

Quality of life and multiple sclerosis

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Introduction. Health-related quality of life (HRQoL) is a complex concept in which evaluation of physical, emotional and social domains of health are included. Since chronic diseases has raised, the importance of HRQoL evaluation has increased, overall in patients with multiple sclerosis (MS) whose HRQoL has shown to be worse than in other chronic diseases.

Aim. To review the information available about the HRQoL in patients with MS to provide an overview of the current situation.

Development. Previously performed clinical trials identified the main factors related to the HRQoL: physical factors (sensitive/motor deficits, fatigue, pain, sexual/bladder dysfunction), psychological factors (depression, anxiety, cognitive disturbances, coping strategies) and social factors (family/social relationships, work activity). The inclusion of HRQoL questionnaires in the patients' follow-up is a relevant issue to optimize its treatment, making easier treatment decision and improving adherence, as well as to reduce the inconveniences derived from medication such as adverse events.

Conclusions. HRQoL evaluation is really complex in patients with MS, being difficult to identify the main domains that impact on HRQoL. However, its regular evaluation provides essential information to improve the symptomatic treatment, increase the adherence to treatment and modify the immunomodulating treatment.

Key words. Health-related quality of life. Multiple sclerosis. Physical functioning. Psychological functioning. Quality of life. Quality of life questionnaire. Social functioning. Treatment.

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Introduction

'Quality of life' is a concept defined by the World Health Organization as the individual's perception regarding their situation in life within their cultural context and values, and in relation to their objectives, expectations, standards, and concerns [1]. It is a complex concept that encompasses physical, mental, and social factors. The context of this concept derives from the individual's perception within three main frames of reference: historical-temporal, cultural, and social [2].

The application of this concept to the field of health leads to the term 'health-related quality of life' (HRQOL), which encompasses the physical, emotional, and social health domains [3]. These domains can be measured objectively by functionally evaluating health status and subjectively by analysing individuals' perceptions, beliefs, and expectations [3].

HRQOL is considered a meaningful measurement of the impact of chronic diseases, of comparison between different diseases, and a way to assess the impact of therapeutic intervention [4]. It has been shown that the chronic disease that generates the worst scores in various aspects related to quality of life is multiple sclerosis (MS) [4-7].

Since the publication of the first study of HRQOL in patients with MS in 1990, numerous studies have been conducted in various countries to determine the impact of different factors of the disease and its treatment on quality of life.

The aim of this paper is to review the information available about HRQOL assessment in patients with MS, allowing us to offer a global view of the current situation.

Impact of multiple sclerosis on the quality of life

The disabling effects of MS trigger a significant detriment in patients' quality of life; this detriment is even higher than that produced by other chronic diseases, as the QOL worsens in at least one third of patients after diagnosis [6]. This detriment is mainly due to the worsening evaluation of several aspects such as vitality, general health, physical function, and social relations. Moreover, a review of 80 HRQOL studies conducted in Canada, Norway, Spain, and the United States has shown that 70% of MS patients were unemployed, with 50% of these cases due only to the MS. Fifty percent of pa-

tients had problems performing house chores and work functions 10 years after disease onset; these patients needed help walking after 15 years and required a wheelchair after 25 years. Moreover, the results of another study showed the existence of a progressive deterioration of HRQOL over the course of the disease, declining to values indicating a state worse than death from a score of 8 on the Expanded Disability Status Scale (EDSS) [7].

Methods of evaluation

The main approaches used to assess the impact of MS in clinical practice are the application of scales such as the Kurtzke EDSS [8] and the Multiple Sclerosis Functional Composite (MSFC) [9]. The EDSS is an easy tool that helps determine the degree of patients' disability. However, the main disadvantages are poor reliability between observers, limited sensitivity to change, nonlinear metric nature, excessive reliance on walking, inadequate quantification of mental and visual function, and failure to assess pain, vitality/fatigue or the level of well-being. The MSFC allows for the assessment of gait and upper limb function and includes a test of cognition. However, it must be performed by qualified personnel and important disabling factors such as fatigue and spasticity must be excluded.

Neither of these scales include the assessment of HRQOL, so several assessment questionnaires, both generic and specific for MS, have been developed (Table). Among the validated HRQOL questionnaires in Spanish are the generic Medical Outcomes Study 36-item Short Form (SF-36) [10-12] and the MS-specific questionnaire Multiple Sclerosis Quality of Life 54 (MSQoL-54) [13, 14]. The SF-36 questionnaire is one of the most widely used; it can be performed in 5-20 minutes and can be self-administered. It is based on the analysis of 36 factors of physical function, bodily pain, general health, vitality, social function, emotional state, and mental health. However, it does not consider other relevant aspects for patients with MS such as sleep problems, sexual disorders, or cognitive disorders.

The MSQoL-54 is a self-administered questionnaire that requires about 15-20 minutes to complete. It is based on the SF-36 and has an additional 18 MS-specific questions related to rest, pain, health concerns, sexual function, cognitive activity, social function, and quality of life in general. The advantages of the MSQoL-54 over other questionnaires are its reliability, the short time necessary for its administration, and the possibility of comparison with

other diseases or with the general population, since it is based on the generic SF-36 [13]. However, it is not well correlated with measures of disability (EDSS) [15] and the 'ground effect' for the physical subscale derived from this structural limitation on the SF-36 [6].

The use of HRQOL questionnaires allows us to evaluate the impact of MS more widely than with other commonly used assessment measures of disease activity such as MRI, relapse rates, and the EDSS or MSFC scales [16]. HRQOL assessments can identify and evaluate both the needs of the patient and the existence of possible complications that are not detected by the physician [6]. These assessments could also be regarded as predictors of the impact of the disease on physical and psychological dimensions [16,17].

Physical factors

The main physical factors that affect the quality of life of patients with MS are functional disability (sensory or motor impairment), fatigue, pain, and urinary or sexual problems [17].

Functional disability

Functional disability has been shown to be correlated with the HRQOL of patients with MS. This disability is not only limited to the deficit, but is also conditioned by the degree of functional limitation in the context of personal health [5]. There is a significant decline in the satisfaction of HRQOL as measured by the Functional Assessment of Multiple Sclerosis (FAMS) in patients with moderate or severe disability (EDSS > 3) compared to those with mild disabilities or no disability [18]. Disability was shown to be significantly related to mobility, symptoms, and emotional well-being (FAMS). Moreover, a study conducted in 166 patients with varied disease progression times (less than 5 years and above 15) showed that abnormal gait and visual function are two important factors that affect functional status as measured by the United Kingdom Disability Scale (UNDS) [19]. Moreover, how the different domains of HRQOL are affected has been shown to be related to the progression of disability over the course of the disease. While in the early stages (EDSS: 0-3) of the disease, the factors that are most affected are bodily pain and vitality, as the disease progresses (EDSS > 6), SF-36 factors related to physical function are affected more [20].

However, the objective functional deficit does not always correspond with patients' subjective perception [19]. According to the EDSS, analysis of the re-

Table. Most commonly used questionnaires for assessing the quality of life of patients with multiple sclerosis.

Generic questionnaires	Areas of assessment
<i>Medical Outcomes Study 36-item Short Form (SF-36)</i> ^a	Physical function, bodily pain, general health, vitality, social function, emotional state, and mental health
<i>World Health Organization Quality of Life (WHOQoL)</i> ^a	Physical and psychological health, level of independence, social relations, environment, personal beliefs
<i>EuroQoL (EQ-5D)</i>	Mobility, self-care, usual activities (limitations), pain/discomfort, anxiety/depression
<i>Functional Status Questionnaire (FSQ)</i>	Self-care, mobility, domestic life
<i>Nottingham Health Profile (NHP)</i>	Pain, physical mobility, sleep, emotional state, energy, social function, work activity, sexual life
<i>Sickness Impact Profile (SIP)</i>	Social and work function, food, sleep/rest, home management, recreation / hobbies
<i>Farmer Quality of Life Index</i>	Functionality and economics, social function, life in general, medical problems
Specific questionnaires	
<i>Multiple Sclerosis Quality of Life 54 (MSQoL-54)</i> ^a	Physical function, bodily pain, general health, vitality, social function, emotional state and mental health, rest, concern for health, sexual function, cognitive activity, and quality of life in general
<i>Functional Assessment of Multiple Sclerosis (FAMS)</i> ^a	Mobility, specific symptoms, emotional disorders, thoughts, fatigue, social, and family aspects
<i>Multiple Sclerosis Quality of Life Inventory (MSQLI)</i>	Physical function, bodily pain, general health, vitality, social function, emotional state, mental health, fatigue, and urinary problems
<i>Multiple Sclerosis International Quality of Life Questionnaire (MuSIQoL)</i>	Daily life activities, psychological well-being, symptoms, social and family function, relation with the sanitary system, sentimental/sexual life, coping, and refusal
<i>RAYS Scale</i>	Physical function, pain, cognitive function, anxiety, depression, sleep disorders, fatigue, sexual function, self-esteem, social and family relations, free time, and work activity
<i>Multiple Sclerosis Impact Scale (MSIS-29)</i>	Physical function, daily/work activities, sleep disorders, mental health, emotional state, social and free time activity
<i>Hamburg Quality of Life Questionnaire in Multiple Sclerosis (HAQUAMS)</i>	Fatigue, mobility, social function, and emotional state
<i>Leeds Multiple Sclerosis Quality of Life (LMSQoL)</i>	Physical, social, and emotional function

^a Validated in Spanish.

relationship between disability and HRQOL has shown mixed results [6,7,16,21]. The EDSS scale primarily reflects the degree of disability objectified by the professional in terms of motor or sensory impairment presented by the patient, with an emphasis on impairments seen in the lower extremities. In addition, assessment of disability has been statistically associated with the following domains of HRQOL (FAMS): mobility, symptoms, and emotional well-being [18]. However, this scale does not assess the

severity as perceived by the patient and is not correlated with HRQOL domains such as pain, emotional state, mental health [22], overall satisfaction, fatigue, social well-being, and other concerns [18].

Fatigue

Fatigue is another consequence of MS that is often seen in patients. However, the assessment of its impact has not received sufficient recognition, in part because it is not considered within the EDSS or in

other questionnaires about the quality of life, such as EuroQoL (EQ-5D) [23].

Studies have shown that the fatigue associated with MS clearly disrupts both the social and professional functioning of patients [24-27], becoming the major cause of unemployment [28]. It has also been shown that fatigue significantly affects the physical and mental aspects of the HRQOL (SF-36), and its influence on the latter is independent of the EDSS score [29].

Pain

Pain is a common symptom of MS, affecting 29-86% of patients [30], and has a negative impact on daily life activities as well as on the HRQOL [30-33]. Its main effects consist of the reduction of vitality, deterioration of physical function, and impairment of mental health (SF-36) [31]. The most important effect seems to occur on mental health, giving rise to a strong correlation with chronic pain –Assessment of Quality of Life Scale (AQoL)– [33] and associated with factors that affect HRQOL, such as fatigue, depression, and sleep disorders (SF-36) [34].

Sexual and urinary problems

Other factors related to the deterioration of the HRQOL of MS patients are the appearance of sexual and urinary problems. A Norwegian study showed that 53% of patients with a score of disability in the EDSS ≤ 4 had sexual problems and 44% had bladder dysfunction [35]. In cases of disability of EDSS > 4 , these percentages increased to 86% and 81%, respectively. Patients with sexual dysfunction had a significant reduction in the quality of life (SF-36) regardless of their disability status (EDSS). Moreover, sexual dysfunction is associated with lower vitality, presence of bodily pain, social function impairment, and a deterioration of mental activity. Subsequent studies confirmed the impact of changes in bladder and sexual quality of life of patients (MSQoL)[36]. Seventy-nine percent of males and 49% of women had moderate or severe bladder dysfunction. With regard to sexual satisfaction, significant differences were found in terms of gender. Fifty percent of men and 15% of women reported being dissatisfied with their sex lives. For men, the main problems was achieving and maintaining an erection, while women had problems reaching orgasm and expressed a lack of sexual interest.

Psychological factors

The psychological state resulting from factors such as depression, anxiety, loss of cognitive functions,

and attitude towards the disease (coping strategies) is also known to impact patients' quality of life [17].

Depression

Depression has been shown to be one of the factors with the greatest impact on HRQOL [37-39]. It has even been regarded as an independent variable associated with the deterioration of HRQOL in relation to the perception of health and the limitations resulting from physical dysfunction (MSQoL-54) [40]. It was also suggested to be an intermediate factor in the effect of disability (EDSS) on mental/general health (SF-36) as well as a moderating factor on the impact of disability (EDSS) on physical function (SF-36) [41]. Several studies have shown the association between depression and the sequelae of MS such as fatigue, physical impairment, cognitive impairment, and pain [42]. In addition, depression has been associated with cognitive impairment, worse adherence to immunosuppressive therapy, and even with the development of suicidal ideation [43].

Given the importance of the consequences of depression and its impact on patients' HRQOL, there should be a systematic assessment of the depressive state of patients with MS after diagnosis and throughout the course of the disease [43]. In this context, various recommendations and management algorithms have been proposed [43,44]. These recommendations and algorithms are based on the initial examination at the time of diagnosis using the Beck Depression Inventory (BDI), followed by a thorough diagnostic interview including questions about previous history of depressive disorders in patients with scores BDI ≥ 13 . If the depression diagnosis is confirmed, patients should be treated with antidepressants or cognitive therapy [43,44].

Anxiety

Anxiety is another factor that has been shown to have significant influence on the deterioration of MS patients' HRQOL [38]. The available information suggests that anxiety may be regarded as an intermediate factor in the effect of disability in three of the four physical health scales of SF-36 [41]. In addition, anxiety modifies the negative effect of disability in three out of the four physical health scales of SF-36 [41].

Cognitive disorders

Cognitive disorders affect 40-60% of patients with MS [45]. Cognitive deterioration is not global, affecting mainly the speed of information processing and episodic and working memory [46], although the condition is usually mild [47]. However, cogni-

tive impairment strongly affects the activities of daily life, affecting patients' personal care, leading to the necessity of help for the performance of household tasks, reduced participation in social activities, and increased unemployment [48-50]. In fact, the first studies that showed this effect have already suggested that cognitive impairment may be an important factor in determining patients' quality of life [50]. Although a study of 29 patients failed to demonstrate the existence of an association between cognitive impairment and quality of life (MSQoL-54) [51], a later study conducted in 209 patients was able to confirm its correlation with the assessment of overall quality of life, mobility, symptoms, fatigue, and emotional/social/family well-being (FAMS) [52]. Therefore, it would be advisable to assess cognitive and emotional functions in order to better understand the perception of HRQOL. However, the level of cognitive function should be considered with caution when analysing HRQOL because the cognitive impairment could produce an overestimation of the patient's HRQOL [53].

Attitude to illness

Assessments of other factors, such as coping strategies, which are efforts to control, reduce, or tolerate threats or overcoming personal limitations, have shown them to influence the mental domain and global assessments of MS patients' HRQOL (MSQoL-54) [54]. Recent studies have provided additional information about the types of coping strategies used by patients with MS, and show that patients use fewer positive strategies addressed at dealing with the problem and more use of avoidant coping strategies [54]. Another study showed differences between the type of MS: secondary progressive (SPMS) and primary progressive (PPMS). SPMS patients had worse mental function (depression and anxiety) and more factors of HRQOL (self-report questionnaire SEP-59) and tended to use more coping strategies that focused on the emotional situation than strategies aimed at the resolution of the cause of the problem. Patients with PPMS had better conditions and preferred instrumental coping strategies directed to the pursuit of material support to cope with their disease [55].

Social factors

Patients with MS often show the stigma that the disease produces on the patient's social network and often lose relationships or friends [56]. The impact of MS in social relationships occurs primarily as a result of the patients' clinical symptoms, worsening

of the disease or its unstable clinical course, fatigue, and limited mobility, which are reflected in the overall quality of life (SF-36) [57]. In addition, family relationships can be affected as a result of frequent arguments and conflicts with caregivers [56]. Although this area is not widely studied, the available evidence confirms the negative impact of the disease on patients' HRQOL (SF-36) and caregivers' 12-item Short Form Health Survey (SF-12) [58]. In both cases, there is a greater degree of problems in the mental domain of the HRQOL. In the case of caregivers, there is a correlation between a reduction in mental health and the existence of anxiety, depression, and a greater number of hours devoted to patient care [58]. In addition, a close relationship with the patient (parent, child, or spouse) has also been shown to relate to the overall deterioration of caregivers' quality of life (SF-36) [57], particularly in the mental domain (SF-12) [58].

A study conducted in patients with newly diagnosed and untreated relapsing-remitting MS (RRMS) has shown that patients with stable employment and at least 13 years of schooling had higher scores in most domains of the MSQoL-54 questionnaire of HRQOL than those who were unemployed and had low education levels [59]. It is common for newly diagnosed MS patients to feel discouraged by the news of a chronic disease with an unpredictable course and the loss of functional capacity, and this can lead to a feeling of inadequacy that can lead to the termination of work or studies. However, it is important to note that unemployment increases the difficulty of adaptation and increases the perception of self-esteem [56] and that patients who continue their academic or occupational activities have a better quality of life [59].

The impact of treatment on quality of life

The evaluation of treatment efficacy is usually based on the evolution of physical function and findings on MRI examinations and does not reflect the global and multidimensional nature of the patients' HRQOL. Beyond the physical function, there are other factors (sensory symptoms, social, psychological, or emotional factors) that greatly influence both the evolution of MS and the effectiveness of treatment and these must be taken into account [60]. These factors change more rapidly than the disability, meaning that, in order to properly adapt treatment strategies to the real needs of patients, detailed analysis of these factors must be performed at more regular intervals [60].

Pharmacotherapy

Despite the fact that there is no cure for MS, various drugs and administration methods have been developed and have been shown to reduce the number of outbreaks and their severity as well as to delay the clinical progression of the disease [17,61-63]. The incorporation of HRQOL questionnaires into the monitoring of patients with MS may serve as a tool to optimise drug therapy. Such treatment may influence the improvement of HRQOL as a result of their impact on disease progression [17]. However, it can also negatively affect some aspects of HRQOL, due to the development of adverse side effects or the limitation of the work/personal autonomy of the patient [17].

Within this framework, adherence to treatment is one of the factors affecting HRQOL. A recent study in a Spanish cohort of 252 patients showed that, in general, patients with good adherence had better scores on the Multiple Sclerosis International Quality of Life (MuSIQoL) of HRQOL questionnaire at baseline and after two years, these patients scored significantly higher in the physical dimensions and symptoms [64]. Patients who were older and who better understood their illness and its treatment had a better compliance. However, the dosing and effectiveness as perceived by patients did not significantly influence compliance or HRQOL [65].

There have been many studies regarding the distinct immunomodulatory therapies and their impact on the HRQOL. A randomised placebo-controlled study in 718 patients with SPMS showed a slightly positive effect on HRQOL –Sickness Impact Profile (SIP)– after treatment with interferon (IFN) β -1b, which reached statistical significance in the physical subscale at 6, 12, and 36 months [66]. Similarly, another randomised placebo-controlled study in patients with SPMS showed a significant improvement in 8 of the 11 subscales of the Multiple Sclerosis Quality of Life Inventory (MSQLI) and a positive tendency in three other studies of patients treated with intramuscular IFN β -1a [67].

In patients with RRMS, the administration of intramuscular IFN β -1a did not result in significant changes on the subscales of the SF-36 questionnaire, except for a decline in the physical function [68]. However, in other studies, this therapy in naïve patients with RRMS led to an alleviation of the disease and an improvement in the HRQOL (EQ-5D), especially in the descriptive part of the utility and anxiety [69].

A comprehensive analysis of patients with MS (including RRMS, SPMS, and PPMS) treated with

immunomodulating agents (IFN β -1a, IFN β -1b, glatiramer acetate) failed to show significant differences in HRQOL measured with either the SF-36 or Subjective Estimation of Quality of Life (SQoL) questionnaires compared to untreated patients [70]. However, other studies showed a significant improvement in the global HRQOL –Leeds Multiple Sclerosis Quality of Life (LMSQoL)– from the first month of treatment with immunomodulatory agents (IFN β -1a, IFN β -1b or glatiramer acetate), reaching a peak at nine months and remaining significantly elevated for the three years of study [71]. This improvement was not correlated with age, duration of illness, or disability (EDSS). Therefore, the choice of treatment for patients should not be selected based on these factors. The number of relapses was also not correlated with HRQOL, which means that this parameter cannot predict the effect of the disease on the HRQOL. Similarly, no significant differences between patients with RRMS and SPMS or between the different drugs used in the treatment were found.

In contrast, there have been proven differences in the impact of different immunomodulatory drugs on other aspects of the HRQOL, such as depression, in MS patients. Some patients treated with IFN β may be more vulnerable to depression, especially those with a history of depression [72,73]. In fact, the negative impact of the treatment with IFN β has been described in the mental domain of HRQOL (MSQoL-54) and depression has shown to be one of the main predictive factors of poor quality of life [74]. However, glatiramer acetate has no negative effect on the development of depression, so it is the treatment of choice in patients with a history of depression [43]. In addition, this drug could have an antidepressant effect due to the increase of the brain-derived neurotrophic factor, the stimulation of neurogenesis, or its anti-inflammatory activity [75,76].

One of the major predictive factors of a poor HRQOL (MSQoL-54) is fatigue [74]. Administration of IFN β and glatiramer acetate has been shown to lead to different scores on the Fatigue Impact Scale (FIS). The administration of glatiramer acetate appears to decrease fatigue in a significantly higher proportion of patients in both the global score of the FIS and the cognitive and physical subscales. Further studies on the effect of glatiramer acetate showed a significant reduction in the intensity of fatigue (FIS) [78] and improvements in the HRQOL (LMSQoL) of patients [79]. It has also been found that a change of IFN therapy to glatiramer acetate contributes significantly to the decline in the perception of fatigue by the patient [80].

The influence of medication on other aspects of HRQOL, such as urinary dysfunction, has not been studied extensively. The limited information shows the beneficial influence of long-term treatment with glatiramer acetate in the development of symptoms of lower urinary tract dysfunction in patients with RRMS, delaying its onset or allowing for symptomatic stabilisation [81].

Most phase III clinical trials aimed at assessing the different pharmacological agents used to treat MS do not include analysis of the HRQOL. The pivotal studies of natalizumab (AFFIRM and SENTINEL) [82] included this kind of evaluation and showed improvement in scores on the subscales of physical and mental health of the SF-36 questionnaire and its correlation with the disability (EDSS), the appearance of relapses, and MRI lesion load. In the AFFIRM study, the administration of natalizumab managed to significantly improve the physical HRQOL score after 24 weeks of treatment, achieving significant improvement in the physical and mental domains of SF-36 after two years. The SENTINEL study also showed that a combination of natalizumab and intramuscular interferon β -1a led to a significant improvement in the physical and mental health domains of HRQOL of SF-36 after two years of treatment. This improvement in HRQOL occurred even in patients with progression of disability or those who relapsed during the study period.

Neurorehabilitation therapy

The effectiveness of neurorehabilitation therapy in MS patients has been demonstrated in several clinical trials. However, the use of multiple rating scales rather than very well specified selection criteria and the increasing lack of multicenter studies, placebo-controlled and appropriate blind methods, as well as the non-homogenous quality results make it necessary to increase the level of evidence [83]. In fact, the impact of rehabilitation on patients' HRQOL is still not clear. A randomised controlled clinical trial showed that physical rehabilitation for three weeks resulted in improved quality of life in patients compared to those who only performed exercises at home, with a significant positive influence on mental health (SF-36) [84]. The beneficial effect of rehabilitation could be partially maintained after the rehabilitation ended, but declined when patients returned to their usual care, which emphasises the importance of continuity of outpatient rehabilitation [85]. The short-term assessment of exercise showed an improvement in the perception of qual-

ity of life of patients who underwent five weekly sessions of 30 minutes for four weeks, mainly in relation to their vitality and social functioning (SF-36) [86]. Studies on the influence of long-term exercise on patients' HRQOL provide contradictory results. While some studies have shown improvement in all domains of the HRQOL (SF-36) in patients who performed at least two exercise sessions of 30 minutes a week for six months [87], other studies did not show an improvement in the HRQOL (MSQoL) after six months of resistance training [88]. In the latter case, we cannot exclude the possible influence of other types of physical activity in improving quality of life [88].

Conclusions

Assessment of HRQOL is complex because of its multifactorial nature, combining clinical, psychological, and social data, and because patients' perception is of particular relevance. In the case of MS, analysis of the HRQOL is even more complex because of the subjectivity associated with various symptoms related to patients' sense of well-being and whose quantification is extremely difficult for the doctor.

Therefore, it is difficult to identify specific domains that interfere most with patients' HRQOL. However, the disability, fatigue, and depression experienced by patients have a remarkable impact on the HRQOL.

The incorporation of periodic assessments of the HRQOL into clinical routine is especially important in patients with MS. These assessments would allow for the identification of possible changes in the various domains of HRQOL and would provide additional information to optimise treatments through appropriate symptomatic treatment or by changing the immunomodulatory treatment.

References

1. The WHOQoL Group. Development of the WHOQoL: rationale and current status. *Int J Mental Health* 1994; 23: 24-56.
2. Minayo MC, Hartz ZM, Buss PM. Quality of life and health: a necessary debate. *Ciencia & Saúde Coletiva* 2000; 5: 7-18.
3. Testa MA, Simonson DC. Assessment of quality-of-life outcomes. *N Engl J Med* 1996; 334: 835-40.
4. Rudick RA, Miller D, Clough JD, Gragg LA, Farmer RG. Quality of life in multiple sclerosis. Comparison with inflammatory bowel disease and rheumatoid arthritis. *Arch Neurol* 1992; 49: 1237-42.
5. Hincapié-Zapata ME, Suárez-Escudero JC, Pineda-Tamayo R, Anaya JM. Calidad de vida en esclerosis múltiple y otras enfermedades crónicas autoinmunes y no autoinmunes. *Rev Neurol* 2009; 48: 225-30.

6. Mitchell AJ, Benito-León J, González JM, Rivera-Navarro J. Quality of life and its assessment in multiple sclerosis: integrating physical and psychological components of wellbeing. *Lancet Neurol* 2005; 4: 556-66.
7. Orme M, Kerrigan J, Tyas D, Russell N, Nixon R. The effect of disease, functional status, and relapses on the utility of people with multiple sclerosis in the UK. *Value Health* 2007; 10: 54-60.
8. Kurtzke JF. Rating neurologic impairment in multiple sclerosis: an Expanded Disability Status Scale (EDSS). *Neurology* 1983; 33: 1444-52.
9. Cutter GR, Baier ML, Rudick RA, Cookfair DL, Fischer JS, Petkau J, et al. Development of a multiple sclerosis functional composite as a clinical trial outcome measure. *Brain* 1999; 122: 871-82.
10. Ayuso-Mateos JL, Lasa L, Vazquez-Barquero JL, Oviedo A, Díez-Manrique JF. Measuring health status in psychiatric community surveys: internal and external validity of the Spanish version of the SF-36. *Acta Psychiatr Scand* 1999; 99: 26-32.
11. Ware JE Jr, Sherbourne CD. The MOS 36-item Short-Form health survey (SF-36). I. Conceptual framework and item selection. *Med Care* 1992; 30: 473-83.
12. Ware JE Jr. SF-36 health survey update. *Spine* 2000; 25: 3130-9.
13. Aymerich M, Guillamón I, Perkal H, Nos C, Porcel J, Berra S, et al. Adaptación al español del cuestionario específico MSQOL-54 para pacientes con esclerosis múltiple. *Neurología* 2006; 21: 181-7.
14. Vickrey BG, Hays RD, Harooni R, Myers LW, Ellison GW. A health-related quality of life measure for multiple sclerosis. *Qual Life Res* 1995; 4: 187-206.
15. Benedict RH, Wahlig E, Bakshi R, Fishman I, Munschauer F, Zivadinov R, et al. Predicting quality of life in multiple sclerosis: accounting for physical disability, fatigue, cognition, mood disorder, personality, and behavior change. *J Neurol Sci* 2005; 231: 29-34.
16. Nortvedt MW, Riise T. The use of quality of life measures in multiple sclerosis research. *Mult Scler* 2003; 9: 63-72.
17. Hernández MA. Tratamiento de la esclerosis múltiple y calidad de vida. *Rev Neurol* 2000; 30: 1242-5.
18. Modrego PJ, Pina MA, Simón A, Azuara MC. The interrelations between disability and quality of life in patients with multiple sclerosis in the area of Bajo Aragón, Spain: a geographically based survey. *Neurorehabil Neural Repair* 2001; 15: 69-73.
19. Heesen C, Bohm J, Reich C, Kasper J, Goebel M, Gold SM. Patient perception of bodily functions in multiple sclerosis: gait and visual function are the most valuable. *Mult Scler* 2008; 14: 988-91.
20. Delgado-Mendilívar JM, Cadenas-Díaz JC, Fernández-Torrico JM, Navarro-Mascarell G, Izquierdo G. Estudio de la calidad de vida en la esclerosis múltiple. *Rev Neurol* 2005; 41: 257-62.
21. Shawaryn MA, Schiaffino KM, LaRocca NG, Johnston MV. Determinants of health-related quality of life in multiple sclerosis: the role of illness intrusiveness. *Mult Scler* 2002; 8: 310-8.
22. Pittock SJ, Mayr WT, McClelland RL, Jorgensen NW, Weigand SD, Noseworthy JH, et al. Quality of life is favorable for most patients with multiple sclerosis: a population-based cohort study. *Arch Neurol* 2004; 61: 679-86.
23. Hemmett L, Holmes J, Barnes M, Russell N. What drives quality of life in multiple sclerosis? *QJM* 2004; 97: 671-6.
24. Freal JE, Kraft GH, Coryell JK. Symptomatic fatigue in multiple sclerosis. *Arch Phys Med Rehabil* 1984; 65: 135-8.
25. Krupp LB, Álvarez LA, LaRocca NG, Scheinberg LC. Fatigue in multiple sclerosis. *Arch Neurol* 1988; 45: 435-7.
26. Krupp LB, LaRocca NG, Muir-Nash J, Steinberg AD. The fatigue severity scale. Application to patients with multiple sclerosis and systemic lupus erythematosus. *Arch Neurol* 1989; 46: 1121-3.
27. Monks J. Experiencing symptoms in chronic illness: fatigue in multiple sclerosis. *Int Disabil Stud* 1989; 11: 78-83.
28. Smith MM, Arnett PA. Factors related to employment status changes in individuals with multiple sclerosis. *Mult Scler* 2005; 11: 602-9.
29. Merkelbach S, Sittinger H, Koenig J. Is there a differential impact of fatigue and physical disability on quality of life in multiple sclerosis? *J Nerv Ment Dis* 2002; 190: 388-93.
30. Bermejo PE, Oreja-Guevara C, Díez-Tejedor E. El dolor en la esclerosis múltiple: prevalencia, mecanismos, tipos y tratamiento. *Rev Neurol* 2010; 50: 101-8.
31. Grasso MG, Clemenzi A, Tonini A, Pace L, Casillo P, Cuccaro A, et al. Pain in multiple sclerosis: a clinical and instrumental approach. *Mult Scler* 2008; 14: 506-13.
32. Brochet B, Deloite MS, Ouallet JC, Salort E, Bonnet M, Jove J, et al. Pain and quality of life in the early stages after multiple sclerosis diagnosis: a 2-year longitudinal study. *Clin J Pain* 2009; 25: 211-7.
33. Khan F, Pallant J. Chronic pain in multiple sclerosis: prevalence, characteristics, and impact on quality of life in an Australian community cohort. *J Pain* 2007; 8: 614-23.
34. Newland PK, Naismith RT, Ullione M. The impact of pain and other symptoms on quality of life in women with relapsing-remitting multiple sclerosis. *J Neurosci Nurs* 2009; 41: 322-8.
35. Nortvedt MW, Riise T, Myhr KM, Landtblom AM, Bakke A, Nyland HI. Reduced quality of life among multiple sclerosis patients with sexual disturbance and bladder dysfunction. *Mult Scler* 2001; 7: 231-5.
36. Nortvedt MW, Riise T, Frugard J, Mohn J, Bakke A, Skar AB, et al. Prevalence of bladder, bowel and sexual problems among multiple sclerosis patients two to five years after diagnosis. *Mult Scler* 2007; 13: 106-12.
37. D'Alisa S, Miscio G, Baudo S, Simone A, Tesio L, Mauro A. Depression is the main determinant of quality of life in multiple sclerosis: a classification-regression (CART) study. *Disabil Rehabil* 2006; 28: 307-14.
38. Fruehwald S, Loeffler-Stastka H, Eher R, Saletu B, Baumhackl U. Depression and quality of life in multiple sclerosis. *Acta Neurol Scand* 2001; 104: 257-61.
39. Lobentanz IS, Asenbaum S, Vass K, Sauter C, Klosch G, Kollegger H, et al. Factors influencing quality of life in multiple sclerosis patients: disability, depressive mood, fatigue and sleep quality. *Acta Neurol Scand* 2004; 110: 6-13.
40. Janardhan V, Bakshi R. Quality of life in patients with multiple sclerosis: the impact of fatigue and depression. *J Neurol Sci* 2002; 205: 51-8.
41. Janssens AC, Van Doorn PA, De Boer JB, Kalkers NF, Van der Meche FG, Passchier J, et al. Anxiety and depression influence the relation between disability status and quality of life in multiple sclerosis. *Mult Scler* 2003; 9: 397-403.
42. Arnett PA, Barwick FH, Beeney JE. Depression in multiple sclerosis: review and theoretical proposal. *J Int Neuropsychol Soc* 2008; 14: 691-724.
43. Ziemssen T. Multiple sclerosis beyond EDSS: depression and fatigue. *J Neurol Sci* 2009; 277: S37-41.
44. The Goldman Consensus statement on depression in multiple sclerosis. *Mult Scler* 2005; 11: 328-37.
45. Brassington JC, Marsh NV. Neuropsychological aspects of multiple sclerosis. *Neuropsychol Rev* 1998; 8: 43-77.
46. Paes RA, Alvarenga RM, Vasconcelos CC, Negreiros MA, Landeira-Fernández J. Neuropsicología de la esclerosis múltiple primaria progresiva. *Rev Neurol* 2009; 49: 343-8.
47. Ryan L, Clark CM, Klonoff H, Li D, Paty D. Patterns of cognitive impairment in relapsing-remitting multiple sclerosis and their relationship to neuropathology on magnetic resonance images. *Neuropsychol* 1996; 10: 176-93.
48. Amato MP, Ponziani G, Rossi F, Liedl CL, Stefanile C, Rossi L. Quality of life in multiple sclerosis: the impact of depression, fatigue and disability. *Mult Scler* 2001; 7: 340-4.
49. Higginson CI, Arnett PA, Voss WD. The ecological validity of clinical tests of memory and attention in multiple sclerosis. *Arch Clin Neuropsychol* 2000; 15: 185-204.
50. Rao SM, Leo GJ, Ellington L, Nauertz T, Bernardin L, Unverzagt F. Cognitive dysfunction in multiple sclerosis. II. Impact on employment and social functioning. *Neurology* 1991; 41: 692-6.

51. O'Connor P, Lee L, Ng PT, Narayana P, Wolinsky JS. Determinants of overall quality of life in secondary progressive MS: a longitudinal study. *Neurology* 2001; 57: 889-91.
52. Benito-León J, Morales JM, Rivera-Navarro J. Health-related quality of life and its relationship to cognitive and emotional functioning in multiple sclerosis patients. *Eur J Neurol* 2002; 9: 497-502.
53. Gerbaud L, Deffond D, Mulliez A, Benausse F, Vernay D, Clavelou P. Cognitive impairment and quality of life in multiple sclerosis patients. *Rev Neurol (Paris)* 2006; 162: 970-9.
54. Goretti B, Portaccio E, Zipoli V, Hakiki B, Siracusa G, Sorbi S, et al. Coping strategies, psychological variables and their relationship with quality of life in multiple sclerosis. *Neurol Sci* 2009; 30: 15-20.
55. Montel SR, Bungener C. Coping and quality of life in one hundred and thirty five subjects with multiple sclerosis. *Mult Scler* 2007; 13: 393-401.
56. Rivera-Navarro J, Morales-González JM, Benito-León J, Mitchell AJ. Dimensión social y familiar: experiencias de cuidadores y personas con esclerosis múltiple. Estudio GEDMA. *Rev Neurol* 2008; 47: 281-5.
57. Aronson KJ. Quality of life among persons with multiple sclerosis and their caregivers. *Neurology* 1997; 48: 74-80.
58. Aymerich M, Guillamón I, Jovell AJ. Health-related quality of life assessment in people with multiple sclerosis and their family caregivers. A multicenter study in Catalonia (Southern Europe). *Patient Prefer Adherence* 2009; 3: 311-21.
59. Patti F, Pozzilli C, Montanari E, Pappalardo A, Piazza L, Levi A, et al. Effects of education level and employment status on HRQoL in early relapsing-remitting multiple sclerosis. *Mult Scler* 2007; 13: 783-91.
60. Foley JF, Brandes DW. Redefining functionality and treatment efficacy in multiple sclerosis. *Neurology* 2009; 72: S1-11.
61. Hernández-Pérez MA. Seguridad y tolerabilidad en la fase inicial del tratamiento con interferón beta-1a 44 microgramos en pauta lenta frente a pauta rápida en pacientes con esclerosis múltiple (estudio PARALEN). *Rev Neurol* 2009; 48: 505-8.
62. Patrucco L, Rojas JI, Cristiano E. Efecto del tratamiento a largo plazo con interferón beta en la gravedad de la esclerosis múltiple remitente-recurrente. *Rev Neurol* 2010; 50: 529-32.
63. Río-Izquierdo J, Montalban X. Natalizumab en esclerosis múltiple. *Rev Neurol* 2009; 49: 265-9.
64. Sánchez-Solano O, Arroyo E, Grau C, Parra JC, You X, on behalf of the Spanish GAO study group. Quality of life in patients with relapsing-remitting multiple sclerosis treated with immunomodulators: 2 years results in Spain. 25th Congress ofECTRIMS. Düsseldorf, Alemania, septiembre de 2009.
65. De Sèze J, Borgel F, Brudon F. Immunomodulator treatments and multiple sclerosis: compliance and factors of adherence to treatment. *Mult Scler* 2007; 13: S46.
66. Freeman JA, Thompson AJ, Fitzpatrick R, Hutchinson M, Miltenburger C, Beckmann K, et al. Interferon-beta 1b in the treatment of secondary progressive MS: impact on quality of life. *Neurology* 2001; 57: 1870-5.
67. Miller M. Assessing the effects of IFNβ-1a on health related quality of life in secondary-progressive MS patients: results from the IMPACT study. 54th AAN Meeting. Denver, EE.UU., abril de 2002.
68. Vermersch P, De Sèze J, Delisse B, Lemaire S, Stojkovic T. Quality of life in multiple sclerosis: influence of interferon-beta 1a (Avonex) treatment. *Mult Scler* 2002; 8: 377-81.
69. Putzki N, Fischer J, Gottwald K, Reifschneider G, Ries S, Siever A, et al. Quality of life in 1000 patients with early relapsing-remitting multiple sclerosis. *Eur J Neurol* 2009; 16: 713-20.
70. Isaksson AK, Ahlstrom G, Gunnarsson LG. Quality of life and impairment in patients with multiple sclerosis. *J Neuro Neurosurg Psychiatry* 2005; 76: 64-9.
71. Lily O, McFadden E, Hensor E, Johnson M, Ford H. Disease-specific quality of life in multiple sclerosis: the effect of disease modifying treatment. *Mult Scler* 2006; 12: 808-13.
72. Mohr DC, Likosky W, Dwyer P, Van der Wende J, Boudewyn AC, Goodkin DE. Course of depression during the initiation of interferon beta-1a treatment for multiple sclerosis. *Arch Neurol* 1999; 56: 1263-5.
73. Goeb JL, Even C, Nicolas G, Gohier B, Dubas F, Garre JB. Psychiatric side effects of interferon-beta in multiple sclerosis. *Eur Psychiatry* 2006; 21: 186-93.
74. Simone LL, Ceccarelli A, Tortorella C, Bellacosa A, Pellegrini F, Plasmati I, et al. Influence of Interferon beta treatment on quality of life in multiple sclerosis patients. *Health Qual Life Outcomes* 2006; 4: 96.
75. Tsai SJ. Glatiramer acetate could be a potential antidepressant through its neuroprotective and anti-inflammatory effects. *Med Hypotheses* 2007; 69: 145-8.
76. Ziemssen T, Reichmann H, Schneider H. Presence of glatiramer acetate-specific TH2 cells in the cerebrospinal fluid of patients with multiple sclerosis 12 months after the start of therapy with glatiramer acetate. *J Neurodegen Regen* 2008; 1: 19-22.
77. Metz LM, Patten SB, Archibald CJ, Bakker JI, Harris CJ, Patry DG, et al. The effect of immunomodulatory treatment on multiple sclerosis fatigue. *J Neurol Neurosurg Psychiatry* 2004; 75: 1045-7.
78. Ziemssen T, Hoffman J, Apfel R, Kern S. Effects of glatiramer acetate on fatigue and days of absence from work in first-time treated relapsing-remitting multiple sclerosis. *Health Qual Life Outcomes* 2008; 6: 67.
79. Jongen PJH, Carton H, Sanders EACM, Seeldrayers P, Fredrikson S, Andersson M, et al, the FOCUS Study Group. FOCUS study: fatigue and quality of life in relapsing-remitting multiple sclerosis patients using glatiramer acetate improved at 6 and 12 months of treatment. 23rd Congress ofECTRIMS. Praga, República Checa, octubre de 2007.
80. Hadjimichael O, Vollmer T, Oleen-Burkey M. Fatigue characteristics in multiple sclerosis: the North American Research Committee on Multiple Sclerosis (NARCOMS) survey. *Health Qual Life Outcomes* 2008; 6: 100.
81. Shvarts PG, Zavalishin IA. Influence of 5-year glatiramer acetate therapy on prevalence of lower urinary tract dysfunction in relapsing-remitting multiple sclerosis. *Mult Scler* 2008; 14: S159-60.
82. Rudick RA, Miller D, Hass S, Hutchinson M, Calabresi PA, Confavreux C, et al. Health-related quality of life in multiple sclerosis: effects of natalizumab. *Ann Neurol* 2007; 62: 335-46.
83. Sastre-Garriga J, Galán-Cartaña I, Montalban X, Thompson A. Neurorehabilitación en esclerosis múltiple. *Neurología* 2005; 20: 245-54.
84. Solari A, Filippini G, Gasco P, Colla L, Salmaggi A, La Mantia L, et al. Physical rehabilitation has a positive effect on disability in multiple sclerosis patients. *Neurology* 1999; 52: 57-62.
85. Freeman JA, Langdon DW, Hobart JC, Thompson AJ. Inpatient rehabilitation in multiple sclerosis: do the benefits carry over into the community? *Neurology* 1999; 52: 50-6.
86. Mostert S, Kesselring J. Effects of a short-term exercise training program on aerobic fitness, fatigue, health perception and activity level of subjects with multiple sclerosis. *Mult Scler* 2002; 8: 161-8.
87. Stroud NM, Minahan CL. The impact of regular physical activity on fatigue, depression and quality of life in persons with multiple sclerosis. *Health Qual Life Outcomes* 2009; 7: 68.
88. Romberg A, Virtanen A, Ruutiainen J. Long-term exercise improves functional impairment but not quality of life in multiple sclerosis. *J Neurol* 2005; 252: 839-45.

Calidad de vida y esclerosis múltiple

Introducción. La calidad de vida relacionada con la salud (CVRS) es un concepto complejo en el que se engloba la valoración de los dominios físicos, emocionales y sociales de la salud. Con el aumento de la prevalencia de pacientes con enfermedades crónicas progresivas, la valoración de la CVRS ha cobrando importancia, especialmente en pacientes con esclerosis múltiple (EM), en los que la CVRS se ha mostrado como una condición más deteriorada que en otras enfermedades crónicas.

Objetivo. Realizar una revisión de la información disponible sobre la CVRS de los pacientes con EM, que permita ofrecer una visión global de la situación actual.

Desarrollo. Los estudios realizados han logrado identificar los principales factores relacionados con la CVRS: factores físicos (alteraciones motoras/sensitivas, fatiga, dolor, problemas sexuales/urinarios), factores psicológicos (depresión, ansiedad, pérdida de funciones cognitivas, actitud frente a la enfermedad) y factores sociales (alteración de relaciones sociales/familiares, actividad laboral). La incorporación de cuestionarios de CVRS en el seguimiento de los pacientes constituye una herramienta para optimizar su tratamiento, facilitando la selección de la terapia, mejorando la adhesión y reduciendo los inconvenientes de la medicación, como la presentación de efectos adversos.

Conclusiones. La CVRS es un aspecto sumamente complejo de analizar en pacientes con EM ya que resulta difícil identificar los dominios específicos que interfieren en mayor medida. No obstante, su valoración periódica proporciona información esencial para mejorar el tratamiento sintomático, incrementar la adhesión al tratamiento y modificar el tratamiento inmunomodulador.

Palabras clave. Calidad de vida. Calidad de vida relacionada con la salud. Cuestionario de calidad de vida. Esclerosis múltiple. Función física. Función psicológica. Función social. Tratamiento.