ORİJİNAL ARAŞTIRMA ORIGINAL RESEARCH

Quality of Life in Patients with Multiple Sclerosis: Relationship with Clinical Variables

Multipl Sklerozlu Hastaların Hayat Kalitesi: İlişkili Klinik Değişkenler

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ABSTRACT Objective: The aim of this study was to evaluate the the quality of life by a specific Quality of life (QoL) instrument and to determine the related clinical variables with QoL status in patients with definite Multiple Sclerosis (MS). **Material and Methods:** Thirty-two MS patients with a mean age of 39±8.7 years were included in this study. Demographic and clinical charcteristics of the patients were recorded. QoL was assessed by Multiple Sclerosis International Quality of Life (MusiQoL) scale. Disability, ambulation, coping with stress, depression, anxiety, fatigue and pain were determined respectively by EDSS (Expanded Disability Status Scale), Functional Ambulation Classification (FAC), Coping with the Stress Scale (CWSS), Beck Depression scale (BDS), Beck anxiety scale (BAS), while pain and fatique was determined by Visual Analogue Scale (VAS) pain and fatigue instruments. **Results:** There were 25 female and 7 male patients with mean disease duration of 8.7±6.7 years and mean score of MusiQoL of 56.5±12.35. Negative correlations were found between MusiQoL with disease duration (r= -0.565 p=0.001), BDS (r=-0.459; p=0.008), BAS (r=-0.568; p=0.038), EDSS (r=-0.708; p= 0.021) and VAS fatigue (r=-0.451; p=0.039). Positive correlations were found between MusiQoL with FAC score (r=0.424; p=0.01) and CWSS (r=0.531; p=0.002). There were no statistically significant correlation between MusiQoL and VAS pain (p>0.05). **Conclusion:** In this study, it was demonstrated that QoL is significantly associated with depression, anxiety, fatigue, ambulation level and the ability to cope with stress. MS symptoms and clinical variables have a negative impact on patients' QoL. In this study, we emphasize the need for registration and evaluation of clinical variables in order to improve QoL in patients suffering from MS.

Key Words: Multiple sclerosis; quality of life; clinical variables

ÖZET Amaç: Bu çalışmanın amacı Multipl Skleroz (MS) tanısı olan hastalarda hastalığa spesifik bir hayat kalitesi değerlendirme ölçeği ile yaşam kalitesini değerlendirmek ve yaşam kalitesi ile klinik değişkenler arasındaki ilişkiyi incelemektir. **Gereç ve Yöntemler:** Yaş ortalaması 39±8,7 yıl olan 32 MS'li hasta çalışmaya dahil edildi. Demografik ve klinik özellikleri kaydedildi. Yaşam kalitesi Multıple Skleroz Yaşam Kalite İndeksi (MSYKİ) ile değerlendirildi. Disabilite, ambulasyon, stresle başa çıkma, depresyon, anksiyete, yorgunluk ve ağrı, sırasıyla Genişletilmiş Özürlülük Durum Ölçeği (GÖDÖ), Fonksiyonel Ambulasyon Skalası (FAS), Stresle Başa Çıkma Ölçeği (SBÇÖ), Beck Depresyon Skalası (BDS), Beck Anksiyete Skalası (BAS) ile değerlendirilirken, ağrı ve yorgunluk Görsel Analog Skala (GAS) ile değerlendiridi. **Bulgular:** 25 kadın, 7 erkek hastanın hastalık süresi ortalama 8.7±6.7 yıl ve ortalama MSYKİ skoru 56.5±12.35 idi. MSYKİ skoru ile hastalık süresi (r= -0,565 p=0,001), BDS (r= -0,459 p=0,008), BAS (r=-0,568 p=0,038), GÖDÖ (r=-0,708 p= 0,021) ve VAS yorgunluk (r=-0,451 p=0.039) arasında negatif yönde anlamlı korelasyon tespit edildi. MSYKİ ile FAS skoru (r=0,424 p=0,01) ve SBÇÖ (r=0,531 p=0,002) skorları arasında da pozitif yönlü anlamlı korelasyon tespit edildi. MSYKİ skoru ile VAS ağrı skoru arasında korelasyon saptanmadı (p>0,05). **Sonuç:** Bu çalışmada yaşam kalitesinin, depresyon, anksiyete, yorgunluk, ambulasyon seviyesi, stres ile başa çıkma becerisi ilişkili olduğu gösterilmiştir. MS semptomları ve klinik değişkenlerinin hastaların yaşam kalitesi üzerinde negatif etkileri vardır. Biz bu çalışmada MS li hastalarda yaşam kalitesinin arttırılabilmesi için klinik değişkenlerin kayıt edilmesi ve değerlendirilmesinin gerekliliğini vurgulamayı amaçladık.

Anahtar Kelimeler: Multiple skleroz; yaşam kalitesi; klinik değişkenler

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Multiple sclerosis (MS) is an immune-mediated and demyelinating chronic progressive disease of the human central nervous system (CNS).[1] The worldwide prevalence and incidence of MS are remarkably increasing. MS is the second leading cause of disability in young adults. It can lead to significant economic and social burden as well as physical disability.[2,3]

Disease activity and clinical course of MS are unpredictable, usually culminating in a wide range of symptoms and functional limitations, among which depression and fatigue being the most commonly observed symptoms.[4] Morever, MS may dramatically affect families due to increased role in responsibilities among the family members, employment challenges, financial problems and social isolation.[5]

The clinical symptoms of MS can have major effects on the status of quality of life (QoL). Therefore, in recent years, the measurement of the health-related quality of life (HRQoL) has begun to play a key role in the assessment of the overall burden of MS.[6]

The HRQoL is used as a major outcome measure for assessing health, evaluating treatment, and managing care. Indeed, clinicians may use HRQoL assessments to check whether interventions have been as effective from the patient's point of view as from the clinician's, and to determine whether further action is required.

Information of which factors are determinants of HRQoL would assist clinicians in choosing the most appropriate interventions.[7-9] Additionally these measurements are being considered increasingly important with regard to monitoring disease progression and treatment effects.[10]

The HRQoL is a complex, multidimensional construct comprised of physical, mental, social, and economic components that can be influenced by various factors, including symptoms-related impact of the disease as well as psychosocial aspects.[5] Furthermore, measuring HRQoL is regarded as a standard part of new MS trials because traditional measurements such as the Expanded Disability Status Scale (EDSS), magnetic resonance imaging, and relapse rate can not exactly assess the HRQoL. It has been shown that the EDSS might not adequately reflect patients' perceptions and the impact of their symptoms.[11] Different aspects of HRQoL in MS patients were reported in previous research papers in the literature, but in the majority of these reports the generic HRQoL indexes were used. Disease-specific instruments focus on particular health problems and are more sensitive for detecting and quantifying small changes.[10,12]

The primarily aim of this study is to evaluate QoL by a specific QoL instrument, which is Multiple Sclerosis International Quality of Life (MusiQoL) questionnaire, and to determine the related factors with HRQoL status in patients with definite MS. Secondarily we aimed to compare the HRQoL and clinical parameters between patients with EDSS level <3,5 and ≥3,5 (severe and mild disability).

MATERIAL AND METHODS

Fourty-five patients with MS referred to the clinic of Physical Medicine and Rehabilitation (PMR), were considered to enroll to the study. Four patients refused to participate in the study. Nine patients were excluded from the study since they do not fulfill the inclusion criteria. Therefore 32 patients with MS were included to the study.

The patients were diagnosed with MS according to McDonald's criteria at least 6 months before recruitment. Demographic properties of the subjects including age, gender, years of education were obtained. Inclusion criteria were as follows: 18-60 years of age, clinically stable for at least 3 months prior study participation, informed consent to participate, willing to complete the self-administered questionnaires. All patients had relapsing remitting type of MS.

Exclusion criteria were as follows: having relapse of the disease in the last month, 23 or lower mini mental statement score, chronic comorbid conditions and/or psychiatric disorders, and antidepressants or corticosteroid therapy during the last month. This study was conducted with approval by local Ethics Committee of Ankara Training and Research Hospital and written informed consent was obtained from all patients.

An experienced neurologist also evaluated patients based on sociodemographic and clinical data, type of MS, EDSS score. Current treatments were also recorded (including disease modifying drugs, current treatment for relapse). QoL was assessed by MusiQoL scale. Functional status, depression, anxiety, cognitive performance and coping with stress were determined by Functional Ambulation Clasification scale (FAC), Beck Depression Scale (BDS), Beck Anxiety Scale (BAS), Mini Mental Status Examination (MMSE) and Coping with Stress Scale (CWSS) respectively. Questionnaire forms of experienced neurologist and physiatrist (UE, FK) were given. Visual analogue scale (VAS) was used to assess the intensity of musculoskeletal pain and fatigue. The presence of motor and sensory deficits as well as urinary incontinancy was recorded.

MEASURES

EXPANDED DISABILITY STATUS SCALE (EDSS)

The EDSS is a commonly used MS rating scale based on the standard neurological examination. It is an MS-specific scale consisting of a neurological assessment quantifying disability in eight functional systems (e.g., sensory functions, cerebellar functions). The assessment of these functional systems yields a sum score ranging from 0 (no neurological impairment) to 10 (death due to MS).[13]

MULTIPLE SCLEROSIS INTERNATIONAL QUALITY OF LIFE (MUSIQOL)

The QoL was measured using a disease-specific instrument MusiQoL, which was previously validated for Turkish MS patients.[11,14,15] The MusiQoL is a self-administered, multi-dimensional, patient-based HRQoL instrument that comprises 31 items and describes the following six dimensions: activity of daily living (ADL) (8 items), psychological well-being (PWB) (4 items), relationships with friends (RFr) (4 items), relationships with family (RFa) (3 items), symptoms (SPT) (3 items) relationships with the healthcare system (RHCS) (3 items), sentimental and sexual life (SSL) (2 items), coping (COP) (2items), and rejection (REJ) (2items). MusiQoL also yields a global index score, which is calculated as the mean of the individual dimension scores. Like the individual scale scores, the composite scores range from 0 to 100, with higher scores indicating a better health outcome.[5,9,16-18] MusiQoL questionnaire has been recently developed and validated for the Turkish MS Patients by a multi-center study.[11]

THE FUNCTIONAL AMBULATION CLASSIFICATION (FAC)

FAC is an ordinal method for classifying mobility. It was designed as an inexpensive measure that requires little time for therapist training and administration. FAC was developed in a cohort of 61 people with stroke or MS. [The FAC has six categories ranging from 0 (non-functional ambulation) to 5 (independent)]. Assessors are required to observe performance over various slopes and surfaces.[19]

COPING WITH STRESS SCALE (CWSS)

The CWSS is a self-administered, multi-dimensional, patient-based instrument that comprises 42 items. The items are summed to obtain a total score that can range from 23 to 115, with higher scores meaning better copping with stress.[20]

BECK DEPRESSION SCALE (BDS)

BDS was developed by Beck et al. and is widely used in measuring depression symptom levels.[21] The validity and relaibilty of this scale for Turkey was determined by Hisli.[22] BDS is recommended for depression screening in MS patients. It consists of 21 items about determining the feeling of the subject in the last week, depressive symptoms incorporating pessimism, feelings of unsuccessfulness, dissatisfaction, feeling guilty, indecisiveness, irritability, fatigue, sleep disorder, loss of appetite, and social regression. Each question has a set of at least four possible answer choices, ranging in intensity. When the test is scored, a value of 0 to 3 is assigned for each answer, then the total score is compared to a key to determine the severity of depression symptoms. The standart cut-offs are as follows: 0-9 indicates no depression symptoms, 10-18 indicates mild depression, 19-29 indicates moderate depression, and 30-63 indicates severe depression.[23]

BECK ANXIETY SCALE (BAS)

Anxiety level of the patients was evaluated with BAS. It contains 21 items related to anxiety symptoms. The respondent is asked to rate how much he or she has been bothered by each symptom over the past week on a 4-point scale ranging from 0 to 3. The items are summed to obtain a total score that can range from 0 to 63. The cut off point are determined as: 0-8 indicates minimal anxiety, 8-15 indicates mild anxiety, 16-25 indicates moderate anxiety, and 26-63 indicates severe anxiety.[24]

MINI-MENTAL STATE EXAMINATION (MMSE)

Thirty simple questions, including time and place of the test, repeating words from a list, arithmetic, language use and comprehension along with basic motor skills were asked to determine dementia and other cognitive impairments. The maximum score is 30. A score of 23 or lower indicates cognitive impairment.[25]

VISUAL ANALOGUE SCALE PAIN (VAS PAIN) AND VISUAL ANALOGUE SCALE FATIGUE (VAS FATIGUE)

VAS (10 cm) was used to assess the intensity of musculoskeletal pain and fatigue.[26,27] For pain intensity, the scale is most commonly anchored by “no pain” (score of 0) and “pain as bad as it could be” or “worst imaginable pain” score of 10 cm).

Statistical Analysis

SPSS (Statistical Package for Social Sciences) 20 software was used for statistical analyses. Measured data were described as the arithmetic mean±standard deviation, whereas categorical data were described as percentages (%). Normal distribution of measured data was examined by Kolmogorov Smirnov test. If the data was normally distributed when comparing both groups, Student’s t test was used. If the data were not normally distributed, Mann-Whitney U test was used. Correlation between MusiQoL scores and other continuous parameters was assessed by Pearson’s correlation analysis. Statistical level of significance was accepted as $p<0.05$.

RESULTS

Thirty-two MS patients with a mean age of 39±8.7 years were included. There were 25 female and 7 male patients with mean disease duration of 8.7±6.7 years. The demographic properties are shown in Table 1. Most patients (16.0-49.9%) had received disease-modifying treatments. Six patients (18.8%) had received azothioprine or methotrexate. Minimal depression was present in 5 patients (15.6%), mild depression in 14 patients (43.8%), moderate depression in 6 patients (18.8%) and severe depression in 7 patients (21.9%). There were 6 patients with minimal anxiety (18.8%), 11 patients with mild anxiety (34.4%), 8 patients with moderate anxiety (25%) and 7 patients with severe anxiety (21.9%).

Clinical measurements are shown in Table 2. Negative correlations were found between MusiQoL with disease duration, BDS, BAS, EDSS and VAS fatigue. Positive correlations were found between MusiQoL with FAC score and CWSS There were no statistically significant correlation between MusiQoL and VAS pain. Correlation between MusiQoL and clinical parameters are demonstrated in Table 3.

Patients were divided into two groups according to EDSS scores determinted as <3,5 and ≥3,5.[28]

The mean score of MusiQoL, BDS, BAS, VAS fatigue, CWSS scores were significantly different

TABLE 1: The demographic properties of the patients.

Variables	Patients (n=32)
Female/ Male n(%)	25/7 (78,1/21,9)
Age:mean± SD year (min-max)	39±8,7 (20-54)
Disease duration: mean± SD year (min-max)	8,7±6,7 (0,6-25)
Education status (%)	
Primary school	25 (78,1)
High school	5 (15,6)
University	2 (6,3)
Occupation (%)	
Housewife	23 (71,9)
Officer	7 (21,8)
Retired	2 (6,3)
Medication (n(%))	
User/Non user	22/10 (68,7/31,3)

TABLE 2: The clinical variables of patients.

	Mean(min-max)
MusiQoL	56.5±12.35(25.2-76.7)
BDS score	20.5±12.8(2-50)
BAS score	18.0±11.4(0-54)
VAS pain score	3.1±2,8 (0-8)
VAS fatigue score	6.0±3,2(0-10)
MMSE score	26.1 ± 4.7(24-30)
FAC score	4.3 ± 1.5(0–5)
CWSS score	92.6 ± 8.5 (73–115)
EDSS score median(min-max)	4 (1,5-6)
EDSS score ≥3,5 n(%)	11 (36,37)
EDSS score <3,5 n(%)	21 (63,63)

MusiQoL: Multiple sclerosis quality of life scale, BDS: Beck Depresion Scale, BAS: Beck Anxiety Scale, VAS fatigue: Visual Analog Scale fatigue, MMSE: Mini-Mental State Examination, FAC: The Functional Ambulation Classification, VAS pain: Visual Analog Scale pain, CWSS: Coping with the Stress Scale.

TABLE 3: Correlation values between MusiQoL scores and clinical variables.

Clinical Variables	MusiQoL	
	r	p
Disease Duration	-0.565	0.001
BDS	-0.451	0.039
BAS	-0.568	0.038
EDSS	-0.708	0.021
VAS fatigue	-0.451	0.039
FAC	0.424	0.01
CWSS	0.531	0.002
VAS pain	-	p>0.05

MusiQoL: Multiple sclerosis quality of life scale, BDS: Beck Depresion Scale, BAS: Beck Anxiety Scale, VAS fatigue: Visual Analog Scale fatigue, pain, FAC: The Functional Ambulation Classification, CWSS: Coping with the Stress Scale, VAS pain: Visual Analog Scale.

between the patients having EDSS score <3,5 and those having ≥3,5. (respectively p=0,01, p=0,008, p=0,005, p<0,001, p=0,032). There was no statistically significant difference between between the patients having EDSS score <3,5 and those having ≥3,5 regarding VAS pain (p=0,055) (Table 4).

DISCUSSION

In this study we have determined that HRQoL MS might be related with disability, disease duration, mobility level, fatigue, mood (anxiety and depression) and the level of coping with stress, in our MS patients. Additionally the MusiQoL, BDS, BAS, VAS fatigue, CWSS scores of the patients with severe disability were found to be worse than in patients with less disability.

There was a negative relationship between disease duration and the QoL scores in our study indicating that patients with longer disease duration had impaired QoL, similar to previous studies which have indicated that HRQoL got worse with longer disease duration.[29,30]

According our resuts, we have indicated that increased disability, depression and anxiety symptoms, fatigue, and physical comorbidity were associated with decreased HRQoL in MS, which were similar with some previous data.[31]

The pathophysiological basis of fatigue in MS is complex and its precise mechanism is unresolved. Fatigue can be defined in a number of ways, as a lack of physical or mental energy or a feeling of tiredness.[32,33] The subjective experience of fatigue is reported by 50-90% of patients with MS according to different studies and often interferes with social or occupational activities. It sometimes becomes the most disabling symptom or the first sign of the disease.[33,34] Fatigue is certainly linked with reduced HRQoL, however the precise way in which fatigue impacts on HRQoL has not been clearly defined. In our study fatigue were found to be related with quality of life in patientswith MS. In a recent study, which supports the results of our study, fatigue as well as depression were independently associated with impaired HRQoL in patients with MS.[35]

A substantial body of evidence demonstrates that HRQoL in MS is associated with impairment and disability as measured by neurological symptoms.[36,37] However, the strength of the correlation varies enormously depending on the methodology and questionnaires of each individual study. Strongly correlation was observed between QoL and disability, which was evaluated with EDSS.[38] We also confirm a strong correlation between QoL and disability level as observed in recent studies.[11,39-42] We have detected there were poorer clinical variables and Qol in higher disability level.

TABLE 4: Comparasion of clinical measurements according to the EDSS score

	EDSS<3,5 (n=11)	EDSS ≥3,5 (n=21)	
	Mean ±SD	Mean ±SD	P
MusiQoL	64,10±13,29	53,99±9,18	0,01[*a]
BDS	12,40±5,21	24,32±13,62	0,008[*b]
BAS	10,60±7,66	21,50±11,44	0,005[*b]
VAS fatigue	3,20±2,70	8,27±1,83	<0,001[*b]
VAS pain	2,79±1,50	3,90±2,67	0,055 [b]
CWSS	89,90±11,96	77,86±10,65	0,032[*b]

MusiQoL: Multiple sclerosis quality of life scale, BDS: Beck Depresion Scale, BAS: Beck Anxiety Scale, VAS fatigue: Visual Analog Scale fatigue, VAS pain: Visual Analog Scale pain, CWSS: Coping with the Stress Scale. a Student's t test was employed. b Mann-Whitney U test was employed. *p<0,05 was statically significant.

Salahi et al defined that disability was the most important predictors for QoL.[41] Özakbaş et al also showed a corelation between EDSS and HRQoL scores in their study group.[42]

Two studies have identified depression as the strongest determinant of impaired quality of life in patients with MS.[39,43] Depression and fatigue are important factors of MS and must not be considered as secondary outcomes, but as an integral part of disease presentation and management.[39] Although the high prevalence of depression in people with MS is widely acknowledged, depression is under-recognised and poorly treated.[43] Implications for depression is common among people with MS, however, depressed patient with MS do not receive adequate treatment for depression which may lead to increased disability and HRQoL.[44] Nourbakhsh et al recently reported that fatigue, depression and disability are closely associated with HRQoL in early MS.[45] Similar to previous data, we determined statistically significant correlation between MusiQoL scores and mental health (depression and anxiety) measurements our study group.

Although we did not detect relation between pain and HRQoL, many previous research reported that pain is an important contributor to HRQoL for patients with MS.[46-48] It may be depended on patients' VAS average which scores were not high in our study group.

Ambulation ability is significantly contributed to individuals' perceptions of independence in ADL domains of self-care, mobility and domestic life. The consequences of those disabilities in ADL and participatory activities include an increased need for caregiving and an adverse impact on patient-reported health status or HRQoL.[49-51] However we observed a significant correlation QoL in our patients. It has been proposed that stress may play a role in the MS disease course, and has been shown to have a strong association with frequency of disease relapses.[25] Therefore strategies that reduce and manage stress may play a role in secondary or tertiary prevention for people with MS by slowing disease course and improving QoL. The HRQoL scale into clinical practice is to provide a comprehensive assessment of a patient's health status from his or her perspective.[52] We have used a specific-QoL questionary-MusiQoL questionary for evaluating HRQoL in patient with MS.

MusiQoL questionnaire is a well-validated MS-specific, self-administered, multidimensional, patient-based QoL instrument.[11] It has not only validated for cross sectional measurements ,but also responsive to disability change in patients with MS. In this study conducted with 524 patients with MS, the MusiQoL index score and specific MusiQoL dimensions, such as relationships with health care system or sentimental and sexual life, were moderately responsive to disability change in patients with MS over the course of a 24-month study.[53] Given the availability of many QoL instruments, little research has surprisingly been conducted to test the responsiveness of QoL tools in MS. Comparisons with responsiveness indices for other QoL instruments in the literature are difficult without a direct head-to-head.[53]

The measured HRQoL is considered an important outcome in population health assessments evaluating treatments and managing care. There are virtually no data regarding psychometrically validated HRQoL instruments designed specifically for patients with MS. Notably, the length of the MusiQoL (31 items) is much shorter than that of other HRQoL instruments available for patients with MS and so may be more compatible with clinical practice. MusiQoL questionnaire would be very useful, not only to explore and confirm its sensitivity to changes, but also to explore its ability to be used in a prognostic purpose.[7]

We have performed further subgroup analysis according to EDSS scores .Our study group was divided into two groups; with patients low disability (EDSS <3,5) and patients with higher disability (EDSS ≥3,5).[28] According this subgroup data HRQoL, depression, anxiety and fatigue parameters were detected in patient s with low level of disability better in patients with higher levels of disability.

There are some limitations of our study. First, our study was conducted on a small an d selected sample. Therefore, the generalizability of these results may be limited and may not be reflecting a naturalistic setting. Second, the sample consisted predominantly of female patients, which might have limited generalizability to men. Third, our sample have disability levels higher than EDSS 6. Our results therefore can be applied only to patients in levels with less pronounced disabilities.

In conclusion, this study demonstrates that significant associations are present between QoL and depression, anxiety, fatigue, ambulation and coping with stress skill of level. It is important for clinicians and people with MS to be aware of above mentioned clinical parameters . The determination and treatment of psychosocial problems, fatigue and disability are needed for comprehensive preventive medical approach and in order to increase QoL in patients suffering from MS.

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