RESEARCH ARTICLE

Health-related quality of life in multiple sclerosis: Links to mental health, self-esteem, and self-compassion

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ABSTRACT

Objective: To examine the association of health-related quality of life (HRQoL) with mental health, self-esteem, and self-compassion in multiple sclerosis (MS) patients.

Method: For this descriptive and cross-sectional study, a total of 89 volunteer Turkish MS patients completed the patient information form, Rosenberg Self-Esteem Scale, Self-Compassion Scale, Hospital Anxiety and Depression Scale, and MS International Quality of Life Questionnaire. Depressed patients were compared with nondepressed patients regarding HRQoL, self-esteem, and self-compassion. Bivariate correlations between HRQoL, self-esteem, self-compassion, and mental health indices were calculated followed by hierarchical regression analyses.

Results: Depressed MS patients had significantly lower HRQoL, self-esteem, and self-compassion compared to their nondepressed counterparts. Hierarchical multiple regression analysis showed that physical HRQoL was significantly predicted by disability status and self-compassion, explaining 48% of the total variance. Anxiety and self-esteem explained 52% of the total variance of psychological HRQoL. Social HRQoL was significantly predicted by depression and self-esteem, which explained 21% of the total variance.

Conclusion: The effects of MS and disability may not be avoidable, but self-related traits including self-esteem and self-compassion can be modified through psychosocial interventions to improve HRQoL. The findings of the current study provided insights into which psychosocial factors to address in improving different domains of HRQoL in MS patients. Cultivating self-compassion may increase HRQoL in the physical domain, while working with self-esteem and self-worth may improve the psychosocial domain.

Keywords: Anxiety, depression, health-related quality of life, multiple sclerosis, self-compassion, self-esteem

INTRODUCTION

Multiple sclerosis (MS) is a chronic, progressive inflammatory autoimmune disease of the central nervous system characterized by demyelination and axonal loss. MS typically occurs between 20 and 40 years of age and is two-fold more common in women (1). The prevalence of MS is highest in North America and West Europe (>100 per 100.000); for Turkey, it is 20-60 per 100.000 (2). MS is the most common non-traumatic cause of neurological disability in young adults (3). The disease generally involves periods of

exacerbation and remission, leading to various symptoms including problems with vision, fatigue, pain, paresis, spasticity, loss of balance, cognitive impairment, and sexual dysfunction (1). Psychiatric comorbidity, particularly depression is very common in MS due to various biochemical, genetic, and social factors (4). It was reported that depression is 20% more prevalent in MS patients than in the general population (5). Compared to other neurological diseases, the prevalence of depression in MS was also reported to be high (6).

Being a chronic disabling disease with an ambiguous course and high psychiatric comorbidity, MS has a profound negative impact on health-related quality of life (HRQoL) (7-9). HRQoL is an important end-point indicator of healthcare, being a multidimensional concept covering physical health, level of independence, psychological health, spirituality, social relationships, and environmental features (10,11). MS patients suffer from psychosocial losses such as losing the ability to work and a narrowing of their social network, which lead to alterations in their self-concept and a reduction in HRQoL in addition to the negative physical and neurological effects of the disease (12,13). Previous studies underscored the role of psychosocial factors including low self-efficacy, low self-esteem, low social support, and maladaptive coping in diminished HRQoL in MS (13-17). Above all, depression was found to be one of the most powerful predictors of HRQoL in MS patients (18-21).

Depression and MS both affect the way people view themselves. The cognitive model of depression posits that depressed individuals show distortions in their self-views and have low self-worth (22). Being a chronic disease leading to neurological disability, MS also influences patients' self-views and self-worth via disease symptoms that impose limitations on role performance and affect multiple roles or self-aspects (wife, mother, executive, jogger, etc.). Charmaz (23) suggested that disease-related experiences lead to changes in a person's self-views and force patients to redefine their self-constructs. Previous research supported this assumption, as it was found that MS patients' self-views, which include constructs such as self-esteem and self-compassion, were lower than those of healthy controls (24-26). Self-esteem refers to the judgment of one's self-worth, whereas self-compassion is defined as approaching oneself in a compassionate manner, being mindful of negative emotions without over-identifying with them, and seeing one's own failures as a natural part of being human (27-29).

Low self-esteem and low self-compassion were consistently associated with poorer mental health outcomes in various samples (30-34). In a similar vein, Taylor and Brown (35,36) argued that having an enhanced sense of self-worth helps people respond adaptively to adverse life events such as being diagnosed with a chronic disease. However, other researchers have reported that inflated levels of self-esteem may result in an unhealthy, self-centered personality which deteriorates well-being (37-41). Unlike self-esteem, which refers to an individual's perceptions of his/her worth, self-compassion is independent of evaluations of self-worth. People high in self-compassion tend to respond positively to negative events such as making a mistake, failing in some endeavor, or experiencing distress due to symptoms of the disease (42). Higher self-compassion corresponds to being mindful toward negative affective states and offering oneself soothing and kindness rather than harsh self-directed criticisms or over-identification with negative feelings and the victim role; whereas high self-esteem may not be such a source of relief during hard times because it is dependent upon self-worth and achievement. In other words, self-compassion seems to be a more preferable strength for people with chronic illness because unlike self-esteem, it is not related to the level of "achievement" (continuing to be able to carry out activities of daily living independently etc.). A self-compassionate MS patient would find it easier to accept his/her condition and show adaptive responses to disease-related problems, which in turn would enhance well-being and HRQoL (43). Previous studies showed that self-compassion is positively related to happiness, quality of life, optimism, positive affect, life satisfaction, and health promoting behaviors, while it is negatively associated with depression, anxiety, neuroticism, and negative affect in various samples including college students and HIV patients (27,28,30,32,33,44-46). Thus, the current study aimed to compare self-esteem and self-compassion in their association with HRQoL dimensions in MS patients.

The level of self-esteem in MS patients compared to the general population and its linkage to various outcome variables have been addressed by researchers before. Beatus et al. (47) indicated that the physical and psychological consequences of MS negatively impact work life, social life, and physical independence, leading to deterioration in self-esteem and self-worth. Indeed, it was reported that MS patients have lower levels of self-esteem compared to healthy controls (24-26). Dlugonski and Motl (48) found self-esteem to be negatively linked to the physical and psychological dimensions of HRQoL

in MS patients. On the other hand, studies that assess self-compassion in MS patients are scarce. In one study, it was found that self-compassion had a positive correlation with HRQoL among MS patients (49).

The number of studies examining the association between self-views and HRQoL in MS patients seems to be limited. Yet both self-esteem and self-compassion can serve as protective psychosocial resources to be promoted through psychosocial interventions in order to improve HRQoL in MS patients and thus contribute to reducing health costs. Based on theoretical accounts regarding the association between self-views and well-being, the current study aimed to test a model where HRQoL domains were regressed on disability status, depression, anxiety, self-esteem, and self-compassion in a sample of MS patients. The secondary aim of the study was to compare self-esteem, self-compassion, and HRQoL in depressed and nondepressed MS patients. The hypotheses of the current study were as follows:

1. Depressed MS patients have significantly lower self-esteem, self-compassion, and HRQoL scores compared to nondepressed MS patients.
2. Disability status, depression, anxiety, self-esteem, and self-compassion predict the physical domain of HRQoL.
3. Depression, anxiety, self-esteem, and self-compassion predict the psychological domain of HRQoL.
4. Depression, anxiety, self-esteem, and self-compassion predict the social domain of HRQoL.

METHOD

Design and Setting
The study was planned as a descriptive and cross-sectional study. It was conducted at the Neurology Department of Dokuz Eylul University Hospital from September to December 2016.

Participants
Patients who attended the MS Clinic of Dokuz Eylul University Hospital for routine check-ups were invited to participate in the study. During the study period, 141 patients attended the clinic and the study sample consisted of 89 eligible patients. Inclusion criteria were being 18-60 years old, agreeing to participate in the study, being able to speak and understand Turkish, and having a definitive diagnosis of MS. Exclusion criteria were having severe cognitive impairment as reported by the attending neurologist, having suffered an exacerbation during the last month, having received corticosteroid treatment in the last month, being pregnant, and being diagnosed with any psychotic disorder.

Measures
Data Collection Form
A data collection form was prepared by the researchers in order to record sociodemographic (sex, age, educational status, marital status, number of children, employment status, and level of income) and clinical characteristics (disease duration, number of past MS attacks, and treatment).

Expanded Disability Status Scale (EDSS): EDSS is a widely used measure of the neurological impact of MS, being a clinical assessment tool that relies on the standard neurological examination as conducted by a medical doctor. It rates disease severity on a scale of 0 (normal) to 10 (death due to MS). Scores between 0 and 3.5 indicate full ambulation, whereas scores of 4.0 and above indicate limited ambulation. A score of 6.0 corresponds to the ability to walk approximately 100 m with assistance on one side, while a score of 6.5 indicates being able to walk 20 meters with bilateral assistance. Individuals with scores of 7.0 and 7.5 need to use wheelchairs (50).

Multiple Sclerosis International Quality of Life Questionnaire (MusiQoL): The MusiQoL is a 5-point Likert-type scale consisting of 31 questions and 9 subscales including activities of daily living (ADL, 8 items), psychological well-being (PWB, 4 items), symptoms (SPT, 4 items), relationships with friends (RFr, 3 items), relationships with family (RFa, 3 items), sentimental and sexual life (SSL, 2 items), coping (COP, 2 items), rejection (REJ, 2 items), and relationships with the healthcare system (RHCS, 3 items). The MusiQoL was developed by Simeoni et al. (51) in order to assess HRQoL in MS patients. The index score is computed as the mean of the subscale scores. All 9 dimensions and the index score are linearly transformed and standardized on a 0 to 100 scale, where 0 indicates the worst possible level of HRQoL and 100 indicates the best level. The Turkish version of the MusiQoL was also developed and tested for validity and reliability by Simeoni et al. (51). In the current study, Cronbach's alpha value of the total MusiQoL was found to be 0.89.

Hospital Anxiety and Depression Scale (HADS): The HADS, which is a 14-item 4-point Likert-type scale, was developed for determining the risk for and severity of depression and anxiety in medical samples (52). This scale is not a diagnostic tool but can be used for determining risk groups on short notice. Validity and

reliability of the Turkish version of the HADS was established and cutoff points for depression and anxiety were reported to be 7 and 10, respectively, for the Turkish population (53). In the current study, Cronbach's alpha coefficients of the depression and anxiety subscales were found to be 0.81 and 0.84, respectively.

Rosenberg Self-Esteem Scale (RSES): This 10-item 4-point Likert-type scale was developed by Rosenberg in order to evaluate global self-esteem (29). The Turkish adaptation of the RSES was conducted by Cuhadaroglu (54), who concluded that the Turkish version of the scale was valid and reliable. Total scores may range between 0 and 30, where higher scores correspond to higher levels of self-esteem. In the current study, Cronbach's alpha coefficient of the RSES was found to be 0.89.

Self-Compassion Scale (SCS): The SCS was developed by Neff (27) in order to evaluate the level of self-compassion in adults. The SCS is a 5-point Likert-type scale with 26 items. The Turkish validity and reliability study of the SCS was carried out by Akin et al. (55). For the Turkish SCS, total self-compassion scores were calculated by adding up all 26 items after reverse scoring. Total scores may range between 26 and 130, where higher scores indicate higher levels of self-compassion. In the current study, Cronbach's alpha coefficient of the total SCS was found to be 0.66.

Data Collection

Ethics approval for the study was granted by the Dokuz Eylul University School of Medicine's Noninvasive Clinical Research Ethics Board (protocol number 2859-GOA, decision number: 2016/22-19). Written informed consent of all patients was obtained. The EDSS scores of the patients were calculated by the second author. The pencil-and-paper instruments took approximately 20 minutes to complete and were individually administered to the participants in a quiet room at the hospital after medical examinations. Participants who had difficulties with the questionnaires due to neurological disability were aided by the first author who read the questions to them and marked their responses.

Statistical Analysis

Data was analyzed using SPSS version 20 (IBM). For regression analysis, subscales of the MusiQoL were combined into composite variables. ADL was combined with SPT to produce a composite physical HRQoL score, PWB was combined with COP and SSL to produce a composite psychological HRQoL score, and RFr, RFa, REJ, and RHCS were combined to obtain a composite social HRQoL score. For statistical analysis, descriptive statistics, independent samples t-test, chi-square test of independence, Pearson correlations, and multiple hierarchical regression analysis were used. Independent samples t-tests were run to compare depressed and nondepressed patients regarding self-esteem, self-compassion, and HRQoL parameters while the chi-square test of independence was used to compare these two groups by sex. The associations between disability status, self-esteem, self-compassion, and HRQoL parameters were examined using Pearson correlations prior to hierarchical regression analyses. The level of statistical significance was set at $p<0.05$ (two-tailed).

RESULTS

Demographic and Clinical Characteristics

The demographic and clinical characteristics of the patients are presented in Table 1. Mean age was 39.78 years (standard deviation [SD]=10.83). Of the patients, 75.3% were female (n=67), 55.1% (n=49) had a Bachelor's degree, 68.5% (n=61) were married, 49.4% (n=44) were employed, and 61.8% (n=55) perceived their economic status as "moderate." Patients' mean EDSS score was 1.51 (SD=1.63) and mean disease duration was 7.26 years (SD=5.49). Mean number of MS attacks experienced was 2.57 (SD=2.52). Among the patients, 65.1% (n=58) used immunomodulator injections.

Comparisons Between Depressed and Nondepressed Patients

According to the HADS cutoff criteria, 39.3% (n=35) of the participants had significant depressive SPT and 24.7% (n=22) had significant anxiety. The self-esteem, self-compassion, and HRQoL scores of the depressed and nondepressed patients were compared using independent samples t-tests. Prior to these analyses, the depressed and nondepressed group were compared by age, disease duration, and EDSS scores using independent samples t-test. It was found that the mean age (t [87]=0.76, p>0.05), disease duration (t [87]=0.28, p>0.05), and EDSS scores (t [87]=0.94, p>0.05) of the two groups did not show significant differences. The depressed and nondepressed patients were also compared by sex using the chi-square test of independence. It was determined that there was no significant interaction between sex and depression status (χ^2 [1]=1.39, p>0.05).

Depressed and nondepressed patients were compared with regard to self-esteem, self-compassion,

Table 1: Demographic and clinical characteristics of the multiple sclerosis patients (n=89)

Variable	Mean	SD	n (%)
Age (range: 20-60 years)	39.78	10.83	
Disease duration (range: 6 months-25 years)	7.26	5.49	
Number of children (range: 0-3)	1.07	1.02	
Number of Multiple Sclerosis attacks (range: 1-15)	2.57	2.52	
EDSS (range: 0-6.5)	1.51	1.63	
Gender			
Female			67 (75.3%)
Male			22 (24.7%)
Perceived income			
Poor			5 (5.6%)
Moderate			55 (61.8%)
Good			28 (31.5%)
Very good			1 (1.1%)
Educational level			
Less than high school			23 (25.8%)
High school			17 (19.1%)
Bachelor's Degree			49 (55.1%)
Marital status			
Married			61 (68.5%)
Single			19 (21.3%)
Divorced			6 (6.7%)
Widowed			3 (3.4%)
Employment			
Employed			44 (49.4%)
Unemployed			36 (40.4%)
Retired			9 (10.1%)
Treatment			
Immunomodulator injection			58 (65.1%)
Oral immunomodulator			17 (19.1%)
Immunosuppressant			4 (4.5%)
No medication			10 (11.3%)

EDSS: Expanded Disability Status Scale, SD: Standard deviation

and HRQoL using independent samples t-tests, where depression status constituted the dependent variable. As depicted in Table 2, nondepressed patients had significantly higher self-esteem (t [87]=5.86, p<0.001) and self-compassion scores (t [87]=3.82, p<0.001) compared to depressed patients. Depressed patients had significantly lower HRQoL in multiple subscales including PWB (t [87]=5.06, p<0.001), RFr (t [87]=3.67, p<0.001), RFa (t [87]=3.91, p<0.001), SSL (t [87]=3.29, p<0.01), COP (t [87]=2.42, p<0.05), and REJ (t [87]=2.80, p<0.05). On the other hand, the ADL (t [87]=1.86, p>0.05), SPT (t [87]=1.72, p>0.05), and

RHCS (t [87]=1.13, p>0.05) subscale scores did not differ by depression status. As for the total HRQoL (t [87]=4.82, p<0.001), physical HRQoL (t [87]=2.09, p<0.05), psychological HRQoL (t [87]=5.48, p<0.001), and social HRQoL scores (t [87]=4.52, p<0.001), depressed patients obtained significantly lower scores compared to their nondepressed counterparts.

Correlation Analysis
Bivariate correlations between disability status, mental health, self-esteem, self-compassion, and HRQoL as well as the mean values pertaining to these variables for

Table 2: Self-Esteem, self-compassion and HRQoL in depressed and nondepressed multiple sclerosis patients

	Depressed (n=35)		Nondepressed (n=54)		t (df=87)	p
	Mean	SD	Mean	SD		
Self-esteem	19.77	3.76	24.90	4.19	-5.86	<0.001
Self-compassion	81.51	16.60	95.51	17.08	-3.82	<0.001
ADL	63.83	27.16	74.18	24.61	-1.86	0.06
PWB	50.17	18.53	69.44	16.89	-5.06	<0.001
SPT	72.50	16.68	79.28	18.95	-1.72	0.08
RFr	63.80	27.56	82.40	20.13	-3.67	<0.001
RFa	73.33	22.84	90.74	18.78	-3.91	<0.001
SSL	52.14	33.55	75.92	33.01	-3.29	0.001
COP	68.92	23.16	81.01	22.87	-2.42	0.02
REJ	72.14	22.90	84.95	19.78	-2.80	0.006
RHCS	84.28	18.60	89.19	20.83	-1.13	0.26
Physical HRQoL	66.73	21.38	75.88	19.33	-2.09	0.04
Psychological HRQoL	55.37	15.61	73.95	15.65	-5.48	<0.001
Social HRQoL	73.51	14.10	86.99	13.51	-4.52	<0.001
Total HRQOL	66.19	11.97	79.33	12.88	-4.83	<0.001

SD: Standard deviation, ADL: Activities of daily living, PWB: Psychological well-being, SPT: Symptoms, RFr: Relationships with friends, RFa=Relationships with family, SSL: Sentimental and sexual life, COP: Coping, REJ: Rejection, RHCS: Relationships with healthcare system, HRQoL: Health-related quality of life

the entire sample were shown in Table 3. It was found that the total HRQoL score had significant positive correlations with self-esteem (r=0.53, p<0.01) and self-compassion (r=0.42, p<0.01) and had significant negative correlations with the EDSS score (r=0.41, p<0.01), depression (r=0.52, p<0.01), and anxiety (r=0.42, p<0.01). Physical HRQoL was significantly and positively associated with self-esteem (r=0.32, p<0.01) and self-compassion (r=0.33, p<0.01) and was significantly and negatively correlated to the EDSS score (r=0.59, p<0.01), depression (r=0.32, p<0.01), and anxiety (r=0.23, p<0.05). Psychological HRQoL had significant positive correlations with self-esteem

(r=0.62, p<0.01) and self-compassion (r=0.52, p<0.01) and significant negative correlation with depression (r=0.58, p<0.01) and anxiety (r=0.59, p<0.01). As for social HRQoL, significant negative correlations with depression (r=0.40, p<0.01) and anxiety (r=0.23, p<0.05) and a significant positive correlation with self-esteem (r=0.36, p<0.01) were found.

Hierarchical Multiple Regression Analysis
Hierarchical linear regression analyses were run to determine whether the independent variables (disability status, depression, anxiety, self-esteem, and self-compassion) predicted HRQoL domains (physical,

Table 3: Bivariate correlations between scale scores

	2	3	4	5	6	7	8	9	Mean	SD
1. EDSS	0.11	-0.02	-0.20	0.001	-0.59**	-0.15	-0.06	-0.41**	1.51	1.63
2. Depression	1	0.62**	-0.54**	-0.45**	-0.32**	-0.58**	-0.40**	-0.52**	5.11	4.13
3. Anxiety		1	-0.54**	-0.41**	-0.23*	-0.59**	-0.23*	-0.42**	7.32	4.46
4. Self-esteem			1	0.63**	0.32**	0.62**	0.36**	0.53**	22.88	4.73
5. Self-compassion				1	0.33**	0.52**	0.16	0.42**	90.01	18.15
6. Physical HRQoL					1	0.47**	0.26*	0.82**	72.28	20.54
7. Psychological HRQoL						1	0.52**	0.80**	66.64	18.03
8. Social HRQoL							1	0.70**	81.69	15.18
9. Total HRQoL								1	74.16	14.03

EDSS: Expanded Disability Status Scale, HRQoL: Health-related quality of life, SD: Standard deviation. *p<0.05, **p<0.01

psychological, and social HRQoL). In all three models, the EDSS score was entered in the first step of the analysis, depression and anxiety were entered in step 2, and self-esteem and self-compassion were entered in step 3. The rationale for entering disability status and mental health indices in the first two steps of the analysis was that these factors are well-known predictors of HRQoL in the literature and therefore should be controlled for prior to examining the associations with self-esteem and self-compassion. Three separate hierarchical linear regression analyses were conducted for predicting each HRQoL domain (Table 4). According to the results, EDSS and self-compassion accounted for 48% of the total variance in physical HRQoL (F(5,

83)=15.36, p<0.001). The results of the hierarchical linear regression analysis conducted in order to predict psychological HRQoL showed that anxiety and self-esteem accounted for 52% of the total variance (F[5, 83]=18.16, p<0.001). As for social HRQoL, depression and self-esteem accounted for 21% of the total variance (F[5, 83]=4.36, p<0.01).

DISCUSSION

The main objective of the current study was to investigate the associations between HRQoL, mental health, self-esteem, and self-compassion in a sample of MS patients. The secondary aim of the study was to

Table 4: Hierarchical Multiple Regression Analyses for Predicting HRQoL Domains						
	R2	ΔR2	ΔF	β (Step 1)	β (Step 2)	β (Step 3)
Dependent Variable:						
Physical HRQoL						
Step 1	0.34	0.34	45.75***			
EDSS				-0.59***	-0.57***	-0.60***
Step 2	0.42	0.08	5.85**			
Depression					-0.17	-0.10
Anxiety					-0.14	-0.12
Step 3	0.48	0.06	4.53*			
Self-esteem						-0.11
Self-compassion						0.31*
Dependent Variable:						
Psychological HRQoL						
Step 1	0.02	0.02	2.07			
EDSS				-0.15	-0.13	-0.08
Step 2	0.43	0.41	30.82***			
Depression					-0.32**	-0.19
Anxiety					-0.39***	-0.26*
Step 3	0.52	0.09	7.71**			
Self-esteem						0.26*
Self-compassion						0.15
Dependent Variable:						
Social HRQoL						
Step 1	0.004	0.004	0.31			
EDSS				-0.06	-0.01	0.05
Step 2	0.16	0.15	7.77**			
Depression					-0.41**	-0.36*
Anxiety					0.02	0.11
Step 3	0.21	0.05	2.64			
Self-esteem						0.34*
Self-compassion						-0.17

EDSS: Expanded Disability Status Scale, HRQoL: Health-related quality of life, *p<0.05, **p<0.01, ***p<0.001.

compare depressed and nondepressed MS patients regarding HRQOL, self-esteem, and self-compassion. It was found that 39.3% of the sample was depressed according to the HADS cutoff point. Kocer et al. (56) found the rate of depression to be 32.3% in a Turkish sample of MS patients. In a meta-analysis conducted by Boeschoten et al. (57), the rate of depression in MS patients was reported to be 30.5%. Our finding is slightly higher than rates found in these studies. This slight difference may be explained by methodological variations such as the assessment tools used (self-report measures vs. clinical diagnostic interviews) and the clinical features of the recruited samples (use of interferon treatment, location of MS lesions, etc.).

Despite the high prevalence of depression found in the study sample, mean self-esteem and self-compassion scores were 22.88 and 90.01, respectively. These figures reflect adequate levels of self-esteem and self-compassion. Moreover, the mean total HRQoL score was found to be 74.16, which also reflects adequate levels of HRQoL. However, mean psychological HRQoL was found to be 66.64, which was lower than the mean total, physical, and social HRQoL scores. This is not surprising considering the high rate of depression found in our study. The relatively adequate levels of self-esteem, self-compassion, and overall HRQOL with a high depression rate found in the study may be explained by the organic nature of depression in MS (58,59). It should also be noted that the mean disability status score of the sample was 1.51, indicating full ambulation. Taken together, these findings suggest that the overall well-being of the patients was at a moderate level, while their level of disability was relatively mild.

In the current study, MS patients were split into two groups according to the HADS cutoff criterion for depression, and these two groups were compared regarding HRQoL, self-esteem, and self-compassion. It was expected that depressed patients would score lower in these outcome measures compared to their nondepressed counterparts. This hypothesis was confirmed as it was found that depressed patients had significantly lower overall, physical, psychological, and social HRQoL, lower self-esteem, and lower self-compassion. On the other hand, two MusiQoL subscale scores, namely "relationships with healthcare system" (RHCS) and ADL, did not show significant differences according to depression status. This suggested that the MS patients, regardless of their depression status, were satisfied with the healthcare they received. The current study was carried out at a single center, not allowing for large variations in the delivery of healthcare. Therefore,

it can be presumed that the study site provided high quality healthcare and all patients agreed with this assessment, regardless of their mood status. Another possible explanation for this finding is that patients may have answered the RHCS questions in a biased way, fearing that giving negative feedback on healthcare might lead to conflict with healthcare professionals and thus negatively impact their treatment. The lack of a significant difference in ADL scores according to depression status can be explained by the fact that our sample had low levels of disability and did not have much difficulty carrying out ADL. It is thought that inclusion of MS patients with higher disability status in the sample would have produced different results, where mean ADL scores would have differed by depression status.

The finding of depressed patients having significantly lower overall, physical, psychological, and social HRQoL, lower self-esteem, and lower self-compassion is not surprising since it is known that depression is linked to deterioration in self-views as well as in HRQoL (22,31,34,60-62). This finding suggests that improvements in HRQoL, self-esteem, and self-compassion may serve as protective factors against nonorganic depressive SPT in MS patients. It should also be noted that although there are an abundance of studies on HRQoL and depression in MS patients (18,63-68), the same is not true for the association between self-compassion and depression. To our knowledge, the current study is the first to compare levels of self-compassion among depressed and nondepressed MS patients. As for the links between self-esteem and depression, our results confirmed that depressed MS patients have lower self-esteem than nondepressed patients, which is in line with previous studies (24,31). However, the cross-sectional design of the current study does not allow us to make inferences regarding the etiology of depression in MS. Longitudinal studies should be conducted in the future to investigate the role of low self-esteem and self-compassion in depression among MS patients.

According to the results of correlation analyses, it was determined that total and physical HRQoL were negatively linked to disability status, depression, and anxiety; whereas they were positively associated with self-esteem and self-compassion. This finding matched those of previous studies (20,21,31,48,49). Psychological HRQoL was negatively associated with mental health indices but not with disability status, while it was positively linked to self-esteem and self-compassion. It was also found that social HRQoL was positively related

to self-esteem and negatively related to depression and anxiety. The association of social HRQoL to self-compassion and disability status was not significant. The lack of a relationship between psychological and social HRQoL and disability confirms that MS has two distinct influences on HRQoL: physical and psychosocial (69). Self-compassion not being related to social HRQoL contradicts previous research (43,70). Among MS patients, social HRQoL increased with perceived self-worth or self-esteem but not with self-compassion. More research is needed in order to understand the relationship of social HRQoL to self-compassion better.

Results of the correlation analyses provided support for our regression models, where HRQoL domains were regressed on disability status, depression, anxiety, self-esteem, and self-compassion. For physical HRQoL, it was hypothesized that disability status, mental health, and self-related variables will emerge as significant predictors. This hypothesis was partially supported and it was found that disability status and self-compassion significantly predicted physical HRQoL. However, the assumption that mental health indices and self-esteem also predict physical HRQoL was falsified by the findings. This result is in line with previous research indicating that self-compassion is a better predictor of well-being than self-esteem since self-esteem is dependent upon self-evaluations and performance, whereas self-compassion refers to a mindful and accepting stance towards both the positive and negative aspects of the self (45). Thus, it is thought that self-compassion is more helpful than self-esteem in adapting to the physical challenges or shortcomings brought about by MS. On the other hand, the mean EDSS score of the study sample was low and this may have confounded the findings. In the current study, self-compassion predicted physical HRQoL in MS patients with low levels of disability, but this association may not be valid for patients with advanced disability. Results obtained in this study need to be replicated in future studies for a better understanding of the association of physical HRQoL with self-views, which would provide knowledge about which psychological constructs to address in interventions aiming to improve perceived physical HRQoL among MS patients.

Psychological HRQoL was significantly predicted by anxiety and self-esteem but not by disability, depression, and self-compassion. Most studies focus on depression in relation to psychological HRQoL, but anxiety emerged as a stronger predictor in the current study. The ambiguous course of MS seems to create anxiety and thus reduce psychological HRQoL in MS patients (64,71,72). Based on these findings, it is suggested for mental health professionals to assess the level of anxiety in MS patients as well as depression routinely. As for social HRQoL, depression and self-esteem were found to be significant predictors. Addressing self-esteem and self-worth in psychosocial interventions designed for MS patients carries the potential to improve perceived psychological and social HRQoL.

Our findings support the assumption that an individual's psychological resources such as self-esteem and self-compassion are associated with HRQoL in MS patients. Results of the current study indicate that MS patients should be screened for depression and anxiety, and their psychological resources including self-esteem and self-compassion could also be evaluated. This procedure should then include referrals of MS patients to psychotherapy in order to help them deal with the ambiguities and disabilities brought about by MS and reduced self-esteem. It is also known that reduced self-esteem makes an individual vulnerable to depression (24,73). Therefore, self-esteem seems to be an important factor to address in MS patients. Furthermore, based on the findings of the current study, it can be proposed that psychotherapy practices for MS patients should include both cognitive behavioral therapies addressing more "traditional" factors related to mental health such as self-esteem and adaptive COP and third-wave therapy programs that cultivate self-compassion, mindfulness, and acceptance. A combination of traditional cognitive behavioral and third-wave therapies would prove beneficial in the case of MS, which is a chronic and potentially disabling disease where individuals cannot always take a problem-focused or active stance in facing disease-related stressors. Helping MS patients to take a mindful, compassionate, and accepting approach toward themselves by cultivating self-compassion would positively impact perceived overall and physical HRQoL.

The strengths of the present study include addressing two self-related constructs in relation to HRQoL in MS patients. Nevertheless, to our knowledge the current study is the first in comparing the associations of self-esteem and self-compassion to well-being or HRQoL in a sample of MS patients. There are also limitations to the present study including being a single-center study and using self-report measures. Another limitation of the current study was that the majority of the patients had relapsing remitting MS, which prevents generalizing study findings to MS patients with a progressive course.

It may not be possible to eliminate nonresponsive MS SPT and disability, but psychological factors are modifiable through evidence-based psychosocial interventions, which may in turn lead to the promotion of HRQoL in MS patients. Findings of the current study confirmed previous research findings on the role of depression and anxiety in reduced HRQoL in MS patients. In this context, routine psychiatric assessment is strongly recommended in MS populations. Healthcare professionals may help increase perceived HRQoL by addressing problems with self-esteem and self-compassion and refer patients to mental health professionals who can implement the necessary psychosocial interventions aimed at altering reduced self-esteem and self-compassion in MS patients. The findings of the current study provide insights into which psychosocial factors to address in improving different domains of HRQoL in MS patients. Cultivating self-compassion may increase HRQoL in the physical domain, while working with self-esteem and self-worth may improve the psychosocial domain.

Contribution Categories		Author Initials
Category 1	Concept/Design	Z.G., E.I.
	Data acquisition	Z.G., E.I.
	Data analysis/Interpretation	Z.G.
Category 2	Drafting manuscript	Z.G.
	Critical revision of manuscript	Z.G., E.I.
Category 3	Final approval and accountability	Z.G., E.I.
Other	Technical or material support	N/A
	Supervision	N/A

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