Measurement of Health-Related Quality of Life in Multiple Sclerosis Patients

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ABSTRACT: ***Background:*** Patient outcomes in multiple sclerosis (MS) have generally been measured by their neurological impairment using specific scales such as the Kurtzke Expanded Disability Status Scale (EDSS). However, this scale does not measure the multiple dimensions of health-related quality of life (HRQOL) such as functional status and general well-being, which are also important outcomes along with disease-specific measurements. ***Methods:*** HRQOL was measured in a group of 97 MS patients using the RAND 36-item Health Survey 1.0. The EDSS score was assigned by the clinic neurologist. Additional data were collected from the clinical record for each patient. ***Results:*** MS patients scored poorly in a number of HRQOL domains such as physical and role functioning and energy or vitality. Disability as quantified by the EDSS correlated only with the physical functioning domain. Regression models were developed to measure the relationship between patient characteristics (independent variables) and HRQOL domains (dependent variables). ***Discussion:*** A number of patient characteristics were associated with higher or lower scores on the HRQOL domains. Of particular interest is the finding that a family history of MS was associated with poorer physical and social functioning as well as more pain and less vitality. The occurrence of seizures had a negative impact on role functioning, social functioning and general health perceptions. HRQOL gives caregivers a broader measure of disease burden than the EDSS alone, and should be useful in planning and monitoring interventions.

RÉSUMÉ: Évaluation de la qualité de vie en relation avec la santé chez des patients atteints de sclérose en plaques. ***Introduction:*** Le devenir des patients atteints de sclérose en plaques (SEP) a généralement été évalué selon leur déficit neurologique mesuré par des échelles spécifiques telle l'échelle étendue d'invalidité de Kurtzke (EEIK). Cependant, cette échelle ne mesure pas les multiples dimensions de la qualité de vie en relation avec la santé (QVRS) tels l'état fonctionnel et le bien-être général qui sont également des résultats importants tout comme les mesures des déficits spécifiques à la maladie. ***Méthodes:*** Nous avons mesuré la QVRS chez un groupe de 97 patients atteints de la SEP au moyen de l'enquête sur la santé en 36 items de Rand 1.0. Le score EEIK a été attribué par le neurologue de la clinique. Des données additionnelles ont été recueillies à partir des dossiers des patients. ***Résultats:*** Les patients atteints de SEP ont obtenu des scores faibles dans plusieurs domaines de la QVRS tels le fonctionnement physique, l'accomplissement d'un rôle et le niveau d'énergie et de vitalité. L'invalidité telle que quantifiée par l'EEIK était corrélée seulement au domaine du fonctionnement physique. Nous avons développé des modèles de régression pour mesurer la relation entre les caractéristiques des patients (variables indépendantes) et les domaines de la QVRS (variables dépendantes). ***Discussion:*** Certaines caractéristiques des patients étaient associées à des scores plus élevés ou plus bas à la QVRS. Il est particulièrement intéressant de constater qu'une histoire familiale de SEP était associée à un fonctionnement physique et social plus médiocre ainsi qu'à plus de douleur et moins de vitalité. La présence de crises convulsives avait un impact négatif sur l'accomplissement de rôles, le fonctionnement social et la perception de la santé en général. La QVRS fournit aux soignants une mesure élargie du fardeau de la maladie par rapport à l'EEIK seule et devrait être utile dans la planification et la surveillance des interventions.

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Multiple sclerosis (MS) is a chronic inflammatory demyelinating disease of the central nervous system. Treatment and follow-up have traditionally been based on a model of care which deals specifically with symptoms and complications. Outcome measures have quantified neurological and physical disabilities, using rating scales such as the Disability Status Scale (DSS) and more recently the Expanded Disability Status Scale of Kurtzke (EDSS).[1,2] However, the EDSS is disease specific, measures disability rather than the multiple dimensions of health related quality of life (HRQOL), and does not allow a comparison between patients with MS and other chronic diseases.

Functional status and general well-being are often used as the basis of the concept of HRQOL. Most conceptualizations include the dimensions of physical, social and role functioning

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as well as mental health and general health perceptions.[3] HRQOL is to be distinguished from quality of life (QOL) because the former is based on health domains which can be measured and quantitated. QOL on the other hand is difficult to conceptualize since it is affected by economic, political, cultural and spiritual factors which are not generally considered to fall under the purview of physicians and health care systems. Since maximizing HRQOL is an important goal of health care, it should serve as an outcome measure along with disease-specific end points.[4]

This study had two purposes; first to measure HRQOL in a group of MS patients and examine the relationships between HRQOL and the Kurtzke EDSS, and second to determine which patient characteristics were significant predictors of HRQOL scores.

Methodology

There are currently 350 active patients with clinically or laboratory-supported definite or probable MS followed at the Multiple Sclerosis Clinic at the Kingston General Hospital. These patients are seen at least once per year for assessment, at which time the level of disability is evaluated using the EDSS. One hundred and ten consecutive patients were approached to participate in this study, and 100 agreed to participate. Those who decided not to participate cited fatigue as the primary reason. The study was approved by the Queen's University Research Ethics Board.

The Rand 36-item Health Survey 1.0 was selected to assess HRQOL. This instrument is self-administered and can be completed in a few minutes. The Rand survey measures eight health domains, including physical functioning (10 items), role limitations due to physical problems (4 items), role limitations due to emotional problems (3 items), social functioning (2 items), bodily pain (2 items), emotional well-being (5 items), energy/vitality (4 items), and general health perceptions (5 items). A single item measures the patient's perception of change in health over the past year, but this item is not included in the scoring. The energy/vitality domain may be particularly relevant to MS patients, and includes items such as 'Did you have a lot of energy?' and 'Did you feel worn out?' as they relate to how the patient has felt in the past four weeks. Each of the eight health domains is scored on a scale ranging from 0 (worst possible health state) to 100 (best possible health state). The reliability and validity of the instrument have been well documented.[5-9]

The EDSS has a 20 point rating scale (0 - 10 with 0.5 point increments) which is based on ratings of disability on eight functional systems that are assessed during the neurological exam. A single score is obtained, with zero signifying no disability and ten death. The EDSS score was assigned by the clinic neurologist.

Both the EDSS and the Rand 36-item Health Survey 1.0 were administered at the time of the annual clinic visit. A clinic nurse was available to assist with questions or difficulties completing the Rand questionnaire. Additional data were collected from the clinical record for each patient. This additional information is listed in Appendix 1, and includes socio-demographic and medical characteristics as well as physiologic measures and interventions. A family history was considered positive if one or more first through third degree relatives had been told they had MS by their physician.

Information was entered into a dBase IV[10] database as it was collected. SYSTAT 3.1[11] was then used to generate the descriptive statistics, Pearson's correlations and multivariate linear regressions analyses. The regression models were developed using a stepwise backwards approach, meaning that individual variables were deleted from the models by a process of elimination based on their lack of statistical significance. Due to the relatively small sample size, all variables with a probability of .15 or less were retained in the models.

Results

The reported results are for a subset of 97 patients, as there were 3 patients for whom there was missing information. The characteristics of the sample are reported in Table 1. Seventy-four had no family history of MS, 22 did have a family history, and one adopted patient did not know. The type of MS was clinically definite[12] for the majority (85), and the clinical course was

Table 1: Sample characteristics.

Gender	Male	33
	Female	64
Family History	No	74
	Yes	22
	Unknown (Adopted)	1
Type of MS	Clinically Definite	85
	Lab-Supported Definite	1
	Clinically Probable	7
	Lab-Supported Probable	4
Clinical Course[12,13]	Chronic Progressive	39
	Relapsing Progressive	13
	Relapsing Remitting	41
	Mild Benign	4
Age	Age	46.98
	Standard Deviation	12.2
Age at Diagnosis	Age	37.31
	Standard Deviation	10.0
EDSS	Not Done	2
	Score = 0	2
	Score = 1	11
	Score = 1.5	5
	Score = 2	8
	Score = 2.5	3
	Score = 3	9
	Score = 3.5	2
	Score = 4	4
	Score = 4.5	3
	Score = 5	3
	Score = 5.5	1
	Score = 6	12
	Score = 6.5	5
	Score = 7	7
	Score = 7.5	13
	Score = 8	5
	Score = 8.5	2

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either chronic progressive (39) or relapsing remitting[13] (41) for most of the sample. Scores on the EDSS were clustered around 1 - 3 in 38 patients, indicative of a fairly low severity, and around 6 - 7 for 37 patients, indicating high severity.

Mean scores for the eight domains of the health survey are presented in Table 2, and Pearson correlation coefficients between these eight domains and the EDSS scores are summarized in Table 3. There was a highly significant relationship between the EDSS score and the physical subscale of the questionnaire (–0.667, $p < 0.001$), indicating that the two are measuring a similar concept. No other relationships were significant, although the correlation between the EDSS score and the social domain approached significance ($p = 0.07$).

Least squares linear regression models were developed to measure the association between the independent variables (Appendix) and the domain scores of the health survey (dependent variables). Initially interventions such as referrals to specialists and use of anti-spasticity, chronic pain and anti-fatigue medications were included in the models. However, there was a high level of colinearity between these variables and the medical and physiologic characteristics indicative of very severe MS. Since only the most severely affected patients required these interventions, the interventions became highly predictive of a poor outcome, rather than the underlying patient characteristics they were associated with. Since the sample size was too small to do subsample analyses, it was not possible to analyze the impact of the interventions within classes of patients. The predictive models discussed below use only the socio-demographic and medical characteristics and the physiologic measures outlined in Appendix 1.

Table 4 outlines the patient variables associated with each of the eight domains of the health survey. The individual relationships are addressed in the discussion below. The overall models for each of the eight subscales were statistically significant, with the F-ratios ranging from 4.509 ($p < 0.005$) for the general health subscale to 18.259 ($p < 0.001$) for the physical subscale. The corresponding adjusted multiple r^2 ranged from .10 for the general health domain to .48 for the physical domain.

Discussion

The first objective of this study was to measure HRQOL and examine for correlations between the different domains and disability as quantified by the EDSS. These patients scored particularly low in the three domains of physical functioning, role limitations due to physical problems, and energy/vitality. For these three domains, patient scores were well below those of a representative sample of the non-institutionalized general US population. This US population consisted of a mixture of males and females aged 45 - 54.[14] The differences between our patient group and the general population reached statistical significance for the physical functioning domain only, possibly due to our small sample size and the resulting large standard deviations.

Two recent abstracts have reported HRQOL in MS patients using the RAND survey in one study[15] and a modified version in the other.[16] MS patients scored lower than the general population on physical and social functioning, role limitations and energy subscales. When compared to diabetics and patients with epilepsy, the MS patients demonstrated lower physical and social functioning. Rudick et al.[17] used a different instrument to measure HRQOL in patients with MS, rheumatoid arthritis and inflammatory bowel disease. Their questionnaire, unlike the RAND survey, provides a total overall score. HRQOL was poorest in the MS group and the highest in the patients with inflammatory bowel disease.

Disability as quantified by the EDSS correlated only with the physical functioning domain, although there was a strong trend with the social domain. However, the RAND survey appears to provide clinicians with much more information about patient functional status than the EDSS. It is our impression that this additional information regarding emotional well-being, vitality, and physical and emotional ability to maintain role function provides useful insights into health status and coping mechanisms, and may assist in planning the care of these patients.

The regression models presented in Table 4 provide useful insights into those variables which determine patient reported health-related quality of life. For the physical functioning domain, patients with a family history of MS, those who need assistive devices and those who have had MS for a longer period of time tend to score lower than those who do not have these characteristics. Patients who are currently working and those who have successfully quit smoking tend to have higher scores. Higher income is the only factor which raises scores in the domain measuring role limitations due to physical problems, while having clinically definite and clinically probable MS, thyroid problems and a longer period of time between onset of symptoms and diagnosis of MS are associated with lower scores

Table 2: Scores on the Rand 36-item Health Survey 1.0*

Subscale	Mean	Standard Deviation
Physical	32.47	27.4
Role Physical	29.12	35.8
Role Emotional	55.67	43.0
Social	60.95	27.8
Pain	67.27	27.7
Emotional Well-being	68.24	20.8
Energy/Vitality	37.84	21.7
General Health	52.01	22.4

* Higher scores indicate better functioning and well-being or less pain.

Table 3: Pearson's correlation coefficients health survey domains and EDSS.

Domain	Correlation with EDSS	Probability
Physical	–0.667	0.001
Role Physical	–0.172	0.101
Role Emotional	0.015	0.889
Social	–0.190	0.070
Pain	–0.004	0.969
Emotional Well-being	–0.021	0.844
Energy/Vitality	–0.135	0.199
General Health	–0.157	0.135

High scores on the EDSS are indicative of poorer function, while high scores on the RAND health survey reflect a better level of functioning and well-being or less pain.

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Table 4: Ordinary least squares regression results for health survey domains, with coefficient and associated p-value.

Domain	Characteristic		COEF	p
Physical	Constant		48.4	0.001
	Family history	0=No 1=Yes	−11.1	0.023
	Currently working	0=No 1=Yes	13.9	0.001
	Used to smoke	0=No 1=Yes	7.5	0.076
	Use of aids	0=No 1=Yes	−21.7	0.001
	Duration (years since onset)		−0.9	0.001
Role Physical	Constant		53.5	0.003
	Income		5.5	0.005
	Clinically definite	0=No 1=Yes	−38.3	0.027
	Clinically probable	0=No 1=Yes	−48.1	0.026
	Thyroid problems	0=No 1=Yes	−27.6	0.051
	Time between onset and diagnosis		−1.7	0.008
Role Emotional	Constant		55.9	0.008
	Age		1.1	0.037
	Relapsing remitting	0=No 1=Yes	−31.5	0.001
	Seizure disorder	0=No 1=Yes	−33.6	0.046
	Assisted with survey	0=No 1=Yes	−23.9	0.016
	Duration (years since onset)		−2.0	0.002
Social	Constant		74.4	0.001
	Family history	0=No 1=Yes	−17.6	0.004
	Number of children		3.8	0.086
	Seizure disorder	0=No 1=Yes	−26.2	0.012
	Other comorbidities	0=No 1=Yes	−12.0	0.044
	Assisted with survey	0=No 1=Yes	−16.8	0.007
	Duration (years since onset)		−0.6	0.030
Pain	Constant		55.3	0.001
	Family history	0=No 1=Yes	−19.4	0.002
	Income		3.8	0.005
	Relapsing progress	0=No 1=Yes	19.0	0.013
	Headaches	0=No 1=Yes	−41.5	0.001
Emotional Well-being	Constant		79.9	0.001
	Gender	0=Male 1=Female	−9.6	0.019
	Income		1.6	0.114
	Relapsing remitting	0=No 1=Yes	−9.6	0.018
	Hist. of depression	0=No 1=Yes	−6.7	0.047
	Assisted with survey	0=No 1=Yes	−21.2	0.001
Energy/Vitality	Constant		38.9	0.001
	Family history	0=No 1=Yes	−10.3	0.036
	Number of children		2.8	0.084
	Relapsing progress	0=No 1=Yes	13.0	0.033
	Assisted with survey	0=No 1=Yes	−12.6	0.009
	Time between onset and diagnosis		−0.8	0.019
General Health	Constant		57.5	0.001
	Thyroid disorder	0=No 1=Yes	−15.8	0.084
	Seizure disorder	0=No 1=Yes	−13.4	0.142
	Assisted with survey	0=No 1=Yes	−14.7	0.005

* Due to the small sample size, all variables with a p-value of .15 or less were retained in the models.

in this domain. For the domain measuring role limitations due to emotional problems, having a relapsing remitting course of MS, a seizure disorder, requiring assistance with completing the health survey and having MS for a longer period of time are associated with lower scores, while increasing age contributes to higher scores. Number of children has a positive impact on the social functioning score, while family history, seizure disorders, other comorbidities, requiring assistance with the questionnaire and longer duration of MS all had a negative impact.

The pain domain is scored in the same manner as the other domains, in that higher scores are indicative of less pain. Both a higher income and a relapsing remitting course of MS correlate with a lower pain level, while a family history of MS and headaches are associated with more pain. Income also had a positive impact on emotional well-being, but having a relapsing remitting clinical course, history of depression, requiring assistance with the health survey, and being female all contribute to lower scores. Number of children and a relapsing progressive clinical course are associated with higher vitality and energy scores, while a positive family history, requiring assistance with the health survey and a longer time between onset of symptoms and diagnosis of MS all contribute to lower scores. Finally, having a thyroid disorder, a seizure disorder and requiring assistance with the health survey were associated with a poorer general health perceptions score.

Most of the patient variables which correlate with domains of the RAND health survey appear both intuitively correct and to have the appropriate effect in terms of the direction of the relationship (positive or negative). However, some of these correlations are worthy of additional discussion.

A family history of MS is associated with lower scores in the physical, social, pain, and energy/vitality domains of the RAND health survey. In our sample 22.7% of patients reported a family history of MS. Although these were not always verified cases of MS, this figure is close to the 19.9% reported in a large population-based study from British Columbia.[18] These results suggest that patients with a family history of MS have a more severe form of the disease as measured by HRQOL. Weinshenker et al.[19] have compared familial and sporadic MS and found no differences in disease severity or rate of progression using the DSS. Our findings are based upon patient-reported HRQOL, a multidimensional construct which would reflect not only disease activity but also psychological variables that may influence patient ratings of health status.

Seizures occur in a small proportion of patients with MS during the course of their illness.[20] This study demonstrates the negative impact of having one or more seizures on the domains of role limitations due to emotional problems, social functioning and general health perceptions.

There were too few patients in laboratory-supported definite and probable MS to compare with clinically definite patients. The finding of lower scores in the relapsing-remitting patients in role limitations due to emotional problems and emotional well-being may reflect a shorter duration of disease with less well-developed coping strategies or the emotional strain of an unpredictable illness.

In summary, HRQOL assessment in MS patients gives caregivers a broader measure of disease burden than the EDSS alone, as well as one that is patient-reported. The results of this study are consistent with published results and indicate that MS patients score poorly in a number of HRQOL domains such as physical and role functioning as well as energy or vitality. Regression models allow one to identify those patient variables which contribute to HRQOL and this information will be useful in planning and monitoring interventions.

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APPENDIX

VARIABLES COLLECTED

Sociodemographic:
- Age
- Sex
- Marital status
- Use of tobacco or alcohol
- Family history of MS
- Employment status at time of diagnosis
- Employment status at the time of registration with the clinic
- Education level
- Economic status (average family income for the year)
- Number of children

Medical Characteristics:
- Type of multiple sclerosis
- Clinical course
- Time since diagnosis
- History of psychological disorders
- Prior use of aids such as wheelchairs or canes
- Symptoms such as cerebellar signs and cognitive changes
- Comorbid conditions:
  - atherosclerotic heart disease
  - hypertension
  - headaches
  - thyroid disorder
  - seizure disorders
  - sleep disorders / apnea
  - other
- Age at onset of first neurological symptoms
- Time between diagnosis and referral to the MS clinic.

Physiologic Measures:
- Magnetic Resonance Imaging
- Oligoclonal banding
- Evoked potentials

Interventions:
- Placement in a chronic care facility
- Referrals to other specialties:
  - physiotherapy
  - occupational therapy
  - supplementary patient education
  - psychiatry
  - urology
- Medications:
  - antispacticity
  - chronic pain
  - anti-fatigue

Intermediate Outcomes:
- Number of bladder infections in the past year
- Continence
- Employment or disability pension
- Hospitalizations for exacerbations and for complications
- Marital separation or divorce in the past year

Final Outcomes:
- Score on EDSS
- Score (and sub-scores) on health survey

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