

Comparison of Upper and Lower Extremity Functions in Primary and Secondary Progressive Multiple Sclerosis Patients

Primer ve Sekonder Progresif Multipl Skleroz Hastalarında Üst ve Alt Ekstremitte Fonksiyonlarının Karşılaştırılması

Nuray ATILLA^a,
Vedat ÇİLİNGİR^a,
Aysel MİLANLIOĞLU^a,
Abdullah YILGÖR^a

^aDepartment of Neurology,
 Van Yüzüncü Yıl University
 Faculty of Medicine,
 Van, TURKEY

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Correspondence:
 Nuray ATILLA
 Van Yüzüncü Yıl University
 Faculty of Medicine,
 Department of Neurology, Van,
 TURKEY/TÜRKİYE
 dr.nurayc@hotmail.com

ABSTRACT Objective: The aim of this study was to find out whether upper extremity is relatively preserved and to what extent it is affected by Primary Progressive Multiple Sclerosis (PPMS) through the evaluation and comparison of upper extremity fine motor skills and walking ability in PPMS and Secondary Progressive Multiple Sclerosis (SPMS) patients with Expanded Disability Status Scale (EDSS) score of 4 and above. **Material and Methods:** A total of 65 progressive Multiple Sclerosis (MS) patients admitted to the Neurology Outpatient Clinic of Yüzüncü Yıl University Faculty of Medicine between January and December 2017 with EDSS scores ranging from 4.0 to 8.5 were included in our study. Expanded Disability Status Scale (EDSS), 9-Hole Peg Test (9-HPT) and Timed 25-Foot Walk (T25FW) Test were applied to the patients. **Results:** 9-Hole Peg Test right hand score of PPMS patients with EDSS score between 5.1 and 6.0 was 32.89±7.42 sec, whereas in SPMS patients within the same score range, it was 56.15±54.57 sec (p>0.05). 9-Hole Peg Test left hand score was found as 39.64±16.71 sec in PPMS patients and 47.51±27.32 sec (p>0.05) in SPMS patients. 9-Hole Peg Test mean score was 36.25±11.83 sec in PPMS patients and 51.83±38.18 sec in SPMS patients (p>0.05). The T25FW test was calculated only for 39 patients who were able to perform all tests. In 14 patients with PPMS, the first-stage T25FW test score was 35.62±22.2 sec, the second-stage score was 36.21±24.73 sec, and the mean T25FW test score was 35.92±22.81 sec. In 25 of SPMS patients, the first-stage T25FW test result was 36.12±32.84 sec, the second-stage T25FW test result was 32.77±26.11 sec, and the mean T25FW test result was 34.4±28.75 sec. **Conclusion:** In PPMS and SPMS patients with EDSS score of 5.1-6.0, the mean EDSS scores were observed to be closer to each other, and in PPMS patients in this group, the upper extremity function was relatively better, although not statistically significant. No significant difference was found between the groups in terms of lower extremity function.

Keywords: Upper and lower extremity function in patients with progressive MS; 9-Hole Peg test (9-HPT) and Timed 25-Foot Walk (T25FW)

ÖZET Amaç: Çalışmamızın amacı Primer Progresif Multipl Skleroz (PPMS) ve Sekonder Progresif Multipl Skleroz (SPMS) hastalarında Genişletilmiş Özürlülük Durum Ölçeği (EDSS) puanı 4 ve üzerinde olan hasta grubunda üst ekstremitte ince motor becerisini ve yürüme becerisini değerlendirip birbiri ile kıyaslayarak, PPMS'de üst ekstremitenin göreceli olarak korunup korunmadığını ve ne derecede etkilendiğini göstermektir. **Gereç ve Yöntemler:** Çalışmamıza 2017 yılı Ocak-Aralık ayları arasında Yüzüncü Yıl Üniversitesi Tıp Fakültesi Nöroloji polikliniğine başvuran EDSS 4,0-8,5 arasında olan toplam 65 progresif Multipl Skleroz (MS) hastası dahil edilmiştir. Hastalara Expanded Disability Status Scale(EDSS, Genişletilmiş Özürlülük Durum Ölçeği), 9-Hole PEG testi (9-HPT, Dokuz delikli çubuk testi) ve Timed 25 Food Walk (25 Adımlı Yürüme Testi, T25FW) testleri uygulandı. **Bulgular:** Genişletilmiş Özürlülük Durum Ölçeği 5.1-6.0 arasındaki hastalarda sağ el testi PPMS hastalarında 32,89±7,42 sn, SPMS hastalarında 56,15±54,57 (p>0,05) sn bulunmuştur. Sol el testi PPMS hastalarında 39,64±16,71 sn, SPMS hastalarında 47,51±27,32 sn (p>0,05) bulunmuştur. Ortalama el testi PPMS hastalarında 36,25±11,83 sn, SPMS hastalarında 51,83±38,18 sn (p>0,05) bulunmuştur. Yürüme testi sadece tüm testleri yapabilen 39 hastada hesaplanmıştır. On dört PPMS hastasında birinci tur yürüme testi 35,62±22,2 sn, ikinci tur yürüme testi 36,21±24,73 sn, ortalama yürüme testi 35,92±22,81 sn bulunmuştur. Yirmi beş SPMS hastasında ise birinci tur yürüme testi 36,12±32,84 sn, ikinci tur yürüme testi 32,77±26,11 sn, ortalama yürüme testi 34,4±28,75 sn bulunmuştur (p>0,05). **Sonuç:** Genişletilmiş Özürlülük Durum Ölçeği skoru 5,1-6,0 arasındaki PPMS ve SPMS hastalarında EDSS ortalaması birbirine daha yakın olduğu ve bu gruptaki PPMS hastalarında üst ekstremitte fonksiyonunu istatistiksel olarak anlamlı olmasa da göreceli olarak daha iyi olduğu görülmüştür. Alt ekstremitte fonksiyonu açısından her iki grup arasında anlamlı fark bulunmamıştır.

Anahtar Kelimeler: Progresif MS hastalarında üst ve alt ekstremitte fonksiyonu; 9-Hole PEG testi (9-HPT, Dokuz delikli çubuk testi) ve timed 25 Food Walk (25 adımlı yürüme testi, T25FW)

Multiple sclerosis (MS) is a chronic neurodegenerative disease of the central nervous system (CNS), characterized by demyelination, axonal degeneration, inflammation, astrogliosis, and it may particularly affect white matter, cortex and deep gray matter.¹

Despite numerous studies, its etiology has still not been fully elucidated. Although the etiopathogenesis of multiple sclerosis (MS) is not fully known, many autoimmune mechanisms have been shown to cause axonal damage and demyelination through recent studies.² It is usually diagnosed in the age range of 15-50, and the average age at diagnosis is 30. The occurrence of symptoms before the age of 15 and after the age of 50 is very rare. The incidence of the disease in females is twice as high as in males.³ In MS occurring at advanced ages gender ratios tend to be equal.

There are 3 subtypes of MS including relapsing remitting (RR) type, secondary progressive type (SP) that enters the progressive stage following the attacks at the onset of the disease, and the primary progressive (PP) type of multiple sclerosis, which follows a progressive course from the onset.⁴ Relapsing Remitting Multiple Sclerosis is the most common subtype (85%) of the disease. Periods with attacks, known to be associated with neurological deterioration, and subsequent periods of silence with complete or partial improvement are observed. Primary Progressive Multiple Sclerosis is the type of MS without attacks, where only progressive deterioration is observed.⁵ In SPMS, neurodegeneration is more prominent than inflammation. When RRMS is left to its natural course, 75% of patients advance to secondary progressive MS.⁶

The upper limb provides the ability to maintain a quality life and perform functions required in daily life such as self-care, sensing and holding. The upper extremity is divided into two groups as proximal and distal upper limb. Fine motor skills are mainly provided by the distal part of upper extremity.^{7,8} Walking ability is one of the most important and valuable functions of daily life for MS patients.^{9,10} Walking dysfunction is the most com-

mon cause of trouble in terms of quality of life.^{9,11} One of the important effects of treatment is the improvement of the quality of life.

In our study, by evaluating and comparing upper extremity fine motor skills and walking ability in PPMS and SPMS patients with Expanded Disability Status Scale (EDSS) score of 4 and above, we tried to determine whether upper extremity is relatively preserved and to what extent it is affected by PPMS. With this study, we aimed to contribute to the literature because our literature review revealed that there was no one-to-one comparison of upper extremity function in primary and secondary progressive MS patients.

MATERIAL AND METHODS

Expanded Disability Status Scale (EDSS), 9-Hole Peg Test (9-HPT) and Timed 25-Foot Walk (T25FW) Test were applied to the patients. 9-Hole Peg Test and T25FW are the components of the multiple sclerosis functional composite (MSFC) test. These tests are used to assess the severity of clinical findings, to monitor disease progression over time, or to assess response to treatment. These are the most widely used quantitative performance measurement tests. They have been developed because of the limitation of EDSS in quantifying disability.¹²

The 9HPT test is a quantitative timed test where fine motor skills are measured. This timed test measures finger dexterity as a measure of the time in seconds. Throughout the test, the patient places the pegs into the empty holes on the 9-hole pegboard. The patient needs a certain period of time to pick up the 9 pegs in order, and place them in empty holes as quickly and safely as possible. The time required for all of these is recorded in seconds. 9-Hole Peg Test is performed for the dominant hand first and then for the non-dominant hand two consecutive times. The average of four trials is taken. The average of two trials for each hand is taken and then converted to average times. Then the average of these two periods is taken. Low scores indicate better hand dexterity. Maximum duration is 5 minutes.

The T25FW test is the most important test for measuring MS patients' functional ambulation in daily life.¹⁰ The patient is directed to one end of a clearly marked 25-foot course and is instructed to walk 25 feet (25 feet, approximately 8 meters) as quickly as possible, but safely. The time is calculated in seconds from the initiation of the instruction to start and ends when the patient has reached the 25-foot mark in the 1st stage. The 2nd stage is calculated in the same way as the patient walks back the same distance. It is applied in two stages and the average of both stages is taken. Patients may use assistive devices (such as a cane) when performing this task.^{13,14}

Expanded Disability Status Scale was developed by Kurtzke in 1983. While EDSS score of 1.0 to 4.5 corresponds to a patient who can walk without any help, EDSS score between 5-9.5 corresponds to a patient with varying degrees of gait disorder. An EDSS score of 10 indicates MS-related death.^{13,14} Although EDSS is an important test in determining disability, it is relatively insensitive in especially upper extremity in advanced stages of the disease as in the case of progressive MS patients.

For the analysis of data, SPSS (V.23) (Statistical Package for the Social Sciences) software was used.

Patients who could not use their hands, RRMS patients, pregnant patients, patients with impaired vision enough to make the test difficult, and patients with disease that would affect upper extremity function such as polyneuropathy, cerebrovascular disease, entrapment neuropathy were excluded from the study.

RESULTS

A total of 65 progressive MS patients admitted to the Neurology Outpatient Clinic of Yüzüncü Yıl University Faculty of Medicine between January and December 2017 with EDSS scores ranging from 4.0 to 8.5 were included in our study. Of these patients, 27 (41.5%) had PPMS, 38 (58.4%) had SPMS and 40 (61.5%) were female and 25 (38.5%) were male. While 20 (30.8%) of the PPMS patients were female and 7 (10.8%) were male, 20 (30.8%) of the

SPMS patients were female and 18 (27.6%) were male. The female/male ratio was 1.6/1. The mean age was 43.1±10.826 (min 23, max 66) years in all patients, 42.7±12.62 (min 23, max 66) years in PPMS patients and 43.39±9.528 (min 28, max 66) years in SPMS patients. The median value of all patients was 40.00. The mean EDSS score was 5.92±1.21 in all patients, 6.25±0.98 in 27 PPMS patients and 5.67±1.30 in 38 SPMS patients.

9-Hole Peg Test right hand score was found as 49.93±40.84 sec in 26 PPMS patients and 51.06±48.28 sec ($p>0.05$) in 34 SPMS patients. Five patients could not use their right hand and could not perform the test. One of these patients had PPMS and 4 had SPMS. 9-Hole Peg Test right hand scores were lower in PPMS patients. 9-Hole Peg Test left hand score was found as 47.81±23.49 sec in 24 PPMS patients and 42.95±21.04 sec ($p>0.05$) in 38 SPMS patients. Three patients, all of whom had PPMS, could not use their left hand and could not perform the test. 9-Hole Peg Test left hand scores were lower in SPMS patients. The mean 9-HPT score for both hands was found as 45.14±25.7 sec in all patients, 43.53±18.75 sec in PPMS patients and 46.26±29.83 sec in SPMS patients ($p>0.05$). The mean 9-HPT scores could not be calculated for a total of 8 patients who could not use their right or left hands.

Patients were grouped according to EDSS scores as the upper extremity function was higher in PPMS for the left hand in all patients. There were 20 patients with an EDSS score of 5.1-6.0, and 7 of these patients had PPMS and 13 had SPMS. Four of the patients in this group were unable to perform the T25FW test, and 1 of these patients had PPMS and 4 had SPMS. The mean EDSS score was 5.9 in the PPMS group and 5.8 in the SPMS group. The mean age was 35.86±10.14 years in the PPMS group and 41.62±7.39 years in the SPMS group. 9-Hole Peg Test right hand score was found as 32.89±7.42 sec in PPMS patients and 56.15±54.57 ($p>0.05$) sec in SPMS patients. 9-Hole Peg Test left hand score was found as 39.64±16.71 sec in PPMS patients and 47.51±27.32 sec ($p>0.05$) in SPMS patients. The mean 9-HPT score for both hands was found as 36.25±11.83 sec in PPMS patients and 51.83±38.18 sec ($p>0.05$) in SPMS patients (Figure 1).

The T25FW test was calculated only for 39 patients who were able to perform all tests. The T25FW test could not be performed in 26 patients who could not walk. In 14 patients with PPMS, the first-stage T25FW test score was 35.62±22.2 sec, the second-stage score was 36.21±24.73 sec, and the mean T25FW test score was 35.92±22.81 sec. In 25 SPMS patients, the first-stage T25FW test score was 36.12±32.84 sec, the second-stage score was 32.77±26.11 sec, and the mean T25FW test score was 34.4±28.75 sec (p>0.05) (Figure 2).

DISCUSSION

Recent studies reveal that white matter lesions during the early course of MS do not impair functional capacity due to the flexibility and excess in neuronal circuits. However, it has been shown that functional or cognitive disorders occur in the case of ongoing damage to the white matter caused by MS or normal neuronal loss and depletion of the brain reserve due to aging.¹⁵ The disability progression of the patient may vary depending on the individual's brain reserve. The brain reserve and le-

sion burden may explain the difference in disability progression among individuals with similar disease duration. Patients with high levels of brain reserve are less likely to experience disability. Deterioration in motor skills due to MS is associated with incapacity to work, decreased quality of life and difficulties in daily life activities.^{9,11,16}

In progressive MS patients, as the disability increases, difficulties can be seen in walking, self-care and daily life activities. The degree of quality of life is important in advanced stages of chronic diseases. In MS patients, as the disease progresses, loss of fine motor skills in upper extremity and walking impairment can be seen in varying degrees. This causes loss of function in patients and therefore negatively affects their daily life activities. The upper extremity is divided into two groups as proximal and distal upper limb. Fine motor skills are mainly provided by the distal upper extremity. Walking is one of the most important and valuable functions of daily life for MS patients.^{8-10,16} In the ORATORIO study (Phase 3, randomized, double-blind, placebo-controlled study evaluating ocre-

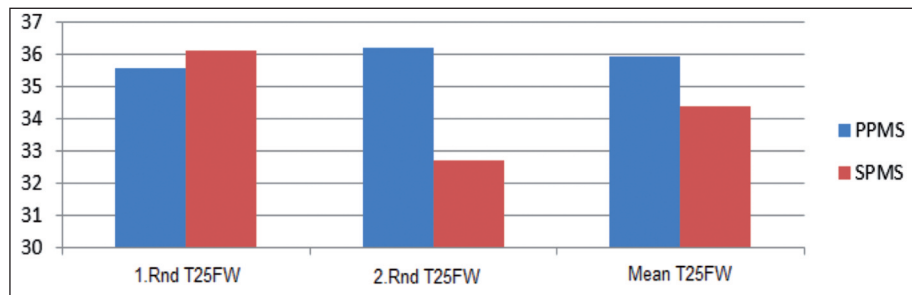


FIGURE 1: Comparison of PPMS and SPMS patients with EDSS score of 5.1-6.0.

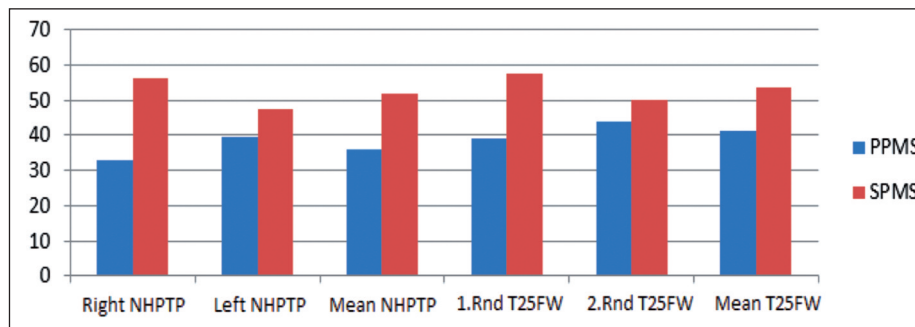


FIGURE 2: Comparison of T25FW test scores in all PPMS and SPMS patients.

lizumab in PPMS), 9-HPT test was applied before and after the treatment in order to evaluate the response to ocrelizumab treatment in PPMS patients, and the response was found to be lower after the treatment.¹⁷ In a study conducted by Tanigawa et al., in which patients with RRMS and patients with progressive MS were compared, the comparison of patients treated for two years and those untreated showed that fine motor skills and walking functions were better in the treated group.¹⁸ In a study by Ontaneda et al., 9-HPT was used to measure the efficacy of fingolimod and rituximab, and significant improvements were observed.¹⁹

Since MS is a progressive disease, as disability increases during the course of the disease, upper and lower extremity functions and work capacity decrease. In many important studies such as ORATORIO studies, upper and lower extremity functions in MS patients, RRMS patients and progressive MS patients were compared with those of healthy control groups, and 9-HPT and T25FW tests were performed, but upper and lower extremity functions were not compared in PPMS and SPMS patients. Since the PPMS patients who participated in our study were in advanced stages of the disease with a higher degree of disability, their upper extremity function was worse. However, in PPMS and SPMS patients with EDSS scores between 5.1-6.0, the mean EDSS score was closer to each other, and the upper extremity function was relatively better in PPMS patients in this group, which was not statistically significant. In PPMS patients, lower extremity function was relatively better, although not statistically significant. No significant difference was found between the groups in terms of lower extremity function.

CONCLUSION

The EDSS score of the upper extremity function was relatively better in patients with PPMS compared to other groups. The fact that we studied

with a small number of patients and that patients in PPMS group had higher EDSS scores were the limitations of our study. We believe that with studies involving multiple centers and more patients, more meaningful results will emerge, and thus our study will shed light on future studies.

Informed Consent

After obtaining the consent no. 05 dated 21.09.2017 from the ethics committee of Van Yüzüncüyıl University Faculty of Medicine, signed informed consent form was obtained from the patients.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: Vedat Çilingir; **Design:** Vedat Çilingir; **Control/Supervision:** Vedat Çilingir; **Data Collection and/or Processing:** Nuray Atilla; **Analysis and/or Interpretation:** Nuray Atilla, Vedat Çilingir; **Literature Review:** Nuray Atilla; **Writing the Article:** Nuray Atilla; **Critical Review:** Vedat Çilingir, Aysel Milanlıoğlu, Abdullah Yılgör; **References and Fundings:** Vedat Çilingir; **Materials:** Nuray Atilla.

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