

Outcome in patients with idiopathic inflammatory myositis: morbidity and mortality

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Abstract

Objective. To assess the long-term outcome of a cohort of 46 patients with idiopathic myositis by assessing both health status, as measured by the SF-36, and cumulative survival probability over a 20-yr follow-up period at a single rheumatology centre.

Methods and results. Forty-six patients under long-term follow-up from 1978 to 1999 were identified from our database. All patients fulfilled three out of four of the Bohan and Peter criteria for myositis. We excluded those with malignancy-associated disease and those with inclusion body myositis. Twenty-three patients (50%) had adult-onset polymyositis, 14 (30.4%) had adult-onset dermatomyositis, one had childhood-onset dermatomyositis and eight (17.4%) had an overlap syndrome (associated with either systemic lupus erythematosus or rheumatoid arthritis). During the course of the disease, seven patients (15.2%) went into full remission, eight (17.4%) had monophasic illness, nine (19.6%) had a relapsing–remitting course, 16 (34.8%) had chronic progressive illness and six (13.04%) died. All patients had significantly lower SF-36 scores in all aspects of health compared with the general population ($P \leq 0.001$). Patients with chronic progressive illness had significantly greater bodily pain ($P \leq 0.05$, *t*-test) than those with a relapsing–remitting illness, but did not differ in other aspects of health. There was no significant difference in the scores in the different domains of the SF-36 between the patients with active disease and those with inactive disease ($0.05 < P < 0.1$). Six of the 46 patients died. Cumulative survival probability was calculated. The five-year survival rate was 95% and the 10-yr survival rate 83.8%.

Conclusion. Patients with myositis report significantly poorer health compared with the general population. Health status and disease activity are important outcome measures in the assessment of patients with myositis.

KEY WORDS: Idiopathic myositis, Morbidity, SF-36, Treatment, Mortality.

The idiopathic inflammatory myopathies constitute a group of systemic autoimmune rheumatic diseases that include polymyositis (PM) and dermatomyositis (DM). They are characterized by chronic inflammation of muscle that results in skeletal muscle weakness, and they frequently cause gastrointestinal, cardiac and pulmonary dysfunction. Morbidity and mortality both remain a significant problem.

The outcome in myositis has been assessed so far in terms of disease activity or mortality. However, it is apparent that a significant proportion of patients with myositis have considerable morbidity due to damage caused by both the disease and its treatment. This is well recognized in patients with rheumatoid arthritis (RA) and is becoming increasingly appreciated for patients

with systemic lupus erythematosus (SLE). In these autoimmune rheumatic diseases, the impact of the disease on the patient is also assessed by a measure of the patient's well-being or 'health status'. There are various validated and reproducible questionnaires available to measure health status, and these have been used in various diseases. However, the use of such health questionnaires, in particular the Medical Outcomes Study Short Form Health Survey (SF-36), has not been studied previously in patients with idiopathic myositis.

We present a cohort of patients who have been followed up by a rheumatology department with a particular interest in the disease. We have previously presented data assessing the morbidity of these patients using muscle strength testing [1]. Our cohort of patients has since grown and we present data on the outcome of these patients over a 20-yr period and the assessment of the patients' health status, as measured by the SF-36, and the calculated cumulative survival probability over a 10-yr follow-up period.

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Patients and methods

Patient selection

The University College London myositis database identified 46 patients who had been followed up prospectively from 1978 to 1999. All patients fulfilled three out of four of the criteria described by Bohan and Peter [2]. Patients with myositis associated with a malignancy and inclusion body myositis were excluded from this study. We analysed the data retrospectively, recording age, sex, date of diagnosis of the myositis, and immunosuppressive therapy. Patients were classified into four subgroups: (1) adult-onset PM (APM); (2) adult-onset DM (ADM); (3) childhood-onset DM; (4) APM or ADM associated with another autoimmune rheumatic disease. Patients with an overlap syndrome had to satisfy the revised criteria of the American Rheumatism Association for SLE [3] or RA [4]. The patients were subclassified into those who had a monophasic illness (a single episode of active disease), relapsing–remitting disease (disease flares associated with disease-free periods), chronic progressive disease (evidence of active disease despite treatment) and remission (this subclass included patients who may also have been in other categories as well as this one). The data were evaluated with respect to demographic features, electromyography (EMG) and muscle biopsy, serological parameters [antinuclear antibodies were tested using rat liver as the substrate, and antibodies to extractable nuclear antigens and Jo-1 by a commercial ELISA (enzyme-linked immunosorbent assay) (Shield Diagnostics, Dundee, UK)], and clinical outcome. Muscle tissue was obtained in most cases by needle biopsy.

Assessment of disease activity

Disease activity was defined as a serum creatine kinase (CK) concentration at least twice the upper limit of normal, as defined by the local reference laboratory.

Assessment of health status

Health status was measured using the SF-36, which measures physical function, role limitations, emotional problems, social function, mental health, general health perception, vitality and pain. Population norms for the SF-36 [5] were used as the control.

Statistical analysis

As the sample size was small, the *t*-test was used to assess the difference between those with active and inactive disease and the difference in health status between the study population and the normal population. Cumulative survival rates were calculated for the patient group using the Kaplan–Meier technique.

Results

Twenty-three patients had APM, 14 had ADM, one had childhood-onset DM and eight had an overlap syndrome associated with SLE or RA. The female: male ratio was 2.5:1 and the ethnic mix was 69.6%

Caucasian, 13% Afro-Caribbean, 13% Asian and 4.3% other. The mean age of diagnosis was 38.9 yr (range 21–67) and the mean duration of symptoms before diagnosis was 10.4 months (range 1–120). Proximal muscle weakness was present in all patients. Table 1 shows disease progression over a follow-up period of 19 yr; approximately a third of the patients had chronic progressive illness. Of the disease-specific antibodies, anti-Jo-1 was detected in only seven out of the 44 patients tested (three of whom also had pulmonary fibrosis). Of the 44 patients tested, 11 were positive for ribonucleoprotein antibodies. Twenty-four patients (52%) were positive for antinuclear antibodies.

All of our patients had been treated with prednisolone, 11% had been managed on prednisolone alone (of these, two patients had monophasic illness, one died and two had mild chronic progressive illness) and 41% had received combined prednisolone and azathioprine. The remainder had invariably had various combinations of methotrexate (26%), cyclosporin (15%), cyclophosphamide (18.7%) and intravenous immunoglobulin G (30.4%) added to prednisolone and azathioprine. Three of our patients had received plasma exchange for chronic progressive disease unresponsive to conventional therapy.

Health status was measured using the SF-36 and was performed in 1999. Thirty-four questionnaires were completed from a possible 36. Four patients were lost to follow-up (six patients had died before the survey was conducted). The mean age of the patients who completed the SF-36 was 52 yr. All patients had significantly lower scores in all aspects of health compared with the general population ($P \leq 0.001$) (Fig. 1). Patients with chronic progressive illness had significantly greater bodily pain ($P \leq 0.05$, *t*-test) than those with relapsing–remitting illness, but did not differ in other aspects of health. There was no significant difference in the scores in the different domains of the SF-36 between the patients with active disease (seven patients) and those with inactive disease (27 patients) ($0.05 < P < 0.1$).

Mortality

Six patients died in our cohort of 46 patients. The cumulative survival probability was calculated. The 5-yr survival rate was 95% and the 10-yr survival rate was 83.8%. The causes of death included cardiac [one myocardial infarction, one hypertrophic obstructive cardiomyopathy and one myocardial necrosis

TABLE 1. Disease progression over 20 yr of follow-up

Disease course	No. of patients (%)	Period of follow-up at time of SF-36 (yr)
Monophasic illness	8 (17.4)	8.6
Full remission	7 (15.2)	11.8
Relapsing–remitting	9 (19.6)	11.5
Chronic progressive	16 (34.8)	13.6
Died	6 (13)	–

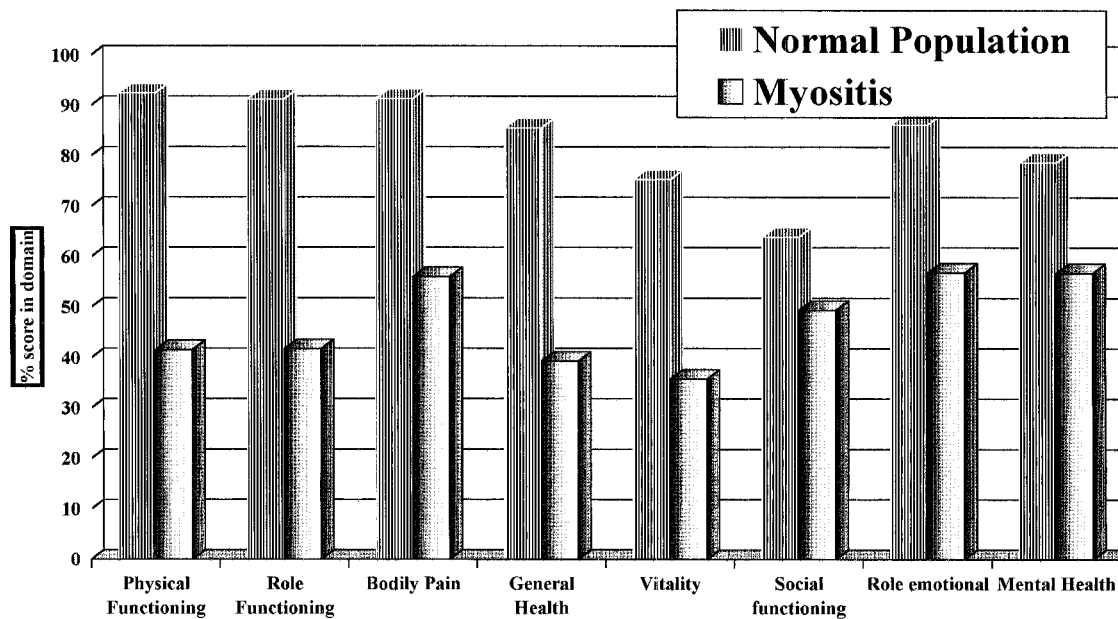


FIG. 1. Comparison of SF-36 scores in the individual domains between the normal population and the patients with myositis.

(this patient also had evidence of pneumonia)], infection (two deaths from pneumonia) and a domestic accident (one patient).

Discussion

We have presented data on patients with myositis who presented to and were followed up in a rheumatology department with a particular interest in the disease. As some of the patients had been referred from other centres, it is possible that the patients in our cohort had more severe disease.

The female: male ratio was 2.4:1, which is similar to that in other studies. Interestingly, all five patients with the overlap syndrome were women and four out of the five had APM.

The CK level was increased in 42 of the 46 patients at the time of diagnosis, and in these patients fluctuations in the level of CK correlated with disease activity. Active disease was defined as a CK level at least twice the upper limit of normal, as defined by the local laboratory. A normal CK level is more common in DM (three out of four of our patients with a normal CK level had DM). The CK level may have been normal because muscle inflammation had not yet developed in the case of DM [6], or because the disease was in the advanced state, causing severe atrophy.

EMG is useful in demonstrating that muscle weakness is myopathic in origin and in excluding neuropathies and other myopathies. An abnormal EMG was recorded in 89.7% of our patients. This is consistent with previous data, in which 90% of patients were found to have an abnormal EMG [7].

Muscle biopsy consistent with an inflammatory myopathy occurred in 88.4% of patients. A negative biopsy is probably the result of sampling errors, as inflammation can be patchy. Magnetic resonance imaging is useful in identifying sites of inflammation in such cases.

All of our patients were treated with steroids. Approximately three-quarters of our patients required the addition of at least one immunosuppressive drug. Generally, the trend is towards the earlier and more frequent use of immunosuppressive agents because of the concerns about steroid side-effects and the improved response to immunosuppressive agents. Methotrexate and azathioprine are the agents used most extensively and there is evidence of their effectiveness when used in combination [8].

Disease progression over a period of 20 yr is shown in Table 1. A third of our patients had chronic progressive illness and a further 20% had relapsing–remitting illness. However, the patient's sense of well-being is affected not only by disease activity but also by accumulated damage and other comorbid conditions and the side-effects of therapies used. Outcome needs to be measured in several ways, e.g. in terms of damage (including muscle strength [1]), disease activity, health status and death.

In order to assess the effects of new therapeutic interventions, we need to determine the effects of disease on the patients' sense of well-being or their health status. Therefore, the measurement of health status needs to be a distinct domain when outcome is assessed in patients with myositis. This concept is now well established in trials in patients with RA, and the use of various health questionnaires in clinical trials is now routine practice. However, to date only two of these questionnaires have been used in patients with myositis. Drouet *et al.*

[9] retrospectively analysed the long-term functional outcome and quality of life in 28 patients with ADM and APM. Quality of life was assessed using the AIMS 1 (Arthritis Impact Measurement Scales) [10]. A third of patients had a rating of 'poor' or 'very poor' on physical activities. This proportion was significantly lower than that reported for the normal population. The disadvantage is that this instrument takes 20 min to complete.

Clarke *et al.* [11] assessed functional status and the factors contributing to disability in a national inception cohort of 257 patients with APM/ADM. Functional disability was assessed using the Health Assessment Questionnaire (HAQ), and data on disease and treatment-related complications were collected. The HAQ was developed for use in patients with RA but has also been used in other conditions. Clarke *et al.* [11] found that the disability index increased with disease duration and that corticosteroid-related morbidity contributed significantly to functional disability. Corticosteroid-related morbidity was defined as vertebral compression fracture (CF) or avascular necrosis (AVN). As expected, patients aged <60 yr who had had no CF or AVN had less disability and slower progression of disability than those aged >60 yr but who had never had CF or AVN and those who had had AVN or CF at any age. This study highlights the importance of damage as a contributor to functional disability; in this case the damage was from steroid-related side-effects.

The SF-36 [5] is used frequently in outcome assessment in clinical trials. It has been validated extensively in a variety of diseases, including RA and SLE. Although some of our patients with myositis also had RA or SLE, the number of patients (8) was small and thus the presence of an overlap condition probably had little effect on our overall SF-36 results. However, it would be of interest to compare in larger studies the SF-36 data of those with myositis alone and those who have myositis and an additional autoimmune rheumatic disease. It is important to obtain an assessment of all these domains as myositis is a chronic disease in which both the disease and the treatments used cause both physical and emotional side-effects.

Patients in our cohort had significantly lower scores in all aspects of health compared with the general population ($P < 0.001$) (Fig. 2). Patients with chronic progressive illness had significantly greater bodily pain than those with relapsing–remitting illness, but did not differ in other aspects of their health. When comparing patients with active disease against those with inactive disease, we were interested to find that there was no significant difference in the health status as measured by the SF-36. We surmise that those with inactive disease may have had increased permanent damage, i.e. damage to their muscles or other organs, which may have contributed to their perceived health status. There is a clear need for internationally agreed indices of activity and damage to address this point. Interestingly, studies in patients with SLE have found no correlation,

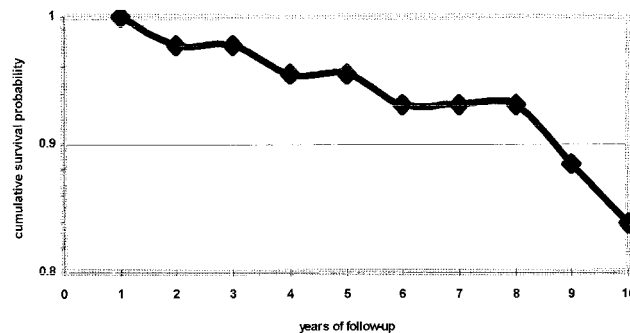


FIG. 2. Cumulative survival probability of patients with idiopathic inflammatory myositis over a 10-yr period.

TABLE 2. Published long-term survival data for patients with myositis

Author	Period	Survival	
		5 yr	> 5 yr
Sultan <i>et al.</i> [present study]	1978–99	95%	83.8% (10 yr)
Hochberg <i>et al.</i> , 1986 [13]	1970–81	80.4%	72.8% (7 yr)
Maugars <i>et al.</i> , 1996 [14]	1973–84	66.7%	55.4% (9 yr)
Medsker <i>et al.</i> , 1971 [15]	1947–68	65%	53% (8 yr)

or only weak associations, between disease activity (as measured by the SLEDAI [Systemic Lupus Erythematosus Disease Activity Index]) and health status [12].

Survival rates for APM/ADM are higher than those before the corticosteroid era. Many factors have contributed to this, such as the earlier use of immunosuppressive agents during the course of disease and better general medical care. The differences may also be due to changes in the case mix, therapy and comorbidity. Long-term prognosis cannot be determined during a follow-up period of less than 5 yr as many cases are still active at this time and the prognosis can improve over time. In Table 2 we have included only studies with a follow-up period of more than 5 yr. Six patients died in our cohort of 46 patients.

Further studies are needed to assess the sensitivity of the SF-36 to change over time and to assess the correlation of the SF-36 with damage. Any clinical trial of a new therapy in patients with myositis must assess three domains when looking at the outcome: disease activity, damage and health status.

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