Subjective symptom impact on quality of life in patients with myotonic dystrophy

CURRENT STATUS: POSTED

Haruo Fujino
Department of Special Needs Education, Oita University and Graduate School of Human Sciences, Osaka University
ORCID: https://orcid.org/0000-0002-8889-1199

Toshio Saito
Department of Neurology, National Hospital Organization Toneyama National Hospital

Masanori P. Takahashi
Department of Functional Diagnostic Science, Osaka University Graduate School of Medicine and Department of Neurology, Osaka University Graduate School of Medicine

Hiroto Takada
Department of Neurology, National Hospital Organization Aomori National Hospital

Takahiro Nakayama
Department of Neurology, Yokohama Rosai Hospital

Osamu Imura
Graduate School of Human Sciences, Osaka University

Tsuyoshi Matsumura
Department of Neurology, National Hospital Organization Toneyama National Hospital

DOI: 10.21203/rs.2.35/v1

SUBJECT AREAS
Interdisciplinary Medicine
Abstract
Background: Although functional impairment in patients with myotonic dystrophy is an important determinant of quality of life (QoL), it is possible that QoL could further be influenced by the subjective evaluation of symptoms. The aim of this study was to investigate the subjective symptom impact on the QoL, after controlling for functional impairment. Methods: Eligible patients with myotonic dystrophy type 1 (DM1) were recruited from four hospitals in Japan. Subjective symptom impact across four domains (muscle weakness, fatigue, pain, and myotonia) and overall QoL were evaluated using the Individualized Neuromuscular Quality of Life (INQoL) questionnaire. Functional impairment was assessed using the modified Rankin scale. Results: Eighty-six patients with DM1 were included in this study. On multiple regression analysis, a portion of the variance in the overall QoL was significantly accounted for by demographic variables and functional impairment (adjusted R² = 0.32). In addition to these variables, subjective symptom impact (muscular weakness, fatigue, and myotonia) explained additional variance in the overall QoL (adjusted R² = 0.80). Difficulties in activities of daily living and participation caused by each symptom consistently predicted overall QoL across three symptom domains (muscular weakness, fatigue, and myotonia). Conclusions: Subjective symptom impact needs to be considered, in addition to functional impairment, when evaluating the QoL of patients with DM1.

Background
Myotonic dystrophy type 1 (DM1) is the most common muscular dystrophy in adults, and is characterized by various symptoms, including progressive muscular weakness, fatigue, and myotonia [1]. These symptoms of the disease often influence patients’ lives, including daily activities and social participation, which negatively impact quality of life (QoL) [2, 3]. Generally, the severity of symptoms of the disease is considered as the strongest predictor of QoL [4]. Functional impairment is one of the major factors that affect activities of daily living and social participation in neuromuscular disorders; however, psychosocial and subjective factors also have a substantial contribution on QoL [5-8]. Recently, patient-reported outcomes have increasingly been considered as important factors in clinical trials [2, 9]. Although the severity of symptoms have been well-studied in neuromuscular
disorders, the impact of subjective assessment of difficulties in activities and participation and the importancel of these difficulties on patients’ assessment of their QoL has not been well investigated. As well, the assessment of symptoms by a clinician and the subjective evaluation of symptoms by patients may differ [10]. Therefore, patients’ QoL could be affected by subjective evaluation of symptom severity and limitations in activities and restriction in participation associated with muscular diseases [11, 12]. Consequently, patients with similar severity of symptoms, their QoL may differ depending on the limitations and restrictions experienced and the importance of these activities and of participation for an individual. Therefore, the subjective feature of the disease burden may affect variability in QoL among patients with DM1. As such, in the current study, we examined the hypothesis that the subjective symptoms impact will explain QoL after controlling for functional impairment.

Methods

Participants

Patients were recruited from four hospitals in Japan (Toneyama National Hospital, Aomori National Hospital, Osaka University Hospital, and Yokohama Rosai Hospital). The eligibility criteria for patients were as follows: genetic or clinical diagnosis of DM1; age ≥18 years; and provision of informed consent, after the procedures had been fully explained. Because the data were collected as part of a larger study, some of the data included in the analysis overlapped with those from our previous study [13].

Ethics, consent and permissions

Informed consent was obtained from all patients participated in this study. This study was conducted in accordance with the World Medical Association's Declaration of Helsinki and was approved by the institutional review board at each institution.

Measures

Subjective symptom impact and QoL

The subjective burden of symptoms and quality of life were measured using the Japanese version of the Individualized Neuromuscular Quality of Life (INQoL) [13, 14] which includes common symptoms
of neuromuscular diseases, i.e., muscular weakness, pain, fatigue, and myotonia. Each symptom domain is evaluated on three scales: a. severity of the symptom, b. difficulties caused by the symptom, and c. the importance of the difficulties caused by the symptom to the person. Symptom scores range from 0 to 100, and indicate subjective impact of each symptom. A higher score indicates greater symptom impact.

The QoL index is calculated from Life domain scales of the INQoL including aspects of independence, social relationships, emotions, and body image, apart from symptom scales. Thus, the QoL index represents a patient's overall QoL on a scale of 0 to 100. A higher score is indicative of worse QoL.

Functional impairment

We assessed functional impairment using the modified Rankin Scale (mRS) [15], which has previously been used as an index of functional impairment in neuromuscular disorders [13, 16]. The mRS was evaluated by each patient’s primary physician, with scores ranging from 0 (no symptoms) to 5 (severe disability).

Statistical analysis

Statistical analyses were performed using R 3.4.1 statistical software (R Core Team, Vienna, Austria). Associations between subjective symptom impact and QoL were evaluated using Pearson’s correlation coefficient. We used a two-step multiple linear regression model to assess the relative contribution of the subjective symptom impact to the overall QoL, after controlling for demographic variables (sex, age, years of education, disease duration, and employment status) and functional impairment (mRS). Because this study did not aim to examine the association between QoL and the molecular pathophysiology of the disease, the number of CTG repeats was not included as an independent variable in multiple regression models. Significant contributing variables were further analyzed using multiple linear regression to evaluate which aspect of subjective evaluation (a. severity of the symptom, b. difficulties caused by the symptom, and c. importance of the difficulties caused by the symptom to the patient) explains QoL. In multiple regression analysis, we also calculated the variance inflation factor (VIF) to assess potential multicollinearity between the predictor variables, where a VIF >10 was indicative of multicollinearity between predictors, and a VIF of 5–10 suggestive of a
multicollinearity problem. We applied a ridge regression analysis if the VIF indicated presence of multicollinearity among variables. The ridge regression is an alternative approach to ordinary least squares (OLS) regression when the predictor variables are strongly correlated. The significance level was set at a two-tailed \( p < 0.05 \).

Results
Eighty-six patients with DM1 were included in this study (Table 1), with the majority having genetically confirmed DM1 (\( n = 79; 92\% \)). The overall QoL was significantly correlated to patients’ subjective symptom impact (Table 2). Functional impairment was also moderately correlated with QoL (\( r = 0.45, p < 0.001 \)).

Demographic variables and functional impairment were entered into model 1, with overall QoL being significantly explained by disease duration and functional impairment (\( F = 7.7, p < 0.001, \text{adjusted } R^2 = 0.32 \) [95% CI: 0.12–0.42]). Longer disease duration and higher functional impairment resulted in lower QoL (Table 3). The subjective symptom impact was then added as a predictor variable (model 2), with the subjective impact in the domains of weakness, fatigue and myotonia explaining a significant proportion of the variance in overall QoL, even after controlling for demographic variables and functional impairment (Table 3). Model 2 explained 80% of the variance in overall QoL (\( F = 35.9, p < 0.001, \text{adjusted } R^2 = 0.80 \) [95% CI: 0.69–0.83]), with higher subjective symptom impact in weakness, fatigue and myotonia resulting in lower QoL. The explained variance in the overall QoL was significantly increased after entering symptom impact (\( F = 46.1, p < 0.001, \Delta R^2 = 0.48 \)), with symptom impact variables (entered in model 2) explaining an additional 71% of the unexplained variance in QoL by the model 1 (\( \text{partial } R^2 = 0.71 \) [95% CI: 0.56–0.76]). VIF values for multicollinearity were not greater than the threshold in either model 1 or 2 (VIF < 3.0).

We further analyzed which aspect of the symptom domains identified as significant predictors in model 2 contributed to the overall QoL. The overall QoL was significantly explained by different aspect depending on the domains (Table 4). Difficulties were a significant predictor of QoL in all three domains (weakness, fatigue and myotonia). In contrast, symptom severity was significant in the fatigue domain (standardized coefficient = 0.32), whereas the importance of the difficulties was
significant in the weakness domain (standardized coefficient = 0.40). However, the VIF was indicative of multicollinearity among variables in weakness (VIF, 3.8–6.7) and fatigue (VIF, 4.1–5.5) domains, with large confidence intervals of coefficients (Table 4). A problem of multicollinearity was also identified in the myotonia domain (VIF, 5.3–9.2), with large confidence intervals of coefficients and an association with overall QoL which was in the direction opposite to the bivariate correlation (e.g., myotonia, severity aspect). Analysis of outcomes using a ridge regression to reduce the influence of multicollinearity provided a similar pattern of coefficients for each item in the domains, although the magnitude of coefficients were reduced relative to the results of the OLS regression (Supplemental Table S1).

Discussion
The subjective symptom impact explained a significant proportion of overall QoL, after controlling for demographic variables and functional impairment, among patients with DM1. Our findings are in agreement with previous studies that have reported disease duration and functional impairment to be associated with QoL [17-19], although the relative contribution of these variables was limited when subjective symptom impact was explained in the present study. In fact, a substantial portion of QoL was explained, in our study group, by patients’ subjective evaluation of the burden caused by muscular weakness, fatigue, and myotonia. Of these subjective factors, muscle weakness was the strongest predictor of QoL, within the domains examined in this study.

Most activities of daily living are strongly influenced by muscle weakness in patients with neuromuscular diseases, which naturally leads to worse QoL, with fatigue and myotonia having an effect on function in social participation and daily activities, to which muscle weakness also contributes [20]. Because QoL is a subjective phenomenon, patient evaluation of symptoms would comprise an important part of QoL in addition to objective assessment of the severity of the disease [2, 3]. As previously reported, the subjective evaluation of the symptom impact may also differ by symptoms [20]. Reducing the burden of these symptoms could be an important target for interventions to improve QoL in patients with myotonic dystrophy. Of note, pain was associated with QoL only in bivariate correlation, indicative that pain had a lower influence on QoL than other
symptom domains evaluated (fatigue, weakness and myotonia), which is in agreement with previous studies [17, 21].

Difficulties caused by each symptom consistently predicted overall QoL across the three symptom domains, with resultant difficulties in activities of daily living directly influencing the physical and social components of QoL [2]. Therefore, improving the burden of fatigue, weakness and myotonia could improve a patient’s QoL. However, careful interpretation of the strength of the influence of these symptoms on QoL due to the potential of bias from multicollinearity, even after applying a ridge regression. Further confirmation in future studies is necessary.

Our study suggest substantial influences of subjective symptom impact on QoL among patients with DM1, which might account for disparity between objective disease severity progression and QoL that has been reported in a few longitudinal studies [22-24]. It is possible that QoL and symptom impact could be influenced by a response shift phenomenon, defined as a change in internal standards [3, 25]. Patients’ perceived impact of the disease is an important mediator of QoL, which may explain the noted variation in QoL among patients with similar severity of a condition. In fact, disease perception is one of the determinants of coping and/or psychological distress [7, 26]. Therefore, although definitive evidence of the effectiveness of psychosocial interventions for patients with muscular diseases is unavailable [27], it is plausible to consider that psychosocial interventions, such as cognitive behavior therapy or neuropsychological interventions, could optimize QoL in these patients [28-30]. A recent randomized controlled trial for fatigued patients with DM1 showed cognitive behavioral therapy could increase patient’s perceived capacity for activity and social participation, whereas there were no significant differences in disease burden and QoL between intervention and standard care group [31]. Although such results were affected by the fact that the intervention did not focused on subjective disease burden and QoL, more direct intervention may be needed [32].

Limitations

The limitations of our study should be acknowledged. First, although the INQoL covers the major components of QoL for patients with DM1, the relative importance of contributing factors could be affected by the underlying concept of QoL measured. Recently, the Myotonic Dystrophy Health Index,
which measures the burden of disease in myotonic dystrophy, is available and has been validated in several languages [33-36]. The INQoL is rather a measure of how disease symptoms impact on the patient’s perspective. The combination of the two instruments would be desirable to detect subjective experience of the disease in patients. Second, we could not examine environmental factors which would affect patients’ QoL, such as social and welfare support which are known to have an impact on patients’ QoL [6]. Third, cognitive impairment, awareness of the disease, and apathy, which are associated with disease severity, may partially moderate associations between subjective evaluation of disease impact and QoL [10, 37, 38].

Conclusions
Our findings indicate that subjective symptom impact affects QoL, in addition to functional impairment, among patients with DM1. Difficulties caused by DM1 symptoms are key predictor of QoL, in addition to severity of symptoms.

Declarations
Ethics approval and consent to participate
All procedures performed in studies involving human participants were in accordance with the ethical standards of the each institutional research committee and with the 1964 Helsinki declaration and its later amendments.

Consent for publication
Not applicable.

Availability of data and material
The datasets generated and/or analysed during the current study are not publicly available due to privacy constraints relating to the ethical approval but are available from the corresponding author on reasonable request.

Competing interests
The authors declare that they have no competing interests.

Funding
This work was supported in part by research grants from the Japan Agency for Medical Research and
Development AMED (Practical Research Project for Rare / Intractable Diseases, 16ek0109172 and 17ek0109259), the Ministry of Health and Welfare of Japan (H28-Nachitou(Nan)-Ippan-030), and the Japan Society for the Promotion of Science KAKENHI (17K14067). The funders had no role in the study design, data collection and analyses, decision to publish, or preparation of the manuscript.

Authors' contributions

HF was critically involved in the design, data collection, the analysis and interpretation of the data and wrote the draft of manuscript. HF, MPT, OI, and TM involved development of study concept. OI was critically involved in the design and interpretation of the data. TS, MPT, HT, TN, and TM were involved in the patient recruitment and the clinical assessments. All authors contributed intellectually to the data interpretation and approved the final manuscript.

Acknowledgements

Not applicable.

Availability of Data and Materials

The datasets generated and/or analysed during the current study are not publicly available due we do not have approval to make the data publically available.

References

1. Turner C, Hilton-Jones D. The myotonic dystrophies: diagnosis and management. J Neurol Neurosurg Psychiatry. 2010;81:358-67.

2. Bann CM, Abresch RT, Biesecker B, Conway KC, Heatwole C, Peay H, et al. Measuring quality of life in muscular dystrophy. Neurology. 2015;84:1034-42.

3. Burns TM, Graham CD, Rose MR, Simmons Z. Quality of life and measures of quality of life in patients with neuromuscular disorders. Muscle Nerve. 2012;46:9-25.

4. Graham CD, Rose MR, Grunfeld EA, Kyle SD, Weinman J. A systematic review of quality of life in adults with muscle disease. J Neurol. 2011;258:1581-92.

5. Bos I, Wynia K, Almansa J, Drost G, Kremer B, Kuks J. The prevalence and severity of disease-related disabilities and their impact on quality of life in neuromuscular diseases. Disabil Rehabil. 2018:1-6.
6. Gagnon C, Mathieu J, Jean S, Laberge L, Perron M, Veillette S, et al. Predictors of disrupted social participation in myotonic dystrophy type 1. Arch Phys Med Rehabil. 2008;89:1246-55.

7. Graham CD, Weinman J, Sadjadi R, Chalder T, Petty R, Hanna MG, et al. A multicentre postal survey investigating the contribution of illness perceptions, coping and optimism to quality of life and mood in adults with muscle disease. Clin Rehabil. 2014;28:508-19.

8. Natterlund B, Ahlstrom G. Activities of daily living and quality of life in persons with muscular dystrophy. J Rehabil Med. 2001;33:206-11.

9. Symonds T, Randall JA, Campbell P. Review of patient-reported outcome measures for use in myotonic dystrophy type 1 patients. Muscle Nerve. 2017;56:86-92.

10. Baldanzi S, Bevilacqua F, Lorio R, Volpi L, Simoncini C, Petrucci A, et al. Disease awareness in myotonic dystrophy type 1: an observational cross-sectional study. Orphanet J Rare Dis. 2016;11:34.

11. Ahlstrom G, Sjoden PO. Coping with illness-related problems and quality of life in adult individuals with muscular dystrophy. J Psychosom Res. 1996;41:365-76.

12. Geirdal AO, Lund-Petersen I, Heiberg A. Understanding the experience of myotonic dystrophy. Mixed method study. J Genet Couns. 2015;24:169-78.

13. Fujino H, Saito T, Takahashi MP, Takada H, Nakayama T, Ogata K, et al. Validation of the Individualized Neuromuscular Quality of Life in Japanese patients with myotonic dystrophy. Muscle Nerve. 2018.

14. Vincent KA, Carr AJ, Walburn J, Scott DL, Rose MR. Construction and validation of a quality of life questionnaire for neuromuscular disease (INQoL). Neurology. 2007;68:1051-7.

15. van Swieten JC, Koudstaal PJ, Visser MC, Schouten HJ, van Gijn J. Interobserver agreement for the assessment of handicap in stroke patients. Stroke. 1988;19:604-7.

16. Seesing FM, van Vught LE, Rose MR, Drost G, van Engelen BG, van der Wilt GJ. The individualized neuromuscular quality of life questionnaire: cultural translation and psychometric validation for the Dutch population. Muscle Nerve. 2015;51:496-500.

17. Laberge L, Mathieu J, Auclair J, Gagnon E, Noreau L, Gagnon C. Clinical, psychosocial, and central correlates of quality of life in myotonic dystrophy type 1 patients. Eur Neurol. 2013;70:308-15.
18. Rakocevic-Stojanovic V, Peric S, Madzarevic R, Dobricic V, Ralic V, Ilic V, et al. Significant impact of behavioral and cognitive impairment on quality of life in patients with myotonic dystrophy type 1. Clin Neurol Neurosurg. 2014;126:76-81.

19. Sansone VA, Panzeri M, Montanari M, Apolone G, Gandossini S, Rose MR, et al. Italian validation of INQoL, a quality of life questionnaire for adults with muscle diseases. Eur J Neurol. 2010;17:1178-87.

20. Heatwole C, Bode R, Johnson N, Quinn C, Martens W, McDermott MP, et al. Patient-reported impact of symptoms in myotonic dystrophy type 1 (PRISM-1). Neurology. 2012;79:348-57.

21. Sansone VA, Ricci C, Montanari M, Apolone G, Rose M, Meola G. Measuring quality of life impairment in skeletal muscle channelopathies. Eur J Neurol. 2012;19:1470-6.

22. Natterlund B, Gunnarsson LG, Ahlstrom G. Disability, coping and quality of life in individuals with muscular dystrophy: a prospective study over five years. Disabil Rehabil. 2000;22:776-85.

23. Peric S, Heatwole C, Durovic E, Kacar A, Nikolic A, Basta I, et al. Prospective measurement of quality of life in myotonic dystrophy type 1. Acta Neurol Scand. 2017;136:694-7.

24. Peric S, Vujnic M, Dobricic V, Marjanovic A, Basta I, Novakovic I, et al. Five-year study of quality of life in myotonic dystrophy. Acta Neurol Scand. 2016;134:346-51.

25. Sprangers MA, Schwartz CE. Integrating response shift into health-related quality of life research: a theoretical model. Soc Sci Med. 1999;48:1507-15.

26. Rose MR, Sadjadi R, Weinman J, Akhtar T, Pandya S, Kissel JT, et al. Role of disease severity, illness perceptions, and mood on quality of life in muscle disease. Muscle Nerve. 2012;46:351-9.

27. Walklet E, Muse K, Meyrick J, Moss T. Do psychosocial interventions improve quality of life and wellbeing in adults with neuromuscular disorders? A systematic review and narrative synthesis. J Neuromuscul Dis. 2016;3:347-62.

28. Graham CD, Kemp S, Radakovic R, Kapur N. Clinical neuropsychology in the management of myotonic dystrophy. Muscle Nerve. 2018;57:701-4.

29. Graham CD, Simmons Z, Stuart SR, Rose MR. The potential of psychological interventions to improve quality of life and mood in muscle disorders. Muscle Nerve. 2015;52:131-6.

30. van Engelen B. Cognitive behaviour therapy plus aerobic exercise training to increase activity in
patients with myotonic dystrophy type 1 (DM1) compared to usual care (OPTIMISTIC): study protocol for randomised controlled trial. Trials. 2015;16:224.

31. Okkersen K, Jimenez-Moreno C, Wenninger S, Daidj F, Glennon J, Cumming S, et al. Cognitive behavioural therapy with optional graded exercise therapy in patients with severe fatigue with myotonic dystrophy type 1: a multicentre, single-blind, randomised trial. Lancet Neurol. 2018;17:671-80.

32. Gagnon C, Gallais B, Laberge L. Myotonic dystrophy type 1: reasons to be OPTIMISTIC. Lancet Neurol. 2018;17:652-3.

33. Gagnon C, Tremblay M, CoTe I, Heatwole C. French translation and cross-cultural adaptation of the Myotonic Dystrophy Health Index. Muscle Nerve. 2018;57:686-9.

34. Heatwole C, Bode R, Johnson N, Dekdebrun J, Dilek N, Heatwole M, et al. Myotonic Dystrophy Health Index: initial evaluation of a disease-specific outcome measure. Muscle Nerve. 2014;49:906-14.

35. Heatwole C, Bode R, Johnson NE, Dekdebrun J, Dilek N, Eichinger K, et al. Myotonic dystrophy health index: Correlations with clinical tests and patient function. Muscle Nerve. 2016;53:183-90.

36. Sansone VA, Lizio A, Greco L, Gragnano G, Zanolini A, Gualandris M, et al. The Myotonic Dystrophy Health Index: Italian validation of a disease-specific outcome measure. Neuromuscul Disord. 2017;27:1047-53.

37. Fujino H, Shingaki H, Suwazono S, Ueda Y, Wada C, Nakayama T, et al. Cognitive impairment and quality of life in patients with myotonic dystrophy type 1. Muscle Nerve. 2018;57:742-8.

38. Peric S, Rakocevic Stojanovic V, Mandic Stojmenovic G, Ilic V, Kovacevic M, Parojcic A, et al. Clusters of cognitive impairment among different phenotypes of myotonic dystrophy type 1 and type 2. Neurol Sci. 2017;38:415-23.

Table 1: Demographic And Clinical Variables Of The Patients
Table 1. Demographic and clinical variables of the patients

|                          | Mean (SD) or Number [%] |
|--------------------------|--------------------------|
| Sex (male/female)        | 39/47 [male 45.3]        |
| Age                      | 46.9 (10.9)              |
| Years of education       | 13.5 (1.9)               |
| Onset age                | 30.4 (13.3)              |
| Disease duration (years) | 16.3 (11.1)              |
| Number of CTG repeats    | 689.8 (447.6)            |
| Employment               | 32 [37.2]                |
| Symptom impact           |                          |
| Weakness                 | 52.1 (26.2)              |
| Pain                     | 21.4 (27.4)              |
| Fatigue                  | 45.3 (27.1)              |
| Myotonia                 | 35.0 (30.3)              |
| Overall QoL              | 45.0 (22.6)              |

QoL: quality of life

Table 2: Correlations Between Subjective Symptom Impact And Overall QoL

|                | Pain | Fatigue | Myotonia | Overall QoL |
|----------------|------|---------|----------|-------------|
| Weakness       | 0.53 | 0.70    | 0.54     | 0.84        |
| Pain           | -    | 0.63    | 0.58     | 0.64        |
| Fatigue        | -    | -       | 0.62     | 0.76        |
| Myotonia       | -    | -       | -        | 0.63        |
| Overall QoL    | -    | -       | -        | -           |

All coefficients were significant (p < 0.001)
QoL: quality of life

Table 3: Multiple Linear Regression Models Predicting Overall QoL In Patients
Table 3. Multiple linear regression models predicting overall QoL in patients

| Predictor variable       | Model 1\(^a\) |       |       | Model 2\(^b\) |       |       |
|-------------------------|---------------|-------|-------|---------------|-------|-------|
|                         | Standardized coefficient | P-value | Standardized coefficient | P-value |
|                         | [95% CI]       |       |       | [95% CI]       |       |       |
| Demographic variables and functional impairment |       |       |       |       |       |       |
| Sex                     | -0.01 [-0.19–0.17] | 0.905 |       | 0.04 [-0.06–0.14] |       |       |
| Age                     | 0.03 [-0.18–0.23] | 0.795 |       | 0.02 [-0.10–0.13] |       |       |
| Years of education      | 0.03 [-0.15–0.22] | 0.725 |       | 0.00 [-0.10–0.10] |       |       |
| Disease duration         | 0.38 [0.18–0.57] | <0.001 |       | 0.09 [-0.02–0.20] |       |       |
| Employment status        | -0.14 [-0.34–0.07] | 0.191 |       | -0.09 [-0.21–0.02] |       |       |
| Functional impairment    | 0.27 [0.06–0.49] | 0.014 |       | 0.12 [0.00–0.24] |       |       |
| Subjective symptom impact |       |       |       |       |       |       |
| Weakness                 |               | 0.40 [0.23–0.57] |       |       |       |       |
| Pain                     |               | 0.10 [-0.04–0.23] |       |       |       |       |
| Fatigue                  |               | 0.22 [0.06–0.38] |       |       |       |       |
| Myotonia                 |               | 0.20 [0.06–0.34] |       |       |       |       |

\(^a\): F = 7.7\(***\), adjusted \(R^2\) = 0.32 [95% CI: 0.12–0.42]
\(^b\): F = 35.9\(***\), adjusted \(R^2\) = 0.80 [95% CI: 0.69–0.83]
\(***\): \(p < 0.001\)

CI: confidence interval
QoL: quality of life

Table 4: Multiple Linear Regression Models Predicting Overall QoL In Patients

| Predictor variable       | Weakness\(^a\) |       |       | Fatigue\(^b\) |       |       | Myotonia\(^c\) |       |
|-------------------------|---------------|-------|-------|---------------|-------|-------|---------------|-------|
|                         | Standardized coefficient [95% CI] | P-value | Standardized coefficient [95% CI] | P-value | Standardized coefficient [95% CI] |       |       |
| Aspect of each symptom  |               |       |       |               |       |       |               |       |
| a. Severity             | 0.08 [-0.14–0.31] | 0.473 |       | 0.32 [0.03–0.60] | 0.029 |       | -0.31 [-0.68] |       |
| b. Difficulties         | 0.40 [0.09–0.70] | 0.011 |       | 0.44 [0.11–0.78] | 0.010 |       | 0.75 [0.25–] |       |
| c. Importance           | 0.40 [0.12–0.67] | 0.005 |       | 0.04 [-0.29–0.36] | 0.832 |       | 0.21 [-0.24-] |       |

\(^a\): F = 68.1\(***\), adjusted \(R^2\) = 0.70 [95% CI: 0.58–0.77]
\(^b\): F = 38.6\(***\), adjusted \(R^2\) = 0.57 [95% CI: 0.41–0.66]
\(^c\): F = 23.7\(***\), adjusted \(R^2\) = 0.44 [95% CI: 0.27–0.55]
\(***\): \(p < 0.001\).

CI: confidence interval
QoL: quality of life

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

Supplemental Table.docx
