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ABSTRACT

Background Quality of life (QoL) assessment allows healthcare professionals to appreciate the patient perspective of their disease. This can help us make a better choice from among the various ways we currently measure the severity of a muscle disease such as inclusion body myositis (IBM). However, we cannot assume that QoL in IBM is just related to disease severity as psychosocial factors may play an important role in determining QoL.

Methods Sixty subjects with IBM had assessments of disease severity and concurrent assessment of mood and QoL using the Short-Form 36 (SF-36).

Results There were significant reductions in Physical functioning, Role physical, General health and Social functioning domains of the SF-36. Functional disability was more indicative of the broader effects of IBM on SF-36 than was the muscle strength sum score. Mood was relatively independent of disease severity and had a different profile of effects on SF-36 domains. Up to 14% of the effect of functional disability on some aspects of QoL was mediated through mood.

Conclusions The functional disability caused by IBM reduces QoL, but psychosocial factors such as mood affect QoL directly and by influencing the degree to which disease severity reduces QoL. Further study should follow the effects of IBM on QoL over time and look at the influence of other psychosocial factors. Such studies may point to psychosocial interventions that may help improve QoL in IBM even if the disease itself cannot be treated.

Inclusion body myositis (IBM) is a late-onset, slowly progressive, painless, inflammatory myopathy resulting in impaired mobility, difficulty with stairs, falls, problems with handgrip and, in some cases, significant swallowing dysfunction. The nature and extent of the impact on quality of life (QoL) has not been specifically studied for IBM. Information on QoL may give a more realistic assessment of the effectiveness of healthcare interventions particularly when, as is the case with IBM, these are not directed at cure but at the management of chronic disability. In clinical trials it is becoming increasingly important to show that the intervention has improved QoL as well as improving some objective measurement of disease severity. Direct measurement of muscle strength either by manual muscle testing (MMT) or by qualitative muscle testing (QMT) using a computer-assisted strain gauge may be the gold standard for assessing muscle disease severity. However, these techniques tend to yield numerical results, the practical impact of which is difficult to appreciate. A disease severity measure that more closely relates to QoL may be a better outcome measure for a clinical trial.

It may seem reasonable to assume that QoL in chronic muscle disease such as IBM would be related to disease severity and duration of disease. However, in other chronic diseases, there is a "disability paradox" with unexpectedly high levels of QoL perhaps due to goal restructuring with a re-setting of internal expectations, a phenomenon called "response shift".[1 2] Response shift emphasises the importance of psycho-social factors, such as depression and coping abilities, on QoL. Psychosocial factors may act either independently or by mediating the effects of disease severity on QoL.

The Muscle Study Group conducted two randomised controlled trials in IBM using Avonex (interferon beta; Biogen, Boston, Massachusetts, USA) at low and then high dose.[3 4] Data on QoL as assessed by the Short-Form 36 (SF-36)[5] was collected during both trials, as well as data on disease severity and depression. In this publication, we take the opportunity to examine more specifically the QoL data with the following aims: (1) to describe the effect of IBM on QoL, (2) to determine the extent to which QoL is related to disease severity, (3) to establish which of the alternative assessments of IBM severity most closely relates to QoL, (4) to determine whether depression might influence (ie, mediate) the relationship between disease severity and QoL as opposed to it merely impacting on QoL.

METHODS

We used the baseline prerandomised assessment data from all subjects enrolled in two randomised six-month clinical trials of interferon beta (Avonex).[3 4] These studies had ethical approval, and all subjects had given informed consent. Subjects had definite or possible IBM. QoL was measured using the SF-36 V.1 and the SF-36 scores were expressed as SD from the published US normal values (Z score).[6] Muscle strength was assessed by maximum voluntary isometric contraction testing and MMT. Muscle mass was estimated by measuring lean body mass using dual energy *x* ray absorptiometry. Objective functional tests included the timed Purdue Pegboard, time to walk 15 ft and time to rise from a chair. Subjective functional abilities were assessed using the Amyotrophic Lateral Sclerosis Functional Rating Scale (ALS-FRS). Mood was assessed using the Beck Depression Inventory (BDI). We also had data on the duration of IBM from time of first symptoms. Statistical analysis was done using SPSS V.15.0 software.

We used simple correlation analysis and multiple regressions to test whether depression has a mediator effect by checking whether the following four

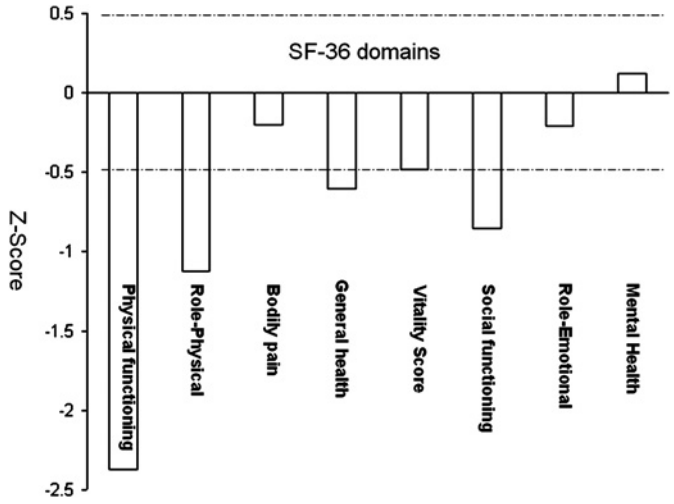

Figure 1 Standardised Short-Form 36 (SF-36) scores in 60 subjects with inclusion body myositis; Z score represents number of SD from the normal.

conditions applied: (1) was disease severity (the independent factor) associated with QoL (the dependent factor); (2) was disease severity (the independent factor) associated with depression (the proposed mediator); (3) was depression (the proposed mediator) associated with QoL (the dependent factor); (4) did the contribution of disease severity to QoL become weaker when we controlled for the effect of depression.[7 8]

RESULTS

We had data from 60 subjects (22 females, 38 males) with a mean age of 64.47 years (SD 8.47). Duration of disease ranged from 0 to 10.8 years (mean 4.35 years, SD 2.96). Web table 1 gives the descriptive data for the disease severity measures, the SF-36 domains and the BDI at baseline.

Standardised SF-36 domain Z scores were calculated using t test with normal population values (figure 1). All SF-36 domains except Mental health were reduced with the reductions being significant for Physical functioning, Role physical, General health, Vitality and Social functioning domains. As expected, MMT total, upper and lower sum scores were strongly correlated with QMT scores (data not shown). ALS-FRS score, timed walk and timed stand strongly correlated with MMT sum scores, but dual energy *x* ray absorptiometry, lean body mass and Purdue Pegboard time were not so well correlated with MMT. Disease severity was not correlated with the duration of disease and was only weakly correlated with age (Web table 2).

MMT, timed stand, time walk and ALS-FRS score severity measures were strongly correlated with the Physical functioning domain of SF-36 questionnaire. Timed walk showed additional moderate correlation with Social functioning and Role emotional domains, whereas ALS-FRS showed additional moderate correlation with Role physical, Vitality and social functioning scores (Web table 3). Neither age of patient nor duration of disease had any strong or moderate correlation with any of the SF-36 domains.

There was no strong or moderate correlation between the BDI score and any of severity of disease measures. There was a mild correlation between ALS-FRS and BDI (correlation coefficient −0.32, $p<0.001$). The BDI score was strongly correlated with the General health, Vitality score, Social functioning and Mental health domains of the SF-36 and moderately correlated with the Physical functioning, Role physical, Bodily pain domains (web table 3).

Disease severity (as measured by ALS-FRS) was significantly correlated with QoL and depression was correlated with both disease severity and QoL (web table 4). The association between disease severity (the independent variable) and most of QoL domains (dependent variables) was significantly reduced by the inclusion of depression as the mediating variable in these correlations. Between 1 and 14 per cent of the effect of disease severity on different domains of QoL was mediated by depression (web table 4).

DISCUSSION

This study shows that IBM does affect QoL with the effects being most evident for some of the physical domains of the SF-36. The physical disability is sufficient to have significant impact on Social functioning. The smallest effects were on Bodily pain, Role emotional and Mental health domains. Some of these effects are predictable considering that IBM is characterised by muscle weakness causing physical disability but with pain not being a recognised feature of this disease.

There have not been any previous studies of QoL in IBM, and only limited comparison of our results with QoL studies using SF-36 in other adult muscle diseases is possible. One study only reported the Bodily Pain domain of the SF-36 and found Bodily Pain scores for post polio syndrome (47.4 (24.2)), Charcot-Marie-Tooth (49.8 (21.9)) and various muscle diseases (61.4 ± 26.4) were significantly lower than the published US normative data (75.2 ± 23.7).[9] The mean Bodily Pain score for IBM was 68.6 (27.2), which for our sample was not significantly different from the published US normal data. Two studies reported the full SF-36 scores (table 1).[10 11] SF-36

Table 1 SF-36 domain scores for various neuromuscular diseases

	Mean (SD)				
	This paper	Boyer *et al*[10]	Kalkman *et al*[11]		
SF-36 domains	IBM (n=60)	NMD (n=108)	FSHD (n=139)	MyoDys (n=322)	CMT 1 (n=137)
Physical functioning	24.21 (19.59)	36 (33)	45.2 (31.4)*	48.4 (28.2)*	53.1 (26.4)*
Role-physical	38.75 (41.02)	58 (40)*	47.9 (42)	48.2 (39.7)	48.9 (39)
Bodily pain	68.61 (27.17)	63 (26)	66.6 (23.8)	75.4 (25.3)	68.5 (25.5)
General health	57.69 (20.67)	46 (20)*	51.7 (21.6)	40.5 (22.3)*	52.5 (20.7)
Vitality score	47.06 (21.27)	48 (21)	NA	NA	NA
Social functioning	66.04 (26.85)	69 (25)	71.6 (24.2)	69.9 (24.3)	67.5 (24.3)
Role-emotional	75.71 (37.05)	65 (40)	69.5 (41.6)	73.9 (37.6)	67.4 (41.6)
Mental health	78.34 (15.68)	63 (19)*	72.6 (17)	72.7 (18)	68.9 (19.2)*

*Significant difference from IBM figure at $p<0.01$.
CMT 1, Charcot-Marie-Tooth type 1; FSHD, facioscapulohumeral dystrophy; IBM, inclusion body myositis; NA, not available; NMD, various neuromuscular diseases; SF-36, Short-Form 36.

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Physical function scores are significantly lower for IBM than for other muscle diseases, but as patients with IBM are older, this may just reflect the known lowering of SF-36 Physical function scores with age. Mental health domain was less affected in IBM perhaps because those with IBM are generally older and may expect a degree of infirmity with age.

The major effects of IBM on SF-36 physical domains are related to disease severity as measured by MMT and QMT. The alternative measures for disease severity that most strongly correlated with MMT were ALS-FRS score, timed walk and timed stand. Although these measures, like MMT, had strong correlation with the SF-36 Physical functioning domain, timed walk and especially ALS-FRS had additional correlations with SF-36 domains. This may mean that the more diverse impacts of IBM on QoL are more accurately related to functional measures rather than to an impairment measure such as MMT. The ALS-FRS may relate to more SF-36 domains because it taps into more of the functional impairments seen with IBM than does time walk. Thus, an appropriate measure for disease severity in QoL studies of muscle disease might be a broad-based functional scale. This statement would also argue for the promotion of functional measures as a primary clinical trial outcome measure given the drive towards choosing outcome measures that are more meaningful for patients. An additional advantage of such scales is that some can be self-administered by patients making them useful for mail surveys.

Depression as measured by the BDI had a stronger effect on mental domains of the SF-36 but with moderate effect also on physical domains. The effects of mood on QoL were independent of disease severity, but up to 14% of the effect of disease severity on some domains of QoL was mediated through depression. The important effects of mood on QoL coupled with the fact that it is eminently treatable means that assessment and treatment of mood would be very worthwhile in the overall management of IBM.

This is a study of patients with IBM who have enrolled in an interventional clinical trial. As such, the data pertain to this particular population of patients, which may not be representative of all patients with IBM. Patients enrolling in a clinical trial may have different mental health status, attitudes and function, either because enrolment means they are sufficiently motivated or because the trial inclusion criteria may have certain requirements, such as sufficient function or other features. Thus, further studies are required on a larger sample to confirm these findings.

Although we do have longitudinal data over 6 months, the SF-36 scores did not change significantly. There was a very small trend towards improvement on the SF-36 mental component summary score.[3 4] Thirteen-one of the patients showed a decline in ALS-FRS scores, but whether these declines were significant is hard to say in the absence of functional natural history data. A previous natural history study highlighted that fluctuations in muscle strength can occur either way if measured over the course of just a few months, and so it would be surprising if the ALS-FRS would change enough in 6 months so as to affect QoL.[12] It is also unlikely that the 6 months duration of the current studies would be long enough to expect any significant psychosocial changes to affect QoL independently of IBM severity. We do need more information on how QoL changes during the course of IBM, starting with the impact of the definitive diagnosis, the adjustment thereafter and the effect of the progressive functional impairments. Future studies could also include other psychosocial measures, such as illness perceptions and coping strategies that, like mood, may also play a major role in the determination of QoL either directly influencing QoL or else acting as a mediator between disease severity and QoL. If such effects are confirmed, this may give us additional means to improve overall QoL even while we await the treatment that will improve QoL by curing IBM.

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Competing interests None.

Ethics approval This study was conducted with the approval of the institutional review board of four US centres and the LREC approval from King's College Hospital London, UK.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

1. **Albrecht GL,** Devlieger PJ. The disability paradox: high quality of life against all odds. *Soc Sci Med* 1999;**48**:977—88.
2. **Sprangers MA,** Schwartz CE. Integrating response shift into health-related quality of life research: a theoretical model. *Soc Sci Med* 1999;**48**:1507—15.
3. **Muscle Study Group.** Randomized pilot trial of INF1a (Avonex) in patients with inclusion body myositis. *Neurology* 2001;**57**:1566—70.
4. **Muscle Study Group.** Randomized pilot trial of high-dose betaINF-1a in patients with inclusion body myositis. *Neurology* 2004;**63**:718—20.
5. **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.
6. **Ware JE Jr,** Kosinski M, Gandek B, *et al*. The factor structure of the SF-36 Health Survey in 10 countries: results from the IQOLA Project. International Quality of Life Assessment. *J Clin Epidemiol* 1998;**51**:1159—65.
7. **Baron RM,** Kenny DA. The moderator—mediator variable distinction in social psychological research: conceptual, strategic, and statistical considerations. *J Pers Soc Psychol* 1986;**51**:1173—82.
8. **Sobel ME.** Asymptomatic confidence intervals for indirect effects in structural equation models. *Sociol Methodol* 1982;**13**:290—312.
9. **Abresch RT,** Carter GT, Jensen MP, *et al*. Assessment of pain and health-related quality of life in slowly progressive neuromuscular disease. Am.J Hosp.Palliat. *Care* 2002;**19**:39—48.
10. **Boyer F,** Morrone I, Laffont I, *et al*. Health related quality of life in people with hereditary neuromuscular diseases: an investigation of test-retest agreement with comparison between two generic questionnaires, the Nottingham Health Profile and the Short Form-36 items. *Neuromuscul Disord* 2006;**16**:99—106.
11. **Kalkman JS,** Schillings ML, van der Werf SP, *et al*. Experienced fatigue in facioscapulohumeral dystrophy, myotonic dystrophy, and HMSN-I. *J Neurol Neurosurg Psychiatr* 2005;**76**:1406—9.
12. **Rose MR,** McDermott MP, Thornton CA, *et al*. A prospective longitudinal natural history study of inclusion body myositis; implications for clinical trials. *Neurology* 2001;**57**:548—50.

APPENDIX

Muscle Study Group: members involved with both IBM trials

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