

## The Evaluation of the Relationship Between the Frequency of Urologic Symptoms and the Disease Progression with Multiple Sclerosis

Multipl Skleroz Hastalarında Ürolojik Semptom Sıklığının Hastalık Progresyonu ile İlişkisinin Değerlendirilmesi

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### Özet

**Amaç:** Çalışmamızda Multipl Skleroz (MS) hastalarında ürolojik semptomların hastalık progresyonu ile ilişkisinin belirlenmesi amaçlanmıştır.

**Gereç ve Yöntemler:** Çalışmaya yeni tanı almış Multipl Skleroz (YTMS) tanılı 11 hasta, Relapsing Remitting Multipl Skleroz (RRMS) tanılı 9 hasta, Sekonder Progresif Multipl Skleroz (SPMS) tanılı 6 hasta ve 10 tane sağlıklı kontrol dahil edilmiştir. Tüm gruplara genel nörolojik muayene sonrasında EDSS (Genişletilmiş özürülük durum ölçeği), MSFC (Multipl sklerozda fonksiyonel kapasite ölçeği) hesaplandı. Daha sonra tüm gruplardan ayrıntılı biokimyasal tetkikler yapıldı. Hasta grubu ve kontrol grubu hastalarına Üroloji AD tarafından alt üriner sistem yakınmaları, inkontinans ve cinsel fonksiyon açısından IPSS (Uluslararası prostat semptom skoru), ICIQ-SF (Uluslararası İnkontinans Sorgulaması), IIEF (Uluslararası Eretil Disfonksiyon Testi) ve FSFI (Kadın Seksüel Fonksiyon İndeksi) formları dolduruldu. Ayrıca hasta grubuna İstanbul Medeniyet Üniversitesi Göztepe Eğitim Araştırma Hastanesi Üroloji Anabilim Dalı tarafından işeme disfonksiyon değerlendirmesi amacı ile ürodinamik çalışma yapıldı.

**Bulgular:** Gruplar arasında yaş, eğitim yılı ve cinsiyet arasında anlamlı bir fark saptanmamıştır. Multipl Skleroz hastalarında hastalık süresi ilerledikçe inkontinans sıklığında artış olduğu görülmüştür. IPSS, IPSS-QOL, ICIQ-SF skorlarında YTMS, RRMS, SPMS ve sağlıklı kontrol grupları arasında

### Abstract

**Objektive:** Our aim is to determine the relationship between Multiple Sclerosis (MS) disease progression and urological symptoms.

**Material and Methods:** We enrolled patients with Newly Diagnosed MS (n: 11), RRMS (n: 9), SPMS (n:6) and healthy control subjects (n:10). Neurological examination was done in all groups. Furthermore, patient groups were evaluated with EDSS (Expanded Disability Status Scale) and MSFC (functional capacity in multiple sclerosis scale). Routine blood biochemistry tests were done. All patients and the subjects in the control group were evaluated in regard to lower urinary tract symptoms by the following questionnaires: incontinence and sexual function in terms of IPSS (International Prostate Symptom Score), ICIQ -SF (International Incontinence Questionnaire), IIEF (International Index of Erectile Dysfunction Test) and FSFI (Female Sexual Function Index). In addition, all the patients were evaluated by urodynamic studies in order to examine the voiding function.

**Results:** There were no differences between the group in respect to age, years of education and gender. As the disease duration increase, the frequency of incontinence was found to increase. PSS, IPSS-QOL, ICIQ-SF scores of newly diagnosed MS, RRMS, SPMS and healthy control groups were statistically significant. There was a correlation between EDSS score and urological symptoms. There was no relationship between disease duration and urological symptoms. Due to inadequate number of male patients in the study, IIEF

anlamli fark olduđu saptanmıřtır. Semptom sorgulamaları ile EDSS skoru korele bulunmuřtur. Semptom sorgulamaları ve hastalık süresi arasında iliřki gösterilememiřtir. Çalışma grubumuzun sayısının yeterli olmaması nedeniyle erkek hastalarda sorgulanan IIEF -5 testinde YTMS, RRMS, SPMS ve sađlıklı kontrol grupları arasında anlamlı bir fark saptanmamıřtır. IIEF-5 testi ile EDSS ve hastalık süresi arasında iliřki gösterilememiřtir. Çalışma grubumuzun sayısının yeterli olmaması nedeniyle kadın hastalarda bakılan FSFI testinde YTMS, RRMS, SPMS ve sađlıklı kontrol grupları arasında anlamlı bir fark görölmemiřtir. FSFI skoru ile EDSS skoru ve hastalık süresi arasında iliřki gösterilememiřtir. Çalışmamızda en sık saptadıđımız ürodinamik patoloji detrusor aşırı aktivitesi (DO) olmuřtur. SPMS grubunda mesane kapasitesi deđerlerinin daha düşük bulunduđu görölmüřtür. EDSS skoru ve 25 adım yürüme skoru arttıka mesane kapasitesinin azaldığı görölmüřtür. Mesane kapasitesi ve hastalık süresi arasında iliřki gösterilememiřtir.

**Sonuç:** Multipl skleroz hastalarında alt üriner sistem semptomları sık görölmektedir. Bu semptomların hastaların yařam kaliteleri üzerinde ciddi etkileri vardır bu nedenle erken tanı konulup tedavi edilmesi MS hasta takibinde önemli bir basamağı oluřturmaktadır.

**Anahtar Kelimeler:** Multipl Skleroz, Ürolojik Semptomlar, Ürodinami, Özürlölük

## INTRODUCTION

Multiple sclerosis is a chronic disease that usually occurs with exacerbations and remissions in young adults, affects the central nervous system white matter in multiple localization, and is thought to be the result of complex interactions of genetic and environmental factors.

Sixty-ninety percent of patients have intracranial plaques. Suprasacral spinal cord involvement is 80%, and in this case, urodynamic detrusor-sphincter dys-synergia is seen (1). Sacral involvement is 20% (1) In this case, insufficient detrusor contraction is seen. In these patients, dysfunction of the lower urinary tract is common and severely impairs the quality of life of patients. More than 80% of MS patients have lower urinary dysfunction. The incidence is approximately 96% over ten years of disease (1,2). Fifty-one percent of lower urinary tract dysfunction has been reported, even in patients with short-term disease (3). The most common symptoms; tightness, frequent urination, and urinary incontinence (1,2).

The aim of this study; in patients with multiple sclerosis; to determine whether there is a relationship

score did not differ significantly between the groups. There was no relationship between EDSS score, disease duration and IIEF. Due to inadequate number of the female patients in the study, FSFI score did not differ significantly between the groups. There was no relationship between EDSS score, disease duration and FSFI.

The most attractive result of our study is the urodynamic detrusor overactivity (DO). Bladder capacity was found to be low in SPMS. EDSS score and 25 step walk score increases while bladder capacity has been reduced. There was no relationship shown between duration of disease and bladder capacity.

**Conclusion:** Patients with Multiple Sclerosis (MS) have a very high prevalence of lower urinary tract symptoms. These symptoms have a great impact on patient quality of life. Therefore, early recognition and treatment is an important step in care of MS patients.

**Keywords:** Multiple Sclerosis, Urologic Symptoms, Urodynamic Disability

between urological complaints, disease progression, multiple sclerosis subtype, EDSS score, and MSFC.

## MATERIAL AND METHODS

A total of 80 volunteers (51 females, 29 males) who applied to the outpatient clinics of the Neurology Department of Marmara University Pendik Training and Research Hospital. Newly diagnosed Multiple Sclerosis (NDMS), Relapsing Remitting Multiple Sclerosis (RRMS) and Seconder Progressive Multiple Sclerosis (SPMS) patients were followed up and control group, who are in the same age, gender and education level, no neuropsychological disease was detected.

Ethics Committee approval was obtained from the Ethics Committee of Marmara University Faculty of Medicine.

(Protocol Code: 09.2014.0017-70737436-050.06.04-1400076918) All the patients and the control group were informed about the purpose of the study and how to do this, and the informed consent form was signed. The study included 36 subjects (23 females, 13 males) who agreed to participate in the study.

EDSS and MSFC scores of the patient and control groups were calculated. Then, urodynamic study was

**Table.1** Gender Distribution for newly diagnosed MS, RRMS, SPMS and Control Groups

Group	N (toplaml)	N (women)	N (man )
NDMS	11 (30,6 %)	7 (19,4%)	4 (11,1%)
RRMS	9 (25%)	7 (19,4%)	2 (5,6%)
SPMS	6 (16,7%)	3 (8,3%)	3 (8,3%)
Control	10 (27,8%)	6 (16,7%)	4 (11,1%)

NDMS=Newly Diagnosed Multiple Sclerosis, RRMS= Relapsing Remitting Multiple Sclerosis, SPMS= Seconder Progressive Multiple Sclerosis

**Table 2.** Age Descriptive Statistics for newly diagnosed MS, RRMS, SPMS and Healthy Control Groups

Variable	Group	N	Average
Age	Control	10	36,70
RRMS	NDMS	11	34,00
SPMS	PPMS	9	41,44
Control	SPMS	6	44,33

NDMS=Newly Diagnosed Multiple Sclerosis, RRMS= Relapsing Remitting Multiple Sclerosis, SPMS= Seconder Progressive Multiple Sclerosis

**Table 3.** Incidence of Incontinence by Groups

	N	Incontinence (-)	Incontinence (+)
Control group	10	10 (100,0%)	0 ( ,0%)
NDMS	11	10 (90,9 %)	1 ( 9,1%)
RRMS	9	5 (55,6 %)	4 (44,4 %)
SPMS	6	0 ( ,0%)	6 (100,0 %)

NDMS=Newly Diagnosed Multiple Sclerosis, RRMS= Relapsing Remitting Multiple Sclerosis, SPMS= Seconder Progressive Multiple Sclerosis (p =0,0001)

performed by the Istanbul Medeniyet University Göztepe Training and Research Hospital Urology Department. Stories of patients prior to urodynamics were obtained, urinalysis, urine culture and urinary system ultrasonography were performed. IPSS (International Prostate Symptom Score) IPSS-OOL (International Urine Satisfaction Survey), ICIQ-SF (International Incontinence Questionnaire), IIEF (International Erectile Dysfunction Questioning), FSFI (Female Sexual Function Index), Turkish-validated forms were filled. The urine culture taken before urodynamic investigation was performed if there was no reproduction. If there was reproduction, the patient was re-evaluated after appropriate antibiotic treatment. Before urodynamic investigation procedure, post-void residue was performed with 10 Fr urethral catheters. Urodynamics process was performed according to ICS standards. The bladder was filled with sterile SF at room temperature of 30 cc / min. During filling, respectively; first urinary sensation, first urination, normal voiding desire, strong voiding desire, and maximal bladder ca-

capacity (highest pressure that the patient could resist without urination) were measured. During the measurement, when the patient was in the lithotomy position after giving 200 cc, the urine leakage with valsalva was examined. If there is no escape, it is repeated every 100cc. Uroflowmetry (urine flow rate measurement) was performed after urodynamic investigation.

SPSS 20 program was used for statistical analysis. Significance levels were calculated by using one-way analysis of variance (ONE-WAY ANOVA) to look at the difference between age and education variables in NDMS, RRMS, SPMS and healthy control groups. P <0.05 was considered significant.

Descriptive statistics were calculated for the variables used in the research in the first stage of the research analysis. The calculated descriptive statistics include arithmetic mean (M), standard deviation (SD), median, minimum score, and maximum score statistics.

After the calculation of the descriptive statistics, the differences between the research groups NDMS, RRMS, SPMS and healthy control groups were exam-

**Table 4.** Distribution of Urodynamics Results in Newly diagnosed MS, RRMS and SPMS Groups.

		Urodynamics Results						Total
		No urodynamic investigation	DO	DO+DSD	DSD	DU	Normal	
Control	N	10	0	0	0	0	0	10
	%	90,9%	0,0%	0,0%	0,0%	0,0%	0,0%	27,8%
NDMS	N	0	1	1	0	1	7	11
	%	0,0%	25,0%	33,3%	0,0%	100,0%	53,8%	30,6%
RRMS	N	1	1	0	2	0	5	9
	%	9,1%	25,0%	0,0%	66,7%	0,0%	38,5%	25,0%
SPMS	N	0	2	2	1	0	1	6
	%	0,0%	50,0%	66,7%	33,3%	0,0%	7,7%	16,7%
Total	N	11	4	3	3	2	13	36
	%	30,6%	11,1%	8,3%	8,3%	5,6%	36,1%	100,0%

NDMS=Newly Diagnosed Multiple Sclerosis, RRMS= Relapsing Remitting Multiple Sclerosis, SPMS= Seconder Progressive Multiple Sclerosis, DO= Detrussor Overactivity , DSD= Detrussor Sphincter Dyssynergia, DU=Detrussor Hypoactivity (p =0,0001)

ined with non-parametric Kruskall-Wallis Test. If there was a significant difference between the Kruskall-Wallis Test and the NDMS, RRMS, SPMS and healthy control groups, Tukey HSD multiple comparison analysis was used to determine which groups were present.

## RESULTS

Thirty-nine patients who admitted to Marmara University Neurology Clinic and accepted to participate in the study were included in the study. There were 10 healthy controls (6 female, 4 male), 11 NDMS patients (7 female, 4 male), 9 RRMS patients (7 female, 2 male), 6 SPMS patients (3 female, 3 male) in groups

There was no significant difference between groups for gender (p = 0.724), age (p = 0.10) and educational level (p= 0.46).

EDSS and MSFC scores; EDSS (p= 0.0001), 25 Step Walking (p= 0.0001) 9 Hole Dominant (p= 0.0001), 9 Hole Nondominant (p= 0.0001) scores were significantly different between groups. RRMS group for EDSS scores differed according to NDMS (p= 0,015),

SPMS (p= 0,0001) and control groups (p= 0,0001). Twenty-five Step walking test, SPMS group was found to be different according to NDMS (p= 0.0001), RRMS (p= 0.0001) and control group (p= 0.0001). According to 9-hole Dominant Test, SPSS group, NDMS (p= 0.001) and healthy controls (p= 0.0001), RRMS group was found to be different according to healthy control group (p= 0.001). For the 9-Hole Nondominant Test, the SPMS grade was found to be significantly different from NDMS (p = 0,003), RRMS (p= 0,07) and control group (p= 0,001) No significant difference was found

between the groups for the cognitive test.

There was a significant difference between the groups in terms of incontinence frequency ( $p=0.0001$ ).

IPSS, IPSS-QoL, ICIQ-SF tests and NDMS, RRMS, SPMS and control group were compared and IPSS ( $p=0.02$ ), IPSS-QoL ( $p=0.002$ ), ICIQ-SF ( $p=0.0001$ ) scores were significantly different between groups. In the IPSS test, between the SPMS group and control group ( $p=0.026$ ), in the IPSS-QoL test, between control group and RRMS ( $p=0.068$ ) and SPMS ( $p=0.001$ ), in the ICIQ-SF test, between SPMS and control group ( $p=0.019$ ) a significant difference was found.

Correlation analysis between disease duration and IPSS, IPSS-QoL, ICIQ-SF tests showed no parallelism between disease duration and IPSS, IPSS-QoL, ICIQ-SF tests ( $p>0.05$ ).

IIEF-5 test which is for male gender, NDMS, RRMS, SPMS and control groups were compared and no significant difference was observed between the groups ( $p=0.288$ ). Two men did not want to answer questions. Correlation analysis between EDSS and disease duration was not correlated with the IIEF-5 test ( $p>0.05$ ).

In the FSFI test in female sex, NDMS, RRMS, SPMS and control groups were compared and no significant difference was observed between the groups ( $p=0.267$ ). One woman from the control group, two women from the NDMS group, three women from the RRMS group, and one woman from the SPMS group did not want to answer the questions. There was no correlation between FSFI score and EDSS score and disease duration ( $p>0.05$ ).

Urodynamic study (including pressure flow analysis) was performed in 25 patients. Urodynamic findings were normal in 52% ( $n=13$ ) of patients. In NDMS group, urodynamic study was performed in 11 patients; 7 patients had normal results. In RRMS group, urodynamic study was performed in 8 patients; 5 patients had normal results. In the SPMS group, urodynamic study was performed in 6; 1 patient had normal results. NDMS, RRMS and SPMS groups were compared with urodynamic findings and a significant difference was observed between the groups ( $p=0.0001$ ). Urodynamic study demonstrated that 16% ( $n=4$ ) of

MS patients who underwent urodynamic study, have Detrusor overactivity (DO), 12% ( $n=3$ ) have Detrusor sphincter dyssynergia (DSD), 12% ( $n=3$ ) have DSD and DO and 8% ( $n=2$ ) have Detrusor hypoactivity (DU). DSD observed in RRMS ( $n=2$ ) and SPMS ( $n=1$ ).

Bladder capacity was compared in NDMS, RRMS and SPMS groups and there was a significant difference between the groups. ( $p=0.042$ ) In the Tukey HSD which is multiple comparison test, a significant difference was found in the newly diagnosed MS and SPMS groups ( $p=0.039$ ).

There is a negative correlation between the EDSS and the bladder Capacity ( $p=0.008$ ). A negative correlation was found between 25 step walking and bladder capacity ( $p=0.003$ ). Correlation analysis between disease duration and bladder capacity showed no association. Q max and newly diagnosed MS, RRMS, SPMS groups were compared with ANOVA Test and no significant difference was found between groups ( $p>0.005$ ).

## DISCUSSION

As a progressive disease of the central nervous system, Multiple Sclerosis has a dynamic process. Assessment of disability during the course of the disease is of key importance, and is particularly important in determining the treatment decision (8).

EDSS is the most widely used and well-defined scale for the evaluation of MS patients, but EDSS is an ambulation index for moderate scores (4). MSFC is a quantitative scale developed in 1994 under the leadership of the US MS Society and finalized in 1999 (5,6). Lower extremity, upper limb functions and cognitive functions are tested. 25 steps walking are used for lower extremity functions. For upper extremity functions, 9-hole nail is used. For cognitive functions, a 3-second version of the Paced Auditory Serial Additional Test (PASAT) is used (PASAT-3).

A recent study has shown that MSFC is more sensitive than EDSS, both during acute attack treatment follow-up and disease follow-up (7). In addition, MSFC seems to be superior to EDSS in the follow-up of immunomodulatory therapy (8). On the other hand, the lack of visual functions constitutes the weaknesses of

MSFC (9,10). In our study, EDSS and MSFC scores between the groups; In the EDSS scores, the RRMS group was found to be different according to the newly diagnosed MS, SPMS and healthy controls, while the MSFC evaluation was different in terms of the SPMS group, newly diagnosed MS, RRMS and healthy control groups. A positive relationship was found between EDSS, 25 step walking, 9 hole dominant, 9 hole non-dominant scores, and a negative relationship between EDSS and cognitive scores.

In our study, a significant difference was observed in incontinence frequency variable between groups. As the disease duration progressed, the incidence of incontinence increased. This result was found to be similar to other studies (11,12,13).

In our study, there was a significant difference between the SPMS group and healthy controls in the IPSS test. It is associated with IPSS scores and disability status (EDSS). The relationship between urinary tract complaints and EDSS has also been shown in other previous studies (12,14,15,16). In the study of Ukkonen et al. There was no relationship between urinary symptoms and EDSS in PPMS patients (17). In the study of Porru et al. There was no relationship between EDSS and lower urinary tract symptoms (18). There was no parallel between the duration of disease and the IPSS score. This result was similar to the previous studies (15,19).

There was a significant difference between healthy controls and RRMS and SPMS in IPSS-QOL test. While there was no relationship between IPSS-QOL score and disease duration, there was a positive relationship between EDSS score. Similarly, the study of Araki et al. Showed no significant correlation with IPSS-QOL score and disease duration and a significant correlation with EDSS score (15). There was no correlation between IPSS-QOL and MSFC values.

The ICIQ-SF test is a test developed for the diagnosis of urinary incontinence. In our study, there was a significant difference between the SPMS group and healthy controls for the ICIQ-SF score. The ICIQ-SF score was associated with EDSS score and MSFC values, but not with disease duration. Since the ICIQ-SF questionnaire

was not used in previous studies, our findings could not be compared with the literature data.

In the IIEF-5 test in male sex, no significant difference was observed between the groups. The correlation between the IIEF-5 test and EDSS and disease duration was not correlated. Dachille et al. With 124 male patients (20); 25 patients (20.1%) had severe erectile dysfunction (IIEF score <10); In our study, only 1 patient (0.02%) showed severe erectile dysfunction.

In FSFI test in female sex, no significant difference was observed between groups. There was no relationship between FSFI score and EDSS score and disease duration. In other studies, the FSFI score has been shown to be negatively correlated with EDSS score and disease duration (21,22).

A significant difference was observed between the newly diagnosed MS, RRMS and SPMS groups when compared with the Urodynamic results. In our study, urodynamic findings were found to be normal in 52% of urodynamic patients. The second most common urodynamic finding was detrusor overactivity (DO) with 16%. Detrusor sphincter dyssynergia (DSD) was seen in 12%, DSD and DO 12% of urodynamic patients. Detrusor hypoactivity (DU) was 8%. In other studies, DO and DSD are the most common urodynamic findings in patients with Multiple Sclerosis (11,12,23,24,13). In A study by Cox et al. have shown a relationship between MS lesion location and DSD but not disease progression and gender (26). In another study by Porru et al., Detrusor hypoactivity (DU) was the most common urodynamic abnormality in Multiple Sclerosis patients (18).

When bladder capacity was compared between groups, there was a difference between newly diagnosed MS and SPMS groups. Bladder capacity values were found to be lower in SPMS group. In our study, the relationship between bladder capacity and EDSS and 25-step walking test was found. As the EDSS score and the 25-step walking score increased, the bladder capacity decreased. There was no relationship between bladder capacity and disease duration.

No difference was found between the groups in terms of peak flow velocity (Qmax) and voiding re-

sidual urine (PMR) and no relationship was found between EDSS score, MSFC values and duration of disease. In a study by Kirchhof et al., a linear relationship between PMR and disability was shown (25).

Some limitations in the present study must be pointed out. First, a weakness of the present study the number of patients especially men patients in groups was not sufficient. Second, we didn't measure bladder capacities by voiding diary initially.

## CONCLUSION

Lower urinary tract symptoms are common in patients with multiple sclerosis and urodynamic findings are related to disability status. These symptoms have serious effects on the quality of life of patients, so early diagnosis and treatment is an important step in MS patient follow-up.

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