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Health-Related Quality of Life in Huntington's Disease: Which Factors Matter Most?

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Abstract: The aim of this article was to determine which aspects of Huntington's disease (HD) are most important with regard to the health-related quality of life (HrQOL) of patients with this neurodegenerative disease. Seventy patients with HD participated in the study. Assessment comprised the Unified Huntington's Disease Rating Scale (UHDRS) motor, cognitive and functional capacity sections, and the Beck Depression inventory. Mental and physical HrQOL were assessed using summary scores of the SF-36. Multiple regression analyses showed that functional capacity and depressive mood were significantly associated with HrQOL, in that greater impairments in HrQOL were associated with higher levels of depressive mood and lower functional capacity. Motor symptoms and cognitive function were not found to be as closely linked with HrQOL. Therefore, it can be concluded that, depressive mood and greater functional incapacity are key factors in HrQOL for people with HD, and further longitudinal investigation will be useful to determine their utility as specific targets in intervention studies aimed at improving patient HrQOL, or whether other mediating variables. As these two factors had a similar association with the mental and physical summary scores of the SF-36, this generic HrQOL measure did not adequately capture and distinguish the true mental and physical health-related HrQOL in HD. © 2008 Movement Disorder Society

Key words: Huntington's disease; health-related quality of life; SF-36; functional capacity; depressive mood; motor; cognition

Huntington's disease (HD) is a neurodegenerative disorder involving compromised motor function, cognitive impairment, changes in behaviour and personality, and emotional difficulties. It represents a great challenge to those who are facing the disease, as the many facets of HD make treatment and management particularly difficult, especially as there is currently no cure or disease modifying treatment available. Comprehensive care has been identified as essential involving a multidisciplinary team working with the patient, their family, spouse and those at risk of developing HD.[1] Three goals have been reported as being important in providing this comprehensive care and these are reducing the burden of symptoms, maximizing function, and ensuring that patients are aware of the future development and acquisition of signs and symptoms. All these combine to impact on health-related quality of life (HrQOL) and ultimately the primary objective of treatment is to improve the quality of life of the patient and their families.[1]

HrQOL is defined as "optimum levels of physical role (e.g., work, carer, parent) and social functioning, including relationships and perceptions of health, fitness, life satisfaction and well-being."[2] As increasing the HrQOL is the ultimate goal, it is rational to ascertain what factors affect HrQOL and how this can be improved for the patient and their family. Although studies have found that patients'[3,4] and indeed their spouses'[5,6] illness perception and coping mechanisms are associated with the HrQOL of patients with HD, only one study has directly examined disease-related

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factors and their relationship with HrQOL of patients' with HD.[7] Helder et al. found that for physical and psychosocial dimensions of the Sickness Impact Profile (SIP), disease-related variables (i.e., motor symptoms, cognitive impairment and disease duration) explained only the former but not the latter. However, depressive mood, which is common in patients with HD was not examined.[8] Since then, Ho et al.[9] validated two generic HrQOL instruments recommending the use of the SF-36 (over the SIP), and this is increasingly being used in this population. Therefore, this study examined motor, cognitive, mood, functional, demographic, and clinical variables, to determine which was most tightly linked with HrQOL in patients with HD, as measured by the SF-36. It was hypothesized that the strength of association between different disease-related variables may be different for physical and mental/psychosocial HrQOL on this instrument, with motor symptoms contributing more toward the former, and depressive mood toward the latter dimension.

PATIENTS AND METHODS

Patients were recruited from the outpatient HD clinic at the Brain Repair Centre Cambridge, UK. There were no specific exclusion criteria as we attempted to maximize diversity of the sample by approaching all patients at the clinic. The final sample comprised patients who volunteered to participate and were able to read and write in English. All assessments and measures were conducted once and collected on the same day (or in a few exceptions, within 6 months) by staff at the clinic. The sample comprised 70 participants (35 male and 35 female patients), with a mean age of 50.13 years ($\pm$11.91), and average disease duration of 7.42 years ($\pm$3.39). Thirty three were on medication (primarily antipsychotics and antidepressants), 26 were unmedicated, and there was no data for 11 participants. The average age when participants left education was 17.20 years ($\pm$2.48).

Motor symptoms were always assessed by the same experienced rater, using the Unified Huntington's Disease Rating Scale (UHDRS).[10] We separated the UHDRS total motor score into subscores for "oculomotor," "bradykinesia/finemotor," "rigidity," "dystonia," and "chorea," with higher scores indicating greater motor impairment.

Functional ability was assessed using the UHDRS Total Functional Capacity (TFC) scale as this has been widely used. It comprises items about occupation, finances, domestic chores, activities of daily living, and care level. The scale provides a total score ranging from 0 to 13, with 13 being normal functioning and 0 being severely impaired in functional capacity.

Cognition was assessed using verbal fluency and symbol digit tests from the UHDRS cognitive assessment. The total score represents the raw number of correct responses, with higher scores indicating better cognitive function.

The level of depressive mood was measured using the Beck Depression Inventory (BDI).[11] The BDI is a 21 item self-rating questionnaire giving a total score of the perceived level of depressive mood in an individual. The total score range is from 0 to 63, with scores of 0 to 9 indicating no depressive mood, 10 to 18 indicating mild to moderate depressive mood, 19 to 29 moderate to severe depressive mood, and more than 30 indicating severe depressive mood.

Health-related quality of life was assessed using the SF-36, because this scale has been validated in this sample and is the currently recommended HrQOL measure for patients with HD.[9] The SF-36 contains 36 items that break down to score eight dimensions, such as physical functioning, bodily pain, and vitality. The eight dimensions are rated on a 0 to 100 scale with 100 being no impairment of HrQOL and 0 being severe impairment. Further to these two summary scales, the physical summary score and the mental summary score, can be calculated from the eight dimension scores to give an overall assessment of physical health and mental health-related HrQOL. These are standardized using a norm based mean of 50 and standard deviation of 10, with lower scores indicating poorer HrQOL.

DATA ANALYSIS AND RESULTS

The mean scores of all assessments are detailed in Table 1. These results indicate that the mental summary score was slightly better than the physical summary score. On average, patients scored less than or close to one standard deviation below control norms (from Jenkinson et al.[12]) on all SF-36 subscales except for Mental Health, Energy/Vitality and Bodily Pain. The mean BDI score fell in the normal range, but had a large standard deviation, as did cognitive measures.

Pearson correlations were computed to assess the relationship between the mental summary score and the physical summary score and the five UHDRS motor subscores, the UHDRS total motor score, the BDI, the TFC and the cognitive scores (Table 2). Lower SF-36 mental and physical summary scores were associated with the presence of depressive symptoms and poorer functional capacity. In addition, the

TABLE 1. *Mean scores and standard deviations on all assessments*

Clinical feature	Assessment	Mean	Standard deviation
Motor	*UHDRS motor*		
	Oculomotor	5.56	4.71
	Bradykinesia/fine motor	9.69	7.97
	Rigidity	0.99	1.31
	Dystonia	1.54	2.56
	Chorea	6.60	5.34
	UHDRS total motor	24.37	18.26
Cognition	*UHDRS cognition*		
	Verbal fluency	27.67	12.08
	Symbol digit	27.34	12.54
Functional ability	*UHDRS function*		
	Total functional capacity	9.00	3.49
Depressive mood	*UHDRS function*	7.60	7.11
	Beck Depression Inventory		
	Quality of life: SF36		
	Physical functioning	66.80	34.11
	Role functioning—physical	50.60	44.58
	Bodily pain	84.45	22.97
	General health	57.43	23.69
	Vitality	59.21	23.69
	Social functioning	61.75	22.13
	Role functioning—emotional	57.62	48.13
	Mental health	71.70	19.58
	Physical summary score	26.43	39.11
	Mental summary score	19.35	41.60

UHDRS, Unified Huntington's Disease Rating Scale.

physical summary score was associated with the presence of cognitive measures and motor problems, except for dystonia.

SF-36 Mental Summary Score

Multiple regression was run first with the Mental summary score entered as the outcome variable and the five UHDRS motor subscores as the predictors in a single block. Next, further analyses were conducted with the following blocks of variables, i.e., with the two cognitive function scores, then with the BDI score and the TFC score, and finally with the demographic and clinical data (age, sex, age left education, disease duration, and on or off medication). To reduce the number of factors entered into the final analysis, only significant predictors from prior blocked analyses were included, i.e., the UHDRS bradykinesia/fine motor subscore, the BDI score, the TFC score, and medication (see Table 3 for results). The four predictor variables were found to account for 63.6% of the variance in the Mental Summary Score. On examining the standardized beta coefficients and the related *t* tests for each individual predictor, only the BDI and TFC were significantly associated with the mental summary score.

SF-36 Physical Summary Score

A second multiple regression analysis was then run using the Physical summary score as the outcome variable, with the same blocks of analysis as with the mental summary score. To reduce the number of factors entered into the final analysis, only significant predictors from prior blocked analyses were included, i.e., the UHDRS bradykinesia/fine motor subscore, the BDI score, the TFC score, age, and medication. These were entered as the predictors in the final analysis (see Table 4 for results). In this model, the predictor variables were found to account for 64.2% of the variance in the Physical summary score. On examining the standardized beta coefficients and the related *t* tests for each individual predictor, only the BDI and TFC were significantly associated with the Physical summary score.

TABLE 2. *Correlations between SF-36 mental summary score and physical summary score with disease-related measures*

	Mental summary score		Physical summary score	
	Pearson correlation	Sig. (1-tailed)	Pearson correlation	Sig. (1-tailed)
Oculomotor	−0.002	0.493	−0.257	0.016*
Bradykinesia/fine motor	−0.180	0.068	−0.470	0.000*
Rigidity	0.012	0.459	−0.228	0.029*
Dystonia	0.063	0.302	−0.175	0.073
Chorea	−0.140	0.123	−0.322	0.003*
UHDRS total motor	−0.111	0.181	−0.407	0.000*
BDI	−0.721	0.000*	−0.507	0.000*
TFC	0.424	0.000*	0.680	0.000*
Verbal fluency	0.039	0.376	0.206	0.045*
Symbol digit	0.038	0.388	0.291	0.013*

*$P < 0.05$.

UHDRS, Unified Huntington's Disease Rating Scale; BDI, Beck Depression Inventory; TFC, Total Functional Capacity Scale.

TABLE 3. *Results of multiple regression analysis on the outcome variable SF-36 mental summary score with disease-related predictors*

Predictors	Unstandardized coefficients		Standardized coefficients		
	B	Std. Error	Beta	*t*	Sig.
(Constant)	3.462	21.313		0.162	0.872
Bradykinesia/fine motor	0.415	0.634	0.085	0.655	0.515
BDI	−3.513	0.491	−0.639	−7.155	0.000
TFC	3.961	1.537	0.354	2.577	0.013
Medication	7.471	8.133	0.091	0.919	0.362

$R^2 = 0.636$; Adjusted $R^2 = 0.609$.
BDI, Beck Depression Inventory; TFC, Total Functional Capacity Scale.

DISCUSSION

This objective of this study was to determine which clinical factors were particularly linked to HrQOL in patients with HD. We found that depressive mood and functional ability were key factors associated with HrQOL, rather than motor and cognitive aspects of the disease. This contrasts with the one other study we are aware of which reported the significance of motor symptoms only in contributing toward total HrQOL.[7] However, there are several methodological differences between this study and the previous study, principally the noninclusion of mood and functional capacity in the latter study. Our study shows that when all these disease-related factors are considered together, the two factors most critically linked to HrQOL are indeed depressive mood and functional ability. These are also key factors impacting HrQOL in Parkinson's disease,[13–17] where like HD, depressive mood is common. Our findings illustrate the importance of low mood and functional ability in patients with HD, and that it is these two factors that are significantly associated with HrQOL, rather than more discrete motor and cognitive impairments, demographic or clinical factors.

Another key methodological difference with the previous study[7] was the use of a different, albeit generic, HrQOL instrument (SIP). Helder found that although the UHDRS total motor score was significantly associated with physical HrQOL, the lack of impact of disease-related variables on psychosocial HrQOL prompted Helder to suggest that a generic HrQOL instrument may not have adequately captured HrQOL in patients with HD. We used another generic instrument the SF-36, due to its advantages over the SIP[9] and found that after including mood and functional capacity measures, there was a lack of differentiation between illness-related variables associated with physical and mental (i.e., psychosocial) HrQOL. The fact that only these same two factors were significantly associated with (and to a very similar extent) both the physical and mental dimensions of HrQOL has important methodological implications for the assessment of HrQOL in HD. It highlights the limitation of using generic HrQOL scales and reinforces the importance of work toward creating a disease-specific instrument for HD,[18] better suited to capturing the unique constellation of HD signs and symptoms on HrQOL.

As the present study was cross-sectional in design, it remains for these findings to be corroborated by larger future studies. We did not systematically collect demographic data from patients who did not choose to

TABLE 4. *Results of multiple regression analysis on the outcome variable SF-36 physical summary score with disease-related predictors*

Predictors	Unstandardized coefficients		Standardized coefficients		
	B	Std. Error	Beta	*t*	Sig.
(Constant)	−15.591	29.361		−0.531	0.598
Bradykinesia/fine motor	−0.247	0.680	−0.047	−0.363	0.718
BDI	−2.429	0.523	−0.415	−4.647	0.000
TFC	6.518	1.642	0.547	3.969	0.000
Age	−0.162	0.319	−0.046	−0.508	0.614
Medication	3.914	8.815	0.045	0.444	0.659

$R^2 = 0.642$; Adjusted $R^2 = 0.608$.
BDI, Beck Depression Inventory; TFC, Total Functional Capacity Scale.

participate, and therefore acknowledge that this is a limitation of the present study. From previous work,[9] however, we know that HD nonresponders in questionnaire research are not likely to differ from responders on the UHDRS total motor scale and independence scale scores, although they may be younger and affected by HD for longer. Comprehensive large-scale longitudinal studies will be necessary to elucidate further the complex interplay between a broad range of disease-related and psychosocial factors, with the unfolding natural history of participants over time.

At present, this study establishes for the first time that the key factors with regard to HrQOL in a HD population are depressive mood changes and functional disability. Further longitudinal investigation will be useful to determine their potential utility as specific targets in intervention studies aimed at improving patient HrQOL, or whether other variables are mediating this link. This study also provides a better understanding of the perspective of patients with HD with regards to which clinical features are most pertinent to their health-related quality of life. Therefore, while the trend for research into potential biomarkers and development of discrete clinical measures in HD is important, it is also essential not to lose sight of global aspects of function and well-being, which are more "ecologically valid" from the patients' perspective. It, therefore, behoves us to develop and refine these assessment tools accordingly.

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