

# Myositis Multidisciplinary Clinic in a Tertiary Referral Center

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**Background:** Idiopathic inflammatory myopathies (IIM) are a rare heterogeneous group of diseases characterised by chronic skeletal muscle inflammation, but other organs are also frequently involved. IMM represent a diagnostic challenge and a multidisciplinary approach is important to ensure successful diagnosis and adequate follow-up of these patients.

**Objective:** To describe the general functioning of our multidisciplinary myositis clinic, highlighting the benefits of multidisciplinary team management in patients with confirmed or suspected IIM and to characterise our clinical experience.

**Methods:** Description of the organization of a dedicated multidisciplinary myositis outpatient clinic, supported by IMM specific electronic assessment tools and protocols based on our Portuguese Register - Reuma.pt. In addition, an overview of our activity between 2017 and 2022 is provided.

**Results:** An IIM multidisciplinary care clinic, based on a close collaboration between Rheumatologists, Dermatologists and Physiatrist is detailed in this paper. One hundred and eighty-five patients were assessed in our myositis clinic; 138 (75%) of those were female, with a median age of 58 [45–70] years. At the last appointment, 130 patients had a confirmed IIM diagnosis, and the mean disease duration was 4 [2–6] years. The most frequent diagnosis was dermatomyositis (n = 34, 26.2%), followed by antisynthetase syndrome (n = 27, 20.8%) and clinically amyopathic/paucimyopathic dermatomyositis (n = 18, 13.8%). Twenty-four patients (18.5%) were on monotherapy and 94 (72.3%) were on combination therapy.

**Conclusion:** A multidisciplinary approach is important to ensure the correct diagnosis and follow-up of these patients. A myositis clinic, with a standardised practice at a tertiary hospital level, contributes to a standardization of care and opens research opportunities.

**Keywords:** inflammatory myopathies, rheumatology, dermatology, rehabilitation medicine, multidisciplinary clinic

## Introduction

Idiopathic inflammatory myopathies (IIM) are heterogeneous, systemic inflammatory diseases that share muscle inflammation as a hallmark. Besides muscles, skin, joints, lungs and gastrointestinal tract are frequently involved. IIM are rare diseases with an estimated prevalence of 10 in 100 000 individuals.<sup>1,2</sup> The diagnosis is often a challenge and usually requires clinical evaluation, testing for autoantibodies and other complementary diagnosis exams like electromyography (EMG), muscle magnetic resonance imaging (MRI) or muscle biopsy. Furthermore, IIM in adults might be associated with malignancies with an increased risk of 2- to 7- fold compared to the general population.<sup>3</sup>

Multidisciplinary teams are the core model for managing complex chronic conditions.<sup>4</sup> Therefore, several specialties are usually required for optimal care of myositis patients, to provide the most differentiated care to patients, avoiding the delay of diagnosis and allowing the timely initiation of adequate treatment.<sup>5,6</sup>

In 2017, the Rheumatology Department of Centro Hospitalar Universitário Lisboa Norte (CHULN), Lisbon Academic Medical Center (CAML) established a dedicated multidisciplinary outpatient clinic for patients with suspected or confirmed IIM. The main goals of this IIM clinic are to standardise the diagnostic investigation and avoid delays in treatment onset. It can also improve patient satisfaction through fewer visits and consistent clinical communication and promote enrolment in research studies or clinical trials.

This experience-based manuscript describes the general functioning of our multidisciplinary IIM outpatient clinic. We describe the assessment tools embedded in the myositis module of Reuma.pt – the Portuguese Rheumatic Diseases Register (<https://reuma.pt/en/>), emphasising the benefits of multidisciplinary team management. In addition, the manuscript provides an overview of our activity with a brief description of the patients evaluated between July 2017 and May 2022.

## Material and Methods

### Multidisciplinary Myositis Outpatient Clinic

#### Description

The Rheumatology Department of CHULN developed a dedicated multidisciplinary myositis outpatient clinic in July 2017. Currently, the myositis outpatient clinic is carried out by 2 rheumatologists, supported at least by 1 resident, taking care weekly of 6 to 9 patients. Once a month, a physiatrist and a dermatologist participate in the appointments and jointly evaluate around 12 patients. Whenever necessary, a neurologist is also present to perform a more detailed neurologic examination and to discuss differential diagnosis of IIM. We perform ultrasound guided muscular biopsies at our department and there is a direct pathway with a neuropathologist for muscular biopsy analysis each time there is a procedure. A fresh muscle sample is immediately prepared for light microscopy (hematoxylin-eosin, Gomori trichrome and periodic acid Schiff stain), enzyme histochemistry (succinate dehydrogenase, cytochrome-c-oxidase, combined cytochrome-c-oxidase/succinate dehydrogenase, myosinic ATPase, myophosphorylase), and immunohistochemistry (CD3, CD20, CD68, MHC class I).

In addition, a monthly joint clinic with pulmonologists and radiologists is available if interstitial lung disease (ILD) is identified or suspected and otolaryngologists/gastroenterologists give support to patients with dysphonia/dysphagia.

Adult patients with confirmed/suspected IIM or with other connective tissue diseases having myositis as a significant feature are evaluated in our myositis clinic. The rheumatologist is at the core of the multidisciplinary team, coordinating it, integrating the various health professionals' contributions, and being co-responsible for all treatment decisions.

The organised IIM clinic structure enables the establishment of clinical and scientific objectives, the implementation of a standardised intervention plan, and the assessment of its efficacy. In addition, individual patients' particularities and preferences are incorporated into the decision process, influencing diagnostic and therapeutic plans whenever appropriate. The combination of this up-to-date specialised care and patient-centred medicine ensures a high-quality personalised healthcare service for patients with IIM. Besides, a standardised electronic clinical record promotes clinical rigor and ensures the precision and detail of data collection.

### Development

An integrated care system was designed and implemented for this clinic and is revised every three years to ensure excellent and up-to-date clinical care. It contains a general description of the clinic, including the health professionals involved, associated infrastructures, and clinical guidelines. The clinical guidelines include referral and discharge criteria, the diagnostic criteria used, and treatment recommendations.

Focus areas recognised as crucial in the development of the myositis clinic are depicted in [Table 1](#).

### Clinical Approach and Complementary Diagnostic Exams

IIM diagnosis is based on clinical symptoms and clinical examination in combination with blood tests, including creatine kinase (CK) and autoantibodies, EMG, MRI and muscle biopsy histopathology.<sup>7</sup> Whenever necessary, a skin biopsy is also performed.

**Table I** Focus Areas of the Myositis-Clinic Team

Focus Area	
Principles for referral	<ul style="list-style-type: none"> <li>• Diagnosis/clinical suspicion of inflammatory myopathy or overlap syndrome with dominant myositis component</li> </ul>
Infrastructure and technology	<ul style="list-style-type: none"> <li>• Dedicated physical space where appointments occur in the 2 hospitals belonging to CHULN: Hospital de Santa Maria and Hospital Pulido Valente</li> <li>• Electronic medical records used (Reuma.pt/Myositis module) includes disease activity assessment tools and allow the standardised collection of data for research</li> <li>• Quick access when requesting blood tests for diagnostic (immunoblot for testing for myositis-specific and myositis-associated antibodies) and follow-up purposes</li> <li>• Ultrasound guided muscular biopsy</li> <li>• Neuropathology facilities for muscle biopsies</li> </ul>
Appointments	<ul style="list-style-type: none"> <li>• Scheduled rheumatology appointments</li> <li>• Scheduled joint rheumatology-physiatry-dermatology appointments</li> </ul>
Meetings	<ul style="list-style-type: none"> <li>• Weekly dedicated biologics decision clinic</li> <li>• Monthly discussion with pneumologists and radiologists dedicated to parenchymal lung diseases</li> <li>• Monthly discussion with a musculoskeletal radiologist</li> <li>• Digital conference discussions of clinical cases with international experts – Clinical Patient Management System (CPMS)</li> </ul>
Organisation of human resources	<ul style="list-style-type: none"> <li>• The team is composed of two rheumatologists, one physiatrist and one dermatologist</li> </ul>

In a patient with a suspected IIM, a correct evaluation of muscle strength is essential. Muscle strength is measured by Manual Muscle Testing 8 (MMT-8), which has high practicality<sup>8</sup> but should be performed by a trained examiner. The modified skin Disease Activity Score (skin DAS) is always performed and allows for evaluating the cutaneous disease evolution. The number of painful, swollen joints and joints with limited range of motion are also registered. Due to the IIM's systemic involvement, a complete evaluation with cardiac and pulmonary auscultation is mandatory.

In our centre, we use the EUROLINE Autoimmune Inflammatory Myopathies 16 Ag (IgG) immunoblot for testing for myositis-specific [anti-complex nucleosome remodeling histone deacetylase (anti-Mi2a, anti-Mi2b), anti-melanoma differentiation-associated gene 5 (anti-MDA5), anti-transcription intermediary factor 1 $\gamma$  (anti-TIF1  $\gamma$ ), anti-histidyl transfer RNA synthetase (anti-Jo1), anti-threonyl-tRNA synthetase (anti-PL7), anti-alanyl-tRNA synthetase (anti-PL12), anti-isoleucyl-tRNA synthetase (anti-OJ), anti-glycyl-tRNA synthetase (anti-EJ), anti-small ubiquitin-like modifier-1 activating enzyme (anti-SAE), anti-signal recognition particle (anti-SRP), anti-nuclear matrix protein 2 (anti-NXP2)]; and myositis-associated [anti-Ro52, anti-Ku, anti-U1ribonucleoprotein (anti-U1RNP), anti-polymyositis/systemic sclerosis (PmScl100, anti-PmScl75)] antibodies. This is a fast and helpful method in terms of future monitoring and prognosis. A full blood count, inflammatory markers, and the serum concentrations of creatinine, aspartate transaminase (AST), alanine transaminase (ALT), CK, aldolase, myoglobin, lactate dehydrogenase (LDH) and urine sediment examination are requested in the first appointment and repeated in every appointment for follow-up of disease activity and treatment side effects. Tests for myositis differential diagnosis are also performed, including infectious diseases (like Human Immunodeficiency Virus, influenza, Cocksackieviruses, Echoviruses, *Borrelia burgdorferi*), endocrine disorders (especially thyroid function), electrolyte disturbances and vitamin D deficiency.

An ultrasound guided muscle biopsy is performed on every patient that consents the procedure. Samples are evaluated by dedicated pathologists and also stored at the institutional biobank (Biobanco-IMM, CAML) for future research. Biobanco-IMM, CAML was approved by the National Data Protection Authority and by the CAML ethics committee. In selected patients, EMG and muscle MRI are also performed in the diagnostic phase. EMG of affected muscles usually displays a myopathic pattern (the motor unit action potential is short, small and polyphasic), being useful to integrate with other clinical and laboratorial variables in the work out phase.<sup>7,9</sup> Whenever symptoms are unclear, an MRI of the skeletal muscle is valuable for identifying the sites of major inflammation and can help select the anatomical structure for

the muscle biopsy. In addition, it supports the differential diagnosis by depicting the pattern of affected muscles, helping in distinguishing between the different subtypes of myositis and ruling out other types of myopathy.<sup>7</sup> Whole-body MRI may add relevant information and evaluate all muscle groups simultaneously. However, whole-body MRI remains time-consuming, and consequently uncomfortable for patients<sup>10</sup> and is not widely available in several centres. In our myositis clinic, MRI is usually performed on the thighs or other muscles possibly involved, according to the previous clinical evaluation.

A nailfold capillaroscopy is also requested at disease onset for every patient. Some studies suggest that changes in nailfold capillaries may have a role at diagnosis, with dermatomyositis (DM) and antisynthetase syndrome (ASS) patients showing more alterations than polymyositis (PM) patients.<sup>11</sup> Nailfold capillaroscopy alterations may reflect disease activity in DM<sup>11,12</sup> and some studies found an improvement of nailfold capillaroscopy alterations with immunosuppressive therapy in IIM.<sup>11,13</sup> Once there are no definite recommendations, the decision to repeat the exam is decided on a case-by-case basis.

When the IIM diagnosis has been confirmed, other organ involvements should be searched for.<sup>1</sup> Thus, a baseline assessment also includes chest radiography and lung function tests. If pulmonary involvement is suspected, high-resolution computed tomography (HRCT) is performed. An electrocardiogram (ECG) and Doppler echocardiography are part of the initial evaluation, and its repetition depends on clinical evolution, once the frequency of cardiopulmonary evaluation in the course of IIM is not well defined.<sup>14</sup> A formal assessment by otolaryngologists/gastroenterologists is requested in case of dysphonia or dysphagia. Adult-onset IIM is associated with increased cancer risk, especially within three years of the myositis diagnosis.<sup>15</sup> The most common cancer subtypes are lung, ovary, colorectal, lymphoma, breast, and nasopharyngeal and thus these organs and systems are carefully reviewed during history taking and physical examination.<sup>3,15</sup> Particular care is applied for patients at the highest risk of cancer: age >40 years at IIM onset, persistent high disease activity, dysphagia, cutaneous necrosis, DM diagnosis and the presence of anti-TIF1-gamma and anti-NXP2. Male sex, anti-SAE1, anti-HMGCR, anti-Mi2, anti-MDA5 antibodies and the subtypes clinically amyopathic dermatomyositis (CADM), PM and necrotizing myopathy are also associated with an intermediate risk.<sup>15</sup> If these risk factors are absent, we only perform a complete blood count, liver function tests, erythrocyte sedimentation rate, C-reactive protein, protein electrophoresis, urinalysis and plain chest x-ray radiograph. When the patient has one or more of those risk factors, we additionally perform a complete malignancy screening, including thoraco-abdomino-pelvic computed tomography (CT), endoscopy and colonoscopy, mammography, pelvic examination and prostate-specific antigen (PSA) measurement at the time of diagnosis. Positron emission tomography/CT (PET/CT) can also be an important screening test; however, it is not widely available.

Functional assessment questionnaires are performed in every appointment, as described in the next section.

## The Added Value of Reuma.pt

In 2008, the Portuguese Society of Rheumatology launched the Rheumatic Diseases National Register (Reuma.pt), which is accessed through an electronic medical record application.<sup>16,17</sup> Reuma.pt login is assured by username and password, which are unique to each rheumatologist, and users can only visualise data from their centre's patients. Registered patients must sign an informed consent stating if their clinical data can be registered by the assisting physicians and whether it can be used for clinical research. Besides, patients have a dedicated area that can be accessed online to complete the patient-reported outcomes.

Reuma.pt has several modules organised according to the patient's diagnosis, contributing to the standardisation of procedures among the Portuguese Rheumatology departments (Figure 1). There is a specific myositis module available since April 2019, developed by us and used in daily practice in our clinic. The Reuma.pt/myositis module displays a table of contents where standard items and disease-specific items are collected (Figure 2). These data also allow us to assess the prevalence of clinical and immunological manifestations in the Portuguese IIM population.

Several specific disease activity scores are evaluated in this protocol: MMT-8 and Childhood Myositis Assessment Scale (CMAS) for children for muscle involvement, modified skin DAS and other skin features (like the presence of calcinosis, cutaneous ulcers, oedema, mechanic hands, etc.) for skin involvement, the Myositis Intention to Treat Activity Index (MITAX) for joint, gastrointestinal, pulmonary and cardiovascular involvements.



The Reuma.pt registry has protocols available for the prospective registration of 13 different rheumatic diseases.

In addition, Reuma.pt has two generic protocols to record data on other rheumatic diseases, both occurring in children and adults.

Since 2014, Reuma.pt has made available English protocols for all the rheumatic diseases described above.

Rheumatoid arthritis (RA)

Early arthritis (EA)

Spondyloarthritis (SpA)

Vasculitis

Psoriatic arthritis (PsA)

Osteoarthritis (OA)

Juvenile Idiopathic Arthritis (JIA)

Scleroderma

Systemic Lupus Erythematosus (SLE)

Sjögren's syndrome

Auto-inflammatory syndromes (AIS)

Myositis

Osteoporosis/osteoporotic fractures

**Figure 1** Modules available on Reuma.pt.

<a href="#">Myositis Protocol</a> <a href="#">Others</a> <a href="#">List of Visits</a> <a href="#">Exit Reuma.pt</a>			
General data	Disease assessment	Complementary exams	Vaccines and tuberculosis
Identification	<b>Joints</b>	Lab results	
Clinical situation	MMT8	GI involvement	Vaccines
Labor situation	<b>VAS</b>	Imaging	Tuberculosis screening
Diagnosis criteria	Skin evaluation	Physical Examination	
Classification Crit. 2017	Calcinosis		Drugs and Adverse events
General clinical data/Manif.	Ulcers		
Immunological manifestations	Clinical features		
Diagnostic complementary exams	<b>HAQ</b>		<b>Medications</b>
Alcohol / Tobacco	MITAX		<b>Adverse events</b>
Surgeries	EQ5D		
Procedures	HADS		Clinical observations
Associated Conditions	SF36		
Neoplasms	FACIT		Notes/Plan
	WPAI		Graphic Evolution
	IPAQ		Chart Evolution
			Visit report

**Figure 2** Myositis module on Reuma.pt.



In this specific module, we can also include information on associated malignancies. In addition, questionnaires to assess the functional impact of the disease are also available: Health Assessment Questionnaire (HAQ), 36-Item Short-Form Survey (SF-36), EuroQol-5D (EQ5D), Hospital Anxiety and Depression Scale (HADS), Functional Assessment of Chronic Illness Therapy (FACIT), and Work Productivity and Activity Impairment (WPAI).

Reuma.pt can easily upload blood test results, enabling prospective laboratory data monitoring. In addition, it also has fields for the registry of other exams' results, such as EMG, muscle MRI or muscle biopsy. Furthermore, we can add information about extra-articular manifestations and exam results (like endoscopy or lung function tests). Finally, it also allows the recording of the patient's treatment and evaluation of efficacy and safety. These medical records are clinically very valuable and at the same time can be used for research.

This project was approved by the Ethics Committee of the Lisbon Academic Medical Center. Furthermore, Reuma.pt was approved by the National Data Protection Authority and the local ethics committees of the participating centres.

## Results

### Experience

A total of 185 patients (corresponding to 831 outpatient clinical appointments) were referred and assessed in the CHULN myositis clinic between July 2017 and May 2022. Of these, 138 (75%) were female, with a median age of 58 [45–70] years.

Patients' referrals to the CHULN myositis clinic came from General Rheumatology clinics ( $n = 84$ ; 45.4%), General Practitioner ( $n = 34$ ; 18.4%), Dermatology ( $n = 17$ ; 9.2%), other Rheumatology subspecialty clinics ( $n = 13$ , 7%), Pneumology ( $n = 11$ , 5.9%), Internal Medicine ( $n = 11$ ; 5.9%), Neurology ( $n = 9$ ; 4.9%), Oncology ( $n = 2$ ; 1.1%), Emergency Department ( $n = 2$ ; 1.1%), Immuno-allergology ( $n = 1$ ; 0.5%) and Infectiology ( $n = 1$ ; 0.5%).

At the time of the last evaluation, 130 (70.3%) patients had a confirmed inflammatory myopathy, and 55 had a non-confirmed previously suspected IIM. The median disease duration at the last appointment of patients with a confirmed IIM was 4 [2–6] years.

Among the 55 patients with previously suspected inflammatory myopathy, there was 1 case of mitochondrial myopathy, 1 case of glycogenosis type IX, 1 case of myopathy secondary to subclinical hypothyroidism, 1 case of myopathy secondary to glucocorticoids, 1 case of systemic lupus erythematosus, 1 case of primary Sjögren's syndrome, and 4 cases of fibromyalgia. The other patients had idiopathic CK elevation or are still in etiologic investigation.

Demographic, clinical and immunological features of patients with confirmed inflammatory myopathies at the time of this assessment are described in Table 2. Six patients had myositis-associated neoplasia and in all of them the diagnosis was identified during cancer screening. There were 2 cases of breast cancer, 1 case of ovarian cancer, 1 case of multiple myeloma, 1 case of prostate cancer, and 1 case of rectal cancer. Most were females (83%,  $n = 5$ ), but all of them had a myositis subtype that implied complete malignancy screening: 3 cases of DM and 3 cases of PM. Five had an age at diagnosis superior to 40 years (83%,  $n = 5$ ). The sixth patient was a 35-year-old female with a DM diagnosis. No patient had persistent high disease activity or cutaneous necrosis, but dysphagia was documented in 2 cases. One of the patients with dysphagia had positivity to anti-Mi2. Anti-SAE1 was identified in another patient with DM diagnosis.

Glucocorticoids (GC) are still in use by 93 patients (71.5%). After GC, the most frequent current treatments are hydroxychloroquine ( $n = 63$ ; 48.5%), methotrexate ( $n = 40$ ; 30.8%) and mycophenolate mofetil ( $n = 26$ ; 20%).

### Internal Collaborations

All patients who are candidates for bDMARD therapy are discussed in a weekly biologics' decision clinic. This joint meeting brings together all medical members of the Rheumatology department, benefitting from the group experience and knowledge. It allows detailed discussions of each case, focusing on the patient's current disease activity, previous and current treatment, and prognosis to define the best treatment option.

Monthly, there is an ILD multidisciplinary meeting with pneumologists, radiologists and rheumatologists. Here, challenging cases of patients with lung involvement are discussed, and diagnostic and treatment choices are made in a multidisciplinary environment. Also, there is a monthly multidisciplinary Rheumatology/Radiology meeting where

**Table 2** Demographic, Clinical and Immunological Profile of the Patients Followed at Our Myositis Outpatient Clinic

	<b>DM (n=34, 26.2%)</b>	<b>Antisynthetase Syndrome (n=27, 20.8%)</b>	<b>CADM (n=18, 13.8%)</b>	<b>MCTD (n=17, 13.1%)</b>	<b>Overlap Syndromes* (n=14, 10.8%)</b>	<b>PM (n=10, 7.7%)</b>	<b>UCTD (n=8, 6.2%)</b>	<b>Necrotising Myopathy (n=2, 1.5%)</b>
<b>Demographics</b>								
Median age at onset, years [IQR]	46 [38–62]	50 [38–66]	55 [47–62]	33 [25–50]	55 [34–69]	61 [52–71]	56 [45–69]	57 (minimal 26, maximal 87)
Female, N (%)	20 (59%)	22 (82%)	13 (72%)	14 (82%)	12 (86%)	8 (80%)	6 (75%)	2 (100%)
Median disease duration [IQR]	4 [3–14]	4 [3–12]	3 [2–4]	5 [3–8]	3 [2–5]	5 [1–7]	3 [2–5]	7 (minimal 6, maximal 8)
<b>Clinical features</b>								
Median modified DAS skin [IQR] of last appointment	2 [0–2]	0 [0–2]	1 [0–2]	0 [0–1]	1 [0–2]	0	0 [0–2]	0
Median MMT-8 [IQR] of last appointment	80 [75–80]	80 [78–80]	80 [76–80]	80 [79–80]	79 [74–80]	80 [70–80]	80 [80–80]	66 (minimal 52; maximal 80)
Arthritis (52; 40%)	7 (21%)	19 (70%)	7 (39%)	12 (71%)	5 (36%)	1 (10%)	1 (13%)	0
RF (52; 40%)	4 (12%)	13 (48%)	5 (28%)	13 (76%)	10 (71%)	0	7 (88%)	0
Lung disease (n=38; 29%)	NSIP (29; 22%)	3 (9%)	16 (59%)	2 (11%)	1 (6%)	3 (21%)	1 (10%)	3 (38%)
	UIP (5; 4%)	0	3 (11%)	0	0	2 (14%)	0	0
	COP (2; 1.5%)	1 (3%)	0	1 (6%)	0	0	0	0
	LIP (1; 0.8%)	0	1 (4%)	0	0	0	0	0
	DIP (1; 0.8%)	0	0	0	0	0	1 (10%)	0
Mechanic hands (24, 18%)	3 (9%)	11 (41%)	5 (28%)	1 (6%)	2 (14%)	0	2 (25%)	0
Dysphagia (19; 15%)	3 (9%)	4 (15%)	2 (11%)	2 (12%)	3 (21%)	2 (20%)	1 (13%)	2 (100%)
Gastroesophageal reflux disease (11; 8%)	1 (3%)	1 (4%)	1 (6%)	3 (18%)	2 (14%)	1 (10%)	2 (25%)	0
Malignancy (8; 6%)	3 (9%)	0	0	0	0	3 (30%)	0	0
Calcinosis (7; 5%)	4 (12%)	1 (4%)	0	0	1 (7%)	0	1 (13%)	0

(Continued)

Table 2 (Continued).

		<b>DM (n=34, 26.2%)</b>	<b>Antisynthetase Syndrome (n=27, 20.8%)</b>	<b>CADM (n=18, 13.8%)</b>	<b>MCTD (n=17, 13.1%)</b>	<b>Overlap Syndromes* (n=14, 10.8%)</b>	<b>PM (n=10, 7.7%)</b>	<b>UCTD (n=8, 6.2%)</b>	<b>Necrotising Myopathy (n=2, 1.5%)</b>
Heart involvement (n=4; 3%)	Myocarditis (2; 1.5%)	0	0	1 (6%)	0	0	1 (10%)	0	0
	Atrioventricular block (1; 0.8%)	1 (3%)	0	0	0	0	0	0	0
	Pericardial effusion (1; 0.8%)	0	0	0	0	1 (7%)	0	0	0
Death (2; 1.5%)		0	0	0	0	1 (7%)	1 (10%)	0	0
<b>Antibodies</b>									
Antinuclear antibody (78; 60%)		17 (50%)	19 (70%)	6 (33%)	16 (94%)	11 (79%)	3 (30%)	5 (63%)	1 (50%)
Anti-Ro52 (36; 28%)		7 (21%)	16 (59%)	2 (11%)	4 (24%)	4 (29%)	3 (30%)	0	0
Anti-Jo1 (17; 13%)		0	17 (63%)	0	0	0	0	0	0
Anti-U1RNP (17; 13%)		0	0	0	16 (94%)	1 (7%)	0	0	0
Rheumatoid factor (11; 8%)		2 (6%)	1 (4%)	1 (6%)	5 (29%)	1 (7%)	0	0	1 (50%)
Anti-Mi2b (11; 8%)		4 (12%)	1 (4%)	5 (28%)	0	0	1 (10%)	0	0
Anti-Mi2a (6; 5%)		4 (12%)	0	1 (6%)	0	0	1 (10%)	0	0
Anti-Ku (6; 5%)		3 (9%)	0	1 (6%)	0	2 (14%)	0	0	0
Anti-PmScl75 (6; 5%)		0	0	0	0	5 (36%)	0	1 (13%)	0
Anti-MDA5 (5; 4%)		2 (6%)	0	2 (11%)	0	1 (7%)	0	0	0
Anti-PL7 (5; 4%)		1 (3%)	4 (15%)	0	0	0	0	0	0
Anti-PmScl100 (5; 4%)		2 (6%)	0	0	0	3 (21%)	0	0	0
Anti-SAE (4; 3%)		3 (9%)	0	1 (6%)	0	0	0	0	0
Anti-SRP (4; 3%)		0	0	1 (6%)	0	0	1 (10%)	1 (13%)	1 (50%)
Anti-PL12 (3; 2%)		0	2 (7%)	0	0	0	0	1 (13%)	0



Anti-NXP2 (3; 2%)	3 (9%)	0	0	0	0	0	0	0
Anti-EJ (2; 1.5%)	1 (3%)	0	1 (6%)	0	0	0	0	0
Anti-Tiflg (2; 1.5%)	1 (3%)	0	1 (6%)	0	0	0	0	0
Anti-ThTo (2; 1.5%)	0	0	0	0	0	0	2 (25%)	0
Anti-Scl70 (1; 0.8%)	0	0	0	0	1 (7%)	0	0	0
Anti-RNA-polimerase 3 (1; 0.8%)	0	0	0	0	1 (7%)	0	0	0
Anti-NOR90 (1; 0.8%)	0	0	0	0	1 (7%)	0	0	0
Treatment								
Oral glucocorticoids (93; 72%)	24 (71%)	21 (78%)	9 (50%)	16 (94%)	11 (79%)	9 (90%)	2 (25%)	1 (50%)
Hydroxychloroquine (63; 48%)	15 (44%)	11 (41%)	10 (56%)	12 (71%)	9 (64%)	0	6 (75%)	0
Methotrexate (40; 31%)	14 (41%)	6 (22%)	4 (22%)	8 (47%)	3 (21%)	3 (30%)	1 (13%)	1 (50%)
Mycophenolate mofetil (26; 20%)	3 (9%)	13 (48%)	2 (11%)	1 (6%)	4 (29%)	2 (20%)	0	1 (50%)
Azathioprine (16; 12%)	5 (15%)	1 (4%)	1 (6%)	5 (29%)	3 (21%)	1 (10%)	0	0
Rituximab (11; 8%)	0	2 (7%)	2 (11%)	1 (6%)	2 (14%)	1 (10%)	0	1 (50%)
Immunoglobulin (11; 8%)	3 (9%)	1 (4%)	1 (6%)	2 (12%)	1 (7%)	2 (20%)	0	1 (50%)
Tacrolimus (5; 4%)	2 (6%)	1 (4%)	1 (6%)	1 (6%)	0	0	0	0
Cyclosporine (2; 1.5%)	0	1 (4%)	0	1 (6%)	0	0	0	0
Cyclophosphamide (1; 0.8%)	0	0	1 (6%)	0	0	0	0	0
Leflunomide (1; 0.8%)	0	1 (4%)	0	0	0	0	0	0
TNFi (1; 0.8%)	1 (3%)	0	0	0	0	0	0	0

**Note:** \*Overlap syndrome included patients with DM/PM and systemic sclerosis or rheumatoid arthritis, or systemic erythematosus lupus.

**Abbreviations:** CADM, clinically amyopathic/paucimyopathic dermatomyositis; COP, cryptogenic-organising pneumonia; DAS, disease activity score; DIP-Desquamative interstitial pneumonia; DM, dermatomyositis; ILD, interstitial lung disease; LIP, lymphocytic interstitial pneumonitis; MCTD, mixed connective tissue disease; MMT, manual muscle test; NSIP, nonspecific interstitial pneumonia; PM, polymyositis; RP, Raynaud phenomenon; TNFi, tumor necrosis factor inhibitor; UCTD, undifferentiated connective tissue disease; UIP, usual interstitial pneumonia.

musculoskeletal imaging exams, like muscle MRI, can be discussed. Although there is no formal scheduled meeting with Neurology, there is direct contact with a Neuropathologist to perform urgent muscle biopsy histopathologic analysis and discuss their results.

## External Collaborations and Scientific Activity

Given the large volume of patients at our myositis clinic and the close collaboration of our group with other centres, we integrate local and multicentric networks and studies. Since 2017 our centre has been included in the European Reference Network on Rare and Complex Connective Tissue and Musculoskeletal Diseases (ERN-ReCONNET). ERN-ReCONNET is a virtual network involving healthcare providers from reference centres across Europe and promotes optimal patient management and the development of common clinical practice guidelines.<sup>18</sup> Besides, elements of our centre are part of The International Myositis Society (iMyoS) and The International Myositis Assessment and Clinical Studies Group (IMACS). Thereby, members of the myositis clinic can participate in digital conference discussions of clinical cases with international experts.

Scientific projects in the field of myositis are ongoing and one example of international collaboration is the participation of several members in EULAR-ACR Classification Criteria for Antisynthetase Syndrome (CLASS project).

The team has been scientifically active, contributing with their experience for the progress of knowledge in inflammatory myopathies.<sup>19–30</sup>

## Discussion

IIM may pose significant clinical challenges and different health professionals play a vital role in providing adequate, evidence-based, cost-effective care.<sup>31</sup> Multidisciplinary teamwork involves coordinated efforts from professionals with diverse backgrounds and expertise, coming together to manage patients, aiming for the best care. Maintaining the structure of a multidisciplinary clinic requires coordination and teamwork, facilitating communication between peers and increasing the involvement of patients in decisions.

Physical rehabilitation is essential for treating patients with IIM since several studies reported the benefits of exercise on disease activity and inflammation.<sup>32–34</sup> Physiotherapy sessions should be prescribed, and several individually tailored physical exercises to enhance muscle strengthening and aerobic capacity are taught to patients.

Skin involvement is frequent in IIM, but cutaneous manifestations may be variable.<sup>35</sup> The skin lesions may precede or follow myositis and could be the main manifestation of the disease. Discussions regarding the choice of therapy are adjusted to fit the needs and expectations of each patient.

The close contact with the Neurology Department allows for support in the differential diagnosis of noninflammatory myopathies.

Despite the significant variability of specialities that refer patients, most come from other rheumatologists, demonstrating the recognition of the benefit of the multidisciplinary clinic.

As has been reported in the literature,<sup>2</sup> there is a female predominance in our cohort. The clinical features of our patients show multiorgan involvement. Almost 30% of patients had associated ILD, an important cause of morbidity and mortality. The most frequent lung manifestation was nonspecific interstitial pneumonia, as described in the literature.<sup>36</sup>

As expected, DM was the most frequent type of inflammatory myopathy. The most common manifestations in these patients were arthritis ( $n = 7$ , 21%), lung involvement ( $n = 4$ , 12%), Raynaud phenomenon ( $n = 4$ , 12%) and calcinosis ( $n = 4$ , 12%). The most prevalent myositis-specific antibody was anti-Mi2 ( $n = 8$ , 23.5%), which is in agreement with the estimated prevalence.<sup>35</sup>

CADM defines a subgroup of patients with predominant skin involvement and includes both patients with amyopathic dermatomyositis and patients with hypomyopathic dermatomyositis.<sup>1</sup> Anti-Mi-2 e anti-MDA5 antibodies were the two most frequent myositis-specific antibodies in CADM patients.

ASS is characterised by multiple organ involvement. Myositis, ILD, arthritis, Raynaud's phenomenon, mechanic's hands and skin rashes are typical.<sup>27</sup> The hallmark is the presence of anti-aminoacyl-tRNA synthetase (ARS) antibodies, anti-Jo1 being the most common. In our cohort, anti-Jo1 was identified in 17 (63%) of our patients. In addition, anti-Ro52 was identified in 16 (59%) patients, which supports the idea that most ASS patients also have anti-Ro52

autoantibodies.<sup>27</sup> As expected, it was in this group of patients that arthritis, lung disease and mechanic's hands were more common. In overlap myositis, autoantibodies typical of other connective tissue diseases were common, as expected.

A myositis-associated neoplasia was diagnosed in 6 patients. Five of the cancer subtypes were the most usually described: breast, ovary, prostate and colorectal.<sup>3,37</sup> There was also one case of multiple myeloma. All patients had high-risk factors for neoplasia and the diagnosis emerged in the cancer screening, following the myositis diagnosis. All of them had a high-risk myositis subtype: 3 cases of DM and 3 cases of PM. Malignancy is described in 25% of patients with DM and 10–15% of PM patients in the literature.<sup>37</sup> In our DM cohort, malignancy was only detected in 9% of cases, but more diagnoses may emerge in the coming years. On the other hand, malignancy was diagnosed in 30% of PM patients, the highest rate among all IIM subtypes. However, the age at diagnosis in this group of patients was also higher, and it is known that older patients have a higher risk of malignancy.<sup>36,38</sup> Five patients had an age of diagnosis superior to 40 years. Dysphagia, one of the clinical risk factors, was documented in two cases. Regarding antibodies, one patient had positivity to anti-Mi2 and another to anti-SAE1. Although there are a small number of disease-related malignancies in our cohort, we are alert to the possibility of their appearance in the following years. Malignancy is one of the leading causes of death in patients with myositis,<sup>36</sup> and our practice is to perform malignancy screening tests whenever justified, as explained previously.

Undifferentiated connective tissue disease (UCTD) patients in our cohort had a low median disease duration. Therefore, we believe some UCTD patients may still develop a well-defined connective tissue disease in the future. The two patients with immune-mediated necrotising myopathy had severe myopathy and dysphagia. They have no other extra-muscular manifestations, in agreement with what has been most commonly described in the literature for this disease subtype.<sup>36</sup>

In adults, we typically initiate treatment with high-dose glucocorticoids and a steroid-sparing agent at the time of IIM diagnosis. The DMARD choice depends on the main manifestations, but methotrexate, azathioprine, or mycophenolate mofetil are the most common choices.<sup>37</sup> Those three agents are usually used in mild to moderate muscle disease.<sup>37,39</sup> Methotrexate is often the first option as it is effective on arthritis, one of the most common manifestations in our patients, and has a quick onset on action on muscle disease, comparing to other agents like azathioprine.<sup>34</sup> Mycophenolate mofetil is the preferred option when ILD is present, as it is generally effective, well tolerated and has fewer potential side effects than cyclophosphamide.<sup>34,40</sup> It works well in myositis as well as the rash of DM.<sup>34</sup> Azathioprine is an alternative to mycophenolate mofetil when ILD is present and has adequate efficacy on muscle disease.<sup>34,40</sup> In our cohort, these three agents are the most frequently used DMARDs after hydroxychloroquine. The extensive use of hydroxychloroquine may be explained by the fact that DM was the most frequent IIM subtype in our cohort since we use hydroxychloroquine primarily for treating DM's cutaneous manifestations.

As previously explained, in our myositis clinic, there is a standardised collection of data, namely demographic, clinical, laboratorial and therapeutic data. Every appointment is registered in Reuma.pt/Myositis and thus it is possible to monitor the clinical evolution of the patient, as well as laboratorial changes and response to therapy. This also allows multiple-network integrations and collaboration on national and international projects, once there is a constant updating and easy data collection.

## Conclusions

Multidisciplinary clinics contribute to a better coordination of the medical care, consolidation of medical knowledge and clinical skills development. A formal standardised approach to IIM, including patient pathways for diagnosis and follow-up, improves the quality-of-care delivered and supports the organization of research. Collaboration between different departments leads to a quicker and more complete clinical evaluation and is essential to increase the chances of successful management of IIM patients. The continuous registry of patients in Reuma.pt/Myositis has been essential for standardising care and leveraging research.

## Disclosure

Dr Inês Cordeiro reports being a BMS employee, outside the submitted work. The authors report no other conflicts of interest in this work.

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