Exercise Limitation in Patients with Polymyositis*

Cullen A. Hebert, M.D.; Timothy J. Byrnes, M.D.; Bruce A. Baethge, M.D.; Robert E. Wolf, M.D.; and Gary T. Kinasewitz, M.D., F.C.C.P.

To examine the hypothesis that patients with inflammatory muscle disease have impairments in cardiac and/or pulmonary function that are masked by peripheral muscle weakness, complete FFTs, echo/Doppler studies and exercise testing were performed in 11 patients with polymyositis. Maximal inspiratory and expiratory pressures and expiratory flow rates were normal. One patient had evidence of restrictive lung disease; two had a reduced Dsb. Seven patients had evidence of pulmonary hypertension. Only three patients had normal aerobic capacity; $V_{O_2}$ max in the other 8 patients was 46±8 percent of predicted when they stopped exercising. Four patients had a normal $O_2$ pulse; seven patients had a reduced $O_2$ pulse while five of seven patients exceeded 85 percent of their target heart rate. We conclude that while asymptomatic impairments in pulmonary function are uncommon in polymyositis, the incidence of pulmonary hypertension is high, but symptoms may be masked by the peripheral muscle weakness.

*From the Section of Pulmonary and Critical Care Medicine, Section of Rheumatology and Section of Cardiology, Louisiana State University Medical Center, Shreveport (Drs. Hebert, Byrnes, Baethge and Wolf), and the Pulmonary and Critical Care Section, University of Oklahoma Health Science Center, Oklahoma City (Dr. Kinasewitz).

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Reprint requests: Dr. Baethge, Department of Medicine/Rheumatology, PO Box 33932, Shreveport 71130

LVDD = left ventricular internal dimension, diastole; LVIDS = left ventricular internal dimension, systole; EF = ejection fraction; LVEDV = left ventricular end-diastolic volume; LVESV = left ventricular end-systolic volume; $V_{DVT}$ = dead-space to tidal volume ratio; MID = maximum inspiratory pressure; MEP = maximum expiratory pressure

Polymyositis is a systemic disease characterized by degeneration and inflammation of striated muscle. Although it primarily affects the proximal limb muscles, it also can involve the respiratory musculature. Occasionally this respiratory muscle dysfunction can produce symptomatic restrictive lung disease in the absence of radiographic evidence of parenchymal disease. However, dyspnea usually occurs because of radiographically apparent diffuse interstitial inflammation or fibrosis, which may contribute to the patient’s morbidity and even progress to overt respiratory insufficiency.

Because patients with polymyositis may have a limitation of their exercise performance due to peripheral muscle fatigue, the effects of the inflammatory muscle disease on the cardiopulmonary response to exercise have not been examined. The purpose of this study was to determine if patients with polymyositis have impairments of cardiopulmonary function which are masked by their peripheral muscle weakness.

METHODS

All patients with polymyositis hospitalized or seen in the rheumatology clinics at Louisiana State University Medical Center in Shreveport and two university-affiliated medical centers during the period of July 1987 to June 1988 were eligible for inclusion in the study. Subjects were identified by review of discharge diagnoses and clinic records at those institutions. The diagnosis of polymyositis was made by the established criteria of Bohan and Peters. Dermatomyositis was diagnosed when the above criteria were satisfied and the characteristic heliotrope rash also was present. Patients were excluded if they had associated collagen vascular disease at the time of the study or if they were unable to exercise.

The patients underwent an initial clinical evaluation by a rheumatologist (B.B., R.W) to ascertain disease activity. Clinical activity was defined as the presence of constitutional symptoms, muscle weakness and abnormal serum muscle enzyme values. Biochemical activity was defined as elevation of muscle enzyme levels in the absence of clinical examination findings. Patients without clinical or biochemical evidence of polymyositis were considered to have inactive disease. The disease duration was defined from date of onset of active disease to the time of the exercise study. Polymyositis was considered chronic if there was persistent disease activity despite appropriate medical therapy for at least one year.

Cardiac evaluation included a routine 12-lead electrocardiogram and an echocardiogram with Doppler flow studies; M-mode and two dimensional echocardiography with Doppler were performed by the cardiologist (T.B.) using a General Electric Pass II echocardiographic machine (General Electric, Inc., Rancho Cordova, CA). Particular attention was directed to the pulmonic valve for evidence of pulmonary hypertension. The diagnosis of pulmonary hypertension was determined via: (1) measurement of the depth of the a-dip, (2) the presence or absence of systolic notch of the pulmonic valve, and (3) measurement of the acceleration time by Doppler flow studies. Reduction of the a-dip (less than 2 mm) or systolic notch of the pulmonic valve were considered suggestive of pulmonary hypertension. Pulsed Doppler echocardiograms were obtained with either a 2.5 or 3.5 kHz transducer in the parasternal and four-chamber views. Pulsed Doppler was employed in the right ventricular outflow tract to record the flow signal just proximal to the pulmonic valve. The acceleration time was determined as the duration from the onset of pulmonary flow to the peak flow. The acceleration times were not corrected for heart rate. Normal acceleration time in our laboratory is 144 (±15.3) ms. An acceleration time of less than 114 ms was considered diagnostic of pulmonary hypertension. Secondary criteria were abnormalities of
pulmonic valve motion, ie, reduction of the a-dip or systolic notching of the pulmonic valve. All pulsed Doppler signals were recorded on videotape and analyzed off-line with the cardiac calculation package. Measurements were made using a parasternal long axis view. The left ventricular diastolic and systolic dimensions were measured using the M-mode. Volumes were calculated from the formula of Teichholz et al at both end-diastole and end-systole:

\[ \text{Diastole} = (LVIDD)^2 \times \frac{1}{2.4 + LVIDD} \]

\[ \text{Systole} = (LVIDS)^2 \times \frac{1}{2.4 + LVIDS} \]

The EF was calculated from the following equation:

\[ \text{EF} \% = \frac{LVEDV - LVESV}{LVEDV} \times 100 \]

Pulmonary evaluation included posteroanterior and lateral chest radiographs with subjects erect and complete PFTs. All chest radiographs were reviewed by two authors (C.H., C.K.). Pulmonary hypertension was diagnosed by chest radiograph when the hilar to thoracic ratio exceeded 0.36. Pulmonary function tests performed included spirometry, and the measurement of lung volumes and DLb. The FVC, FEV₁, FEV₁/FVC, and MVV were determined with a pneumotachograph spirometer (Medical Graphics Corp, St. Paul, MN). Functional residual capacity was determined by open-circuit nitrogen washout technique, and TLC, RV, and RV/TLC ratio were calculated. The Dco was determined and corrected for carboxyhemoglobinemia. Maximum inspiratory and expiratory pressures were measured at TLC and RV, respectively, using a water-filled manometer. All values obtained were also expressed as percent predicted using standard prediction formulas. 

Exercise capacity was determined during a multistage incremental exercise test with instantaneous breath-by-breath measurements and analysis of gas exchange. The exercise protocol consisted of 2-minute stages with 10-W increments performed on a cycle ergometer (Mijnhardt, model KEM-3, Bunsch, Holland) until the patient reached a symptom-limited Vo₂ max. Heart rate was monitored on a cardiotachometer (Biegel Cardiac Monitor, model 302, Morden, Surrey, England). Expiratory flow was determined with a heated linear pneumotachograph, shock-mounted variable pressure transducer (±2.0 cm H₂O) and a carrier demodulator while the patient breathed through a high flow, low-resistance, low-dead-space valve (Hans-Rudolph No. 3800). The concentration of CO₂ and O₂ in expired air was determined by a rapid responding infrared absorption analyzer and zirconia fuel cell sensor, respectively (CadNet System 2001, Medical Graphics Corp, St. Paul, MN). All gas and flow measurements were corrected for ambient temperature, barometric pressure and water vapor. From the expired gas Pco₂, Pco₃, and Ve, O₂ consumption, and CO₂ production were derived. The Vb/Vr was estimated from the mean and end-tidal expired CO₂ concentrations. Oxygen pulse was calculated by dividing the O₂ consumption by the heart rate. The arterial oxygen saturation during rest and exercise was measured by pulse oximetry (Nellcor, model N-100, Hayward, CA). Maximal oxygen uptake was defined as the highest O₂ consumption obtained during the symptom-limited exercise test.

Statistics

All data are expressed as mean ± SD. Student's t test for unpaired data was used to compare differences between patients with and without pulmonary hypertension and between those with and without active disease. We accepted p<0.05 to indicate statistical significance.

Results

A total of 19 patients with polymyositis were identified at the three institutions. Six patients were excluded because they were unable to exercise (one with aseptic necrosis of the hip, one with retinal detachment, two with acute myopathy which precluded their exercise ability, one with hepatic encephalopathy, one with Graves' disease/atrial fibrillation). Thirteen patients were eligible for the study. Two patients refused to participate. The data from the remaining 11 patients are reported.

The clinical characteristics of the study patients are indicated in Table 1. Five patients had definite polymyositis, four patients had definite dermatomyositis, and two patients had probable polymyositis by criteria of Bohan and Peters. All patients studied had a positive muscle biopsy with characteristic features of inflammatory myopathy. The mean age of the patients was 46 (±16) years. There were four males and seven females. Only three patients (No. 2, 3 and 7) were smokers. Six patients had active disease and five patients inactive disease. The disease duration was 42 (±38) months with a range from 6 to 114 months. Five patients had coexisting illness; three had hypertension and two had diabetes.

A routine 12-lead electrocardiogram was normal in only two of 11 patients. Nonspecific ST segment changes were present in seven patients, one patient had right atrial enlargement, one had left atrial enlargement with evidence of a previous myocardial infarction, one had left ventricular hypertrophy, and another had right bundle branch block. Echocardiographic data revealed all patients to have normal left ventricular ejection fractions (mean, 69 ± 11 percent). In contrast to normal left ventricular function, seven patients had echocardiographic evidence of pulmonary hypertension (Table 1). The diagnosis of pulmonary hypertension was based on a reduced acceleration time with associated pulmonic valve motion abnormalities in five patients and on the basis of secondary criteria in two patients (No. 5 and 8) in whom technically adequate Doppler studies could not be obtained. All Doppler studies were performed at heart rates between 60 to 100 beats per minute except for patient 1 (54 beats per minute) and patient 7 (56 beats per minute). Correcting the acceleration time for heart rate would not have changed the results in either patient.

Six patients had no radiographic evidence of parenchymal lung disease, but two of these individuals had an increased hilar/thoracic index suggestive of pulmonary hypertension (Table 1). Four patients had increased interstitial markings consistent with mild pulmonary fibrosis. One patient had unsuspected left lower lobe atelectasis without evidence of other parenchymal disease.

Resting pulmonary function is illustrated in Figure 1. All patients had normal maximum inspiratory pressures. Only one patient (No. 10) had an abnormally
## Table 1—Clinical Characteristics of Study Patients

<table>
<thead>
<tr>
<th>Patients</th>
<th>Age/Sex</th>
<th>Disease Criteria*</th>
<th>Duration (Months)</th>
<th>Activity†</th>
<th>ECG‡</th>
<th>Chest Radiograph‡</th>
<th>Pulmonary Hypertension§</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>30/F</td>
<td>1-4</td>
<td>114</td>
<td>Inactive</td>
<td>ST-T</td>
<td>Normal</td>
<td>AT, VN</td>
</tr>
<tr>
<td>2</td>
<td>33/F</td>
<td>1,2,4,5</td>
<td>6</td>
<td>Inactive</td>
<td>Normal</td>
<td>Normal, ↑ HT index</td>
<td>AT</td>
</tr>
<tr>
<td>3</td>
<td>56/F</td>
<td>1,2,4,5</td>
<td>96</td>
<td>Inactive</td>
<td>RAE</td>
<td>↑ ↑ Interstitial markings</td>
<td>Absent</td>
</tr>
<tr>
<td>4</td>
<td>64/F</td>
<td>1-4</td>
<td>24</td>
<td>Active, B,C</td>
<td>LVH</td>
<td>Cardiomegaly with interstitial markings</td>
<td>AT, AD, VN</td>
</tr>
<tr>
<td>5</td>
<td>57/F</td>
<td>1,2,4</td>
<td>6</td>
<td>Active, B,C</td>
<td>Old MI, LAE, ST-T</td>
<td>Cardiomegaly, ↑ HT index</td>
<td>+ +, AD</td>
</tr>
<tr>
<td>6</td>
<td>52/F</td>
<td>1-5</td>
<td>66</td>
<td>Active, B</td>
<td>ST-T</td>
<td>Normal</td>
<td>AT, VN</td>
</tr>
<tr>
<td>7</td>
<td>37/M</td>
<td>1-5</td>
<td>60</td>
<td>Active, B,C</td>
<td>Sinus bradycardia</td>
<td>Normal</td>
<td>Absent</td>
</tr>
<tr>
<td>8</td>
<td>63/F</td>
<td>1-4</td>
<td>42</td>
<td>Inactive</td>
<td>ST-T</td>
<td>↑ Interstitial markings, fibrosis borderline cardiomegaly</td>
<td>+ +, AD</td>
</tr>
<tr>
<td>9</td>
<td>63/M</td>
<td>1-4</td>
<td>12</td>
<td>Active, B</td>
<td>ST-T</td>
<td>LLL atelectasis</td>
<td>Absent</td>
</tr>
<tr>
<td>10</td>
<td>44/M</td>
<td>1,2,4</td>
<td>29</td>
<td>Inactive</td>
<td>ST-T</td>
<td>↑ Interstitial markings</td>
<td>AT</td>
</tr>
<tr>
<td>11</td>
<td>51/M</td>
<td>1-4</td>
<td>7</td>
<td>Active, B,C</td>
<td>ST-T, RBBB</td>
<td>Normal</td>
<td>Absent</td>
</tr>
</tbody>
</table>

*1 = proximal muscle weakness; 2 = elevated muscle enzymes; 3 = positive electromyogram; 4 = positive muscle biopsy; 5 = rash of dermatomyositis.
†Chronic disease is the persistence of disease activity for one year despite continuous appropriate medical therapy. B = biochemical evidence. C = clinical evidence.
‡ST-T = ST-T wave abnormalities; RAE = right atrial enlargement; LAE = left atrial enlargement; MI = myocardial infarction; LVH = left ventricular hypertrophy; RBBB = right bundle branch block; LLL = left lower lobe; HT = hilal-thoracic.
§Echocardiographic criteria. AT = abnormal acceleration time; AD = A-dip; VN = pulmonic valve notching; + + = technically inadequate Doppler study.

**Figure 1.** Resting pulmonary data in patients with polymyositis. Data expressed as percent predicted except for FEV/FVC ratio which is observed percentages. Solid triangles, pulmonary hypertension but no active disease; solid circles, no pulmonary hypertension and no active disease; open triangles, pulmonary hypertension and active disease; open circles, no pulmonary hypertension but active disease.
low maximum expiratory pressure. Patient 3 had a mild reduction in the TLC, and patients 2 and 10 had mild reductions in diffusing capacity. No patient had evidence of obstructive ventilatory impairment.

Figure 2 illustrates the data during maximal exercise. The maximal work load ranged from 11 to 71 percent of predicted. The mean aerobic capacity or $\overline{V}O_2$ max was 57 percent (±20) but again the individual values were scattered over a wide range. Minute ventilation at maximal exercise, expressed as the percentage of the MVV, suggested the patients did not have a ventilatory limitation to exercise since the $V_e$/MVV ratio did not exceed 60 percent in any individual. No patient desaturated as measured by pulse oximetry. Despite the trend for patients with pulmonary hypertension to have higher $V_d$/$V_t$ ratios at end-exercise.
than those without pulmonary hypertension, this difference did not achieve statistical significance.

Figure 3 illustrates the relationship between the \( O_2 \) pulse and heart rate achieved at \( V_{O_2} \) max. The majority (nine of 11) of patients stopped exercising because of peripheral muscle fatigue while two (patients 2 and 11) complained of dyspnea. Four patients had normal \( O_2 \) pulse, as percent predicted. Three of these four patients also had a normal \( V_{O_2} \) max while patient 1 only reached 70 percent of the target heart rate before the onset of peripheral muscle fatigue. Seven patients had a decreased \( O_2 \) pulse. In five of these seven (patients 3, 4, 8, 10 and 11) the maximal heart rate exceeded 85 percent of predicted, suggesting an impaired stroke volume response and therefore cardiac limitation to exercise. Two others (patients 5 and 7) with a low \( O_2 \) pulse developed peripheral muscle fatigue prior to reaching their target heart rate.

DISCUSSION

Pulmonary hypertension was first reported as a consequence of dermatomyositis in the late 1950s.\(^{17}\) The pulmonary hypertension was thought to be the result of degenerative and occlusive changes in the smaller branches of the pulmonary artery tree. In an autopsy series, Denbow et al\(^{18}\) examined the lungs and cardiovascular system of 20 patients with polymyositis. Four of 20 patients had small vessel disease characterized by smooth muscle hyperplasia of the medial portion of the blood vessel wall which was confined to the myocardium and lungs without involvement of other organs. More recently, another case report emphasized the severity of pulmonary hypertension in a patient with polymyositis.\(^{19}\) Postmortem examination of the pulmonary vasculature revealed fibrous intimal proliferation of the small pulmonary arteries. The pulmonary parenchyma revealed focal interstitial fibrosis.\(^{19}\)

The association of other collagen vascular diseases with pulmonary hypertension is more widely recognized. The incidence of pulmonary hypertension in patients with progressive systemic sclerosis is 33 percent and in those with the CREST variant, the incidence increases to approximately 50 percent.\(^{20}\) The pulmonary vascular changes involve the small- and medium-sized pulmonary arteries and arterioles. These changes may range from intimal proliferation with narrowing of the vessel to almost complete obliteration of the lumen.\(^{20}\) Pulmonary vascular lesions also occur in patients with progressive systemic sclerosis who have no evidence of pulmonary hypertension, suggesting that the vascular lesions are the cause rather than the result of pulmonary hypertension.\(^{21}\)

The clinical recognition of pulmonary hypertension in the absence of overt right heart failure may be difficult. Prior to the development of echocardiographic techniques right heart catheterization was the only method of establishing the diagnosis. However, echocardiography, particularly with the Doppler study, has been shown to be a sensitive, noninvasive technique for determining the presence of pulmonary hypertension.\(^{22,23}\) The results of the present study in which seven of 11 patients with polymyositis had echocardiographic evidence of pulmonary hypertension suggests that pulmonary vascular involvement is common in this disorder. Ventilation and perfusion scans were obtained in the first three patients with pulmonary hypertension to exclude possible pulmonary embolism. All three patients had normal or low probability scans so that further scanning was not thought to be clinically indicated.

In contrast to the subtle manifestations of pulmonary hypertension, parenchymal lung involvement in polymyositis usually is readily apparent. The majority of such patients complain of dyspnea. While restrictive dysfunction due to respiratory muscle weakness can develop in the absence of a normal chest radiograph, most patients with parenchymal involvement have radiographic evidence of diffuse interstitial disease.\(^{24,25}\) Histologic examination of biopsy or autopsy specimens, or both, reveals nonspecific interstitial pulmonary fibrosis.\(^{22,23}\)

The \( V_{D} \)/\( V_{T} \) ratio may be increased at end-exercise due to either parenchymal or pulmonary vascular disease.\(^{24}\) Although Jones and Goodwin\(^{25}\) have reported abnormal increases in the \( V_{D} \)/\( V_{T} \) ratio during exercise in patients with pulmonary vascular disease, D’Alonzo et al\(^{26}\) found that the typical response observed in nine of 11 patients with pulmonary hypertension was a fall in the \( V_{D} \)/\( V_{T} \) ratio during exercise. We failed to observe a consistent response in the patients with pulmonary hypertension in the present study and their \( V_{D} \)/\( V_{T} \) ratio at end-exercise was not significantly different from that of the patients without pulmonary hypertension.

The majority, nine of 11 patients, stopped exercising because of peripheral muscle fatigue. Two stopped at a low work load with a subnormal heart rate response, suggesting that peripheral muscle weakness limited their exercise tolerance. However, five patients had a heart rate response exceeding 80 percent of their predicted target heart rate and a low \( O_2 \) pulse, suggesting a cardiac limitation to exercise. In contrast, none of the patients had evidence of a ventilatory limit to their exercise capacity.

In summary, we found that symptomatic impairments in pulmonary function are uncommon in patients with polymyositis. Unsuspected pulmonary hypertension is extremely common in polymyositis patients and the reduced \( O_2 \) pulse during exercise suggests that cardiac performance also may be impaired in these patients. The clinical significance of
these findings cannot be determined from this study. In the majority of patients, peripheral muscle fatigue appears to be a major factor contributing to the impairment in exercise performance.

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