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The importance of depression and anxiety for perceived health status in younger and older patients with multiple sclerosis⁵

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⁵Submitted

Abstract

Higher levels of depression and anxiety have a negative impact on the disease process in multiple sclerosis (MS) patients. The aim of this study was to explore whether there are the discrepancies in the association of depression and anxiety with perceived physical and mental health status, and whether these associations differ between younger and older MS patients.

The study sample consisted of 223 MS patients who were divided into two age groups: those under 45 years ($n=149$) and those age 45 years or older ($n=74$). A model consisting of age, gender, marital status, EDSS, depression and anxiety explained 46.6% of the variance in perceived physical health status and 60.8% of the variance in perceived mental health status in the total sample. Depression was significantly associated with perceived physical health status in both younger ($p\leq 0.05$) and older ($p\leq 0.001$) MS patients. Depression was also significantly related to perceived mental health status in both age groups ($p\leq 0.001$). Anxiety, however, was significantly associated with perceived physical and mental health status in the younger age group ($p\leq 0.05$; $p\leq 0.001$), but not in the older one.

The role of depression is always present in MS patients with regard to their perceived health status, mainly to perceived physical health status in the older group and to perceived mental health status in the younger one. The role of anxiety is more important in younger MS patients than among older patients with regard to their perceived health status.

Introduction

Multiple sclerosis (MS) is a chronic and unpredictable neurological disease that varies from a mild course with minimal disabilities to a rapidly progressing or fluctuating course resulting in disabilities. No reliable indicators exist to assure patients that their status will remain stable or that disabilities will not arise or progress. Furthermore, patients are confronted with symptoms that frequently and unpredictably vary with respect to their form and intensity, sometimes even daily (1). Symptoms include sensory and motor loss, fatigue, difficulties with balance, ataxia, muscular weakness, pain, cognitive impairments and mood disorders. MS is the most common cause of neurological disability in young adults (2).

Disablement status has been found to be reflected in the perceived health status of the chronically ill (3). With the progression of a disability, it is primarily physical functioning that shows a decrease in perceived health status in patients with MS. As previous studies have reported,

a higher level of functional disability has negative consequences on perceived health status in MS patients (4, 5). The clinical impact of MS on perceived health status can be quantified and assessed in clinical trials and in everyday practice in order to optimize individual patient care (6, 7). Many neurological scales associated with functional disability are used to measure perceived health status in MS patients (8). When MS patients are compared to controls, they score significantly lower than the general population in disability measures (4, 8-10).

Depressed mood and anxiety are among the most commonly described symptoms of MS. MS patients may develop depression as an understandable reaction to their experiencing a chronic disease and having to live with its consequences (11, 12). Anxiety, along with a high level of distress, occurs mostly in the first years of diagnosis (13). High levels of depression and anxiety were found to be negatively associated with physical and mental health status in chronically ill patients (14-16). The negative impact of depressive symptoms on perceived health status in MS patients has also been demonstrated (7). In some studies, depression seems to be associated with worse scores in self-reported questionnaires, independent of the clinical course or disability status of the MS patients (5, 17). Statistically, as many as 60% of patients with MS experience major depression, and the suicide rate among those with MS is 7.5 times higher than that of the age-matched general population (12).

Perceived health status, measured using the SF-36 questionnaire, has been evaluated as an appropriate instrument for measuring general health. It assesses four physical health domains and four mental health domains, and MS patients show lower scores for both the physical health summary scale and for the mental health summary scale in the SF-36 than the general population (18).

Within the context of this study, age is an important factor that might play a role in perceiving health, assessing functional disability and evaluating psychological well-being. Older age seems to be related to lower scores in perceived health status (7), though the association of depression and anxiety with age in MS patients is still unclear. Some studies have reported the prevalence of a greater risk of depression in younger MS patients. When younger and older MS patients are compared, the younger patients appeared to be more depressed than the older ones. Other studies have revealed a high rate of anxiety prevalence, with higher levels of anxiety at disease onset (19-21).

This study was conducted because younger and older MS patients might differ in evaluating their psychological well-being and health status. The aim of this study was to explore whether there are discrepancies in the association of depression and anxiety with perceived physical and mental health status, and whether these associations differ in younger (<45 years) and older (≥45 years) MS patients. We expected depression

and anxiety in MS patients to be significantly associated with perceived physical and mental health status, even when controlled for the relevant sociodemographic and clinical variables. We also expected this relationship to differ between younger (<45 years) and older (≥45 years) MS patients.

Methods

Patients and procedures

MS patients from neurology outpatient clinics and members of MS clubs were included in the study. Outpatient clinics were addressed and MS patients were recruited from those who were eligible to participate. The sample consisted of 223 MS patients from the eastern part of Slovakia. Data were collected from December 2003 to January 2006. Firstly, questionnaires, invitation letters and written informed-consent forms were sent to participants' homes by post. After two weeks, a trained interviewer spoke with the MS patients personally in a neurological outpatient clinic. A neurologist then carried out a neurological examination immediately after each interview. These examinations were performed by the same neurologist for all patients. One phone call to again arrange an interview was made to those patients who did not come the first time.

This cross-sectional study consisted of several self-reported questionnaires, a semi-structured interview and physical examinations on a voluntary and anonymous basis. Socio-demographic data, including age, gender, marital status, living situation, education level, employment status, family life and disease history, were ascertained from the interview. Depression, anxiety and perceived health status were obtained from the questionnaires. Clinical data, including functional disability, disease duration and clinical course, were assessed by the neurologist. Questionnaires were translated from English into Slovak, and then the Slovak version was translated back into English and compared with the original version. Measures were tested in a pilot study with 10 MS patients. Exclusion criteria were as follows: non-Slovak-speaking patients, cognitive impairment determined by a Mini-Mental State Examination (MMSE) score of <24 (22), a history of psychiatric or medical conditions affecting the outcomes of the study and pregnancy.

Each patient provided a signed informed-consent form before participating in the study. The local Ethics Committee of the University Hospital approved the study on December 17th, 2002.

Measures

The Kurtzke Expanded Disability Status Scale (EDSS) is based on the neurological testing of functional systems: pyramidal, cerebellar,

brainstem, sensory, bowel and bladder, visual, mental and "other". Disability caused by MS is graded on a continuum from 0 (normal neurological examination) to 10 (death caused by MS) (23). This measure, with its widespread use, remains the most frequently used scoring system in MS in neurological practice. It belongs to the category of physician-oriented measures, as information is based on an objective neurological examination, which in this study was performed by the same neurologist on all respondents (24).

Psychological well-being was assessed with the Hospital Anxiety and Depression Scale (HADS) (25). The scale consists of 14 items, 7 of which are related to depression and 7 to anxiety. Patients respond on a 4-point scale (0=absent and 3=definitely present/severe), and the score ranges from 0 to 21, with a higher score implying that depression or anxiety is present to a larger extent. The score identifies non-cases (a score of 7 or smaller), doubtful cases (a score from 8-10) and definitive cases (a score of 11 or higher) (25). Cronbach's alpha for depression was 0.79 and for anxiety 0.81 in this study.

The Short Form-36 Health Survey (SF-36) was originally used as a generic indicator of health status in population surveys and evaluative studies of health policy (26). The SF-36 includes the measurement of the eight dimensions of health: 1. physical functioning (ten items), 2. role limitation due to physical health (four items), 3. bodily pain (two items), 4. social functioning (two items), 5. general health (five items), 6. mental health, covering psychological distress and well-being (five items), 7. role limitations due to emotional problems (three items), and 8. vitality, energy or fatigue (four items). In addition, one question covers changes in health status over the past year (one item). We used the physical health summary scale (perceived physical health status) and the mental health summary scale (perceived mental health status). All item scores were coded and transformed into a scale of 0 (poor health) to 100 (optimal health) (26, 27). Cronbach's alpha for the SF-36 total score in the present sample was 0.93; for the physical health summary scale it was 0.90, and for the mental health summary scale 0.89.

To improve functioning or to simply stop the decrease in functional ability, different therapeutic strategies are used in MS patients (24). Disease-modifying drugs (DMD) are a commonly used approach, and in Slovakia DMD were, until recently, accessible predominantly for MS patients aged 45 year or younger suffering mainly from relapsing-remitting or secondary-progressive clinical courses (28). This is the reason why we chose 45 years old as our cut-off point. All patients in our sample of <45 years used DMD's.

It is important to control for variables that can frequently influence study outcomes. Many studies in recent years have found associations between sociodemographic variables, functional disability and health

status in patients with MS. Patients who were younger, were male, were engaged and who had low functional disability reported better perceived health status (4, 29-31).

Statistical analysis

Firstly, the sociodemographic variables (age, gender, marital status), clinical variables (EDSS, disease duration, clinical course), psychological well-being (depression, anxiety) and perceived health status (physical and mental health summary scales) were described. Pearson's correlations were used for testing the associations between the examined variables. The cut-off age of 45 years in this sample was based particularly on the prescription of DMD to MS patients. The Mann-Whitney U test was conducted to determine the differences in scores between younger (<45 years) and older (≥ 45 years) age subgroups of MS in sociodemographic variables, clinical variables, psychological well-being and perceived health status. Finally, hierarchical multiple regression analyses were performed using the "enter method" in order to identify how much of the variance of dependent variables (physical and mental health summary scales) may be explained by age, gender, marital status, functional disability, depression and anxiety. Hierarchical multiple regression analyses were performed for the total sample, as well as for samples of younger (<45 years) and older (≥ 45 years) MS patients (final results presented in Table 3).

Data were analysed using the Statistical Package for the Social Sciences, v.16.0 (SPSS).

Results

Basic description of the sample

In general, the respondents (n=223) were of middle age (mean age 38.9 ± 10.8 years), consisted of more women than men (67.3% females), were married or cohabiting (64.6%), had secondary education (54.6%) and were not employed (59.4%). The main study variables with means and standard deviations for the whole sample and for the two age groups of MS patients (<45 years and ≥ 45 years) are described in Table 1. The younger group significantly differed statistically from the older age group in more often living alone/single, shorter disease duration, lower EDSS and a more frequent a relapsing-remitting course. Furthermore, the younger group had less depression, better perceived physical health status and better perceived mental health status (Table 1).

The 223 questionnaires represented a response rate of 52.0%. Non-respondents (45.1 ± 10.5 years) were significantly older than the participants (38.9 ± 10.8 years) ($p < 0.05$), though there were no statistically significant

differences between the non-respondents and the participants regarding gender.

Table 1 Description of the study sample and two age groups of MS patients: <45 years of age and ≥45 years of age

Variables ^a	Total sample (n=223)	<45 age group (n=149)	≥45 age group (n=74)
	n (%) or mean±SD	n (%) or mean±SD	n (%) or mean±SD
Age	38.9±10.8	32.7±6.9***	51.2±4.9***
Gender			
Women	67.3%	69.8%	62.2%
Marital status			
Living alone/single	35.4%	44.3%***	17.6%***
Married/cohabiting	64.6%	55.7%	82.4%
Disease duration	5.8±5.2	4.9±4.4***	7.6±6.3***
EDSS	3.1±1.5	2.7±1.5***	3.7±1.3***
Clinical course			
Relapsing-remitting	70.9%	83.7%***	45.2%***
Secondary-progressive	13.2%	4.8%	30.1%
Primary-progressive	15.9%	11.6%	24.7%
HADS			
Depression	4.5±3.6	4.2±3.5*	5.3±3.8*
Anxiety	7.1±4.2	6.8±4.2	7.6±4.2
SF-36			
Physical Summary ^b	48.1±20.4	53.0±20.1***	37.7±16.7***
Mental Summary ^b	56.7±16.0	58.6±16.6**	53.0±14.0**

Note:

*p<.05; **p<.01; ***p<.001

^aThe significance test on the differences between subgroups of younger and older MS patients was on the Mann-Whitney U test on continuous variables; ^bhigher scores indicate “better functioning”; EDSS=Expanded Disability Status Scale; HADS=Hospital Anxiety and Depression Scale; SF-36=Short Form-36 Health Survey

Correlations between study variables

Table 2 demonstrates the significant cross-sectional relationships between the variables used in this study. Marital status (married/cohabiting) is significantly correlated with better physical and mental health status in MS patients. Age, disease duration, EDSS, clinical course, depression and anxiety are strongly associated negatively with the physical summary scale. Age, EDSS, clinical course, depression and anxiety are strongly associated negatively with the mental summary scale.

Table 2 Pearson's correlations between the studied variables

	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.
1. Age	-									
2. Gender	ns	-								
3. Marital status	-.42***	ns	-							
4. Disease duration	.34***	ns	ns	-						
5. EDSS	.33***	ns	ns	.40***	-					
6. Clinical course	.36***	ns	ns	.31***	.64***	-				
7. Depression	.23***	ns	ns	ns	.18**	.18**	-			
8. Anxiety	.13*	ns	-.14*	ns	ns	ns	.55***	-		
9. Physical Summary	-.42***	ns	.17*	-.23***	-.54***	-.37**	-.44***	-.37***	-	
10. Mental Summary	-.25***	ns	.16*	ns	-.27***	-.26***	-.72***	-.63***	.64***	-

Note:

*p<.05; **p<.01; ***p<.001

Gender 1=men, 2=women; Marital status 1=married/cohabiting, 2=living alone/single; ns=no significance; EDSS=Expanded Disability Status Scale

Perceived physical health status

Table 3 shows that 46.6% of the variance of perceived physical health status in the whole group of MS patients was explained by a model consisting of age, gender, marital status, EDSS, depression and anxiety. EDSS appeared to be the strongest variable associated with perceived physical health status in the total sample ($\beta = -0.44$, $p \leq 0.001$) (Table 3).

The variance in perceived physical health status explained in both age groups was very similar: 39.8% in the younger group and 38.8% in the older group of MS patients. Discrepancies were found with regard to the importance of EDSS and anxiety in the younger group (<45 years) and of depression in the older (≥ 45 years). EDSS was the strongest variable associated with perceived physical health status in the younger age group (<45 years) ($\beta = -0.47$, $p \leq 0.001$), while depression was the stronger variable related to perceived physical health status in the older age group (≥ 45 years) ($\beta = -0.39$, $p \leq 0.001$). Anxiety was significantly associated statistically, albeit weakly, with perceived physical health status in the younger age group (<45 years) ($\beta = -0.16$, $p \leq 0.05$), but not in the older one (≥ 45 year) ($\beta = -0.17$, not significant) (Table 3).

Perceived mental health status

In the total sample of MS patients, 60.8% of the variance in perceived mental health status was explained by a model consisting of age, gender, marital status, EDSS, depression and anxiety. Anxiety appeared to be the strongest variable associated with perceived mental health status in the sample of all MS patients ($\beta = -0.32$, $p \leq 0.001$) (Table 3).

In younger MS patients (<45 years), 65.0% of the variance in perceived mental health status was explained by a model consisting of age, gender, marital status, EDSS, depression and anxiety, while the same model explained 47.2% of the variance in perceived mental health status in older MS patients (≥ 45 years). Depression appeared to be the strongest variable associated with perceived mental health status in both age groups ($\beta = -0.49$, $p \leq 0.001$; $\beta = -0.47$, $p \leq 0.001$ respectively), with higher explained variance in younger MS patients (<45 years). Anxiety was significantly associated with perceived mental health status in the younger age group (<45 years) ($\beta = -0.37$, $p \leq 0.001$), but not in the older one (≥ 45 years) ($\beta = -0.20$, not significant) (Table 3).

Table 3 Final results from the hierarchical multiple regression analyses: sociodemographic variables, EDSS, depression and anxiety on perceived physical and mental health status in the total sample, and in younger (<45) and older (≥45) MS patients

Total sample			Age groups			
			<45		≥45	
Physical health						
status SF-36	<i>Adjusted R²</i>	<i>β</i>	<i>Adjusted R²</i>	<i>β</i>	<i>Adjusted R²</i>	<i>β</i>
Age	16.7%	-.19***	6.0%	-.20**	0.3%	.07
Gender	0.0%	-.03	0.0%	-.07	0.0%	-.03
Marital status	0.0%	.05	0.0%	-.02	3.6%	.17
EDSS	19.0%	-.44***	24.2%	-.47***	13.7%	-.38***
Depression	3.6%	-.24***	2.3%	-.20*	10.3%	-.39***
Anxiety	7.3%	-.15*	7.3%	-.16*	10.9%	-.17
Σ Adjusted R ²	46.6%		39.8%		38.8%	
Mental health						
status SF-36	<i>Adjusted R²</i>	<i>β</i>	<i>Adjusted R²</i>	<i>β</i>	<i>Adjusted R²</i>	<i>β</i>
Age	6.4%	-.05	3.9%	-.09	3.7%	-.02
Gender	0.6%	-.03	0.0%	.00	4.0%	-.15
Marital status	0.0%	.04	0.0%	.02	3.3%	.11
EDSS	4.3%	-.16***	3.0%	-.13*	4.1%	-.21*
Depression	16.4%	-.50***	42.6%	-.49***	16.0%	-.47***
Anxiety	33.1%	-.32***	15.5%	-.37***	16.1%	-.20
Σ Adjusted R ²	60.8%		65.0%		47.2%	

Note:

*p<.05; **p<.01; ***p<.001

EDSS=Expanded Disability Status Scale

Discussion

The aim of this study was to explore whether there are discrepancies in the association of depression and anxiety with perceived physical and mental health status, and whether these associations differ in younger (<45 years) and older (≥45 years) MS patients. Less depression and less anxiety were associated with better perceived physical and mental health status in the total sample. MS patients without depressed mood and anxiety reported significantly better perceived physical health status than those with depression and anxiety when controlled for age, gender, marital status and EDSS. Similarly, less depressed and less anxious MS patients assessed perceived mental health status as significantly better when controlled for age, gender, marital status and EDSS. Our results regarding perceived health status as a dependent variable are in line with previous findings (4, 29-32).

The described model, which includes depression and anxiety, explained the lower variance in the difference in perceived physical health status (46.6%) compared with perceived mental health status (60.8%) in the total sample. While EDSS was the strongest variable explaining perceived physical health status, depression and anxiety appeared to be the main variables explaining most of the variance in perceived mental health status. Janssens et al (33) showed that the EDSS explained much, but not all, of the variance in the physical scale of SF-36, suggesting that other additive determinants were involved. An important difference between the instruments is that the EDSS aims to assess objective clinical status, whereas the SF-36 is a subjective evaluation of physical functioning as perceived by the patient (33).

A low score in depression was associated with better perceived physical health status, while a low score in anxiety appeared to be significantly related to better perceived physical health status in younger MS patients, but without significant association in the older age group. These findings provide some support for the results of more recent studies, which have suggested that more symptoms of depression and anxiety were significantly associated with worse perceived physical and mental health status presented by the SF-36 health summary scales and with poorer quality of life in MS patients (17, 30, 33).

A low score in depression was associated with better perceived mental health status in both age groups, with a higher explained prevalence of depression in younger MS patients. This finding is comparable to the results of some studies in which younger adults reported higher levels of depressive symptoms than older adults with MS (34, 35). Depression can result from individual reactions to MS-related disability, its symptoms and from the disease process itself (14). A low score in anxiety was significantly related to perceived mental health status only in the younger age group. The relationship between anxiety and mental health in younger patients was studied in a survey of recently diagnosed MS patients whose mean age was 37.5 ± 9.5 years. More symptoms of anxiety were associated with poorer physical and mental health in this sample (33).

The existence of unique features in the national health care system in the past may lead to a certain limitation of this study. In particular, the inaccessibility to DMD for MS patients over age 45 may affect the differences when evaluating symptoms of depression and anxiety in comparison to patients from other countries in this age cohort. Also, the MS patients participating in this study were significantly younger than the non-respondents. We may assume, then, that the non-respondents were largely members of the older MS group and with the longest disease duration, and that they were possibly the most affected group, a fact that might have prevented them from participating in the study. The results therefore cannot be extended and generalized to the whole MS population,

as a larger proportion of the oldest group of MS patients compared with the younger group was missing from this study. In addition, the outcomes of this cross-sectional study cannot be causally determined. The current survey can only imply causal pathways, not prove them. Longitudinal data are needed to further unravel the complex interplay between psychological well-being and changes in perceived health status during and after DMD treatment in Slovak MS patients.

Summary and implications

In a summary of the study findings, depression showed its importance for evaluating the perceived health status in all MS patients. Therefore depression should be carefully screened for in all MS patients, regardless of sociodemographic factors and clinical variables. Among the most used therapeutic agents, β -interferon (a DMD) is being widely adopted in relapsing-remitting MS (28). In our sample, patients below the age of 45 years had been treated with β -interferon 1a or 1b. It was recognized that among the potential drug-related side effects, there was a possible association with an increased risk of depression, a fact which has been debated (36). If depression occurs in MS patients, it is hard to conclude that the reason is as a side effect of DMD or no accessibility to using DMD or any other reason. As DMD moderately reduces the number and severity of attacks, the number of new lesions on magnetic resonance imaging and progression (37), it may be that older MS patients who had no access to DMD feel the impossibility of coping with the disease as their younger colleague patients are able to, which might lead to a depressed mood. Symptoms of anxiety could be connected with perceived physical and mental health in younger MS patients, despite their use of DMD. This could be explained by distress caused by possibly worsening functional disability at a younger age, which was significantly associated with impairment, and its consequences on education, employment and leisure-time physical activity, and with the restricted social network. With regard to older MS patients, they could have built up during treatment with DMD useful coping strategies during the years of disease and thus are able to cope with anxiety when older. Determining the factors that could have an impact on an MS patient's perceived health status might help with decision-making during the planning of interventions, treatments and services aimed at enhancing health status or quality of life (30).

The clinical importance of this study is that MS patients possessing higher levels of depression and anxiety have a greater likelihood of perceiving health status more negatively than those who are less depressed and less anxious. According to the result of the study, health care providers would expect that MS patients suffering from depression and anxiety may

evaluate their health as worsened. It may be therefore important to assess the symptoms of depression and anxiety of MS patients and to treat them in order to contribute to a patient's perceived health status.

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