

Original article

Survival and associated comorbidities in inclusion body myositis

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Abstract

Objective. To evaluate survival and associated comorbidities in inclusion body myositis (IBM) in a population-based, case-control study.

Methods. We utilized the expanded Rochester Epidemiology Project medical records-linkage system, including 27 counties in Minnesota and Wisconsin, to identify patients with IBM, other inflammatory myopathies (IIM), and age/sex-matched population-controls. We compared the frequency of various comorbidities and survival among groups.

Results. We identified 50 IBM patients, 65 IIM controls and 294 population controls. Dysphagia was most common in IBM (64%) patients. The frequency of neurodegenerative disorders (dementia/parkinsonism) and solid cancers was not different between groups. Rheumatoid arthritis was the most common rheumatic disease in all groups. A total of 36% of IBM patients had a peripheral neuropathy, 6% had Sjögren's syndrome and 10% had a haematologic malignancy. T-cell large granular lymphocytic leukaemia was only observed in the IBM group. None of the IBM patients had hepatitis B or C, or HIV. IBM patients were 2.7 times more likely to have peripheral neuropathy, 6.2 times more likely to have Sjögren's syndrome and 3.9 times more likely to have a haematologic malignancy than population controls. IBM was associated with increased mortality, with a 10-year survival of 36% from index, compared with 67% in IIM and 59% in population controls. Respiratory failure or pneumonia (44%) was the most common cause of death.

Conclusions. IBM is associated with lower survival, and higher frequency of peripheral neuropathy, Sjögren's syndrome and haematologic malignancies than the general population. Close monitoring of IBM-related complications is warranted.

Key words: inclusion body myositis, case-control study, large granular lymphocytic leukemia, peripheral neuropathy, Sjögren's syndrome

Rheumatology key messages

- Compared to population controls, patients with inclusion body myositis (IBM) have lower survival.
- Peripheral neuropathy, Sjögren's syndrome, and T-cell large granular lymphocytic leukemia are more common in IBM.
- The frequency of neurodegenerative disorders and solid cancers was similar to population controls.

Introduction

Inclusion body myositis (IBM) is a progressive muscle disease associated with distinctive clinical and histopathological characteristics. IBM histopathological findings include a combination of an inflammatory exudate invading

non-necrotic muscle fibres, and disrupted protein homeostasis as witnessed by the presence of rimmed vacuoles and congophilic inclusions [1, 2]. The congophilic inclusions consist of a wide spectrum of protein aggregates reminiscent of neurodegenerative diseases of ageing, such as amyloid- β peptides, ubiquitin, phosphorylated tau and TDP-43 [3–5]. Despite these common histopathological features, the prevalence of neurodegenerative diseases in IBM patients has not been evaluated in comparison to the general population. Interestingly, more than expected frequency of peripheral neuropathy has been reported in IBM patients, and it remained unclear whether this was purely related to age or comorbidities [6, 7]. Given the

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inflammatory component on muscle biopsy and the poorly understood disease pathogenesis, several studies evaluated the association of IBM with various disorders: immune-mediated such as rheumatic diseases, infectious such as hepatitis C and HIV, and neoplastic such as chronic T-cell large granular lymphocytic (T-LGL) leukaemia [8–12]. However, the majority of the literature derives from cross-sectional retrospective studies performed at referral centres, as most population-based studies focussed on evaluating the prevalence of the disease [13–19]. Reported IBM prevalence varies widely between studies, with an estimated overall prevalence of 24.8–45.6 per million according to a meta-analysis [13–20]. Furthermore, most previous studies reported that IBM does not affect longevity, by comparing to life expectancy in general population databases [21, 22]. A head-to-head comparison in a case-control population-based study is lacking.

The Rochester Epidemiologic Project (REP), started about half a century ago, is a comprehensive medical records linkage system for all residents of Olmsted County, Minnesota, USA [23]. Mayo Clinic and Olmsted Medical Center being the only healthcare systems in Olmsted county makes the REP an ideal setting for population-based studies including calculation of incidence and prevalence of diseases. This resulted in several epidemiologic projects on various diseases including inclusion body myositis [14, 24]. In the most recent study, we identified 20 patients with IBM who lived in Olmsted county (population of about 150 000) between 1980 and 2019 [24]. In that study, we reported the highest prevalence of IBM to date (182 per million in people 50 years of age or older). The long-term follow-up over 40 years enabled us to provide detailed information about the natural history of the disease. We also found shorter survival in IBM patients; however, the study was limited by the low number of patients given the small population of Olmsted county. This also precluded a comprehensive evaluation for associated comorbidities.

In 2010, the REP population was expanded (expanded REP) to include 27 counties in Southern Minnesota and Western Wisconsin, to capture a population of >700 000 [25]. The large expanded REP population facilitated population-based studies on rare diseases such as IBM, and allowed us to identify 50 patients with IBM seen between 2010 and 2019, only five of whom were included in previous Olmsted county studies [14, 24]. In this study, we aimed to evaluate the association of IBM with the various aforementioned neurological, immune-mediated, infectious and neoplastic disorders, in a large case-control, population-based study. We also aimed to evaluate whether IBM affects survival, by head-to-head comparison with age and sex-matched controls. In addition, we aimed to compare the findings in IBM patients to a group of patients with other idiopathic inflammatory myopathies (IIM).

Methods

Study population

The study was approved by the Institutional Review Boards of the Mayo Clinic and of Olmsted Medical Center. The study was considered minimal risk by both Institutional Review Boards; therefore, the requirement for informed consent was waived. However, records of any patient who had not provided authorization for their medical records to be used for research, as per Minnesota statute 144.335, were not reviewed.

Case ascertainment

We searched the medical records-linkage system of the expanded REP to identify participants who had the diagnosis codes for IBM using ICD9 and ICD10 codes (359.71, G72.41), polymyositis (710.4, M33.20, M33.21, M33.22, M33.29) and dermatomyositis (710.3, M33.10, M33.11, M33.12, M33.13, M33.19). We then performed a manual chart review and review of muscle biopsy reports of the identified patients to classify patients into IBM vs IIM. We included in the IBM group patients fulfilling European Neuromuscular Centre (ENMC) 2011 diagnostic criteria for clinico-pathologically defined, clinically-defined, or probable IBM [26]. We included in the IIM groups patients with the following entities: dermatomyositis, overlap myositis, antisynthetase syndrome, immune-mediated necrotizing myopathy and nonspecific myositis [27, 28]. Patients with myositis were excluded from the IIM control group if there was clinical suspicion for IBM (not fulfilling ENMC diagnostic criteria), or if the available information was not sufficient to exclude IBM. We also excluded patients with limited information regarding the diagnosis in their chart.

Matching

Index date consisted of the first time the patient was coded for the diagnosis of IBM. Each IBM patient was individually matched by age (within a year) and sex, with six population controls from the REP database seen during the same calendar year. As we expected the number of individuals with other IIM to be limited and the IIM population to be younger, each IBM patient was individually matched by age (± 15 years) and sex to one or two IIM cases.

Data collection

The medical records of cases and controls were electronically searched to extract patients' demographics, tobacco use and education level at index date. For IBM disease characteristics, we searched diagnostic codes for dysphagia, gastrostomy tube, impaired gait and wheelchair use. Patients' prescribed medication lists were electronically pulled and manually reviewed to abstract data regarding the use of immunosuppressant drugs. For IBM

patients, we performed a manual chart review to determine the indication for corticosteroid treatment.

Regarding the associated conditions, we electronically pulled data by diagnostic codes for the following entities of interest: neurodegenerative disorders (any form of dementia, Parkinson's disease, or other Parkinsonian disorders), peripheral neuropathy, peripheral neuropathy-associated conditions (diabetes mellitus, vitamin B12 deficiency, thyroid dysfunction and monoclonal gammopathy), rheumatic diseases (RA, lupus erythematosus, Sjögren syndrome and scleroderma), malignancy of any type, haematologic cancers, and infections (hepatitis B and C, and HIV). Infectious etiologies were also searched for by serological testing data. We also retrieved mortality data including cause of death and death certificates. All diagnostic codes were reviewed for accuracy. We then performed a manual chart review of the following variables that cannot be ascertained solely based on diagnostic codes: peripheral neuropathy, Sjögren syndrome, malignancy of any type (including haematologic) and cause of death (chart review and death certificate review). For malignancies, we included the malignancies that occurred within 5 years preceding match date or any time afterwards. For recurring cancers (such as skin cancers), they were only included if they occurred for the first time during the defined time frame.

Statistics and data analysis

Descriptive summaries are presented as frequency and percentage for categorical variables, and mean (s.d.) for continuous variables. Statistical analysis was carried out using JMP[®] 13 and SAS version 9.4 (SAS Institute Inc., Cary, NC, USA) statistical software. Comparison among the three groups was performed using Kruskal–Wallis, χ^2 or Exact test as appropriate. All of the tests were two sided. When the *P*-value for an outcome comparing the three groups reached statistical significance (<0.05), groups were then compared in a pairwise manner using Wilcoxon Rank Sum, χ^2 or Exact test as appropriate. This was followed by logistic regression to evaluate for the association between the outcomes of interest (comorbidities with *P* < 0.05) and the groups, while adjusting for age at index; reported as odds ratios and [95% CI]. Time-to-death as an end point was analyzed using Kaplan–Meier method and Cox proportional hazard regression.

Results

Demographics and baseline characteristics

Fifty patients fulfilled the 2011 ENMC criteria for IBM and included 31 clinicopathologically-defined, 16 clinically-defined and three probable IBM. We identified 69 IIM controls: 32 with dermatomyositis, 13 with anti-synthetase syndrome, five with overlap myositis, 17 with nonspecific myositis and two with necrotizing autoimmune myopathy. Demographic data is shown in

Table 1. Patients in the IIM group were on average 6.5 years younger and more commonly females. All IBM patients were white, one of them Hispanic; racial and ethnic distribution of IBM patients are not different from those of the catchment area. There was no difference in the use of tobacco or educational level between groups. Dysphagia was most common in IBM group, as IBM patients were 7.6 [3.8, 14.9] times more likely to have dysphagia than population controls (*P* < 0.0001). There was a trend for IBM patients to have more dysphagia than IIM patients; however, this became less evident adjusting for age: odds ratio of 1.6 [0.7, 3.6] (*P* = 0.23). In contrast, IBM patients were 3.7 [1.5, 9] times more likely to have impaired gait compared with the IIM group (*P* = 0.0036), and 4.2 [2.1, 8.7] times compared with the population controls (*P* < 0.0001). A small number of patients were coded for the use of a wheelchair; nevertheless, this was most common in the IBM group. Regarding medication exposure during the study period, 22 (44%) IBM patients and 29 (44.6%) IIM patients were treated with corticosteroids for their condition. Comparing the group of IBM patients who were treated with corticosteroids vs the ones who were not, there was no statistically significant difference in age at index (mean: 71.5 vs 74.4 years, respectively), sex (50% males vs 64.3%), the presence of dysphagia (68.2% vs 60.7%), gait difficulty (77.3% vs 71.4%) or follow-up duration (40.8 vs 58.1 months, *P* = 0.074). Patients were maintained on varying doses of oral prednisone. They were usually started on a high dose of oral prednisone followed by a slow taper. The mean reached high dose was 43.4 mg/day (s.d. 19.5). Duration of treatment was highly variable with a mean of 5.5 years (s.d. 7.2). 25 (38.5%) IIM and 17 (34%) IBM patients were treated with an immunosuppressant drug (IIM: MTX, AZA, MMF, cyclosporin, or rituximab; IBM: MTX or MMF).

Association with neurological conditions

Results are shown in **Table 2**. There was no statistically significant difference in the frequency of Alzheimer's or Parkinson's diseases between the groups. Peripheral neuropathy was more common in IBM and IIM patients than population controls. IBM patients were 2.7 [1.4, 5.3] times more likely to have a peripheral neuropathy than population controls (*P* = 0.0033). Diabetes mellitus, thyroid dysfunction and vitamin B12 deficiency were not more common in IBM group to explain the increased frequency of peripheral neuropathy. There was a trend for increased frequency of a monoclonal gammopathy of uncertain significance in the IBM group that did not reach statistical significance (could be due to small sample size).

Association with rheumatic diseases

Rheumatic diseases were more common in IBM and IIM patients than population controls (**Table 2**). RA was the most common rheumatic disease in all groups. IBM patients were 6.4 [1.3, 33.2] times more likely to have Sjögren's syndrome than population controls (*P* = 0.026).

TABLE 1 Demographics and baseline characteristics of patients

Variable	IBM (n = 50)	IIM (n = 65)	Population controls (n = 294)
Demographics			
Age (years)	73.5 (10.39)	67.4 (10.98)**	73.0 (10.44)
Sex: male	29 (58)	25 (38.4)	173 (58.8)
Race, n (%)			
Black	0 (0.0%)	2 (3.1)	1 (0.3)
Asian	0 (0.0%)	1 (1.5)	12 (4.1)
Other/mixed	0 (0.0%)	3 (4.6)	3 (1.0)
White	50 (100)	59 (90.8)	277 (94.2)
Unknown	0 0	0 0	1 (0.3)
Hispanic, n (%)	1 (2)	1 (1.5)	8 (2.7)
Weight (kg)	80.1 (14.54)	77.6 (20.25)	79.0 (17.69)
Height (cm)	170.1(10.88)	165.9 (9.86)	167.7 (9.72)
Tobacco use			
Current or former smoker	7 (17.1)	6 (11.5)	31 (16.1)
Unknown	9	13	101
Education level			
Primary	1 (2.2)	0 0	8 (2.9)
Secondary	16 (34.8)	24 (38.1)	89 (32.1)
Tertiary	29 (63)	39 (61.9)	180 (65.5)
Unknown	4	2	17
Disease characteristics			
Dysphagia****	32 (64)	30 (46.2)#	61 (20.8)****
Gastrostomy tube*	3 (6)	5 (7.7)	5 (1.7)
Impaired gait****	37 (74)	24 (36.9)****	128 (43.5)****
Wheelchair use**	5 (10)	1 (1.5)*	5 (1.7)*

Categorical variables are displayed as *n* (percentage), and continuous variable as mean (s.d.). The *P*-value corresponding to comparison of the three groups is shown in the first column, *P*-value for IBM vs IIM group is shown in 'IIM' column, and *P*-value for IBM vs population controls is shown in 'Population controls' column. * $0.01 \leq P\text{-value} < 0.05$; ***P*-value < 0.01 ; ****P*-value < 0.001 ; *****P*-value < 0.0001 ; #*P*-value = 0.057. IBM: inclusion body myositis; IIM: inflammatory myopathy.

Association with malignancies

A total of 135 patients developed 155 malignancies within 5 years preceding match date or any time afterwards. Among the 20 patients with more than one malignancy, 15 had skin cancer. There was no difference in the frequency of patients with solid cancers between the groups as shown in Table 2. The distribution of various cancer types per group is shown in Supplementary Fig. S1, available at *Rheumatology* online. However, haematologic malignancies were most common in IBM group, and IBM patients were 3.9 [1.2, 12.6] times more likely to have a haematologic malignancy than population controls ($P = 0.021$). Although IBM patients were 2.8 [0.6, 12.9] times more likely to have a haematologic malignancy than IIM patients, the difference did not reach statistical significance ($P = 0.18$), which may be due to limited sample size given the wide 95% CI. Chronic T-cell large granular lymphocytic leukaemia was only observed in IBM group. In both patients, the diagnosis of T-LGL leukaemia preceded the diagnosis of IBM. The first patient presented with lymphocytosis, neutropenia and elevated lactate dehydrogenase level, and had bone marrow involvement. She was diagnosed with T-LGL leukaemia 3 years prior to the diagnosis of IBM. The patient passed away from respiratory failure

attributed to IBM, 13 years after IBM symptom onset. The second patient presented with neutropenia and had bone marrow involvement. She was diagnosed with T-LGL leukaemia, and then a year and a half later she was diagnosed with IBM. Haematologic malignancies in IIM group were all B-cell lymphomas. The most common haematologic malignancy in population controls was diffuse large-B-cell lymphoma. None of the IBM patients and one of the IIM patients with haematologic malignancies was exposed to an immunosuppressant (AZA).

Association with infectious etiologies

The number of patients with infectious diseases of interest was low in all groups, with no difference in frequency between groups. None of the IBM patients had hepatitis B, hepatitis C or HIV. We then evaluated the test positivity rates (number of patients with positive serology/total number of tested patients $\times 100$) for participants with available serological testing. For hepatitis B, the positivity rate was 0% (0/8) for IBM, 0% (0/29) for IIM and 6.45% (2/31) for population controls ($P > 0.05$). For hepatitis C, the positivity rate was 0% (0/9) for IBM, 2.9% (1/34) for IIM and 1.8% (1/57) for population controls ($P > 0.05$). The second patient with hepatitis C was identified by ICD

TABLE 2 Inclusion body myositis-associated conditions

	IBM (n = 50)	IIM (n = 65)	Controls (n = 294)
Neurological			
Dementia	3 (6)	7 (10.8)	31 (10.5)
Parkinson's disease	2 (4)	2 (3.1)	17 (5.8)
Peripheral neuropathy**	18 (36)	15 (23.1)	51 (17.4)**
Conditions that may cause a peripheral neuropathy:			
• Diabetes mellitus [†]	16(32)	19(29)	129(44)
• Hypo/Hyperthyroidism*	11(22)	31(48)**	87(30)
• Vitamin B12 deficiency	3(6)	3(5)	8(3)
• Monoclonal gammopathy of uncertain significance	4(8)	1(2)	8(3) [#]
Rheumatological			
Lupus erythematosus***	0	6(9) [†]	1(<1)
Systemic scleroderma***	1(2)	7(11)	0
Sjögren syndrome*	3(6)	2(3)	3(1)*
RA	4(8)	8(12)	13(5)
Any of the above***	8(16)	19(29)	15(5)**
Malignancies			
Malignancy of any type	20 (40)	23 (35.4)	92 (31.3)
Solid cancers	16 (32)	21 (32.3)	88 (29.9)
Haematologic malignancies*	5 (10)	3 (4.6)	8 (2.7)*
• Lymphoma	Diffuse large B cell (1) Marginal zone (1)	Hodgkin's (1) Waldenstrom (1) Diffuse large B cell (1)	Diffuse large B cell (4) Marginal zone (1)
• Leukaemia	TLGL(2)	0	CLL(1)
• Myeloma	Multiple myeloma (1)	0	0
• Myelodysplastic syndrome	0	0	2
Infectious			
Hepatitis B	0 0	0 0	2 (0.7)
Hepatitis C	0 0	1 (1.5)	2 (0.7)
HIV	0 0	0 0	0 0

P = comparison of the three groups; NS: not significant with *P* >0.05, *P*₁ = IBM vs IIM, *P*₂ = IBM vs Categorical variables are displayed as *n* (percentage). The *P*-value corresponding to comparison of the three groups is shown in the first column, *P*-value for IBM vs IIM group is shown in 'IIM' column, and *P*-value for IBM vs population controls is shown in 'population controls' column. *0.01 ≤ *P*-value < 0.05; ***P*-value < 0.01; ****P*-value < 0.001; *****P*-value < 0.0001; [#]*P*-value = 0.06. IBM: inclusion body myositis; IIM: inflammatory myopathy.

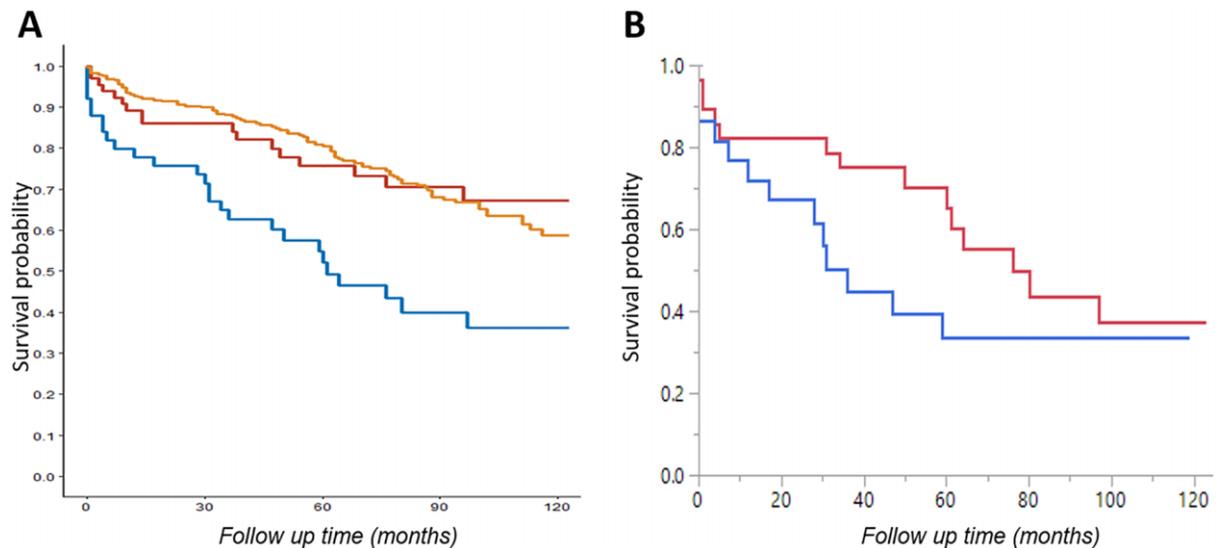
code. For HIV, the number of tested patients was 10 in IBM, 20 in IIM and 38 in population controls.

Survival outcomes

Mean follow up time from index was 51 (39.3) months for IBM, 65 (42.2) for IIM and 71 (37.3) for population controls. Mean age at death was 79.3 (8.5) for IBM patients, 77.5 (9.12) for IIM patients and 83.6 (6.68) for population controls (*P* = 0.021). Patients with IBM had lower survival than IIM patients and population controls as shown in (Fig. 1) (*P* < 0.0001). Survival for IBM patients, IIM patients and population controls respectively was as follows: 75%, 86% and 90% at 2 years, 52%, 76% and 81% at 5 years, and 36%, 67% and

59% at 10 years. The most common causes of death were respiratory failure or pneumonia (44.4%), cancer (14.8%), and old age and medical comorbidities (14.8%) in IBM group; cancer (47%), respiratory failure (17.6%) and cardiovascular (11.8%) in IIM group; and cancer (24.1%), cardiovascular (24.1%) and respiratory failure or pneumonia (13.8%) in population controls. We then evaluated whether any of the following univariates were predictors of mortality in IBM patients: age at index, sex, dysphagia or any of the associated comorbidities (peripheral neuropathy, Sjögren's syndrome, rheumatic disease of any type, haematologic malignancy, and malignancy of any type). Age at index and probably dysphagia were the only predictors, with a hazard ratio per 1 year increase of 1.06 [1.01, 1.11] (*P* = 0.025) for age,

Fig. 1 Survival outcomes



(A) Kaplan–Meier survival curves comparing IBM patients (blue line), inflammatory myopathy patients (red line) and population controls (orange line). (B) Clear separation in survival curves for IBM patients treated with corticosteroids (blue line) compared with untreated IBM patients (red line). IBM: inclusion body myositis.

and a hazard ratio of 2.6 [0.98, 6.97] for dysphagia but with a P -value of 0.054. Given that IIM patients were younger and more commonly females, we compared survival between the three groups with group, age and sex as multivariables. IBM and IIM were associated with increased mortality risk compared with population controls, with hazard ratio per 1 year increase of 2.69 [1.74, 4.15] ($P < 0.0001$) for IBM, and 2.11 [1.22, 3.65] ($P = 0.0078$) for IIM. However, IBM was not associated with increased mortality risk compared with IIM. We then compared survival between patients treated with corticosteroids vs not (Fig. 1). Patients treated with corticosteroids had a median survival of 31 months compared with 76 months in the untreated group. However, this did not reach statistical significance ($P = 0.2$), which could be due to the small sample size and low event rate as shown in Fig. 1. There was no difference in survival based on treatment with corticosteroids in the IIM group, or based on treatment with other immunosuppressant drugs in either group (data not shown).

Discussion

Herein, we demonstrate in a population-based, case-control study, the increased frequency of peripheral neuropathy, haematologic malignancies and Sjögren syndrome in IBM. Furthermore, we show that IBM patients have lower survival compared with population controls.

Despite the similarities between IBM and other neurological diseases of ageing, the frequency of dementia and Parkinson's disease in IBM was not different from population controls. However, IBM patients were 2.7 times more likely to have peripheral neuropathy than population

controls. Peripheral neuropathy in IBM is considered independent of the myopathic process, as witnessed by the lack of correlation with disease severity or duration, and the lack of inflammation or tubulofilamentous aggregates on nerve biopsy [29, 30]. Interestingly, the presence of peripheral neuropathy has been reported to be associated with treatment unreponsiveness in patients with polymyositis [6]. While this finding could be because peripheral neuropathy in these patients is simply a marker of inclusion body myositis, which is inherently refractory to treatment, nerve involvement in IBM and its contribution to the clinical phenotype and disease course is yet to be explored [31]. In contrast to previous studies, diabetes mellitus was not more common in IBM or IIM patients compared with population controls [32, 33].

While rheumatic diseases are expected to be more prevalent in IIM patients, we demonstrate they are also more common in IBM, namely Sjögren syndrome. Sjögren syndrome has been reported in patients with IBM; however, the nature of the relationship between the two disorders is not well understood [16]. It may be due to underlying genetic predisposition, as seen in a study from Western Australia, where patients with IBM and Sjögren syndrome were more likely to be carriers of HLA-DR3 and the 8.1 MHC ancestral haplotype [34]. The frequency of Sjögren syndrome in our study is relatively similar to previously reported in most recent studies (10–12%) [16, 34].

Inclusion body myositis pathologic hallmark is the invasion of nonnecrotic muscle fibres by a well-orchestrated inflammatory infiltrate, with highly differentiated, cytotoxic T cells in the front line [35, 36]. When prospectively screened, 58% of IBM patients had aberrant populations of large granular T cells [36]. However, the

presence of a T-LGL clone (T-LGL lymphocytosis) does not necessarily mean that the patient has T-LGL leukaemia. The demarcation line between the two entities remains blurry [37]. T-LGL leukaemia is a very rare lymphoproliferative disorder and little is known regarding its pathogenesis, dysregulated signalling pathways, and treatment options [38]. Our two patients were diagnosed with leukaemia based on the presence of associated cytopenias and bone marrow involvement. It was postulated that chronic antigenic stimulation in IBM may result in clonal expansion of a T-LGL population, or vice versa, the T-LGL clone may invade muscle tissue and cause IBM [36, 39]. However, in both of our patients, the diagnosis of T-LGL leukaemia preceded that of IBM, and preceded the onset of muscle weakness in at least one patient (details are unclear for the second patient). It is noteworthy that similar association with T-LGL clonal expansion has been observed in certain immune-mediated disorders such as RA and Sjögren syndrome [40, 41].

Given the low prevalence of hepatitis B, C and HIV in the local population as witnessed by the low prevalence in the control group, and given the lack of any IBM patient in our cohort with any of these disorders, we cannot draw any conclusions regarding the association with IBM based on our study results. However, hepatitis C seropositivity is reported in 28% of Japanese patients with IBM, which is less likely to be the case in our IBM population as none of the tested nine patients was seropositive; these results are relatively similar to those reported in a Brazilian study [42].

Traditionally, IBM is not considered to affect longevity, and survival is reported to be similar to the life expectancy of the general population in France and the Netherlands [21, 22]. We demonstrate in our study that survival is reduced in IBM patients when compared with age- and sex-matched controls. IBM patients died on average 3 years younger than population controls. These results are similar to those reported in Norway and Olmsted county [16, 24]. Our reported 10-year survival of 36% from match date (mean age at match date was 73.5 years) was relatively similar to the 42% 10-year survival from diagnosis (mean age at diagnosis was 69.9 years) reported by Dobloug *et al.* [43]. The risk of death in our study was influenced by age at match and probably by the presence of dysphagia. In previous reports, survival was mainly influenced by age at diagnosis [21, 43]. Similar to previous reports, the death in IBM patient was most commonly related to respiratory complications including respiratory failure or pneumonia [24, 43–47]. In contrast, the most common cause of death in IIM group was cancer, similar to population controls. Lastly, there was a trend for lower survival in IBM patients treated with corticosteroids, which is intriguing and has not been previously reported. Benveniste *et al.* reported that IBM patients treated with glucocorticosteroids or other immunosuppressants needed a walking aid sooner than untreated patients, with no difference in the rate of progression to a wheelchair [21]. In our study, there was no clear difference

baseline characteristics between the treated and untreated patients. It remains unclear whether the difference in survival is a direct effect of the use of corticosteroids, vs other confounding factors. Nevertheless, there is no evidence that treatment with corticosteroids has any benefit in IBM patients, and thus it should be avoided.

Our study has several limitations. The rarity of IBM and IIM limited our sample size, and our ability to further stratify by sex. Likewise, some of the comorbidities of interest such as various rheumatic diseases were uncommon as well. The vast majority of our patients and controls were white, limiting generalizability to other races. Additionally, it is possible that some subjects were diagnosed with one of the diseases of interest at a medical facility outside of the records-linkage system and were never coded for such diagnosis in our system. It is noteworthy that the first time a patient is coded for a condition may not necessarily reflect the diagnosis date. However, given the large amount of data in epidemiologic studies, any search method has to be based on diagnosis codes. Nevertheless, we performed a chart review to confirm the accuracy of various diagnoses as mentioned in the methods section. Additional limitations are inherent to the retrospective design of the study and the variability in the work-up obtained in each study participant. Lastly, having a control group would help mitigate to some extent some of the study limitations.

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Data availability statement

Data not provided in the article and additional information on methods and materials may be shared upon request.

Supplementary data

Supplementary data are available at *Rheumatology* online.

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