C-Reactive Protein and Body Mass Index Predict Outcome in End-Stage Respiratory Failure*

Noël J. M. Cano, MD, PhD; Claude Pichard, MD, PhD; Hubert Roth, Eng; Isabelle Court-Fortuné, MD; Luc Cynober, PharmD, PhD; Michèle Gérard-Boncompain, MD; Antoine Cuvelier, MD, PhD; Jean-Pierre Laaban, MD, FCCP; Jean-Claude Melchior, MD; Jean-Claude Raphaël, MD; Christophe M. Pison, MD, PhD; and the Clinical Research Group of the Société Francophone de Nutrition Entérale et Parentérale

Study objective: To determine the predictive factors of morbidity and mortality in patients with end-stage respiratory disease.

Design: Prospective, multicenter cohort study.

Setting: Thirteen outpatient chest clinics within the Association Nationale de Traitement à Domicile de l’Insuffisance Respiratoire.

Participants: Stable adult patients with chronic respiratory failure receiving long-term oxygen therapy and/or home mechanical ventilation (n = 446; 182 women and 264 men; aged 68.5 ± 12.1 years [± SD]); Respiratory diseases were COPD in 42.8%, restrictive disorders in 36.3%, mixed respiratory failure in 13.5%, and bronchiectasis in 7.4%. Recruitment was performed during the yearly examination. Patients with neuromuscular diseases and sleeping apnea were excluded.

Measurements and results: Hospitalization days and survival were recorded during a follow-up of 14.3 ± 5.6 months. Body mass index (BMI), serum albumin, and transthyretin levels were considered for their predictive value of outcome, together with demographic data, underlying respiratory disease, respiratory function, hemoglobin, C-reactive protein, smoking habits, oral corticosteroid use, and antibiotic treatment courses. Overall, 1.8 ± 1.7 hospitalizations (cumulative stay, 17.6 ± 27.1 days) were observed in 254 of 446 patients (57%). Independent predictors of hospitalization were oral corticosteroids, FEV1, and plasma C-reactive protein. One-year and 2-year cumulative survivals were 93% and 69%, respectively. Plasma C-reactive protein, BMI, PaO2 on room air, and oral corticosteroids independently predicted survival in multivariate analysis.

Conclusion: Besides established prognosis factors such as FEV1 and PaO2, nutritional depletion as assessed by BMI and overall systemic inflammation as estimated by C-reactive protein appear as major determinants of hospitalization and death risks whatever the end-stage respiratory disease. BMI and C-reactive protein should be included in the monitoring of chronic respiratory failure. Oral corticosteroids as maintenance treatment in patients with end-stage respiratory disease are an independent risk factor of death, and should be avoided in most cases.

(CHEST 2004; 126:540–546)

Key words: body mass index; C-reactive protein; long-term oxygen therapy; noninvasive ventilation; survival

Abbreviations: BMI = body mass index; HMV = home mechanical ventilation; LTOT = long-term oxygen therapy; NS = not significant

Chronic respiratory diseases are set to become the third leading cause of death in the world.1 In patients with end-stage respiratory disease receiving long-term oxygen therapy (LTOT) and/or home mechanical ventilation (HMV), the median survival is approximately 3 years.2 In face of this growing public health problem, it is of primary importance to identify the determinants of survival.2,3 Chronic respiratory failure due to COPD is more and more regarded as a wasting disease.3–6 In patients with COPD, whatever the stage and the type of recruitment, the impact of malnutrition on survival is established.4,7–9 In patients receiving LTOT and/or HMV, regardless of the underlying disease, a French cooperative study2 showed that body mass index (BMI) predicted survival. We previously reported the high prevalence of malnutrition in neuromuscular and nonneuromuscular outpatients receiving LTOT and/or HMV.10
The present study focuses on the nonneuromuscular patients and aims to determine the predictive factors of the outcome by the longitudinal follow-up of a 446-patient cohort.

**MATERIALS AND METHODS**

**Participants**

Thirteen outpatient clinics within the Association Nationale de Traitement à Domicile de l’Insuffisance Respiratoire network participated in a prospective survey of hospitalization and death risks in patients receiving home LTOT and/or HMV. Recruitment was performed during the yearly examination as required for reimbursement of home treatment fees. Thus, 446 patients (182 women and 264 men; mean age, 68.5 ± 12.1 years [± SD]) were included in a cohort study. The minimum planned follow-up was 1 year. Inclusion criteria were age > 18 years, LTOT and/or HMV for > 3 months, PaO₂ on room air ≤ 8 kPa at initiation of home treatment, and informed consent to examination of nutritional status. Exclusion criteria were neuromuscular diseases, sleep apnea syndrome treated with continuous positive airway pressure, history of exacerbation during the last 3 months, and any condition likely to affect the prognosis within 6 months. Patients with neuromuscular disease (n = 96) were excluded since they present with an intrinsic skeletal muscle disease. Recent exacerbation, < 3 months, was an exclusion criterion because stable condition was needed to study the potential role of systemic and chronic inflammation. Four respiratory disease groups were considered: COPD corresponding to patients with non-failly irreversible bronchial obstruction, bronchiectasis defined on chest CT pattern, restrictive disorders including pulmonary fibrosis and chest wall diseases, and mixed respiratory failure combining restrictive and obstructive defects. This observational study was approved by the French Commission Nationale Informatique et Liberté, and patients gave their informed consent for their participation.

*From the Département de Nutrition (Dr. Cano), Clinique Résidence du Parc, Marseille, France; Service de Nutrition Clinique (Dr. Pichard), Hôpitaux Universitaire de Genève, Genève, Switzerland; Département de Médecine Aiguë Spécialisée (Mr. Roth and Dr. Pison), CHU, Grenoble, France; Service de Pneumologie (Dr. Court-Fortune), CHU, Saint-Etienne, France; Service de Biochimie A (Dr. Cynober), AP-HP, Hôpitaux Universitaires de Paris, France; Service de Pneumologie (Dr. Cuvelier), CHU, Rouen, France; Service de Pneumologie (Dr. Cuvellier), CHU, Rouen, France; Service de Pneumologie et de Réanimation Respiratoire (Dr. Laaban), AP-HP, Hôtel-Dieu, Paris, France; Service des Maladies Infectieuses (Dr. Melchior), AP-HP, Hôpital Raymond Poincaré, Garches, France; and Service de Réanimation Médicale (Dr. Raphael), AP-HP, Hôpital Raymond Poincaré, Garches, France. Funding was provided by Société Francophone de Nutrition Entérale et Parentérale, Astra-Zeneca France. Manuscript received July 31, 2003; revision accepted February 12, 2004. Reproduction of this article is prohibited without written permission from the American College of Chest Physicians (e-mail: permissions@chestnet.org). Correspondence to: Noël J. M. Cano, MD, PhD, Département de Nutrition, Clinique Résidence du Parc, Rue Gaston Berger, 13010 Marseille, France; e-mail: njm.cano@wanadoo.fr.

**Methods**

Body weight and height were recorded at the time of enrollment. Serum albumin, transthyretin (prealbumin), and C-reactive protein levels were determined using conventional methods. Participating laboratories agreed to a blinded quality control. Malnutrition was defined as BMI ≤ 20, or serum albumin < 35 g/L, or serum transthyretin < 200 mg/L. Blood gases were measured on room air, except in 10 of 191 patients with COPD, 4 of 33 patients with bronchiectasis, 10 of 162 patients with restrictive disorders, and 4 of 60 patients with mixed respiratory failures due to the patient’s dependence on LTOT and/or mechanical ventilation. Blood gases were also measured with LTOT and/or HMV. Respiratory function was assessed by FEV₁, FVC, and 6-min walking distance test on room air. Smoking habits were classified into three categories: nonsmokers, active smokers, and ex-smokers (withdrawal from tobacco > 3 months). Corticosteroid users were defined as patients who received oral corticosteroids for > 3 months during the previous year. The number of antibiotic treatment courses was recorded over the same period.

Mean follow-up was 429 ± 169 days, and maximum follow-up was 1,144 days. Two outcome parameters were prospectively recorded: mortality and the number of days of hospitalization. BMI, serum albumin, and transthyretin levels were considered for their predictive value of outcome, together with demographic data, underlying respiratory disease, respiratory function, hemoglobin, C-reactive protein, smoking habits, oral corticosteroid use, and antibiotic treatment courses.

**Statistical Analysis**

Data distribution of continuous variables was tested using skewness and kurtosis tests. Normally distributed data are reported as mean ± SD and nonnormally distributed as median. Analysis of variance was used to compare normally distributed variables between the respiratory disease groups, with post hoc analysis using Fisher predicted least significant difference test when allowed. When data were not normally distributed, the Kruskal-Wallis test was used with post hoc analysis using Mann and Whitney test with Bonferroni correction. Contingency tables were used for categorical variables. Univariate and multivariate regression analyses were used to study the determinants of hospitalization duration. For survival analysis, parameters having a significant impact on survival after univariate Cox model analysis were tested in a multivariate Cox proportional model analysis. Kaplan-Meier graphs and log-rank tests were performed in order to study the influence of potential predictors on survival. Statview 5 software (SAS Institute; Cary, NC) was used for statistical analysis.

**Results**

Demographic data, causes of respiratory failure, blood gases, and lung function test results are given in Tables 1, 2. COPD represented 42.8% of patients, restrictive disorders represented 36.3%, mixed respiratory failure represented 13.5%, and bronchiectasis represented 7.4%. COPD was the most common respiratory disease in male patients (58.4%), and restrictive disorders were the most common respiratory disease in female patients (54.4%). The median PaO₂ in room air of 57 mm Hg shows the severity of
respiratory failure. Restrictive disorders showed the highest values of PaO2 in room air, and COPD shows the highest FVC and the lowest FEV1/FVC ratio. Restrictive disorders (mainly chest wall diseases and kyphoscoliosis) showed the highest PaO2, the lowest FVC, and the highest FEV1/FVC ratio. Mean duration of LTOT and/or HMV was 69.3 ± 56.2 months (median, 51.0 months). The 6-min walking test distance was 233 ± 113 m and did not differ significantly with the underlying disease.

Restrictive disorders were characterized by a longer home treatment (56.0 ± 62.8 months). Home treatment was LTOT in 179 patients, noninvasive HMV in 247 patients, and invasive HMV with tracheostomy in 20 patients. The percentage of patients requiring mechanical ventilation varied according to the cause of respiratory disease: 35% in COPD, 77% in bronchiectasis, 88% in restrictive disorders, and 62% in mixed respiratory failure (χ² = 108.6, p < 0.0001). Hypoxemia was well corrected by LTOT and/or HMV (Table 1), whereas hypercapnea was only corrected in patients receiving HMV (data not shown). Smoking habits varied according to sex: nonsmokers represented, respectively, 47.1% of all patients, 82.4% of women, and 22.7% of men; active smokers represented 5.6%, 3.3%, and 7.2%; and ex-smokers represented 47.3%, 14.3%, and 70.1% (χ² = 155, p < 0.0001). Smoking habits also varied with the cause of respiratory failure: smoking history was found in 79.6% of COPD cases, 36.4% of bronchiectasis cases, 24.7% of restrictive disorders cases, and 53.3% of mixed respiratory failure cases (χ² = 111.7, p < 0.0001). Oral corticosteroid use > 3 months in the previous year was recorded in 11.7% of patients, 13.6% in patients with COPD, 9.1% in patients with bronchiectasis, 10.5% in patients with restrictive disorders, and 10.0% in patients with mixed respiratory failure (χ² = 1.29, not significant [NS]). Fifty-nine percent of patients received at least one antibiotic treatment course (median of two courses among these patients). The number of antibiotic courses varied according to underlying disease: 1.70 ± 0.15 in patients with COPD, 2.82 ± 0.45 in patients with bronchiectasis, 0.85 ± 0.12 in patients with restrictive disorders, and 1.32 ± 0.17 in patients with mixed respiratory failure (analysis of variance, p < 0.0001). Figure 1 shows the prevalence of malnutrition as defined by BMI < 20, serum albumin < 35 g/L, or serum transthyretin < 200 mg/L, according to the underlying re-

Table 1—Demographic Data and Blood Tests According to Disease Groups

<table>
<thead>
<tr>
<th>Variables</th>
<th>Age (Mean ± SD)</th>
<th>Male:Female Ratio</th>
<th>PaO2 (kPa on Room Air)</th>
<th>PaO2 (kPa LTOT/HMV)</th>
<th>PaCO2 (kPa on Room Air)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients (n = 446)</td>
<td>71.0 (68.5 ± 12.1)</td>
<td>1.45</td>
<td>7.58 (7.90 ± 1.64)</td>
<td>11.01 (11.88 ± 6.09)</td>
<td>6.12 (6.30 ± 2.30)</td>
</tr>
<tr>
<td>COPD (n = 191)</td>
<td>72.01 (70.5 ± 9.2)</td>
<td>4.16</td>
<td>7.24 (7.33 ± 1.19)</td>
<td>10.24 (11.15 ± 6.85)</td>
<td>6.18 (6.46 ± 3.33)</td>
</tr>
<tr>
<td>Bronchiectasis (n = 33)</td>
<td>67.01 (63.9 ± 13.3)</td>
<td>0.65</td>
<td>7.26 (7.29 ± 0.95)</td>
<td>10.79 (10.81 ± 1.98)</td>
<td>6.37 (6.53 ± 1.67)</td>
</tr>
<tr>
<td>Restrictive disorders (n = 162)</td>
<td>71.0 (66.8 ± 14.6)</td>
<td>0.64</td>
<td>8.71 (8.75 ± 1.91)</td>
<td>12.10 (13.10 ± 6.46)</td>
<td>6.04 (6.09 ± 0.55)</td>
</tr>
<tr>
<td>Mixed respiratory failure (n = 60)</td>
<td>71.0 (69.4 ± 11.4)</td>
<td>1.31</td>
<td>7.55 (7.73 ± 1.47)</td>
<td>11.16 (11.67 ± 2.98)</td>
<td>6.25 (6.24 ± 0.96)</td>
</tr>
</tbody>
</table>

p Value: 0.0027 < 0.0001 < 0.0001 < 0.0001

*Data are presented as median (mean ± SD), except for PaO2/FVC, for which values were normally distributed, Kruskal-Wallis and Mann and Whitney post hoc tests for FVC and FEV1/FVC, analysis of variance and post hoc test of Fisher for FEV1/FVC.
| With COPD. |
| With bronchiectasis. |
| With restrictive disorders. |
| With mixed respiratory failure. |

Table 2—Lung Function According to Disease Groups

<table>
<thead>
<tr>
<th>Variables</th>
<th>FVC, % Predicted</th>
<th>FEV1, % Predicted</th>
<th>FEV1/FVC, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients (n = 446)</td>
<td>54.7 (56.3 ± 17.8)</td>
<td>36.9 (39.9 ± 16.8)</td>
<td>0.57 ± 0.18</td>
</tr>
<tr>
<td>COPD (n = 191)</td>
<td>63.61 (64.1 ± 15.5)</td>
<td>35.1 (38.6 ± 16.0)</td>
<td>0.47 ± 0.15</td>
</tr>
<tr>
<td>Bronchiectasis (n = 33)</td>
<td>53.21 (53.8 ± 20.2)</td>
<td>30.71 (31.6 ± 11.3)</td>
<td>0.49 ± 0.12</td>
</tr>
<tr>
<td>Restrictive disorders (n = 162)</td>
<td>45.61 (49.1 ± 16.5)</td>
<td>39.11 (43.8 ± 18.2)</td>
<td>0.71 ± 0.14</td>
</tr>
<tr>
<td>Mixed respiratory failure (n = 60)</td>
<td>47.61 (50.1 ± 16.5)</td>
<td>35.9 (39.0 ± 16.6)</td>
<td>0.60 ± 0.15</td>
</tr>
</tbody>
</table>

p Value: < 0.0001 0.0016 < 0.0001

*Data are presented as median (mean ± SD), except for FEV1/FVC, for which values were normally distributed, Kruskal-Wallis and Mann and Whitney post hoc tests for FVC and FEV1, analysis of variance and post hoc test of Fisher for FEV1/FVC.
spiratory disease. BMI was < 20 in 18.7%, serum albumin was < 35 g/L in 19.6%, and transthyretin was < 200 mg/L in 22.4%. C-reactive protein was > 10 mg/L in 27.3% of all patients. Patients with bronchiectasis had the highest prevalence of elevated C-reactive protein (54.5%), while patients with restrictive disorders had the lowest (17.4%).

Overall, 1.8 ± 1.7 hospitalizations accounting for a mean cumulative stay of 17.6 ± 27.1 days were recorded in 254 of 446 patients (57%). Hospitalization rates were not influenced by the cause of respiratory failure (NS). In univariate regression analysis, factors associated with the risk of hospitalization were oral corticosteroid use (p < 0.0001), FEV₁, C-reactive protein (p < 0.01), PaO₂ on room air, and 6-min walking test distance (p < 0.05). Age, sex, and etiology of chronic respiratory failure were not associated with the risk of hospitalization. Only oral corticosteroid use (χ² = 10.1, p = 0.0002), FEV₁ (χ² = 7.4, p = 0.005), and C-reactive protein (χ² = 4.6, p < 0.03) appeared as independent predictors of hospitalization in the multivariate analysis.

One-year and 2-year cumulative survivals were 93% and 69%, respectively. Determinants of survival according to Cox univariate and multivariate model analysis are given in Table 3. Survival was not influenced by age, sex, etiologies of respiratory failure, PaO₂ with LTOT and/or HMV, and the type of home respiratory assistance. Four parameters were independently associated with survival in the multivariate analysis: C-reactive protein, BMI, PaO₂ on room air, and oral corticosteroids (Table 3). The

Table 3—Determinants of Survival According to Cox Univariate and Multivariate Model

<table>
<thead>
<tr>
<th>Variables</th>
<th>p Value</th>
<th>χ²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Univariate analysis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral corticosteroids*</td>
<td>&lt; 0.0001</td>
<td></td>
</tr>
<tr>
<td>C-reactive protein</td>
<td>&lt; 0.001</td>
<td></td>
</tr>
<tr>
<td>PaO₂ room air</td>
<td>&lt; 0.001</td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td>&lt; 0.01</td>
<td></td>
</tr>
<tr>
<td>Serum albumin</td>
<td>&lt; 0.05</td>
<td></td>
</tr>
<tr>
<td>FVC, % predicted</td>
<td>&lt; 0.05</td>
<td></td>
</tr>
<tr>
<td>Active smoking</td>
<td>&lt; 0.05</td>
<td></td>
</tr>
<tr>
<td>6-min walking test</td>
<td>&lt; 0.05</td>
<td></td>
</tr>
<tr>
<td>Serum transthyretin</td>
<td>0.05</td>
<td></td>
</tr>
<tr>
<td>Multivariate analysis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C-reactive protein</td>
<td>0.009</td>
<td>6.81</td>
</tr>
<tr>
<td>BMI</td>
<td>0.010</td>
<td>6.63</td>
</tr>
<tr>
<td>PaO₂ room air</td>
<td>0.016</td>
<td>5.79</td>
</tr>
<tr>
<td>Oral corticosteroids*</td>
<td>0.018</td>
<td>5.60</td>
</tr>
</tbody>
</table>

*Corticosteroid users were defined as patients receiving oral corticosteroids for > 3 months during the previous year.
influence of each of these predictors of survival is depicted in Figure 2, showing Kaplan-Meier graphs and log-rank tests.

**DISCUSSION**

Chronic respiratory failure remains of poor prognosis in spite of LTOT and HMV. The aim of this work was to prospectively determine factors of hospitalization rates and survival in patients with home-treated respiratory failure. Outpatients included in this cohort study were characterized by severe and stable respiratory failure secondary to various etiologies. The main result was that survival was independently correlated with systemic inflammation, malnutrition, hypoxemia, and oral corticosteroid use. It is noticeable that, in these patients with end-stage respiratory diseases, the cause of respiratory failure did not influence the outcome.

One limitation of this study could be the heterogeneity of the underlying respiratory diseases. However, in the present series, patients with COPD, restrictive diseases, mixed respiratory failure, and bronchiectasis were not different according to PaO$_2$, 6-min walking test, exposure to oral corticosteroid, BMI, and serum albumin levels. Despite differences according to age, gender, pulmonary function test results, need for mechanical ventilation, smoking habits, number of antibiotic courses, and inflammation, a similar outcome was observed whatever the underlying respiratory disease, suggesting a final common pathway at this stage of severe respiratory insufficiency.

One of the main concerns in chronic respiratory failure patients is to identify determinants of hospitalization. As a matter of fact, hospitalization is associated with a high mortality rate during the following year, and is responsible for the main source of costs in patients with COPD. Hospitalizations were found to be independently determined by oral corticosteroid use, low FEV$_1$, and elevated C-reactive protein. The role of systemic corticosteroid use in peripheral muscle weakness, a recognized factor of health-care utilization, already established in COPD, was extended to other end-stage respiratory disease in the present study. The impact of low FEV$_1$ on the occurrence of exacerbations is admitted in the setting of COPD. Data from the present series demonstrate the predictive value of low FEV$_1$ on the hospitalization risk whatever the cause of chronic respiratory failure.

The influence of hypoxemia on survival and the interest of oxygen therapy have clearly been demonstrated during COPD in the early 1980s in randomized...
controlled studies, and more recently as a risk factor for hospitalization for acute exacerbation during COPD. Similarly, the prognostic effect of low BMI has already been documented in patients with home-assisted respiratory failure and particularly during COPD. A major potentially modifiable risk is the use of prolonged oral corticosteroids. In a retrospective study, oral corticosteroid therapy has been shown to be responsible for a dose-related increase in mortality risk in ambulatory patients with COPD admitted to a rehabilitation center. Similar adverse effects of oral corticosteroids have been observed in prospective studies, in women with COPD receiving LTOT, and after hospitalization for acute exacerbation of COPD. Our data showed that the pejorative effect of systemic corticosteroids also concerns home-treated end-stage respiratory diseases. This observation is important to consider since positive effects of prolonged oral corticosteroids are not established in COPD, bronchiectasis, chest wall disease, advanced diffuse infiltrative diseases, or mixed respiratory failure. Myopathy is one of the most severe complications of prolonged treatment with oral corticosteroids. In patients with COPD, corticosteroids adversely affect both respiratory and peripheral muscle function. As the decrease in the muscle amino acid reservoir is associated with alterations of several key physiologic functions such as tissue regeneration and immune defense, muscle wasting due to oral corticosteroids may explain their detrimental consequences on patient outcome.

The main finding of this study was that systemic inflammation, as evaluated by serum C-reactive protein, was related to the risk of hospitalization and appeared to be the best prognostic indicator of survival. Although the relationship between C-reactive protein and survival is well recognized in cardiovascular diseases, it had not been previously demonstrated in chronic respiratory failure. These data support the concept that a subgroup of patients with chronic respiratory failure suffers from a systemic inflammation, which in turn may account for an increased morbidity and mortality.

Routine monitoring and management of patients with chronic respiratory failure rely mostly on $P_{aO_2}$ in room air and FEV$_1$. C-reactive protein and BMI now appear of clinical relevance to assess the risk of hospitalization and death and should be included in the follow-up of patients receiving LTOT or HMV. This work stresses that, in patients with end-stage respiratory disease, maintenance treatment with oral corticosteroids is an independent risk factor of death and should be avoided in most cases.

ACKNOWLEDGMENT: The physicians responsible for patient recruitment were Fison C, Pépin JL, Département de Médecine Aiguë Spécialisée, CHU, Grenoble; Cuvelier A, Tengang B, Muir JF, Service de Pneumologie, CHU, Rouen; Jang G, Service de Médecine, CH, Briançon; Chailleux E, Ordonneau JR, Service de Pneumologie, CHU, Nantes; Beumel E, Centre Médiacal de Gravenard, Genilac; Beuret F, Canamela A, Service de Réanimation, CH, Roanne; Perrin Ch, Service de Pneumologie, CHU, Nice; Lahrousse J, Diehl JL, Service de Réanimation Médicale, AP-HP, Boucicaut, Paris; Caillaud D, NGuen LT, Service de Pneumologie, CHU, Clermont-Ferrand; Mallart A, Perez Th, Service de Pneumologie, CHU, Lille; Tschopp JM, Service de Pneumologie, MT, Suisse. Dan Veale corrected the English-language text.

REFERENCES
onomic evaluation of acute exacerbations of chronic bronchitis and COPD. Chest 2002; 121:1449–1455
26 Decramer M, Stas KJ. Corticosteroid-induced myopathy involving respiratory muscles in patients with chronic obstructive pulmonary disease or asthma. Am Rev Respir Dis 1992; 146:800–802
28 Gosselink R, Troosters T, Decramer M. Peripheral muscle weakness contributes to exercise limitation in COPD. Am J Respir Crit Care Med 1996; 153:976–980