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ORIGINAL ARTICLE

Predictors of Reduced Health-Related Quality of Life in Adult Patients With Idiopathic Inflammatory Myopathies

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Objective. **Extensive studies on health-related quality of life (HRQoL) in idiopathic inflammatory myopathies (IIMs) are lacking. Our objective was to document HRQoL and to identify factors associated with a reduced HRQoL in patients with IIM.**

Methods. **A total of 1,715 patients (median age 49.9 years, 70% female, 87% white) who met probable or definite Bohan and Peter criteria or Griggs criteria for myositis were included from the Myovision registry. HRQoL was ascertained using the Short Form 12 (SF-12) health survey questionnaire. HRQoL physical component summary (PCS) and mental component summary (MCS) scores in relation to different patient and disease characteristics were compared to scores from matched normative data from the US general population and rheumatoid arthritis (RA) patients. Bivariate and multiple linear regression analyses were performed to assess the association between HRQoL and patient and disease parameters.**

Results. **The mean SF-12 summary scores were significantly lower in IIM patients than in the normative and RA populations. A diagnosis of inclusion body myositis, older age, patient-reported negative effect of disease on work, presence of another co-occurring autoimmune disease, polypharmacy, and IIM-associated lung disease and joint involvement were significantly associated with lower PCS scores. Lower MCS scores were associated with joint involvement and a negative effect of disease on work.**

Conclusion. **In this large study of patient-reported outcomes in IIM, an association was found between multiple disease characteristics and reduced HRQoL, mostly in the physical domain. In the US, the HRQoL of IIM patients was found to be lower than that of the general population and RA patients.**

INTRODUCTION

The idiopathic inflammatory myopathies (IIMs), including dermatomyositis (DM), polymyositis (PM), and inclusion body myositis (IBM), are chronic systemic inflammatory conditions that can involve almost any organ system but primarily affect muscle (1). Although the prognosis for IIM has improved significantly in the past few decades with advances in medications and health care (2,3), IIM still has a significant impact on the health-related quality of life (HRQoL) of patients (3–6). HRQoL is a multidimensional concept that includes domains related to physical, mental, emotional, and social functioning and is focused on the impact that health status has on quality of life (7).

Extensive research has been conducted on HRQoL in other rheumatic diseases, such as rheumatoid arthritis (RA) (8,9), juvenile idiopathic arthritis (10,11) and systemic lupus erythematosus (SLE) (12). However, there are few sizable studies assessing HRQoL in patients with

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Significance & Innovations

- This large registry study demonstrates that the idiopathic inflammatory myopathies (IIMs) have a more profound negative impact on health-related quality of life (HRQoL), compared to rheumatoid arthritis and the general US population as measured by the Short Form 12.
- This study identifies multiple disease parameters associated with a reduced physical component summary score of HRQoL in IIM.
- Similar to HRQoL studies in other rheumatologic diseases, this study shows little influence of demographic or disease parameters on the mental component of HRQoL in IIM.

IIM (4–6,13–16). Due to the rarity of these conditions, previous studies had small sample sizes, which prohibited adequately powered statistical comparisons to delineate patient or IIM factors associated with HRQoL outcomes (16,17).

The Myositis Association provides support to myositis patients and their families, and its database now includes more than 10,000 IIM patients. The National Myositis Registry (named Myovision) is operated by the association and provides a wide range of self-reported information about both adult and pediatric patients with IIM, including demographics, clinical manifestations, medications, and environmental exposures that may be associated with these diseases. This patient registry also collected information on HRQoL at enrollment.

Using the Myovision registry, we attempted to document the degree of HRQoL impairment in adult IIM patients, comparing this to RA patients and to a normal healthy population. Further, we wished to identify predictors of outcomes associated with lower than expected HRQoL among the major IIM clinical groups.

PATIENTS AND METHODS

Registry participants and survey procedures. This exploratory, cross-sectional study evaluated patients who enrolled in the Myovision registry. Myovision enrollment packages were mailed between December 2010 and July 2012 to 9,049 patients on The Myositis Association mailing list in the US and Canada. Additional myositis patients could also enroll by responding to study advertisements or by accessing The Myositis Association website and requesting to participate. Enrollment packages contained a patient questionnaire, as well as the study consent form and a return postage-paid envelope.

Potential participants were given the option to complete the paper version of the questionnaire or an online electronic version. Patient data were not entered into the database until a signed consent form was received. Only patients who met probable or definite Bohan and Peter criteria (18,19) for dermatomyositis or polymyositis, or possible or probable criteria for inclusion body myositis (20), based on questionnaire data, were included in the Myovision registry database. The diagnosis was also ascertained via a partial sample of the patient population seen the National Institutes of Health (NIH). The diagnosis reported on the questionnaire was compared to that in their NIH medical or research record.

The Myovision questionnaire included 83 questions that encompassed patient demographics, disease-related information, environmental exposures, and questions regarding work, school, and leisure activities, as well as HRQoL. Patients were not reimbursed for their participation in the study. For missing data or inconsistent responses to the Myovision questions, respondents were contacted again by phone, e-mail, and mail. These quality assurance procedures were conducted by personnel from The Myositis Association and the National Institute of Environmental Health Sciences. The Cincinnati Children's Hospital Medical Center Institutional Review Board approved the study.

HRQoL assessment tool. Patients ages 18 years or older at the time of questionnaire completion also received version 2 of the Short Form 12 (SF-12) HRQoL instrument. The SF-12 has been shown to have similar performance characteristics as the SF-36 and was used because of its ease of completion compared to other HRQoL scales (21–23). The SF-12 questionnaire is an abbreviated version of the SF-36 questionnaire and is a short 4-week recall questionnaire addressing 12 different items in 8 different domains (physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health). Four domain scores (physical functioning, role-physical, role-emotional, and mental health) are based on responses to 2 items each, whereas the scores of the remaining domains are based on a single item. Two summary measures can be derived from the SF-12: the physical component summary (PCS) score and the mental component summary (MCS) score. The SF-12 allows for complete scoring of summary measures even when select item responses are missing, provided that at least 1 item in a 2-item domain is answered.

The different health domains and summary scores are presented as normalized T scores with a mean of 50 and an SD of 10 (24). The means and SDs used in scoring originate from the 1998 US general population norms derived from responses to the National Survey of Functional Health Status. The factor score coefficients come from the 1990 US general population norms (24).

HRQoL data of age- and sex-matched US normative population and RA patients were derived from a national probability sample of US noninstitutionalized adults who participated in the internet-based 2009 QualityMetric PRO Norming Study (23). A total of 8,719 individuals participated in this study, and 6,012 of these individuals received items from the standard version of the SF-12. As part of the survey, all respondents were asked "Have you ever been told by a doctor or other health professional that you had any of the following conditions?" accompanied by a list of more than 40 common health

conditions, which included RA. Of the 6,012 patients who received a survey including the SF-12, 463 answered yes for RA (24).

HRQoL predictors of interest. We identified a priori a series of demographic and clinical variables that we hypothesized were associated with differences in HRQoL in IIM. The variables included were as follows: sex, race, age at diagnosis, age at enrollment in Myovision, disease duration, IIM effects on work and school, presence of co-occurring autoimmune diseases or cancer, treating physician type (rheumatologist versus nonrheumatologist), number of medications used for the treatment of IIM (more than 1 immunomodulator versus 1 or no medications), associated pulmonary disease, joint swelling, dysphagia, and geographic location of residence. The patient's addresses were geocoded using ArcGIS, version 10.1. The assigned latitudes and longitudes associated with the patients' addresses at the time of enrollment were used to categorize them into 4 US Census Bureau regions at the time of enrollment.

Statistical analysis. Analyses of all adult Myovision registry patients, as well as of those in the different myositis clinical groups, i.e., DM, PM, and IMB, were performed. The juvenile DM group was not included due to its insufficient sample size. Descriptive statistics (medians with interquartile ranges and frequencies) of the demographic data of the Myovision registry population were performed. Using analysis of variance (ANOVA), we compared the SF-12 domain scores and the 2 summary measure scores (PCS and MCS) of registrants with IIM to those of the healthy and RA populations.

Bivariate analysis was conducted via *t*-tests to assess the difference in mean PCS and MCS scores for each of the independent variables assessed. One-way ANOVA was used to compare PCS and MCS scores across the 4 census regions. Multiple linear regression analyses were used to identify significant HRQoL predictors in the total IIM population and in the DM, PM, and IBM groups. All 13 predictors of interest were included in the multivariate analyses, even if they were found to be nonsignificant in the bivariate analysis. Both forward-selection and backward-elimination methods were used to fit an appropriate model for predicting PCS or MCS score. The significance threshold for keeping a variable in the model was set a priori at a P value of 0.1, except for candidate predictors previously identified to be relevant based on the bivariate analysis. Notably, relevant predictors were identified irrespective of the predictor selection approach (backward or forward selection).

Adjusted least squares means and SEs of PCS and MCS scores by IIM group were generated using generalized linear models. The covariates included were the same as those in the multiple linear regression analyses described above. As this was an exploratory study, P values were not adjusted for multiple tests of hypotheses. Univariate analyses were performed using GraphPad Prism 6 software, and SAS, version 9.3, was used to conduct the ANOVA and multivariate analyses.

RESULTS

Demographic data. A total of 1,956 patients (22% of the 9,049 to whom packets were mailed) consented to participate in the study and returned completed questionnaires (Figure 1). Of these, 1,806 patients met IIM diagnostic criteria. HRQoL information (SF-12 questionnaire answers) was available for 1,648 adult patients, of whom 702 had DM, 481 had PM, and 465 had IBM. There were 67 adult patients with juvenile-onset disease (juvenile DM or juvenile PM) who were not included in this study.

The median age at diagnosis among all patients (n = 1,806) was 49.9 years (interquartile range [IQR] 37.3–59.6 years). As expected, IBM patients were significantly older (62.3 years [IQR 55.5–68.2]) at the time of diagnosis than DM and PM patients (46.4 years and 47.8 years, respectively; $P < 0.0001$ for both). There were 1,262 female patients (70%), with a greater female predominance in DM (84%), but a larger male predominance (60%) in IBM ($P < 0.0001$). The vast majority of participants were white (87% in the total patient group and 93.6% in the IBM group). African Americans comprised 6% of the total and 12% of the PM group. Disease duration at the time of enrollment was 9.2 years (IQR 5.3–13.6) for the total patient group, without a significant statistical difference among the IIM patient groups.

To assess the accuracy of the self-reported diagnosis, we assessed 121 patients of the total 1,806 patients (6.7%) who were patients at the NIH. Of these, the patient's reported diagnoses matched the NIH physician's diagnoses in 105 (87%).

Comparison of HRQoL scores in IIM compared to the general and RA populations. As shown in Table 1, IIM

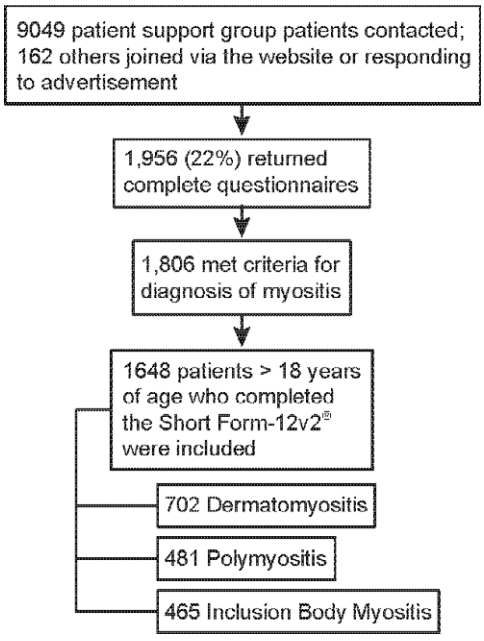

Figure 1. Flow diagram for patient inclusion in the study.

Table 1. Burden of disease relative to an age- and sex-matched US sample*

SF-12 domain	Myositis (n = 1,715) Mean	SE	No.	General population (n = 6,012) Mean	SE	F†	Difference P‡	ES§
Physical functioning	33.90	0.26	6,028	48.54	0.20	2,000.4	< 0.0001	−1.01
Role-physical	35.18	0.27	6,026	48.73	0.20	1,618.5	< 0.0001	−0.91
Bodily pain	42.58	0.28	6,007	49.43	0.21	380.6	< 0.0001	−0.45
General health	41.62	0.28	6,024	49.21	0.21	482.1	< 0.0001	−0.50
Vitality	42.38	0.26	5,997	50.80	0.21	639.1	< 0.0001	−0.55
Social functioning	40.94	0.29	6,009	50.55	0.21	720.3	< 0.0001	−0.62
Role-emotional	42.02	0.32	6,024	51.29	0.21	593.8	< 0.0001	−0.59
Mental health	47.04	0.25	6,026	52.24	0.21	257.2	< 0.0001	−0.34
PCS score	35.56	0.26	6,009	47.84	0.20	1,382.7	< 0.0001	−0.84
MCS score	47.26	0.27	6,012	52.52	0.21	241.8	< 0.0001	−0.35

* SF-12 = Short Form 12; SE = standard error; ES = effect size (Cohen's *d*); PCS = physical component summary; MCS = mental component summary.
† F statistic for analysis of variance with sample as a between-subjects factor.
‡ All *P* values are statistically significant.
§ A negative effect size indicates the myositis population has a numerically smaller mean and that the burden of disease is greater than in the general population.

negatively impacted all health domains captured by the SF-12 questionnaire in comparison to the general population, with the most profound negative effect (based on effect size [ES]) on the physical functioning (ES = −1.01) and role-physical (ES = −0.91) domains. With respect to overall physical function and mental health, both PCS and MCS scores were significantly lower among those with IIM compared to the healthy US population sample. When compared to RA patients, all domain scores (apart from bodily pain) and both summary scores were significantly lower in IIM patients (Table 2).

HRQoL scores among IIM groups. PCS scores differed significantly among different IIM groups, with IBM showing the most profound impact on overall physical function (mean IBM 30 versus PM 34.7 versus DM 39). Conversely, MCS did not significantly differ among IIM subtypes (mean IBM 46.6, PM 46.7, and DM 47.7).

Differences in HRQoL based on patient demographics and clinical characteristics. In the bivariate analysis of the study population (n = 1,648), nonwhite patients had significantly worse mean ± SD PCS scores (mean ± SD 33.6 ± 10.2 versus 35.7 ± 10.9; $P < 0.0001$) and MCS scores (mean ± SD 44.9 ± 11.6 versus 47.5 ± 10.9; $P = 0.003$) compared to whites. The PCS scores were significantly lower for older patients at diagnosis (median >50 years; mean ± SD 33.9 ± 9.5 versus 37.2 ± 11.8; $P < 0.0001$) and for older patients at enrollment (median >60 years; mean ± SD 33.5 ± 9.5 versus 37.5 ± 11.7; $P < 0.0001$), but the mean ± SD MCS scores for older patients

Table 2. Burden of disease relative to an age- and sex-matched US RA sample*

SF-12 domain	Myositis (n = 1,715) Mean	SE	RA (n = 463) Mean	SE	Difference F†	P‡	ES§
Physical functioning	33.90	0.26	41.65	0.83	79.3	< 0.0001	−0.61
Role-physical	35.18	0.27	42.01	0.83	61.1	< 0.0001	−0.53
Bodily pain	42.58	0.28	41.53	0.85	1.4	0.2419	0.08
General health	41.62	0.28	43.81	0.78	6.9	0.0084	−0.17
Vitality	42.38	0.26	46.93	0.76	32.0	< 0.0001	−0.38
Social functioning	40.94	0.29	44.44	0.87	14.7	0.0001	−0.26
Role-emotional	42.02	0.32	45.18	0.94	10.2	0.0014	−0.21
Mental health	47.04	0.25	48.68	0.79	3.9	0.0478	−0.14
PCS score	35.56	0.26	40.47	0.82	32.5	< 0.0001	−0.39
MCS score	47.26	0.27	48.96	0.79	4.2	0.0415	−0.14

* RA = rheumatoid arthritis; SF-12 = Short Form 12; SE = standard error; ES = effect size (Cohen's *d*); PCS = physical component summary; MCS = mental component summary.
† F statistic for analysis of variance with sample as a between-subjects factor.
‡ All *P* values except that for bodily pain are statistically significant.
§ A negative effect size indicates the myositis population has a numerically smaller mean and that the burden of disease is greater than in the RA population.

Table 3. Multivariate analysis of the full Myovision sample for PCS and MCS scores*

HRQoL predictor	PCS		MCS	
	β (SE)	*P*	β (SE)	*P*
Polymyositis†	−4.28 (0.59)	< 0.001‡	−1.00 (0.67)	0.140
Inclusion body myositis†	−8.94 (0.80)	< 0.001‡	−1.10 (0.83)	0.189
Female	−0.09 (0.58)	0.882	Rem.	Rem.
White	1.49 (0.80)	0.063	1.08 (0.91)	0.239
Age at enrollment	−0.08 (0.02)	< 0.001‡	0.02 (0.03)	0.551
Disease duration	Rem.	Rem.	0.08 (0.04)	0.087
Effect on work	−5.43 (0.61)	< 0.001‡	−3.52 (0.69)	< 0.001‡
Treated by rheumatologist	1.57 (0.59)	0.008‡	Rem.	Rem.
Lung disease	−3.48 (0.58)	< 0.001‡	−0.80 (0.66)	0.226
Dysphagia	−0.56 (0.50)	0.263	−0.96 (0.57)	0.093
Joint swelling	−2.85 (0.53)	< 0.001‡	−2.92 (0.60)	< 0.001‡
Multiple immunomodulators	−2.61 (0.55)	< 0.001‡	−1.00 (0.62)	0.109
Cancer diagnosis	Rem.	Rem.	1.53 (0.74)	0.038
Autoimmune disease overlap	−1.52 (0.58)	0.009‡	Rem.	Rem.

* PCS = physical component summary score; MCS = mental component summary score; HRQoL = health-related quality of life; SE = standard error; rem. = removed from analysis by backward elimination.
† Relative to dermatomyositis.
‡ Statistically significant.

at diagnosis (mean ± SD 47.7 ± 10.9 versus 46.8 ± 11.1; $P = 0.096$) and at enrollment (mean ± SD 48.0 ± 11.0 versus 46.4 ± 10.8; $P = 0.002$) were higher. Disease duration did not significantly change the PCS score among all patient groups, but MCS score was better in DM patients with a longer than median disease duration (mean ± SD 45.8 ± 10.8 versus 48.5 ± 10.3; $P = 0.0007$).

Both the PCS and MCS scores were lower among patients who reported that their disease affected their ability to work compared to the total patient group (mean ± SD 33.7 ± 10.0 versus 40.7 ± 11.3; $P < 0.0001$ and mean ± SD 46.3 ± 11.1 versus 50.4 ± 9.9; $P < 0.0001$, respectively). In the DM group, the PCS score was significantly lower among patients with an associated autoimmune disease (mean ± SD 36.0 ± 11.3 versus 40.0 ± 11.6; $P < 0.0001$). However, patients with associated cancer had a better MCS score than the total patient group (mean ± SD 46.9 ± 11.1 versus 48.6 ± 10.5; $P = 0.017$). When the treating physician was a rheumatologist, the PCS score was significantly higher in the total patient group (mean ± SD 37.1 ± 11.5 versus 33.0 ± 9.3; $P < 0.00001$), but the PCS score was lower in IBM patients when the treating physician was a rheumatologist (mean ± SD 29.3 ± 6.9 versus 30.8 ± 6.6; $P = 0.044$).

Both the PCS and MCS scores were significantly lower in patients who reported more systemic disease involvement, such as having a history of lung disease (mean ± SD PCS 32.2 ± 9.6 versus 36.8 ± 11.1; $P < 0.0001$; mean ± SD MCS 45.6 ± 11.5 versus 47.8 ± 10.8; $P = 0.0003$), difficulty swallowing (mean ± SD PCS 34.4 ± 10.4 versus 37 ± 11.3; $P < 0.0001$), or joint swelling (mean ± SD PCS 34.1 ± 10.3 versus 36.3 ± 11.1; $P < 0.0001$; mean ± SD MCS 45.3 ± 10.9 versus 48.4 ± 10.9; $P < 0.0001$). Region of residence did not significantly impact the PCS or MCS score when the entire study population was considered in the analysis.

Multivariate analyses. In the multivariate analyses of the total IIM patient group (Table 3), older age at enrollment, patient report of a negative effect of disease on work performance, associated autoimmune disease, lung disease, and presence of joint disease, as well as use of multiple medications, were all associated with significantly lower PCS scores. Notably, care of an IIM patient by a rheumatologist was associated with a higher PCS score. The MCS was negatively influenced by a history of arthritis and a negative effect on work.

Patients with a diagnosis of cancer had a higher MCS score and there was a tendency for a higher MCS score among patients with longer disease duration. As shown in Table 4, these results were quite consistent in the IIM group multivariate analysis. A reported effect on work and a history of arthritis were the most constant parameters with a negative effect on both PCS and MCS scores in all 3 IIM groups. In the IBM group, fewer parameters influenced the PCS and MCS scores, compared with the DM and PM groups. Treatment by a rheumatologist negatively influenced both the PCS and the MCS score in the IBM group. Geographic region did not significantly influence the MCS or PCS score in the multivariate analysis (data not shown).

DISCUSSION

Results from this large registry study of adult patients with IIM showed that overall HRQoL is reduced in comparison to either a healthy population or to RA patients. The current study also identified an association with multiple variables and reduced HRQoL, most of which are in the physical health domain. These included older age, effect of disease on work, the presence of another autoimmune disease, lung disease, joint involvement, and use of multiple medications. The reduction in

Table 4. Multivariate analysis of myositis groups for PCS and MCS scores*

Variable	Dermatomyositis		Polymyositis		Inclusion body myositis	
	PCS	MCS	PCS	MCS	PCS	MCS
Disease duration	Rem.	0.14 (0.06)	Rem.	Rem.	Rem.	0.14 (0.06)
P		0.024†				0.233
Effect on work	−7.45 (1.02)	−3.81 (1.00)	−4.60 (1.16)	−4.06 (1.27)	−2.82 (0.83)	−2.82 (1.40)
P	< 0.001†	< 0.001†	< 0.001†	0.001†	< 0.001†	0.044†
Treated by rheumatologist	2.94 (1.03)	2.37 (1.02)	Rem.	Rem.	−1.22 (0.81)	−3.00 (1.33)
P	0.004†	0.02†			0.133	0.025†
Lung disease	−4.16 (0.93)	−0.98 (0.92)	−4.02 (1.03)	Rem.	−0.73 (0.92)	−2.80 (1.57)
P	< 0.001†	0.285	< 0.001†		0.428	0.076
Dysphagia	−1.68 (0.84)	Rem.	Rem.	Rem.	Rem.	−2.30 (1.16)
P	0.046†					0.048†
Joint swelling	−3.39 (0.84)	−2.76 (0.83)	−1.89 (0.99)	−4.07 (1.09)	−1.75 (0.80)	Rem.
P	< 0.001†	< 0.001†	0.058	< 0.001†	0.029†	
Multiple immunomodulators	−1.82 (0.93)	Rem.	−3.24 (0.98)	−0.36 (1.08)	−1.79 (0.82)	Rem.
P	0.049†		0.001†	0.736	0.029†	
Autoimmune disease overlap	−2.26	Rem.	Rem.	Rem.	Rem.	Rem.
P	0.013†					

* Values are the parameter estimate (standard error). Only significant variables are shown. PCS = physical component summary; MCS = mental component summary; rem. = removed from analysis by backward elimination.
† Statistically significant.

HRQoL found in the current study is consistent with various other smaller studies that compared IIM patients to the general population (4,13,14), as well as analyses assessing all studies in aggregate (16). Other studies have shown comparable reduced HRQoL scores in other rheumatic diseases, including SLE, RA, and Sjögren's syndrome (12,16,25–27).

A well-recognized, reliable set of demographic, disease, environmental, or time-related predictors of HRQoL in IIM has yet to be identified. Our findings relating to predictors of HRQoL in IIM are consistent with a number of earlier studies in some respects, but do vary from others. Somewhat surprisingly, for example, disease duration was not associated with reduced HRQoL in this and some earlier studies (4,28), while other authors have found a rather strong association between the two (14,29). This may be due to variations in study design, sample size, or instruments used to assess HRQoL, or in the underlying clinical and therapeutic heterogeneity of the IIM groups themselves.

Rheumatic diseases are well-known to be one of the most common chronic conditions limiting a person's ability to remain in paid employment (30,31), perhaps due to associated fatigue, pain, and emotional and interpersonal issues (32). Indeed, the most significant independent predictor of reduced HRQoL physically and mentally in the current study was a patient-reported negative effect of their disease on their ability to work. Ponyi et al (14) reported that 42% of patients with IIM were unable to work at some point in life due to their disease and that 70% were mildly to moderately disabled despite inactive disease. The inability to remain gainfully employed due to IIM likely contributes to a further reduction in HRQoL. The authors suggest this finding might be partially explained by the increased use of glucocorticoid medications and their secondary side effects, such as osteoporosis.

MCS scores were actually higher in patients with longer disease duration, in older patients, and in patients with associated cancer. This apparent discrepancy has been reported in other studies of IBM (6) and IIM (4). This perhaps could be ascribed to the disability paradox (33), which refers to the phenomenon in which patients with chronic disease report unexpectedly high levels of HRQoL, perhaps due to resetting of internal expectations through a process of disease assimilation, termed "response shift" (34,35), or to improved coping strategies. Health care providers and significant others are known to underestimate patients' QOL in comparison to the patients' own evaluation (36). It is worth mentioning that few studies to date have evaluated the disability paradox and response shift in rheumatic or inflammatory diseases.

IBM patients had the most profoundly reduced physical function among IIM patients. Although this finding was not consistently reported previously (4,6,13,14), it is not surprising. IBM has a different demographic profile, with an older age of onset (usually >50 years of age) and greater male predominance (2:1 male:female ratio) (36,37). Furthermore, there is a concern that IBM may have a degenerative component (38) and it is known to be associated with greater long-term disability, including progressive weakness, resulting in significant walking difficulties and wheelchair use (39). IBM is typically treated by neurologists rather than rheumatologists, and is very resistant to treatment (38). Interestingly, treatment by a rheumatologist negatively impacted HRQoL scores in this subgroup, and this may be consistent with a large natural history study that suggests that certain treatments with immunosuppressive agents may modestly exacerbate the progression of disability in IBM (39). These

differences may explain why HRQoL was lower among IBM patients compared to the other groups.

A major strength of this study is the large sample size, enabled by the use of the Myovision patient registry. Use of the registry underlies what also may be the study's major weakness. Conducting large, statistically valid studies of health outcomes in rare diseases is extremely challenging and often must rely on nonverifiable patient-reported data. A number of steps were taken, however, in an attempt to address this issue. We attempted to ensure that the data were accurate and complete, including clarification of answers to questions in which interpretation of the response was unclear or missing, by contacting patients again to verify their responses or complete missing data, and by including range and acceptable-value checks in the data entry software. Recently, registries have facilitated an increase in the scope of research regarding IIM and have permitted some of the first detailed phenotypic descriptions of the IIM groups as well as their individual clinical and serologic classifications (39,40).

One limitation of this study might be the use of the SF-12 rather than the SF-36 for the assessment of HRQoL. The SF-36 is the recommended HRQoL assessment tool and patient-reported outcome measure for the evaluation of response to therapy in myositis by the International Myositis Assessment and Clinical Studies Group (17,41). Indeed, the SF-12 has been used in only a few studies of HRQoL in IIM (6,13,15), which makes comparisons of results from this study to others more difficult. Also, the SF-12 does not directly address fatigue as a component of HRQoL, which is regarded today as a major component of HRQoL in RA (42) and in adult- and juvenile-onset SLE (43,44). Nonetheless, the SF-12 is easier and quicker to complete than the SF-36 and has been shown to have similar performance characteristics (19,20).

Another limitation, inherent in the use of patient-reported outcomes, as performed in this study, is the propensity for bias, specifically survivor and participation bias. Only 22% of the patients who received the questionnaire packets responded to the survey. We know that only surviving patients and patients well enough to complete the questionnaire took part in this study, thereby perhaps reflecting a group of patients with less morbidity. However, this consideration might make the results of this study even more compelling. Also, as this is a cross-sectional descriptive study, one cannot deduce cause and effect. For example, the negative reported effect on work could be both the cause and the consequence of poor health status. We should also note that we have little data regarding the comparison populations used in this study. For example, respondents reported a diagnosis of RA in the RA population, but we do not have any further information regarding the severity of their disease or its treatment.

In summary, we report a profound reduction, especially in physical function, among IIM patients compared to RA patients and to the general US population. A history of lung and joint involvement, treatment-resistant disease, and the diagnosis of IBM are the most relevant disease-specific risk factors for poor HRQoL in IIM identified in this study. Further adequately powered studies are needed to assess the strength of the potential relationships between HRQoL and demographic, disease, clinical, and environmental characteristics among IIM patients. Conflicting results from earlier studies are likely attributable to the small sample sizes used and heterogeneity among the IIM groups. Additionally, little information is known regarding the patterns of change of HRQoL in IIM patients after therapy and over time. Existing and future patient registries may provide the most feasible method for carrying out such studies.

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All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be submitted for publication. Dr. Miller had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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