delivery was reported in 54.7% of cases, while 45.3% were born vaginally. The majority (94.3%) were full-term births. Gender distribution was nearly equal, and 94.7% had been breastfed. Mental health diagnoses in children were commonly reported by their parents, with 17.4% of children reported to have been diagnosed with depression and 27.9% with anxiety. Among the children, 17.4% had allergic diseases, 3.2% had anemia, and 1.6% had psychiatric diagnoses such as attention-deficit/hyperactivity disorder. A small number were reported to have chronic conditions, including polycystic ovary syndrome and MS (each 0.8%), while rare conditions (each 0.4%) included tuberculosis, epilepsy, thyroid cancer, SLE, and others. The most commonly mentioned allergens were pollen, house dust, and metals. The most frequently reported allergens were pollen, house dust, and metals. Based on parental reports, the children's academic performance was comparable to the national average.

CONCLUSION Children of individuals with MS generally exhibit favorable health and developmental outcomes. However, the relatively high frequency of allergic conditions and the presence of mental health concerns reported by parents highlight the need for continued monitoring and supportive interventions. These findings emphasize the importance of considering the broader psychosocial environment in the comprehensive care of families affected by MS.

052

Pregnancy and Breastfeeding in Women with Multiple Sclerosis: Do Maternal Choices Influence Disease Activity and Disability?

Yasemin Şimşek, Can Caliskan, Ela Zengin, Serkan Ozakbas

INTRODUCTION Multiple sclerosis is a chronic, immune-mediated neurological condition that primarily affects young women of reproductive age. Understanding how pregnancy and postpartum factors - particularly breastfeeding - influence disease activity and disability progression is essential for guiding individualized treatment decisions and improving outcomes for women living with multiple sclerosis.

OBJECTIVES The primary objective of this study is to examine whether breastfeeding has a modifying effect on relapse rates and disability status before and after pregnancy in women with multiple sclerosis.

METHODS This retrospective analysis included women with multiple sclerosis from our cohort who had experienced at least one pregnancy. Variables assessed included multiple sclerosis subtype (relapsing-remitting, secondary progressive, primary progressive, clinically isolated syndrome), mode of delivery, relapses count before and after pregnancy, clinician-rated disability scores before and after pregnancy, breastfeeding status, and breastfeeding duration.

RESULTS A total of 726 patients were included in the study. Among them, 603 women (90.8%) breastfed, while 67 (9.2%) did not. No significant differences were found between the groups in terms of multiple sclerosis subtype distribution ($p = 0.086$) or worsening in disability scores ($p = 0.353$). Group comparisons revealed no significant differences between breastfeeding and non-breastfeeding participants in birth weight, relapses count before and after pregnancy, disability scores, age, age at disease onset, or disease duration (all $p > 0.05$). There was a small but statistically significant negative correlation between relapse counts before and after pregnancy ($r = -0.194$, $p < 0.001$). The post-pregnancy relapse showed moderate positive correlations with both pre- and post-pregnancy disability scores ($r = 0.349$, $p < 0.001$; $r = 0.345$, $p < 0.001$, respectively). The effect of time on relapse rates and disability scores from pre- to post-pregnancy was statistically significant (relapses: $p = 0.008$; disability scores: $p = 0.016$). However, these changes did not differ significantly between breastfeeding and non-breastfeeding groups ($p > 0.05$).

CONCLUSION This study highlights that pregnancy, and the postpartum period are dynamic phases in the disease course of women with multiple sclerosis, characterized by changes in relapse activity and disability progression. While a temporal effect was evident, breastfeeding did not independently influence these outcomes. Nevertheless, larger prospective and controlled studies are warranted to further clarify the role of breastfeeding within the broader context of postpartum disease modulation and to investigate potential immunological mechanisms involved.

SECTION VIII

Disease-Modifying Therapies: Long-Term Real-World Outcomes

10 ABSTRACTS

053

Long-Term Effects of Ocrelizumab on Motor and Cognitive Functions in Progressive Multiple Sclerosis: A Three-Year Follow-Up Study

Ergi Kaya, Asiye Tuba Ozdogar, Gözde Deniz Ünal, Turhan Kahraman, Serkan Ozakbas

INTRODUCTION Ocrelizumab has been shown to delay disability progression and improve fatigue, quality of life, and cognitive function in relapsing-remitting multiple sclerosis. However, evidence regarding its long-term effects on physical and cognitive functions in progressive MS remains limited.

OBJECTIVES To evaluate the long-term effects of ocrelizumab on extremity function and cognitive performance in individuals with progressive MS (pwPMS) over a three-year period.

METHODS This retrospective cohort study included patients diagnosed with primary or nonactive secondary progressive MS. Upper and lower extremity function, cognitive performance, and disability status were assessed at treatment initiation and after three years of continuous ocrelizumab therapy. Fine motor skills of the upper limbs were evaluated using the Nine-Hole Peg Test (9HPT), while lower limb performance was assessed with the Timed 25-Foot Walk (T25FW). Cognitive functions were examined using the Symbol Digit Modalities Test (SDMT), California Verbal Learning Test (CVLT), and Brief Visuospatial Memory Test (BVMT). The Expanded Disability Status Scale (EDSS) was used to monitor disability progression.

RESULTS Thirty individuals with progressive MS receiving ocrelizumab were included in the study. The mean baseline EDSS score was 5.52±1.68. While EDSS scores remained stable over the follow-up period, significant improvements were observed in verbal and visuospatial memory. Specifically, CVLT and BVMT scores improved significantly. No statistically significant changes were detected in SDMT, 9HPT, or T25FW performance.

CONCLUSION Ocrelizumab was associated with preserved motor performance and stable disability levels over three years in patients with progressive MS. In addition, notable improvements in cognitive domains such as verbal and visuospatial memory suggest that ocrelizumab may exert beneficial effects beyond physical disability. These findings support its potential as a disease-modifying treatment with cognitive protective benefits in progressive MS.

054

Five-Year Real-World Outcomes of Fingolimod in Multiple Sclerosis: Long-Term Effectiveness and Treatment Continuation Patterns

Serkan Ozakbas, Said Alizada, Ulvi Samadzade, Can Caliskan

INTRODUCTION Long-term real-world data on fingolimod therapy are essential to evaluate its sustained clinical benefit and tolerability in patients with multiple sclerosis (MS).

OBJECTIVES This study aimed to assess five-year treatment outcomes, reasons for discontinuation, and predictors of disease progression.

METHODS This retrospective cohort study included 989 patients who initiated fingolimod therapy in or before 2019. Demographic, clinical, and treatment-related data were analyzed. Expanded Disability Status Scale (EDSS), annualized relapse rate (ARR), and treatment persistence were evaluated over a five-year period. Statistical analyses included paired-samples t-tests, Wilcoxon signed-rank tests, chi-square tests, and correlation analyses.

RESULTS Among the 693 patients who completed at least five years of therapy, the mean age was 44.91 ± 10.43 years and 69.3% were female. Mean age at disease onset was 27.72 ± 8.80 years, mean disease duration was 17.19 ± 7.23 years, and mean treatment duration was 7.50 ± 2.22 years. Baseline EDSS (2.09 ± 1.85) showed a modest but statistically significant improvement at year five (1.86 ± 1.98; $p < .001$). EDSS improvement was observed in 32.9% of patients, while 13.3% showed worsening. Mean ARR was 0.0736 ± 0.20. Annual effectiveness rates declined gradually from 94.6% in year one to 79.1% in year five. Treatment persistence decreased to 65.7% by the fifth year. Among 123 patients with known discontinuation reasons, 64.2% cited lack of efficacy. Male patients were more likely to discontinue due to inefficacy than females (OR = 2.76; 95% CI: 1.13-6.71; $p = 0.023$). No significant associations were found between EDSS worsening and age, disease duration, or treatment duration.

CONCLUSION In this large real-world cohort, fingolimod was associated with low relapse rates and overall clinical stability over a minimum of five years. While many patients remained on therapy for extended periods - a notable outcome in long-term MS management - treatment persistence gradually declined. Discontinuation due to inefficacy emerged as a key reason for stopping therapy, particularly among male patients. These findings support the value of fingolimod in selected patients, while underlining the need for individualized treatment strategies over time.

055

Longitudinal Impact of Fingolimod on Disease Course in Multiple Sclerosis: A Three-Year Pre- and Post-Treatment Analysis

Said Alizada, Ulvi Samadzade, Can Caliskan, Orkhan Mammadov, Serkan Ozakbas

INTRODUCTION Fingolimod is a widely used oral disease-modifying therapy (DMT) for multiple sclerosis (MS), known for reducing relapse rates and delaying disease progression.

OBJECTIVES This study aimed to assess the clinical impact of fingolimod by comparing disease activity and progression over three years before and after treatment initiation.

METHODS A retrospective analysis was conducted on 657 MS patients treated with fingolimod, including 596 with relapsing MS and 61 with secondary progressive MS. Key clinical measures, including Expanded Disability Status Scale (EDSS) scores, annualized relapse rate (ARR), and no evidence of disease activity (NEDA-3) status, were assessed at three time points: three years before fingolimod initiation, at treatment initiation, and three years post-treatment.

RESULTS Among relapsing MS patients (mean age 45.0 ± 10.2; 69.5% female), ARR significantly declined from 0.34 before treatment to 0.08 after three years of fingolimod therapy, while mean EDSS remained stable (1.48 pre-treatment, 1.48 at initiation, 1.43 post-treatment). Notably, 69.6% of patients achieved NEDA-3. Patients who attained NEDA-3 were older (45.64 vs. 43.55 years, $p=0.021$), had longer disease duration (5.84 vs. 5.09 years, $p=0.005$), and a lower baseline EDSS (1.22 vs. 2.07, $p<0.001$) compared to NEDA-3-negative individuals. In secondary progressive MS patients (mean age 50.2 ± 10.9; 65.6% female), EDSS scores increased from 5.12 pre-treatment to 6.10 post-treatment over the six-year period, indicating ongoing disability progression. However, ARR decreased from 0.61 to 0.27. Only 16.4% of these patients achieved NEDA-3, and those who did had significantly higher baseline EDSS scores (6.11 vs. 4.94, $p=0.002$). No significant differences in age or disease duration were observed between NEDA-3-positive and NEDA-3-negative patients.

CONCLUSION Fingolimod demonstrated strong efficacy in reducing relapse rates and maintaining overall clinical stability in relapsing MS patients, with a substantial proportion achieving NEDA-3. In secondary progressive MS, while ARR declined, disability progression remained evident, underscoring the need for more effective treatment options for this patient subgroup. These findings reinforce fingolimod's long-term disease-modifying effects in relapsing MS and provide valuable insights into patient characteristics associated with better treatment outcomes.

056

Sustained Effectiveness or Inevitable Discontinuation? Five-Year Real-World Outcomes of Teriflunomide Therapy in Multiple Sclerosis

Serkan Ozakbas, Said Alizada, Ulvi Samadzade, Can Caliskan

INTRODUCTION Long-term evaluation of disease-modifying treatments (DMTs) is crucial for optimizing multiple sclerosis (MS) management.

OBJECTIVES While pivotal trials suggest stable efficacy, real-world data often reveal a progressive decline in treatment effectiveness. This study investigates the five-year clinical outcomes of teriflunomide, focusing on its long-term efficacy, discontinuation patterns, and patient retention rates using an intention-to-treat (ITT) approach.

METHODS A retrospective cohort study was conducted on 292 patients treated with teriflunomide for at least five years. Annual clinical effectiveness, reasons for treatment discontinuation, and disability progression were assessed. ITT analysis was applied to evaluate real-world treatment retention rates.

RESULTS The mean age at disease onset was 31.7 years (SD=10.1), with 65.9% female participants. Baseline EDSS was 1.55±1.71, increasing slightly to 1.63±1.89 at the final follow-up. Mean ARR remained low (0.0774 ± 0.0126). Over five years, 166 patients (56.8%) discontinued treatment, primarily due to inefficacy (74.1%) and adverse events or personal reasons (25.9%). ITT analysis revealed a steady decline in treatment continuation: 84.25% remained on teriflunomide after year one, decreasing to 76.03% (year 2), 66.10% (year 3), 57.19% (year 4), and 43.15% (year 5). Interestingly, patients discontinuing teriflunomide for inefficacy in year two showed better clinical outcomes with subsequent treatments compared to pivotal trial data. Older age (p=0.016) and later disease onset (p=0.017) significantly correlated with worsening EDSS.

CONCLUSION Teriflunomide exhibits strong initial clinical effectiveness but demonstrates a progressive decline over time, with increasing discontinuation rates. ITT analysis underscores that while long-term retention is relatively low, close monitoring may allow for sustained effectiveness in a subset of patients. Furthermore, early identification of suboptimal responders may improve overall treatment strategies, as those switching due to inefficacy appear to achieve better outcomes on alternative therapies. Personalized treatment approaches remain essential for maximizing long-term disease control.

057

Five Years of Ocrelizumab in MS: Clinical Stability and Subtle Cognitive Gains

Serkan Ozakbas, Ulvi Samadzade, Gözde Deniz Ünal, Can Caliskan, İrem Kara, Said Alizada

INTRODUCTION Ocrelizumab is a CD20-directed monoclonal antibody approved for the treatment of both relapsing and primary progressive multiple sclerosis (MS). While its short-term efficacy has been well established, real-world data on long-term outcomes remain limited.

OBJECTIVES This study aimed to evaluate the clinical trajectory and disease activity in patients treated with Ocrelizumab for five years or longer.

METHODS Patients who received Ocrelizumab for five or more years were included. Annualized relapse rate (ARR), Expanded Disability Status Scale (EDSS) scores, and relapse history were assessed at treatment initiation and at the end of the follow-up period (or the most recent visit for ongoing treatment). Physical performance (Timed 25-Foot Walk [T25FW], Nine-Hole Peg Test [9-HPT]) and cognitive performance (Symbol Digit Modalities Test [SDMT], California Verbal Learning Test-Second Edition [CVLT-II], and Brief Visuospatial Memory Test-Revised [BVMT-R]) were evaluated in patients with available data at both time points.

RESULTS Patients who initiated Ocrelizumab in 2019 or earlier were included. Ten patients discontinued treatment before completing five years for reasons other than lack of efficacy. Clinical data from 241 patients (61.8% female) who received treatment for at least five years were analyzed. The mean age at evaluation was 52.6 years (SD=10.45), with a mean age at disease onset of 30.91 years (SD = 9.76) and a mean disease duration of 21.10 years (SD=8.58). The mean EDSS score increased slightly from 5.23 (SD = 1.81) at baseline to 5.40 (SD=1.90) at follow-up, representing a statistically significant but clinically modest progression ($p<0.05$). EDSS worsened in 85 patients, improved in 41, and remained unchanged in 113. The mean ARR during follow-up was 0.0095 (SD=0.048), indicating minimal inflammatory activity. Functional test scores showed no significant change: T25FW times increased from 50.47 to 65.99 seconds ($p=0.185$), 9-HPT from 37.81 to 38.01 seconds ($p=0.933$), and SDMT from 39.65 to 41.97 ($p=0.119$). In contrast, cognitive performance improved significantly in verbal and visuospatial memory: CVLT-II scores increased from 47.72 to 53.05 ($p=0.016$), and BVMT-R from 22.27 to 24.64 ($p=0.022$).

CONCLUSION In patients receiving Ocrelizumab for five years or more, overall clinical stability was preserved, with very low relapse rates and only minimal physical disability progression. Interestingly, while functional measures such as walking speed and manual dexterity remained stable, significant improvements in verbal and visuospatial memory were observed. These findings suggest that long-term Ocrelizumab therapy may contribute to cognitive resilience, possibly reflecting a neuroprotective effect beyond its anti-inflammatory properties.

058

Ten-Year Long-Term Efficacy of Fingolimod in Relapsing Multiple Sclerosis: Sustained Disease Control and Relapse Prevention in Long-Term Users

Serkan Ozakbas, Said Alizada, Can Caliskan, Ulvi Samadzade

INTRODUCTION Fingolimod is a well-established oral disease-modifying therapy (DMT) for relapsing multiple sclerosis (MS). This study focuses on the long-term efficacy of fingolimod, evaluating patients who have been continuously treated with the therapy for at least ten years.

OBJECTIVES The goal is to assess relapse rates, disease progression, and the overall stability of the disease in this unique cohort.

METHODS A total of 217 MS patients (62.2% female; mean age: 47.89 ± 9.24 years) who have been on fingolimod therapy for at least ten years were retrospectively analyzed. Key variables included age, age at disease onset, disease duration, annualized relapse rate (ARR), and disease progression. Statistical methods such as paired t-tests, Wilcoxon tests, Pearson correlation, and logistic regression were applied to the data.

RESULTS The mean ARR was 0.0378 ± 0.0686, with values ranging from 0 to 0.49, indicating sustained low relapse activity over the ten-year period. Of the patients, 87.1% (n = 189) remained clinically stable, while 11.5% (n = 25) experienced disease progression. There were no statistically significant differences between progression and non-progression groups in terms of age, age at disease onset, or disease duration. Additionally, 33 patients (15.2%) discontinued fingolimod during the follow-up, with 14 discontinuing due to lack of efficacy and 19 due to adverse effects or personal preferences.

CONCLUSION Fingolimod continues to be highly effective in maintaining disease control and preventing relapses in patients who have been using it for at least ten years. The majority of patients remained stable, with a low relapse rate observed over the extended period. These results further support the long-term use of fingolimod as an effective therapeutic option for managing relapsing MS. Further research is needed to identify factors that influence disease progression and to optimize long-term treatment strategies for MS patients.

059

Dimethyl Fumarate in the Long Run: Five-Year Stability and Cognitive Gains in Relapsing Multiple Sclerosis

Serkan Ozakbas, Ulvi Samadzade, Gözde Deniz Ünal, Can Caliskan, İrem Kara, Said Alizada

INTRODUCTION Dimethyl fumarate (DMF) is an oral disease-modifying therapy (DMT) for relapsing-remitting multiple sclerosis (RRMS), with well-established short- and mid-term efficacy. However, data on its long-term impact remain limited.

OBJECTIVES This study aimed to assess five-year clinical, physical, and cognitive outcomes in people with MS (pwMS) treated with DMF.

METHODS PwMS who initiated DMF in 2019 or earlier were included. Annualized relapse rate (ARR), Expanded Disability Status Scale (EDSS) scores at treatment initiation and final follow-up, and - where available - physical (Timed 25-Foot Walk [T25FW], Nine-Hole Peg Test [9HPT]) and cognitive (Symbol Digit Modalities Test [SDMT], California Verbal Learning Test-Second Edition [CVLT-II], Brief Visuospatial Memory Test-Revised [BVMT-R]) outcomes were evaluated.

RESULTS A total of 126 patients initiated DMF during the inclusion period. Treatment was discontinued by 28 patients due to lack of efficacy and by 31 patients for other reasons. Sixty-seven patients (64.2% female) remained on DMF for ≥5 years and were included in the final analysis. The mean age at disease onset was 32.75 years, mean disease duration was 12.73 years, and the average duration of DMF use was 5.87 years. EDSS scores showed no significant change over the treatment period (baseline: 1.67; year 5: 1.73; $p > 0.05$), and the ARR was 0.04. Among 28 patients with available physical performance data, no significant changes were observed in T25FW (baseline: 5.75 s; year 5: 5.79 s; $p > 0.05$) or 9HPT (baseline: 21.67 s; year 5: 21.48 s; $p > 0.05$). In contrast, all three cognitive measures showed statistically significant improvement. SDMT scores increased from 46.69 to 49.38 ($p = 0.026$); CVLT-II from 46.85 to 53.44 ($p = 0.009$); and BVMT-R from 24.96 to 27.85 ($p = 0.006$).

CONCLUSION Five-year DMF therapy in RRMS was associated with sustained disease stability, low relapse rates, and preserved physical function. Notably, cognitive performance modestly improved, suggesting a potential long-term cognitive benefit of DMF treatment.

060

Three Years Before, Three Years After: Longitudinal Outcomes of Natalizumab Therapy in Relapsing Multiple Sclerosis

Ulvi Samadzade, Orkhan Mammadov, Said Alizada, Can Caliskan, İrem Kara, Serkan Ozakbas

INTRODUCTION Natalizumab, a monoclonal antibody targeting α4-integrin, is a well-established disease-modifying therapy (DMT) for relapsing multiple sclerosis (MS).

OBJECTIVES This study assesses its long-term impact by comparing key clinical parameters and disease activity over three years before and after treatment initiation.

METHODS A retrospective analysis was conducted on 131 MS patients treated with natalizumab for at least three years (122 RRMS, 9 SPMS). Clinical outcomes, including annualized relapse rate (ARR), Expanded Disability Status Scale (EDSS) scores, and no evidence of disease activity (NEDA-3), were evaluated over two three-year periods: pre- and post-treatment.

RESULTS At baseline, the mean age was 36.47 years, and 79.4% of patients were female. Natalizumab treatment led to a 93.8% reduction in ARR, from 2.08 in the three years before treatment to 0.13 in the three years after ($p < 0.001$). EDSS remained relatively stable, with values of 1.569 pre-treatment, 1.847 at treatment initiation, and 1.466 after three years. Notably, 84% of patients achieved NEDA-3, indicating substantial disease control.

CONCLUSION Over a six-year observational period, natalizumab demonstrated robust and sustained efficacy, significantly reducing relapse rates and maintaining clinical stability. The high NEDA-3 rate (84%) underscores its potential in achieving long-term disease control and minimizing disability progression in relapsing MS.

061

Six-Year Disease Trajectory in Multiple Sclerosis: A Pre- and Post-Ocrelizumab Treatment Analysis

Ulvi Samadzade, Said Alizada, Can Caliskan, Orkhan Mammadov, İrem Kara, Serkan Ozakbas

INTRODUCTION Ocrelizumab, a humanized anti-CD20 monoclonal antibody, has been shown to effectively reduce disease activity and delay disability progression in both relapsing and progressive forms of multiple sclerosis (MS). This study aimed to evaluate the clinical trajectory of MS patients during the three years preceding and following the initiation of ocrelizumab therapy.

OBJECTIVES This study aimed to evaluate the clinical trajectory of MS patients during the three years preceding and following the initiation of ocrelizumab therapy.

METHODS We conducted a retrospective analysis of 268 people with multiple sclerosis (pwMS) treated with ocrelizumab. Patients were stratified into relapsing-remitting MS (RRMS, n=138) and progressive MS (PMS; 111 secondary progressive MS, 19 primary progressive MS; total n=130) groups. Clinical outcomes were assessed by comparing annualized relapse rates (ARR) in the three years before and after treatment initiation. Expanded Disability Status Scale (EDSS) scores were recorded at three time points: three years before treatment, at the time of initiation, and three years post-initiation. In the post-treatment period, the proportion of patients achieving no evidence of disease activity (NEDA-3) - defined as the absence of clinical relapses, confirmed disability progression, and new or enlarging MRI lesions - was also evaluated.

RESULTS The mean age of the cohort was 53.2 years (SD = 12.1), with 63.4% female. The average age at MS onset was 30.8 years (SD = 10.2), and the mean disease duration was 22.3 years (SD = 8.8). In the RRMS group, the ARR declined significantly from 0.35 (SD = 0.34) in the three years before treatment to 0.014 post-treatment ($p < .001$). EDSS scores remained stable (baseline: 3.57, SD = 1.76; year 3: 3.54, SD = 1.90; $p = .765$). In the PMS group, the ARR decreased from 0.31 (SD = 0.35) to 0.0077 (SD = 0.05) after treatment ($p < .001$), with EDSS scores showing no significant change (baseline: 6.27, SD = 0.91; year 3: 6.36, SD = 0.91; $p = .080$). Notably, NEDA-3 was achieved in 46.0% of RRMS patients and 54.6% of those with progressive MS over the three-year follow-up, highlighting the broad efficacy of ocrelizumab across different MS phenotypes.

CONCLUSION This six-year observational window reveals that ocrelizumab substantially suppresses disease activity in both relapsing and progressive MS. The therapy was associated with a marked reduction in relapse rates and stabilization of disability over time. The achievement of NEDA-3 in a considerable proportion of patients, including those with progressive forms of MS, underscores the potential of ocrelizumab to effectively modify disease trajectory even in long-standing and advanced cases.

062

Ocrelizumab Improves Visual Memory and Preserves Cognition in Progressive Multiple Sclerosis

Serkan Ozakbas, Gözde Deniz Ünal, Can Caliskan, Ulvi Samadzade

INTRODUCTION Multiple sclerosis (MS) is a chronic neurological disease characterized by both motor and cognitive decline. In the progressive forms of MS, neurodegeneration accelerates, leading to significant cognitive impairment. While the impact of disease-modifying therapies (DMTs) on physical disability is well-documented, their effects on cognitive function, especially over the long term, remain underexplored.

OBJECTIVES This study investigates cognitive and physical changes in progressive MS patients receiving Ocrevus (ocrelizumab) therapy over a three-year period, with a specific focus on visual memory performance.

METHODS A cohort of 125 progressive MS patients undergoing Ocrevus treatment was included in this study. Neurological and neuropsychological assessments were conducted at two time points, approximately three years apart. The assessment battery included the Timed 25-Foot Walk (T25FW), 9-Hole Peg Test (9HPT), Symbol Digit Modalities Test (SDMT), California Verbal Learning Test-II (CVLT-II), Brief Visuospatial Memory Test-Revised (BVMT-R), and the Expanded Disability Status Scale (EDSS). Paired-sample t-tests and effect size analyses (Cohen's d) were used to assess longitudinal changes.

RESULTS Patients ranged in age from 33 to 84 years, with a mean age of 54.82 ± 10.01 years. The average disease duration was 23.17 ± 9.95 years, with a mean age at onset of 31.66 ± 12.31 years. EDSS scores significantly increased from 5.65 to 5.82 ($p = .015$), with a small effect size (Cohen's $d = -0.226$). In contrast, BVMT-R scores improved significantly from 18.64 to 21.16 ($p < .001$), demonstrating a moderate effect size (Cohen's $d = -0.411$), indicating cognitive improvement. Other cognitive measures, including SDMT and CVLT-II, showed minor and non-significant changes, while physical performance measures (T25FW, 9HPT) demonstrated minimal fluctuations without clinical significance.

CONCLUSION This study demonstrates that Ocrevus therapy not only mitigates the progression of physical disability in progressive MS but also leads to significant cognitive improvements, particularly in visual memory. The moderate effect observed in BVMT-R, despite the concurrent progression of EDSS, reinforces the importance of cognitive assessment in routine clinical monitoring and further supports the use of Ocrevus as a comprehensive therapeutic strategy for progressive MS. Despite the worsening of physical disability as reflected by EDSS over the three-year follow-up, Ocrevus treatment led to a notable improvement in visual memory performance. The increase in BVMT-R scores suggests that cognitive decline is not inevitable in progressive MS and can potentially be mitigated through appropriate therapeutic interventions. The disconnect between physical disability and cognitive outcomes underscores the multidimensional therapeutic benefits of Ocrevus, particularly its potential to preserve cognitive function.

SECTION IX

Treatment Safety, Infections and Wearing-Off

7 ABSTRACTS

063

No Significant Association Between Lymphocyte Count and Infection Risk in Fingolimod-Treated MS Patients

Ela Zengin, Asiye Tuba Özdoğar, Yasemin Şimşek, Can Caliskan, Serkan Ozakbas

INTRODUCTION Fingolimod is an oral disease-modifying therapy (DMT) that was introduced as the first oral treatment for relapsing multiple sclerosis (MS). It works by preventing the migration of lymphocytes into the central nervous system. A known side effect of fingolimod is peripheral lymphopenia, which raises concerns about the potential increased risk of infections, including COVID-19, herpes zoster, and other pathogens. However, it remains unclear whether the degree of lymphopenia correlates with the incidence of clinically significant infections. This study aims to explore the relationship between lymphocyte count and infection risk in fingolimod-treated MS patients.

OBJECTIVES To investigate the relationship between lymphocyte count and the incidence of infections, including COVID-19, herpes zoster, and other infections, in MS patients treated with fingolimod. The study also examines whether different degrees of lymphopenia, classified by WHO grading, are associated with increased infection risk.

METHODS This retrospective cohort study included MS patients receiving fingolimod treatment. The study classified lymphocyte counts into five categories: normal (≥1000/μL), Grade 1 lymphopenia (800- 999/μL), Grade 2 lymphopenia (500-799/μL), Grade 3 lymphopenia (200-499/μL), and Grade 4 lymphopenia (<200/μL). The incidence of COVID-19, herpes zoster, and other infections was analyzed across these categories to determine any significant associations.

RESULTS The study included 1,197 MS patients. Of these, 13% (156 patients) developed COVID-19, 1.9% (23 patients) developed herpes zoster, and 23 patients had other infections. For COVID-19, no significant differences in infection incidence were observed between the lymphocyte count groups. For herpes zoster, a significantly higher incidence was found in patients with Grade 3 lymphopenia (200-499/μL) compared to other groups ($p = 0.004$). For other infections, no significant differences were found between the lymphocyte count groups.

CONCLUSION In this cohort of MS patients treated with fingolimod, no significant association was found between lymphocyte count and the overall risk of infection, including COVID-19 and other infections. Although herpes zoster was more common in patients with moderate lymphopenia (Grade 3), this trend was not observed in patients with severe lymphopenia (Grade 4). These results suggest that lymphocyte count alone is not a strong predictor of infection risk in MS patients on fingolimod. Fingolimod continues to be an effective treatment option, and vaccination against varicella-zoster virus may be an important preventive measure for those at higher risk for herpes zoster. Further studies are needed to investigate other factors contributing to infection risk in this population.

064

Viral Seroprevalence and Risk of Reactivation in MS Patients Treated with Ocrelizumab: A Real-World Cohort Study

Ela Zengin, Yasemin Şimşek, Can Caliskan, Serkan Ozakbas

INTRODUCTION Ocrelizumab, a humanized monoclonal antibody targeting CD20-positive B cells, has demonstrated efficacy in reducing disease activity in both relapsing and primary progressive multiple sclerosis (MS). Despite its clinical benefits, the immunosuppressive nature of ocrelizumab raises concerns regarding infectious complications, particularly the reactivation of hepatitis B virus (HBV). While cases of HBV reactivation have been reported in patients receiving ocrelizumab without antiviral prophylaxis, data on the potential impact of ocrelizumab on hepatitis A (HAV), hepatitis C (HCV), and human immunodeficiency virus (HIV) infections remain limited.

OBJECTIVES This study aimed to investigate the prevalence of HBV, HAV, HCV, and HIV markers in patients with MS undergoing ocrelizumab therapy and to evaluate the incidence of viral reactivation in this population.

METHODS Patients receiving ocrelizumab therapy were retrospectively evaluated. Demographic, clinical, and laboratory data were collected, including MS subtype, disease duration, disability status, and viral serologies. Patients with positive serological markers were monitored annually, and antiviral prophylaxis was administered when indicated.

RESULTS A total of 273 MS patients treated with ocrelizumab were included in the analysis. The majority were women, and relapsing-remitting MS was the most common subtype, followed by secondary progressive and primary progressive MS. The average age at treatment initiation was in the mid-forties, with a mean disease duration exceeding 16 years. Initial disability scores indicated moderate impairment, with no significant progression observed during ocrelizumab treatment. Clinical relapse activity was also markedly suppressed. In terms of viral serologies, anti-HBs positivity was detected in 7.0% of patients, while 4.4% had positive anti-HAV results. HBsAg was identified in 1.5% of patients, and 0.4% tested positive for anti-HBc total. All patients with HBV markers received antiviral prophylaxis, and no reactivation was observed during follow-up. Additionally, one patient tested positive for anti-HCV and another for anti-HIV. The HIV-positive patient received antiretroviral therapy prior to ocrelizumab initiation, and no viral complications were reported during treatment.

CONCLUSION This study emphasizes the importance of routine viral screening and individualized prophylactic strategies in MS patients receiving ocrelizumab. With proper monitoring and appropriate antiviral measures, ocrelizumab can be administered safely even in patients with positive viral serologies. These findings support the feasibility of maintaining effective MS control while minimizing infectious risks in this vulnerable population.

065

No Serological Evidence of Hepatitis or HIV Reactivation in a Real-World Cohort of MS Patients Treated with Cladribine

Ela Zengin, Yasemin Şimşek, Can Caliskan, Serkan Ozakbas

INTRODUCTION Cladribine, a purine nucleoside analogue, selectively depletes B and T lymphocytes and is an effective oral disease-modifying therapy (DMT) for relapsing multiple sclerosis (MS). While its immunosuppressive mechanism raises concerns regarding the risk of opportunistic infections, current data indicate no significant increase in infections other than herpes zoster. However, real-world data on the risk of hepatitis virus reactivation or HIV in cladribine-treated patients remain scarce and inconclusive.

OBJECTIVES To assess the serological profiles of hepatitis A, B, C, and HIV in patients with MS receiving cladribine therapy, aiming to clarify potential infectious risks in real-world clinical practice.

METHODS This was a retrospective observational study based on routine annual viral serology screening of patients diagnosed with MS and treated with cladribine at a single center. Serological markers included hepatitis B surface antigen (HBsAg), hepatitis B surface antibody (anti-HBs), hepatitis B core total antibody (anti-HBc total), hepatitis A virus antibody (anti-HAV), hepatitis C virus antibody (anti-HCV), and human immunodeficiency virus antibody (anti-HIV).

RESULTS A total of 223 patients (74.4% female; mean age: 39.9 ± 11.5 years) were included. The average disease duration was 11.4 ± 6.9 years, and the mean time since cladribine initiation was 2.7 ± 1.3 years. All patients tested negative for anti-HBc total, anti-HCV, and anti-HIV (100%). HBsAg positivity was detected in one patient (0.4%), while anti-HBs was positive in 3 patients (1.3%). Anti-HAV was positive in 4 individuals (1.8%). No cases of active hepatitis or HIV infection were found.

CONCLUSION In this real-world cohort of MS patients treated with cladribine, no serological evidence of active hepatitis B, hepatitis C, or HIV infection was observed. The absence of viral reactivation or new infections during follow-up supports the favorable infectious safety profile of cladribine in clinical settings. Nevertheless, given the immunomodulatory effects of the drug, continued vigilance through routine serological monitoring is recommended. These findings contribute valuable real-world data to the limited literature on infectious risk under cladribine therapy and may help guide clinicians in the long-term management of MS patients receiving this treatment.

066

Serological Profiles in Natalizumab-Treated Multiple Sclerosis Patients: No Alarming Signals for Hepatitis or HIV

Ela Zengin, Yasemin Şimşek, Can Caliskan, Serkan Ozakbas

INTRODUCTION Natalizumab, a humanized monoclonal antibody targeting α4-integrin, is an effective treatment for relapsing-remitting multiple sclerosis (RRMS). Although it is not broadly immunosuppressive, concerns persist regarding the risk of opportunistic viral infections, including herpesvirus encephalitis. However, limited data exist on the prevalence or reactivation of other viral infections such as hepatitis B (HBV), hepatitis C (HCV), hepatitis A (HAV), and human immunodeficiency virus (HIV) in patients receiving natalizumab. Clarifying the serological profile for these viruses is essential for informing screening and prevention strategies in clinical practice.

OBJECTIVES To investigate the hepatitis and HIV serological profiles of RRMS patients treated with natalizumab, in order to better understand the potential infectious risks associated with this therapy.

METHODS This retrospective observational study included patients with RRMS undergoing natalizumab treatment. As part of routine annual follow-up, serological evaluations were performed, including testing for hepatitis B surface antigen (HBsAg), hepatitis B surface antibody (anti-HBs), hepatitis B core total antibody (anti-HBc IgG), hepatitis A virus antibody (anti-HAV), hepatitis C virus antibody (anti-HCV), and human immunodeficiency virus antibody (anti-HIV).

RESULTS A total of 63 patients were evaluated. The majority were female (87.3%), with a mean age of 33.38 ± 6.91 years and a mean disease duration of 9.78 ± 5.40 years. The average duration of natalizumab therapy was 2.98 ± 2.91 years (range: 1-15 years). All patients tested negative for HBsAg, anti-HCV, and anti-HIV. Anti-HBs positivity was observed in 30.2% of patients, while one patient (1.6%) tested positive for anti-HBc IgG, consistent with prior exposure to HBV. The remaining 98.4% were negative for anti-HBc. HBV vaccination was documented in 28.6% of patients. Anti-HAV IgG was positive in 9.5% of the cohort, indicating past exposure or immunization.

CONCLUSION This cohort of RRMS patients receiving natalizumab therapy demonstrated no evidence of active HBV, HCV, or HIV infection, despite relatively long treatment durations. The low seroprevalence of hepatitis A and hepatitis B antibodies suggests a gap in vaccination coverage, which may pose preventable risks. These findings support the overall viral safety of natalizumab in clinical use but also emphasize the importance of systematic serological screening and timely vaccination, particularly for HBV and HAV, in order to ensure comprehensive patient care.

067

Evaluation of Hepatitis B Virus Status in Patients Treated with Rituximab: A Retrospective Cohort Study

Ulvi Samadzade, Yasemin Şimşek, Serkan Ozakbas

INTRODUCTION Rituximab, a monoclonal anti-CD20 antibody, is widely used in the treatment of autoimmune disorders such as multiple sclerosis (MS), neuromyelitis optica spectrum disorder (NMOSD), and myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD). Despite its efficacy, rituximab poses a potential risk for hepatitis B virus (HBV) reactivation, particularly in patients with prior HBV exposure. Given the clinical significance of HBV reactivation and its potential complications, understanding the HBV status of patients undergoing rituximab therapy is crucial.

OBJECTIVES This study aimed to evaluate the HBV status in patients treated with rituximab and assess the prevalence of past HBV exposure in this cohort.

METHODS Seventy-three patients who had received at least one cycle of rituximab for MS, NMOSD, or MOGAD were retrospectively analyzed. Data collection focused on demographic characteristics, disease-related factors, and HBV serological status. Patients were categorized based on HBV infection status into two groups: those with resolved HBV infection (anti-HBc IgG-positive but HBsAg-negative) and those without HBV infection (HBsAg-negative and anti-HBc IgG-negative). Additionally, vaccination history was recorded to identify patients with vaccine-induced immunity.

RESULTS Among the 73 patients, 15 had MS, 52 had NMOSD, and 6 had MOGAD. The majority of NMOSD patients were female (78.8%), while females represented 53.4% of the MS group and 33.4% of the MOGAD group. The mean age at disease onset was 33.68 (±12.86) years, with a mean disease duration of 11.5 (±9.3) years. The average duration of rituximab treatment was 2.6 (±2.24) years. Notably, 36.5% of NMOSD patients were seropositive for AQP4-Ab. Regarding HBV status, no patients tested positive for HBsAg, anti-HIV, or anti-HCV antibodies. Only one patient (1.3%) had resolved HBV infection, characterized by anti-HBc IgG and anti-HBs positivity. Among HBV-naïve patients, 19 had received HBV vaccination (anti-HBs-positive), while 53 had no history of HBV infection or vaccination (anti-HBs-negative). No cases of acute HBV infection, chronic HBV infection, or occult HBV carriers were identified in this cohort.

CONCLUSION This study underscores the low prevalence of HBV infection in rituximab-treated patients with MS, NMOSD, and MOGAD. While our findings suggest a minimal risk of HBV reactivation in this population, routine HBV screening remains essential, especially in regions with higher HBV endemicity. Future prospective studies are needed to further evaluate the long-term safety of rituximab in patients with prior HBV exposure.

068

Patient-Reported Symptom Fluctuations Between Ocrelizumab Infusions: Wearing-Off or Symptomatic Effect?

Ulvi Samadzade, Sumeyye Cevik, Yasemin Şimşek, Can Caliskan, İrem Kara, Serkan Ozakbas

INTRODUCTION Ocrelizumab, a monoclonal anti-CD20 antibody, is an effective immunomodulatory treatment for both relapsing and progressive forms of MS. While its efficacy in controlling disease activity has been well documented, a subset of patients report transient symptom worsening prior to scheduled infusions.

OBJECTIVES To assess the frequency and clinical features of patient-reported symptom worsening prior to Ocrelizumab infusions, and to investigate whether these fluctuations correlate with fatigue, quality of life, and measures of disability - while also considering the possibility of a transient symptomatic effect rather than a true wearing-off phenomenon.

METHODS Patients with and without wearing-off were compared regarding age, disease duration, fatigue levels, EDSS, annualized relapse rate (ARR), number of relapses, components of the EQ-5D-3L quality of life scale, depression and anxiety scores, and responses to a six-item original survey.

RESULTS The mean age of participants was 46.84 ± 12.60 years; disease duration averaged 17.21 ± 9.17 years, Ocrelizumab use 3.88 ± 1.99 years, and time from symptom onset to diagnosis 3.78 ± 6.14 years. Symptom fluctuations prior to Ocrelizumab infusions were reported by 52 patients (24.8%). Ocrelizumab use duration was significantly longer in this group ($p = 0.002$), but no differences were found in age, sex, disease duration, EDSS, ARR, or fatigue scores ($p > 0.05$). The “usual activities” domain of EQ-5D-3L was significantly lower in this group ($p = 0.016$). EDSS significantly improved from baseline to the last 6 months ($p < 0.001$), while ARR and relapse rate changes were not significant ($p = 0.070$ and $p = 0.083$). No association was found between MS subtype and symptom fluctuations ($p = 0.324$). Among those reporting symptoms, fatigue was most common (78.8%), followed by balance problems (7.7%), gait difficulty (5.8%), sensory symptoms (5.8%), and cognitive issues (1.9%). All described symptoms as moderate and lasting over four weeks. Post-infusion recovery occurred within 1-6 days in 17.3%, 1-2 weeks in 21.2%, 3-4 weeks in 57.7%, and after 5+ weeks in 3.8%.

CONCLUSION Approximately one in four patients receiving Ocrelizumab reported a subjective worsening of symptoms prior to scheduled infusions. These fluctuations, most commonly characterized by fatigue and reduced daily functioning, were not associated with clinical disease activity or relapse. The findings suggest a possible symptomatic effect of Ocrelizumab that may wear off between doses, though a true biological wearing-off cannot be confirmed within the limits of a retrospective design.

069

Not a Relapse, Not Stable: Characterizing the Wearing-Off Window in Multiple Sclerosis Patients on Natalizumab

Ulvi Samadzade, Can Caliskan, Yasemin Şimşek, İrem Kara, Sumeyye Cevik, Serkan Ozakbas

INTRODUCTION Natalizumab, a monoclonal antibody that inhibits leukocyte migration across the blood-brain barrier, is an effective treatment for relapsing multiple sclerosis. However, some individuals report transient symptom worsening in the days leading up to their next infusion, followed by rapid improvement post-infusion - a clinical pattern consistent with the wearing-off phenomenon. Although not linked to relapses or MRI activity, this phenomenon may affect daily functioning, patient satisfaction, and perceived treatment efficacy.

OBJECTIVES To compare clinical, functional, and patient-reported outcomes between patients experiencing wearing-off and those who do not, and to characterize the timing, severity, and nature of symptoms in affected individuals.

METHODS Patients with relapsing multiple sclerosis receiving natalizumab were divided into two groups based on self-reported symptom worsening in the final week prior to infusion and resolution shortly thereafter. Data collected included demographic variables, disease duration, age at onset, EDSS scores, relapse history, fatigue scores, responses to a six-item original questionnaire, and components of the EQ-5D-3L.

RESULTS The study included 66 patients (15 with wearing-off symptoms and 51 without). There were no significant differences between groups in age, disease duration, age at onset, EDSS scores, fatigue levels, or quality of life parameters. In the wearing-off group, all patients (100%) reported moderate symptom severity, typically beginning one week before infusion. Most frequently reported symptoms were fatigue (40.0%) and weakness (33.3%), followed by sensory disturbances, dizziness, and leg spasms. While 60.0% of patients noted improvement within a few days, 40.0% reported recovery shortly after infusion. All wearing-off patients (100%) expressed a perceived need for earlier infusions. A significant overall improvement in EDSS scores was observed during treatment ($p < 0.001$), independent of wearing-off status.

CONCLUSION The wearing-off phenomenon in patients receiving natalizumab appears to represent a reversible symptomatic fluctuation, rather than sustained disease progression. Despite the absence of measurable differences in disability, fatigue, or quality of life scores, the consistent timing and nature of these symptoms - and their resolution post-infusion - suggest a potential short-lived functional decline tied to the pharmacodynamics of natalizumab. While its mechanism remains uncertain, recognizing this phenomenon may improve patient counseling, treatment satisfaction, and potentially guide individualized infusion intervals. Further investigation is warranted to determine whether this represents an unrecognized symptomatic benefit of natalizumab that extends beyond its established role in relapse prevention.

SECTION X

COVID-19 Pandemic

3 ABSTRACTS

070

The Shadow of the Pandemic: Long-Term Disability Patterns in People with Multiple Sclerosis

Serkan Ozakbas, Yasemin Şimşek, Can Caliskan, Tuncay Basaran, Ulvi Samadzade

INTRODUCTION The COVID-19 pandemic may have disrupted both the clinical course of multiple sclerosis (MS) and its ongoing management. Understanding the long-term effects of the pandemic on disability progression is critical for adapting treatment strategies in the post-pandemic era.

OBJECTIVES To evaluate the changes in disability progression among people with MS (pwMS) before and after the COVID-19 pandemic using Expanded Disability Status Scale (EDSS) scores, and to identify the factors associated with disability worsening during the post-pandemic period.

METHODS This cross-sectional cohort study focused on changes in disability status before and after the pandemic period. From a larger population of 4,191 pwMS followed at our center, two matched groups were selected for comparison: those with a confirmed history of COVID-19 infection and those without. EDSS scores were used to evaluate disability progression, and demographic and clinical factors potentially associated with worsening disability were also analyzed.

RESULTS A total of 1,292 pwMS were included in the analysis: 646 individuals in the COVID-19 group and 646 in the control group. In the COVID-19 group, 69.3% were female (n = 448), with a mean age of 44.41 years (SD = 11.58) and mean disease duration of 13.12 years (SD = 8.29). The mean EDSS score decreased slightly from 1.91 (SD = 2.12) pre-pandemic to 1.86 (SD = 2.21) post-pandemic, a statistically significant reduction ($p = 0.038$). Older age ($p = 0.01$) and longer disease duration ($p = 0.01$) were associated with EDSS worsening, while age at disease onset was not ($p = 0.507$). In the control group, the mean EDSS score declined from 1.97 (SD = 1.96) to 1.80 (SD = 2.08) after the pandemic, also a significant change ($p < 0.001$), with a mean reduction of 0.176 points. However, when comparing the overall EDSS change between the two groups, no statistically significant difference was observed ($p > 0.05$).

CONCLUSION Contrary to initial concerns, COVID-19 infection did not appear to accelerate disability progression in pwMS. Both groups exhibited a slight but statistically significant reduction in EDSS scores following the pandemic, possibly reflecting broader changes in care accessibility, lifestyle adjustments, or healthcare delivery during this period. Importantly, age and disease duration, rather than COVID-19 status, emerged as key predictors of disability worsening. These findings highlight the resilience of pwMS in the face of a global health crisis and underscore the need for continued individualized care strategies, particularly for older patients and those with longer disease duration.

071

Emerging Comorbidities and Malignancies in People with Multiple Sclerosis After the COVID-19 Pandemic: A Comparative Study

Can Caliskan, Ergi Kaya, Yasemin Şimşek, Serkan Ozakbas

INTRODUCTION The COVID-19 pandemic has presented unprecedented challenges to healthcare systems and vulnerable populations, including people with multiple sclerosis (pwMS). As the pandemic unfolded, concerns emerged regarding its potential long-term impact on the overall health profile of pwMS. This study aimed to explore whether a history of COVID-19 infection was associated with differences in the frequency and types of newly reported comorbidities and malignancies in this population.

OBJECTIVES To investigate the spectrum and frequency of comorbidities and malignancies reported after the COVID-19 pandemic among pwMS with and without a history of COVID-19 infection.

METHODS This retrospective study included pwMS with and without a history of COVID-19 infection, selected from a large cohort regularly followed at a tertiary MS center. Age- and sex-matched groups were formed to allow for appropriate comparisons.

RESULTS The study included 646 pwMS with confirmed COVID-19 and 646 pwMS without a history of COVID-19. In the COVID-19 group, 69.3% were female (n = 448), and the mean age was 44.41 years (SD = 11.58). The average disease duration was 13.12 years (SD = 8.29), and the mean age at MS onset was 31.29 years (SD = 9.12). In this group, a total of 194 comorbidities were identified: psychiatric disorders (n = 65; 25.2%), neurological disorders (n = 61; 23.6%), cardiovascular diseases (n = 32; 12.4%), endocrine/metabolic disorders (n = 17; 6.6%), respiratory diseases (n = 10; 3.9%), rheumatologic/autoimmune diseases (n = 5; 1.9%), and gynecological/urogenital conditions (n = 4; 1.6%). In the control group, 293 comorbidities were reported: neurological disorders (n = 61; 16.9%), psychiatric disorders (n = 25; 6.9%), cardiovascular diseases (n = 20; 5.5%), endocrine/metabolic disorders (n = 17; 4.7%), and respiratory diseases (n = 7; 1.9%). Although the total comorbidity burden appeared numerically higher in the control group, there was no statistically significant difference between the groups (p = 0.063). Regarding malignancies, 16 cancer cases (2.5%) were identified in the COVID-19 group. Breast cancer was the most frequent (n = 7; 43.8%), followed by thyroid cancer, invasive ductal carcinoma, colorectal cancer, laryngeal cancer, cervical cancer, prostate cancer, lymphoma, and ovarian cancer (n = 1 each; 6.3%). In the control group, 7 malignancy cases (1.1%) were reported, including breast cancer (n = 5; 71.4%) and colorectal cancer (n = 2; 28.6%).

CONCLUSION The findings indicate a possible shift in comorbidities and malignancies among pwMS after the COVID-19 pandemic. While not statistically significant, the higher frequency and variety of conditions in those with prior infection highlight potential emerging risks. These results emphasize the need for ongoing, multidisciplinary follow-up focused on both physical and mental health in the post-pandemic period.

072

Tracing the Long-Term Motor and Cognitive Impact of COVID-19 in Multiple Sclerosis: A Four-Year Within-Subject Controlled Study

Ulvi Samadzade, Can Caliskan, Gözde Deniz Ünal, İrem Kara, Serkan Ozakbas

INTRODUCTION The COVID-19 pandemic has presented significant health challenges worldwide, especially for individuals with chronic neurological disorders such as multiple sclerosis.

OBJECTIVES This study aimed to investigate the effects of COVID-19 infection on motor and cognitive functions in people with MS by comparing their performance two years before and two years after the infection. To ensure accuracy, only patients with motor and cognitive assessments at these two time points were included, allowing for a within-subject longitudinal comparison.

METHODS Participants were categorized into two groups: MS patients with confirmed COVID-19 infection (COVID-MS) and MS patients without COVID-19 (control-MS). The COVID-MS group included individuals with motor and cognitive assessments approximately two years prior to and two years following COVID-19 infection. The control-MS group consisted of patients without COVID-19 who had comparable assessments spaced approximately four years apart, matching the timeline of the COVID-MS group. Motor functions were evaluated using the Timed 25-Foot Walk and the Nine-Hole Peg Test. Cognitive functions were assessed by the Symbol Digit Modalities Test, California Verbal Learning Test, and Brief Visuospatial Memory Test-Revised.

RESULTS In the COVID-MS group, motor performance declined significantly over the study period, with Timed 25-Foot Walk duration increasing from 17.99 seconds two years before infection to 23.96 seconds two years after ($p = 0.014$). The control-MS group showed stable performance over the comparable period (18.21 to 18.44 seconds, $p = 0.612$). Nine-Hole Peg Test times increased slightly in the COVID-MS group (29.88 to 31.42 seconds, $p = 0.091$), while remaining stable in controls (28.76 to 28.95 seconds, $p = 0.735$). Cognitive test scores in the COVID-MS group improved significantly over the same interval: Symbol Digit Modalities Test increased from 41.8 to 45.9 ($p = 0.019$), California Verbal Learning Test from 48.4 to 52.1 ($p = 0.028$), and Brief Visuospatial Memory Test-Revised from 19.2 to 22.7 ($p = 0.002$). The control group showed smaller, non-significant cognitive changes over the four-year interval.

CONCLUSION Comparing assessments two years before and two years after COVID-19 infection, the findings indicate a significant decline in motor function in people with multiple sclerosis following COVID-19, while no comparable decline was observed in the matched control group over the same time frame. Cognitive improvements observed in the COVID-MS group likely represent practice effects rather than genuine recovery. These results underscore the additional risk COVID-19 infection poses for motor deterioration in MS patients and highlight the importance of longitudinal monitoring and targeted interventions following systemic infections in this vulnerable population.

SECTION XI

Neuromyelitis Optica Spectrum Disorder and MOGAD

5 ABSTRACTS

073

Impact of First Demyelinating Event Severity on Long-Term Disability in Neuromyelitis Optica Spectrum Disorder: A Retrospective Cohort Study

Ergi Kaya, Yasemin Şimşek, Serkan Ozakbas

INTRODUCTION Neuromyelitis optica spectrum disorder (NMOSD) is characterized by relapsing demyelinating events of the central nervous system that can range from mild to severely disabling or even life-threatening. Although inflammatory activity is a hallmark of NMOSD, the relationship between the severity of the first demyelinating event and long-term clinical outcomes remains unclear.

OBJECTIVES To investigate whether the severity of the first demyelinating event in NMOSD is associated with subsequent relapse activity and long-term disability.

METHODS This retrospective cohort study included 57 patients diagnosed with NMOSD. The severity of the initial demyelinating episode was categorized based on the Expanded Disability Status Scale (EDSS): mild (0-3.0), moderate (3.5-5.5), and severe (≥6.0). Demographic and clinical data -including age at onset, follow-up duration, EDSS at the last visit, number of relapses after the first event, treatment type, and treatment duration-were analyzed using appropriate statistical methods.

RESULTS A total of 57 patients (73.6% female; mean age: 36.67 ± 13.64 years) were included. Aquaporin-4 antibodies were positive in 24 patients, MOG antibodies in 2, and 31 seronegative patients. The first demyelinating event was classified as mild in 35 patients, moderate in 11, and severe in 11. No significant differences were observed among the severity groups in terms of gender, age, total follow-up duration, treatment type or duration, or NMOSD subtype ($p > 0.05$). Relapse rates following the first event were also similar across the three groups ($p > 0.05$). However, the EDSS score at the last visit remained significantly higher in those with initially moderate or severe relapses (median [IQR]: severe: 6.0 [2.5], moderate: 1.5 [1.5], mild: 1.0 [2.0]; $p < 0.01$).

CONCLUSION Although the severity of the first demyelinating event was not associated with future relapse rates, it was significantly related to long-term disability in NMOSD patients. This suggests that even a single severe attack may have lasting consequences on neurological function. Therefore, early identification of severe initial episodes and timely initiation of effective immunotherapy are crucial for minimizing irreversible damage and optimizing long-term outcomes. These findings highlight the importance of individualized treatment strategies based not only on serostatus and relapse frequency but also on the clinical severity of disease onset.

074

Impact of Aquaporin-4 Serostatus on Disease Activity and Disability in NMOSD: A Five-Year Comparative Study

Ergi Kaya, Yasemin Şimşek, Serkan Ozakbas

INTRODUCTION Neuromyelitis optica spectrum disorder (NMOSD) is a rare, relapsing demyelinating disease of the central nervous system. It includes aquaporin-4 antibody-positive (AQP4+) NMOSD, myelin oligodendrocyte glycoprotein antibody-associated disease, and seronegative NMOSD (SN-NMOSD). Although these subtypes may exhibit similar clinical presentations, comparative data on their prognosis are still limited.

OBJECTIVES To investigate the clinical and prognostic differences between AQP4+ and SN-NMOSD patients during the first five years following diagnosis.

METHODS This retrospective cohort study included 70 NMOSD patients (37 AQP4+, 33 SN-NMOSD). Data collected comprised age at diagnosis, sex, time from first symptom to diagnosis, localization of the first symptom, baseline Expanded Disability Status Scale (EDSS) scores, baseline relapse count, treatment type and duration, total relapse count and EDSS scores at 2 and 5 years, radiological activity during follow-up, and No Evidence of Disease Activity-3 (NEDA-3) status at the second and fifth years. Comparative analyses were performed using appropriate statistical methods.

RESULTS Among the 70 participants (81.4% female; mean age 38.4 ± 12.9 years), no significant differences were found between the AQP4+ and SN-NMOSD groups in terms of age at diagnosis, sex, time to diagnosis, first symptom localization, treatment type, or treatment duration ($p > 0.05$). However, the AQP4+ group had significantly higher baseline EDSS scores, and relapse counts compared to the SN-NMOSD group (EDSS: median 3.0 [IQR 2.75] vs. 2.0 [IQR 0.75], $p = 0.003$; baseline relapse count: 2.0 [IQR 2.0] vs. 2.0 [IQR 1.0], $p = 0.046$). No significant differences were observed between groups in relapse count, MRI activity, or NEDA-3 status at 2 and 5 years ($p > 0.05$). Nonetheless, a trend toward greater long-term disability persisted in the AQP4+ group.

CONCLUSION Although relapse frequency and radiological activity during the five-year follow-up were comparable, AQP4+ NMOSD patients demonstrated a more aggressive disease course at baseline, with higher relapse burden and disability scores compared to those with SN-NMOSD. These findings highlight the importance of early diagnosis and appropriate treatment strategies tailored to serostatus to mitigate long-term disability, particularly in AQP4+ patients.

075

Beyond Relapse Control: A Closer Look at the Wearing-Off Phenomenon in Patients Receiving Rituximab for Neuromyelitis Optica and Myelin Oligodendrocyte Glycoprotein Antibody-Associated Disease

Ulvi Samadzade, Yasemin Şimşek, Can Caliskan, İrem Kara, Sumeyye Cevik, Ela Zengin, Serkan Ozakbas

INTRODUCTION Rituximab, an anti-CD20 monoclonal antibody, is widely used to prevent relapses in neuromyelitis optica spectrum and myelin oligodendrocyte glycoprotein antibody-associated disease. A subset of patients receiving rituximab reports transient worsening of symptoms in the weeks leading up to the next scheduled infusion, with subsequent improvement following re-dosing - a pattern known as the wearing-off phenomenon. This study explores the clinical relevance of this phenomenon and its association with functional and patient-reported outcomes.

OBJECTIVES To compare clinical and functional outcomes between patients with and without the wearing-off phenomenon and assess its association with relapse rate, EDSS, fatigue, and quality of life.

METHODS Patients were classified based on transient symptoms worsening before rituximab infusion and improvement after re-dosing. Data included demographics, disease duration, age at onset, rituximab duration, time to diagnosis, EDSS, relapse count, fatigue scores, EQ-5D-3L, and responses to a six-item questionnaire.

RESULTS The study included 31 patients (26 with neuromyelitis optica [83.9%], 5 with MOGAD [16.1%]). Mean age was 42.13 ± 11.25 years; disease duration averaged 6.32 ± 6.26 years. Rituximab was used for 2.68 ± 2.07 years. EDSS significantly improved from 2.90 ± 1.86 at treatment start to 1.79 ± 1.35 in the last six months ($p < 0.001$). Ten patients (32.3%) experienced wearing-off symptoms - mostly fatigue/weakness (n=5), sensory issues (n=2), gait problems (n=1), and others (n=1). Symptoms emerged ~1 month pre-infusion and resolved within 1-2 weeks post-infusion. Among them, 69.2% felt the need for earlier dosing. Fatigue scores were higher in this group (19.13 ± 7.79 vs. 15.25 ± 6.09), though not significant. Relapse frequency did not change significantly ($p = 0.625$).

CONCLUSION While rituximab is effective in reducing relapses and improving long-term disability in neuromyelitis optica and myelin oligodendrocyte glycoprotein antibody-associated disease, the wearing-off phenomenon - defined by transient symptom worsening shortly before scheduled infusions and subsequent improvement thereafter - may reflect a reversible symptomatic fluctuation rather than true disease activity. These subtle deteriorations, although not captured by relapse-based metrics, can impact patients' daily functioning and treatment satisfaction. Recognizing and addressing this phenomenon may help optimize infusion intervals and prompt further exploration of rituximab's potential symptomatic effects beyond its immunomodulatory role.

076

Characterizing Pain in Neuromyelitis Optica Spectrum Disorder: Prevalence and Clinical Features

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INTRODUCTION Chronic pain is a common symptom that impairs activities of daily living in persons with Neuromyelitis Optica Spectrum Disorder (NMOSD, pwNMOSD). The higher the intensity of pain in pwNMOSD, the worse the physical and emotional quality of life is affected.

OBJECTIVES To determine the prevalence and characteristics of pain in pwNMOSD.

METHODS This cross-sectional study involved a total of 62 pwNMOSD. The Nordic Musculoskeletal Questionnaire (NMQ) was used to determine the participants' pain levels and pain localization. The PainDETECT Questionnaire (PD-Q) was used to differentiate between nociceptive and neuropathic pain. The scores ≤ 12 were considered as presence of musculoskeletal pain and >12 as neuropathic pain. The Preference-Based Multiple Sclerosis Index (PBMSI) was used to measure health-related quality of life. Information such as Expanded Disability Status Scale (EDSS), disease duration and age of the participants were also recorded.

RESULTS The 62 participants included in the study were divided into 3 groups: 14 without pain, 17 with Musculoskeletal Pain (MSP) and 31 with Neuropathic Pain (NP). There was no difference between the groups in terms of age, disease duration and EDSS scores ($p>0.05$). When the pain distribution was analyzed, the regions with the most pain complaints in the last 12 months were neck (n=22, 34.9%), foot-ankle (n=16, 25.4%) and back (n=15, 25.8%), respectively. The frequency of pain sites that prevented work in the last 12 months were neck (n=9, 14.3%), back (n=7, 11.1%) and foot-ankle (n=7, 11.1%). The most common areas of pain in the last 7 days were neck (n=19, 30.2%), foot-ankle (n=16, 25.4%) and back (n=14, 22.2%). When the quality of life of the three groups were compared, there was a difference between PBMSI-Walk, PBMSI-Fatigue and total score. As a result of post-hoc analysis, there was a difference between MSP (0.08±0.23) and NP (0.38±0.40) for PBMSI-Walking. For PBMSI-Fatigue, there was a difference between MSP (0.19±0.28) and NP (0.56±0.35), NP (0.56±0.35) and no pain (0.23±0.39) groups. For the total score, there was a difference between MSP (0.90±0.14) and NP (0.65±0.25), NP (0.65±0.25) and no pain (0.85±0.27) groups.

CONCLUSION The results of this study showed that the neck, back, and foot-ankle were the most common and most disabling pain areas in pwNMOSD, regardless of the age, disease duration, and EDSS score of the participant. However, there was a difference between the groups in the parameters related to gait, fatigue and total quality of life against neuropathic pain.

077

Pregnancy and Disease Activity in Neuromyelitis Optica Spectrum Disorder: A Retrospective Study of Relapse Burden and Disability Progression

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INTRODUCTION Neuromyelitis optica spectrum disorder (NMOSD) is a relapsing inflammatory condition of the central nervous system that predominantly affects women during their reproductive years. The relationship between pregnancy and disease activity is of particular clinical importance, as pregnancy may influence relapse rates and long-term disability outcomes.

OBJECTIVES This study aimed to evaluate the impact of pregnancy on disease activity and disability in individuals with NMOSD by comparing clinical characteristics and relapse profiles before and after pregnancy, as well as assessing changes in EDSS scores.

METHODS This retrospective study included individuals diagnosed with NMOSD from our cohort. Participants were divided into three groups according to pregnancy history: those who became pregnant after their NMOSD diagnosis, those who became pregnant before diagnosis, and those who never became pregnant. Demographic data, age at disease onset, duration of disease, EDSS scores (initial and final), total and pregnancy-related relapses, annualized relapse rates (ARR), and maternal age at delivery were analyzed and compared between groups.

RESULTS Among the 71 participants, 25 (35.2%) had a history of pregnancy. The mean age was 47.63 ± 15.45 years (range: 23-85), and the mean age at disease onset was 37.18 ± 14.27 years. Disease duration averaged 7.45 ± 6.56 years. The mean EDSS score at disease onset was 3.56 ± 2.15, and the final EDSS score was 2.68 ± 2.42. There were no significant differences between the three groups in terms of final EDSS scores or total number of relapses ($p > 0.05$ for both). Among the 25 individuals with a pregnancy history, a significant increase was observed in relapse activity following pregnancy. The mean number of relapses rose from 0.56 ± 1.19 before pregnancy to 2.64 ± 2.45 after pregnancy ($p < 0.05$), and the ARR increased from 0.0226 ± 0.05 to 0.1925 ± 0.25 ($p < 0.05$). Despite this increase in disease activity, most patients did not experience worsening in disability. EDSS worsening, defined as an increase in score over time, was observed in 12 individuals (16.9%). This included 3 patients (4.2%) who became pregnant before their diagnosis and 9 patients (12.7%) who had never been pregnant. Notably, none of the patients who became pregnant after being diagnosed with NMOSD showed EDSS worsening. However, the difference between groups regarding disability progression did not reach statistical significance ($p > 0.05$).

CONCLUSION Although relapse activity significantly increased after pregnancy in individuals with NMOSD, the majority did not experience a corresponding progression in disability. This suggests that with proper monitoring and individualized treatment, pregnancy may not worsen long-term outcomes. These findings highlight the importance of multidisciplinary care and preconception counseling in women with NMOSD planning pregnancy.