RESEARCH ASSOCIATION

ABSTRACT BOOK

# 2024

*Multiple Sclerosis Study Group Research Abstracts*

50 abstracts · 10 thematic sections

# Contents

SECTION I

# Cognitive Function and Its Assessment

9 ABSTRACTS

001

# Is Cognitive Impairment a Predictor of Physical Disability Progression in Multiple Sclerosis Over a Five-Year Period?

Zuhal Abasıyanık, Pinar Yigit, İrem Kara, Gözde Deniz Ünal, Serkan Ozakbas

INTRODUCTION Understanding the relationship between cognitive impairment (CI) and the progression of physical disability in multiple sclerosis (MS) is critical to improving long-term management strategies.

OBJECTIVES To investigate the effect of CI on physical functions over five years in persons with MS (pwMS).

METHODS We enrolled 117 pwMS and 43 healthy controls (HC). Cognitive outcomes were the Symbol Digit Modalities Test (SDMT), California Verbal Learning Test-II (CVLT-II), and Brief Visuospatial Memory Test Revise (BVMT-R). Baseline CI was defined as below 1.5 standard deviations for HC in these three cognitive tests, and impairment in one test was considered a CI. Furthermore, in order to assess the physical status within the MS cohort at baseline, as well as to discern any subsequent deterioration in physical functioning by the fifth year, evaluations encompassing the Expanded Disability Status Scale (EDSS), Timed 25-Foot Walk (T25FW), 6-Minute Walk Test (6MWT), and 9-Hole Peg Test (9HPT) were administered. Repeated measures ANOVA was conducted to investigate time (at baseline vs. fifth years) and group (CI vs. non-CI) effects.

RESULTS A total of 51 individuals with MS, accounting for 43.6% of the sample, were categorized as having cognitive impairment (CI), with a mean Expanded Disability Status Scale (EDSS) score of 1.88 (±1.53). Conversely, 66 individuals with MS (56.4%) did not exhibit cognitive impairment, with a mean EDSS score of 1.36 (±1.33). Notably, impairment observed in the SDMT related to deteriorated performance on the T25FW ($p=0.05$, $\eta p2{:}0.034$), the 9HPT ($p=0.018$, $\eta p2{:}0.052$), and EDSS scores ($p=0.013$, $\eta p2{:}0.057$). In contrast, participation in the CVLT-II was associated with 9HPT performance ($p=0.02$, $\eta p2{:}0.05$), while involvement in the BVMT-R was linked to T25FW outcomes ($p=0.029$, $\eta p2{:}0.042$). Furthermore, individuals demonstrating CI overall exhibited diminished 9HPT performance over the course of five years ($p=0.05$, $\eta p2{:}0.035$).

CONCLUSION Our findings underscore the substantial impact of cognitive impairment on the progression of physical function among MS patients over a five-year duration, underscoring the necessity for comprehensive assessment and management of both cognitive and physical facets of MS for long-term care.

002

# Improving Cognitive Impairment Detection in Multiple Sclerosis: A Focus on the California Verbal Learning Test-Second Edition

İrem Kara, Gözde Deniz Ünal, Pinar Yigit, Zuhal Abasıyanık, Ela Zengin, Serkan Ozakbas

INTRODUCTION The California Verbal Learning Test-Second Edition (CVLT-II) is a widely utilized assessment tool in both clinical and research settings. It aims to evaluate various aspects of cognitive psychology, such as repetition learning, serial position effects, semantic organization, intrusions, and proactive interference. Given that individuals with multiple sclerosis (pwMS) commonly experience difficulties with episodic memory, the CVLT-II is highly recommended for assessing cognitive function in this population.

OBJECTIVES This study seeks to investigate the potential for improvements in the CVLT-II to enhance the detection of cognitive impairment (CI) in pwMS.

METHODS A cohort of 387 pwMS and 40 healthy controls (HCs) underwent assessment using an extended version of the CVLT-II, completing additional practice trials until mastery was achieved in recalling all words. The cut-off value for CI was determined a s 1.5 standard deviations below the mean based on data from the 40 HCs. Individuals performing below this threshold were classified as cognitively impaired.

RESULTS Among the 387 pwMS, CI was detected in one individual when the original version of the CVLT-II was applied, while the extended version identified impairment in 16 individuals. This discrepancy in impairment detection between the original and extended practices of the CVLT-II was found to be statistically significant ($p<.05$).

CONCLUSION The administration of the extended version of the CVLT-II yielded reliable and more frequent detection of CI in episodic memory among pwMS. These findings underscore the importance of utilizing comprehensive assessment tools like the extended CVLT-II in clinical practice to improve the detection and understanding of CI in MS. Further research and refinement of cognitive assessment techniques are warranted to enhance our ability to accurately detect and monitor cognitive dysfunction in pwMS.

003

# Evaluating Cognitive Impairment Detection in Multiple Sclerosis: Advancements in the Brief Visuospatial Memory Test-Revised

İrem Kara, Gözde Deniz Ünal, Pinar Yigit, Zuhal Abasıyanık, Serkan Ozakbas

INTRODUCTION Cognitive impairment (CI) poses a prevalent and concerning challenge in the context of multiple sclerosis (MS). Among the various assessment tools available, the Brief Visuospatial Memory Test - Revised (BVMT-R) stands out as a widely utilized and standardized instrument for evaluating visuospatial learning and memory capacities in both research and clinical settings.

OBJECTIVES The aim of this study is to investigate the potential for enhancements in the BVMT-R to improve the detection of CI in persons with MS (pwMS).

METHODS A cohort comprising 500 pwMS and 40 healthy controls (HCs) underwent assessment using an extended version of the BVMT-R, engaging in practice trials until mastery was achieved in accurately reproducing all drawings. The cut-off value for CI was established as 1.5 standard deviations below the mean based on data obtained from the 40 HCs. Individuals performing below this threshold were classified as cognitively impaired.

RESULTS Among the 500 pwMS, CI was identified in six individuals when the original version of the BVMT-R was applied, whereas the extended version revealed CI in 75 individuals. This discrepancy in impairment detection between the original and extended practices of the BVMT-R was found to be statistically significant ($p<.05$).

CONCLUSION The administration of the extended version of the BVMT-R yielded reliable and more frequent detection of CI in visuospatial learning and memory among pwMS. These findings underscore the importance of employing comprehensive assessment tools like the extended BVMT-R in clinical practice to enhance the detection and understanding of CI in MS. Further research and refinement of cognitive assessment techniques are warranted to improve our ability to accurately detect and monitor cognitive dysfunction in pwMS.

004

# Enhancing Cognitive Impairment Detection in Multiple Sclerosis: Exploring More Sensitive Measurement Tools

Serkan Ozakbas, İrem Kara, Gözde Deniz Ünal, Pinar Yigit, Zuhal Abasıyanık

INTRODUCTION Cognitive impairment (CI) is a pervasive feature of multiple sclerosis (MS) that affects individuals across all stages of the disease. Over time, individuals with MS (pwMS) commonly experience diminished cognitive functioning, which can significantly impact their quality of life and functional independence. The development of standardized cognitive assessment tools, such as the Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS), has facilitated the screening and detection of CI in clinical settings. The utilization of the BICAMS battery has enabled clinicians to reliably identify CI in pwMS.

OBJECTIVES The aim of this study is to investigate the potential for improving the detection of CI in pwMS through enhancements in measurement tools.

METHODS This study enrolled 246 pwMS and 40 healthy controls (HCs) who underwent assessment using an extended version of the BICAMS battery. In the extended version, participants completed additional practice trials for each cognitive test until mastery was achieved: all symbols were counted for the Symbol Digit Modalities Test (SDMT), all words were remembered for The California Verbal Learning Test-Second Edition (CVLT-II), and all drawings were made correctly for the Brief Visuospatial Memory Test-Revised (BVMT-R). The cut-off value for each test was determined as 1.5 standard deviations below the mean based on data from the 40 HCs. Individuals performing below this threshold were classified as having CI in the respective domain. Severity of CI was categorized based on the number of affected domains.

RESULTS Application of the original version of the BICAMS battery revealed single-domain impairment in three out of 246 pwMS, two-domain impairment in three individuals, and no detection of three-domain impairment. Conversely, utilization of the extended version identified single-domain perturbations in thirty-five pwMS, two-domain impairments in seven individuals, and three-domain impairments in five participants. Statistical analysis demonstrated a significant difference in CI detection between the original and extended practice of BICAMS ($p<.05$).

CONCLUSION Implementation of the full version of the SDMT and increased trial repetitions in CVLT-II and BVMT-R resulted in a higher prevalence of CI among pwMS. These findings suggest that the extended version of the BICAMS battery allows for more precise detection of CI, enabling earlier intervention to prevent cognitive decline progression.

005

# Enhancing Cognitive Impairment Detection in Multiple Sclerosis: Exploring the Symbol Digit Modalities Test

İrem Kara, Gözde Deniz Ünal, Pinar Yigit, Zuhal Abasıyanık, Serkan Ozakbas

INTRODUCTION The Symbol Digit Modalities Test (SDMT) is widely recognized as a highly sensitive measure for detecting cognitive impairment in individuals with multiple sclerosis (pwMS). It is renowned for its ability to assess a range of cognitive processes, including visual processing and learning, making it a comprehensive screening tool. Given its extensive use in both clinical and research settings related to MS, it is crucial to delve deeper into the cognitive psychometric profile captured by the SDMT.

OBJECTIVES This study aims to investigate whether enhancements in the administration of the SDMT can lead to improved detection of cognitive impairment in pwMS.

METHODS A cohort of 502 pwMS and 40 healthy controls (HCs) underwent assessment using an extended version of the SDMT. In this extended version, participants completed additional practice trials until mastery was achieved in counting all symbols. The cut-off value for cognitive impairment was determined as 1.5 standard deviations below the mean based on data from the 40 HCs. Individuals performing below this threshold were classified as cognitively impaired.

RESULTS Among the 502 pwMS, cognitive impairment was detected in four individuals when the original version of the SDMT was applied, whereas the extended version identified impairment in 60 individuals. This disparity in impairment detection between the original and extended practices of the SDMT was found to be statistically significant ($p<.05$).

CONCLUSION The administration of the full version of the SDMT led to the reliable and more frequent detection of impairments in processing speed among pwMS. This underscores the importance of utilizing comprehensive assessment tools like the extended SDMT in clinical practice to improve the detection and understanding of cognitive impairment in MS.

006

# A Potential Link Between Chronic Tobacco Smoking and Impaired Visuospatial Memory in People With Multiple Sclerosis

Turhan Kahraman, Irem Kara, Gozde Deniz Unal, Yasemin Simsek, Serkan Ozakbas

INTRODUCTION Multiple sclerosis (MS) frequently results in cognitive impairment, posing significant challenges to affected individuals. Identifying factors contributing to cognitive dysfunction in MS is pivotal for tailored interventions and improved patient well-being. Smoking, a notable modifiable risk factor, is associated with various adverse health outcomes in MS, yet its impact on cognitive function remains unclear.

OBJECTIVES This cross-sectional study aimed to investigate the relationship between smoking status and cognitive function in people with MS.

METHODS The study enrolled 152 participants diagnosed with MS, of whom 76 were smokers and 76 were non-smokers. Cognitive assessment utilized the Brief International Cognitive Assessment for MS (BICAMS), encompassing the Symbol Digit Modalities Test (SDMT), California Verbal Learning Test-II (CVLT-II), and Brief Visuospatial Memory Test-Revised (BVMT-R). Z-scores were derived from normative data, with cognitive impairment defined as scores falling below 1.5 standard deviations from the mean. Pack-year was calculated to measure tobacco exposure. Analysis of covariance (ANCOVA) compared cognitive performance between smokers and non-smokers. Logistic regression predicted impaired cognition based on smoking status, while linear regression analysed the association between pack-year and cognitive function. All analyses controlled for age, education level, and Expanded Disability Status Scale (EDSS) scores.

RESULTS Significant differences emerged between smokers and non-smokers in BVMT-R performance [$F(1, 143) = 10.035$, $p = 0.002$], indicating impaired visuospatial memory in smokers. However, no significant differences were observed for SDMT [$F(1, 143) = 0.687$, $p = 0.408$] or CVLT-II [$F(1, 144) = 2.525$, $p = 0.114$]. Smoking status was associated with an approximately 11.8 times higher likelihood of impaired performance on BVMT-R [OR = 11.8, 95% CI (2.5-55.8), $p = 0.002$], after covariate adjustments. Pack-year exhibited a significant negative association with BVMT-R ($B = -0.149$, $SE = 0.070$, $\beta = -0.167$, $t = -2.117$, $p = 0.036$), explaining 25.6% of the variance in BVMT-R.

CONCLUSION These findings suggest a potential link between chronic tobacco smoking and impaired visuospatial memory in people with MS, underscoring the importance of smoking cessation interventions in this population. Further research is warranted to elucidate the mechanisms underlying this association and explore interventions to mitigate cognitive decline in smokers with MS.

007

# Associating Age of Symptom Onset with Cognitive Impairment Severity in Multiple Sclerosis: A Comparative Study

Gözde Deniz Ünal, Said Alizada, İrem Kara, Yasemin Şimşek, Serkan Ozakbas

INTRODUCTION Cognitive impairment (CI) and associated neurobehavioral symptoms represent common manifestations in individuals diagnosed with multiple sclerosis (MS). However, the factors underlying CI and its influence remain inadequately understood.

OBJECTIVES This study aims to explore the potential correlation between the age of initial symptoms onset (ISO) and the occurrence of CI in individuals with Multiple Sclerosis (pwMS).

METHODS The study encompassed two distinct groups: 986 pwMS with (ISO) between the ages of 18-29, and 986 pwMS between the ages of 30-50. To mitigate potential confounding effects on CI, pwMS were included in the study with matched education levels and ages. A cohort of 467 healthy controls underwent assessment with Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS) battery, with a predetermined cut-off value for CI set at 1.5 standard deviations below the mean. Individuals below this threshold were categorized as exhibiting CI within the respective domain. Severity of CI was stratified based on the number of affected domains: impairment in one domain was classified as having moderate-to-severe CI, those with CI in two domains as severe, and those with CI across all three domains as very severe.

RESULTS Among pwMS manifesting initial symptoms between the ages of 18-29, 93 exhibited moderate-to-severe CI, 34 severe CI, and 26 very severe CI. Conversely, among pwMS experiencing initial symptoms between the ages of 30-50, 154 displayed moderate-to-severe CI, 77 severe CI, and 27 very severe CI.

CONCLUSION This study represents a significant step in investigating the relationship between the age of symptom onset and CI severity in pwMS, the age at which MS symptoms first appear is associated with the severity of CI. Individuals presenting symptoms between the ages of 18-29 were observed to experience a higher prevalence of mild to moderate CI compared to those presenting symptoms between the ages of 30-50. Additionally, more severe CI were noted in individuals with symptom onset at later ages. These findings suggest that early diagnosis and treatment in MS may play a pivotal role in preventing and managing the development of CI. However, these results need to be integrated into clinical practice and corroborated by further research. Future studies will be crucial in gaining a better understanding of the underlying mechanisms of CI and developing more effective treatment and management strategies based on this understanding.

008

# Comparison of the Objective and Subjective Cognitive Fatigue During Relapse and Remission in Individuals With Multiple Sclerosis: Preliminary Results

Serkan Ozakbas, İrem Kara, Pınar Yiğit, Ulvi Samadzade, Tuba Ozdogar

INTRODUCTION A discrepancy between cognitive tests and subjective perception on cognitive functioning is known in people with multiple sclerosis (pwMS). The relationship between subjective and objective cognitive fatigue, especially during relapse and remission, has yet to be fully elucidated.

OBJECTIVES To investigate the differences between relapse and remission periods regarding subjective and objective cognitive fatigue in pwMS.

METHODS This study assessed 23 pwMS at relapse and remission (from one month to three months after relapse). The Symbol Digit Modalities Test (SDMT) was used to determine objective cognitive fatigue. The standard 90-second interval was divided into three 30-second intervals for each test. Scores from the first part (0-30 sec) were subtracted from scores from the last part (61-90 sec). Participants who have negative scores are accepted as having cognitive fatigue. The cognitive subscore of the Modified Fatigue Impact Scale (MFIS) was used to determine subjective cognitive fatigue. Increased score is associated with cognitive fatigue. The Expanded Disability Status Score (EDSS), age, gender, and disease duration were recorded.

RESULTS According to objective cognitive fatigue assessment, five out of 17 patients have cognitive fatigue during relapse and remission. However, there were no significant differences between relapse (1.39±2.54) and remission (2.43±3.26) periods' average objective cognitive fatigue scores (p=0.279). In subjective cognitive fatigue assessment, cognitive fatigue scores were better during remission than relapse (relapse:15.47±10.82, remission: 19.27±9.21, p=0.044).

CONCLUSION Our results indicate that while subjective cognitive fatigue increases during the remission period, objective cognitive fatigue remains unchanged from relapse to remission. Despite a small sample size, detailed objective measures of cognitive fatigue may serve as additional outcomes sensitive to changes in disease status and interventions during and after relapse.

009

# Association Between Vascular Risk Factors and Cognitive Impairment in Multiple Sclerosis: A Cross-Sectional Study

Serkan Ozakbas, Taha Aslan, Ela Simay Zengin, Irem Kara, Yasemin Simsek, Turhan Kahraman

INTRODUCTION Cognitive impairment is a prevalent and disabling feature of multiple sclerosis (MS), yet its aetiology remains complex and multifactorial. Recent evidence suggests a potential interplay between vascular risk factors and cognitive dysfunction in various disease states, prompting investigations into their association in MS.

OBJECTIVES To explore the association between vascular risk factors and cognitive impairment in people with MS. By employing comprehensive cognitive assessment tools, we sought to elucidate the impact of hypertension (HT), hyperlipidaemia (HL), and diabetes mellitus (DM) on cognitive function.

METHODS A cross-sectional study was conducted involving 128 people diagnosed with MS. Cognitive function was assessed using the Brief International Cognitive Assessment for MS (BICAMS), which includes the Symbol Digit Modalities Test (SDMT), the Brief Visuospatial Memory Test-Revised (BVMRT), and the California Verbal Learning Test-II (CVLT-II). Z-scores were calculated based on normative data from 467 healthy controls, with cognitive impairment defined as impairment in at least one BICAMS domain. Logistic regression analysis was performed to predict cognitive impairment, adjusting for age, Expanded Disability Status Scale (EDSS) scores, and sex.

RESULTS The mean EDSS score was 2.9 (SD=2.2), indicating a moderate level of disability. HT was present in 37.5% of patients, HL in 10.9%, and DM in 14.8%. Cognitive impairment was observed in 27.3% of people with MS. After adjusting for covariates, neither HT (p=0.833) nor DM (p=0.511) emerged as significant predictors of cognitive impairment. However, the presence of HL was significantly associated with cognitive impairment, with an odds ratio (OR) of 4.3 (95% CI: 1.3-14.4, p=0.02), indicating a 4.3-fold increased likelihood of cognitive impairment in people with MS with HL compared to those without.

CONCLUSION The identification of HL as a significant predictor of cognitive impairment in people with MS underscores the need for comprehensive assessment and management of vascular risk factors in this population. While HT and DM did not emerge as significant predictors of cognitive impairment in our study, the association between HL and cognitive dysfunction warrants further investigation. Future research should focus on elucidating the underlying mechanisms linking HL to cognitive impairment in MS and exploring potential therapeutic interventions targeting vascular risk factors to mitigate cognitive decline.

SECTION II

# Mobility, Fatigue and Symptoms

6 ABSTRACTS

010

# Prevalence and Correlates of Fear of Falling in People With Multiple Sclerosis Exhibiting No to Mild Disability

Zuhal Abasıyanık, Özge Ertekin, Tuğçe Kara, Turhan Kahraman, Serkan Ozakbas

INTRODUCTION Fear of falling (FOF) is a crucial problem affecting daily life activities in people with multiple sclerosis (pwMS). However, little is known about the prevalence and related factors in pwMS with no to mild disability.

OBJECTIVES This study aimed to investigate the prevalence and related factors of FOF in pwMS.

METHODS A total of 91 pwMS [49 pwMS without disability (EDSS≤1.5), 42 with mild disability (EDSS 2.0 to 3.5)] were enrolled. FOF was assessed using the Fall Efficacy Scale-International (FES-I). Motor outcomes are the Timed 25-foot Walk (T25FW), 6-Minute Walk Test (6MWT), and Multiple Sclerosis Walking Scale (MSWS-12). Cognitive processing speed was assessed using the Symbol Digit Modalities Test (SDMT), and the level of fatigue was measured using the Modified Fatigue Impact Scale (MFIS).

RESULTS The prevalence of FOF was 61.5% in the total group, 44.9% in pwMS without disability, and 81% in pwMS with mild disability. The FES-I was significantly correlated with all the measures (r=0.473 to 0.800) used except for SDMT. Linear regression analysis showed that perceived walking impairment assessed by MSWS-12 and MFIS were significantly associated with FOF, accounting for 67.3% of the variance.

CONCLUSION This study underscores the noteworthy prevalence of FOF in pwMS, even in the early stages, and highlights the importance of integrating patient-reported outcomes to comprehend FOF effectively. Improving gait and preventing fatigue might be effective in reducing FOF in pwMS.

011

# Factors Influencing Self-Reported and Measured Walking Disability in Early-Stage Multiple Sclerosis

Zuhal Abasıyanık, Gözde Deniz Ünal, Serkan Ozakbas

INTRODUCTION Detecting walking impairment is crucial for developing effective interventions in persons with multiple sclerosis (pwMS) from the early phase of the disease. While self-report measures offer valuable insights into patients' subjective experiences, objective measurements provide more precise assessments of physical impairment, highlighting the need for comprehensive evaluations in clinical practice.

OBJECTIVES To investigate the factors related to self-reported and objectively measured walking disability among individuals in the early stages of multiple sclerosis (MS).

METHODS A total of 756 pwMS (EDSS≤2.5 and disease duration ≤5 years) were enrolled in the study (mean EDSS=0.87±0.83). Self-reported walking disability was assessed using the MS Walking Scale (MSWS-12). Walking was assessed objectively using the Timed 25-Foot Walk (T25FW) and 6-Minute Walk Test (6MWT). We also administered the EDSS, Activities-Specific Balance Confidence (ABC) Scale, Modified Fatigue Impact Scale (MFIS), Epworth Sleepiness Scale (ESS), Beck Depression Scale (BDS) and Symbol Digit Modalities Test (SDMT). An exploratory data analysis was performed to examine the influence of the motor and non-motor outcomes on self-reported, and objective walking disability using linear regression analyses.

RESULTS Fatigue (i.e., MFIS) and balance confidence (i.e., ABC) were significant factors affecting perceived walking disability and explained 71% of the variance of the MSWS-12 test. The only determinant was 6MWT and explained 38% of the variance of the T25FW.

CONCLUSION The determinants of objective and perceived walking function may differ, particularly in the early-stage MS. While self-reported walking is influenced by factors such as fatigue and balance confidence, objective walking is influenced by walking capacity. Understanding these distinct relationships holds potential to enhance the management of walking ability in the early MS.

012

# Understanding Factors Influencing Deterioration in Upper and Lower Extremity Outcomes in Multiple Sclerosis

Said Alizada, Asiye Tuba Ozdogar, Gözde Deniz Ünal, İrem Kara, Nurbanu Yapıcı, Serkan Ozakbas

INTRODUCTION In the realm of multiple sclerosis (MS) management, understanding the factors contributing to significant deteriorations in mobility and dexterity is paramount. This retrospective study delves into the intricate web of variables influencing ≥20% worsening in Timed 25-Foot Walk (T25FW) and 9-Hole Peg Test (9HPT) outcomes over approximately one year in MS patients.

OBJECTIVES Our investigation involved a meticulous cross-sectional analysis of MS patients who underwent T25FW and 9HPT tests approximately one year apart.

METHODS Patients were stratified into two distinct groups: those who encountered ≥20% worsening and a control cohort devoid of such deterioration. Various parameters including demographic details, initial Expanded Disability Status Scale (EDSS), disease type, lesion characteristics, and treatment history were meticulously scrutinized. Binary logistic regression was then wielded to decipher the pivotal factors impacting the decline in T25FW and 9HPT outcomes.

RESULTS For the 9HPT cohort, comprising 47 individuals, 12 endured ≥20% worsening while 35 remained stable. Intriguingly, no discernible factors emerged to elucidate the deterioration in 9HPT outcomes. Conversely, in the T25FW cohort encompassing 91 patients, 41 manifested ≥20% worsening while 50 maintained stability. Remarkably, the presence of T1 black holes emerged as a significant contributor to T25FW worsening ($\beta$=4.067, p=0.036), underscoring its prognostic relevance.

CONCLUSION This study offers profound insights into the determinants underpinning ≥20% deterioration in T25FW and 9HPT outcomes among MS patients. Notably, the presence of T1 black holes surfaced as a pivotal factor in precipitating T25FW deterioration, highlighting its clinical significance. These findings hold promise in refining prognostic models and tailoring therapeutic interventions, thereby fostering a more personalised approach to MS management.

013

# Determinants of Fatigue in People with Multiple Sclerosis: An Investigative Analysis

Asiye Tuba Ozdogar, Said Alizada, Yasemin Şimşek, Serkan Ozakbas

INTRODUCTION Fatigue, defined as a feeling of extreme physical and/or mental lack of energy, is a symptom that affects 75-97% of people with multiple sclerosis (MS, pwMS). Determining the related factors to fatigue is an important issue in developing medical treatment and rehabilitation strategies.

OBJECTIVES The aim is to compare disease duration, disability level, polypharmacy, sleep quality, depression levels, and physical performance in pwMS with and without fatigue.

METHODS A total of 512 pwMS were divided into two groups with and without fatigue according to the Modified Fatigue Impact Scale (MFIS), which has a cut-off value of 38 points. The levels of disability, sleepiness, and depression were assessed with the Expanded Disability Status Scale (EDSS), the Epworth Sleepiness Scale (ESS), and the Beck Depression Scale (BDS), respectively. The Timed 25-Foot Walk (T25FW) and the Nine-Hole Peg Test (N-HPT) were used for evaluating the physical performance. The participants' ages, disease duration, MS type, and multiple drug use were recorded.

RESULTS Most participants had the relapsing-remitting MS type (78.1%) and were female (66.4%). The mean age of the participants was 39±12.33. According to the cut-off value of MFIS, 194 (37.89%) participants were fatigued, and 318 (62.10%) were non-fatigued. The mean EDSS, T25FW, NHPT, ESS, and BDS scores were (fatigued: 3.49±2.07; non-fatigued: 2.39±2.27); (fatigued: 26.31±53.86; non-fatigued: 21.36±47.91); (fatigued: 35.87±58.89; non-fatigued: 30.99±41.16); (fatigued: 7.01±4.67; non-fatigued: 4.05±3.57); (fatigued: 18.46±9.80; non-fatigued: 7.51± 6.52), respectively. Of the fatigued participants, 25.8% used one symptomatic drug, 16.4% used two symptomatic drugs, and 6.6% used three or more symptomatic drugs. Binary logistic regression showed that EDSS (β=1.416, p=0.001), BDS (β=1.156, p<0.01), and ESS (β=1.103, p=0.001) were effective factors in the presence of fatigue. However, T25FW, NHPT, BDS, disease duration and multiple drug use were not related factors to the presence of fatigue.

CONCLUSION EDSS score, sleep quality, and depression levels emerged as significant factors contributing to fatigue in pwMS. Therefore, management strategies for fatigue should incorporate interventions targeting EDSS score, sleep quality, and depression. Additionally, given the clinical utility of T25FW and NHPT, future research employing longer-duration assessment methods to explore the impact of fatigue on physical performance is warranted.

014

# Comparative Analysis of Restless Legs Syndrome and Neuropathic Pain Impact on Walking and Balance in Multiple Sclerosis: Clinical and Radiographic Insights

Asiye Tuba Ozdogar, Ergi Kaya, Sinem Ozcelik, Gözde Deniz Ünal, Serkan Ozakbas

INTRODUCTION Restless legs syndrome (RLS) and neuropathic pain are commonly reported by persons with multiple sclerosis (MS, pwMS). Even though RLS and neuropathic pain could affect walking and balance, no studies investigated which is more effective. Moreover, having information regarding magnetic resonance imaging (MRI) could help the understanding of pathophysiological mechanisms.

OBJECTIVES This study aims to explore the effects of RLS and neuropathic pain on walking and balance in pwMS, while also conducting a comparative analysis of MRI results.

METHODS A cohort of 1156 participants were divided into four groups: neuropathic pain (n=115,9.9%), RLS (n=168,14.5%), both neuropathic pain and RLS (n=77,6.7%), and control (have not both neuropathic pain and RLS) (n=796, 68.9%). The Timed 25 Foot Walk Test (T25FW), Multiple Sclerosis Walking Scale-12 (MSWS-12), Timed Up and Go (TUG), Activities-Specific Balance Confidence (ABC) scale, Single-Leg Stand Test (SLST) were used to assess walking and balance. The Expanded Disability Status Scale (EDSS), disease duration, age, and MRI results (presence of supratentorial, infratentorial, and spinal cord lesions) were recorded.

RESULTS EDSS and age were determined as covariate factors. There were no significant differences between groups in T25FW, TUG and SLST performance. However, significant differences were found between groups regarding MSWS-12 and ABC scale ($p<0.05$). According to posthoc analysis, the MSWS-12 score was lower in the control group (19.12±9.51) than in neuropathic pain (26.67±10.95), and both neuropathic pain and RLS (28.79±11.48) groups ($p<0.001$). Also, the RLS group has a lower MSWS-12 score (22.44±10.71) than the neuropathic pain and both neuropathic pain and RLS groups ($p=0.006$ and $<0.001$, respectively). The ABC scale score was higher in the control group (79.94±23.52) than in neuropathic pain (64.79±22.53; $p<0.001$), RLS (70.66±24.59; $p=0.018$), and both neuropathic pain and RLS (61.44±26.94; $p<0.001$) groups. There were no significant differences between groups regarding MRI results ($p>0.05$).

CONCLUSION Neuropathic pain may have a more pronounced impact on perceived walking and balance disability compared to RLS in pwMS. Individuals experiencing both neuropathic pain and RLS demonstrated poorer patient-reported outcomes concerning walking and balance functions. MRI findings did not exhibit significant differences among the studied groups, underscoring the complex interplay of clinical symptoms and radiographic manifestations in MS.

015

# Prevalence and Related Factors of Restless Legs Syndrome in Pediatric-Onset Multiple Sclerosis

Tuba Ozdogar, Ergi Kaya, Nurbanu Yapıcı, Serkan Ozakbas

INTRODUCTION It is well-known that Restless Legs Syndrome (RLS) is more common in adults with multiple sclerosis (MS) than in the general population. However, its prevalence and related factors in the pediatric-onset MS (POMS) group are unknown.

OBJECTIVES This study aimed to investigate the prevalence of RLS and identify related factors in young patients with POMS. Additionally, we aimed to compare the severity of RLS between POMS and adult-onset MS (AOMS) groups.

METHODS A total of 58 people who were diagnosed with MS under the age of 18 years based on McDonald 2017 diagnostic criteria and currently being under the age of 21 years were enrolled. Also, 504 AOMS were included to comparison. The RLS diagnosis was made according to five criteria defined by the International RLS Study Group. The daytime sleepiness and RLS severity were assessed using the Modified Fatigue Impact Scale (MFIS) and the RLS Study Group Rating Scale (RLSSGRS). A Brief International Cognitive Assessment for Multiple Sclerosis was used to determine cognitive performance. Demographic and clinical data such as age, gender, disability level, and disease duration have been recorded.

RESULTS While RLS detected in ten patients (17.2%) in POMS group, 102 (20.2%) had RLS in AOMS group. Although, the average RLSSGRS score was higher in AOMS patients with RLS (18.06±7.3) than POMS patients with RLS (15.18±10.26), it failed to reach to the statistically significant level. The Expanded Disability Status Scale (EDSS) score, disease duration, cognitive functions and daytime sleepiness score were found to be similar between POMS patients with RLS than those without ($p>0.05$). However, mean age was significantly lower in POMS patients with RLS (15.3±10.81) than those without (19.21±1.53) ($p = 0.007$).

CONCLUSION This study revealed a high prevalence of RLS in young patients with POMS. The lower mean age in POMS patients with RLS may explain the similar clinical profiles observed in both RLS-positive and RLS-negative groups. Importantly, the prevalence and severity of RLS were similar between AOMS and POMS groups.

SECTION III

# Disease Progression, PIRA and NEDA

4 ABSTRACTS

016

# Enhancing Disability Progression Assessment in Multiple Sclerosis: Introducing the EDSS-Plus Score

Sinem Ozcelik, Asiye Tuba Ozdogar, Said Alizada, Bilge Piri Cinar, Serkan Ozakbas

INTRODUCTION Current methods for assessing progression in MS, primarily reliant on the Expanded Disability Status Scale (EDSS), may overlook nuanced changes in disability. Incorporating additional measures such as the 9-Hole Peg Test (9HPT) and Timed 25-Foot Walk Test (T25FWT) provides a more detailed evaluation of disease progression.

OBJECTIVES This study aims to develop an EDSS-Plus score that incorporates 9HPT and T25FWT alongside EDSS, to provide a more comprehensive assessment tool for evaluating disability progression in MS and describe PIRA (Progression Independent of Relapse Activity) more qualitatively.

METHODS This prospective study includes people with Relapsing MS (pwRMS). EDSS, 9HPT, and T25FWT raw scores were standardized using z-scores. PIRA was defined as having at least one of these components: EDSS progression, an increase of %20 in T25FT or an increase of %20 in 9PHT that sustain at least 3 months while there was no sign of relapse in the last 30 days before and after the initial increase of disability.

RESULTS 741 pwRMS were enrolled in this study. PIRA was seen in 19.7% with no difference between the treatment groups ($p>0.05$). The EDSS-Plus scores between groups with and without PIRA was found significantly meaningful ($p<0.001$). There was a significant difference between all DMT groups in terms of EDDS Plus score (the first-line:0.28±0.29, the second line:0.16±0.48, the third-line:-0.60±0.98; $p<0.001$). According to the regression model, gender, age, number of relapses, number of previous treatments, and disease duration are not the effective factors in the presence of PIRA. However, the number of relapses (B:-0.45, $p<0.001$) and age (B:-0.17, $p<0.001$) were found to be an effective factor on the EDSS-Plus score (R2:0.268).

CONCLUSION The EDSS-Plus score emerges as a promising tool to redefine PIRA by offering a quantifiable scoring system. Integrating EDSS with functional assessments like 9HPT and T25FWT by incorporating multiple measures into a single score, this approach provides a clearer delineation of disability progression.

017

# Evaluating the Effectiveness of No Evidence of Disease Activity-3 in Managing Progression Independent of Relapse Activity and Relapse-Associated Worsening in Multiple Sclerosis

Sinem Ozcelik, Asiye Tuba Ozdogar, Said Alizada, Serkan Ozakbas

INTRODUCTION NEDA-3 is commonly used to describe disease inactivity in MS, encompassing no evidence of clinical relapses, new MRI activity, or disability progression. However, achieving NEDA-3 does not always equate to the absence of progression, as EDSS and MRI alone may not be sufficient to measure all aspects of disease activity.

OBJECTIVES This study aims to investigate the relationship between achieving NEDA-3 status and the occurrence of PIRA (Progression Independent of Relapse Activity) and RAW (Relapse-Associated Worsening).

METHODS In this retrospective study, patients were categorized based on NEDA-3 status and monitored for PIRA over 17 ± 14.3 months. PIRA was defined as having at least one of the following: EDSS progression, a 20% increase in the Timed 25-Foot Walk Test (T25FT), or a 20% increase in the 9-Hole Peg Test (9HPT) sustained for at least 3 months, without any signs of relapse 30 days before and after the initial increase in disability. RAW was defined as sustained EDSS worsening 90 days post-relapse.

RESULTS A total of 738 (72.5% female) RRMS patients were included in the study. The mean age was 37 ± 11.1 years, and the mean disease duration was 7 ± 6.5 years. NEDA-3 was achieved in 563 (76.3%) patients, while PIRA was observed in 125 (20.6%) patients. A total of 45 (4.7%) patients experienced at least one relapse, with 4 (17.7%) developing RAW. New lesions were observed in 80 (10.8%) patients. The PIRA rate was significantly lower in the NEDA-3-achieving group compared to the non-achievers ($p < 0.001$). Among patients who had relapses, RAW was not associated with higher PIRA rates ($p = 0.661$). According to the regression model, gender, age, number of relapses, number of previous treatments, and disease duration are not effective factors in the presence of PIRA.

CONCLUSION Achieving NEDA-3 status is significantly associated with a reduced incidence of PIRA, underscoring its importance in comprehensive disease management. These findings highlight the need for rigorous monitoring and targeted therapeutic approaches to address progressive disability in MS patients, irrespective of relapse activity. Therefore, while NEDA-3 is a useful measure, it should be complemented with other assessments to fully capture disease progression and improve patient outcomes.

018

# Which One Is More Progressive; Primary, or Secondary Progressive Multiple Sclerosis?

Sinem Ozcelik, Ergi Kaya, Asiye Tuba Ozdogar, Serkan Ozakbas

INTRODUCTION Progressive multiple sclerosis (MS), encompassing primary progressive MS (PPMS) and secondary progressive MS (SPMS), signifies a stage of the disease marked by steadily worsening clinical disability. Despite their clinical similarities, the underlying pathophysiological mechanisms driving progression in PPMS and SPMS remain elusive. Understanding whether PPMS and SPMS share common disease mechanisms or represent distinct entities is paramount for advancing our comprehension and treatment of progressive MS.

OBJECTIVES This study aims to investigate differences in NEDA-3 (No Evidence of Disease Activity) status, EDSS (Expanded Disability Status Scale) changes, and PIRA (Progression Independent of Relapse Activity) rates between PPMS and SPMS. The goal is to determine if PPMS and SPMS are fundamentally distinct diseases or represent a spectrum of the same underlying pathophysiological process with different early-stage clinical manifestations.

METHODS A retrospective cohort study was conducted with age-matched PPMS and SPMS patients. Disease progression was monitored using NEDA-3 criteria, PIRA rates, and new MS lesions on MRI. NEDA-3 status includes no clinical relapses, no new or enlarging MRI lesions, and no disability progression. PIRA was defined by at least one of the following: EDSS progression, a 20% increase in the Timed 25-Foot Walk Test (T25FT), or a 20% increase in the 9-Hole Peg Test (9HPT) sustained for at least 3 months, without signs of relapse 30 days before and after the initial increase in disability.

RESULTS The study included 24 PPMS (41.5% female) and 40 SPMS (62.5% female) patients, matched by age. The mean follow-up duration was 7.4 ± 5.6 months, and the mean age was 52.6 ± 7.2 years. NEDA-3 status was achieved by 14 (58.3%) PPMS and 24 (60%) SPMS patients. PIRA was observed in 9 (37.5%) PPMS and 17 (42.5%) SPMS patients. There were no statistically significant differences between the groups in terms of NEDA-3 achievement, PIRA incidence, or new MS lesions ($p < 0.05$).

CONCLUSION Our study suggests that PPMS and SPMS may share common pathophysiological mechanisms, challenging the traditional view of them as distinct entities. Instead, they may represent varying manifestations of a unified disease process. Continued exploration of these shared pathways is crucial for refining treatment approaches and improving outcomes for individuals with progressive MS.

019

# Impact of Diagnosis and Treatment Timing on Long-Term Outcomes in Multiple Sclerosis: A Comprehensive Study

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

INTRODUCTION The progression of multiple sclerosis (MS) is influenced by a variety of factors. While the number of relapses and the age of onset are commonly researched, the intervals from symptom onset to diagnosis and from diagnosis to treatment initiation have not been thoroughly examined in the literature.

OBJECTIVES This study aims to explore the potential effects of the time from the first symptom to diagnosis (TFSD) and the time from diagnosis to the start of treatment (TDT) on several key measures: the Expanded Disability Status Scale (EDSS) score, the Timed 25-Foot Walk test (T25FW), the Nine-Hole Peg Test (9HPT), and the Brief Cognitive Assessment for Multiple Sclerosis (BICAMS).

METHODS The research included 1337 patients with MS (pwMS) with a 5-year follow-up and 698 pwMS with a 10-year follow-up. During the 5-year follow-up, assessments were made using EDSS, T25FW, 9HPT, and BICAMS scores. For the 10-year follow-up, the evaluation focused exclusively on the EDSS score.

RESULTS The 5-year follow-up results indicated no significant associations between TFSD or TDT and the evaluated parameters ($p > .05$). However, in the 10-year follow-up, a significant positive relationship was found between TFSD and the EDSS score at the tenth year ($p < .05$). This suggests that a longer duration from the first symptom to diagnosis is associated with higher EDSS scores after ten years, indicating greater disability.

CONCLUSION While the timing from symptom onset to diagnosis does not appear to significantly influence outcomes in the short term, it has a pronounced impact on the long-term progression of MS. Early diagnosis and prompt initiation of treatment are crucial for improving long-term outcomes and reducing disability. This study underscores the importance of reducing diagnostic delays to enhance the quality of life and prognosis for individuals with MS. Implementing strategies to expedite the diagnostic process could potentially alter the disease course and improve patient outcomes, highlighting the need for increased awareness and better access to diagnostic resources in clinical practice.

SECTION IV

# Age at Onset

3 ABSTRACTS

020

# Clinical Comparison of Early and Late Onset Multiple Sclerosis at Age 35: Implications for Disease Progression and Management

Ergi Kaya, Taha Aslan, Asiye Tuba Özdoğar, Said Alizada, Serkan Ozakbas

INTRODUCTION The age at which multiple sclerosis (MS) manifests can influence disease progression and outcomes. While early onset MS (EOMS) and adult-onset MS (AOMS) represent distinct subgroups within the MS spectrum, the selection of a specific age threshold for comparison warrants rationale.

OBJECTIVES This study aimed to investigate differences in clinical performance characteristics between individuals with EOMS and AOMS, focusing on their status at the age of 35. By comparing disease progression and disability levels at this milestone age, we sought to identify potential implications for long-term disease management.

METHODS Patients with relapsing-remitting MS were categorized into two groups based on age at MS onset: EOMS (onset before age 18) and AOMS (onset after age 18). Data on Expanded Disability Status Scale (EDSS) scores, demographic variables, disease duration, and number of relapses were retrospectively collected from patients when they reached 35 years of age.

RESULTS A total of 227 patients with MS were included in the study, with 74 classified as EOMS. Disease duration was significantly longer in the EOMS group compared to the AOMS group (mean: 19.36±2.25 vs. 6.38±4.9, $p<0.05$), and the number of relapses was also higher in the EOMS group (mean: 4.66±2.49 vs. 3±2.51, $p<0.05$). At age 35, individuals with EOMS exhibited higher EDSS scores than those with AOMS (mean: 2.9±2.26 vs. 1.36±1.64). Furthermore, a higher proportion of individuals with EOMS experienced secondary progressive MS compared to those with AOMS (13% vs. 6%, $p=0.048$).

CONCLUSION At age 35, individuals with early onset MS demonstrate higher disability levels and a greater number of relapses compared to those with late-onset MS. These findings underscore the importance of early identification and aggressive management strategies for individuals with EOMS to mitigate disease progression and optimize long-term outcomes. Moreover, the observed differences in disease progression between EOMS and AOMS highlight the need for tailored treatment approaches based on age at MS onset. Further research is warranted to elucidate the underlying mechanisms driving these differences and inform personalized therapeutic interventions for individuals with MS.

021

# Comparative Analysis of Disease Progression and Disability Accumulation between Early Onset and Adult Onset Multiple Sclerosis Patients at a Decade Post-Diagnosis

Taha Aslan, Ergi Kaya, Asiye Tuba Özdoğar, Nurbanu Yapıcı, Serkan Ozakbas

INTRODUCTION Early onset multiple sclerosis (EOMS), defined as the onset of MS before the age of 18, and adult-onset multiple sclerosis (AOMS) represent two distinct subgroups within the MS spectrum. EOMS, often considered a rare form of the disease, has been postulated to possess unique clinical features and possibly a more aggressive disease course compared to AOMS. However, studies comparing the clinical characteristics and disease progression between these two subgroups at the same disease duration are scarce.

OBJECTIVES This study aims to investigate the differences in clinical characteristics between patients with EOMS and AOMS, focusing on disease progression and disability accumulation over a ten-year period from the time of MS diagnosis.

METHODS This retrospective study included patients diagnosed with relapsing-remitting MS (RRMS) who were followed up for at least ten years after the initial diagnosis. Patients were stratified into two groups based on the age at MS onset: EOMS (onset before 18 years of age) and AOMS (onset after 18 years of age). Data on Expanded Disability Status Scale (EDSS) scores, demographic variables, and the number of relapses were collected from medical records when patients reached their tenth-year post-diagnosis.

RESULTS A total of 212 patients with RRMS were included in the study, of whom 82 were classified as EOMS. There were no significant differences observed between genders in either subgroup ($p>0.05$). The number of relapses experienced within the first ten years of diagnosis was similar between AOMS and EOMS ($p>0.05$). Additionally, there were no significant differences in EDSS scores between AOMS and EOMS at the ten-year ($p>0.05$). Notably, the incidence of secondary progression was observed to be higher in AOMS compared to EOMS after ten years of disease duration ($p=0.04$).

CONCLUSION Over a ten-year period from the time of diagnosis, disease progression was more pronounced in patients with AOMS compared to those with EOMS. This finding suggests that different immunogenetic and immunosenescence mechanisms may contribute to the observed differences in disease progression between the two subgroups. Further research elucidating the underlying pathophysiological mechanisms driving these disparities is warranted to inform tailored therapeutic approaches for patients with EOMS and AOMS.

022

# Use of High-Efficacy Therapies of Early- and Late-Onset Multiple Sclerosis Compared to Adult-Onset Multiple Sclerosis

Serkan Ozakbas, Taha Aslan, Ergi Kaya, Said Alizada, Tuba Ozdogar

INTRODUCTION While multiple sclerosis (MS) predominantly manifests in adults, onset can occur at various ages, impacting disease characteristics and treatment responses. Early-onset (EOMS) and late-onset MS (LOMS) represent less common subtypes, necessitating tailored therapeutic approaches. However, insights into high-efficacy therapy usage across different age groups remain limited. Understanding treatment patterns, particularly regarding high-efficacy therapies, is essential for optimizing management strategies.

OBJECTIVES This study aims to compare the utilization of high-efficacy therapies among individuals with EOMS, LOMS, and adult-onset MS (AOMS), shedding light on treatment patterns and potential disease aggressiveness across age cohorts.

METHODS A cohort of MS patients was stratified into three groups based on age at onset: EOMS (<18 years), AOMS (20-40 years), and LOMS (>55 years). High-efficacy therapies included ocrelizumab and natalizumab, while other disease-modifying therapies were categorized as non-high-efficacy. Demographic and clinical data, including age, disease duration, relapse history, Expanded Disability Status Score (EDSS), and current treatment regimens, were recorded for analysis.

RESULTS The age and number of relapses were compared, and significant differences were determined (Age: EOMS= 31.31±9.52, AOMS=40.59±9.56, LOMS=59.75±4.74; Number of relapses: EOMS= 6.17±2.81, AOMS=5.81±3.61, LOMS=3.0±2.28). So, those variables are defined as covariates. The ratio of high-efficacy therapies was not different between groups (p=0.268, x2=2.633) (EOMS=29.7%, AOMS=26.1%, LOMS=34.7%). However, there was a significant difference between groups in terms of time (month) switching from non-high-efficacy therapies to high-efficacy therapies (p<0.001, F=32.363) (EOMS= 141.74±91.23, AOMS=108.96±72.29, LOMS=57.60±41.41).

CONCLUSION Our findings suggest a distinct treatment trajectory in LOMS characterized by an expedited transition to high-efficacy therapies, indicative of potentially more aggressive disease behavior. However, the overall utilization of high-efficacy treatments did not significantly vary across age groups. Further investigation is warranted to elucidate the underlying factors influencing treatment decisions and their implications for disease management and prognosis across different age cohorts in MS.

SECTION V

# Pregnancy

5 ABSTRACTS

023

# The Role of Pregnancy in Shaping MS Prognosis: A Five-Year Study

Sinem Ozcelik, Ergi Kaya, Yasemin Şimşek, Tuncay Basaran, Taha Aslan, Serkan Ozakbas

INTRODUCTION Multiple sclerosis (MS) disproportionately affects women of childbearing age. The interplay between pregnancy and MS remains complex, influenced by hormonal shifts and the discontinuation of disease-modifying therapies (DMTs) before conception.

OBJECTIVES This study seeks to shed light on the impact of pregnancy on the five-year prognosis of women with MS. It focuses on women who became pregnant after their MS diagnosis and gave birth more than 27 months (ppwMS) and women who had no pregnancy after their MS diagnosis. (n-pwMS)

METHODS Retrospective data analysis was conducted on ppwMS and n-pwMS. Detailed data collection included information on diagnosis dates, birth dates, pregnancy timelines, prepartum and postpartum relapses (first year after delivery), third and fifth-year Expanded Disability Status Scale (EDSS) scores, magnetic resonance imaging (MRI) activity, and disease-modifying therapy (DMT) usage. To establish a comparable timeline, data on these parameters were similarly recorded for n-pwMS. Statistical analyses were performed to identify any significant differences in outcomes between ppwMS and n-pwMS.

RESULTS Among the 111 ppwMS included in the study, 11 experienced relapses during pregnancy (P+ppwMS), while 100 did not (P-ppwMS). Additionally, 85 n-pwMS were included for comparison. Comparative analysis revealed no significant differences between P-ppwMS and n-pwMS in terms of age at MS diagnosis, time from diagnosis to pregnancy, previous DMT usage, or pre-pregnancy EDSS scores ($p>0.05$). However, within the first three years post-delivery relapse rates were notably higher in P-ppwMS compared to n-pwMS ($p=0.004$). This increased relapse rate in P-ppwMS was further substantiated by the observation that 33 out of 76 relapses occurred during the postpartum period. Despite these findings, there were no significant differences observed in EDSS scores or MRI activity at three and five years post-delivery between P-ppwMS and n-pwMS ($p>0.05$). In P+ppwMS, relapses were seen higher than in p-ppwMS. ($p<0.01$) There was no significant difference between MRI activity and EDSS. ($P>0.05$)

CONCLUSION While pregnancy does not appear to significantly influence the long-term disability outcomes or MRI activity in women with MS, it is associated with an increased risk of relapses, particularly in the immediate postpartum period. These results underscore the importance of closely monitoring pregnant women with MS and implementing strategies to minimize the risk of relapse during and after pregnancy.

024

# Determinants of Postpartum Relapse in Multiple Sclerosis: A Comprehensive Analysis of Demographic and Clinical Factors

Said Alizada, Ulvi Samadzade, Nurbanu Yapıcı, Ergi Kaya, Asiye Tuba Ozdogar, Serkan Ozakbas

INTRODUCTION The intersection of pregnancy and multiple sclerosis (MS), a chronic, potentially debilitating condition affecting the central nervous system, presents a unique window to scrutinize shifts in disease dynamics, especially the frequency and intensity of relapses following childbirth. Given the complexity of MS and its variable trajectory, the postpartum period emerges as a critical juncture to examine fluctuations in disease behavior. This exploration is vital not only for enhancing patient care but also for deepening our grasp of MS's pathophysiology in the context of pregnancy.

OBJECTIVES This investigation aims to dissect the impact of the postpartum interval on MS relapse activity, quantifying the number and incidence of relapses in two distinct phases: up to 6 months post-pregnancy and from 6 to 12 months thereafter. This effort underpins our quest to refine post-pregnancy management protocols for MS sufferers, tailoring interventions to mitigate the risk of relapse and facilitate smoother recovery trajectories.

METHODS In this retrospective cohort analysis, we scrutinized the pregnancy journeys of 239 women with MS. This comprehensive data collection endeavor captured a broad spectrum of variables: age, age at MS diagnosis, interval from diagnosis to pregnancy, gestational age, identity of the last DMT undertaken before conception, and the frequency of relapses both prior to and following pregnancy. Through follow-up over the year succeeding childbirth, we tracked relapse occurrences during the first and second six-month windows, employing robust statistical tools to discern patterns and predictors of postpartum disease activity.

RESULTS Our regression analysis, employing rigorous statistical methodologies, revealed that factors such as age at diagnosis, the interval from diagnosis to pregnancy, gestational age, the nature of the last DMT regimen before pregnancy, and the pre-pregnancy relapse count, did not exhibit a statistically significant correlation with the likelihood of relapses in the initial 6-month postpartum phase (p-values exceeding 0.05). Maternal age emerged as a notable exception, with a positive beta coefficient (β: 1.100, $p = 0.033$), signaling an elevated relapse risk correlating with advancing age during this critical period.

CONCLUSION The findings of this analysis shed light on the landscape of postpartum MS management, pinpointing maternal age as the pre-pregnancy variable with a demonstrable impact on early postpartum relapse risk. The dataset derived from 239 participants buttresses the call for nuanced, age-specific follow-up approaches, enriching strategies deployed in the postpartum care of women with MS, and ultimately, enhancing their health outcomes and quality of life.

025

# Evaluating the Impact of MS Medications on Pregnancy Outcomes: A Retrospective Cohort Study

Ergi Kaya, Yasemin Şimşek, Sinem Ozcelik, Can Caliskan, Serkan Ozakbas

INTRODUCTION Multiple sclerosis (MS) is more frequently diagnosed in women of childbearing age. Managing pregnancy in women with MS (wwMS) can be challenging because many disease-modifying therapies (DMTs) may have potential harmful effects on the fetus. Therefore, clinicians often recommend discontinuing DMTs for a certain period before pregnancy to mitigate these risks.

OBJECTIVES This study aims to evaluate the impact of DMT use during pregnancy on preterm births, miscarriages, and full-term pregnancies in women with MS. Additionally, it seeks to assess the effects of discontinuing DMTs before pregnancy on these outcomes and on MS activity during pregnancy.

METHODS A retrospective analysis was conducted on women with MS. The collected data included pregnancy dates, birth dates, DMT use before and during pregnancy, DMT exposure during pregnancy, and pregnancy outcomes categorized as full-term (≥37 weeks), preterm (28-37 weeks), or miscarriages (≤27 weeks). Additionally, the occurrence of partum relapses was recorded.

RESULTS A total of 226 women with MS and 269 pregnancies were included in this analysis. The outcomes comprised 36 miscarriages, 40 preterm births, and 193 full-term deliveries. The age of women in these groups did not significantly differ ($p>0.05$ for each; mean age: miscarriages 32.25, preterm 30.05, full-term 29.98). The majority of the cohort used interferon (119), glatiramer acetate (47), and fingolimod (47) before pregnancy. Some women who used fingolimod did not discontinue their DMT before pregnancy (18/47), and this did not significantly affect the rates of preterm birth or miscarriage compared to those who stopped their DMT. However, partum relapses were higher in women who discontinued fingolimod before pregnancy ($p<0.019$; 6 of 18 experienced relapses). No significant differences in partum relapse rates were found for other DMTs between those who discontinued use and those who did not ($p>0.05$).

CONCLUSION The findings suggest that exposure to DMTs during pregnancy may not significantly impact the rates of miscarriage or preterm birth. However, discontinuing fingolimod before pregnancy may increase the risk of MS activity during pregnancy. These preliminary results indicate that further extensive research is needed to better understand the relationship between DMT exposure and pregnancy outcomes in women with MS, and to develop guidelines for managing MS treatment during pregnancy.

026

# Investigating the Impact of Pregnancy on Disease Course in Multiple Sclerosis: A Retrospective Analysis

Yasemin Şimşek, Serkan Ozakbas, Ergi Kaya, Sinem Ozcelik, Can Caliskan

INTRODUCTION Multiple sclerosis (MS) is more prevalent in women of childbearing age, prompting questions about the potential influence of pregnancy on disease progression. Pregnancy induces hormonal changes that can modulate the immune system, potentially affecting the course of MS. However, existing literature lacks consensus on the precise effects of pregnancy on MS Progression.

OBJECTIVES This study aims to assess the impact of pregnancies on secondary progression in individuals with MS (pwMS). By analyzing pregnancy data and disease progression timelines, we seek to elucidate any associations between pregnancy history and the risk of secondary progression in MS.

METHODS A retrospective analysis was conducted on a cohort of pwMS who had experienced at least one preterm or term delivery following their MS diagnosis. Data on pregnancy dates, birth dates, number of pregnancies, and time to secondary progression were collected and Analyzed.

RESULTS A total of 453 pwMS with at least one preterm or term delivery were included in the study. Among them, 36 individuals exhibited a progressive disease course (SPMS), while the majority (417) had relapsing-remitting MS (RRMS). Comparative analysis revealed no significant difference in the age of MS diagnosis between the SPMS and RRMS groups ($p>0.05$). However, the age at the first pregnancy was lower in the SPMS group compared to the RRMS group ($P=0.03$). Furthermore, the SPMS group had a higher number of pregnancies compared to the RRMS group ($p=0.02$). Interestingly, there was no discernible correlation between the number of pregnancies and the progression of age.

CONCLUSION Our findings suggest that a higher number of preterm or term pregnancies may be associated with an increased risk of disease progression in MS. This observation could potentially be attributed to extended periods of disease-modifying therapy interruption before, during, and after pregnancy, or hormonal dysregulation of the immune system. Further research is warranted to better understand the underlying mechanisms and to optimize management strategies for women with MS considering pregnancy.

027

# Pregnancy in Multiple Sclerosis and Its Impact on Disease Course

Taha Aslan, Ergi Kaya, Yasemin Şimşek, Sinem Özçelik, Asiye Tuba Özdoğar, Serkan Ozakbas

INTRODUCTION Understanding the effects of pregnancy on the course of MS can provide valuable insights guiding the management of MS during pregnancy and patient counseling.

OBJECTIVES The objective of this study is to assess the impact of pregnancy on relapse rates, MRI activity, and disease progression measured by the Expanded Disability Status Scale (EDSS) score among individuals with multiple sclerosis (MS).

METHODS A total of 117 patients were included in the analysis. Relapse rates, MRI activity, and changes in EDSS score were assessed in the three-year periods before and after pregnancy. Additionally, relapse occurrence during pregnancy and EDSS scores three years prior to and following pregnancy were examined.

RESULTS In the three years before pregnancy, 44.8% (n:52) had no relapses relapses, no MRI activity showed in 46.2% (n:54) of patients. Worsening of EDSS score in the three years before pregnancy not occurred in 59.8% (n:70). Between the three years before and after pregnancy, 88% (n:103) had no worsening of EDSS score, and mean worsening of EDSS score was 0.06±0.80 (min: -4; max: 2). In the three years following pregnancy, 56.4% (n:52) had no relapses, no MRI activity showed in 50.4% (n:59). Worsening of EDSS score in the three years following pregnancy not occurred in 70.1% (n:82). During pregnancy, 12% (n: 14) of pwMS experienced relapses. In the cohort, 24 pwMS were on fingolimod, 9 pwMS were on natalizumab, 49 pwMS were on interferon, and 7 pwMS were on teriflunomide. Among the 14 pwMS who experienced relapses, 6 (%25) were on fingolimod, 4 (%8) were on interferon, 2 (%22) were on natalizumab and 1 was on teriflunomide.

CONCLUSION The findings of this study contribute valuable insights into the complex relationship between pregnancy and MS progression. Despite concerns regarding potential exacerbation of MS symptoms during pregnancy, our results suggest that pregnancy may not significantly worsen the course of the disease. The observed low rates of relapse, stable EDSS scores, and comparable MRI activity before and after pregnancy indicate a relatively benign effect of pregnancy on MS progression. Clinicians can provide reassurance to women with MS who are considering pregnancy, emphasizing that pregnancy may not lead to worsening of their disease. However, it is essential for healthcare providers to closely monitor pregnant women with MS, as a subset of patients may experience relapses during pregnancy, particularly those on certain disease-modifying therapies. Furthermore, while our study provides valuable insights, larger-scale studies with diverse populations are warranted to confirm these findings and better understand the impact of pregnancy on MS progression. Additionally, future research should explore the underlying mechanisms behind the observed outcomes, which may further inform clinical decision-making and improve the overall management of MS in pregnant individuals.

SECTION VI

# Familial Multiple Sclerosis

3 ABSTRACTS

028

# Familial Multiple Sclerosis: Unveiling Disease Progression and Clinical Correlates

Yasemin Şimşek, Said Alizada, Can Caliskan, Serkan Ozakbas

INTRODUCTION In recent years, there has been interest in unraveling the familial aspects of multiple sclerosis (MS) and their implications for disease risk and progression. However, understanding of familial MS eludes us, urging further inquiry into this intriguing facet of the disease.

OBJECTIVES The aim of our study is to delve into the complexities of familial MS by conducting a comparative analysis between familial MS patients and a control group of non-familial MS patients. Our objective is to scrutinize various aspects including cerebrospinal fluid (CSF) results, disease course, Expanded Disability Status Scale (EDSS) scores, disease duration, treatments, and disease subtype, seeking to uncover potential patterns and associations.

METHODS We conducted a retrospective analysis of medical records from our MS cohort to identify cases of familial MS. All patients diagnosed with MS and treated at our clinic between 2013 and 2023 were included in the study. Data on familial relationships were collected through detailed patient interviews and medical records review. For each patient, MS subtype, treatments, current EDSS, date to first onset, date to diagnosis, and CSF results were documented and recorded. Descriptive statistics were used to analyze the relationship between the familial MS group and the control group, disease duration, time to diagnosis, CSF results, EDSS, and MS subtype.

RESULTS Within our cohort, we detected 523 cases of Familial MS. Age groups were equalized, and a control group of 512 non-familial MS patients was established. In the Familial MS group, 78% were diagnosed with RRMS, 3.5% with PPMS, 7.6% with CIS, and 10.9% with SPMS. In the non-familial MS group, these percentages were 76.7% RRMS, 5.2% PPMS, 11.1% CIS, and 7% SPMS. The incidence of secondary progressive MS in the Familial MS group was higher than in the control group ($p=0.030$). However, no significant difference was found between the Familial MS group and the control group concerning disease duration, time to diagnosis, EDSS, treatments, or CSF results (Oligoclonal band, IgG Index, IgM Index) ($p>0.05$).

CONCLUSION Our extensive analysis of the Familial MS Cohort sheds light on potential trends within the disease progression, particularly noting a higher prevalence of Secondary Progressive MS (SPMS), which suggests a potentially accelerated transition to this phase. This study serves as a foundational step towards unraveling the complexities of familial MS and its clinical implications.

029

# Exploring Familial Multiple Sclerosis: Insights from a Cohort Analysis

Serkan Ozakbas, Yasemin Şimşek, Can Caliskan, Sinem Ozcelik

INTRODUCTION Familial multiple sclerosis (MS) has increasingly captured the attention of researchers, presenting a fascinating avenue for exploration within the realm of neurology. This phenomenon, wherein MS occurs in multiple members of the same family, underscores the potential interplay between genetic predispositions and environmental factors in the etiology of the disease. Understanding the familial aspects of MS not only provides valuable insights into disease pathogenesis but also holds implications for risk assessment, prognosis, and therapeutic interventions. Our investigation delves into the familial patterns of MS within our cohort, aiming to unravel the genetic threads that contribute to its manifestation.

OBJECTIVES The aim of our study is to comprehensively examine the prevalence and characteristics of familial MS within our cohort, shedding light on the demographic features, kinship relationships, MS subtypes, and treatment modalities associated with this familial clustering. By elucidating the familial dynamics of MS, we seek to deepen our understanding of its underlying mechanisms and pave the way for personalized approaches to disease management. Through this exploration, we endeavor to contribute to the growing body of knowledge surrounding familial MS, ultimately informing clinical practice and guiding future research endeavors in this field.

METHODS All patients in our cohort for the study were screened for familial MS. While scanning familial data, kinship relationships with neuromyelitis optica spectrum disorder (NMO) and clinically isolated syndrome (CIS) patients were also detected. These kinship relationships were meticulously evaluated and included in our analysis.

RESULTS Among the 3411 MS patients in our cohort, 531 cases of familial MS were identified, yielding a familial MS rate of 14.1%. The majority were female (69.3%), with 40 presenting with CIS (7.5%) and 8 with NMO (1.5%). RRMS constituted the most prevalent subtype (76.8%), followed by SPMS (5.7%) and PPMS (3.4%). Treatment distribution revealed 33.1% on first-line, 35.2% on second-line, and 22% on third-line treatments, while 9.6% received no treatment. We observed 131 families with 2 to 5 patients, totaling 131 index patients and 659 kinship relationships. These included 37.2% first-degree, 11.9% second-degree, and 50.9% third-degree relatives, with diverse familial connections such as siblings, parents, children, and cousins.

CONCLUSION Through our cohort analysis, we shed light on the prevalence and characteristics of familial MS, revealing intriguing insights into its demographic patterns and familial associations. The substantial proportion of familial cases underscores the importance of genetic factors in MS susceptibility. Further investigation into the genetic and environmental determinants of familial MS is warranted to enhance our understanding and improve patient care strategies in this context.

030

# Unraveling the Genetic Threads: Exploring Familial Dynamics and Clinical Profiles in Pediatric-Onset Multiple Sclerosis

Yasemin Şimşek, Can Caliskan, Said Alizada, Serkan Ozakbas

INTRODUCTION Pediatric-onset Multiple Sclerosis (MS) has garnered increasing attention from researchers due to its unique characteristics and potential familial associations. Understanding the familial aspects of MS, especially in pediatric cases, not only enhances our understanding of disease pathogenesis but also holds implications for risk assessment, prognosis, and therapeutic interventions. In this study, we investigate familial patterns of pediatric-onset MS within our cohort to unravel the genetic links contributing to the emergence of MS.

OBJECTIVES Our study aims to comprehensively examine the prevalence and characteristics of pediatric-onset familial MS in our cohort, with a focus on demographic features, kinship relationships, MS subtypes, and treatment methods. By elucidating the familial dynamics of pediatric-onset MS, we aim to deepen our understanding of its underlying mechanisms and pave the way for personalized approaches to disease management. Through this research, we seek to contribute to the body of knowledge regarding pediatric-onset MS, informing clinical practice and guiding future research efforts.

METHODS We conducted a thorough screening for pediatric-onset familial MS among all patients in our study group, meticulously evaluating demographic data, kinship relationships, MS subtypes, and treatment histories. Inclusion criteria encompassed patients diagnosed with MS before the age of 18 and belonging to families with multiple affected individuals.

RESULTS Among 3411 MS patients in our cohort, 251 cases of pediatric-onset MS were identified, yielding a pediatric-onset MS rate of 7.36%. Within the cohort of 523 familial MS cases, 51 cases of pediatric-onset MS were detected, with a prevalence rate of 9.75%. The majority of patients were female (70.5%), and the most common MS subtype was Relapsing-Remitting MS (RRMS) (94%), followed by Secondary Progressive MS (SPMS) (6%). Primary Progressive MS (PPMS) cases were not observed. Among patients with available CSF analysis (n=31), 77.4% exhibited abnormal MS-typical findings, with 51% showing a high IgG index. Treatment distribution included 23.5% receiving primary care, 49% receiving secondary care, and 27.5% receiving tertiary-level treatment. The average Expanded Disability Status Scale (EDSS) score was 1.3. Eighteen patients had familial ties to MS, with six serving as index patients.

CONCLUSION Our study sheds light on the familial patterns and clinical characteristics of pediatric-onset MS, highlighting the potential genetic basis of the disease and emphasizing the importance of familial history in disease susceptibility. By enhancing our understanding of this complex disease, we can better inform clinical practice and improve patient outcomes in the future.

SECTION VII

# Comorbidities

5 ABSTRACTS

031

# The Co-Occurrence of Hashimoto Thyroiditis and Multiple Sclerosis: Implications for Prognosis and Clinical Management

Ergi Kaya, Gözde Deniz Ünal, İrem Kara, Serkan Ozakbas

INTRODUCTION Hashimoto thyroiditis (HT) and multiple sclerosis (MS) are autoimmune conditions that may coexist, potentially influencing disease progression and prognosis. Understanding the prevalence of HT in the MS population and its impact on MS prognosis is crucial for optimizing clinical management strategies.

OBJECTIVES This study aimed to investigate the prevalence of HT among individuals with MS and assess how the presence of HT affects the prognosis of MS over a five-year period.

METHODS A retrospective analysis was conducted, involving the review of medical records of individuals diagnosed with MS. Demographic data, Expanded Disability Status Score (EDSS) at diagnosis and follow-up, magnetic resonance imaging (MRI) findings, relapse history, depression diagnosis, and initial symptoms were recorded. Individuals with HT-related MS (htMS) were compared with an equal number of MS patients (pwMS) without HT (non-htMS).

RESULTS Out of 3501 pwMS, 57 (1.6%) had a concomitant diagnosis of HT, with all affected individuals being female. HT was observed in 0.1% of the general population, indicating a significantly higher prevalence in pwMS. Although both HT and MS are more common in females, the exclusive presence of HT among female subjects suggests a potential gender-specific predisposition. Comparative analysis between htMS and non-htMS groups revealed no significant differences in demographic characteristics, disease duration, initial symptom presentation, or EDSS scores at diagnosis or follow-up. Furthermore, MRI activity, relapse rates, and achievement of no evidence of disease activity 3 (NEDA-3) status were comparable between the two groups at the second-year follow-up.

CONCLUSION HT is more prevalent in pwMS compared to the general population, primarily affecting females. However, its co-occurrence does not significantly influence MS prognosis within the initial five years following diagnosis. These findings underscore the importance of considering comorbid autoimmune conditions in the management of MS, although further research is warranted to elucidate long-term implications and potential therapeutic implications. Additionally, gender-specific factors may contribute to the observed associations, necessitating tailored approaches to patient care and monitoring

032

# The Impact of Hashimoto's Thyroiditis on Cognitive and Physical Impairment in Individuals with Multiple Sclerosis

Gözde Deniz Ünal, İrem Kara, Yasemin Şimşek, Ergi Kaya, Serkan Ozakbas

INTRODUCTION Multiple sclerosis (MS) and Hashimoto's thyroiditis (HT) are often co-occurring autoimmune conditions. HT is characterized by autoimmune inflammation of the thyroid gland, typically leading to irregular production of thyroid hormones. On the other hand, MS is a chronic inflammatory disease of the central nervous system, typically resulting in demyelination and neuronal loss. Both conditions are rooted in complex etiological and pathophysiological mechanisms and can exhibit considerable variability in their clinical and pathological features.

OBJECTIVES The primary objective of this study is to compare cognitive and physical functions between individuals with MS diagnosed with and without HT. Understanding how an additional comorbidity such as Hashimoto's thyroiditis may impact the cognitive and physical status of individuals with MS is crucial both clinically and in research contexts. The findings of this study may contribute to identifying additional factors to consider in the management of individuals with MS and subsequently inform better clinical decision-making.

METHODS This retrospective study enrolled 34 females with MS and HT (mean age: 44.00±11.00, mean EDSS: 1.54±1.74) and 204 age and disease duration-matched women with MS without a diagnosis of HT. Cognitive function was assessed using the Symbol Digit Modalities Test (SDMT), California Verbal Learning Test Second Edition (CVLT-II), and Brief Visuospatial Memory Test-Revised (BVMT-R), while physical function was evaluated using the Timed 25-Foot Walk (T25FW) and 9-Hole Peg Test (9-HPT).

RESULTS Among individuals diagnosed with HT, mean scores were 48.47±14.47 for SDMT, 54.44±12.84 for CVLT-II, 25.97±6.28 for BVMT-R, 11.22±30.08 for T25FW, and 21.97±8.26 for 9HPT. In comparison, individuals without HT had mean scores of 47.32±14.36 for SDMT, 54.20±13.00 for CVLT, 25.19±6.81 for BVMT-R, 12.52±32.44 for T25FW, and 23.23±20.35 for 9-HPT. Statistical analysis revealed no significant differences between the two groups on any measurement ($p>0.05$).

CONCLUSION While HT, as an autoimmune process, may impact cognitive functions, our findings suggest that it does not lead to additional cognitive or physical impairment in individuals with relapsing-remitting MS. The presence of HT among individuals with MS did not significantly influence cognitive and physical impairment, as evaluated by the various measures utilized in this study.

033

# Epilepsy Prevalence and Characteristics in Patients with Multiple Sclerosis: Implications for Disease Management

Ergi Kaya, Ulvi Samadzade, Gözde Deniz Ünal, Ela Zengin, Serkan Ozakbas

INTRODUCTION Epilepsy is recognized as a potential comorbidity in multiple sclerosis (MS), adding complexity to disease management. The co-occurrence of epilepsy and MS presents clinical challenges and may impact disease progression and management. Understanding the prevalence and characteristics of epilepsy in MS patients is crucial for optimizing treatment strategies and improving patient outcomes.

OBJECTIVES This study aimed to investigate the prevalence of epilepsy and characterize patients with epilepsy and MS (pwE&MS) in terms of clinical features. By identifying patterns and associations, we sought to enhance our understanding of the relationship between epilepsy and MS.

METHODS A retrospective analysis was conducted on a cohort of MS patients to determine the prevalence of epilepsy and examine clinical characteristics associated with pwE&MS. Data on epilepsy diagnosis, disease duration, gender, disease progression, past history of depression, and location of initial symptoms were collected and analyzed.

RESULTS Among 3,463 MS patients, 1.9% had a diagnosis of epilepsy, with 10 of them exhibiting secondary progressive MS (SPMS). The prevalence of seizures was higher in the SPMS group (2.4%), with most experiencing their first seizure after disease progression, potentially related to cortical atrophy observed in SPMS. Epilepsy typically occurred after the diagnosis of MS, with a mean onset of 117.92 months (standard deviation = 102.3, range: 0-447) post-diagnosis. There was no significant difference in the location of initial symptoms between pwE&MS and MS-only patients. However, the prevalence of depression was approximately twofold higher in pwE&MS compared to MS-only patients (34% vs. 17%, $p < 0.05$).

CONCLUSION Our findings highlight the increased prevalence of seizures in MS patients, particularly in the progressive phase of the disease. The association between epilepsy and disease progression underscores the need for comprehensive monitoring and management strategies in MS patients with epilepsy. Additionally, the higher prevalence of depression in pwE&MS suggests the importance of addressing mental health concerns in this population. Further research is warranted to elucidate the underlying mechanisms and optimize therapeutic approaches for pwE&MS.

034

# Prevalence of Various Cancer Types Among Multiple Sclerosis Patients: Insights from a Retrospective Analysis

Said Alizada, Yasemin Şimşek, Serkan Ozakbas

INTRODUCTION Comorbidities, including cancer, present significant challenges in the management of individuals with multiple sclerosis (MS). Understanding the prevalence of different cancer types within the MS population is crucial for tailoring effective patient care and treatment strategies.

OBJECTIVES This retrospective analysis aims to investigate the prevalence of various cancer types among MS patients.

METHODS A retrospective analysis was conducted on 3460 MS cases diagnosed between 2015 and 2023 to assess the frequency of different cancer types within the cohort.

RESULTS Among the 3460 MS cases analyzed, 68% were female (n=2353) and 32% were male (n=1107). A total of 50 cases were diagnosed with cancer, with 40 cases in females and 10 cases in males. Breast cancer emerged as the most prevalent cancer type, representing 46% of total cases (n=23), with a prevalence rate of approximately 0.98%. Comparing this to the general female population in Turkey, where the age-standardized incidence rate (ASIR) of breast cancer in 2020 was estimated to be 42.4 per 100,000 females, suggests a notably lower prevalence among female MS patients. Other less common cancer types included thyroid cancer (8%, n=4), prostate cancer (4%, n=2), colon cancer (4%, n=2), and various other cancers.

CONCLUSION Our analysis highlights the varying prevalence rates of different cancer types among MS patients, with breast cancer being notably lower among female MS patients compared to the general female population in Turkey. Understanding these patterns is crucial for tailoring comprehensive care strategies to address the unique needs of MS patients, including cancer screening and management protocols. Additionally, a broader spectrum of cancer types was observed among MS patients, indicating the necessity for tailored screening and management approaches to address these diverse needs effectively.

035

# Impact of Body Weight on Five-Year Progression in Multiple Sclerosis: A Longitudinal Study

Gözde Deniz Ünal, Zuhal Abasıyanık, Yasemin Şimşek, Ela Zengin, Serkan Ozakbas

INTRODUCTION Obesity has been implicated as a risk factor for the development of multiple sclerosis (MS), yet its influence on disability progression remains poorly elucidated.

OBJECTIVES To investigate the effect of body weight on disability progression in persons with MS

METHODS This single-center longitudinal study included 123 persons with MS (pwMS). Disability level (EDSS), walking (Timed 25-Foot Walk and 6-Minute Walk Test) , manual dexterity (9-Hole Peg Test), and cognitive functions (Symbol Digit Modalities Test, California Verbal Learning Test, and Brief Visuospatial Memory Test-Revised) were compared at baseline and at year 5 between overweight [body mass index, BMI ≥25 kg/m2) and non-overweight (BMI <25 kg/m2) pwMS. The repeated measures ANOVA (RMANOVA) was conducted for time (baseline vs. 5th years) and group (overweight vs. non-overweight pwMS) effects.

RESULTS Sixty-seven pwMS (54.5%) were classified as non-overweight (mean EDSS:1.291.14) and 56 pwMS (45.5%) were overweight (mean EDSS:1.811.54). There was no change in EDSS scores in both groups at two time points (0.17 decrease in non-overweight group, 0.14 decrease in overweight group. The RMANOVA revealed no significant effects of time*group interaction on any physical and cognitive outcome measures.

CONCLUSION These findings suggest that, despite concerns regarding obesity in disease development, it may not precipitate deterioration in physical and cognitive function over time. This observation may be attributed to the relatively low EDSS levels in our sample and the maintenance of these levels over time.

SECTION VIII

# Biomarkers and Pharmacogenetics

7 ABSTRACTS

036

# Effect of Fc-γ Receptor Polymorphism on the Cognitive Functions in Patients With Multiple Sclerosis Treated With Ocrelizumab: A Retrospective Study

Pinar Yigit, Mukaddes Gumustekin, Muharrem Gurkan, Serkan Ozakbas

INTRODUCTION The Fc gamma receptors (FCGR) 2A and 3A gene polymorphisms has been reported with the susceptibility to multiple autoimmune diseases. Our study presents initial findings on the impact of the FCGR genetic variants on the cognitive functions in patients with multiple sclerosis (pwMS).

OBJECTIVES To assess the association between Fc-γ receptor polymorphisms with the cognitive functions in pwMS treated with ocrelizumab.

METHODS Two hundred pwMS (83 relapsing-remitting MS, 117 progressive MS, mean age 48.29, disease duration 16.99, EDSS 4.94, 64.4% female) receiving ocrelizumab were enrolled. The Brief International Cognitive Assessment for MS scores (BICAMS) in the last four years were recorded retrospectively. FCGR2A-131 and FCGR3A-158 gene polymorphisms were screened from blood samples. The dependent and independent samples t-test were used to assess cognitive performance. Hierarchical regression analysis was used to determine the effect of the genetic variations on cognitive performance. Demographic (age, gender, education) and clinical outcomes (MS form, disease duration, pre-post treatment EDSS) were entered in the first step, and genetic variations in the second step. NEDA-4 definition consists of the Symbol Digit Modalities Test (SDMT) as the fourth component.

RESULTS FCGR2A-131 and FCGR3A-158 polymorphisms were determined in 66% and 75.5% of pwMS, respectively, and 48.5% in both genes. The whole BICAMS scores were improved significantly in the first year ($p<0.05$). The FCGR2A polymorphism is associated with lower SDMT and California Verbal Memory Test results at baseline [$F(10,153) = 6.751$; $F(10,153) = 9.441$, $p<0.05$, respectively]. NEDA-4 improved by 68.5-79.6% during two years.

CONCLUSION The results showed that FCGR2A-131 gene polymorphism was related to cognitive functions in pwMS. The pharmacogenetic markers may be useful in evaluating the treatment efficacy of ocrelizumab in terms of cognitive status.

037

# The Association of Fc-γ Receptor Polymorphism With Efficacy in Patients With Multiple Sclerosis Treated With Ocrelizumab: A Retrospective Study

Pinar Yigit, Mukaddes Gumustekin, Muharrem Anil Gurkan, Ergi Kaya, Serkan Ozakbas

INTRODUCTION The Fc gamma receptors (FCGR) 2A and 3A gene polymorphisms have been associated with the clinical response to cell-depleting antibodies. This study firstly investigated the relationship between FCGR genetic variants and clinical response to ocrelizumab treatment.

OBJECTIVES To evaluate the association of Fc-γ receptor polymorphism with efficacy in patients with multiple sclerosis (pwMS) treated with ocrelizumab.

METHODS Our study included 200 patients with MS, comprising 83 with relapsing-remitting MS (RRMS) and 117 with progressive MS (PMS) receiving ocrelizumab (mean age 48.29, disease duration 16.99, EDSS 4.94, 64.4% female). The neurological assessments in four years of pwMS were recorded retrospectively. FCGR2A-131 and FCGR3A-158 gene polymorphisms were analysed from blood samples taken during routine controls. The associations between single-nucleotide polymorphisms and clinical outcomes were analyzed using chi-square tests, independent t-tests, and 2x2 mixed design ANOVA for the differences between two MS forms. The alpha level was set as <0.05.

RESULTS FCGR2A-131 and FCGR3A-158 polymorphisms were determined in 66% and 75.5% of pwMS respectively, and 48.5% in both genes. The FCGR2A polymorphism in PMS was significantly more than RRMS (68.7% vs 45.5%, respectively). There was no significant difference between the genetic variant groups in terms of EDSS and NEDA-3. The proportion of patients with increased EDSS was significantly higher in pwMS with heterozygous mutations of FCGR2A-131 and FCGR3A-158. The interaction between MS courses and measurement time was not significantly in EDSS changes during treatment [F (1, 191)=0.320, p=0.572].

CONCLUSION The heterozygous genotypes of FCGR2A-131 and FCGR3A-158 polymorphism adversely affects the treatment response. The results provide crucial information on Fc receptor polymorphisms for future clinical trials using OCR therapy.

038

# CXCL13 as a Biomarker for Cognitive Impairment in Multiple Sclerosis: An Investigative Study

Nurbanu Yapıcı, Cavid Baba, Sumeyye Cevik, Özge Sağıcı, Yavuz Dogan, Serkan Ozakbas

INTRODUCTION Cognitive impairment in multiple sclerosis (MS), occurring in 35-65% of patients, can be detected independently of other neurological symptoms even in the earliest stages and is associated with increased future disability.

OBJECTIVES This study aims to examine the relationship between CXCL13 and early cognitive involvement.

METHODS Thirty-nine newly diagnosed individuals with relapsing-remitting MS (RRMS) were assessed using the Brief Repeatable Battery of Neuropsychological Tests (BRBN), the Brief International Cognitive Assessment for MS (BICAMS), and the Stroop test at the beginning of the study. Approximately one year later, 31 patients were reassessed with BICAMS, 29 with BRBN, and 28 with the Stroop test. Test results below 1.5 standard deviations from normative data were considered impaired. Cognitive impairment was classified if there were abnormalities in 2 out of 5 tests for BRBN and 1 out of 3 tests for BICAMS. Baseline cerebrospinal fluid (CSF) CXCL13, CXCL13 index, and serum CXCL13 levels were measured for all 39 patients. The Mann-Whitney U test was used to compare CXCL13 parameters between groups. The relationship between test results and CXCL13 parameters was evaluated using Spearman correlation analysis.

RESULTS When comparing the groups with and without impairment in initial BRBN or BICAMS tests, serum CXCL13 was higher in the non-impaired group (p=0.033). In the group with impairment in the initial Brief Visuospatial Memory Test (BVMT), CSF CXCL13 (p=0.059) and CXCL13 index (p=0.047) were higher. Serum CXCL13 was higher in the group without impairment in the final BVMT test and the initial Selective Reminding Test (SRT) (both p=0.068). CSF CXCL13 was higher in the group without impairment in the California Verbal Learning Test (CVLT) first test (p=0.023), while the CXCL13 index was higher in the group with impairment in the Stroop post-test (p=0.016).

CONCLUSION This study reveals a complex relationship between CXCL13 levels and cognitive impairment in MS. Higher CSF CXCL13 and CXCL13 index values were linked to poorer cognitive outcomes, suggesting greater neuroinflammation and cognitive decline. Conversely, higher serum CXCL13 levels were associated with better cognitive performance, indicating a possible protective role. These findings suggest that CXCL13 levels in both CSF and serum could be important biomarkers for cognitive prognosis in MS. Further research is needed to identify affected cognitive domains and understand the protective mechanisms of serum CXCL13.

039

# Biomarker Chronicles: Investigating CXCL13 and Parvalbumin in Multiple Sclerosis Management

Nurbanu Yapıcı, Sümeyye Çevik, Cavid Baba, Seda Dastan, Yavuz Doğan, Serkan Ozakbas

INTRODUCTION Predicting prognosis in multiple sclerosis (MS) is crucial for effective patient management and treatment decisions. Reliable biomarkers are essential for achieving this goal. Among these, CXCL13 and parvalbumin have shown promise in their association with MS outcomes.

OBJECTIVES This study explores the link between cerebrospinal fluid (CSF) and serum levels of CXCL13 and parvalbumin with clinical and radiological outcomes in MS, highlighting their potential in predicting disease course and treatment response.

METHODS We analyzed CSF and serum levels of CXCL13 and parvalbumin in 39 individuals with relapsing-remitting multiple sclerosis (RRMS) using Enzyme-Linked ImmunoSorbent Assay (ELISA). Additionally, the CXCL13 index was calculated. Demographic data, Expanded Disability Status Scale (EDSS) assessments, Timed 25 Foot Walk Test (T25FW) results, Nine-Hole Peg Test (9HPT) outcomes, and neuroimaging characteristics of RRMS individuals were recorded. Follow-up assessments were conducted approximately one year later, with repeat EDSS assessments and physical tests in 32 RRMS individuals.

RESULTS Negative parvalbumin levels were observed in individuals with RRMS, suggesting limited utility as an early prognostic biomarker in those with short disease duration. No significant correlations were found between age at diagnosis, time from first symptom to diagnosis, initial EDSS, and CSF or serum CXCL13 levels in RRMS individuals. Furthermore, there were no significant differences in CXCL13 parameters between female and male groups. However, a significant negative correlation was found between follow-up EDSS and serum CXCL13 levels. Serum CXCL13 was notably lower in RRMS patients with a 20% increase in T25FW compared to those without an increase. Additionally, CSF CXCL13 and CXCL13 index were higher in RRMS individuals without spinal cord lesions compared to those with lesions.

CONCLUSION The findings contribute to our understanding of CXCL13 and parvalbumin as potential biomarkers in MS management. Negative parvalbumin levels suggest limited prognostic value in short disease duration, while serum CXCL13 levels correlate with disease outcomes, indicating its potential as a prognostic indicator and treatment response predictor. Unexpectedly, higher CSF CXCL13 levels in those without spinal cord lesions warrant further investigation. These findings underscore the importance of continued biomarker research to improve early prognosis prediction and personalized treatment in MS.

040

# Does the Association of CXCL13 and CSF Profile in MS Support the Role of CXCL13 as a Potential Prognostic Biomarker?

Nurbanu Yapıcı, Sumeyye Cevik, Cavid Baba, Yavuz Dogan, Serkan Ozakbas

INTRODUCTION The examination of cerebrospinal fluid (CSF) in individuals with multiple sclerosis (MS) is crucial for diagnosis, differential diagnosis, predicting disease activity, and providing prognostic information. Higher IgG and IgM indices are known to be associated with worse clinical outcomes. Evidence suggests that CSF levels of CXCL13, a B cell chemoattractant, also have predictive value for future disease activity.

OBJECTIVES This study aimed to investigate the relationship between classical CSF parameters and CSF CXCL13, serum CXCL13, and the CXCL13 index.

METHODS The study included 39 newly diagnosed individuals with relapsing-remitting multiple sclerosis (RRMS). CSF and serum CXCL13 levels were measured using the enzyme-linked immunosorbent assay (ELISA) method. For participants with matching CSF and serum samples, the CXCL13 index was calculated using the formula (CSF/Serum CXCL13) / (CSF/Serum albumin). The linear relationships between CSF protein level, albumin level, number of OCB bands, IgG index, IgM index, and CXCL13 parameters were evaluated using Spearman correlation analysis. Additionally, the CXCL13 parameters of different groups - OCB positive vs. negative, IgG index> 0.7 vs. ≤ 0.7, and IgM index> 0.1 vs. ≤ 0.1 - were compared using the Mann-Whitney U test.

RESULTS The analysis revealed no significant correlation between CSF protein, albumin levels, Q albumin value (CSF albumin(mg/L) / serum albumin(mg/dl)), and the number of OCB bands with CSF and serum CXCL13 levels or the CXCL13 index ($p>0.05$). However, there was a positive correlation between the CSF IgG index and both CSF CXCL13 levels ($r=0.381$, $p=0.017$) and the CXCL13 index ($r=0.394$, $p=0.034$). Notably, CSF CXCL13 levels were higher in the group with an IgG index> 0.7 compared to the group with an IgG index ≤ 0.7 ($p=0.052$). Similarly, the CXCL13 index was higher in the group with an IgG index> 0.7 ($p=0.048$). Additionally, CSF CXCL13 levels were higher in the group with an IgM index> 0.1 compared to those with an IgM index ≤ 0.1 ($p=0.040$).

CONCLUSION This study indicate that there is a significant correlation between CSF CXCL13 levels and the CXCL13 index with the IgG index, suggesting that higher levels of CSF CXCL13 and a higher CXCL13 index are associated with increased intrathecal immunoglobulin synthesis. Furthermore, the elevated CSF CXCL13 levels in groups with higher IgG and IgM indices support the potential role of CSF CXCL13 and the CXCL13 index as prognostic biomarkers for future disease activity in MS patients.

041

# The Oligoclonal Band Dilemma: Decoding its Role in Predicting Relapsing-Remitting Multiple Sclerosis Progression

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

INTRODUCTION Understanding the prognostic factors influencing the clinical course of relapsing-remitting multiple sclerosis (RRMS) is crucial for optimizing patient management strategies. Oligoclonal bands (OCBs) in cerebrospinal fluid have been proposed as a potential prognostic marker, yet their association with disease progression remains debated. This study aims to elucidate whether OCB positivity (OCB+) correlates with worse clinical outcomes compared to OCB negativity (OCB-) over 2 and 5 year periods in RRMS patients.

OBJECTIVES The objective of this retrospective study is to investigate the prognostic implications of OCB positivity in RRMS patients by comparing clinical outcomes, including Expanded Disability Status Scale (EDSS) scores, attack frequency, and progression to secondary progressive MS (SPMS), between OCB+ and OCB-groups over 2 and 5 year intervals.

METHODS A cohort of 2324 RRMS patients, comprising 1613 females (69.4%) and 711 males (30.6%), was retrospectively analyzed. OCB status was determined, with 1915 (82.4%) classified as OCB+ and 409 (17.6%) as OCB-. Clinical outcomes were assessed at 2 and 5 year intervals. Statistical analyses included independent samples t-tests for EDSS scores and attack rates, and chi-squared tests for SPMS progression rates between OCB+ and OCB-groups.

RESULTS At the 2 year follow-up, no significant differences were observed in EDSS scores ($p = 0.734$) or attack rates ($p = 0.464$) between OCB+ and OCB-patients. Progression to SPMS within 2 years also showed no significant difference ($p = 0.633$). Similarly, at the 5 year follow-up, EDSS scores ($p = 0.615$) and attack rates ($p = 0.549$) remained statistically insignificant between the two groups. However, a significant difference in 5 year progression to SPMS was noted ($p = 0.024$), with a higher proportion of OCB+ patients progressing compared to OCB-patients.

CONCLUSION The presence of oligoclonal bands does not significantly impact disability progression or attack frequency over 2 and 5 year periods in RRMS patients. While no difference was observed in SPMS progression at 2 years, a significant discrepancy emerged at the 5 year mark, suggesting a potential prognostic role for OCB positivity in long-term disease evolution. Further research is warranted to elucidate the underlying mechanisms driving these differences and to refine prognostic models in RRMS.

042

# Examining Classical Cerebro-Spinal Fluid Biomarkers in Primary Progressive Multiple Sclerosis: Implications for Prognosis

Nurbanu Yapıcı, Ergi Kaya, Yasemin Şimşek, Serkan Özakbaş

INTRODUCTION Primary progressive multiple sclerosis (PPMS) presents unique challenges in diagnosis and prognosis assessment. Oligoclonal bands (OCB), immunoglobulin G (IgG), and IgM index are pivotal cerebrospinal fluid (CSF) biomarkers for PPMS diagnosis, yet their prognostic value remains underexplored.

OBJECTIVES This study aims to comprehensively investigate the prevalence and clinical significance of classical CSF biomarkers, including OCB, IgG, and IgM index, in individuals with PPMS. Additionally, we aim to compare these biomarker profiles between PPMS and relapsing-remitting multiple sclerosis (RRMS) cohorts to discern any distinctive features that may inform prognosis and guide personalized treatment strategies.

METHODS We conducted a retrospective analysis of PPMS patients diagnosed according to the 2017 McDonald criteria. Demographic data, follow-up duration, expanded disability score (EDSS) at baseline and follow-up, OCB, IgG index, IgM index positivity, initial symptom localizations, and T1 black hole presence in magnetic resonance imaging (MRI) were collected. OCB positivity was defined as type 2 or 3 OCB result, IgG index positivity as ≥ 0.7, and IgM index positivity as ≥ 0.1. Patients were categorized into OCB+/-, IgM+/-, and IgG+/- groups.

RESULTS Of the PPMS patients, 73.1% were OCB-positive, 29% were IgM index positive, and 50% were IgG index positive. OCB and IgG index positivity resembled cerebrospinal fluid characteristics of relapsing-remitting multiple sclerosis patients (70% OCB positivity, 47% IgG index positivity). However, IgM index positivity was slightly lower in PPMS compared to RRMS (29% vs. 38%). Median follow-up duration was 3.55 years, with no significant differences between OCB+/-, IgM+/-, and IgG+/- groups. No variations were observed in gender, diagnosis age, duration between first symptom and diagnosis, initial symptom localizations, and EDSS worsening among the groups. The OCB+ group exhibited more T1 black holes on MRI compared to the OCB-group (p=0.032).

CONCLUSION PPMS patients exhibit higher IgM index positivity compared to RRMS, suggesting potential differences in disease pathogenesis. Furthermore, the presence of oligoclonal bands may indicate more severe MRI findings, emphasizing its relevance in PPMS prognosis assessment. Further research is warranted to elucidate the prognostic implications of these classical biomarkers in PPMS management.

SECTION IX

# Treatment and Real-World Evidence

4 ABSTRACTS

043

# Natalizumab Treatment Outcomes and Safety Profile in Women with Multiple Sclerosis: Insights from Real-world Data

Yasemin Şimşek, Zuhal Abasıyanık, Ulvi Samadzade, Serkan Ozakbas

INTRODUCTION Multiple sclerosis (MS) predominantly affects young women, and Natalizumab stands as a significant treatment modality impacting disease progression and reducing disease activity. However, a comprehensive evaluation of the safety and efficacy of Natalizumab specifically in women remains lacking.

OBJECTIVES This study aimed to assess the efficacy and safety profile of Natalizumab in the treatment of MS among women. By delving into real-world data, this investigation seeks to provide insights into treatment outcomes and potential side effects of Natalizumab in women with MS characterized by high disease activity.

METHODS This cross-sectional study recruited 167 women diagnosed with MS and currently undergoing Natalizumab treatment. Medical records were meticulously reviewed to collect comprehensive data on disease progression parameters, including Expanded Disability Status Scale (EDSS) scores, relapse rates, and details of current and prior treatments. Additionally, participants underwent semi-structured interviews conducted by a skilled MS nurse to gather in-depth information regarding participants' pregnancy and childbirth experiences, including details on Natalizumab use during pregnancy and breastfeeding.

RESULTS Among the 167 women receiving Natalizumab treatment for MS, various patterns of Natalizumab use during pregnancy and breastfeeding were observed. Natalizumab treatment was discontinued in 61.1% of patients, with reasons including confirmation of pregnancy, adverse events, positive John Cunningham virus (JCV) status, disease progression, lack of efficacy, cancer diagnosis, and patient preference.

CONCLUSION This real-world study provides valuable insights into the utilization and outcomes of Natalizumab treatment among women with MS. Importantly, the study highlights the complexities involved in managing MS in women, particularly concerning treatment decisions in the context of pregnancy and disease progression. While Natalizumab remains a crucial therapeutic option for managing MS, the decision-making process regarding its use must consider individual patient factors, including pregnancy status and disease activity. The observed discontinuation rates underscore the need for ongoing monitoring and evaluation of treatment effectiveness and safety.

044

# Impact of Treatment Change on Long-Term Disease Outcomes in Multiple Sclerosis: Beyond Ineffectiveness

Nurbanu Yapıcı, Ulvi Samadzade, Yasemin Şimşek, Irem Kara, Turhan Kahraman, Serkan Özakbaş

INTRODUCTION Multiple sclerosis (MS) is a chronic inflammatory disease of the central nervous system (CNS) characterized by inflammation, demyelination, gliosis, and axonal damage, particularly affecting young adults. Disease-modifying therapies (DMTs) alter the course of MS through immunosuppression or immunomodulation. Despite considerations of the side effect profiles and effectiveness of DMTs during clinical follow-up, determining the right medication at the right time can still be challenging for clinicians.

OBJECTIVES The aim of this study was to compare relapse rates among people with MS who switched DMTs due to side effects with those who switched DMTs for other reasons, such as lack of efficacy, pregnancy, or scheduled stop.

METHODS A retrospective analysis was conducted on a cohort of 337 people diagnosed with MS who had undergone treatment changes and were followed up for 10 years. Patients were divided into two groups based on the reason for treatment discontinuation: side effects (n=253, 75%) and lack of efficacy/pregnancy/scheduled stop (n=84, 25%). Demographic and clinical characteristics were compared between the two groups using the Mann-Whitney U test. The primary outcome measure was the number of relapses after treatment discontinuation.

RESULTS There were no significant differences in sex, age, disease duration, disease type, or Expanded Disability Status Scale (EDSS) scores between the two groups ($p>0.05$). However, patients who discontinued DMT due to side effects experienced significantly more relapses after switching medications [median = 2, interquartile range (IQR) = 0-3] compared to those who discontinued due to pregnancy or inefficacy (median = 1, IQR = 0-2) ($p<0.001$).

CONCLUSION The findings of this study underscore the significant impact of treatment change on long-term disease outcomes in individuals with multiple sclerosis (MS), particularly when considering factors beyond treatment ineffectiveness. Patients who discontinued DMTs due to side effects experienced a higher number of relapses after switching medications compared to those who discontinued due to pregnancy or inefficacy. This highlights the importance of careful consideration of treatment decisions, especially when managing adverse effects, to optimize patient outcomes.

045

# Impact of Early Treatment Modification on Long-Term Outcomes in Treatment-Naive Multiple Sclerosis Patients: Adverse Reactions and Compliance Challenges

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INTRODUCTION Multiple sclerosis (MS) is an autoimmune demyelinating and neurodegenerative disease of the central nervous system. Early initiation and continuous adherence to treatment are recognized as crucial in mitigating disability progression in individuals with MS.

OBJECTIVES Evaluation of 5-year outcomes of naive patients with MS who discontinued disease-modifying medications due to side effects or noncompliance within the first year.

METHODS Patients were categorized into two groups: those who discontinued the drug within the first year due to side effects or incompatibility and those who used it continuously for 5 years. There were no significant differences between the groups in terms of age and gender. Both groups included treatment-naive patients. Outcome evaluation included the number of attacks, EDSS scores, and conversion to secondary progression after an average of 5 years in both groups.

RESULTS Seventy-two MS patients were included in the first group, and 37 MS patients were included in the second group. In the first group, 66.7% (n=48) of patients were female, and 33.3% (n=24) were male. In the second group, 67.57% (n=25) were female, and 32.43% (n=12) were male. At the end of 5 years, the EDSS score (Mean difference 1.625, 95% CI 0.887; 2.363, $p<0.001$) and relapse frequency (Mean difference 1.217, 95% CI 0.715; 1.719, $p<0.001$) were significantly lower in patients who used medication for 5 years compared to those who stopped taking medication within 1 year. In the first group, the percentage of patients who transitioned to the secondary progressive phase was 22% (n=16). No transition to the secondary progressive phase was observed in the second group.

CONCLUSION Early discontinuation of treatment due to side effects or noncompliance may lead to unfavorable clinical outcomes, including disease progression and increased relapse frequency. Therefore, clinicians should prioritize the selection of DMDs with favorable tolerability profiles and engage in proactive patient education and monitoring to optimize treatment adherence and long-term outcomes in individuals with MS. Further research is warranted to elucidate the underlying factors contributing to treatment discontinuation and to develop strategies to mitigate this challenge in clinical practice.

046

# Exploring the Impact: An Analysis of Cladribine Treatment in Multiple Sclerosis Management

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INTRODUCTION Cladribine, a promising disease-modifying therapy (DMT), offers potent immunomodulatory effects with a favorable safety profile. However, its impact on cognitive and physical function in multiple sclerosis (MS) patients warrants further investigation.

OBJECTIVES This abstract presents a comprehensive evaluation of the efficacy and safety of cladribine treatment in people with MS (pwMS), focusing on cognitive and physical outcomes besides clinical outcomes.

METHODS A cohort of 125 participants diagnosed with MS underwent treatment with cladribine. Thirty participants underwent cognitive and physical assessments. The assessments were conducted at baseline (T0) and follow-up (first year=T1). Cognitive function was evaluated using the Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS) battery, including the California Verbal Learning Test (CVLT), Brief Visuospatial Memory Test-Revised (BVMTR), and Symbol Digit Modalities Test (SDMT). Physical function was assessed through the Timed 25-Foot Walk (T25FW) and Nine-Hole Peg Test (N-HPT). The Expanded Disability Status Scale (EDSS), disease duration, age, presence of new attacks, and new MRI findings were recorded.

RESULTS The mean age and disease duration were 36.22±10.65 and 8.04±6.41, respectively. Cladribine treatment led to significant improvements in verbal and visual memory components of cognitive function, evidenced by markedly higher performance on CVLT (T0:56.94±12.02, T1:61.59±10.67) and BVMTR (T0:27.75±5.38, T1:29.44±5.35) tests at follow-up. However, no significant differences were observed in physical function measures (T25FW and N-HPT) or information processing speed (SDMT scores) between baseline and follow-up assessments. Notably, only a small percentage of participants experienced new attacks during the treatment period (n=5, 4%), and few participants had new MRI findings (n=2, 1.6%) in the third and fourth years.

CONCLUSION The low incidence of new attacks and new MRI lesions observed in participants under cladribine treatment underscores its efficacy in managing disease activity and progression. These findings suggest that cladribine treatment not only improves cognitive function but also reduces the likelihood of disease relapses and new lesion formation, indicating its potential as a highly effective therapeutic option for managing MS symptoms. Further research is warranted to elucidate its impact on physical function and long-term safety profiles.

SECTION X

# Neuromyelitis Optica Spectrum Disorder

4 ABSTRACTS

047

# Familial Patterns and Clinical Correlates of Neuromyelitis Optica: Insights from a Cohort Study

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INTRODUCTION The existence of cases where both neuromyelitis optica (NMO) and multiple sclerosis (MS) occur within the same family suggests a potential proximity between these two diseases. This phenomenon underscores the complex interplay between genetic predispositions and environmental factors in the etiology of NMO. Understanding the familial aspects of NMO not only enriches our understanding of disease pathogenesis but also holds implications for risk assessment, prognosis, and therapeutic strategies. In this context, our research endeavors to elucidate familial patterns within our cohort, aiming to unravel the genetic underpinnings contributing to the emergence of NMO.

OBJECTIVES Our study aims to comprehensively assess the prevalence and characteristics of familial NMO in our cohort, shedding light on demographic features, consanguinity, and treatment modalities associated with this familial clustering. By deciphering the familial dynamics of NMO, we seek to deepen our understanding of its underlying mechanisms and explore potential similarities with MS to pave the way for personalized approaches to disease management.

METHODS We conducted a thorough screening for familial neuromyelitis optica spectrum disorder (NMO) among all patients in our study group, with simultaneous identification of familial multiple sclerosis (MS) kinship relationships. These relationships were meticulously evaluated and incorporated into our analysis.

RESULTS Among 91 NMO patients in our cohort, we identified 8 cases of familial NMO, resulting in a familial NMO rate of 8.8%. The majority of affected individuals were women (n=6), with an average Expanded Disability Status Scale (EDSS) score of 2.3. Treatment regimens included rituximab for 6 patients and azathioprine for 2 patients. Four patients had familial ties to MS, forming 4 familial MS clusters. The observed familial relationships included mother-daughter, brother-brother, cousins, nephew-uncle, and nephew-aunt pairs.

CONCLUSION Our cohort analysis reveals intriguing insights into NMO, particularly in relation to familial clustering and its potential association with MS. The notable prevalence of familial cases underscores the significance of genetic factors in NMO susceptibility and suggests a possible shared genetic basis between NMO and MS. Understanding these dynamics is pivotal for tailored interventions and family-centric approaches to NMO management. Further exploration of the genetic and environmental determinants of familial NMO is imperative to enhance our understanding and optimize patient care strategies.

048

# Kinematic Analysis of Gait Parameters in Patients Affected by Neuromyelitis Optica Spectrum Disorders: A Comparative Study

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INTRODUCTION Neuromyelitis optica spectrum disorder (NMOSD) represents a chronic inflammatory and autoimmune condition characterized by a range of debilitating symptoms, including impaired vision, sensory loss, pain, fatigue, and limb spasms. Among these challenges, gait abnormalities hold particular significance due to their profound impact on the daily functioning and overall well-being of affected individuals. However, the nuanced features of gait impairment in NMOSD necessitate further elucidation.

OBJECTIVES To comprehensively analyze the spatiotemporal parameters of gait in patients with NMOSD (pwNMOSDs) compared to healthy subjects (HS).

METHODS 10 pwNMOSDs and 9 HS, matched for age and gender, were recruited for this investigation. PwNMOSDs included in the study were specifically chosen from individuals exhibiting low disability, categorized with 0 or 1 in the pyramidal functional system. The evaluation of gait parameters, including cadence, walking speed, stride length, gait cycle duration, initial contact angle (ICA), toe-off angle (TOA), and step duration, was conducted using the APDM Movement Monitoring inertial sensor system. Data were collected during a 2-minute walk test completed by all participants.

RESULTS The study cohort comprised pwNMOSDs with a mean age of 47±14.82 years, EDSS score of 1.45±0.93 (range: 0 to 2.5), and disease duration of 6.67±4.80 years. In the HS group, the mean age was 50.67±12.54 years. The female-to-male ratio was 7:3 in pwNMOSDs and 6:3 in HS. Significant differences were observed between groups in gait speed (pwNMOSDs=1.24±0.15 vs. HS=1.59±0.20, $p<0.001$), stride length (pwNMOSDs=1.22±0.11 vs. HS=1.46±0.18, $p=0.002$), and total distance covered during the 2-minute walk test (pwNMOSDs=136.80±19.04 vs. HS=185.67±29.93, $p<0.001$). However, no significant differences were found between groups in cadence (pwNMOSDs=121.80±10.54 vs. HS=130.28±9.35, $p=0.082$), gait cycle duration (pwNMOSDs=0.99±0.09 vs. HS=0.93±0.07, $p=0.098$), initial contact angle (ICA) (pwNMOSDs=25.33±6.05 vs. HS=27.83±3.34, $p=0.288$), toe-off angle (TOA) (pwNMOSDs=37.53±5.18 vs. HS=39.36±3.57, $p=0.389$), and step duration (pwNMOSDs=0.50±0.05 vs. HS=0.46±0.04, $p=0.098$).

CONCLUSION This study provides objective insights into gait parameters affected in mild disability pwNMOSDs, revealing differences in gait speed, stride length, and total distance covered during the 2-minute walk test. Notably, the inclusion of pwNMOSD with low pyramidal scores suggests that observed differences between groups may be attributable to the cumulative impact of the disease. These findings hold clinical relevance for informing rehabilitation strategies tailored to the specific needs of this population.

049

# Can the Age of the First Symptom for Neuromyelitis Optica Be Used to Predict Cognitive Impairment?

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INTRODUCTION Cognitive functions, including working memory, attention, word fluency, and information processing speed, are known to be impacted in individuals with multiple sclerosis (pwMS). Despite the clinical similarity of cognitive complaints between persons with neuromyelitis optica (pwNMO) and pwMS, there is a paucity of research addressing cognitive impairment (CI) in NMO literature.

OBJECTIVES The aim of this study is to investigate the potential association between the age of initial symptoms onset (ISO) and the presence of CI in pwNMO.

METHODS This study comprised two groups: 11 pwNMO with ISO between the ages of 18-29 and 15 pwNMO with ISO between the ages of 30-50. To mitigate potential confounding effects on CI, pwNMO were included in the study with matched education levels and ages. A cohort of 467 healthy controls underwent assessment using the Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS) battery, with a predefined cut-off value for cognitive impairment set at 1.5 standard deviations below the mean. Individuals performing below this threshold were classified as exhibiting CI in the respective domain. Severity of CI was stratified based on the number of affected domains: individuals with impairment in one domain were classified as having moderate-to-severe impairment, those with impairment in two domains as severe, and those with impairment across all three domains as very severe.

RESULTS None of the pwNMO with ISO between the ages of 18-29 exhibited CI. However, among those with ISO between the ages of 30-50, 3 demonstrated moderate-to-severe cognitive impairment, 1 severe cognitive impairment, and 1 very severe cognitive impairment.

CONCLUSION The results of this study indicate a potential link between the age of ISO and CI in individuals with pwNMO. Specifically, none of the individuals who experienced ISO between the ages of 18-29 exhibited CI, whereas among those with ISO between the ages of 30-50, a notable proportion demonstrated varying degrees of CI.These findings suggest that a later onset age of NMO symptoms may contribute to an increased risk of CI. Therefore, early initiation of treatment could be vital in preventing and managing CI in pwNMO. Further research is warranted to validate these findings and elucidate the underlying mechanisms driving this association.

050

# Comparative Analysis of Comorbidities in Neuromyelitis Optica Spectrum Disorders and Multiple Sclerosis: Insights into Disease Pathogenesis and Management

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INTRODUCTION Comorbidities play a significantly impact the clinical management and prognosis of Neuromyelitis Optica Spectrum Disorders (NMOSD) and Multiple Sclerosis (MS) and are known to influence disease outcomes and treatment strategies in NMOSD and MS. However, the comparative analysis of comorbidities between these two conditions remains limited. Understanding the prevalence and spectrum of comorbidities in NMOSD and MS can provide valuable insights into disease pathogenesis and guide clinical management decisions.

OBJECTIVES This study aimed to detect and compare the spectrum and prevalence of common comorbidities in NMOSD patients, comparing them with those observed in MS. By elucidating differences in comorbidity profiles, we sought to enhance our understanding of disease-specific manifestations and inform tailored management approaches.

METHODS A retrospective analysis of medical records was conducted for individuals diagnosed with NMOSD and MS. The presence of comorbidities, including hypertension, type 2 diabetes mellitus, herpes zoster, systemic lupus erythematosus (SLE), psychiatric diseases, neuropathic pain, and avascular necrosis was documented. Comparative analyses were performed to assess differences in comorbidity prevalence between NMOSD and MS cohorts.

RESULTS A total of 83 NMOSD and 2674 MS patients were included in the study, with a predominance of females in both groups (79% NMOSD, 68% MS). NMOSD patients exhibited a significantly higher prevalence of systemic lupus erythematosus (4.83% vs. 0.03%), hypertension (15.6% vs. 8.2%), type 2 diabetes mellitus (10% vs. 4.6%), avascular necrosis (6% vs. 1.6%), and herpes zoster (4.8% vs. 0.8%) compared to MS patients ($p < 0.05$). However, neuropathic pain, psychiatric diseases, and malignancies showed similar prevalence rates between NMOSD and MS cohorts ($p > 0.05$).

CONCLUSION Our findings highlight distinct comorbidity profiles between NMOSD and MS patients, with NMOSD demonstrating a higher prevalence of certain comorbidities such as systemic lupus erythematosus, hypertension, type 2 diabetes mellitus, avascular necrosis, and herpes zoster. These differences may reflect underlying pathogenic mechanisms unique to NMOSD, including lesion localization and immune dysregulation. Understanding the differential comorbidity burden in NMOSD and MS can inform targeted management strategies and improve patient care outcomes.