DEMOGRAPHIC AND CLINICAL FEATURES OF INCLUSION BODY MYOSITIS IN NORTH AMERICA

A. DAVID PALTIEL, PhD,[1,2] EINAR INGVARSSON, MBA,[2] DONALD K. K. LEE, PhD,[2] RICHARD L. LEFF, MD,[3] RICHARD J. NOWAK, MD,[4] KURT D. PETSCHKE, BS,[1] SETH RICHARDS-SHUBIK, PhD,[5] ANGE ZHOU, PhD,[2] MARTIN SHUBIK, PhD,[2] and KEVIN C. O'CONNOR, PhD[4]

[1] Yale School of Public Health, New Haven, Connecticut, USA
[2] Yale School of Management, New Haven, Connecticut, USA
[3] Richard L. Leff, MD, LLC, Chadds Ford, Pennsylvania, USA
[4] Department of Neurology, Yale School of Medicine, 300 George Street, Room 353J, New Haven, Connecticut, USA 06511
[5] H. John Heinz III College, Carnegie Mellon University, Pittsburgh, Pennsylvania, USA

ABSTRACT: *Introduction*: Few studies of the demographics, natural history, and clinical management of inclusion body myositis (IBM) have been performed in a large patient population. To more accurately define these characteristics, we developed and distributed a questionnaire to patients with IBM. *Methods*: A cross-sectional, self-reporting survey was conducted. *Results*: The mean age of the 916 participants was 70.4 years, the male-to-female ratio was 2:1, and the majority reported difficulty with ambulation and activities of daily living. The earliest symptoms included impaired use and weakness of arms and legs. The mean time from first symptoms to diagnosis was 4.7 years. Half reported that IBM was their initial diagnosis. A composite functional index negatively associated with age and disease duration, and positively associated with participation in exercise. *Conclusions*: These data are valuable for informing patients how IBM manifestations are expected to impair daily living and indicate that self-reporting could be used to establish outcome measures in clinical trials.

Muscle Nerve **52**: 527–533, 2015

Inclusion body myositis (IBM) is both an autoimmune and degenerative disorder of skeletal muscle of unknown etiology.[1–3] Patients with IBM experience slowly progressive muscle weakness that can occasionally be asymmetric. Muscles most frequently affected include finger and wrist flexors, quadriceps, and the muscles of the lower leg. This muscle involvement is a consistent pattern that is evident clinically and can also be visualized through imaging.[4] The disease manifests as slowly progressive hand and finger grip impairment and difficulty with ambulation. The etiology and pathogenesis of IBM are understood poorly, but aging, genetics, and environment may each play a role.[5,6] IBM is typically sporadic in nature (often termed sIBM) and most often occurs after age 45.[7] The prevalence of IBM in North America has not been reported. However, limited studies in the United States estimate the prevalence per million in Connecticut at 10.7 and at 71 in a single county in Minnesota.[8] A national survey in Australia reported that the disease affects 14.9 per million individuals, and this prevalence increases to 51.3 per million when the estimate is restricted to people over age 50.[9]

The literature on the demographics and clinical history of patients with IBM comprises a very limited number of studies, each of which involves a very small sample of patients. These studies include a cross-sectional study of 64 patients[10]; a long-term observational study of 136 patients at 2 separate centers[11]; a study of 51 patients, in which 23 participated in a 1-year follow-up[12]; separate clinical studies of 18[13] patients and 15 patients[14]; and a study focused on demographic features of 73 patients in Japan.[15] In addition the Myositis Association of America (renamed The Myositis Association [TMA]) compiled a report of their survey that included 364 adult patients with sporadic IBM. Collectively, these studies offer a limited and highly localized portrait of the general and clinical characteristics of sporadic IBM, including the mean age of patients, age of onset, period between symptoms and diagnosis, which muscle groups are most affected, and daily living tasks that are difficult. As a means to consolidate findings from these studies into a valuable metric, the Muscle Study Group (MSG)[16] developed an IBM Functional Rating Scale (IBMFRS). This was used to evaluate 30 IBM patients in a placebo-controlled trial. The scale is based on 10 questions related to tasks associated with daily living.

The rarity of such studies and their limited number of included patients emphasize the difficulty of performing studies in IBM. Moreover, given the rarity of the disease, surveys of considerable size are not possible in single centers. Accordingly, we undertook a self-reporting survey of IBM patients in North America to collect both clinical and demographic data from a relatively large

cohort of subjects. There were 4 aims of this study. The first was to describe the demographics of the IBM patient population; the second was to describe the nature of IBM disability by characterizing the trajectory of disease symptoms, its impact on activities of daily living, and its effect on quality of life; the third was to ascertain the means of diagnosis; and the fourth was to determine whether the natural history of disease varies between population groups. The survey included questions related to demographics, diagnosis, clinical care, and daily living queries that build upon the IBMFRS.

MATERIALS AND METHODS

Survey Implementation. We developed the questionnaire (Supplementary Table S1, which is available online), with guidance from experts in the fields of rheumatology, neurology, economics, operations research, patient registry design, and health care management policy. The survey was implemented in both electronic and paper formats. The electronic version was prepared using the online design, distribution, and analysis software of Qualtrics, a market research and enterprise feedback organization (www.qualtrics.com). A sample of persons with IBM was assembled with the help of 2 patient organizations. TMA is an international organization of roughly 9,000 patients living with inflammatory muscle diseases, including IBM (www.myositis.org). TMA sent an electronic message on our behalf to its approximately 1,400 IBM members with known email addresses. A reminder email was also sent to these persons 2 weeks later. Individuals were asked to voluntarily complete the survey anonymously by means of the Qualtrics online website. Persons who felt uncomfortable or unable to complete the survey online were provided with information to obtain a hard-copy version. TMA mailed a paper copy of the cover letter, consent form, and survey to approximately 1,500 U.S. and Canadian IBM patients in its database who lacked an email address. The Muscular Dystrophy Association (MDA) is a nonprofit health agency dedicated to finding treatments and cures for neuromuscular diseases, including IBM (www.mda.org). The MDA posted a brief article in *Quest*, its online newsletter, (quest.mda.org) describing the survey and providing a link to the Qualtrics website. MDA also e-mailed the article to its registered IBM patients.

The original survey did not include a sufficient query to accurately determine the time between the appearance of symptoms and the date of first diagnosis. We, therefore, created a supplementary survey (Supplementary Table S1) that asked 2 short questions about symptom onset and time of diagnosis. We also asked again for year and place of birth so that we could match these supplemental survey responses with those of the original survey without asking respondents to reveal their protected identity. The request to patients to participate in this supplementary survey was emailed to patients in the TMA database, and an article about the supplemental survey also appeared in the MDA *Quest* newsletter.

Inclusion and Exclusion Criteria. We included all the records submitted (paper or electronic) by patients confirming a diagnosis of IBM. A few participants ($n = 10$) responded indirectly through a caregiver (a spouse or child), and several participants ($n = 29$) asked (and received) permission to respond on behalf of a deceased loved one; these records were included. Exclusion was only applied in instances of duplication. Duplicate records were identified first by examining records for matching year and place of birth. Records that matched in these 2 categories were then examined for matching in 6 additional categories: gender, ethnicity, height, education level, annual income, and marital status. Duplicates that matched in all 8 categories were eliminated.

Ethics. All patients provided informed consent to participate in the survey. The survey instrument, which included the questionnaire, accompanying consent forms, and data management protocols, was approved by the Human Research Protection Program at Yale School of Medicine. No identifiers or any other information that could be used to identify or locate survey respondents were collected. At no time did either TMA or MDA share their mailing lists with the investigators. Completion and submission of surveys was completely voluntary and anonymous.

Statistical Analyses. Column statistics were calculated with Microsoft Excel. The MEANS procedure for calculating latency was performed with Statistical Analysis System (SAS) software. A composite index of function was constructed as the sum of response scores (0–6) over 10 categories of disability measured in the survey (cutting food and handling utensils, dressing, fine motor tasks, handwriting, hygiene, sit to stand, swallowing, turning in bed/adjusting covers, walking, and climbing stairs). A higher composite index reflects greater ability. To explore the relationships between age, time since onset of disease, and exercise on overall functional status, fixed effects models were fitted to the composite index. The models included combinations of the following variables: age, gender, time since diagnosis (in years), the type of the exercise in which a respondent engages, and the

Table 1. Age and gender of the survey participants.		
Demographic category	Respondents $n = 916$	Responding yes (%)
Age		
< 40	3	0.33
40–49	27	2.9
50–59	157	17.1
60–69	303	33.1
70–79	292	31.9
≥ 80	134	14.6
Gender	916	
Men	613	66.9
Women	303	33.1

hours spent on that exercise in a week. To evaluate different aspects of the relationship with exercise, we estimated 3 separate fixed effects models that included indicators for either: any participation in exercise, type of exercise, or hours of exercise per week. These models also included age and gender as control variables. An algorithm was applied to deal with missing data if a respondent did not answer a question and to deal with multiple variables. All computations were performed using Statistical Analysis System 9.3 (SAS). Least squares (LS) means for each exercise category (defined by type of exercise and hours per week), 95% confidence intervals (CIs) for pairwise differences in LS means, and P-values for these pairwise comparisons were generated. Normal probability plots and residual plots were used to assess the assumptions of the model.

RESULTS

Participation and General Demographics. We received a total of 973 responses (795 online; 178 paper), of which 57 were considered duplicates. The online survey response rate was 795/1,400 (56.7%) based on the original TMA email solicitation. Additional online responses were received following the announcement in the TMA newsletter that could not be attributed exclusively to the email solicitation. The response rate for the mailed paper surveys was 178/1500 (11.8%). Of the collective 916 unique respondents 613 (66.9%) were men, yielding a male:female ratio of 2:1 (Table 1). The mean age of the subjects was 70.4 (SD, 10.2) years (Table 1). The age range was 32–100 years. The majority (65.0%) of the subjects were between ages 60 and 80 years. Only 3 (0.3%) of the 916 respondents were less than age 40 years. Additional demographics that were collected included race, living arrangements, employment, height, and weight (Supplementary Table S2). The race of the responding majority was white (95.5%), and their ethnicity was non-Hispanic/Latino (97.3%). Many

of the respondents were retired (75.3%). Most respondents still lived at home (91.7%), and a high fraction lived with a spouse (75.6%). The likelihood of residing in an assisted living facility was higher for those respondents living alone (10.0%) than for those living with a spouse (1.5%). The weight and height distributions of the respondents were unremarkable. However, the body mass index (BMI) of a considerable fraction (43%), was greater than 27.

Ambulation and Daily Living. Daily living was evaluated through questions we developed using the IBMFRS disability scale[16] as a guide. While the validity of the IBMFRS for self-administration is not yet established, such an assessment is beyond both the exploratory scope of this study and our use of the IBMFRS in guiding the development of our survey. Our questions included rating scales of difficulty in daily tasks including handwriting, eating, fine motor tasks, dressing, standing, walking, and climbing stairs (Supplementary Table S3). Among these assessments, those that were notably influenced by the disease were standing from sitting and walking. Many subjects reported that rising from the sitting position requires use of arms (44.5%) or requires assistance from a device or person (34.2%). Similarly, the majority of subjects reported difficulty with walking, as only 5.7% qualified their ability as normal. Difficulty included unsteadiness while walking (17.0%), dependence on an assistive device (24.6%), or dependence on a wheelchair (26.6%). Disability was apparent in stair climbing assessment. The majority of subjects (56.8%) reported inability to climb stairs, while a further 17.4% depend on hand rails or additional support (17.3%). Two-thirds (66.2%) reported inability to walk more than a block. Nearly half of the subjects (46.6%) reported participation in some form of exercise.

A majority of subjects reported that IBM produced either extreme (41.2%) or considerable (32.6%) interference with work both in and out of the home, while very few (2.0%) indicated that it had no influence. Similarly, most subjects reported that IBM influenced their energy levels some (23.7%), all (32.0%), or most (37.7%) of the time. Slightly more than half (55.3%) operated a motor vehicle alone, and the majority traveled away from home. More than half indicated that the disease influenced their mood toward depression. Only a third of the respondents (36.7%) reported that eating or swallowing was unaffected, while nearly half reported difficulty swallowing (44.0%), and 12.0% reported that they choke frequently. Tasks that require motor skills, including handwriting, handling utensils, dressing, hygiene, adjusting in
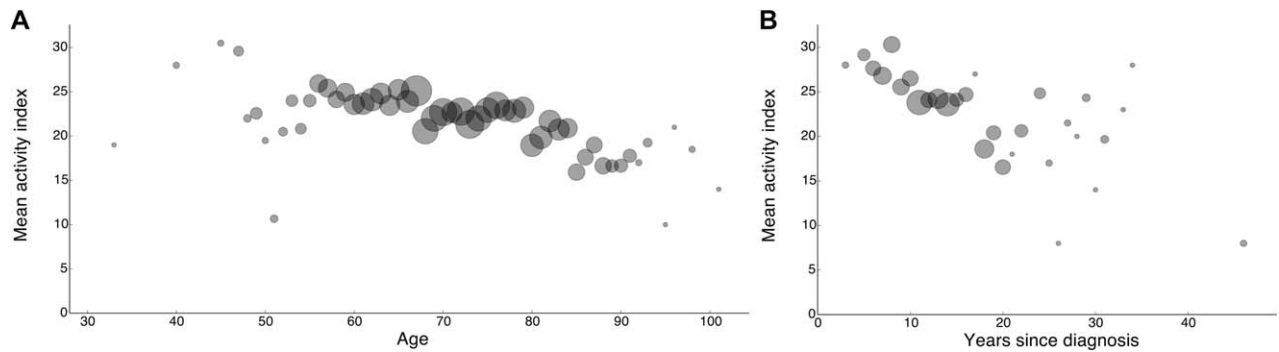
FIGURE 1. Age and disease duration associate with disability in patients with IBM. A functional index, calculated from 10 scores reporting ambulation and daily living activities, negatively associated with both the age of respondents and the number of years since diagnosis. The mean of the functional activity index was plotted against the age (years) of respondents **(A)** or disease duration **(B)** indicated by the number of years since the diagnosis of IBM. The size of the data points in each graph represents the relative number of respondents in each group.

bed, and fine motor skills were all influenced in many subjects and were rarely reported as normal. Despite these difficulties, 58.4% of the subjects reported that they did not employ assistance in their activities of daily living.

Diagnosis. Subjects were asked several questions related to their diagnosis and clinical care (Supplementary Table S4). Regarding the symptom(s) that compelled them to first seek medical care, the majority cited weakness (69.9%) as the chief ailment followed by difficulty in climbing stairs (59.6%), falls (56.8%), or impaired use of arms and legs (53.4%). Fewer reported fatigue (32.0%) and trouble swallowing (23.0%). The time between the observation of these initial symptoms and diagnosis was greater than 2 years in nearly half of the subjects (45.9%). Other respondents reported shorter intervals: between 1 and 2 years in 22.8%;

6 and 12 months in 14.3%, and less than 6 months in the remaining 15.8% of subjects. The mean latency between disease onset and establishment of diagnosis was 4.7 years for the subset of patients ($n = 280$) who completed the second follow-up survey. This value compares favorably with estimates (5.7 years) from other series that report this metric[13,14,17,18] Approximately half of the subjects (50.9%) reported their initial diagnosis as IBM. The other half was diagnosed initially with polymyositis (18.8%) or arthritis (4.3%), and the remainder did not know or were diagnosed with another disease that was not disclosed. This initial diagnosis was provided to the majority of the subjects (69.3%) by a neurologist. Both rheumatologists (14.4%) and primary care providers (10.7%) provided the initial diagnosis in a noticeably smaller subset. Neurologists provided the first diagnosis of IBM in 78.3% of the subjects. Nearly all
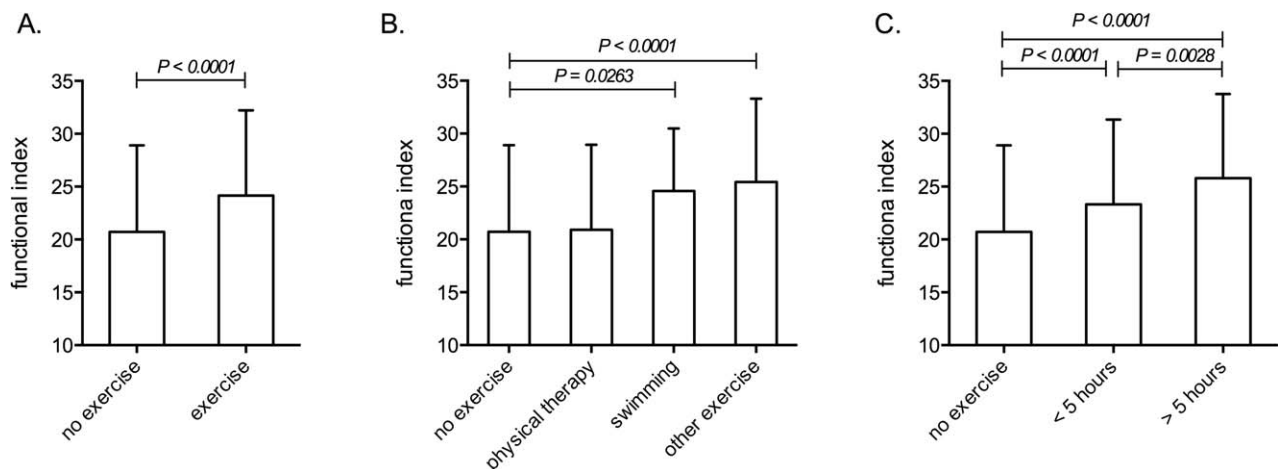

FIGURE 2. Participation in exercise associates with better function in patients with IBM. A functional index, calculated from scores reporting ambulation and daily living activities, was compared among survey respondents. Three fixed effects models were estimated that include age and gender, as well as indicators for either: any participation in exercise **(A)**, or type of exercise (swimming, physical therapy, or other unspecified forms of exercise) **(B)**, or hours of exercise per week **(C)**. Using these indicators, comparisons were made relative to no exercise **(A–C)**, and between types of exercise **(B)** or hours of exercise **(C)**. Statistical significant differences are indicated.

(90.8%) reported that a muscle biopsy was associated with the diagnosis of IBM. Finally, almost all (97.7%) had no knowledge of IBM remissions through their own experience or that of other patients.

Factors Correlated with Function and Disability. A functional index was used to determine whether disability was associated with demographics and daily living. There was an association between age and functional ability ($P < 0.0001$), indicating that older respondents experienced greater disability (Fig. 1A). Similarly, for every year since diagnosis, there was an average decrease of 0.38 in the overall functional index ($P < 0.0001$), highlighting disease progression and impairment (Fig. 1B). We also found associations between exercise and degree of function (Fig. 2) by comparing the functional index of subjects who exercised (controlling for age and gender) to that of subjects who did not. We observed that participation in exercise was significantly associated ($P < 0.0001$) with increased functional ability (Fig. 2A). Subjects who participated in swimming or other unspecified forms of exercise reported greater functional ability (Fig. 2B) than respondents who did not exercise ($P = 0.0263$ for swimming and $P < 0.0001$ for unspecified forms). Participation in physical therapy was not associated significantly ($P = 0.5042$) with increased functional ability (Fig. 2B). The amount of time spent exercising was associated significantly with increased functional ability. Respondents who spent either up to 5 h or more than 5 h per week had significantly higher functional index scores ($P < 0.0001$ for both categories) compared with respondents who did not exercise (Fig. 2C). Moreover, respondents who spent more than 5 h per week participating in exercise had greater functional ability ($P = 0.0028$) than those whose exercise was limited to 5 h or less (Fig. 2C).

DISCUSSION

Overall, our data set agreed very well with the existing literature on IBM. We obtained a male:female ratio of 2:1 which is in agreement with several other studies[11,12,15,18,19] However, other observational studies of IBM report ratios that are more extreme (6:1)[14] and also closer to equal distribution between genders (1.25:1).[13] IBM is reported rarely in patients less than age 40 years[11,14]; our data reflected this, in that only 0.3% of the respondents were less than age 40 years. The rate of functional decline over time in IBM patients varies based on the age of onset. Those in whom the disease onset occurs between 40 and 59 years progress more slowly than those whose onset occurs between ages 60 and 79 years.[20] Given that IBM develops slowly and starts insidiously, by the

time medical help is pursued there is already significant muscle weakness, atrophy, and advanced degeneration even in clinically strong muscles. Our data reflect this, in that a large fraction (nearly 70%) of respondents reported muscle weakness as the reason for seeking medical advice. Only half of the subjects reported IBM as their initial diagnosis, indicating that misdiagnosis of IBM is common. Other studies that queried this also reveal that rates of initial misdiagnosis can reach as high as 85%.[18] Neurologists, confirming another survey, most often perform evaluations and provide a diagnosis of IBM.[18] These findings highlight that patients suspected of having myositis should be directed to clinicians who specialize in inflammatory myopathies. Overall, our study provided data that were in alignment with several prior clinical studies, indicating that self-reporting may be valuable for acquiring outcome measures in clinical studies of IBM.

A few interesting patterns emerged from our *post-hoc* analysis of associations. We observed that approximately three-fourths of the respondents lived at home with a spouse. Respondents living alone were much more likely to reside in an assisted living facility than respondents who lived with a spouse. These data taken together may reflect that spousal help is an important contributing factor in keeping those with the disease in their homes. We also focused our inquiry of associations with the degree of disability. Given the progressive nature of the disease it was not unexpected that individuals with longer disease duration experienced less ability in ambulation and tasks accompanying daily living. The same was true of age. Older subjects also experienced increased disability compared with their younger counterparts. Interestingly, participation in exercise and duration of participation were strongly associated with increased ambulation and performance of daily living tasks. Exercise provides several beneficial effects in polymyositis and dermatomyositis.[21] Although studies in IBM are few, it appears to prevent loss of muscle strength/deterioration.[22,23] While the associations we found do not suggest causality, we cannot discern whether exercise slows disability or if persons with less severe disability are more likely to exercise, they warrant further exploration.

Although this study has provided a wealth of information, the limitations must be considered. The origin of this study was founded in the objective to build a national registry of IBM patients and the associated demographics and clinical data. Any study, such as ours, in which a convenience sample is used, includes inherent bias. Self-reporting allows a single study to cover a huge

geographic area and therefore a very large cohort of subjects; further research is needed, however, to confirm the validity of our question set for self-administration. Among the obvious limitations are that a clinical evaluation was not performed, thus the possibility that some respondents have not been properly diagnosed remains. However, our data set matches other surveys of these patients, and more than 90% reported undergoing muscle biopsy during diagnosis. We are aware that surveys conducted in the context of patient care will capture a wide diversity of patients. Our online survey would exclude those unfamiliar with the Internet. We sought to address this limitation by including a standard mail version of the survey. Additional comorbidities were not queried which may have contributed to conditions that we ascribed to IBM. Overall, our data derived from several queries was in agreement with several other studies, suggesting the validity of our data set in light of these limitations. Finally, we did not include a question that would allow us to distinguish between hereditary inclusion body myopathy and sporadic IBM. Hereditary inclusion body myopathy encompasses a heterogeneous group of vacuolar myopathies that can be either autosomal recessive or dominant[24]; they are rare, as a very small number of cases have been reported.[24–26] Although the 2 diseases share several pathologic features, hereditary inclusion body myopathy is not associated with an intramuscular lymphocyte infiltrate, thus it is termed a myopathy rather than a myositis, and the disease spares the quadriceps. Additionally, unlike sporadic IBM, which mostly affects individuals over age 50 years, the clinical onset of hereditary inclusion body myopathy usually occurs in individuals aged between 20 and 40.[27] Given the age of onset of our subjects, that none of the respondents reported knowing any family members with IBM, and that this disease is extraordinarily rare, we reason that our data include very few, if any cases of hereditary inclusion body myopathy.

The results are of value for 2 main purposes. The first is that these data will be valuable for informing patients of the manifestations of the disease. They may help clinicians explain to their IBM patients their prognoses and specifically what they can expect to experience in their daily lives based on the experiences of a large group of their peers. Second, further value may be realized by overcoming the absence of standardized outcome measures able to capture meaningful changes connected with disability and quality of life. We suggest that self-reporting surveys of patients with IBM are accurate in terms of assessing demographics and, more importantly, evaluating disability. Thus, such instruments may be considered for use as outcome measures for clinical trials, as this approach could reduce considerably both clinic visits and, by extension, the costs of clinical trials.

REFERENCES

1. Greenberg SA. Pathogenesis and therapy of inclusion body myositis. Curr Opin Neurol 2012;25:630–639.
2. Amato AA, Barohn RJ. Inclusion body myositis: old and new concepts. J Neurol Neurosurg Psychiatry 2009;80:1186–1193.
3. Schmidt J, Dalakas MC. Inclusion body myositis: from immunopathology and degenerative mechanisms to treatment perspectives. Expert Rev Clin Immunol 2013;9:1125–1133.
4. Cox FM, Reijnierse M, van Rijswijk CS, Wintzen AR, Verschuuren JJ, Badrising UA. Magnetic resonance imaging of skeletal muscles in sporadic inclusion body myositis. Rheumatology (Oxford) 2011;50:1153–1161.
5. Askanas V, Engel WK, Nogalska A. Pathogenic considerations in sporadic inclusion-body myositis, a degenerative muscle disease associated with aging and abnormalities of myoproteostasis. J Neuropathol Exp Neurol 2012;71:680–693.
6. Hohlfeld R, Engel AG, Goebels N, Behrens L. Cellular immune mechanisms in inflammatory myopathies. Curr Opin Rheumatol 1997;9:520–526.
7. Rose MR. 188th ENMC International Workshop: Inclusion Body Myositis, 2–4 December 2011, Naarden, The Netherlands. Neuromuscul Disord 2013;23:1044–1055.
8. Wilson FC, Ytterberg SR, St Sauver JL, Reed AM. Epidemiology of sporadic inclusion body myositis and polymyositis in Olmsted County, Minnesota. J Rheumatol 2008;35:445–447.
9. Needham M, Corbett A, Day T, Christiansen F, Fabian V, Mastaglia FL. Prevalence of sporadic inclusion body myositis and factors contributing to delayed diagnosis. J Clin Neurosci 2008;15:1350–1353.
10. Badrising UA, Maat-Schieman ML, van Houwelingen JC, van Doorn PA, van Duinen SG, van Engelen BG, et al. Inclusion body myositis. Clinical features and clinical course of the disease in 64 patients. J Neurol 2005;252:1448–1454.
11. Benveniste O, Guiguet M, Freebody J, Dubourg O, Squier W, Maisonobe T, et al. Long-term observational study of sporadic inclusion body myositis. Brain 2011;134(Pt 11):3176–3184.
12. Cortese A, Machado P, Morrow J, Dewar L, Hiscock A, Miller A, et al. Longitudinal observational study of sporadic inclusion body myositis: implications for clinical trials. Neuromuscul Disord 2013;23:404–412.
13. Lindberg C, Persson LI, Bjorkander J, Oldfors A. Inclusion body myositis: clinical, morphological, physiological and laboratory findings in 18 cases. Acta Neurol Scand 1994;89:123–131.
14. Amato AA, Gronseth GS, Jackson CE, Wolfe GI, Katz JS, Bryan WW, et al. Inclusion body myositis: clinical and pathological boundaries. Ann Neurol 1996;40:581–586.
15. Nakanishi H, Koike H, Matsuo K, Tanaka F, Noda T, Fujikake A, et al. Demographic features of Japanese patients with sporadic inclusion body myositis: a single-center referral experience. Intern Med 2013;52:333–337.
16. Jackson CE, Barohn RJ, Gronseth G, Pandya S, Herbelin L. Inclusion body myositis functional rating scale: a reliable and valid measure of disease severity. Muscle Nerve 2008;37:473–476.
17. Lotz BP, Engel AG, Nishino H, Stevens JC, Litchy WJ. Inclusion body myositis. Observations in 40 patients. Brain 1989;112(Pt 3):727–747.
18. Felice KJ, North WA. Inclusion body myositis in Connecticut: observations in 35 patients during an 8-year period. Medicine 2001;80:320–327.
19. Chahin N, Engel AG. Correlation of muscle biopsy, clinical course, and outcome in PM and sporadic IBM. Neurology 2008;70:418–424.
20. Peng A, Koffman BM, Malley JD, Dalakas MC. Disease progression in sporadic inclusion body myositis: observations in 78 patients. Neurology 2000;55:296–298.
21. Alemo Munters L, Alexanderson H, Crofford LJ, Lundberg IE. New insights into the benefits of exercise for muscle health in patients with idiopathic inflammatory myositis. Curr Rheumatol Rep 2014;16:429.

22. Arnardottir S, Alexanderson H, Lundberg IE, Borg K. Sporadic inclusion body myositis: pilot study on the effects of a home exercise program on muscle function, histopathology and inflammatory reaction. J Rehabil Med 2003;35:31–35.
23. Alexanderson H, Lundberg IE. Exercise as a therapeutic modality in patients with idiopathic inflammatory myopathies. Curr Opin Rheumatol 2012;24:201–207.
24. Askanas V, Engel WK. Sporadic inclusion-body myositis and hereditary inclusion-body myopathies: current concepts of diagnosis and pathogenesis. Curr Opin Rheumatol 1998;10:530–542.
25. Sivakumar K, Semino-Mora C, Dalakas MC. An inflammatory, familial, inclusion body myositis with autoimmune features and a phenotype identical to sporadic inclusion body myositis. Studies in three families. Brain 1997;120(Pt 4):653–661.
26. Sivakumar K, Dalakas MC. The spectrum of familial inclusion body myopathies in 13 families and a description of a quadriceps-sparing phenotype in non-Iranian Jews. Neurology 1996;47:977–984.
27. Simmons Z, Towfighi J. Sporadic inclusion body myositis and hereditary inclusion body myopathy. J Clin Neuromuscul Dis 2002;3:122–132.