Movement Disorders
Vol. 17, No. 5, 2002, pp. 1064–1067

Quality of Life in Stiff-Person Syndrome

Willibald Gerschlager, MD,[1,2]* Anette Schrag, MD, PhD,[1] and Peter Brown, MD[1]

[1]*Sobell Department of Motor Neurosciences and Movement Disorders, Institute of Neurology, Queen Square, London, United Kingdom*
[2]*Department of Neurology, University of Vienna, Vienna, Austria*

Abstract: Stiff-person syndrome (SPS) is a rare, chronic disorder characterized by painful spasm and stiffness. We investigated the quality of life (QoL) in SPS patients, and identified factors associated with impairment in patients' QoL. Twenty-four SPS patients (10 men, 14 women; mean age ± S.D., 52.6 ± 9.5 years) completed the medical outcomes study Short Form health survey (SF-36), the Beck Depression Inventory (BDI), and a questionnaire asking for sociodemographic and clinical details. Extent of the disease was assessed using a distribution of stiffness score. SPS patients showed markedly reduced mean scores for all dimensions of the SF-36 when compared to norms from the general population of the United Kingdom. QoL scores showed a strong correlation with the extent of the disease. Depression was a common finding; 14 of 24 patients had depressive symptoms as evidenced by the BDI. There was a significant and strong correlation between the BDI score and several SF-36 subscores. This is the first study to address QoL in patients with SPS. We have shown that SPS has a significant impact on patients' reported QoL. The association between depression and QoL highlights the importance of recognizing and treating depression in SPS. © 2002 Movement Disorder Society

Key words: stiff-person syndrome; quality of life

Stiff-person syndrome (SPS) is a rare, chronic disorder characterized by painful spasms and stiffness. Classically, contraction of axial muscles leads to spontaneous and reflex spasms as well as axial rigidity resulting in lumbar hyperlordosis.[1] Diagnosis is supported by the finding of anti-GAD autoantibodies in the blood or cerebrospinal fluid.[2–5] Many patients suffer from diabetes mellitus type I (DM I) or other autoimmune disorders, suggesting an autoimmune basis.[2,6] However, patients in whom rigidity and spontaneous and reflex spasm involve one or more limbs rather than axial muscles are being increasingly recognized.[3,4,7,8] Both the classical form of SPS as well as variants involving the limbs may lead to progressive disability and significant impairment of well being.

*Correspondence to: Willibald Gerschlager, MD, Department of Neurology, University of Vienna, Währinger Gürtel 18-20, A-1090 Vienna, Austria. E-mail: willibald.gerschlager@univie.ac.at

Received 11 October 2001; Revised 22 January 2002; Accepted 12 February 2002

Published online 6 May 2002 in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/mds.10235

Health-related quality of life (QoL) is increasingly recognized as a valid measure in health care that takes into account the patients' own perspective of health. QoL measurements encapsulate not only the physical impact of chronic illness but also the emotional and social consequences of having a chronic condition. Little is known about the impact of SPS on QoL. The goal of this study was to assess the QoL in a cohort of SPS patients and identify clinical and sociodemographic variables that are associated with impaired QoL. Because SPS is a rare condition, we anticipated that numbers would be relatively small and we limited our analysis to testing whether age, sex, disease duration, distribution of stiffness, presence of autoimmune disease (including DM I), and depression affected QoL.

PATIENTS AND METHODS

Patients

Patients were classified as having the classical form of SPS[3] or variants involving the limbs according to established criteria.[3,4,9] Patients were recruited through two

routes. Patients who had received a diagnosis of SPS (n = 18) at the National Hospital for Neurology and Neurosurgery were invited to participate. Reports of 6 of the patients have been published recently.[10] In addition, patients were approached through a self-help group of people with SPS (n = 6). The neurologists of patients in the latter group were contacted for medical details. All patients were asked to complete and return questionnaires within 2 weeks in a stamped, addressed envelope. All subjects gave their informed consent prior to participation, and the study was carried out with approval of the local Ethical Committee. During the study, patients received the following treatment for SPS: clonazepam (n = 12), diazepam (n = 7), baclofen (n = 17), intravenous immunoglobulin (n = 6), prednisolone (n = 3), azathioprine (n = 2), cyclophosphamide (n = 1), and gabapentin (n = 3).

Measures

Disease Severity.

There are no widely accepted and validated clinical rating scales to assess the severity or extent of SPS. We adapted the distribution of stiffness scoring system[11] as an objective measure to assess the extent of disease. Involvement of each of the following areas provides a score of one and summation of the scores results in a maximum score of 5: lower trunk, upper trunk, both legs, both arms, face. This information was obtained through the patients' notes (n = 18) or the patients' neurologists (n = 6).

Health-Related Quality of Life.

QoL was assessed using the medical outcomes study short form health survey (SF-36). The SF-36 is a generic, self-administered instrument, which has been widely used in several chronic disorders.[12,13] The questionnaire contains 36 questions from which eight different subscores can be calculated (physical and social functioning, physical and emotional role limitations, mental health, energy, pain, and general health perceptions), and a physical and mental summary score can be derived from these. The maximum score of 100 indicates the best possible health state. Published norms are available from the general population of the United Kingdom for various age groups.[14]

Depression.

The Beck Depression Inventory (BDI)[15] was used to assess depression. The BDI is a 21-item questionnaire with answer options from 0 to 3 and a maximum score of 63. The cut-off point for depression was 10, which has been used in the evaluation of patients with somatic illnesses.[16] Depression was categorized as follows: 0 to 9, null to minimal; 10 to 17, mild to moderate; 18 or higher, moderate to severe depression.

Sociodemographic and Clinical Features.

We constructed a questionnaire to address sociodemographic and clinical variables. In addition, the neurologists of the patients recruited through the self-help patient organization were asked to provide the following information: (1) the results of anti-GAD antibody testing, if performed; (2) the results of electromyographic analysis; (3) the distribution of stiffness (see above) as assessed clinically at the last visit.

Statistical Analysis

Mean values were compared using the Mann Whitney *U* test. The relationship of ordinal or interval variables was assessed using Spearman's rank correlations. We determined the relationship between age, disease duration, distribution of stiffness and depression, and the scores of the SF-36. Significance levels were Bonferroni-corrected for multiple comparisons.

RESULTS

Clinical and Sociodemographic Characteristics

Thirty-two patients were contacted. The response rate was 78.1%, and the completion rate among the responders was 96%. One patient had to be excluded from the study because the questionnaires were not filled in correctly. Therefore, this study included 24 patients who completed the questionnaires, of whom 21 had predominantly axial and 3 limb involvement (Table 1). Those 8 patients who did not participate (1 died, 4 declined, 3 moved residence and contact details were not available) did not differ with respect to age, age at onset, and sex from those who participated. On average, the diagnosis was made 3.0 ± 2.2 years after the first symptom had been noticed. Seventeen patients were positive for anti-GAD antibodies and 7 patients tested negative for anti-

TABLE 1. *Clinical and demographic characteristics of 24 SPS patients*

Characteristic	Total (n = 24)	Men (n = 10)	Women (n = 14)	*P*
Age (yr)	52.6 ± 9.5	53.7 ± 9.9	51.8 ± 9.4	0.4
Age at onset (yr)	45.6 ± 9.3	47.0 ± 9.9	44.6 ± 9.0	0.2
Disease duration (yr)	7.0 ± 4.2	6.7 ± 4.1	7.2 ± 4.5	0.3
Distribution of stiffness	2.9 ± 1.1	2.3 ± 0.9	3.3 ± 1.1	0.2
BDI	10.9 ± 7.9	11.3 ± 10.4	10.6 ± 6.0	0.3

Data presented as mean score ± SD. *P* values refer to differences between men and women (Bonferroni-corrected). Distribution of stiffness scores range from 0 to 5.

BDI, Beck Depression Inventory score (range, 0–63); SPS, stiff-person syndrome.

GAD antibodies. Twelve of the 24 patients had DM I. Seven of the 24 patients had additional autoimmune diseases such as pernicious anemia (n = 3), thyroid disease (n = 3), myasthenia gravis (n = 1), Sjogren's syndrome (n = 1), and vitiligo (n = 1). Men and women, those with and without limb involvement and those with and without anti-GAD antibodies, DM I or other autoimmune diseases, did not differ significantly with respect to age, disease duration, or BDI score. Women scored worse in the distribution of stiffness score (Table 1), but this was not statistically significant.

Eleven of 24 patients were retired due to the condition, 5 were retired for other reasons, 1 was unemployed, and 7 patients were still employed. All but 3 patients were married and lived with their families.

SF-36 Scores

The results of the SF-36 scores are shown in Figure 1. The patients showed markedly reduced mean scores for all dimensions of the SF-36 compared to published norms available from the general population of the United Kingdom[14] of the age group 45 to 54 years. In particular, SPS patients scored poorly in the SF-36 subscores physical functioning and social functioning. Women had slightly poorer SF-36 physical summary scores than men (30.9 [S.D. 9.7] vs. 40.4 [SD 8.2]), but this difference was not statistically significant. Patients with or without diabetes or other autoimmune disease did not differ with respect to their SF-36 scores.

Correlation of Measures of Disease Severity with the SF-36

The distribution of stiffness score showed a negative correlation with the SF-36 subscores general health perception and vitality. Perhaps due to the small sample size, these findings were not statistically significant. Disease duration did not correlate with any of the SF-36 scores (Table 2).

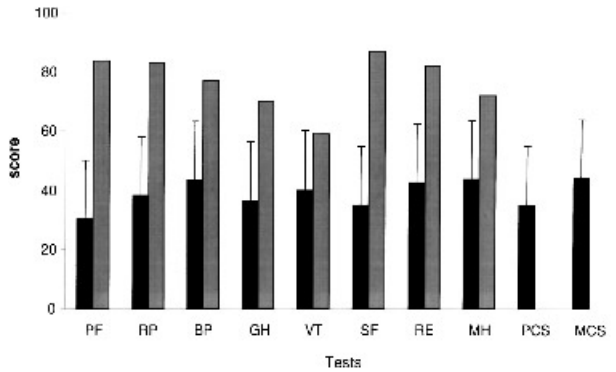

FIG. 1. Results (mean ± S.D.) of the eight dimensions and the two summary scores of the SF-36 in SPS patients (black bars) and the general UK population of the age group 44 to 54 years (grey bars; Brazier et al., 1992). PF, physical functioning; RP, role limitations physical; BP, bodily pain; GH, general health perceptions; VT, vitality; SF, social functioning; RE, role limitations emotional; MH, general mental health; PCS, physical summary score; MCS, mental summary score. A maximum score of 100 indicates the best possible health state.

Beck Depression Inventory

Ten patients had a BDI score between 10 and 17, indicating mild to moderate depression, and 4 patients had a score higher than 17, indicating moderate to severe depression. Ten patients had a score between 0 and 9 (no depression). The BDI score had a significant negative correlation (Table 2) with the SF-36 mental summary score and with the SF-36 scores of physical role limitation, vitality, social functioning, emotional role limitation, and general mental health.

DISCUSSION

This study is the first to report on QoL in a reasonable sample of SPS patients. We found that QoL is markedly impaired in all domains of the SF-36, when compared with norms from the general population of the United Kingdom.[14] In particular, SPS patients had impaired functioning in the subscores social functioning and physical functioning of the SF-36. This finding suggests that SPS patients have difficulties performing their normal social activities in addition to the physical problems caused by the disease and may reflect a tendency to withdraw from social activities. Corresponding with clinical observation, pain also seems to be a significant feature of SPS as demonstrated by the reduced SF-36 QoL score for pain, indicating significant experience of pain.[3,11]

The QoL subscores general health perceptions and vitality tended to be lower in patients with a higher extent of stiff areas, as assessed in the distribution of stiffness score. Yet, there was no correlation between disease duration and SF-36 scores. This may reflect the fact that,

TABLE 2. *Spearman correlation coefficients of the quality of life (SF-36) scores with clinical characteristics*

SF-36 scores	Age (yr)	Disease duration	Distribution of stiffness	BDI
Physical functioning	−0.51	−0.23	−0.26	−0.25
Role limitations, physical	−0.11	0.16	−0.30	−0.54[a]
Bodily pain	−0.21	−0.07	−0.39	−0.31
General health perceptions	0.18	0.07	−0.57	−0.49
Vitality	−0.02	0.14	−0.58	−0.75[a]
Social functioning	0.16	0.23	−0.39	−0.66[a]
Role limitations, emotional	0.14	0.40	−0.18	−0.64[a]
General mental health	0.19	0.27	−0.34	−0.74[a]
Physical summary score	−0.42	−0.25	−0.38	−0.19
Mental summary score	0.29	0.39	−0.31	−0.75[a]

[a]$P < 0.05$ (Bonferroni corrected).
BDI, Beck Depression Inventory score.

after a few years, classical SPS, from which most patients in this study suffered, is no longer a progressive disease. Alternatively, this lack of correlation may be explained by the patients' increased adaptation to a chronic disorder after longer disease duration.

Depression, as assessed by the BDI, was a common finding in the current study. Fourteen of 24 patients had depressive symptoms and 4 of the 14 patients had scores in the moderate to severe depression range. We could not identify any particular sociodemographic and clinical variables associated with depression. This association between depression and QoL score is in keeping with that reported in other chronic disorders.[17–19] In addition, there are reports of an association of SPS and psychiatric symptoms. Recently, it was described that 4 of 9 patients with SPS had task-specific fear months before the onset of motor symptoms and 6 of 9 developed task-specific fear after the onset of motor symptoms.[20] Yet, only 1 SPS patient developed depression after the onset of motor symptoms. Tinsley and coworkers[21] found that 12 of 24 SPS patients had psychiatric morbidity, including anxiety, depression, and substance abuse. The authors speculated that abnormalities of the GABA-system cause not only neurological features but are responsible for psychiatric symptoms as well. However, an alternative explanation is the reverse causality of severe, chronic illness inducing depression and anxiety. Further prospective studies are required to investigate this question. Independent of the causal relationship, the demonstrated association between depression and impaired QoL underscores the importance of recognizing and treating depression in these patients, especially as treating depression in medical conditions may improve QoL.[22]

The main limitation of the current study is the small sample size as, due to the rarity of the disease, only 24 patients were included. In addition, there was some inhomogeneity in the group of patients studied. Three had involvement of the limbs rather than classical axial SPS, and the study included patients testing positive as well as negative for the anti-GAD antibody. However, it is noteworthy that there was no significant difference between QoL scores of those with limb involvement and those with classic axial SPS or those with and without anti-GAD antibodies.

In conclusion, we have shown that SPS has a significant impact on patient-reported QoL and that more extensive stiffness is associated with worse QoL scores. In addition, depression was also common in patients with SPS and appeared to be associated with worse QoL in these patients. The results of this study highlight the importance of recognizing and treating depression in this condition.

REFERENCES

1. Moersch FP, Woltman HW. Progressive fluctuating muscular rigidity and spasm (stiff man syndrome): report of a case and some observations in 13 other cases. Mayo Clin Proc 1956;31:421–427.
2. Solimena M, Folli F, Aparisi R, et al. Autoantibodies to GABA-ergic neurons and pancreatic beta cells in stiff-man syndrome. N Engl J Med 1990;322:1555–1560.
3. Barker RA. Revesz T, Thom M, Marsden CD, Brown P. Review of 23 patients affected by the stiff man syndrome: clinical subdivision into stiff trunk (man) syndrome, stiff-limb syndrome, and progressive encephalomyelitis with rigidity. J Neurol Neurosurg Psychiatry 1998;65:633–640.
4. Brown P, Marsden CD. The stiff man and stiff man plus syndromes. J Neurol 1999;246:648–652.
5. Shaw PJ. Stiff-man syndrome and its variants. Lancet 1999;353: 86–87.
6. Blum P, Jancovich J. Stiff-person syndrome: an autoimmune disease. Mov Disord 1991;6:12–20.
7. Brown P, Rothwell JC, Marsden CD. The stiff leg syndrome. J Neurol Neurosurg Psychiatry 1997;62:31–37.
8. Saiz A, Graus F, Valldeoriola F, Valls-Sole J, Tolosa E. Stiff-leg syndrome: a focal form of stiff-man syndrome. Ann Neurol 1998; 43:400–403.
9. Lorish TR, Thorsteinsson G, Howard FM. Stiff-man syndrome updated. Mayo Clin Proc 1989;64:629–636.
10. Gerschlager W, Brown P. Effect of treatment with intravenous immunoglobulin on quality of life in patients with stiff-person syndrome. Mov Disord 2002:DOI 10.1002/mds.10043.
11. Dalakas MC, Fujii M, Li M, McElroy B. The clinical spectrum of anti-GAD antibody-positive patients with stiff-person syndrome. Neurology 2000;55:1531–1535.
12. McHorney CA, Ware JE Jr, Raczek AE. The MOS 36-item short-form health survey (SF-36). II. Psychometric and clinical tests of validity in measuring physical and mental health constructs. Med Care 1993;31:247–263.
13. Schrag A, Jahanshahi M, Quinn N. How does Parkinson's disease affect quality of life? A comparison with quality of life in the general population. Mov Disord 2000;6:1112–1118.
14. Brazier JE, Harper R, Jones NMB, et al. Validating the SF-36 health survey questionnaire: a new outcome measure for primary care. Br Med J 1992;305:160–164.
15. Beck AT, Ward C, Mendelsohn M, et al. An inventory for measuring depression. Arch Gen Psychiatry 1961;4:561–567.
16. Beck AT, Steer RA, Garbin MG. Psychometric properties of the Beck Depression Inventory: twenty-five years of evaluation. Clinl Psychol Rev 1988;8:77–100.
17. Schrag A, Jahanshahi M, Quinn N. What contributes to quality of life in patients with Parkinson's disease? J Neurol Neurosurg Psychiatry 2000;69:308–312.
18. Karlsen KH, Larsen JP, Tandberg E, Maeland JG. Influence of clinical and demographic variables on quality of life in patients with Parkinson's disease. J Neurol Neurosurg Psychiatry 1999;66: 431–435.
19. Williams LS, Weinberger M, Harris LE, et al. Measuring quality of life in a way that is meaningful to stroke patients. Neurology 1999;53:1839–1843.
20. Henningsen P, Clement U, Küchenhoff J, Simon F, Meinck HM. Psychological factors in the diagnosis and pathogenesis of stiff-man syndrome. Neurology 1996;47:38–42.
21. Tinsley JA, Barth EM, Black JL, Williams DE. Psychiatric consultations in stiff-man syndrome. J Clin Psychiatry 1997;58:444–449.
22. Lamberg L. Treating depression in medical conditions may improve quality of life. JAMA 1996;276:857–858.