Validity and Reliability of the Turkish Version of the Multiple Sclerosis-Related Symptom Checklist

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ABSTRACT

Introduction: Multiple sclerosis (MS) is a disease that causes different symptoms in each attack and has an individual-specific course. Detailed questioning and recording of MS symptoms is important for developing a management plan for individual-specific symptoms. The present study was planned to evaluate the validity and reliability of the Turkish version of "Multiple Sclerosis-Related Symptom Checklist" (MS-RS), which has been developed for patients to personally follow-up the symptoms they experience.

Methods: The study was conducted in the outpatient MS clinic of the İstanbul University İstanbul Faculty of Medicine between January and October 2013 and included a sample group of 148 patients who were aged >18 years, could easily communicate, had a definite diagnosis of MS, and had no other medical problems besides MS. The data were collected using patient information forms, including sociodemographic and MS-RS forms. To assess the linguistic validity, the Likert-type scale with 26 items was first applied to a group of 30 patients. Confirmatory factor analysis was used to test the construct validity. Furthermore, the correlation of the scale with the Expanded Disability Status Scale

(EDSS), Hospital Anxiety and Depression Scale (HADS), Mini-Mental Status Evaluation (MMSE) scale, and Multiple Sclerosis Quality of Life Scale-54 (MSQL-54) was evaluated.

Results: The scale comprised five factors with factor loading values between 0.39 and 0.86. The item-total correlation coefficients revealed values of 0.27–0.88. The Cronbach's alpha reliability coefficient for the whole scale was determined to be 0.89 and for the subscales to be 0.60–0.85. The test–retest analysis revealed no difference between the scale and its subscales in terms of invariance with time ($p>0.05$). Moreover, MS-RS was significantly correlated with EDSS, HADS, MMSE, and MSQL-54.

Conclusion: The Turkish version of MS-RS is a valid and reliable scale that can be used in the Turkish population.

Keywords: Multiple sclerosis, multiple sclerosis-related symptom checklist, validity, reliability

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INTRODUCTION

Multiple sclerosis (MS) is a disorder of the central nervous system (CNS) and is characterized by inflammation, demyelination, remyelination, and axonal degeneration (1). Because MS usually appears in young adults, patients may remain disabled for many years (2,3,4). MS lesions can develop at any point in the brain and spinal cord, and this damage may be observed in various severity, resulting in a wide range of symptoms (1), including motor, sensory, and visual problems; ataxia; spasticity; pain; cognitive collapse; neuropsychiatric findings; chronic fatigue; sleep disorders; and sphincter dysfunction (5,6,7,8,9,10). Accurately describing these symptoms and administering the appropriate treatment are of major importance for improving the patient's quality of life (11,12,13).

The symptoms of MS are closely associated with each other. For example, chronic fatigue is frequently accompanied by pain and depression (9,14). The holistic therapy of these interacting symptoms is important for effectively planning disease management. The complex relationship among the symptoms can be determined only by a detailed query. Furthermore, following up the symptoms by the patient him/herself and sharing the relevant information obtained with the health staff would strengthen the cooperation between the patient and doctor and between the patient and nurse. Thus, providing active participation to the treatment and gaining self-management skills to the patient, may provide increased awareness of symptoms, ability to overcome symptoms, control of comorbid conditions, limitation of the physiological and psychological effects of the disease, prevention of dependency, and increased quality of life (9,15,16,17).

Although there are a significant number of scales for scoring the functional status and quality of life in MS, the number of scales for evaluating the symptoms of MS is limited. Furthermore, many of the latter scales evaluate the symptoms individually and not globally. Such scales fail to examine all symptoms together as a whole and their relationship with each other and prolong the time required for evaluating the patient. Multiple Sclerosis-Related Symptom Checklist (MS-RS), introduced by Gulick in 1989, is a scale that can describe all symptoms in one form, can provide a

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holistic approach, is easy to use, and enables patients to evaluate their own symptoms (18). This study aimed to demonstrate the validity and reliability and to evaluate the psychometric features of the Turkish version of MS-RS in patients with MS.

METHODS

Design, Sampling, and Place

This methodological and descriptive study was performed in patients with MS who were followed up in the outpatient MS clinic of the Istanbul University Istanbul Faculty of Medicine between January and October 2013. The sample size was decided to be 130 ($26 \times 5 = 130$) because the sample number should be at least five times the number of scale items in order to perform factor analysis in scale validity and reliability studies (19). The study included 148 patients with definite MS who were aged >18 years, could easily communicate, and had no attack for at least 1 month.

Ethical Aspect

Prior to the study, written permission was obtained from Elsie Gulick for adapting and using MS-RS in the Turkish population. In addition, ethical approval of the Istanbul Faculty of Medicine, where the study was to be conducted, was obtained (No: 2012/1717-1277). Written consent was also obtained from patients in the sample group who had volunteered to participate in the study.

Data Collection

The forms were filled out by investigators during face-to-face interviews with patients who were eligible. The interviews were conducted in a separate room in the outpatient clinic. The patient information form and MS-RS were applied to the patients. The patient information form, prepared by the investigators in line with the literature, included information regarding the patient's personal and MS characteristics (type of the disorder, duration, medications, comorbidities, functional status, etc.). To assess the time invariance, the same forms were applied to 35 patients in the same sample group 15 days after the first interview (test-retest) (20).

MS-RS, comprising 26 items, includes five subgroups [motor (seven items), brainstem (four items), sensory (four items), neuropsychiatric problems (three items), and elimination (six items) subgroups] and two independent items (fatigue and difficulty sleeping). The answers were of 6-point Likert type (Never=0, almost never=1, occasionally=2, usually=3, almost always=4, and always=5). In the scale, the minimum point that can be obtained is 0 and the maximum is 130, and high points show increased symptom load. To assess the correlation between the sub-dimensions of the scale, other scales that are frequently used in MS studies, namely the Multiple Sclerosis Quality of Life Scale-54 (MSQL-54) (21,22), Expanded Disability Status Scale (EDSS) (23), Mini-Mental Status Evaluation (MMSE) scale (24), and Hospital Anxiety and Depression Scale (HADS) (25,26) were also applied.

Linguistic Validity

The linguistic validity was assessed as described in the literature (27,28). After translating the scale into Turkish by two different translators and presenting it to the expert panel, the translations were turned into a single form. This single translated form was back translated to English and sent to Gulick, who developed the scale, to acquire her opinion. The content validity index of the scale was calculated to be 0.95. The pilot application of the scale was performed in 30 subjects, and thus, the final version of the scale was obtained (20,29).

Statistical Analysis

The obtained data were analyzed and evaluated using the Statistical Package for the Social Sciences 21.0 (SPSS IBM Statics, NY, USA) and LISREL 8.5 package programs. Descriptive statistics (number, percentage, mean, and standard deviation) were used for evaluating the data. The internal consistency of the scale was evaluated with Cronbach's alpha coefficient and item-total correlations. Because the scale data revealed no normal distribution, non-parametric statistical tests were used. The test-retest data were assessed using the Spearman's correlation analysis. The confirmatory factor analysis (CFA), goodness-of-fit statistics, and Mann-Whitney U test were performed. A 95% confidence interval was used, and statistical significance level was set at a *p* value of <0.05.

RESULTS

In the patient group, the mean age was 35.1 ± 10.5 (min-max, 18-62) years; 73.6% (*n*=109) were females and 61.5% (*n*=91) of patients had high school or university education. Most patients were married. Patients had the diagnosis of MS for a mean of 7.5 months, and most of them were being followed up as cases of relapsing-remitting MS. Seventy-five percent of patients were ambulatory. Of all patients, 42.6% (*n*=63) were depressive, and their mean MMSE scores were calculated as 28 ± 1.6 (min-max, 28-30) (Table 1).

In the adaptation of MS-RS to Turkish, CFA was performed to evaluate the construct validity. The goodness-of-fit indices (GFIs), root mean square error of approximation (RMSEA), and standardized root mean square residual (SRMR) that were obtained by the factor analyses were studied. The RMSEA value of the model was determined to be 0.053. Furthermore, its chi-square value was found to be statistically significant ($\chi^2=339.67$; *n*=148, *sd*=240, $\chi^2/df=1.41$, *p*=0.001). In this context, it was accepted that CFA showed data fitting the hypothesized measurement model. The data were found to be within good compliance limits because the value of $\chi^2/sd=339.67/240=1.41$ was calculated to be <2. The factor loads of MS-RS according to the results of CFA are presented in Table 2. To test the reliability of the scale, item-subscale correlations, test-retest correlations, and the Cronbach's alpha values were calculated (Table 3). Of the 26 items in the scale, the coefficients of the item-subscale and subscale-total correlations were determined to be 0.53-0.87 and 0.57-0.81, respectively, with a positive and statistically significant relationship in between (*p*<0.001). In the test-retest analysis of the sample group, including 35 patients, the Spearman's correlation coefficients were found to be 0.68-0.90. The Cronbach's alpha reliability coefficients, which were calculated to evaluate the internal consistency, had values of 0.60-0.89. Mean MS-RS scores of the patients were 42.3 ± 18.7 (min-max, 9-99), with the highest score belonging to the subscale of the fatigue item, motor and elimination (high symptom burden in the mentioned item and subscales).

To support the construct validity, the scale scores were evaluated according to sociodemographic and MS characteristics. With respect to the relationship between the means of MS-RS and age, fatigue (*r*=0.183, *p*=0.026), motor (*r*=0.25, *p*=0.002), and MS-RS total scores (*r*=0.18, *p*=0.026) were significantly related to age. When the symptom scores were studied according to gender, it was determined that females had higher symptom burdens than males in terms of fatigue (*Z*=2.023, *p*=0.043) and subscales of sensory (*Z*=-3.29, *p*=0.001), elimination (*Z*=-2.75, *p*=0.006), and MS-RS total (*Z*=-2.55, *p*=0.011). The patients with under-high school education received higher scores for all symptoms, except for insomnia, than patients with higher education levels; in other words, they had a higher symptom burden; however, only their elimination (*Z*=-2.24, *p*=0.025) and MS-RS total scores (*Z*=-2.29, *p*=0.022) were found to be significant.

Table 1. Sociodemographic and clinical features of patients with MS (n=148)

Characteristics	n	%
Age (X±SD, Range)	35.1±10.5	(18–62)
Gender		
Male	39	26.4
Female	109	73.6
Education		
High school/University	91	61.5
Primary or secondary school	57	38.5
Employment		
Employed	50	33.8
Housewife	65	43.9
Student	9	6.1
Retired	10	6.8
Disability pensioner	3	2.0
Unemployed	11	7.4
Marital status		
Single/divorced/widowed	51	34.5
Married	97	65.5
Time since diagnosis (months) (X±SD, range)	7.5±5.9	(0.5–36)
Type of MS		
Relapsing remitting	114	77.0
Secondary progressive	28	18.9
Primary progressive	6	4.1
Use of disease modifying therapy		
Yes	108	73.0
No	40	27.0
Comorbidity		
Yes	35	23.6
No	113	76.4
EDSS		
Ambulatory (EDSS 0–3.5)	111	75.0
Ambulatory with assistance (EDSS 4–6)	31	20.9
Dependent (EDSS 6.5–9)	6	4.1
HADS-Anxiety (X±SD, range)	7.32±4.49	(0–18)
Anxious	37	25.0
Not anxious	111	75.0
HADS-Depression (X±SD, range)	6.61±3.92	(0–18)
Depressive	63	42.6
Not depressive	85	57.4
MMSE (X±SD, range)	28±1.6	24–30
EDSS: Expanded Disability Status Scale; HADS-A: Hospital Anxiety and Depression Scale- Anxiety; HADS-D: Hospital Anxiety and Depression Scale-depression; MMSE: Mini-Mental State Examination; X±SD: Mean±standard deviation		

Higher means of MS-RS motor points were observed for non-working group of patients than for working group of patients ($p=0.022$).

With the increase in time passed since the diagnosis, there were also increases in motor ($r=0.24$, $p=0.002$), elimination ($r=0.027$, $p=0.001$), and

Table 2. Factor loadings: multiple sclerosis-related symptom checklist (MS-RS) (n=148)

	M	B	S	NP	E
1. Fatigue*					
2. Arm weakness	0.57				
3. Leg weakness	0.73				
4. Spasms	0.68				
5. Tremors	0.50				
6. Knee locking or collapsing	0.66				
7. Balance problems	0.72				
8. Falling	0.65				
9. Double vision		0.69			
10. Blurred vision		0.72			
11. Difficulty swallowing		0.39			
12. Forgetfulness		0.39			
13. Difficulty sleeping*					
14. Loneliness				0.78	
15. Depression				0.86	
16. Anxiety				0.64	
17. Pain			0.55		
18. Burning sensation			0.61		
19. Numbness			0.63		
20. Pins and needle sensation			0.49		
21. Increased urinating frequency: DAY					0.48
22. Increased urinating frequency: NIGHT					0.61
23. Trouble making toilet: DAY					0.48
24. Trouble making toilet: NIGHT					0.52
25. Difficulty in starting to urinate					0.41
26. Urinary infection or burning					0.43
M: Motor; B: Brainstem; S: Sensory; NP: Neuropsychiatric; E: Elimination					
*The factor loading has not been calculated because those items are independent and do not belong to any subgroup.					

total ($r=0.21$, $p=0.011$) scores. When the relationship between the patients' mean scores and MS type was studied, patients with progressive MS had higher scores for all subscales and the total scale than patients with relapsing MS ($p<0.001$). Patients with comorbidity had higher fatigue scores than patients without comorbidity ($z=-2.013$, $p=0.044$). There was no significant difference in MS-RS scores among patients in terms of DMT use ($p>0.05$).

When the relationship between MS-RS and functional status was studied, there were significant correlations between MS-RS and EDSS and between MMSE and HADS. Moreover, there were significant and moderately strong correlations with MSQ-54 scores (Table 4).

DISCUSSION

MS-RS is a scale developed by Gulick et al. (18) for patients with MS to follow-up the symptoms they experience. The scale comprises 26 items and five subscales covering motor, brainstem, sensory, neuropsychiatric, and elimination symptoms (18). In our study, after providing linguistic validity, psychometric evaluations were made. Furthermore, CFA was performed to study the construct validity and to evaluate whether the

items were adequately represented in the subscales and whether the subscales were adequate for explaining the specific construct of the scale or not. Items with a factor load of 0.39–0.86 were grouped under five factors and as in the original scale, had a five-factor construct, including motor, brainstem, sensory, neuropsychiatric, and elimination symptoms. According to GFI (chi-square, RMSEA, SRMR, AIC, CAIC, and ECVI), the model was within the limits of acceptable concordance. In view of these results, the scale was found to have adequate construct validity.

For the reliability analysis of the scale, from the methods cited in the literature, the item-subscale correlation, Cronbach's alpha test (internal consistency), and test–retest (time invariance) were used. A positive statistically significant relationship is expected among the item-subscale correlations and between the contribution of every item of the scale to its subscale and contribution of each subscale to the total scale. Although there are different values of the lower limit of this coefficient in the literature, 0.20 is generally accepted as the lowest level, and items with correlation coefficient of 0.30–0.40 and >0.40 demonstrate “good” and “very good” discrimination, respectively, and thus, therefore reliable (29). In view of these findings, the item-subscale and subscale-total correlations in the Turkish version of MS-RS were found to have a range of 0.53–0.87 and 0.57–0.81, respectively, and no item required exclusion from the scale.

One of the recommended methods for evaluating the reliability in Likert-type scales is determination of the Cronbach's alpha reliability coefficient

Table 3. Turkish version of MS-RS: Descriptive statistics, Cronbach' alpha values, and test–retest correlations (n=148)

Subscale	Mean±SD	Cronbach's alpha	Test–Retest	
			r	p
Motor	1.8±0.9	0.83	0.90	0.001
Brainstem	1.3±0.7	0.60	0.71	0.001
Sensory	1.6±0.9	0.65	0.64	0.001
Neuropsychiatric	1.4±0.9	0.85	0.89	0.001
Elimination	1.8±0.8	0.75	0.68	0.001
MS-RS total	42.3±18.7	0.89	0.85	0.001
Fatigue*	3.0±1.0	-	0.71	0.001
Difficulty sleeping*	1.5±1.5	-	0.74	0.001

*The Cronbach's alpha value has not been calculated because those items are independent and do not belong to any subgroup

(20). Gulick (18,30,31) reported the Cronbach's alpha reliability coefficient for the subscales to be 0.66–0.86 and for the whole scale to be 0.87–0.89. The results of our study are compatible with those of the original studies, and the high (0.89) total Cronbach's alpha coefficient of the scale shows the presence of high internal consistency (0.60–0.85) in all subscales.

One of the methods used for evaluating the reliability of scales is the test–retest, which tests the time invariance. In our Turkish scale, the test–retest demonstrated correlation coefficients to be 0.68–0.90, similar to those in the original scale (18,30). These results show that our scale has the capacity to provide similar values in repeated measurements and is consistent. These results prove that the Turkish version of MS-RS is a reliable scale to be applied to patients with MS.

In addition, to support the construct validity of MS-RS, the scale scores were evaluated according to the sociodemographic and clinical features. The mean age of patients with MS participating in the study was 35.1±10.5 (min–max, 18–62) years, with most patients being in the young–middle-age group. The relationship between the mean MS-RS scores and age, fatigue, motor, and total scores were significant but weakly related to age. The patient group comprised 73.6% (n=109) females and 26.4% (n=39) males. MS is more prevalent in females than in males, with a female:male ratio of 2-3:1 (32). In terms of the relationship between symptom scores and gender, the symptom burdens of fatigue, sensory and elimination subscores, and total scores were higher in women than in men. Women are more aware of their symptoms (33) than men because of biological and cultural reasons (34). Furthermore, fatigue is more prevalent in women than in men (35), whereas motor and spinal symptoms rather than sensory symptoms are more prevalent in men (34). Because health behavior is an important factor in the follow-up of symptoms, the educational level of our patient group was also studied. The group with an under high school education level received higher scores for all symptoms, except for insomnia, than the group with higher education level; in other words, the symptom burden of the group with under high school education was higher. However, only the elimination and total scores of this group were found to be significant. In studies based on patient report, low educational level of the patient is associated with negative outcomes (36). Our results that are compatible with those in the literature support the construct validity of our Turkish version of MS-RS.

The predominating MS subtype in our sample was relapsing–remitting MS (77%, n=114). This percentage is similar to those stated in the literature, although there are different distributions of subtypes according to the characteristics of the sample (37,38). When mean scores of patients according

Table 4. Correlations of MS-RS scores with EDSS, MMSE, HADS, and MSQ-54 (n=148)

Scales	Motor		Brainstem		Sensory		Neuropsychiatric		Elimination		MS-RS Total	
	r	p	r	p	r	p	r	p	r	p	r	p
MS-RS												
EDSS	0.74	0.001	–0.16	0.337	0.00	0.991	0.15	0.371	0.54	0.001	0.56	0.001
MMSE	–0.23	0.167	–0.06	0.722	–0.01	0.925	–0.21	0.214	–0.40	0.017	–0.34	0.043
HADS-A	0.14	0.394	0.31	0.064	0.17	0.314	0.50	0.002	0.23	0.173	0.23	0.173
HADS-D	0.29	0.082	0.29	0.089	0.30	0.080	0.48	0.003	0.43	0.008	0.43	0.008
MSQ54-PHC	–0.61	0.001	–0.37	0.001	–0.56	0.001	–0.46	0.001	–0.47	0.001	–0.71	0.001
MSQ54-MHC	–0.47	0.001	–0.42	0.001	–0.45	0.001	–0.54	0.001	–0.41	0.001	–0.62	0.001

HADS-A: Hospital Anxiety and Depression Scale-anxiety; HADS-D: Hospital Anxiety and Depression Scale-depression; MSQ-54PHC: Multiple Sclerosis Quality of Life Scale-54-physical health composite; MSQ-54-MHC: Multiple Sclerosis Quality of Life Scale-54-mental health composite

to the MS type were studied, as expected (39), patients with progressive MS received higher scores in all subscales and total scale than patients with relapsing–remitting MS. Moreover, parallel to the time since the diagnosis, motor, elimination, and total scores of MS-RS increased but with a weak correlation in between. This situation may be because of the predominance of patients with relapsing–remitting MS in our sample group.

Because the study was conducted in the outpatient clinic, most patients were ambulatory (EDSS, 0–3.5; 75%). According to HADS, 25% of patients had anxiety and 42.6% were depressive. Mean MMSE scores of the sample group were 28 ± 1.6 (min–max, 24–30), and the group showed good mental functions. To further support the construct validity of the scale, the relationship between scales for evaluating the functional status of MS-RS (EDSS, MMSE, and HADS) and quality of life scale (MSQL-54) was assessed. A significant and strong correlation was found between EDSS and MS-RS motor subscale and MS-RS total. Gulick et al. (40) reported that EDSS scores given by the doctor are significantly compatible with those symptoms (of all MS-RS subscales) expressed by the patient. Furthermore, a significant negative relationship was found between MMSE and MS-RS total. As expected, HADS anxiety and depression scores were found to be correlated with the neuropsychiatric subscale. However, MS-RS total scores showed a correlation with HADS depression but not with the HADS anxiety scores. In summary, a significant relationship was determined between the functional status scales and corresponding subscales in MS-RS and also MS-RS total scores (except HADS anxiety).

Patients with MS frequently experience symptoms, and the severity of these symptoms seriously affects the patients' quality of life (41,42). Likewise, in our study, we found that a negative relationship at moderate–strong level of significance was present between MS-RS and the physical and mental health composite scores of MSQL-54 and that increase in symptom load decreased the patients' quality of life.

Some limitations of this study should be considered when results are interpreted such as the study was conducted in an outpatient clinic with most patients being ambulatory and symptoms not being longitudinally followed up. Furthermore, some symptoms, such as sexual dysfunction, cognitive symptoms, and dysmetria, could not be sufficiently evaluated because of the structure of the original questionnaire (i.e., limitation of the original questionnaire).

In conclusion, the Turkish version of MS-RS was determined to be a valid and reliable scale that could be used for evaluating symptoms in patients with MS. Patients with MS, which is a chronic neurological disease, experience various symptoms throughout their lives. The follow-up of these symptoms by the patients would increase the awareness of symptoms, decrease comorbidity, provide the chance for early intervention against symptoms, and increase the quality of life.

Practical evaluation of the symptoms experienced by patients with MS using MS-RS can be useful in clinical practice. We suggest the use of this form in prospective patient studies in the future and also suggest testing the sensitivity of the form for determining the changes in the clinical manifestations of patients with MS.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of İstanbul University İstanbul School of Medicine (No: 2012/1717-1277).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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REFERENCES

1. Compston A, Coles A. Multiple sclerosis [seminar]. *Lancet* 2008; 9648:1502-1517. [\[CrossRef\]](#)
2. Goodin DS. The epidemiology of multiple sclerosis: insights to disease pathogenesis. *Handb Clin Neurol* 2014; 122:231-266. [\[CrossRef\]](#)
3. Melcon MO, Correale J, Melcon CM. Is it time for a new global classification of multiple sclerosis? *J Neurol Sci* 2014; 344:171-181. [\[CrossRef\]](#)
4. Heydarpour P, Khoshkish S, Abtahi S, Moradi-Lakeh M, Sahraian MA. Multiple Sclerosis Epidemiology in Middle East and North Africa: A Systematic Review and Meta-Analysis. *Neuroepidemiology* 2015; 44:232-244. [\[CrossRef\]](#)
5. Feinstein A, DeLuca J, Baune BT, Filippi M, Lassman H. Cognitive and neuropsychiatric disease manifestations in MS. *Mult Scler Relat Disord* 2013; 2:4-12. [\[CrossRef\]](#)
6. Hickman SJ, Raoof N, McLean RJ, Gottlob I. Vision and multiple sclerosis. *Mult Scler Relat Disord* 2014; 3:3-16. [\[CrossRef\]](#)
7. Patti F, Vila C. Symptoms, prevalence and impact of multiple sclerosis in younger patients: a multinational survey. *Neuroepidemiology* 2014; 42:211-218. [\[CrossRef\]](#)
8. Shahrbanian S, Duquette P, Kuspinar A, Mayo NE. Contribution of symptom clusters to multiple sclerosis consequences. *Qual Life Res* 2015; 24:617-629. [\[CrossRef\]](#)
9. Newland PK, Lorenz R, Budhathoki C, Jensen MP. The presence of symptoms with comorbid conditions in individuals with multiple sclerosis (MS) *Clin Nurs Res* 2015. pii: 1054773815592817.
10. Tabrizi FM, Radfar M. Fatigue, sleep quality, and disability in relation to quality of life in multiple sclerosis. *Int J MS Care* 2015; 17:268-274. [\[CrossRef\]](#)
11. Henze T, Rieckmann P, Toyka KV. Symptomatic treatment of multiple sclerosis. Multiple Sclerosis Therapy Consensus Group (MSTCG) of the German Multiple Sclerosis Society. *Eur Neurol* 2006; 56:78-105. [\[CrossRef\]](#)
12. de Sa JC, Airas L, Bartholome E, Grigoriadis N, Mattle H, Oreja-Guevara C, O'Riordan J, Sellebjerg F, Stankoff B, Vass K, Walczak A, Wiendl H, Kieseier BC. Symptomatic therapy in multiple sclerosis: a review for a multimodal approach in clinical practice. *Ther Adv Neurol Disord* 2011; 4:139-168. [\[CrossRef\]](#)
13. Newland PK, Flick LH, Thomas FP, Shannon WD. Identifying symptom co-occurrence in persons with multiple sclerosis. *Clin Nurs Res* 2014; 23:529-543. [\[CrossRef\]](#)
14. Gupta S, Goren A, Phillips AL, Dangond F, Stewart M. Self-reported severity among patients with multiple sclerosis in the U.S. and its association with health outcomes. *Mult Scler and Relat Disord* 2014; 3:78-88. [\[CrossRef\]](#)
15. Motl RW, Snook EM, McAuley E, Gliottoni RC. Symptoms, self-efficacy, and physical activity among individuals with multiple sclerosis. *Res Nurs Health* 2006; 29:597-606. [\[CrossRef\]](#)
16. Gulick EE, Namey M, Halper J. Monitoring my multiple sclerosis: a patient-administered health-assessment scale. *Int J MS Care* 2011; 13:137-145. [\[CrossRef\]](#)
17. Kalina JT. Clutter Management for Individuals with Multiple Sclerosis. *Int J MS Care* 2014; 16:117-122. [\[CrossRef\]](#)
18. Gulick EE. Model confirmation of the MS-Related Symptom Checklist. *Nurs Res* 1989; 38:147-185. [\[CrossRef\]](#)
19. DeVellis RF. Scale development: Theory and applications. 2nd ed. Sage Publications, California; 2003.
20. Polit DF, Beck CT. Essentials of nursing research: Appraising evidence for nursing practice 7th ed. Philadelphia, PA: Lippincott, Williams & Wilkins; 2010.
21. Idiman E, Uzunel F, Ozakbas S, Yozbatiran N, Oguz M, Callioglu B, Gokce N, Bahar Z. Cross-cultural adaptation and validation of multiple sclerosis quality of life questionnaire (MSQOL-54) in a Turkish multiple sclerosis sample. *J Neurol Sci* 2006; 15:77-80 [\[CrossRef\]](#)

22. Tülek Z. Düzenli sağlık kontrolüne alınan multipl sklerozlu hastalarda yaşam kalitesinin belirlenmesi, İstanbul Üniversitesi Sağlık Bilimleri Enstitüsü Hemşirelik Doktora Tezi, 2006, İstanbul.
23. Kurtzke JF. Rating neurological impairment in multiple sclerosis: An Expanded Disability Status Scale (EDSS). *Neurology* 1983; 33:1444-1452. [\[CrossRef\]](#)
24. Folstein MF, Folstein SE, McHugh PR. Mini-Mental State: A practical method for grading the cognitive state of patients for clinician. *J Psychiatr Res* 1975; 12:189-198. [\[CrossRef\]](#)
25. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983; 67:361-70. [\[CrossRef\]](#)
26. Aydemir Ö, Güvenir T, Küey L, Kültür S. Hastane anksiyete ve depresyon ölçeği Türkçe formunun geçerlilik ve güvenilirliği. *Türk Psikiyatri Dergisi* 1997; 8:280-287.
27. Beaton DE, Bombardier C, Guillemin F, Ferraz MB. Guidelines for the process of cross-cultural adaptation of self-report measures. *Spine (Phila Pa)* 1976; 2002; 25:3186-3191. [\[CrossRef\]](#)
28. Gjersing L, Caplehorn JR, Clausen T. Crosscultural adaptation of research instruments: Language, setting, time and statistical considerations. *BMC Med Res Methodol* 2010; 10:13. [\[CrossRef\]](#)
29. Burns N, Grove SK. The practice of nursing research appraisal, synthesis, and generation of evidence. 6th ed. St.Louis, MO: Saunders; 2009.
30. Gulick EE. Symptom and activities of daily living trajectory in multiple sclerosis: a 10-year study. *Nurs Res* 1998; 47:137-146. [\[CrossRef\]](#)
31. Gulick EE, Yam ML, Touw MM. Work performance by persons with multiple sclerosis: Conditions that impede or enable the performance of work. *Int J Nurs Stud* 1989; 26:301-311. [\[CrossRef\]](#)
32. Niedziela N, Adamczyk-Sowa M, Pierzchala K. Epidemiology and clinical record of multiple sclerosis in selected countries: a systematic review. *Int J Neurosci* 2013; 124:322-330. [\[CrossRef\]](#)
33. Vlahiotis A, Sedjo R, Cox ER, Burroughs TE, Rauchway A, Lich R. Gender differences in self-reported symptom awareness and perceived ability to manage therapy with disease-modifying medication among commercially insured multiple sclerosis patients. *J Manag Care Pharm* 2010; 16:206-216. [\[CrossRef\]](#)
34. Bove R, McHenry A, Hellwig K, Houtchens M, Razaz N, Smyth P, Tremlett H, Sadovnick AD, Rintell D. Multiple sclerosis in men: management considerations. *J Neurol* 2016 Jan 2. doi: 10.1007/s00415-015-8005-z. [\[CrossRef\]](#)
35. Simpson S Jr, Tan H, Otahal P, Taylor B, Ponsonby AL, Lucas RM, Blizzard L, Valery PC, Lechner-Scott J, Shaw C, Williams D, Ausimmune/AusLong Investigators Group, van der Mei I. Anxiety, depression and fatigue at 5-year review following CNS demyelination. *Acta Neurol Scand*. 2016 Jan 12. doi: 10.1111/ane.12554. [\[CrossRef\]](#)
36. Fernández O, Baumstarck-Barrau K, Simeoni MC, Auquier P; MusiQoL study group. Patient characteristics and determinants of quality of life in an international population with multiple sclerosis: assessment using the MusiQoL and SF-36 questionnaires. *Mult Scler* 2011; 17:1238-1249. [\[CrossRef\]](#)
37. Leray E, Morrissey S, Yaouanq J, Coustans M, Le Page E. Long-term survival of patients with multiple sclerosis in West France. *Mult Scler* 2007; 13:865-874. [\[CrossRef\]](#)
38. Birnbaum G. Multiple sclerosis: Clinician's guide to diagnosis and treatment. 2nd Ed. New York: Oxford University Press; 2013.
39. Yamout B, Issa Z, Herlopian A, El Bejjani M, Khalifa A, Ghadie AS, Habib RH. Predictors of quality of life among multiple sclerosis patients: a comprehensive analysis. *Eur J Neurol* 2013; 20:756-764. [\[CrossRef\]](#)
40. Gulick EE, Cook SD, Troiano R. Comparison of patient and staff assessment of MS patients' health status. *Acta Neurol Scand* 1993; 88:87-93. [\[CrossRef\]](#)
41. Garg H, Bush S, Gappmaier E. Associations Between Fatigue and Disability, Functional Mobility, Depression, and Quality of Life in People with Multiple Sclerosis. *Int J MS Care* 2015 doi: 10.7224/1537-2073.2105-013
42. Newland PK, Lorenz R, Budhathoki C, Jensen MP. The presence of symptoms with comorbid conditions in individuals with multiple sclerosis (MS) *Clin Nurs Res* 2015 Jun 29. pii: 1054773815592817.