Polymyositis and Dermatomyositis: Short Term and Longterm Outcome, and Predictive Factors of Prognosis

ISABELLE MARIE, ERIC HACHULLA, PIERRE-YVES HATRON, MARIE-FRANCE HELLOT, HERVE LEVESQUE, BERNARD DEVULDER, and HUBERT COURTOIS

ABSTRACT. ***Objective.*** To assess short term and longterm outcome of polymyositis (PM) and dermatomyositis (DM), and predictive variables of PM/DM course.

Methods. The medical records of 77 consecutive patients with PM/DM were reviewed. The criteria for PM/DM diagnosis were based upon Bohan and Peter criteria.

Results. Thirty-one patients (40%) achieved remission of PM/DM, whereas 33 (43%) improved and 13 (17%) worsened their clinical status. Short term recurrences of PM/DM (during tapering of therapy) occurred in 36 patients and longterm recurrences (after discontinuation of therapy) in 9 patients. PM/DM were associated with both decreased functional status and quality of life at longterm followup: (1) only 52% of patients considered to be in remission experienced a return to previous normal activities; and (2) 45% of the other patients with nonremitting PM/DM still had a marked reduction of activities (as shown by the disability scale of the Health Assessment Questionnaire). Overall mortality was as high as 22%, and the main causes of death were cancer and lung complications. Factors associated with PM/DM remission were younger age and shorter duration of clinical manifestations prior to therapy initiation. Variables associated with poor outcome of PM/DM were older age, pulmonary and esophageal involvement, and cancer.

Conclusion. Our series shows both high morbidity and mortality related to PM/DM, emphasizing that management of PM/DM patients at an early stage is required. Lung complications (i.e., aspiration pneumonia due to PM/DM related esophageal dysfunction and ventilatory insufficiency) were one of the main causes of death in our series, indicating that investigating for subclinical esophageal and lung impairment should become an integral part of initial PM/DM evaluation. The presence of poor prognostic factors should prompt both close followup and aggressive therapy in patients with PM/DM. (J Rheumatol 2001;28:2230–7)

Key Indexing Terms:
POLYMYOSITIS DERMATOMYOSITIS THERAPY
OUTCOME PROGNOSIS PREDICTIVE FACTORS

Polymyositis (PM) and dermatomyositis (DM) are chronic idiopathic inflammatory disorders, affecting the striated muscles, the skin, and other organs. PM and DM are still considered to be associated with high morbidity and mortality rates, as high as 4 to 50%[1-17], principally related to life threatening muscle weakness and cardiac and lung complications[1-6,9,14,16,18]. Few series have analyzed longterm outcome and prognostic factors in PM/DM[1-6,14,16-19], which prompted us to conduct this retrospective study. Our aims were (1) to assess short term and longterm outcome, including functional course, complications, survival rate, and mortality in 77 consecutive patients with PM/DM; and (2) to determine predictive variables of recovery and also factors associated with poor outcome of PM/DM.

From the Department of Internal Medicine, Centre Hospitalier Universitaire de Rouen-Boisguillaume, Rouen; the Department of Internal Medicine, Centre Hospitalier Universitaire de Lille, Lille; and the Department of Biostatistics, Centre Hospitalier Universitaire de Rouen-Boisguillaume, Rouen, France.

I. Marie, MD, PhD, Department of Internal Medicine, CHU de Rouen-Boisguillaume and CHU de Lille; E. Hachulla, MD, PhD; P-Y. Hatron, MD, PhD; B. Devulder, MD, PhD, Department of Internal Medicine, CHU de Lille; M-F. Hellot, ScD, Department of Biostatistics, CHU de Rouen-Boisguillaume; H. Levesque, MD, PhD; H. Courtois, MD, PhD, Department of Internal Medicine, CHU de Rouen-Boisguillaume.

Address reprint requests to Dr. I. Marie, 16 rue Arthur Duval, 76300 Sotteville-lès-Rouen, France.

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MATERIALS AND METHODS

Patient population. Seventy-seven consecutive patients with a diagnosis of DM (n = 36) and PM (n = 41) were studied. All patients were seen at the University of Lille and University of Rouen medical centers as inpatients or outpatients between 1983 and 1998. No patient had other connective tissue disorders. Diagnosis of PM and DM was based on Bohan and Peter criteria[20,21]: symmetric muscle weakness, increased muscle enzymes, myopathic changes on electromyography, typical histologic findings on muscle biopsy, and characteristic dermatologic signs. PM and DM were considered definite in 50 patients who presented at least 4 manifestations, and probable in 27 patients with 3 manifestations.

All 77 patients had an initial prospective standardized evaluation of organ involvement, which resulted in the detection of systemic complications that included Raynaud's phenomenon, dysphagia with manometric

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esophageal impairment, dysphonia, cardiac dysfunction (evaluated by electrocardiogram and echocardiography), and peripheral neuropathy. Pulmonary involvement was investigated by pulmonary function tests (PFT) and computerized tomography (CT) scan of the lungs. The presence of interstitial lung disease (ILD) was confirmed if patients had bilateral shadowing on CT scan associated with PFT abnormalities manifested by restrictive changes (vital capacity < 80%) and transfer factor < 70% predicted[11]. Ventilatory insufficiency due to respiratory striated muscle weakness was dichotomized, as described[22]: (1) severe hypoventilation, determined by hypercapnic respiratory failure requiring intubation and mechanical ventilation[22]; and (2) moderate hypoventilation, characterized by restrictive pattern on PFT (i.e., decreased lung volumes, with vital capacity < 80%) without evidence of ILD[22].

Patients also underwent biochemical analysis, including creatine kinase (CK) (U/l) and aldolase (U/l). Autoantibody screening [antinuclear antibodies (ANA), anti-J01 antibody] was performed; myositis-specific autoantibodies were not tested (anti-signal recognition particle, anti-Mi-2 antibodies), as detection of these antibodies is not yet available in our hospitals.

Patients had a minimal followup duration of 18 months, although patients who died before 18 month followup were also included. The functional course of all patients was assessed for: (A) muscle functional disability according to the disability scale of the Health Assessment Questionnaire (HAQ), which is divided into 8 variables, i.e., dressing and grooming, arising, eating, walking, hygiene, reach, grip, and activity[23]; and (B) biochemical (CK, aldolase) and electromyographic abnormalities. The outcome of PM/DM patients was defined as (1) remission: disappearance of skin manifestations, stable increase of muscle strength, normal function of major organs, normalization of both serum muscle enzyme levels and electromyographic abnormalities, persisting after therapy discontinuation; (2) improvement: when muscle and skin signs, function of involved major organs, and biochemical data improved with therapy; (3) deterioration: when muscle and skin signs, function of involved major organs, and biochemical findings worsened despite therapy. Moreover, PM/DM was defined as: (1) "monocyclic": patients remained free of all clinical and biochemical signs of disease and were taking no medication at 24 months after PM/DM diagnosis; and (2) "chronic continuous": persistent active PM/DM or continuation of medication beyond 24 months after PM/DM diagnosis.

Recurrences of PM/DM were diagnosed on the basis of the following criteria: clinical relapse (i.e., muscle and/or dermatologic manifestations), biochemical relapse (i.e., increase of serum muscle enzymes for which there was no other explanation). PM/DM recurrences were further divided into short term and longterm recurrences; short term recurrences occurred during tapering of therapy and longterm recurrences after termination of therapy.

Both survival and current status were based on hospital records (i.e., data obtained during routine followup visit) or by contacting patients from September to December 1998. The HAQ[23] was again used to evaluate functional disability of PM/DM patients. Particular attention was further paid to the development of 3 steroid related complications: myopathy, avascular necrosis of bone, and osteoporotic vertebral fracture. Finally, the cause of death was determined through hospital or physician records.

Measurement of prognostic factors. Prognostic factors were determined at time of PM/DM diagnosis. First, we evaluated factors associated with PM/DM remission. Patients were divided into 2 groups: patients who achieved PM/DM remission and patients who did not. Clinical data, biochemical findings, electromyographic and histologic features were compared between these 2 groups of patients. Second, we assessed factors of PM/DM poor prognosis. Patients were divided into 2 groups: patients who deteriorated or died due to PM/DM and patients who did not. The above variables were compared between these 2 groups of patients.

Statistical analysis. Analyses were performed using StatXact version 3.0 (Cytel Software Corporation, Cambridge, MA, USA) and StatView version 5.0. For group comparisons involving binary data, we used either the chi-square test or Fisher's exact test depending on the sample size. Comparisons involving continuous data were by Mann-Whitney test. We also calculated the corresponding odds ratio and either asymptotic or exact 95% confidence intervals (CI), depending on the sample size. To control for multiple testing, we applied Bonferroni correction, which consists of multiplying the p value by the number of outcomes analyzed (32 in this series); the results were regarded as significant when adjusted p values were < 0.0016 (i.e., 0.05/32). Unadjusted p values are reported in Tables 4 and 5. Only adjusted p values are reported in the text. Additionally, comparisons of pulmonary involvement variables were controlled for cancer using the Mantel-Haenszel test. Finally, cumulative survival rates were calculated, using the Kaplan-Meier test for the whole series.

RESULTS

General background. The 77 consecutive patients with PM/DM consisted of 33 men and 44 women, with a median age 52 years (range 3–86). Age-specific frequency rates in PM/DM patients were: (1) ≤ 25 years: n = 8 [6 patients were ≥ 18 yrs; 2 patients (3 and 12 yrs, respectively) were included in the study as they still had active PM/DM after age 16 years]; (2) 26–44 years: n = 17; (3) 45–64 years: n = 28; and (4) ≥ 65 years: n = 24.

The median duration of first clinical symptoms before PM/DM diagnosis was 4 months (range 0.5–120). The median HAQ score for the cohort at PM/DM diagnosis was 1; HAQ-specific frequency scores in patients were: (1) 0 < HAQ ≤ 0.5: n = 27; (2) 0.5 < HAQ ≤ 1: n = 20; (3) 1 < HAQ ≤ 1.5: n = 13; (4) 1.5 < HAQ ≤ 2: n = 7; (5) 2 < HAQ ≤ 2.5: n = 3; and (6) 2.5 < HAQ ≤ 2.75: n = 7.

The clinical characteristics of patients are shown in Table 1. Thirty-two (42%) patients developed pulmonary involvement: (1) 14 patients had ILD; (2) 15 patients had ventilatory insufficiency due to respiratory striated muscle weakness (without underlying ILD) (14 patients had moderate hypoventilation and one had severe hypoventilation with hypercapnic respiratory failure requiring mechanical ventilation); and (3) 13 patients had aspiration pneumonia. They presented associated esophageal dysfunction (n = 5), ventilatory insufficiency (n = 7), ILD (n = 3), and cancer (n = 6), and 7 patients received steroids at a daily dose of 1 mg/kg.

Sixteen patients (22%) had cancer; cancer was metastatic (n = 7) or localized (n = 9). Among the patients with cancer,

Table 1. General characteristics of the patient population (n = 77).

Patient Characteristics	n (%)
Raynaud's phenomenon	24 (32)
Arthralgias/arthritis	20 (31)
Esophageal involvement	22 (29)
Dysphonia	6 (8)
Pulmonary involvement	32 (42)
Cardiac impairment	5 (6)
Peripheral neuropathy	3 (4)
Malignancy	16 (22)
Nailfold capillaroscopic microangiopathy	28 (37)
Antinuclear antibodies	36 (47)

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15 had DM. Cancer onset preceded PM/DM initial clinical signs in 2 patients (8 mo; 29 mo in a patient with chronic lymphoid leukemia), was concurrently identified in association with PM/DM in 11 patients, and developed after PM/DM diagnosis in 3 patients (3, 10, and 18 mo).

Thirty-six patients (47 %) had ANA and 6 (8%) anti-J01 antibody. Nailfold capillaroscopy showed microangiopathy in 28 patients (37%), with enlargement of capillary loops (26/28). Electromyography revealed myogenic abnormalities in 64 patients (84%). Muscle biopsy specimens confirmed evidence of PM/DM in 60 patients (80%), demonstrating inflammatory infiltrates (58/60), muscle fiber necrosis (41/60), and vascular damage (21/60).

Therapy. All patients were given high dose steroid therapy initially (range 0.5–1.5 mg/kg per day), which resulted in clinical improvement in 61% of cases at 3 month followup. Median duration of steroid therapy in PM/DM patients was 3 years (range 1 mo–14 yrs). Finally, 37 patients (48%) received steroids as a monotherapy.

PM/DM patients were further treated with immunosuppressive agents. Twenty-three patients received methotrexate (MTX) for a median duration of 10 months, which resulted in improvement of PM/DM in 70% of cases (16/23); MTX therapy had to be discontinued due to severe cytomegalovirus related colitis secondary to pancytopenia (n = 1) and hepatic cytolysis (n = 3). Fourteen patients received azathioprine for a median duration of 6 months, resulting in improvement of PM/DM in 57% of cases (8/14); one patient had hepatic cytolysis, requiring discontinuation of azathioprine. Two patients with PM/DM refractory to either MTX or azathioprine alone were successfully given combined therapy of MTX and azathioprine. Twelve patients received cyclophosphamide for a median duration of 5.5 months, permitting resolution of clinical signs in 3 of them (25%); the 9 patients who were unsuccessfully given cyclophosphamide had PM/DM refractory to MTX (n = 5), azathioprine (n = 2), and intravenous immunoglobulins (IVIG) (n = 2). Three patients with PM/DM refractory to other cytotoxic drugs received cyclosporine, resulting in clinical improvement in 2 of them. Finally, 24 patients were given IVIG [1 g/kg for 2 days monthly for a median duration of 6 months (range 3–11 mo)], resulting in clinical improvement in 92% of cases; the 22 patients (10 PM, 12 DM) who successfully received IVIG had PM/DM refractory to steroids alone (n = 16), MTX (n = 5), azathioprine (n = 3), and cyclophosphamide (n = 2).

Outcome. The median followup duration of PM/DM patients was 4 years (range 1 mo–24 yrs). The outcome of patients with PM/DM is summarized in Table 2.

Thirty-one patients (40%) had remission of PM/DM; 14 of these patients had "monocyclic" PM/DM. Thirty-three other patients (43%) had improvement of PM/DM. The 13 remaining patients (17%) had deterioration of PM/DM. Forty-nine patients (64%) had "chronic continuous" PM/DM. None of the 14 patients who died within one to 22 months after PM/DM diagnosis had a monocyclic course of the disease.

Table 2. Outcome of patients with PM/DM (n = 77).

	Patients, n (%)
Resolution	31 (40)
Improvement	33 (43)
Deterioration	13 (17)
Disease course	
Monocyclic	14 (18)
Chronic continuous	49 (64)
Recurrence	45 (58)
During tapering of high dose steroids or stable maintenance treatment	21 (27)
During tapering of low dose steroids (< 20 mg/day)	15 (19)
Off treatment	9 (12)
Mortality	17 (22)

PM/DM recurred in 45 patients (25 PM, 20 DM). Short term recurrence was encountered in 36 patients (47%); 15 of these patients received steroids at daily doses lower than 20 mg at time of onset of PM/DM recurrence. The prevalence of PM and DM patients experiencing short term recurrence of disease was similar (20 vs 16); the total number of recurrence (37 vs 31) was not different in PM and DM patients. Multiple short term recurrences (≥ 2 per patient) were also similar in DM (8/16) and PM (10/20) patients. The characteristics of short term recurrence in PM patients were as follows: clinical (7/37), biochemical (11/37), and both clinical and biochemical (19/37) relapses. DM patients developed cutaneous (9/31), biochemical (3/31), both clinical muscle and biochemical (8/31), and both clinical (cutaneous and muscle) and biochemical (11/31) relapses. Longterm clinical recurrence of PM/DM was noted in 9 patients (12%; 5 PM, 4 DM). Duration of PM/DM therapy, prior to longterm recurrence, in these patients ranged from 2.5 to 10 years; 4 patients had a previous history of steroid refractory PM/DM. Time of onset of PM/DM recurrence after therapy termination ranged as follows: 3 months (n = 1), 6 months (n = 2), one year (n = 3), 2 years (n = 2), and 9 years (n = 1); we failed to find a correlation between the length of previous therapy and time of PM/DM recurrence onset.

Survival and mortality. Figure 1 provides the survival curve of patients with PM/DM. Survival of PM/DM patients was 83%, 82%, 77%, and 61% at one, 2, 5, and 15 years, respectively. The overall mortality rate was 22% (17/77). The characteristics of patients with PM/DM who died are shown in Table 3. Death was due to cancer in 8 patients. Six other patients died from pulmonary complications that included one pulmonary hypertension due to ILD and 5 aspiration pneumonia; the 5 patients with aspiration pneumonia concomitantly had esophageal motor dysfunction (n = 3), moderate ventilatory insufficiency (n = 3), and cancer (n =

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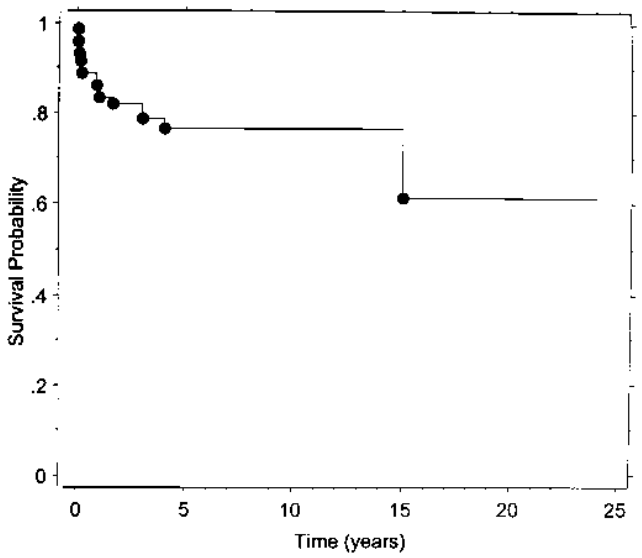

Figure 1. Survival curve of 77 patients with PM/DM. Number of available patients: 68 at one year followup, 34 at 5 year followup, 14 at 10 year followup, and 5 at 15 year followup.

3); cancer in the latter patients included localized (n = 1), metastatic (n = 1), and stable chronic lymphoid leukemia without therapy (n = 1). An additional patient died from generalized muscle weakness, and the 2 remaining patients died from other disorders.

Longterm functional outcome. The median HAQ score, for the cohort, at longterm followup was 0.25 (range 0–1.75). The longterm functional outcome of the 31 PM/DM patients who achieved PM/DM remission is shown in Figure 2. It was characterized by: (1) complete disappearance of clinical manifestations, with a return to previous normal activities in 16 patients (52%); (2) persistent muscle effort fatigue with moderate decreased activities (HAQ score < 0.75) in 10 patients; (3) death due to disorders other than PM/DM complications in 2 patients (6%); and (4) 3 other patients were alive but could not be contacted.

The longterm functional outcome of the remaining patients with nonremitting PM/DM was as follows: (1) persistent muscle effort fatigue (HAQ score < 0.75) in 17 patients (55%); (2) marked decrease of muscle weakness, with severe reduction of activities (0.75 < HAQ score ≤ 1.5) in 12 patients (39%); and (3) the 2 remaining patients require a wheelchair (HAQ score > 1.5) (6%).

The functional disability of our patients with PM/DM was also due to the adverse effects of steroid therapy, including steroid related muscle weakness (n = 11), avascular necrosis of the femoral head (n = 1), and osteoporotic vertebral fracture (n = 3).

Predictive factors. Factors associated with remission. Patients who achieved remission of PM/DM were younger than those who did not (48 vs 53 yrs; p = 0.0526). The median duration of clinical symptoms before PM/DM diagnosis tended to be shorter in patients who experienced PM/DM remission, although not significantly so [3 mo (range 1–24 mo) vs 5.5 mo (range 0.5–120 mo); p = 0.1165].

Neither PM nor DM (41% vs 39%; p = 0.8182) was more frequent in patients with PM/DM remission than in those without. As shown in Table 4, clinical manifestations were not predictive of PM/DM remission. Serum CK levels were similar in patients who presented PM/DM remission compared to those who did not: (1) initial CK levels > 5000 U/l (14% vs 11%; p = 0.7224); (2) initial normal CK levels (36% vs 38%; p = 1); and (3) CK level reversion to normal 2 months after initiation of PM/DM therapy (47 vs 42%; p = 1).

Table 3. Mortality among 17 PM/DM patients.

Patient	Age (yrs)/Sex	Subset	ED	Cancer	Lung	Duration of Disease	Cause of Death
1	86 F	DM	–	+	—	1 yr	Cancer
2	74 M	DM	+	+	—	3 mo	Cancer
3	67 F	DM	–	+	—	11 mo	Cancer
4	22 F	DM	+	–	—	15 yrs	Biliary pancreatitis
5	48 M	PM	+	+	Pneumonia/insufficiency	4 yrs	Pneumonia
6	66 F	PM	–	–	Insufficiency	1.5 mo	Liver cirrhosis
7	63 F	PM	–	–	ILD	3 yrs	Pulmonary hypertension / ILD
8	59 M	DM	+	–	Pneumonia/insufficiency	3 mo	Pneumonia
9	67 M	DM	–	+	—	1.5 mo	Cancer
10	65 M	DM	+	+	Pneumonia	1 mo	Pneumonia
11	69 F	PM	+	+	Insufficiency	11 mo	Generalized muscle weakness
12	81 M	DM	+	+	Pneumonia	20 mo	Cancer
13	39 F	DM	–	+	—	2 yrs	Cancer
14	75 F	DM	–	+	—	2 mo	Cancer
15	69 F	DM	–	+	Pneumonia	1 mo	Pneumonia
16	82 M	PM	–	–	Pneumonia/insufficiency	1 mo	Pneumonia
17	53 M	DM	–	+	—	1 yr	Cancer

ED: esophageal dysfunction.

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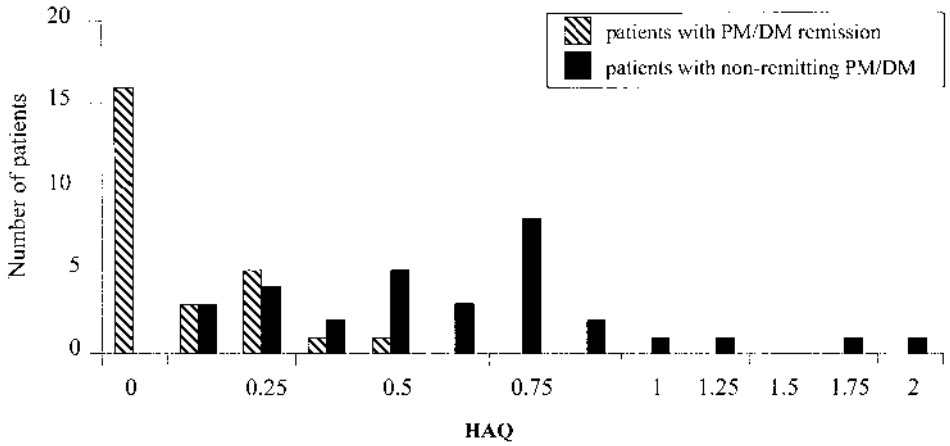

Figure 2. Distribution scores of the Health Assessment Questionnaire (HAQ) at longterm followup of PM/DM.

Table 4. Clinical, biochemical, capillaroscopic, and histologic factors associated with PM/DM remission.

	PM/DM Remission (n = 31)	Nonremitting PM/DM (n = 46)	p	OR	95% CI
Clinical manifestations					
Initial myalgias, %	90	87	0.7326	1.40	0.27–9.34
Initial muscle weakness, %	87	91	0.7072	0.64	0.11–3.78
Raynaud's phenomenon, %	47	23	0.0308	2.98	1.09–8.13
Esophageal dysfunction, %	29	26	0.7760	1.16	0.42–3.21
Dysphonia, %	10	6	0.6800	1.54	0.19–12.23
Joint involvement, %	36	27	0.4701	1.48	0.51–4.33
Pulmonary impairment, %	39	43	0.6771	0.82	0.32–2.07
Cancer, %	13	87	0.1527	0.41	0.12–1.42
Biochemical, capillaroscopic, histologic features					
CK, median (range)	437 U/l (10–8,260)	491.5 U/l (13–27,356)	0.7592		
Aldolase, median (range)	9.6 U/l (1.5–66)	4.8 U/l (1.8–63)	0.1497		
Antinuclear antibodies, %	45	48	0.8182	0.90	0.36–2.24
Anti-J01 antibody, %	6	9	1.0000	0.67	0.06–5.09
Characteristic microangiography at nailfold capillaroscopy, %	48	33	0.2054	1.87	0.71–4.93
Muscle biopsy					
Inflammatory infiltrates, %	72	84	0.2269	0.50	0.16–1.56
Muscle fiber necrosis, %	45	64	0.1130	0.46	0.18–1.21
Vascular damage, %	21	34	0.2158	0.50	0.17–1.51

p values are obtained with Mann-Whitney tests; p values regarded as significant when < 0.0016 (i.e., 0.05/32).

Finally, therapy was not different in patients with PM/DM remission compared to other patients for MTX (19% vs 37%; p = 1), azathioprine (10% vs 24%; p = 1), cyclophosphamide (13% vs 18%; p = 1), and IVIG (19% vs 39.1%; p = 1).

Factors associated with deterioration and death. Results are shown in Table 5. Patients who experienced PM/DM deterioration and death related to PM/DM were older (65 vs 50 yrs; p = 0.0111). The median duration of first clinical symptoms before PM/DM diagnosis tended to be longer in these patients [2 mo (range 0.5–120) vs 4 mo (range 1–120)], although not significantly (p = 0.0975).

Patients with PM/DM who deteriorated more often had cancer compared to patients who did not (p < 0.0001). Pulmonary involvement was more frequent in patients who deteriorated or died due to PM/DM (p = 0.0352). Among pulmonary disorders, only aspiration pneumonia (p < 0.0001) was more common in patients with PM/DM deterioration versus those without; pneumonia remained more frequent in patients with PM/DM deterioration after control for cancer status, using the Mantel-Haenszel test (p = 0.029). Serum CK levels were similar in patients who experienced PM/DM deterioration and in those who did not: (1) initial CK levels > 5000 U/l (10% vs 13%; p = 1); (2) initial

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Table 5. Clinical, biochemical, capillaroscopic, and histologic variables associated with PM/DM deterioration and death related to PM/DM complications.

	Deterioration and Death due to PM/DM (n = 15)	Absence of Deterioration and Death due to PM/DM (n = 62)	p	OR	95% CI
Clinical manifestations					
Initial myalgias, %	76	93	0.0568	0.25	0.04–1.32
Initial muscle weakness, %	76	95	0.0311	0.18	0.03–1.08
Raynaud's phenomenon, %	35	31	0.7740	1.17	0.39–3.46
Esophageal dysfunction, %	33	25	0.4646	1.50	0.50–4.46
Dysphonia, %	10	7	0.6617	1.37	0.11–10.43
Joint involvement, %	26	33	0.6171	0.74	0.22–2.43
Pulmonary impairment, %	71	30	0.0011	5.73	1.90–17.31
Aspiration pneumonia	55	4	< 0.0001	29.33	4.85–293.40
Ventilatory insufficiency	45	12	0.0074	6.00	1.49–24.69
Interstitial lung disease	19	18	1.0000	1.08	0.22–4.42
Cancer, %	62	6	< 0.0001	27.08	5.42–168.90
Biochemical, capillaroscopic, histologic features					
CK, median (range)	483 U/l (13–27,356)	602 U/l (10–10.063)	0.5895		
Aldolase, median (range)	5.4 U/l (1.8–55)	8.1 U/l (1.5–66)	0.5156		
Antinuclear antibodies, %	48	46	0.9257	1.05	0.38–2.86
Anti-J01 antibody, %	10	8	1.0000	1.29	0.11–9.85
Characteristic microangiography at nailfold capillaroscopy, %	33	42	0.5397	0.70	0.23–8.16
Muscle biopsy, %					
Inflammatory infiltrates	81	79	1.0000	1.14	0.28–5.59
Necrosis of muscle fibers	57	56	0.9147	1.06	0.38–2.94
Vascular damage	48	21	0.0237	3.39	1.15–10.02

p values obtained with Mann-Whitney tests; p values regarded as significant when < 0.0016 (i.e., 0.05/32).

normal CK levels (23% vs 15%; p = 0.4481); and (3) reversion to normal CK levels 2 months after initiation of PM/DM therapy (0% vs 12%; p = 0.1465).

Finally, therapy did not differ in PM/DM patients who deteriorated compared to patients who did not for: MTX (14% vs 36%; p = 1), azathioprine (5% vs 23%; p = 1), cyclophosphamide (14% vs 16%; p = 1), and IVIG (10% vs 39%; p = 0.384).

DISCUSSION

Few investigators have evaluated short term and longterm outcome in PM/DM[2-7,9,15-18,23-29]. Uthman, *et al*[17], in a series of 30 patients with PM/DM, reported that as high as 77% of patients achieved PM/DM remission. In our study, we clearly demonstrated a marked poorer outcome of PM/DM. We observed that only 40% of patients achieved PM/DM remission, whereas 43% improved and 17% worsened their clinical status. Our study considered 77 consecutive patients without prior selection based on clinical or biologic presentation, which tends to be representative of the entire PM/DM population. Our findings confirm other data, showing the PM/DM remission rate varying from 25 to 70%[6,7,10,17,18,24,27]. Further, our data are in accord with previous series that mention relapse rates as high as 23 to 60% in PM/DM[9,26,27,29]. In our study, short term recurrence, observed during therapy tapering, was encountered in 47% of PM/DM patients; roughly half of these recurrences were noted in patients receiving low dose steroid therapy (< 20 mg daily). Prevalence of short term recurrence was similar in PM and DM patients (49% vs 44%), and notably multiple recurrences. However, biochemical subclinical relapses were more frequent in PM patients. Interestingly, DM patients experienced either cutaneous or muscle relapses separately, suggesting that pathologic mechanisms may be differentially reactivated in patients' skin or muscle[29]. Longterm recurrence of PM/DM after therapy withdrawal is less frequent, occurring in 6 to 43% of patients for up to 33 years after disease remission[9,26,27,29]. In our population, 9 patients (12%) had longterm recurrences of PM/DM, with similar recurrence rate in PM and DM patients (10% vs 14%); recurrences more often manifested during the first year following discontinuation of PM/DM therapy (6/9), although later recurrences were still possible. We failed to find a correlation between the length of previous therapy and time of PM/DM recurrence onset. Finally, both steroid and cytotoxic drugs could be discontinued in only 40% of our patients who remained stable after therapy discontinuation at a median followup of 4 years. Our data confirm other authors' results noting that therapy could be discontinued in 17.6 to 58% of cases[17].

PM/DM are still considered to have a high morbidity leading to decreased functional status[16,25,27], although

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Maugars, *et al*[18] found that 90% of patients experienced insignificant muscular disability at 3 year followup. In our study we have shown that PM/DM are associated with a marked decrease of patients' functional status at longterm followup. We have therefore found that, among PM/DM patients considered to be in remission, only 52% experienced a return to normal previous activities, whereas the remaining patients in this group still complained of decreased quality of life ($0 < HAQ\ score < 0.75$) despite our ability to control active muscle inflammation in these patients. We further noted that longterm functional outcome of the surviving patients with nonremitting PM/DM was particularly poor, as a marked reduction of activities ($HAQ > 0.75$) was present in 45% of them. In the present series, decreased functional disability was mainly due to PM/DM activity and complications, although it was also related, in part, to adverse effects of steroid (myopathy and osteoporosis). Finally, because we noted a correlation between higher scores of HAQ and reduced functional status, we suggest that although the disability scale of the HAQ has not yet been validated in patients with myositis, it may represent a helpful test for measuring muscle functional disability in PM/DM.

In previous series analyzing the survival of PM/DM patients, survival ranged from 72–84%, 34–73%, and 42–85% at 2, 5, and 10 years, respectively[1,2,4-6,14,16-19]. Our findings also underscore that PM/DM are associated with decreased survival, although we have observed slightly higher survival rates than previously reported: 83%, 77%, and 61% of patients were still alive at one, 5, and 15 year followup, respectively. These data may be explained by better management of PM/DM patients compared with older series. PM/DM has further been reported to be associated with increased mortality, with a total mortality rate ranging from 4 to 50%[1-10,14-17]. Cancer, lung, and cardiovascular complications are generally cited as the most common causes of death in PM/DM patients[1,2,5-7,9,10,12,16,19]. In our series, the overall mortality rate was 22%. Among the 17 PM/DM patients who died, the first cause of death was cancer in 47% of cases. As cancer was principally diagnosed concurrently or within one year after PM/DM diagnosis, PM/DM longterm survivors may not require extensive screening measures beyond those recommended for the general population. Only Chow, *et al*[30] in 539 patients also mentioned that excess cancer incidence declined with increasing years since initial diagnosis of PM/DM: 6-fold during the first year, lower during the 2nd year, and no significant excess in subsequent years of followup. The second cause of death in our patients was pulmonary complication (35% of cases), mainly aspiration pneumonia occurring during the first 2 months after PM/DM diagnosis. Aspiration pneumonia was more often due to PM/DM related esophageal motor involvement and moderate ventilatory insufficiency (with decreased cough reflex and inability to take the maximum inspiration[22]) in these patients. Our findings therefore indicate that the search for both subclinical esophageal motor dysfunction and ventilatory insufficiency should be systematically performed during the initial evaluation of PM/DM patients, as these variables are contributing factors of life threatening aspiration pneumonia.

From a practical point of view, the knowledge of prognostic factors of PM/DM course appears essential in order to improve patient management. Previous investigators have described variables of PM/DM remission. In our experience, younger age (48 vs 53 yrs) tended to be correlated with PM/DM remission ($p = 0.052$), confirming other data[2,9,10]. Shorter duration of clinical manifestations prior to therapy initiation also tended to predict PM/DM remission, although not significantly, as reported[2,5-7,9,24]; only 9% of patients whose PM/DM was diagnosed within a period > 18 months between symptom onset and therapy institution achieved remission. A more favorable response in patients treated at an early stage of PM/DM may be related to a lower extent of histologic irreversible muscle damage. A correlation between greater gains in muscle strength and higher serum CK levels has further been described in PM/DM[24], although we were unable to find a relationship between initial serum CK levels and PM/DM remission. On the other hand, numerous variables have been reported as predictive of PM/DM poor outcome. In the present series, we noted a correlation between older age and deterioration in PM/DM patients (65 vs 50 yrs), which confirms other data[1–5,8,9,12,14,16]. We also noted that pulmonary involvement was a predictive factor of PM/DM deterioration, in accord with previous results[1,3,9,11,12,14]. Among pulmonary disorders, only aspiration pneumonia was associated with PM/DM deterioration. Because aspiration pneumonia was mainly due to PM/DM related esophageal motor dysfunction and moderate ventilatory insufficiency and more often occurred early during the course of PM/DM, our findings highlight that the search for both esophageal involvement and ventilatory insufficiency should be performed during the initial evaluation of PM/DM patients; this evaluation should include: (1) esophageal manometry, which may reveal dysfunction of striated muscle motor activity and low pressure in the upper esophageal sphincter[13]; (2) PFT, which may show a restrictive pattern and decreased maximal inspiratory and expiratory pressures[22]; and (3) chest radiograph, which may reveal atelectasis, small lung volumes, diaphragmatic elevation[22]. Our data further suggest that patients with clinical/subclinical pulmonary involvement may require more aggressive therapy with short term efficacy[13]. Moreover, cancer was a predictive factor of PM/DM deterioration, confirming previous data[1-3,5-7,12]; however, 7 patients underwent adequate therapy of localized cancer, which indicates that the risk of cancer in PM/DM should be recognized, resulting in appropriate therapy of cancer[12]. As

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cancer mainly occurred in older patients with DM[12], we suggest that the search for cancer should be systematically carried out initially in these patients; other authors also noted that recurrence of skin or muscle signs and a poor response to therapy should prompt investigations for underlying cancer in patients with PM/DM[7,12,31]. Finally, few authors have suggested that a normal CK may indicate poor prognosis in PM/DM[32]. Our findings emphasize the absence of correlation between blood CK levels and PM/DM outcome.

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