

The effect of initial complaints and third year MRI lesion load on EDSS of multiple sclerosis patients

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Abstract

Aim: We aimed to investigate the effect of initial complaints and third-year MRI lesion burden on Expanded Disability Status Scale (EDSS) of Multiple Sclerosis Patients.

Materials and Methods: Patients who were admitted to the Mustafa Kemal University Faculty of Medicine Neurology clinic and diagnosed with Multiple Sclerosis according to Mc Donald diagnostic criteria were included in the study. The initial symptoms of patients, MRI lesion burden at the end of the third year, and the EDSS score were recorded retrospectively from the patient files. 74.5 % of the participants were female and 25.5 % were male. The most common initial symptoms were: Sensory symptoms, vision symptoms, pyramidal tract symptoms, and polysymptomatic. The mean age of the patients was 33.4. Mean EDSS was found to be 1.8 ± 1.3 . The total number of lesions in the brain was 14.8 ± 4.83 on average.

Results: If patients compared according to the initial symptoms at the end of the third year, the highest EDSS score was at the polysymptomatic onset group, the second-highest score was at the motor onset group. The patients with the initial symptoms of motor or polysymptomatic group had a higher mean EDSS score than the patients with the initial symptoms of vision, sensorial symptoms, or cranial neuropathy. When we examine the relationship between MRI lesion load at the end of the third year and the EDSS score, there is a strong positive correlation between them. Patients who have more lesions in the brain on MRI studies have higher average EDSS scores than patients who have fewer lesions in the brain.

Conclusion: We found that the initial symptoms are directly related to the third-year EDSS score and the prognosis of the disease. We found that there was a significant relationship between the number of lesions in the brain on MRI studies at the end of the third year and the mean EDSS score.

Keywords: Multiple sclerosis; MRI lesion load; EDSS; initial symptom

INTRODUCTION

Multiple sclerosis (MS) is the central nervous system disease that is frequently seen in young people and causes the most disability among non-traumatic reasons. MS is grouped clinically according to the presence of attacks and the course of disability as clinically isolated syndrome, relapsing MS and progressive MS (1). Relapses typically start within hours-days and complaints can continue for days to weeks. In the beginning, patients fully recover after relapses, later, with the attacks, there is an accumulation of disability and patients go to secondary progressive stage (SPMS). The clinic of the disease occurs as a result of the interaction between focal inflammation and demyelination, as well as axonal damage.

Signs and symptoms of multiple sclerosis may overlap

with many other diseases; therefore, clinical features are still very important in diagnosing the disease. A complete medical history and a complete neurological examination are essential for diagnosis. The Kurtzke Expanded Disability Status Scale (EDSS) is a scoring system used to assess the level of disability in MS patients. While the normal neurological examination EDSS score is expressed as 0, the unilateral support requirement for the walk represents the EDSS score 6.0, and EDSS score 0 means death due to MS (2).

Although EDSS is still a gold standard scoring system in the assessment of disability, it is criticized for excessive focus on lower limb function loss, and it's being inadequate to assess cognitive loss and clinical changes (3).

MRI has a very important place in diagnosing MS and

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its' importance is gradually increasing. Lesions are characteristically observed in MRI as a cerebral or spinal plaque. Plaques are typically detected in MRI at periventricular, juxtacortical, infratentorial, and spinal localization (4). When most of the lesions seen on MRI are evaluated pathologically, it is found to be compatible (5).

It is known that patients who develop clinically definitive MS also have a higher lesion burden on MRI during admission. The high lesion load during admission also shortens the clinical definitive MS development. Also, lesion burden can be effective in the long-term course of the disease.

Many studies have demonstrated that among all initial complaints, sensory symptoms, and cranial nerve dysfunction such as optic neuritis are associated with good prognosis whereas pyramidal, cerebellar and brainstem involvement has been associated with poor prognosis. Although there is no consensus among experts on this subject, both benign and malignant forms of MS have been identified. Benign MS is a retrospective diagnosis characterized by sparse episodes that do not leave serious sequelae, with a low lesion load detected on MRI. Patients with EDSS scores ≤ 3 15 years after the onset of the disease are considered benign MS (6).

The purpose of this study was to investigate the effect of initial symptoms and third-year MRI lesion load on EDSS of MS patients.

MATERIALS and METHODS

In this retrospective cohort study, we aimed to investigate the effect of initial symptoms and third-year MRI lesion load on EDSS of Multiple Sclerosis Patients.

A total of 153 patients who admitted to the neurology clinic of Mustafa Kemal University Faculty of Medicine Hospital were included in the study, and 74.5% (114) of the participants were female and 25.5 % (39) were male. These patients were diagnosed according to McDonald diagnostic criteria for multiple sclerosis and the first symptoms at the hospital admission were studied retrospectively from patient files.

MRs of patients taken in the third year after diagnosis were evaluated by a specialist radiologist, retrospectively and demyelinating plaque numbers were determined. The patient who didn't have cranial MRI at the end of the third year or disease duration is shorter than 3 years were excluded from the study.

EDSS scoring system was used to determine the disability level of MS patients and EDSS scores of the patients were obtained from patient file records.

Our study was approved by the Clinical Study Ethics Committee of Mustafa Kemal University Tayfur Ata Sökmen Medical Faculty (Approval no: 25, dated 05.06.2014).

Data were electronically recorded for analysis. Frequency tables, correlation analysis, Student's t-test, one-way ANOVA and Chi-square test were used to analyze data.

RESULTS

In this study, 74.5 % (114) of the study participants were female and 25.5 % (39) were male. When we look at the most common first three initial symptoms, they were: Sensory symptoms 29.4 % (45), visual symptoms 19.6 % (30), pyramidal tract symptoms and polysymptomatic 17.6 % (27) (Table 1).

Table 1. Sex and Initial symptoms of the patients participating in the study

	Number	%
Female	114	74.5
Male	39	25.5
Sensory	45	29.4
Visual	30	19.6
Motor	27	17.6
Polysymptomatic	27	17.6
Cerebellar	13	8.5
Cranial	11	7.2

*p<0.05 **p<0.01

The mean age of the patients was 33.4 years old at the end of the third year. The smallest of the patient's age was 17 and the oldest one was 57. Mean EDSS was found to be 1.8 ± 1.3 . When we assess the total number of lesions in the brain at the end of the third year, an average of 14.8 ± 4.83 , the number of lesions of at least 9, and the number of most lesions was 30 (Table 2).

Table 2. The total number of lesions in the brain, Age and the EDSS of the participants

	Mean	Standard Deviation	Minimum	Maximum
Age	33.4	9.79	17	57
EDSS	1.8	1.3	1	7
Total Number of Lesions	14.8	4.83	9	30

Patients participating in the study, if they compared according to the initial symptoms, average EDSS scores of patients with polysymptomatic onset were highest (2.7) the second-highest score was at the motor onset group (2.5).

The difference between initial symptoms of the participants and mean EDSS scores was statistically significant ($p < 0.001$).

Motor or polysymptomatic onset group had a higher mean EDSS score than the visual or sensorial onset group and that was statistically significant ($p < 0.05$).

Polysymptomatic onset group had a higher mean EDSS score than the cranial neuropathy onset group and that was statistically significant ($p < 0.05$) (Table 3).

Table 3. Relationship between initial symptom and EDSS

	Number	Mean	EDSS			p
			Standard Deviation	Minimum	Maximum	
Polysymptomatic	27	2.7	1.71	1	7	<0.05
Motor	27	2.5	1.45	1	6	<0.05
Cerebellar	13	2.1	1.90	1	7	0.05
Cranial	11	1.4	0.82	1	3	<0.05
Visual	30	1.4	0.86	1	4	<0.05
Sensory	45	1.1	0.40	1	3	<0.05
Total	153	1.8	1.34	1	7	

We investigate the relationship between MRI lesion load at the end of the third year and the EDSS score, there is a strong positive correlation between them and this relationship was found to be statistically significant ($p<0.05$, $R=0.586$).

Patients who have more lesions in the brain on MRI studies (14-30) have a higher mean EDSS score (2.4 ± 1.57) than patients who have fewer lesions (9-13) (1.2 ± 0.65) and that was statistically significant ($p<0.05$) (Table 4).

Table 4. Relationship between total number of MRI lesions and EDSS

Total Number of MRI Lesions	Number of patients	EDSS		
		Mean EDSS	Standard Deviation	p
9-13	74	1.2	0.65	0.001
14-30	79	2.4	1.57	

DISCUSSION

Many studies have examined the sociodemographic features and their role in the prognosis of Multiple Sclerosis. In this study, we aimed to investigate the effect of initial symptoms of the disease and third-year MRI lesion load on EDSS of MS patients.

More than 90 % of patients diagnosed with clinically definitive MS have typical white matter lesions on MRI. However, CNS lesions caused by other diseases may also appear similar to MS lesions. Diseases that can cause these lesions include: Small-vessel disease, ischemia, hypertensive encephalopathy, CADASIL, systemic lupus erythematosus (SLE), Acute disseminated encephalomyelitis (ADEM), Behçet's disease, sarcoidosis, Lyme disease, other vasculitides and human T-cell lymphotropic virüs (HTLV)-1. For this reason, white matter lesions over 50 years old, which can be observed due to ischemic lesions, may complicate the diagnosis of MS (7). In small-vessel disease, juxtacortical U-fibers are not affected, and in T2 / FLAIR there is a dark band between the lesion in the white matter and the cortex. In hypertensive encephalopathy, white matter lesions are located in the frontal and parietal lobes and rarely in the occipital lobes. They are not observed in the temporal

lobes. Only in CADASIL, temporal lobes can be affected early. With a few exceptions, spinal cord lesions are rare in CNS diseases. These exceptions are; ADEM, sarcoidosis, Lyme disease, and SLE. Spinal cord lesions are usually not longer than 1-2 vertebral segments. Other pathologies such as neuromyelitis optica (NMO) spectrum disorders, Behçet's disease, tumors (such as glioblastoma), syphilis should be considered in longer lesions. MS lesions rarely have a mass effect (distinction from abscess and space-occupying tumoral lesions). Contrast enhancement lasts 1-2 months, and may rarely extend to a maximum of three months. Longer contrast enhancement requires consideration of other pathologies (8).

In the course of MS, the cranial MRI lesion burden is not always associated with the degree of clinical disability. Despite a small number of lesions, these patients' disabilities may be higher, whereas the others have a large number of lesions detected by MRI but their disability may be less. A few possible reasons can be said to explain this situation: localizations, where lesions occur, can be clinically silent areas, lesions in the spinal cord can cause great disability even if small and MRI may be inadequate to detect clinically relevant lesions in localizations such as cortex, brain stem and basal ganglia (9).

In this study, 153 patients were enrolled and all patients had a history of at least 3 years of disease. In the literature, the female to male ratio was 2-3 /1 (10). In our study, this ratio was found to be 2.9 / 1.

When we look at the initial symptoms of the cohort studied in London, 45 % sensory, 17 % optic neuritis, 20 % motor, 13 % diplopia/vertigo, and 13 % imbalance/ataxia as listed. When we look at the initial symptoms in our study, sensory symptoms (29.4 %), visual symptoms (19.6 %), motor symptoms, and polysymptomatic onset (17.6 %) as we sorted.

We have the evidence that initially affected 2 or more system indicates poor prognosis in MS. Initially, MS patients with 2 or more system involvement, they reached high EDSS scores earlier than MS patients with monosymptomatic onset (11-13). Patients participating in the study, we compared according to the initial symptoms on EDSS at the end of the third year, the highest score was at the polysymptomatic onset group, the second-highest score was at the motor onset group. There is a statistically significant difference is detected between mean EDSS score and initial symptoms of the participants ($p < 0.001$). Motor or polysymptomatic onset group are with the higher average EDSS score than the visual or sensorial onset group and that was statistically significant ($p < 0.05$). Polysymptomatic onset group is with the higher mean EDSS score than the cranial neuropathy onset group and that was statistically significant ($p < 0.05$).

Sailer and colleagues observed that MS patients who were followed for 10 years, the total MRI lesion load was related significantly with EDSS (14). In the early stages of the disease, the amount of pathological changes detected in MRI T2-weighted images, provides the clinical course of the disease, and an estimate of future disability. Grimaud and colleagues studied brain lesions at 15 MS patients with nine MRI parameters and EDSS were determined (15). There is a strong relationship was found between EDSS and the four parameters (Proton density in total lesion load, MTU, calculated T1 and T1 hypointense lesion load) indicating the size and pathology of the lesions. Such parameters may be useful in monitoring therapy in MS, however, further studies should be made to use these techniques in practice.

The use of multiple MRI parameters together will probably give more information about the prediction of clinical status, working with new techniques, such as diffusion MRI and MRS are made for this purpose. These techniques, giving detailed information about the integrity of the myelin and axon and enabling the measurement of the atrophy, so this condition exhibits more objective tips on disability (15, 16).

MRI has a very important role in the diagnosis of MS. It can be used to evaluate the efficacy of treatment in clinical trials as a paraclinical measurement. There is 2 superiority of MRI follow up to clinical follow up at MS patients, more objective, and is more susceptible to pathological events.

However, despite this, the correlation between clinical and MRI findings in MS is weak. Sometimes, despite a large number of lesions, a minimal disability can be detected, conversely, a small number of lesions may cause much more disability. Therefore, to determine the disease activity and to understand the evolution of the disease, we should work on new MRI techniques to increase the sensitivity of MRI (15, 17-19).

In this study, showing a direct correlation between EDSS and MRI findings is very difficult. Various MR techniques, contrast-enhanced MRI, follow-up MRI or the other methods which can provide valuable information were previously studied during episodes of attack or remission or at another different time (14, 15, 17). In this study, only the total number of plaques could be investigated. But we can say that disability was associated with total lesion burden (20).

When we look at the total number of lesions in the brain, the average was 14.8 ± 4.83 , a minimum of 9 and a maximum of 30 lesions were detected. We investigate the relationship between MRI lesion load at the end of the third year and the EDSS score, there is a strong positive correlation between them and this relationship was found to be statistically significant ($p < 0.05$, $R = 0.586$).

As a result of our study, a statistically significant relationship was found between MRI lesion load at the end of the third year and the initial symptoms of the patients and the mean EDSS score.

CONCLUSION

In this study, a statistically significant difference was found between initial symptoms and mean EDSS scores of multiple sclerosis patients. It was determined that there was a strong positive correlation between total MRI lesion load and EDSS scores at the end of the third year and this relationship was statistically significant. However, follow-up of cases, it seems too short to prove the existence of such a relationship exactly because MS disability is an evolving situation over the years rather than months. Therefore, to say that there is a strong correlation between the EDSS and MRI abnormalities in this study, the future vice-versa should not imply that come to a result. Maybe if these patients are followed for 10 years longer, more accurate results may be obtained.

Short follow-up of patients, such as 3 years, focusing only on the number of lesions, not investigating other parameters such as localization or lesion size, and not linking the treatment patterns of patients can be listed as the limitations of the study. Future studies are needed to reveal all the parameters related to MS prognosis.

Conflict of interest : The authors declare that they have no competing interest.

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