

Aging with MS

Michela Ponzio¹, Andrea Tacchino¹, Paola Zaratini¹, Mario Alberto Battaglia², Giampaolo Bricchetto¹

¹Department of Research, Italian Multiple Sclerosis Foundation, Genoa, Italy; ²Department of Life Science, University of Siena, Italy

Introduction Even though Multiple Sclerosis (MS) is often described as a disease of young and middle aged adults, about 10% of all people with MS (PwMS) are over the age of 65. Although the proportion of elderly PwMS is relatively small, the general and disability-specific trends towards increasing life expectancy suggest that their numbers are likely to increase over time [1,2]. Few studies evaluated what it means to grow old with a disability as MS, and what are the unmet needs for these patients.

Objects To identify the aspects changing with aging in PwMS.

Methods Data, derived from the project "A New Functional Profile to Monitor the Progression of disability in MS", were collected on consecutive outpatients or in-home rehabilitation patients attending the North Italy Rehabilitation units (Genoa, Padua, Como, Aosta, Brescia, Vicenza). We analyzed the first visit data (before to any rehabilitation treatment) including only patients with relapsing-remitting and secondary-progressive form.

Analysis Participants were divided in two groups, based on age (≥ 60 and < 60 years). Differences between groups were evaluated using univariate analysis (χ^2 or Mann-Whitney U test), and a logistic regression model was performed to test the relationship between explanatory variables selected in univariate analysis ($p < 0.10$) and the subjects age ($< 60y$ and $\geq 60y$). Collinearity was assessed for logistic regression model using variance inflation factor (VIF) and Tolerance techniques. The final model only includes significant predictors, after selection using the likelihood ratio test.

Clinical scales collected during the visit

Outcome	Clinical Scale
Disability level	Expanded Disability Status Scale (EDSS)
Fatigue in terms of physical, cognitive, and psychosocial functioning	Modified-Fatigue Impact Scale (M-FIS)
	M-FIS1 subscale cognitive fatigue
	M-FIS2 subscale physical fatigue
Functional Independence as cognitive and social skills, communication, sphincter control, personal care, locomotion and mobility	M-FIS3 subscale psychosocial fatigue
	Functional Independence Measure (FIM)
	FIM1 subscale cognitive and social skills
	FIM2 subscale communication
	FIM3 subscale sphincter control
	FIM4 subscale personal care
Life Satisfaction	Life Satisfaction Index (LSI)
	Montreal Cognitive Assessment (MoCA)
Cognitive impairment	Montreal Cognitive Assessment (MoCA)
Attention impairment	Symbol Digit Modality Test (SDMT)
Cognitive and attention impairment and information processing speed	Paced Auditory Serial Addition Task 3 (PASAT 3)
	Overactive Bladder Questionnaire (OAB-Q)
Bladder problems	Hospital Anxiety and Depression Scale (HADS)
	HADS1 subscale anxiety
Depression and anxiety	HADS2 subscale depression

A total of **466** PwMS were included in the analysis, mean age was $55,3 \pm 12,9$ years, 68,2% were female

Univariate Analysis

Variables		< 60 y (n=297)	≥ 60 y (n=169)	P value
Sex, (%)	Male	27.3%	39.6%	0.006
	Female	72.7%	60.4%	
Diagnosis, (%)	Relapsing-Remitting (RR)	57.4%	20.7%	<0.001
	Secondary-Progressive (SP)	42.7%	79.3%	
EDSS, mean (SD) score		4.8 (2.3)	6.2 (2.0)	<0.0001
MoCA, mean (SD) score		23.7 (4.5)	20.7 (4.5)	<0.0001
SDMT, mean (SD) score		38.3 (15.4)	25.4 (14.2)	<0.0001
PASAT3, mean (SD) score		30.1 (18.3)	19.7 (17.2)	<0.0001
HADS 1, mean (SD) score		7.2 (4.3)	6.2 (4.3)	0.007
HADS 2, mean (SD) score		5.3 (3.7)	5.0 (3.3)	0.649
FIM 1, mean (SD) score		19.9 (1.9)	19.6 (2.4)	0.634
FIM 2, mean (SD) score		13.5 (1.3)	13.4 (1.4)	0.203
FIM 3, mean (SD) score		12.4 (2.4)	11.1 (3.7)	<0.0001
FIM 4, mean (SD) score		37.8 (7.4)	33.2 (10.4)	<0.0001
FIM 5, mean (SD) score		11.8 (4.0)	9.3 (4.2)	<0.0001
FIM 6, mean (SD) score		18.0 (4.8)	15.5 (5.9)	<0.0001
LSI, mean (SD) score		12.6 (4.7)	11.4 (4.3)	0.006
MFIS 1, mean (SD) score		14.4 (10.6)	12.0 (9.6)	0.031
MFIS 2, mean (SD) score		20.2 (9.1)	21.7 (8.0)	0.100
MFIS 3, mean (SD) score		3.4 (2.3)	3.9 (2.5)	0.026
OAB-Q, mean (SD) score		21.9 (10.9)	22.0 (11.0)	0.954

PwMS over 60y show:

- > % Male
- > % Secondary-Progressive
- > Disability level (\uparrow EDSS)
- > Cognitive impairment (\uparrow MoCA)
- > Attention and cognitive impairment and information processing speed (\downarrow SDMT, \downarrow PASAT3)
- < Anxiety (\downarrow HADS 1)

- < Sphincter control (\downarrow FIM 3)
- < Personal care (\downarrow FIM 4)
- < Locomotion (\downarrow FIM 5)
- < Mobility (\downarrow FIM 6)
- < Life satisfaction (\downarrow LSI)
- > Cognitive fatigue (\uparrow MFIS 1)
- > Psychosocial fatigue (\uparrow MFIS 3)

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Logistic Regression Model

Variables associated with aging ($\geq 60y$ vs. $< 60y$)

Variabili	Full Model			Reduced Model		
	OR	95% CI	P value	OR	95% CI	P value
SDMT	0.96	0.93-0.99	0.008	0.96	0.94-0.98	<0.001
LSI	0.95	0.89-1.01	0.125	0.94	0.88-1.00	0.056
HADS1	0.91	0.85-0.98	0.017	0.93	0.87-0.99	0.026
Diagnosis	1.58	1.13-2.20	0.007	1.54	1.17-2.04	0.002
EDSS	1.05	0.84-1.30	0.672			
MoCA	0.99	0.92-1.07	0.805			
PASAT3	0.99	0.97-1.01	0.303			
MFIS2	0.99	0.94-1.03	0.557			
MFIS3	1.11	0.96-1.29	0.147			
FIM3	0.91	0.81-1.03	0.143			
FIM4	1.05	0.97-1.13	0.204			
FIM5	0.95	0.86-1.05	0.312			
FIM6	1.05	0.92-1.19	0.513			
Sex	1.11	0.62-1.99	0.725			

Hosmer-Lemeshow goodness-of-fit statistic, $p=0.460$

- Attention impairment (\downarrow SDMT)
- Life satisfaction (\downarrow LSI)
- Anxiety (\downarrow HADS1)
- Diagnosis (SP)

Conclusioni Aging involves changes and deterioration of PwMS health. Many skills are decreased and some symptoms become more important. However, as shown by multivariate analysis, with aging the psychosocial aspects are more impacting with respect to physical aspects. To note that the variables associated with aging were: less attention capacity (mean score SDMT (25.4) lower also to that considered non-pathological (34.2 observed in normal population) [3]; the lower level of satisfaction and well-being measured by LSI (11.4 vs. 12.6); lower level of anxiety also considering the clinical cut-off ≥ 8 [4] identifying anxiety disorders in 36% of people over 60 compared to 46% of subjects aged < 60 years ($p = 0.042$) and higher frequency of subjects with SP diagnosis.

In conclusion, in a debilitating disease as MS, in addition to the progressive MS form are the cognitive (attention impairment) and psychosocial factors (life satisfaction) that impact on aging, while the anxiety appears diminish.