Prognostic Value of the Hematocrit in Patients With Severe COPD Receiving Long-term Oxygen Therapy*

Arnaud Chambellan, MD; Edmond Chailleux, MD; Thomas Similowski, MD, PhD; and the ANTADIR Observatory Group†

Background: Although traditionally associated with polycythemia, COPD has a systemic inflammatory component that could interfere with erythropoiesis. This study describes the distribution and prognostic value of the hematocrit in patients with severe COPD receiving long-term oxygen therapy (LTOT).

Methods: A total of 2,524 patients with COPD, FEV1/vital capacity (VC) < 70%, FEV1 < 80% of predicted, and PaO2 < 7.3 kPa in whom a hematocrit was available at entry was identified between 1980 and 1999 in the French Association Nationale pour le Traitement à Domicile de l'Insuffisance Respiratoire chronic respiratory insufficiency and home-care database (male/female ratio, 5/1; mean ± SD age, 68 ± 10 years for men, and 70 ± 10 years for women). Correlations between hematocrit, demographic data, and pulmonary function data were examined. A multivariate Cox proportional hazard regression was performed to identify prognostic factors.

Results: Mean hematocrit was 45.9 ± 7.0% in men and 43.9 ± 6.0% in women (< 39% in 12.6% of men, and < 36% in 8.2% of women) according to the World Health Organization definition of anemia. Hematocrit was negatively correlated with age (r = −0.245) and FEV1/VC (r = −0.068) and was positively correlated with PaCO2 (r = 0.161) and body mass index (r = 0.127). Multivariate analysis found hematocrit to be an independent predictor of survival, hospital admission rate, and cumulative duration of hospitalization. The 3-year survival was 24% (95% confidence interval, 16 to 33%) when the hematocrit was < 35%, and 70% (63 to 76%) when the hematocrit was ≥ 55%.

Conclusions: A low hematocrit is not uncommon in LTOT/COPD patients. Hematocrit is negatively associated with mortality and morbidity. Whether the association is causative or not and whether or not corrective measures are warranted remain to be determined.

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Key words: anemia; COPD; erythropoietin; hematocrit; long-term oxygen therapy; survival

Abbreviations: ANTADIR = Association Nationale pour le Traitement à Domicile de l’Insuffisance Respiratoire; BMI = body mass index; BODE = body mass index, airflow obstruction, dyspnea, and exercise capacity; CI = confidence interval; IL = interleukin; LTOT = long-term oxygen therapy; TNF = tumor necrosis factor; VC = vital capacity

COPD is, according to a widely disseminated definition,1 “a disease state characterized by airflow limitation that is not fully reversible,” where “the airflow limitation is usually both progressive and associated with an abnormal inflammatory response of the lungs to noxious particles or gases” (the main source of which is tobacco smoke). Besides spirometric abnormalities, bronchopulmonary lesions lead to ventilation-perfusion imbalance and the ensuing gas exchange abnormalities. FEV1 and hypoxemia are strong prognostic markers,2,3 and long-term oxygen therapy (LTOT) has been shown to improve survival.4,5 The deleterious effects of hypoxemia proceed from the effects of tissue hypoxia on cell metabolism.

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and organ function. Among these effects, the stimulation of erythropoietin production can lead to a compensatory erythrocytosis that is traditionally viewed as a typical of COPD.

COPD also has a systemic inflammatory dimension. Patients with COPD often exhibit raised levels of proinflammatory cytokines, e.g., interleukin (IL)-1, IL-6, tumor necrosis factor (TNF)-α, chemokines (IL-8, monocyte chemotactic protein-A), and C-reactive protein. The expression of neutrophil adhesion molecules is increased, and there are changes in neutrophil functions, and many other perturbations. In some COPD patients, this could contribute to an increased energy expenditure, promoting muscle wasting, nutritional imbalance, and weight loss. Weight loss in patients with COPD has been correlated with serum TNF-α levels and has a negative prognostic value. COPD-related inflammation could also impair erythropoiesis, as do other chronic inflammatory processes. Hemoglobin levels in COPD patients would then reflect the balance between the stimulation of erythropoiesis by hypoxia and its depression by inflammation.

Inadequate hemoglobin levels could aggravate tissue hypoxia and carry a negative prognostic impact. Hints as to the plausibility of this scenario exist in the literature. Blood cell transfusion in anemic COPD patients reduces minute ventilation and the work of breathing, suggesting that correcting low hemoglobin levels could alleviate dyspnea and improve exercise capacity. In a small set of anemic ventilator-dependent COPD patients, raising hemoglobin levels to > 12 g/dL seemed to improve patients enough to make ventilator weaning possible. A reduced hematocrit was found to be an independent predictor of poor outcomes in COPD patients following elective open abdominal aortic aneurysm resection. In the COPD population from which Celli et al derived the prognostic value of a multidimensional index combining four variables (body mass index [BMI], airflow obstruction, dyspnea, and exercise capacity [BODE index], the patients who died had a significantly lower hematocrit (mean ± SD, 39 ± 5%) than those who survived (42 ± 5%).

The present study was conducted to look for a putative association between hematocrit and prognosis in severe COPD patients receiving LTOT. The data were extracted, over a period of 20 years, from a large national database in France maintained by the Association Nationale pour le Traitement à Domicile de l’Insuffisance Respiratoire (ANTADIR). This database has already been used, for example, to describe the main prognostic factors in various types of chronic respiratory insufficiency, or to relate BMI to outcome in this population.

### Materials and Methods

#### Organization of the ANTADIR Observatory

The ANTADIR is a French national nonprofit associative network of 23 regional associations founded in 1981 to ensure health-care support and technical follow-up to disabled patients requiring domiciliary oxygen support, mechanical ventilation, or continuous positive airway pressure. Since its foundation, ANTADIR has maintained a comprehensive demographic database or “observatory,” providing a unique national register allowing epidemiologic surveys in large cohorts of patients with various types of chronic respiratory diseases. Individual patient records derive from the single document filled in by prescribing physicians for the reimbursement of costs by the French social security system. Available information includes demographic data (age, sex, height, and weight) and clinical data (diagnosis, room air arterial blood gases and hematocrit, pulmonary function tests, and smoking status). Prescriptions, hospitalizations, treatment withdrawals, and deaths are registered by the regional associations using common software and compiled together by ANTADIR, which manages the national database and produces an annual report.

#### Patients

Among the patients registered in the database, 11,366 had a clinical diagnosis of COPD with a FEV1/VC ratio < 70% and a FEV1 < 80% of predicted. Room air PaO2 was < 7.3 kPa in 6,111 cases. The initial hematocrit was available in 2,524 of these patients (2,097 men and 427 women), who constitute the study cohort (Table 1). In this population, women were older than men and were more likely to be nonsmokers than ex-smokers or current smokers. Although they had been prescribed oxygen, 10.2% of the patients were reported as current smokers (men, 9.9%; women, 11.3%).

#### Hematocrit

Hematocrit values considered for analysis were those recorded with the arterial blood gases retained to prescribe LTOT. Six hematocrit categories (21 to 34%, 35 to 39%, 40 to 44%, 45 to 49%, 50 to 54% and ≥ 55%) were defined for the purpose of statistical calculations.

#### Table 1—Demographic and Functional Characteristics of the Patients by Sex

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Men (n = 2,097)</th>
<th>Women (n = 427)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>68 (10)</td>
<td>70 (10)</td>
</tr>
<tr>
<td>Smoking status, No. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoker</td>
<td>163 (9.9)</td>
<td>40 (11.3)</td>
</tr>
<tr>
<td>Ex-smoker</td>
<td>1,438 (87.7)</td>
<td>717 (57.7)</td>
</tr>
<tr>
<td>Nonsmoker</td>
<td>38 (2.3)</td>
<td>80 (11.0)</td>
</tr>
<tr>
<td>FEV1, L</td>
<td>0.92 (0.37)</td>
<td>0.66 (0.23)</td>
</tr>
<tr>
<td>FEV1, % predicted</td>
<td>34 (13)</td>
<td>37 (13)</td>
</tr>
<tr>
<td>VC, L</td>
<td>2.26 (0.71)</td>
<td>1.49 (0.51)</td>
</tr>
<tr>
<td>VC, % predicted</td>
<td>61 (19)</td>
<td>63 (19)</td>
</tr>
<tr>
<td>FEV1/VC, %</td>
<td>41 (12)</td>
<td>47 (12)</td>
</tr>
<tr>
<td>PaO2, kPa</td>
<td>6.5 (0.7)</td>
<td>6.4 (0.7)</td>
</tr>
<tr>
<td>Pao2, kPa</td>
<td>6.4 (1.2)</td>
<td>6.7 (1.1)</td>
</tr>
<tr>
<td>BMI, kg/m2</td>
<td>24 (5)</td>
<td>25 (7)</td>
</tr>
<tr>
<td>Hematocrit, %</td>
<td>45.9 (6.8)</td>
<td>43.9 (6.3)</td>
</tr>
</tbody>
</table>

*Data are expressed as mean (SD) unless otherwise indicated. †Available for 2,450 patients.
Anthropometric Data and Pulmonary Function Tests

The BMI was calculated as the ratio of weight to height squared from the data available in the initial patients records. Spirometric values obtained in body temperature and pressure, saturated, conditions were expressed as percentages of predicted values.16

Outcomes

The annual death rate, annual hospital admission rate, and annual number of days spent in the hospital were computed from the follow-up records.

Statistical Analysis

In the 2,524 studied patients, the associations between hematocrit and age, BMI, and pulmonary function tests were studied by linear correlation and represented graphically for each hematocrit category. The population survival was calculated from the onset of LTOT by the actuarial and Kaplan-Meier methods with a closing date of January 1, 2001. The study of prognostic factors was performed using the log-rank test and Cox semiparametric models as previously described.14,15 The influence of hematocrit, age, sex, BMI, arterial blood gases, and pulmonary function tests on the annual rate of hospital admissions and on the number of days spent in the hospital were studied by univariate regression followed by a multivariate stepwise regression. These patients were also compared to the 3,587 patients with a FEV1/VC ratio of a hematocrit value in men than in women (5.9%). Hematocrit was significantly higher in women, 5.9%). Hematocrit was significantly higher in men and women (5.6, p < 0.001), and was negatively correlated with age (r = 0.245, p < 0.001) and positively correlated with PaO2 (r = 0.161, p < 0.001) and BMI (r = 0.127, p < 0.001), but there was no significant correlation between hematocrit and PaO2 (r = 0.033, p = 0.095). A weak negative correlation existed between hematocrit and FEV1/VC (r = 0.054, p < 0.001), and between hematocrit and FEV1 percentage of predicted (r = 0.006) [Fig 1]. Current smokers had significantly higher hematocrit values than ex-smokers or non-smokers (Table 2).

Survival

At the time of analysis, 1,842 patients had died, 266 were alive, and 416 were unavailable for follow-up by the ANTADIR system (two thirds of those were known to have stopped oxygen for motives such as alleged poor tolerance or a personal wish; one third was known to have entered a long-term care facility). The mean duration of follow-up was 10 years. The overall median survival was 3.0 years. Survival was increased when the hematocrit was high and reached the longest duration in polycythememic patients (p < 0.001, log-rank test) [Fig 2]. The 3-year survival rate was 24% (95% confidence interval [CI], 16 to 33%) in patients with a hematocrit < 35%; 36% (95% CI, 31 to 42%) in patients with a hematocrit between 35% and 39%; 47% (95% CI, 43 to 51%) in patients with a hematocrit between 40% and 44%; 51% (95% CI, 47 to 55%) in patients with a hematocrit between 45% and 49%; 59% (95% CI, 54 to 64%) in patients with a hematocrit between 50% and 54%; and 70% (95% CI, 63 to 76%) in patients with a hematocrit ≥ 55%.

Multivariate analysis ranked age, hematocrit, BMI, PaO2, sex, and FEV1 percentage of predicted as prognostic factors, in descending order (Table 3). The prognostic influence of the hematocrit was significant in both men and women. The interactions between correlated variables (hematocrit and BMI, hematocrit and FEV1, hematocrit and PaO2) were not significant predictors of survival.

Admission Rate and Hospital Length of Stay

For the 1,799 patients with a follow-up of at least 1 year, the annual hospitalization rate was 1.17 ± 1.21 (median, 0.86) and the average number of days in the hospital was 25.1 ± 35.1 (median, 13.3). Univariate analysis showed that hematocrit was negatively correlated with the rate (r = -0.091, p = 0.001) and duration (r = -0.095, p < 0.001) of hospitalizations (Fig 3). This correlation, although weak, was the second strongest found in the data set after the correlation with between BMI and hospitalizations.

Patients with a hematocrit < 35% were hospitalized 1.41 ± 1.24 (mean ± SD) times per year, with 31.5 ± 42.8 days in the hospital per year. However, patients with a hematocrit ≥ 55% were hospitalized 0.96 ± 0.99 times a year on average, with a mean annual time spent in the hospital of 17.5 ± 23.4 days. Stepwise multivariate regression selected BMI (p < 0.001), hematocrit (p < 0.002), PaCO2 (p = 0.002), and age (p = 0.027) as predictive factors of the annual admission rate, whereas hematocrit (p < 0.001), BMI (p = 0.008), and age (p = 0.017) were predictive of the annual duration of hospitalization.

Comparison of the Patients With and Without a Known Hematocrit Value

These two groups of patients were not significantly different regarding the sex ratio, age, tobacco smoking...
status, PaO₂, VC, and FEV₁. The patients with a known hematocrit value had a marginally but significantly higher PaCO₂ (48.8 ± 8.8 mm Hg vs 48.2 ± 9.0 mm Hg) and lower BMI (23.2 ± 6.6 kg/m² vs 23.7 ± 6.6 kg/m²). The outcomes were slightly better in the group with an unknown hematocrit than in the group with a known hematocrit (median survival, 1,154 days vs 1,086 days [p = 0.016, log-rank]; admission rate, 1.07 ± 1.19 vs 1.18 ± 1.21 [p = 0.003]; length of stay, 21.3 ± 31.2 days vs 25.1 ± 35.1 days [p < 0.001]).

**Discussion**

This study shows that in a large population of COPD patients treated with LTOT, the prevalence of a low hematocrit at the time the prescription of oxygen is far from negligible (12.6% of the men and 18.5% of the women meeting the World Health Organization definition of anemia [hematocrit < 39%]²⁷). In this particular population, the study also points to a strong association between hematocrit and long-term survival in this population.

These findings seem to contrast with commonly held views. Although an apparent lack of polycythemic response to hypoxia has been noted in COPD patients in early studies, red cell mass has consistently been found increased and anemia never

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**Table 2—Hematocrit by Sex and Smoking Habits**

<table>
<thead>
<tr>
<th>Hematocrit, %†</th>
<th>Men</th>
<th>Women</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoker</td>
<td>49.0 (7.1)</td>
<td>45.9 (7.5)</td>
<td>48.4 (7.3)</td>
</tr>
<tr>
<td>Ex-smoker</td>
<td>45.5 (6.6)</td>
<td>44.2 (6.4)</td>
<td>45.3 (6.6)</td>
</tr>
<tr>
<td>Non-smoker</td>
<td>44.3 (5.7)</td>
<td>42.8 (5.9)</td>
<td>43.2 (5.9)</td>
</tr>
</tbody>
</table>

*Data are expressed as mean (SD).
†Hematocrit is higher in smokers vs ex-smokers and nonsmokers.
‡p < 0.001.
§p < 0.024.
reported with a prevalence such as the one we found. Polycythemia in COPD has been assigned no effect on survival\textsuperscript{22} or a negative effect.\textsuperscript{4,5}

**Cohort Characteristics, Prognostic Impact, and Shape of Risk**

The patients in our cohort were mostly elderly people of the male gender (83%). As expected, they had severe COPD (mean FEV\textsubscript{1} in men, 0.92 $\pm$ 0.37 L/s; in women, 0.68 $\pm$ 0.23 L/s; median survival, 3.0 years). Hematocrit was negatively correlated with age, a common finding in geriatric medicine.\textsuperscript{23} It was also correlated, less strongly, with BMI and PaO\textsubscript{2}. Age and the male gender were identified as negative prognostic factors by the Cox model. This model also indicated that increasing values of PaO\textsubscript{2}, BMI, and FEV\textsubscript{1} percentage of predicted were significantly associated with a better prognosis. These results fit with established facts in COPD.\textsuperscript{4,5,24,25} In addition, the Cox model showed that each 5% increase in hematocrit was associated with improved survival, and that hematocrit was the strongest prognostic factor next to age. Even though cross-correlation did exist between some of the model variables, none of their interactions had a significant effect.

The 10-year actuarial survival curve (Fig 2) shows a strong correlation between each 5% stratum of hematocrit and the mortality rate, particularly within the first years. The annual hospital admission rate and the cumulative hospital length of stay were highest in the patients with the lowest hematocrit levels and decreased in a roughly linear manner with hematocrit. This observation may be viewed as surprising, as a U-shaped risk could have been expected, but it may be due to the relatively small number of patients with high or very high hematocrit values. Further studies will be necessary to determine whether the hematocrit-associated risk is gradual or if it has a threshold.

Hypercappnia was positively correlated with hematocrit. If one equates hypercappnia with disease severity, the inverse correlation of hematocrit with survival is consistent with these observations.

Table 3—*Multivariate Study of Prognostic Factors by Cox Model*

<table>
<thead>
<tr>
<th>Factors</th>
<th>Relative Risk (95% CI)</th>
<th>t Test</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, by 10 yr</td>
<td>1.42 (1.35–1.51)</td>
<td>12.6</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Hematocrit, by 5%</td>
<td>0.86 (0.83–0.89)</td>
<td>−8.0</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>BMI, by 5 kg/m\textsuperscript{2}</td>
<td>0.87 (0.84–0.91)</td>
<td>−7.4</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>PaO\textsubscript{2}, by 5 mm Hg</td>
<td>0.86 (0.82–0.90)</td>
<td>−6.1</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Sex, female vs male</td>
<td>0.74 (0.65–0.85)</td>
<td>−4.5</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>FEV\textsubscript{1}, % predicted, by 10%</td>
<td>0.93 (0.89–0.97)</td>
<td>−3.5</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

*Relative risk of death for a given increase of each significant variable in the final multivariate Cox model calculated by stepwise selection (n = 2,490). A relative risk > 1 indicates a poorer prognosis for higher values of the variable (age). Sex was coded 0 for men and 1 for women; a relative risk < 1 indicates a better prognosis for women.
vival may then seem paradoxical. However a low hemoglobin level stimulates ventilation and could thus be responsible for “artificially” low values of PaCO$_2$. Of note, our first study from the ANTADIR database showed that in COPD patients receiving LTOT, a low PaCO$_2$ had a negative prognostic value.

Limitations and Strength of the Study

The study has limitations. First, it is a retrospective observational study, and as such it tells nothing on the causative nature of a statistical association between a risk factor and a given outcome. Second, the only hematocrit value considered is the one noted at the time of the initiation of LTOT. As a result, the prognosis value of the dynamics of the hematocrit over time is unknown, as are on the impact of the compliance with oxygen therapy and of changes in smoking status. Third, the study pertains to a fraction of the relevant population, because a hematocrit was available in only one third of the patients meeting the inclusion criteria. A hematocrit should be gathered systematically on ANTADIR forms, and why this is not the case is only too obvious. The comparison of the population with and without known hematocrit values shows only slight differences in characteristics, but indicate differences in prognostic suggesting that somehow clinicians might note down hematocrit in more severe patients. However, we feel that this does not intrinsically undervalue our results, which are what they are in the population studied. Fourth, there is no possibility to identify, from the database, the existence of comorbidities that could either be specific etiologies for the decrease in hemoglobin (eg, chronic renal failure or GI bleeding) or intrinsically aggravate the prognosis. Finally, the database has been in operation over a long time period, during which treatments for COPD and patterns of healthcare use have changed, which may have influenced the hematocrit.

These limitations must be taken into account (see “Perspectives”) but also weighted against the strengths of the study. The principal of these strengths lie in the size of the cohort and in the nature of the database from which it was derived. Indeed, the ANTADIR observatory has been continuously recording data from LTOT patients 25 years, and from 23 regions of France. Therefore, we were able to study a very large population of patients characterized in a standard manner in terms of demographic data, pulmonary function tests, and intercurrent events. Although not a typical epidemiologic database (such as the Framingham database, in which all patients are followed up at fixed intervals to collect complete information), the characteristics of the ANTADIR database are such that selection and censoring biases are not likely to be major. The 10-year average follow-up adds weight to our observations.

Possible Mechanisms of Anemia in COPD

Anemia increases in prevalence with age, which may account in part for our observations. GI bleeding; chronic renal failure; deficiencies in vitamin B$_{12}$, folate, or iron; and myelodysplastic syndromes can coexist with COPD, and should not be overlooked in anemic COPD patients. Chronic infections, chronic
inflammation, and neoplastic diseases cause the so-called anemia of chronic disease, also a feature of chronic heart failure where anemia is an independent risk factor for mortality. These diseases can all coexist with COPD, but COPD itself might cause anemia of chronic disease. A full review of the possible mechanisms is beyond the scope of this article, but some facts warrant attention. In the anemia of chronic disease, shortened survival of RBCs is thought to result from raised levels of IL-1 and TNF. These findings are common in COPD and exaggerated during exacerbations. IL-1 and TNF also decrease the erythropoietin response to hypoxia, impede iron utilization, and impair marrow erythropoietic response. Low hemoglobin levels in COPD patients undergoing elective abdominal aortic aneurysmectomy, found than a low preoperative hematocrit was significantly associated with a poor outcome. From these observations, it may be postulated that COPD patients are rendered more sensitive to anemia, acute or chronic, by the prevailing tissue hypoxia. In the BODE index study, hematocrit was significantly lower in the patients who died than in those who survived. That this variable was not selected by the statistical process in the BODE index may be surprising in view of our observations. However, the populations of patients are very different, ours being restricted to patients with very severe COPD needing LTOT.

Conclusion and Perspectives

Because of the limitations outlined above, this study cannot be more than a token of the putative clinical relevance of anemia in severe COPD patients. It is, however, an important addition to the existing anecdotal evidence pointing to this common sense possibility. In our view, the observations presented are a strong incentive for confirmatory prospective studies assessing the prognostic value of low hemoglobin levels in severe COPD patients, and in other forms of respiratory insufficiency. It would be useful to assess the effects of oxygen therapy on the production of erythropoietin. Finally, the question of the correction of hemoglobinemia in COPD should be raised and the corresponding pathophysiologic and prognostic effects assessed. Meanwhile, clinicians should be aware that anemia can be an issue in COPD patients; seeking and correcting associated factors such as GI bleeding or folate deficiency is probably particularly important in this setting.

The Relationship Between Low Hematocrit and Mortality

Anemia is associated with increased mortality in patients with end-stage renal insufficiency, malignancy, acute myocardial infarction and chronic heart failure, surgical patients in general, and critically ill patients. In some cases, the causative nature of the association is suspected because correcting hemoglobinemia improves prognosis. In heart failure patients, open studies suggest that the correction of anemia with erythropoietin improves ejection fraction, reduces symptoms, decreases hospitalizations, and reduces mortality. These data however need confirmation. In other situations, correcting hemoglobinemia does not have a positive influence on the prognosis.

In COPD patients, Cappell and Nadler observed increased mortality in cases of upper-GI bleeding as compared to control subjects (odds ratio, 4.3; 95% CI, 1.22 to 14.8; p < 0.01). Upchurch et al., in 158

References

7 Wouters EF. Chronic obstructive pulmonary disease: 5. Systemic effects of COPD. Thorax 2002; 57:1067–1070