HEALTH-RELATED QUALITY OF LIFE IN MULTIPLE SCLEROSIS PATIENTS WITH ACCOMPANYING DISEASES

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ABSTRACT

INTRODUCTION: Multiple sclerosis (MS) is a progressive demyelinating neurologic disease characterized by a different extent of comorbidity. Everyday life is challenging for these patients because of physical and psychological impairments.

AIM: The purpose of this study was to comparatively analyze the relationships between several health-related quality of life aspects of MS patients' in cases of accompanying diseases.

MATERIALS AND METHODS: Health-related quality of life of 80 MS patients, 56 females and 24 males, at a mean age of 49 years, was examined by means of Short Form-36 questionnaire. Forty patients presented with at least one accompanying chronic disease.

RESULTS: These patients presented with similar Expanded Disability Status Scale scores of 2.0 or 2.5. Most questionnaire scores differed between MS patients with and without comorbidity. Usually, comorbidity additionally worsened patients' quality of life. There were statistically significant differences between the patients with MS alone and those with MS and comorbidity concerning depression ($t=5.877$; $p<0.0001$); the troubles with concentration/thinking ($t=4.822$; $p<0.0001$); troubles with memory ($t=4.020$; $p<0.0001$); feeling of fatigue ($t=4.148$; $p<0.0001$), and feeling of happiness ($t=-3.399$; $p<0.001$).

CONCLUSION: The hot topic of the health-related quality of life of the patients with MS and comorbidities necessitates further interdisciplinary research. Correct treatment and follow-up of MS patients and particularly of those with common accompanying cardiovascular and other neurological diseases could contribute to long-lasting preservation of acceptable individual quality of life. *Scr Sci Med.* 2017;49(4):35-41

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INTRODUCTION

Multiple Sclerosis (MS) is a chronic autoimmune disease that affects the central nervous system and has a high impact on the health-related quality of life of patients, their families and society (1). In MS, everyday life is challenging for these patients because of physical (fatigue, pain, visual damage, weakness, mobility disorders, and bladder and bowel dysfunction) and psychological impairments (worsened cognition, depression, reduced social interaction, and increased reliance on others). The associ-

ation of comorbidity with health-related quality of life and disability progression results in comorbidity being an area of increasing importance in MS research (1). MS is one of the most common causes of neurological disability in young adults and its prevalence is increasing throughout Europe (2). Usually, rates of mortality and comorbidities are higher in MS patients compared to non-MS ones. With prevalence rates ranging from 2 per 100 000 inhabitants in Japan to greater than 100 per 100 000 inhabitants in Northern Europe and North America, the burden of MS is similarly unevenly influenced by longevity and comorbid disorders (2).

In an observational, cross-sectional, descriptive study, MS prevalence rate among the general population, including non-Spanish individuals, in Health District III in the Region of Murcia, Spain, was 71.9 per 100 000 inhabitants but among the native Spanish population it was 82.0 per 100 000 inhabitants (3).

A cross-sectional, observational study of the burden and costs of MS was endorsed by the European Multiple Sclerosis Platform and carried out in collaboration with national MS societies and local clinical and economic experts in 16 countries (Austria, Belgium, Czech Republic, Denmark, France, Germany, Hungary, Italy, Netherlands, Poland, Portugal, Russia, Spain, Sweden, Switzerland and the United Kingdom) (4). Costs for a total of 16 808 MS patients at a mean age of 51.5 years were reported from a societal perspective adjusted for purchasing power parity (PPP) in 2015. Work capacity declined from 82% to 8% and utility diminished from normal population values to less than zero with advancing disease. The mean costs were 22 800€ PPP in mild, 37 100€ PPP in moderate, and 57 500€ PPP in severe disease. Of them, healthcare accounted for 68%, 47% and 26%, respectively. Fatigue and cognitive difficulties were reported by 95% and 71% of the study participants, respectively, and exerted a significant independent effect on utility.

After an international workshop devoted to the most relevant comorbidities in MS, a series of recommendations for observational studies were suggested (5). One should establish age- and gender-specific incidence and prevalence estimates for five comorbidities (depression, anxiety, hypertension, hyperlipidemia, and diabetes mellitus); evaluate the effect of seven comorbidities (depression, anxiety, hypertension, diabetes mellitus, hyperlipidemia, chronic lung disease, and autoimmune diseases) on disability, quality of life, brain atrophy and other imaging parameters, healthcare utilization, employment, and mortality, including age, sex, race/ethnicity, socioeconomic status, and disease duration as potential confounders; harmonize study designs across jurisdictions as well as conduct such studies worldwide.

AIM

The purpose of this study is to comparatively analyze the relationships between several health-related quality of life aspects of MS patients' in case of accompanying diseases.

MATERIALS AND METHODS

Our study covered a total of 80 MS patients, 56 females and 24 males, at a mean age of 49 years. Of them, 40 patients presented with MS alone and 40 did with MS and with one to seven accompanying diseases affecting different organs and systems. The gender distribution of both groups is summarized in Table 1 while patients' distribution according to gender and age is illustrated on Fig. 1.

Health-related quality of life was assessed by means of Short Form-36 (SF-36) questionnaire and Expanded Disability Status Scale (EDSS).

Attention was paid to the influence of MS and its comorbidity during the preceding four weeks on the following symptoms and parameters of health-related quality of life: self-assessment of health status, presence of happiness, physical pain, fatigue, depres-

Table 1. Gender distribution of MS patients without and with comorbidity

Diagnosis	males		females		total	
	n	%	n	%	n	%
MS only	9	11.25	31	38.75	40	50.00
MS with comorbidity	15	18.75	25	31.25	40	50.00
total	24	30.00	56	70.00	80	100.00

Fig. 1. MS patients' distribution according to age and gender

Table 2. MS influence on the frequency of some parameters of patients' health-related quality of life

Parameter	males (n=24)		females (n=56)		total (n=80)	
	n	%	n	%	n	%
health status self-assessed as good	12	50.00	31	55.36	54	53.75
being always happy	3	12.50	6	10.71	9	11.25
no effect on physical pain at all	8	33.33	27	48.21	35	43.75
no feeling of fatigue at all	1	4.17	1	1.79	2	2.50
no depression at all	17	70.83	39	69.64	56	70.00
no anxiety at all	6	25.00	10	17.86	16	20.00
no troubles with concentration/thinking	8	33.33	21	37.50	29	36.25
no troubles with fixation of attention	5	20.83	20	35.71	25	31.25
no troubles with memory	15	62.50	30	53.57	45	56.25

sion, and anxiety, as well as on troubles with concentration/thinking, fixation of attention, and memory.

Statistical data processing was performed by means of correlation analysis (Pearson's coefficient) and *t*-test. Statistical significance was considered at *p*-value less than 0.05.

RESULTS

MS patients' distribution according to age and EDSS scores is demonstrated on Fig. 2. Two EDSS scores were mainly established - of 2.0 and 2.5.

Fig. 2. MS patients' distribution according to age and EDSS scores

The effects of MS on the frequency of some parameters of patient's health-related quality of life were summarized in Table 2. The effects of MS alone and of MS with comorbidity on the frequency of these patient's health-related quality of life parameters were compared in Table 3.

The comparison of five parameters of health-related quality of life between the patients with MS alone and those with MS and comorbidity by means of *t*-test revealed the following statistically significant differences: concerning depression - $t=5.877$;

$p<0.0001$; concerning troubles with concentration/thinking - $t=4.822$; $p<0.0001$; concerning troubles with memory - $t=4.020$; $p<0.0001$; concerning the feeling of fatigue - $t=4.148$; $p<0.0001$, and concerning the feeling of happiness - $t=-3.399$; $p<0.001$.

The significant correlations between health-related quality of life scores and some parameters in MS patients are listed in Table 4.

There were certain other significant negative correlations between some parameters such as patient's gender, on the one hand, and anxiety ($R=-0.379$; $p<0.05$) and troubles with memory ($R=-0.343$; $r<0.05$), on the other hand; EDSS scores, on the one hand, and depression ($R=-0.320$; $p<0.05$), troubles with fixation of attention ($R=-0.330$; $p<0.05$) and troubles with memory ($R=-0.346$; $p<0.05$), on the other hand, as well as between health status self-assessment, on the one hand, and feeling of fatigue ($R=-0.566$; $p<0.01$), anxiety ($R=-0.438$; $p<0.01$), and troubles with memory ($R=-0.473$; $p<0.01$), on

Table 3. Influence of MS without and with comorbidity on the frequency of some parameters of patients' health-related quality of life

Parameter	MS (n=40)				MS and comorbidity (n=40)			
	males (n=9)		females (n=31)		males (n=15)		females (n=25)	
	n	%	n	%	n	%	n	%
health status self-assessed as good	5	55.55	19	61.29	7	46.67	12	48.00
being always happy	2	22.22	6	19.35	1	6.67	0	0
no effect on physical pain at all	5	55.55	19	61.29	3	20.00	8	32.00
no feeling of fatigue at all	0	0	1	3.23	1	6.67	2	2.50
no depression at all	8	88.89	31	100.00	9	60.00	8	32.00
no anxiety at all	5	55.55	10	32.26	1	6.67	0	0
no troubles with concentration/ thinking	4	44.44	17	54.84	4	26.67	4	16.00
no troubles with fixation of attention	1	11.11	18	58.06	4	26.67	2	8.00
no troubles with memory	8	88.89	25	80.65	7	46.67	5	20.00

Table 4. Significant correlations between health-related quality of life scores and some parameters in MS patients ($p<0.01$)

Parameter	Pearson's coefficient - R
health status self-assessment	-0.597
influence upon social activities	-0.750
EDSS scores	-0.503
feeling of happiness	-0.565
feeling of fatigue	0.413
depression	0.667
anxiety	0.503
troubles with memory	0.526
troubles with concentration/ thinking	0.479
troubles with fixation of attention	0.494

the other hand. There were some significant positive correlations between the health status self-assessment, on the one hand, and influence upon social activities ($R=0.473$; $p<0.01$), feeling of happiness ($R=0.428$; $p<0.01$) and depression ($R=0.372$; $p<0.05$), on the other hand, as well as between the influence upon social activities, on the one hand, and feeling of happiness ($R=0.539$; $p<0.01$), on the one hand. There were certain significant negative correlations between the influence upon social activities, on the one hand, and depression ($R=-0.625$; $p<0.01$), troubles with memory ($R=-0.435$; $p<0.01$), troubles with concentration/thinking ($R=-0.372$; $p<0.05$), anxiety

($R=-0.368$; $p<0.05$) and troubles with fixation of attention ($R=-0.315$; $p<0.05$), on the one hand as well as between depression, on the one hand, and feeling of happiness ($R=-0.591$; $p<0.01$), on the one hand. In addition, depression correlated significantly positively with troubles with memory ($R=0.543$; $p<0.01$), anxiety ($R=0.520$; $p<0.01$), feeling of fatigue ($R=0.472$; $p<0.01$), troubles with concentration/thinking ($R=0.454$; $p<0.01$) and troubles with fixation of attention ($R=0.421$; $p<0.01$), on the one hand.

DISCUSSION

It is noteworthy that most questionnaire scores differ between MS patients with and without comorbidity. Usually, comorbidity additionally worsens patients' quality of life. Our results are similar to those reported in the most recent foreign literature available.

The most common comorbidities in MS patients, such as depression, anxiety, arterial hypertension, hyperlipidemia, and chronic lung disease are common even at the time of MS diagnosis. Some 19% of individuals have sought care for depression by this time, while 11.1% of subjects have sought care for anxiety (6,7) indicating that comorbidities are a concern throughout the disease course.

International differences in MS health outcomes and associated factors were assessed in a cross-sectional survey of a total of 2401 participants from 37 countries in Australasia, Europe, and North America (8). There were some differences between these re-

gions in disability, physical and mental health quality of life, fatigue, and depression. However, most differences disappeared after adjusting for sociodemographic, disease, and lifestyle factors in multivariable regression models. Adjusted odds for disability were higher in Europe (OR: 2.17, between 1.28 and 3.67 at 95% CI) and North America (OR: 1.79, between 1.28 and 2.51 at 95% CI) than in Australasia.

The results from a cross-sectional study exploring the associations between pain, demographic factors and disease in an international sample of MS patients recruited online demonstrated substantial pain of moderate/severe intensity and interfering at least moderately with work/household or enjoyment of life in the past four weeks in 682 out of 2362 patients (in 28.9% of the cases) (9). Substantial pain was associated with fatigue (OR: 6.7, between 4.9 and 9.3 at 95% CI), depression (OR: 4.0, between 3.2 and 5.19 at 5% CI), anxiety (OR: 2.4, between 1.9 and 2.9 at 95% CI), and lower mental health quality of life (mean difference: -14.7, between -16.6 and -12.8 at 95% CI).

Fatigue is one of the most debilitating symptoms in MS considerably interfering with patients' daily functioning. The psychometric properties of the Finnish version of the Fatigue Severity Scale (FSS) were evaluated by means of self-administered questionnaires among 553 MS patients at a mean age of 53.8 ± 11.4 years and a mean patient-defined disease severity, EDSS of 4.0 ± 2.5 (10). The mean FSS score was 4.5 ± 1.7 . The score was ≥ 4.0 in 65% of the cases. The FSS showed moderate/high correlations with the perceived burden of the disease, quality of life and disease severity, whereas, age or gender did not exert any significant effect on the FSS score.

The Multiple Sclerosis Impact Scale-29 (MSIS-29) is a patient-reported outcome sensitive to short-term change in MS. Its questions cover both physical and psychological quality of life. MSIS-29 questionnaires were completed by 2126 MS patients during a 10-year retrospective cohort study (11). Both higher baseline MSIS-29 physical and psychological scores were associated with reduced survival time (HR: 5.7, between 3.1 and 10.5 at 95% CI; $p < 0.001$ and HR: 2.8, between 1.8 and 4.4 at 95% CI; $p < 0.001$, respectively). The MSIS-29 physical scores were associated with

survival time independent of age, sex, and patient-reported EDSS score in a Cox regression analysis.

The psychometric properties of the Finnish version of the MSIS-29 were evaluated among 553 MS patients as these self-administered questionnaires captured information on demographics, disease characteristics and severity (12). A perceived quality of life (EuroQol 5D-3L instrument) and FSS were made use of, too. The data quality for MSIS-29 was excellent, with 99.5% computable scores for the MSIS-29 physical scale and 99.3% for the MSIS-29 psychological one. The physical subscale showed highest correlations with measures of physical functioning, such as disease severity and the mobility domain of the quality of life while the psychological subscale demonstrated highest correlations with self-reported fatigue and the anxiety/depression domains of the quality of life. MSIS-29 physical scores related strongly to disease severity whereas the MSIS-29 psychological scores increased in mild disease but declined in more severe disease forms.

The direct and indirect influences of physical comorbidity, symptoms of depression and anxiety, fatigue, and disability on health-related quality of life in 949 adult MS patients were evaluated in a cross-sectional path analysis (1). Disability status most strongly affected health-related quality of life ($\beta = -0.52$) closely followed by depressive symptoms ($\beta = -0.50$). There were small direct associations of physical comorbidity and anxiety with health-related quality of life ($\beta = -0.08$ and $\beta = -0.10$, respectively). They were stronger when indirect effects through other variables (depression or fatigue) were considered, too, such as physical comorbidity ($\beta = -0.20$) and anxiety ($\beta = -0.34$).

Out of 2399 respondents with MS within an international sample in Australia, 67.2% reported at least one comorbidity, with back pain (36.2%), depression (31.7%), anxiety (29.1%) and arthritis (13.7%) being most prevalent and most limiting in daily activities (13). Increasing number of comorbidities was related to worse quality of life, increased odds of disability and prior relapse.

The application of an online survey completed by 42 members of the Consortium of Multiple Sclerosis Centers concerning the tools available to assess the presence of depression, anxiety, and sleep disorder

ders in MS demonstrated that nearly 93% of them asked about depression and 81% did about anxiety (14). However, the use of validated tools to do so was infrequent which highlighted a gap in the implementation of evidence available.

A retrospective cohort study of 222 MS patients at a mean age of 45.5 ± 12.5 years was carried out using electronic medical records from 19 primary care centres in Catalonia and Asturias, Spain (15). The mean EDSS score was 3.2 ± 2.0 . Depression (in 32.4%), dyslipidemia (in 31.1%), arterial hypertension (in 23.0%) and obesity (in 22.5% of the cases) were the most common comorbidities. The patients with an EDSS ≥ 4.0 showed a significantly higher number of comorbidities (OR=2.2, between 1.7 and 3.0 at 95% CI; $p < 0.001$).

A systematic review for evaluation of the criterion validity of anxiety screening tools for measuring the anxiety in MS showed that strikingly, only four studies met their inclusion criteria, and only one tool, the Hospital Anxiety and Depression Scale, presented with adequate sensitivity and specificity rates (16).

Anxiety effects on coping, emotional processing, emotional balance and depression in 189 MS patients from three hospitals in France were analyzed in a cross-sectional study by a battery of questionnaires encompassing the following domains: anxiety and depression; emotional processing; positive and negative emotions; alexithymia, and coping (17). Anxiety was a strong predictor of depression, in both a direct and indirect way, and explained 48% of the variance of depression. It had an indirect impact on depression via 'unregulated emotion' subscale of the Emotional Processing Scale and via negative emotions. Gender and functional status (measured by the EDSS) played a modest role. Non-depressed MS patients reported high levels of negative emotions and low levels of positive ones.

The analysis of the relationship between the social support network and health-related quality of life in 150 consecutive MS patients at a mean age of 41.7 ± 10.4 years (range, 18-70 years) and a mean EDSS score of 2.5 ± 2.4 (range, 0-9) in Portugal revealed a statistically significant correlation between the structure of this social support network and the health-related quality of life (18).

CONCLUSION

Our recent results and abundant literature data convincingly indicate that the hot topic of the health-related quality of life of the patients with MS and comorbidities necessitates further interdisciplinary research. Correct treatment and follow-up of such patients and particularly of those with common accompanying cardiovascular and other neurological diseases could contribute to long-lasting preservation of acceptable individual quality of life.

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