EXTENDED REPORT

Long-term outcome in polymyositis and dermatomyositis

I M Bronner, M F G van der Meulen, M de Visser, S Kalmijn, W J van Venrooij, A E Voskuyl, H J Dinant, W H J P Linssen, J H J Wokke, J E Hoogendijk

Ann Rheum Dis 2006;**65**:1456–1461. doi: 10.1136/ard.2005.045690

See end of article for authors' affiliations

Correspondence to: M de Visser, Department of Neurology, Academic Medical Centre, University of Amsterdam, PO Box 22660, 1100 DD Amsterdam, The Netherlands; m.devisser@amc.uva.nl

Accepted 30 March 2006
Published Online First 10 April 2006

Background: Although polymyositis and dermatomyositis are regarded as treatable disorders, prognosis is not well known, as in the literature long-term outcome and prognostic factors vary widely.
Aim: To analyse the prognostic outcome factors in polymyositis and adult dermatomyositis.
Methods: We determined mortality, clinical outcome (muscle strength, disability, persistent use of drugs and quality of life) and disease course and analysed prognostic outcome factors.
Results: Disease-related death occurred in at least 10% of the patients, mainly because of associated cancer and pulmonary complications. Re-examination of 110 patients after a median follow-up of 5 years showed that 20% remained in remission and were off drugs, whereas 80% had a polycyclic or chronic continuous course. The cumulative risk of incident connective tissue disorder in patients with myositis was significantly increased. 65% of the patients had normal strength at follow-up, 34% had no or slight disability, and 16% had normal physical sickness impact profile scores. Muscle weakness was associated with higher age (odds ratio (OR) 3.6; 95% confidence interval (CI) 1.3 to 10.3). Disability was associated with male sex (OR 3.1; 95% CI 1.2 to 7.9). 41% of the patients with a favourable clinical outcome were still using drugs. Jo-1 antibodies predicted the persistent use of drugs (OR 4.4, 95% CI 1.3 to 15.0).
Conclusions: Dermatomyositis and polymyositis are serious diseases with a disease-related mortality of at least 10%. In the long term, myositis has a major effect on perceived disability and quality of life, despite the regained muscle strength.

Idiopathic inflammatory myopathies comprise a heterogeneous group of disorders, including polymyositis, dermatomyositis and sporadic inclusion body myositis (s-IBM). Although polymyositis and dermatomyositis are regarded as treatable disorders, prognosis is not well known, as in the literature long-term outcome and prognostic factors vary widely.[1–15] Mortality ranges from 4% to 45% of patients,[1–6 10 11 15] and favourable long-term outcome varies between 18% and 90%.[1 4 5 7 9–11 15] Predictors of poor outcome include old age,[4 5 7 9–11 14] male sex,[7 9 14 15] dysphagia,[3 6 7 10] longstanding symptoms before diagnosis or treatment,[1 2 4 5 9–11] various types of myositis,[2 4 7 10 11 14] pulmonary or cardiac involvement,[4 6 7 10 11 14] and the presence of antisynthetase or anti-signal recognition particle (SRP) auto-antibodies.[8 13 15] Differences in reported outcome and prognostic factors may be due to several methodological shortcomings. In most studies on outcome in polymyositis and dermatomyositis, diagnostic criteria did not specifically exclude patients with s-IBM,[1 3–7 10 11 14 15] which can easily be misdiagnosed as polymyositis.[16 17] Secondly, reports have varied with respect to treatments received by the patients, outcome measures and follow-up time.[1 3–5 7 8 10]

In this study, we assessed the long-term outcome of a large group of adult patients with polymyositis and dermatomyositis, including survival, development of associated disorders, clinical condition and course, and prognostic factors.

METHODS

Patients

Diagnoses and demographic data of the investigated patient population have been described previously.[18] In short, we reviewed the clinical data and muscle biopsy specimens at presentation of 268 patients (>16 years of age) with ''myositis'' or ''possible myositis'' diagnosed in the period 1977–98. In total, 103 patients were excluded because of suspected s-IBM, rhabdomyolysis or muscular dystrophy (n = 73), insufficient clinical data to determine the disease course (n = 18), absence of biopsy specimen (n = 4) or lack of muscle biopsy abnormalities (n = 8). The remaining 165 patients were classified according to the following predefined criteria:

1. Definite polymyositis (subacute onset, proximal weakness or muscle soreness without skin changes, inflammatory myopathy with mononuclear cells surrounding and preferably invading individual non-necrotic muscle fibres in the endomysium)[19]
2. Definite dermatomyositis (subacute onset, proximal weakness or muscle soreness with characteristic skin abnormalities of dermatomyositis or perifascicular muscle atrophy)
3. Unspecified myositis (clinical polymyositis: subacute onset, proximal weakness or muscle soreness without skin changes, histopathologically characterised by inflammatory myopathy with perimysial/perivascular localisation of mononuclear cells in the muscle biopsy specimen, without additional endomysially located cell infiltrate)
4. Possible myositis (clinical polymyositis: subacute onset, proximal weakness or muscle soreness without skin changes, serum creatine kinase levels raised more than double and necrotising myopathy).

Abbreviations: CTD, connective tissue disorder; MRC, Medical Research Council; MSA, myositis-specific autoantibodies; s-IBM, sporadic inclusion body myositis; SIP, Sickness Impact Profile; SRP, signal recognition particle

Subclassification of each of these categories into isolated myositis, myositis associated with a connective tissue disorder (CTD; in the presence of a well-defined CTD at presentation[20–24]) or myositis associated with malignancy (in the presence of a malignancy diagnosed <2 years before presentation of myositis[25]) resulted in the following diagnoses: isolated polymyositis (polymyositis with endomysial cell infiltrates), n = 9 (5%); dermatomyositis, n = 59 (36%; 54 isolated, 3 with CTD, 2 with malignancy); unspecified myositis (clinical polymyositis with perivascular/perimysial cell infiltrates), n = 65 (39%; 38 isolated, 26 with CTD, 1 with malignancy); and possible myositis (clinical polymyositis with necrotising myopathy), n = 32 (19%; 29 isolated, 3 with CTD).

The medical ethics committees of all participating centres approved the study protocol.

Data extraction from clinical charts

The following data were extracted from the clinical files: age at presentation, sex; history of referral; disease duration (time span from start of symptoms to start of treatment) before initiation of treatment; severity of weakness at presentation; diagnosis of lung involvement; development of cancer (<2 years after onset of myositis) or of CTD (during the entire follow-up period); laboratory features at initial evaluation, type, dose and duration of treatment modalities; adverse effects of drugs; and cause of death. We also recorded the disease course (see below). Myositis-specific autoantibodies (MSAs; antibodies to Jo-1, other tRNA synthetases, Mi-2 and signal recognition particle (SRP)) were determined in all patients examined at follow-up.[26]

Outcome assessment

Death was regarded as disease-related if caused by cancer diagnosed 2 years before or after the onset of myositis, pulmonary complications, cardiac complications in patients < 40 years without cardiac history, complications of prednisone or other immunosuppressive treatment, or complications specifically related to a CTD.

Two investigators (IMB and MFGvdM) personally assessed muscle strength, disability, quality of life and persistent use of drugs in patients who had a follow-up duration of at least 1 year. Muscle strength was tested manually and scored according to the Medical Research Council score (MRC). By adding up the scores of 12 proximal and distal upper and lower limb muscles, and head flexors and extensors, a sum score was calculated, resulting in a maximum score of 130 for normal muscle strength.[27] Disability was assessed by the modified Rankin scale (score 0, no disability; score 5, totally dependent), a short index of global disability, well validated for several neurological disorders and also applied in neuromuscular diseases.[28] Three of the subscales (body care and movement, walking, and mobility) of the Sickness Impact Profile (SIP) score, a well-validated quality-of-life test, are aggregated into a physical dimension.[29–31] In a Dutch population of healthy people aged 41–50 years, the mean physical SIP score was 1.6%.[31] Physical SIP scores >1.6% were defined as abnormal.

For the prognostic factor analysis, cut-off scores were determined. Significant muscle weakness was arbitrarily defined as an MRC sum score of <128, thus allowing for one muscle group to be rated bilaterally with an MRC grade 4. Considerable disability was assigned a modified Rankin score of ⩾3 (moderate handicap, symptoms that significantly restrict lifestyle and prevent totally independent existence). Finally, the use of prednisone at >10 mg/day or other immunosuppressive or immunomodulating drugs at follow-up was used as an outcome for the analysis of prognostic factors.

Assessment of prognostic factors

The following prognostic factors for death and unfavourable outcome were analysed: age at onset of myositis (> or <60 years), sex, classification of myositis at presentation, disease duration before initiation of treatment (> or <6 months) and presence of MSAs in survivors only. In all models we adjusted for duration of follow-up.

Assessment of clinical course

Disease course was defined as monocyclic, according to the criteria used by Huber *et al*[32] in juvenile dermatomyositis, when the patient remained in remission (no detectable clinical or biochemical disease activity, and off all drugs) after 24 months since diagnosis. Disease course was designated as polycyclic when the patient had recurrence of disease activity (as determined by clinical or biochemical parameters) after remission, and as chronic continuous when there was persistent disease or continuation of drugs beyond 24 months after diagnosis. We determined whether disease course differed according to age at onset, diagnosis at onset, sex and MSAs.

Statistical analyses

Groups were compared using Student's t test or Mann–Whitney U test for continuous variables and the χ^2 test for categorical variables. Log rank test was used to compare hazard rates. All tests were two sided, and a p value <0.05 was considered significant.

Cox proportional hazards regression analysis and logistic regression analyses were used to assess the prognostic factors predicting death and unfavourable outcome, respectively. The hazard ratio or odds ratio (HR/OR) and 95% confidence interval were used as measure of association. Subsequently, predictors that were univariately associated with death or unfavourable outcome (HR/OR with p values <0.25) were included in a multivariate regression model (full model) to evaluate their independent contribution. Model reduction was carried out by excluding predictors with p values >0.05, such that a final model was derived, including independent predictors of death and unfavourable outcome. To prevent overoptimism in future populations and to validate the model internally, the regression coefficients of each predictor in the final models needed to be subjected to shrinkage. For this, a heuristic shrinkage factor was calculated as follows: (full model χ^2−p)/full model χ^2, where p is the number of predictors considered. This shrinkage factor was used as a multiplier for the regression coefficients of the selected predictors.[33] The prognostic ability of the models to discriminate between patients with and without poor outcome was shown by the area under the receiver operating characteristic curve.[34]

All analyses were carried out using SPSS software V.10.

RESULTS

Follow-up time, treatment and development of associated disorders during follow-up

There were 120 women and 45 men, with a mean age of 45 years (standard deviation (SD) 17 years, range 16–80 years). Median follow-up period was 5 years (mean (SD) 6.0 (4.4) years, range 1–23 years). In all, 157 patients (95%) were treated with prednisone. Treatment was started within 3 months after onset of symptoms in 51% of patients and within 1 year in 87% of patients. In 125 patients (76%) prednisone was given in a dose of at least 1 mg/kg body weight/day for at least 4 weeks. In total, 94 patients (57%) were subsequently treated with one (n = 61) or more (n = 33) immunosuppressive or immunomodulating agents because of failure of the prednisone or impossibility of tapering off. Drugs used included azathioprine (n = 72),

Table 1 Prognostic factors of death, disability, muscle strength and persistent immunosuppressive treatment

		Full model		Final model			
	n	Predictor	HR/OR (95% CI)	Predictor	HR/OR (95% CI)	ROC area (95% CI)	HR/OR after bootstrapping
Disease-related mortality	148*	Malignancy	7.4 (1.4 to 38.1)	Malignancy	7.8 (1.5 to 40.4)	—	6.0
		Interval from clinical manifestation to treatment <6 months	7.6 (1.0 to 57.3)	Interval from clinical manifestation to treatment <6 months	7.7 (1.0 to 58.0)		5.9
		Age >60 years	2.7 (1.0 to 7.3)	Age >60 years	2.7 (1.0 to 7.5)		2.4
		Unsp myositis and CTD	0.4 (0.06 to 3.2)				
Disability (Rankin score ⩾3)	108†	Male sex	3.2 (1.1 to 9.1)	Male sex	3.1 (1.2 to 7.9)	0.6 (0.5 to 0.7)	2.0
		Age >60 years	2.1 (0.6 to 7.0)				
		Interval from clinical manifestation to treatment >6 months	2.6 (0.9 to 7.3)				
		DM	0.5 (0.1 to 1.6)				
		Unsp myositis	2.4 (0.7 to 8.1)				
		Duration of follow-up (years)	0.9 (0.8 to 1.0)				
Muscle strength (MRC <128)	110	Male sex	2.6 (0.9 to 7.0)			0.6 (0.5 to 0.7)	
		Age >60 years	3.4 (1.1 to 10.3)	Age >60 years	3.6 (1.3 to 10.3)		2.3
		Unsp myositis and CTD	0.3 (0.03 to 2.1)				
		PM	2.5 (0.4 to 14.0)				
Persistent treatment	98‡	Jo-I	4.1 (1.2 to 14.1)	Jo-I	4.4 (1.3 to 15.0)	0.7 (0.6 to 0.8)	3.1
		PM	0.3 (0.04 to 3.1)	Duration of follow-up (years)	0.9 (0.8 to 1.0)		0.9
		Duration of follow-up (years)	0.9 (0.8 to 1.0)				

CTD, connective tissue disorder; DM, dermatomyositis; final model, multivariate analysis with $p<0.05$; full model, multivariate analysis with $p<0.25$; MRC, Medical Research Council; PM, polymyositis (defined by endomysial cell infiltrates); ROC, receiver operating characteristic; Unsp myositis, unspecified myositis (clinical PM, with perimysial and perivascular cell infiltrates).
*In 8 of the 161 patients, the cause of death was unknown and in 5 patients, information on disease duration before was missing; these patients were excluded from the analysis.
†Two missing values.
‡Twelve missing values.

methotrexate (n = 41), ciclosporin (n = 15), cyclophosphamide (n = 6), intravenous immunoglobulins (n = 14) or plasmapheresis (n = 3). Adverse effects of the drugs were reported in 125 patients (76%), including Cushing appearance (n = 71), psychiatric symptoms (n = 35), osteoporosis (n = 29), infections (n = 29), peptic symptoms (n = 23), hyperglycaemia (n = 18), hypertension (n = 16), acne (n = 10), glaucoma (n = 5), cataract (n = 5) and aseptic necrosis of the femur head (n = 1).

A malignancy was diagnosed within 2 years after onset of myositis in five patients with dermatomyositis, in three patients with unspecified myositis (clinical polymyositis) and in two patients with possible myositis (colon (n = 2), lung (n = 2), breast, stomach, renal cell, ovarian or oral squamous cell carcinoma, and Hodgkin's lymphoma (all n = 1)). Development of a CTD during follow-up was diagnosed in one patient with dermatomyositis (systemic lupus erythematosus) and in 10 of 38 patients with isolated unspecified myositis (clinical polymyositis), including scleroderma (n = 4), systemic lupus erythematosus (n = 3), Sjögren's syndrome, rheumatoid arthritis and mixed CTD (all n = 1). The cumulative risk of incident CTD in patients with unspecified myositis was 6% at 6 months, 17% at 1 year and 33% at 7 years. This risk was significantly different from the CTD risk in the rest of the patients, in whom it remained at 1% after 6 months ($p<0.001$, log rank test). Lung involvement occurred in 24 patients (15%) and included lung fibrosis (n = 9), restrictive pattern at respiratory function testing (n = 8), isolated alveolitis (n = 3), interstitial pneumonia (n = 3) and pleuritis (n = 1). Patients with lung involvement had Jo-1 autoantibodies significantly more often (44%) than patients without lung involvement (14%; $p = 0.007$).

Mortality

In all, 34 patients (21% of the 161 patients who could be traced) had died after a median follow-up of 4 years (range 0.1–20 years). The cause of death was unknown in eight patients. Myositis-related death appeared in 18 patients (11%) and occurred until 9 years after onset of myositis (median 2 years, range 0.1–9 years). Causes of death were associated cancer (n = 7), pulmonary complications (n = 4), lethal adverse effect of drugs (n = 4), CTD (n = 2) or cardiac complication of myositis (n = 1). Table 1 shows factors predicting disease-related mortality.

Death was regarded as not disease-related in another eight patients, including one patient who died after a stroke, one because of suicide and two because of cancer, which occurred >5 years after myositis was diagnosed. In four elderly patients who died because of heart failure, we considered a relationship with myositis unlikely as the myositis was not active at the time of death.

Outcome in surviving patients

In all, 110 of 131 surviving patients (84%) were personally re-examined after a median follow-up of 5 years (mean (SD) 6.9 (4.4) years, range 1–23 years). There were no statistically significant differences with regard to age, sex, serum creatine kinase activity at onset, type of myositis, duration of clinical manifestations before treatment initiation, severity of weakness at presentation, or whether treatment was given in a second-line or third-line setting between the re-examined patients and the 21 patients who were lost to follow-up (n = 4, 3%) or refused to be re-examined (n = 17, 13%; data not shown).

Tables 2 and 3 present the results of outcome assessments in re-examined patients at follow-up, categorised by

Table 2 Favourable and poor outcome in surviving patients categorised by diagnosis

	Disability (Rankin score) n (%)*		Muscle strength (MRC sum score) n (%)		Quality of life (phSIP) n (%)		Treatment at FU n (%)	
	0–1	3–5	130	<128	<1.6%	>10.8%†	No	Yes‡
PM (n = 6)								
Isolated (n = 6)	0 (0)	2 (33)	2 (33)	3 (50)	1 (17)	5 (83)	2(33)	1(17)
+ CTD (n = 0)	—	—	—	—	—	—	—	—
+ mal (n = 0)	—	—	—	—	—	—	—	—
DM (n = 41)								
Isolated (n = 37)	14 (38)	6 (16)	22 (60)	9 (24)	8 (22)	17 (46)	14(38)	15(41)
+ CTD (n = 3)	2 (67)	0 (0)	3 (100)	0 (0)	0 (0)	1 (33)	2(67)	0(0)
+ mal (n = 1)	1(100)	0 (0)	1 (100)	0 (0)	0 (0)	0 (0)	1(100)	0(0)
Unsp myositis (n = 40)								
Isolated (n = 24)	7 (29)	8 (33)	17 (71)	7 (29)	5 (22)	11 (47)	9(38)	11(46)
+ CTD (n = 16)	3 (19)	3 (19)	13 (81)	1 (6)	2 (13)	10 (63)	3(19)	8(50)
+ mal (n = 0)	—	—	—	—	—	—	—	—
Poss myositis (n = 23)								
Isolated (n = 21)	9 (43)	6 (29)	12 (57)	6 (29)	1 (5)	8 (42)	9(43)	9(43)
+ CTD (n = 2)	1 (50)	1 (50)	1 (50)	1 (50)	0 (0)	1 (50)	1(50)	1(50)
+ mal (n = 0)	—	—	—	—	—	—	—	—
Total (%)	37 (34)	26 (24)	71 (65)	27 (25)	17 (16)	53 (51)	41(37)	45(41)

CTD, connective tissue disorder; DM, dermatomyositis; FU, follow-up; mal, malignancy; MRC, Medical Research Council; phSIP, physical dimension of the Sickness Impact Profile (mean phSIP score in healthy persons is 1.6%,[31] median phSIP score in our study population was 10.8%, three missing values); PM, polymyositis (defined by endomysial cell infiltrates); Poss myositis, possible myositis (clinical PM with necrotising myopathy); Unsp myositis, unspecified myositis (clinical PM, with perimysial and perivascular cell infiltrates); +, with.
*Values are given for favourable and poor outcome; number of patients with neither a poor nor a favourable outcome are not shown.
†Median physical SIP score in total population.
‡Prednisone >10 mg/day or immunosuppressive drug.

diagnostic group and myositis-specific autoantibody, respectively. At follow-up, 24% of the patients had considerable disability (Rankin score 3–5) and 25% of the patients had muscle weakness (MRC sum score <128). Abnormal physical SIP scores were found in 84% of the patients. In all, 41% of the patients were using prednisone (>10 mg) or immunosuppressive treatment at follow-up. The median total SIP score was 12.2% and the median physical SIP score 10.8%. All 37 patients without disability (Rankin score 0 or 1) had complete normal muscle strength (MRC 130): 15 (41%) of these patients were still on drugs and 23 (62%) had abnormal physical SIP scores. All patients with a normal physical SIP score (n = 17) had complete normal muscle strength and no (n = 14) or slight (n = 2) (Rankin score 2) disability.

The analyses of prognostic factors in surviving patients are presented in table 1. Significant disability was predicted by male sex (OR 3.1; 95% CI 1.2 to 7.9) and muscle weakness by age >60 years (OR 3.6; 95% CI 1.3 to 10.3). The presence of Jo-1 autoantibodies predicted the persistent use of drugs (OR 4.4; 95% CI 1.3 to 15.0). Among the patients who still used drugs at the time of re-examination, the Jo-1-positive patients (n = 10) had significantly more lung involvement (50%) than the Jo-1-negative group (n = 28, 11%; p = 0.019). Duration of follow-up was not related to disability or muscle strength. An inverse relationship existed between duration of follow-up and persistent use of drugs (OR/year increase in follow-up 0.9; 95% CI 0.8 to 1.0). Outcome was not significantly different between the various myositis subtypes or groups defined by presence of various MSAs.

The receiver operatoring characteristic areas for the three final models predicting significant disability, muscle weakness and treatment dependency indicated that in 61%, 61% and 70% of the patients, respectively, outcome can be predicted correctly using these models (table 1).

Clinical course of myositis in surviving patients

In the 104 re-examined patients with a follow-up time of at least 2 years, disease course was monocyclic in 21 patients (20%), polycyclic in 21 patients (20%) and chronic continuous in 62 patients (60%). Fifteen patients with a polycyclic

Table 3 Outcome in surviving patients, categorised by myositis-specific autoantibodies

	Disability Rankin score n (%)		Muscle strength n (%) MRC sum score n (%)		Quality of life phSIP n (%)		Treatment at FU n (%)	
	0–1	3–5	130	<128	<1.6%	>10.8%§	No	Yes¶
Jo-1 (n = 14)††	5 (36)‡	4 (29)	8 (57)	5 (36)	1 (7)	8 (57)	4 (29)	9 (64)*
Synthetase† (n = 6)	1 (17)	3 (50)	3 (50)	2 (33)	0 (0)	5 (100)	1 (17)	4 (67)
Mi-2 (n = 20)	9 (45)	5 (25)	14 (70)	4 (20)	4 (20)	10 (50)	8 (40)	8 (40)
SRP (n = 3)	1 (33)	0 (0)	2 (67)	0 (0)	0 (0)	3 (100)	1 (33)	2 (67)
No MSA (n = 56)	19 (34)	12 (21)	35 (63)	14 (25)	10 (18)	25 (45)	23 (41)	16 (29)**

MRC, Medical Research Council; phSIP, physical dimension of the sickness impact profile (mean phSIP score in healthy persons is 1.6%,[31] median phSIP score in our study population was 10.8%); MSA, myositis-specific autoantibody.
*p = 0.04 compared with Jo-1-negative patients.
†Anti-synthetase auto-antibodies, other than Jo-1.
‡N (% in each of the myositis-specific auto-antibody group).
§Median physical SIP score in total population.
¶Prednisone>10 mg/day or immunosuppressive drug.
**p = 0.02 compared with MSA-positive patients.
††Myositis-specific antibodies determined in 94 patients, 5 patients had two MSAs.

Table 4 Disease course in surviving patients with follow-up of at least 2 years (n = 104)

	Monocyclic	Polycyclic or chronic continuous
Number of patients	21	83
Mean age in years (SD)	42 (19)	42 (14)
Women, n (%)	15 (71)	64 (77)
Diagnosis		
Polymyositis (%)	0 (0)	5 (6)
Dermatomyositis (%)	10 (48)	29 (35)
Unspecified myositis (%)	5 (24)	34 (41)
Possible myositis (%)	6 (29)	15 (18)
MSAs present (%)*	7 (41)	3 (41)

MSA, myositis-specific autoantibodies; polymyositis, myositis defined by endomysial cell infiltrates; unspecified myositis, clinical polymyositis; with perimysial and perivascular cell infiltrates; possible myositis, clinical polymyositis with necrotising myopathy.
*Myositis-specific antibodies determined in 92 patients.

course had one relapse, six patients had two relapses. Follow-up duration, age, sex, types of myositis and the presence of MSAs were not significantly associated with the type of disease course (table 4).

DISCUSSION

Our study shows that patients with dermatomyositis and polymyositis have a mortality risk of >10% to die of a cause related to their disease, mostly cancer, especially during the first years after onset of myositis. This disease-related mortality may even be an underestimation, as in one quarter of deaths the cause was unknown. This high mortality is impressive, especially when comparing this number with a healthy population of Dutch people with the same mean age, in which the 5-year mortality is about 1–2% (Statistics Netherlands; www.cbs.nl). Cancer was not restricted to dermatomyositis, but also occurred in patients with unspecified myositis (clinical polymyositis), which shares histopathological features with dermatomyositis,[18] and in immune-mediated necrotising myopathy, designated here as possible myositis. Immune-mediated necrotising myopathy has been reported to be associated with malignancy.[35 36] Patients with an isolated unspecified myositis (clinical polymyositis) have also a chance of about one in four to be diagnosed with an associated CTD after onset of myositis. Lung involvement was not found frequently in our study, but this can be an underestimation, as not all patients were sytematically screened for this.

Most of the survivors have a chronic continuous or polycyclic disease course. In the long term, half the patients are still taking a low dosage of drugs, and one quarter (especially older men) are left with significant disability or muscle weakness. Only 20% of our re-examined patients were off all drugs, without any signs of active disease, at least 2 years after adequate treatment of one single period of myositis. This is in line with the results of another investigation in adult patients with polymyositis and dermatomyositis.[11] As 25–42% of patients with juvenile dermatomyositis had a monophasic course, this corroborates the notion that age is a strong predictor.[32 37 38]

At long-term follow-up, 65% of patients who survived had normal strength, 34% had no or slight disability, and only 16% had normal scores on the quality-of-life scale. This discrepancy between outcome measures is consistent with three recent observations[11 12 15] and is not disease-specific. It has also been found in Guillain–Barré syndrome, showing disabling persistent fatigue in patients who ultimately regained normal muscle strength.[39] Doctors who treat patients with myositis should be aware of this insensitivity of the MRC score.

Not surprisingly, disease-related death was associated with age and associated cancer, but no other prognostic factors, especially no differences between myositis subtypes, were found.

We could not confirm several factors often reported to be a determinant of unfavourable outcome, such as duration of symptoms before treatment.[1 2 4 5 9–11] It should be borne in mind that in previous investigations, patients with IBM (who usually have insidious onset, and therefore a longer duration until treatment) may well have been misdiagnosed as having polymyositis. Furthermore, our Jo-1-positive patients did not do worse in terms of muscle strength, disability or quality of life in the long term, although we and others have observed a high drug dependency in Jo-1-positive patients, possibly related to the more frequent occurrence of lung involvement.[8]

Finally, we also found no indication that type of myositis determines the outcome. In this study, we have carefully excluded patients with IBM and have distinguished myositis subtypes based not only on clinical characteristics (absence or presence of skin abnormalities) but also on histopathological features as described recently elsewhere.[18] In the previous study, we found that only a small proportion of patients without skin changes showed endomysial mononuclear cells surrounding and invading non-necrotic muscle fibres as described by Arahata and Engel[19] in patients with polymyositis. In contrast, the largest proportion of our patients without skin abnormalities and therefore clinically considered to be having polymyositis according to the classification of Bohan and Peter[40] (designated here as unspecified myositis) showed histopathological features suggestive of a primary microangiopathy as in dermatomyositis. In our study, the outcomes of polymyositis (designated as unspecified myositis), dermatomyositis and necrotising myopathy (designated here as possible myositis) were essentially similar, whereas patients with polymyositis as defined by the presence of endomysial mononuclear cells surrounding and invading non-necrotic muscle fibres tended to have a somewhat worse outcome. This is in line with the results from our previous study that some of these patients developed signs of IBM in the course of their disease.[18] However, some of the myositis groups, including the polymyositis group, were small, which hampers statistical calculations. Our findings will be of value for the current initiatives to adapt diagnostic and classification criteria for the idiopathic inflammatory myopathies, which followed our earlier publication.

ACKNOWLEDGEMENTS

This study was financially supported by the Prinses Beatrix Fonds, The Hague, The Netherlands.

Authors' affiliations

I M Bronner*, M de Visser, Department of Neurology, Academic Medical Centre, University of Amsterdam, Amsterdam, The Netherlands
M F G van der Meulen*, J H J Wokke, J E Hoogendijk, Department of Neurology, University Medical Centre Utrecht, Utrecht, The Netherlands
S Kalmijn, Julius Centre for Health Sciences and Primary Care, University Medical Centre Utrecht
W J van Venrooij, Department of Biochemistry, Centre for Molecular Life Sciences, Radboud University Nijmegen, Nijmegen, The Netherlands
A E Voskuyl, Depertment of Rheumatology, Free University Hospital Amsterdam, Amsterdam
H J Dinant, Department of Clinical Immunology and Rheumatology, Academic Medical Centre
W H J P Linssen, Department of Neurology, St Lucas Andreas Hospital Amsterdam, Amsterdam

*These authors contributed equally to this work.

Competing interests: None.

REFERENCES

1 **DeVere R**, Bradley WG. Polymyositis: its presentation, morbidity and mortality. *Brain* 1975;**98**:637–66.
2 **Bohan A**, Peter JB, Bowman RL, Pearson CM. A computer-assisted analysis of 153 patients with polymyositis and dermatomyositis. *Medicine* 1977;**56**:255–83.
3 **Carpenter JR**, Bunch TW, Engel AG, O'Brien PC. Survival in polymyositis: corticosteroids and risk factors. *J Rheumatol* 1977;**4**:207–14.
4 **Henriksson KG**, Sandstedt P. Polymyositis–treatment and prognosis. A study of 107 patients. *Acta Neurol Scand* 1982;**65**:280–300.
5 **Tymms KE**, Webb J. Dermatopolymyositis and other connective tissue diseases: a review of 105 cases. *J Rheumatol* 1985;**12**:1140–8.
6 **Hochberg MC**, Feldman D, Stevens MB. Adult onset polymyositis/dermatomyositis: an analysis of clinical and laboratory features and survival in 76 patients with a review of the literature. *Semin Arthritis Rheum* 1986;**15**:168–78.
7 **Chwalinska-Sadowska H**, Maldykowa H. Polymyositis-dermatomyositis: 25 years of follow-up of 50 patients disease course, treatment, prognostic factors. *Mat Med Polona* 1990;**3**:213–18.
8 **Love LA**, Leff RL, Fraser DD, Targoff IN, Dalakas M, Plotz PH, *et al*. A new approach to the classification of idiopathic inflammatory myopathy: myositis-specific autoantibodies define useful homogeneous patient groups. *Medicine* 1991;**70**:360–74.
9 **Fafalak RG**, Peterson MGE, Kagen LJ. Strength in polymyositis and dermatomyositis: best outcome in patients treated early. *J Rheumatol* 1994;**21**:643–8.
10 **Maugars YM**, Berthelot JMM, Abbas AA, Mussinin JMD, Nguyen JMD, Prost AM. Long-term prognosis of 69 patients with dermatomyositis or polymyositis. *Clin Exp Rheum* 1996;**14**:263–74.
11 **Marie I**, Hachulla E, Hatron PY, Hellot MF, Levesque H, Devulder B, *et al*. Polymyositis and dermatomyositis: short term and long term outcome, and predictive factors of prognosis. *J Rheumatol* 2001;**28**:2230–7.
12 **Chung YL**, Mitchell HL, Houssien DA, Al-Mahrouki H, Carr AJ, Scott DL. A comparative study of outcome in myositis and other musculoskeletal disorders assessed using the Nottingham Health Profile. *Clin Exp Rheumatol* 2001;**19**:447–50.
13 **Hengstman GJD**, Brouwer R, Vree Egberts WTM, Seelig HP, Jongen PJ, van Venrooij WJ, *et al*. Clinical and serological characteristics of 125 Dutch myositis patients. *J Neurol* 2002;**249**:69–75.
14 **Danko K**, Ponyi A, Constantin T, Borgulya G, Szegedi G. Long term survival of patients with idiopathic inflammatory myoapathies according to clinical features. A longitudinal study of 162 cases. *Medicine* 2004;**83**:35–42.
15 **Ponyi A**, Borgula G, Constantin T, Vancsa A, Gergely L, Danko K. Functional outcome and quality of life in adults with idiopathic inflammatory myositis. *Rheumatology* 2005;**44**:83–8.
16 **van der Meulen MF**, Hoogendijk JE, Jansen GH, Veldman H, Wokke JH. Absence of characteristic features in two patients with inclusion body myositis. *J Neurol Neurosurg Psychiatry* 1998;**64**:396–8.
17 **Griggs RC**, Askanas V, DiMauro S, Engel A, Karpati G, Mendell JR, *et al*. Inclusion body myositis and myopathies. *Ann Neurol* 1995;**38**:705–13.
18 **van der Meulen MFG**, Bronner IM, Hoogendijk JE, Burger H, van Venrooij WJ, Voskuyl AE, *et al*. Polymyositis: an overdiagnosed entity. *Neurology* 2003;**61**:316–21.
19 **Arahata K**, Engel AG. Monoclonal antibody analysis of mononuclear cells in myopathies. I: quantitation of subsets according to diagnosis and sites of accumulation and demonstration and counts of muscle fibers invaded by T cells. *Ann Neurol* 1984;**16**:193–208.
20 **Arnett FC**, Edworthy SM, Bloch DA, McShane DJ, Fries JF, Cooper NS, *et al*. The American Rheumatism Association 1987 revised criteria for the classification of rheumatoid arthritis. *Arthritis Rheum* 1988;**31**:315–24.
21 **Tan EM**, Cohen AS, Fries JF, Masi AT, McShane DJ, Rothfield NF, *et al*. The 1982 revised criteria for the classification of systemic lupus erythematosus. *Arthritis Rheum* 1982;**25**:1271–7.
22 **Vitali C**, Bombardieri S, Moutsopoulos HM, Jonsson R, Moutsopoulos HM, Alexander EL, *et al*. Assessment of the European classification criteria for Sjögren's syndrome in a series of clinically defined cases: results of a prospective multicentre study. The European Study Group on Diagnostic Criteria for Sjögren's Syndrome. *Ann Rheum Dis* 1996;**55**:116–21.
23 **Subcommittee for Scleroderma Criteria of the American Rheumatism Association Diagnostic and Therapeutic Criteria Committee**. Preliminary criteria for the classification of systemic sclerosis (scleroderma). *Arthritis Rheum* 1980;**23**:581–90.
24 **Kasukawa R**. Mixed connective tissue disease. *Intern Med* 1999;**38**:386–93.
25 **Buchbinder R**, Forbes A, Hall S, Dennet X, Giles G. Incidence of malignant disease in biopsy-proven inflammatory myopathy. A population based cohort study. *Ann Intern Med* 2001;**134**:1087–95.
26 **Brouwer R**, Hengstman GJ, Vree Egberts W, Ehrfeld H, Bozic B, Ghirardello A, *et al*. Autoantibody profiles in the sera of European patients with myositis. *Ann Rheum Dis* 2001;**60**:116–23.
27 **Notermans NC**, Wokke JHJ, Fransen H, van der Graaf Y, Vermeulen M, van den Berg LH, *et al*. Chronic idiopathic polyneuropathy presenting in middle or old age: a clinical and electrophysiological study of 75 patients. *J Neurol Neurosurg Psychiatry* 1993;**56**:1066–71.
28 **Swieten JC van**, Koudstaal PJ, Visser MC, Scouten HJA, van Gijn J. Interobserver agreement for the assessment of handicap in stroke patients. *Stroke* 1988;**19**:604–7.
29 **Berger M**, Bobbitt RA, Carter WB, Gilson BS. The Sickness Impact Profile: development and final revision of a health status measure. *Med Care* 1981;**19**:787–805.
30 **Read JL**, Quinn RJ, Hoefer MA. Measuring overall health: an evaluation of three important approaches. *J Chromi Dis* 1987;**40**(Suppl 1):S7–21.
31 **Jacobs HM**, Luttik A, Touw-Otten FWMM, de Melker RA. The Sickness Impact Profile; results of a validation study of the Dutch version. *Ned Tijdschr Geneeskd* 1990;**134**:1950–4.
32 **Huber AM**, Lang B, LeBlanc CMA, Birdi N, Bolaria RK, Malleson P, *et al*. Medium- and long-term functional outcomes in a multicenter cohort of children with juvenile dermatomyositis. *Arthritis Rheum* 2000;**43**:541–9.
33 **Van Houwelingen JC**, Le Cessie S. Predictive value of statistical models. *Stat Med* 1990;**9**:1305–25.
34 **Hanley JA**, Mc Neil BJ. The meaning and use of the area under a receiver operating characteristic (ROC) curve. *Radiology* 1982;**143**:29–36.
35 **Bronner IM**, Hoogendijk JE, Wintzen AR, van der Meulen MF, Linssen WH, Wokke JH, *et al*. Necrotising myopathy, an unusual presentation of a steroid-responsive myopathy. *J Neurol* 2003;**250**:480–5.
36 **Vosskamper M**, Korf K, Franke F, Schachenmayr W. Paraneoplastic necrotizing myopathy: a rare disorder to be differentiated from polymyositis. *J Neurol* 1989;**236**:489–90.
37 **Ng Y**, Ouvrier RA, Wu T. Drug therapy in juvenile dermatomyositis: follow-up study. *J Child Neurol* 1998;**13**:109–12.
38 **Bernsen Spencer CH**, Hanson V, Singsen BH, Bernstein BH, Kornreich HK, King KK. Course of treated juvenile dermatomyositis. *J Pediatr* 1984;**105**:399–408.
39 **Bernsen RAJAM**, de Jager AEJ, Schmitz PIM, van der Meché FGA. Long-term impact on work and private life after Guillain-Barré syndrome. *J Neurol Sci* 2002;**201**:13–17.
40 **Bohan A**, Peter JB. Polymyositis and dermatomyositis. *N Engl J Med* 1975;**292**:344–177, 403–7.