Patterns of longitudinal trajectories of pain in patients with inflammatory myopathies

Sirs,

Idiopathic inflammatory myopathies (IIM) have historically been considered a disease of painless weakness (1). However, recent studies indicate that pain can be present in up to 80% of patients (2-5). Despite the high prevalence and burden of pain, longitudinal pain trajectories of patients with IIM are currently unknown. Understanding the temporal course of pain in these patients can inform clinicians about risk stratification and provide mechanistic clues. In this study, we aimed to investigate longitudinal changes in pain levels in patients with IIM.

This is a retrospective cohort study using FORWARD Databank, a longitudinal registry of adults with rheumatic diseases recruited from rheumatology clinics in the US. Patients were asked to complete biannual questionnaires related to their sociodemographics, disease activity, comorbidities, medications, and symptoms (6). Pain, fatigue, and patient global disease activity were assessed using numeric rating scale (ranging from 0–10). Health-related quality of life and physical function were assessed with Short Form-36 and Health Assessment Questionnaire-II, respectively. Patients with IIM who had pain scores at ≥2 visits were included.

Pain trajectories were modelled using latent mixed models using a threshold link function for pain (lcmm package, R version 4.4.3). Models included time as a fixed effect with random intercepts and slopes for each patient. The optimal number of latent classes was determined with Akaike and Bayesian Information Criteria. We compared the characteristics of the two groups with t tests for continuous and chi square/Fisher's exact test for categorical variables at the time of study entry.

A total of 147 patients with IIM (mean age: 54.6 [±13.8], female 78.9% and White 70%) were included in the study. Patients had a mean of 9.0 [±7.7] study visits. Two groups of patients were identified based on their longitudinal pain trajectories: "improving" (57%; n=84) and "stable" (43%; n=63) (Fig. 1). Pain levels of the "improving" group started at 4.31 out of 10.00 and improved by 0.14 per year. Baseline sociodemographic variables, disease subgroups, and comorbidities were comparable between the two groups. Compared to the "stable" group, the patients in the "improving" group had significantly higher pain (4.9 *vs*. 2), fatigue (5.7 *vs*. 3.5), patient global disease activity (4.8 *vs*. 2.8), joint swelling (44.6% *vs*. 18.0%), joint pain (77.0% *vs*. 45.9%), muscle pain (78.4% *vs*. 44.3%), weakness (81.1% *vs*. 61.9%), photosensitivity (30.6% *vs*. 16.1%), and rash (39.7% *vs*. 19.7%) at the study entry (Table I). Because pain trajectories closely mirrored changes in patient global disease activity (Fig. 1), longitudinal relationship between patient global disease activity and pain levels were further examined with multivariable linear mixed-effects models. After adjusting for age, race, body mass index, education level, depression, anxiety, and analgesic use, increase in patient global disease activity (β^=0.33, $p<0.0001$) was significantly associated with worsening pain levels over time.

To our knowledge, this is the first study to demonstrate the heterogeneous nature of pain trajectories in patients with IIM. While most patients experienced improvement in their pain levels over time, a substantial subset reported persistently "stable" pain levels. Importantly, patients with "improving" trajectory had indicators of higher baseline disease activity such as rash and weakness, suggesting that pain in this group may be more directly related to underlying inflammatory disease process that could be more likely to improve over time. In contrast, "stable" pain trajectory with lower disease activity may reflect contribution from nociplastic pain process. These findings suggest that better control of disease activity may play an important role in improving pain levels for a subset of patients with IIM. We acknowledge that the absence of physician global disease assessment, muscle enzymes and manual testing are limitations of our study, therefore future longitudinal studies using these measures of disease activity could shed further light on this relationship. In conclusion, the pain levels show an improvement in nearly 60% of the patients with IIM over time, while the rest have "stable" pain levels. Patients with "improving" pain trajectory are more likely to have active disease. A close link between pain trajectories and myositis disease activity suggests that pain could be a clinical manifestation of IIM.

Table I. Baseline characteristics of myositis patients with "improving" and "stable" pain trajectories.

Variables	**"Improving" pain trajectory** (n=84)	**"Stable" pain trajectory** (n=63)	*p*-value
Sociodemographic features			
Age	53.9 (13.8)	55.6 (13.8)	0.4
Sex (male)	16 (19.0%)	12 (20.0%)	0.9
Race (White)	62 (79.5%)	54 (91.5%)	0.053
Smoking history	42 (50.0%)	25 (39.7%)	0.2
BMI	28.1 (6.7)	28.6 (6.7)	0.7
Education (yrs)	14.0 (2.1)	14.4 (2.0)	0.2
Annual income ($1,000s)	51.7 (31.3)	58.6 (31.0)	0.2
Total number of study visits	8.1 (7.1)	10.2 (8.1)	0.1
Rheumatology visits in the past 6 months (≥ 3 visits)	43 (58.1%)	23 (49.0%)	0.03*
IIM subtype (DM)	30 (35.7%)	19 (30.2%)	0.6
Clinical outcomes			
Pain NRS (0-10)	4.9 (2.6)	2.0 (2.4)	<0.001*
Fatigue NRS (0-10)	5.7 (3.1)	3.5 (3.1)	<0.001*
Patient global dis activity (0-10)	4.8 (2.6)	2.8 (2.3)	<0.001*
HAQ-II (0-3)	1.2 (0.6)	0.9 (0.8)	0.02*
SF-36 PCS (0-100)	33.2 (9.3)	39.1 (11.8)	0.002*
SF-36 MCS (0-100)	45.1 (12.7)	50.5 (10.9)	0.01*
Comorbidities			
RDCI (0-9)	2.3 (1.8)	1.9 (1.5%)	0.2
Fibromyalgia	32 (41.0%)	15 (26.8%)	0.09
Osteoarthritis	14 (16.7%)	13 (20.6%)	0.5
Raynaud's phenomenon	15 (20.5%)	12 (19.7%)	0.9
Depression	28 (37.8%)	10 (16.4%)	0.006*
Anxiety	20 (27.0%)	11 (17.7%)	0.2
Diabetes mellitus	12 (14.3%)	5 (7.9%)	0.2
Cancer	13 (15.5%)	9 (14.3%)	0.8
Symptoms (last 6 months)			
Shortness of breath	21 (29.2%)	19 (30.6%)	0.9
Joint swelling	33 (44.6%)	11 (18.0%)	0.001*
Joint pain	57 (77.0%)	28 (45.9%)	<0.001*
Muscle pain	58 (78.4%)	27 (44.3%)	<0.001*
Muscle weakness	60 (81.1%)	39 (61.9%)	0.01*
Photosensitivity	22 (30.6%)	10 (16.1%)	0.05*
Pleurisy	12 (16.7%)	4 (6.6%)	0.07
Rash	29 (39.7%)	12 (19.7%)	0.01*
Medications			
NSAIDs	35 (44.3%)	11 (17.5%)	0.001*
Opioids	24 (30.4%)	8 (12.7%)	0.01*
Glucocorticoids	43 (54.4%)	34 (54.0%)	0.9

Data is represented as n (%) or mean (standard deviation). *p-values <0.05

BMI: body mass index; IIM: idiopathic inflammatory myopathy; DM: dermatomyositis; HAQ-II: health assessment questionnaire II; SF-36: short form 36; PCS: physical component summary; MCS: mental component summary; NRS: numeric rating scale; RDCI: rheumatic disease comorbidity index; NSAIDs: non-steroidal anti-inflammatory drugs.

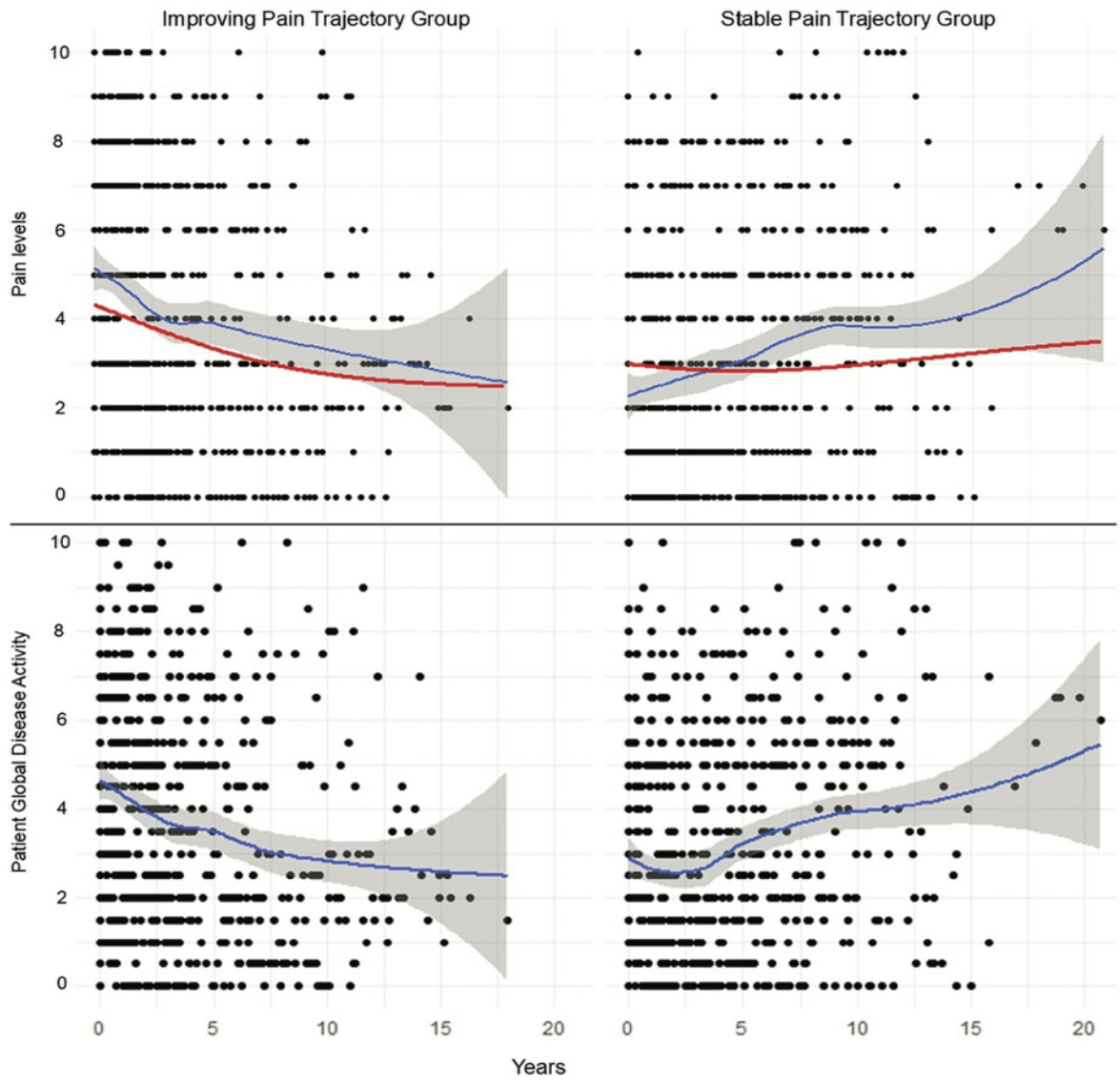

Fig. 1. Longitudinal pain trajectories of adults with IIM and the corresponding change in patient global disease activity in each group.
Blue line with grey area: LOESS line with confidence interval; Red line: trajectory line.

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