

Clinical factors to predict a poor prognosis and refractory disease in patients with polymyositis and dermatomyositis associated with interstitial lung disease

Sirs,

Interstitial lung disease (ILD) is a serious complication and a poor prognostic factor in patients with polymyositis (PM) and dermatomyositis (DM) (1, 2). Some patients show progressive ILD that is often refractory to corticosteroid (CS) treatment, resulting in a fatal outcome (3-5). Although immunosuppressive drugs, including cyclosporine A (CYA), intravenous cyclophosphamide (IVCY) and methotrexate (MTX) has been shown to be effective (4-8), these were effective when they were started early in the course of ILD (4, 6). Therefore, it is important to predict a poor prognosis and poor response to CS at the initial presentation. We retrospectively investigated the clinical factors, collected at diagnosis, which are associated with a poor prognosis and refractory disease in patients with PM/DM associated with ILD. This study was approved by the ethics committee.

From 2001 to 2005, 61 idiopathic PM/DM patients with ILD, 15 men and 46 women with a mean (\pm SD) age of 53.6 \pm 1.8 years, were analyzed. They consisted of 25 PM patients, 19 classic DM patients, and 17 clinically amyopathic dermatomyositis (CADM) patients. The median duration of follow-up was 35 months (0.1-78 months). Patients with cancer-associated myositis and overlap syndrome were excluded. The diagnosis of PM/DM was based on Bohan and Peter's criteria (9) except for CADM, which was based on the Gerami's definition. (10). All patients were treated with CS (maximum dose of 25 to 100 mg/d). Immunosuppressive/immunomodulating drugs were given to 34 (56%) patients (CYA: 28, IVCY: 5, tacrolimus: 5, azathioprine: 5, MTX: 2, IVIG: 1). Eleven patients (4 PM, 3 classic DM, and 4 CADM) died (fatal group). Among 50 patients, whose ILD remitted or improved, eight (2 classic DM and 6 CADM) were given two immunosuppressive drugs (refractory group), and 42 patients (21 PM, 14 classic DM, and 7 CADM) were treated with CS with or without one immunosuppressive drug (responsive group).

The clinical factors were analysed using a Cox proportional hazards model, comparing fatal and refractory groups with responsive group. On univariate analysis, CADM, skin ulcer, LDH/CK ratio >1, negative anti-Jo-1 antibody, PaO₂/FiO₂ ratio <400, and chest x-ray score (0 = no lesion; 1 = lesions limited in the bottom of the lung; 2 = lesions limited to the lower half of the lung; 3 = lesions in the lower and upper areas of the lung; and 4 = diffuse lesions) >2 were associated with fatal or refractory disease. Because the PaO₂/FiO₂ ratio and the chest x-ray score

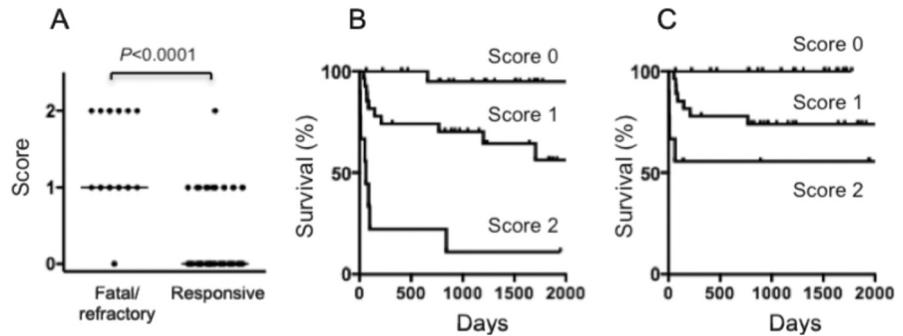


Fig. 1. Evaluation of the clinical scoring system. **A.** Comparison of the scores between fatal/refractory patients and responsive patients. The scores of the two groups are significantly different ($p < 0.0001$). **B.** Survival curves defined by the time to the introduction of the second immunosuppressive/immunomodulating agent or death by current score. Patients were divided into three groups according to the score (score 0, $n = 23$; score 1, $n = 27$; score 2, $n = 9$). The survival curves are significantly different ($p < 0.0001$ and $p = 0.047$ for trend). **C.** Survival curves showing the time to death by current score ($p < 0.0024$ and $p = 0.208$ for trend).

represent the severity of ILD, these two items were combined as PaO₂/FiO₂ <400 OR chest x-ray score >2. On multivariate analysis, PaO₂/FiO₂ <400 OR chest x-ray score >2 (HR 5.09, 95%CI 1.69-15.39, $p = 0.004$) and LDH/CK >1 (HR 3.71, 95%CI 1.17-11.72, $p = 0.026$) were significant independent factors. Based on these results, we propose a preliminary simple score, the number of positive risk factors to predict a poor prognosis and refractory disease. In 59 patients, who had an adequate data set, the scores were significantly different between fatal/refractory cases and responsive cases (Fig. 1A, $p < 0.0001$). The sensitivity and specificity of the cut-off ≥ 1 were 95% and 55%, respectively. The survival curves of the endpoint, the time to the introduction of second immunosuppressive/immunomodulating agents or death correlated with the score ($p = 0.0007$, $p = 0.047$ for trend, Fig. 1B). Survival curves that indicate the time to death also showed a similar trend, although it was not significant ($p = 0.0024$, $p = 0.208$ for trend, Fig. 1C).

The present study showed that the preliminary prediction is valid and may serve as a guide to deciding the initial therapeutic strategy in the treatment of PM/DM associated with ILD. It is necessary to validate this scoring system using a larger cohort.

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