Journal of Neuroimmunology 293 (2016) 54–58

Contents lists available at ScienceDirect

Journal of Neuroimmunology

journal homepage: www.elsevier.com/locate/jneuroim

# Factors that impact health-related quality of life in neuromyelitis optica spectrum disorder: anxiety, disability, fatigue and depression

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ARTICLE INFO

*Article history:*
Received 4 January 2016
Received in revised form 10 February 2016
Accepted 15 February 2016

*Keywords:*
Neuromyelitis optica
Quality of life
Anxiety
Depression
Fatigue

ABSTRACT

*Aims:* Neuromyelitis optica spectrum disorder (NMOSD) is associated with reduced health-related quality of life (HRQOL). This study aimed to investigate factors that impact HRQOL in NMOSD.
*Methods:* A series of questionnaires were completed by 73 patients to assess the relationships between HRQOL and fatigue, depression, anxiety and sleep disorder. We also evaluated the contributions of clinical characteristics to HRQOL. Correlation and regression analysis were conducted to identify factors that negatively impact HRQOL in NMOSD.
*Results:* Pearson's correlation analysis showed that reduced HRQOL was strongly correlated with anxiety ($r = -0.77$, $P = 0.000$), fatigue ($r = -0.75$, $P = 0.000$) and depression ($r = -0.73$, $P = 0.000$); and moderately correlated with disability ($r = -0.53$, $P = 0.000$) and sleep disorder ($r = -0.59$, $P = 0.000$). Stepwise regression analysis further revealed that anxiety was the best predictor of both the global and physical composite scores of HRQOL, followed by disability, fatigue and depression (global composite, $r^2 = 0.76$, $P = 0.000$; physical composite, $r^2 = 0.71$, $P = 0.000$). Depression, fatigue and anxiety were the main predictors of the mental health composite score of HRQOL ($r^2 = 0.69$, $P = 0.000$). Other factors did not have an effect on HRQOL.
*Conclusions:* This study revealed factors that impact HRQOL in NMOSD and provided the first demonstration that anxiety, disability, fatigue and depression are independent predictors of poor HRQOL in NMOSD.


## 1. Introduction

Neuromyelitis optica (NMO) is a severe central nervous system demyelinating disorder that usually results in more disabling symptoms and a worse prognosis than multiple sclerosis (MS) (Wingerchuk et al., 2006, 2007). A highly specific serum aquaporin-4 IgG antibody (AQP4 IgG) is considered closely related to NMO and helps define neuromyelitis optica spectrum disorder (NMOSD), which includes both NMO patients and AQP4 IgG-positive patients who display a limited NMO phenotype (Wingerchuk et al., 2007). In recent years, numerous studies have indicated that patients with MS experience worse HRQOL than the general population and have revealed important predictors of reduced quality of life, including depression, disability, fatigue and sleep disorder (Amato et al., 2001; Auty et al., 1998; Clavelou et al., 2009; Lobentanz et al., 2004; Tanriverdi et al., 2010). However, compared to the extensive study of HRQOL in MS, sufficient investigations of HRQOL in NMOSD are lacking (Chanson et al., 2011). Therefore, this study aimed to assess the relationships between HRQOL and clinical characteristics, sleep disorder, fatigue, anxiety and depression and to explore factors that contribute to the impairment of HRQOL in NMOSD.

## 2. Methods

### 2.1. Patients

We consecutively recruited 73 patients with NMOSD who visited the Neurology Department of West China Hospital, Sichuan University during September 2014 and August 2015. The inclusion criteria were as follows: (1) Satisfied the diagnostic criteria for NMOSD according to the 2007 revised criteria for NMOSD (Wingerchuk et al., 2007); and (2) 18–70 years old. The exclusion criteria were as follows: (1) Coexistence of other chronic disorders that could significantly affect HRQOL; (2) not able to complete all questionnaires with the assistance of doctors; and (3) severe disability that prevented completion of the relevant assessments. Clinical characteristics (including age, gender, disease duration, annual relapse rate (ARR), and treatment with immunosuppressants) were recorded for each patient. The degree of disability was evaluated by two neurologists and was based on the Expanded Disability Status Scale (EDSS) score (Kurtzke, 1983).The presence of AQP4-IgG in serum was tested with a transfected cell-based assay (Waters et al., 2012). This study was approved by the Medical Ethics

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http://dx.doi.org/10.1016/j.jneuroim.2016.02.011
0165-5728/

Committee of the West China Hospital, Sichuan University and was performed in accordance with the ethical standards of the Declaration of Helsinki. All patients provided informed consent prior to their inclusion in the study.

### 2.2. Questionnaires

#### 2.2.1. HRQOL

The Multiple Sclerosis Quality of Life-54 items (MSQOL-54) was used to evaluate HRQOL. This questionnaire has been extensively used in MS and has high test–retest reliability and internal consistency (Vickrey et al., 1995).The Chinese version of the MSQOL-54 has been translated and validated (Kang et al., 2009). The MSQOL-54 contains 52 items in addition to 2 single-item measurements and is grouped into 14 scales, including changes in health; physical functioning; role limitation-physical; role limitation-emotional; pain; emotional well-being; energy; health perception; social functioning; health distress; cognitive functioning; sexual functioning; sexual satisfaction and overall quality of life. The mean score can range from 0 to 100, with higher scores indicating better HRQOL. Composite scores for the two underlying dimensions of physical and mental health were a weighted sum of 52 of the 54 items of the MSQOL-54 (Vickrey et al., 1995).

#### 2.2.2. Fatigue

The Fatigue Impact Scale (FIS) was used to assess chronic fatigue in the NMOSD patients (Fisk et al., 1994). The FIS is a self-report instrument that evaluates patients' perceptions of the functional limitations caused by fatigue over the past month (Fisk et al., 1994). It consists of 40 questions that are distributed among 3 subscales—cognitive, physical and psychosocial functioning. The global scores range from 0 to 160, and higher scores indicate more severe fatigue. The FIS has also shown good test–retest reliability and has been validated for both MS and the general population (Fisk et al., 1994; Mathiowetz, 2003).

#### 2.2.3. Depression and anxiety

The 21-item Hamilton Depression Rating Scale (HAMD) was used to evaluate depressive symptoms (Hamilton, 1967). The score can range from 0 to 64 points, and the cut-off point is 16; a score of 0–16 indicates the absence of depression, 17–33 indicates moderate depression, and above 33 indicates serious depression (Mottram et al., 2000). Anxiety symptoms were assessed with the 14-item Hamilton Anxiety Rating Scale (HAMA); scores on this scale range from 0 to 56 points (Hamilton, 1959). A score of less than 7 indicates no anxiety, 7–14 indicates mild anxiety, 15–21 indicates moderate anxiety, 22–29 indicates obvious anxiety, and above 29 indicates severe anxiety (Maier et al., 1988).

#### 2.2.4. Sleep disorder

Sleep disorder was assessed using the Pittsburgh Sleep Quality Index (PSQI), which is a self-reported scale used to assess sleep disorder over the past month (Buysse et al., 1989). It consists of seven composite scores: sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbance, use of sleep-related medication and daytime dysfunction. The global PSQI score ranges from 0 to 21, with higher scores indicating worse sleep quality. The cut-off point is 5; a global score greater than 5 indicates the potential presence of a sleep disorder (Buysse et al., 1989).

The HAMD and HAMA questionnaires were administered by a psychologist, while the others were completed by the patients themselves in the presence of two neurologists, who assisted the patients with reading and understanding the items.

## 3. Statistical analysis

The IBM SPSS Statistics version 21.0 software was used to perform the relevant analyses. The demographic and clinical characteristics are shown as means or counts. The Mann–Whitney U test was used to compare composite scores of HRQOL among subgroups of gender (women and men), AQP4 IgG status (positive and negative) and treatment with immunosuppressants (with and without). The effect of the location of the lesions, which was determined with MRI, on HRQOL was determined using one-way ANOVA. Pearson's correlation was used to explore the relationships between the dependent measure (HRQOL) and the independent variables, including age, disease duration, ARR, disability (EDSS), sleep disorder, fatigue, anxiety and depression. A stepwise linear regression model was used to further assess the predictors of poor HRQOL. The correlations between HRQOL and the variables were represented by r values, which ranged between $-1$ and $+1$. The greater the absolute value of r, the stronger the correlation. In the regression analysis, the $r^2$ values indicate the percentage of the variability in HRQOL explained by the predictors. A value of $P < 0.05$ was considered significant.

## 4. Results

### 4.1. Main clinical characteristics and composite scores

We finally enrolled 73 patients with NMOSD who met the inclusion criteria. Of these, 51 patients (70%) were outpatients, and 34 patients (47%) were being treated with immunosuppressants (including mycophenolate mofetil and azathioprine). The main demographic and clinical characteristics and composite scores of these patients are presented in Table 1. The subjects completed all of the questionnaires except for items related to the sexual function (89%) and satisfaction with sexual function (90%) dimensions of the MSQOL-54.

### 4.2. No difference in HRQOL among the gender-, AQP4 IgG status- and immunosuppressant therapy-based subgroups

We did not observe a significant difference in HRQOL among the gender-, AQP4 IgG status- and immunosuppressant therapy-based subgroups using the Mann–Whitney U-test ($P > 0.05$). However, the patients who were AQP4 IgG-positive had better cognitive function subscale scores than those who were negative ($68.67 \pm 16.32$ vs. $56.94 \pm 19.49$, $P = 0.023$). Furthermore, compared to the patients

**Table 1**
Clinic characteristics and composite scores of the subjects.

| Clinical characteristics and composite scores | Value | Range |
|---|---|---|
| Gender (F/M), N (%) | 67(91%)/6(9%) | |
| Age, mean ± SD, years | 40.05 ± 11.18 | (18–70) |
| Disease duration, mean ± SD, years | 4.28 ± 4.27 | (0.1–18) |
| ARR,mean ± SD | 1.12 ± 0.69 | (0.22–4) |
| EDSS,mean ± SD | 2.79 ± 1.78 | (0–8) |
| AQP4 IgG positive/negative, N (%) | 49(73%)/18(27%) | |
| With/without immunosuppressants, N (%) | 34(47%)/39(53%) | |
| MRI lesions | | |
| Brain lesions(B) | 7(10%) | |
| Cervical lesions(C) | 15(21%) | |
| Thoracic lesions(T) | 14(19%) | |
| Cervical plus thoracic lesions | 20(27%) | |
| Brain plus spinal cord lesions | 17(23%) | |
| MSQOL, mean ± SD (0–100) | 48.3 ± 17.19 | (13–82) |
| FIS, mean ± SD (0–84) | 65.63 ± 40.98 | (5–149) |
| PSQI, mean ± SD (0–21) | 7.74 ± 4.4 | (1–21) |
| Poor/good sleeper, N (%) | 50(68%)/23(32%) | |
| HAMD, mean ± SD (0–64) | 12.07 ± 7.71 | (0–37) |
| Depression/no depression, N (%) | 18(25%)/55(75%) | |
| HAMA, mean ± SD (0–56) | 11.85 ± 7.57 | (0–35) |
| Anxiety/no anxiety, N (%) | 50(68%)/23(32%) | |

F, Female; M, Male; SD, standard deviation; ARR, Annual Relapse Rate; EDSS, Expanded Disability Status Scale; MSQOL, Multiple Sclerosis Quality of Life-54 Items; FIS, Fatigue Impact Scale; PSQI, Pittsburgh Sleep Quality Index; HAMD, Hamilton Depression Rating Scale; HAMA, Hamilton Anxiety Rating Scale.