Prevalence of macrocytosis in patients with chronic obstructive pulmonary disease

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Abstract

Background Macrocytosis is a common finding in the hospital and community setting, generally attributed to alcoholism, vitamin B-12 and folate deficiencies and certain medications. Only few studies have reported macrocytosis in chronic obstructive pulmonary disease (COPD).

Aim The aim of this study was to determine the prevalence of increased mean red cell volume (MCV) in COPD in an out-patient setting and to analyse its relationship to respiratory parameters.

Methods Ninety patients were retrospectively evaluated over a one year period. Patient demographics, smoking history, dyspnoea score, forced expiratory volume (FEV1) and haematological parameters were recorded from their medical charts. Macrocytosis was defined as a MCV ≥ 94 fl.

Results Twenty-one patients demonstrated macrocytosis giving a prevalence of 23.3%. Mean MCV (SD) of patients with and without macrocytosis was 97.5 fl (4.9) and 87.7 fl (7.5) respectively. FEV1 was significantly higher in patients with macrocytosis (p=0.03) There were no significant differences in body mass index (BMI), dyspnoea scores or current smoking status between patients with and without macrocytosis.

Conclusion Macrocytosis is a frequent finding in COPD patients attending an outpatient pulmonary clinic.

Key words: macrocytosis, chronic obstructive pulmonary disease, mean cell volume, prevalence

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Introduction

Red cell macrocytosis has been frequently described in the hospital and community setting. Macrocytosis is commonly attributed to alcoholism, B12 and folate deficiencies, or certain medications (1,2).

Less well known is that macrocytosis can be a finding in patients with COPD. One recent study has demonstrated that macrocytosis was present in almost half of hypoxic COPD patients (3), while another study demonstrated that macrocytosis was present in 29% of COPD patients without respiratory insufficiency (4).

Apart from those studies, there have only been a limited number of small studies describing macrocytosis in COPD patients. The primary aim of our study was to determine the prevalence of macrocytosis in stable COPD patients in an outpatient setting and to determine whether macrocytosis in that setting was associated with respiratory parameters.

Materials and methods

Study design and patients

We retrospectively reviewed the medical charts of all COPD patients (ICD-9 code: 496; chronic airway obstruction) attending the outpatient pulmonary clinic at Changhua Christian Hospital, Changhua City, Taiwan for a one year period (March 2008 to 2009). Excluded were patients with documented vitamin B-12 or folate deficiency and patients with a high alcohol intake.

From the medical charts we recorded the patients demographics (gender, age, weight, height, diagnosis), spirometry data (FEV1), smoking history (current smoker, ex-smoker for >12 months, never smoker), alcohol intake (non-drinker, occasional drinker, moderate drinker), modified Medical Research Council dyspnea score (5), and haematological parameters (red cell count, haemoglobin, haematocrit, mean cell volume and platelet count). Body mass index (BMI) was calculated by dividing weight (Kg) by height squared (M²).

Spirometry and laboratory methods

FEV1 was determined on a MasterScreen CPX (VIASYS Health Care, Hoechberg, Germany) according to ATS spirometry standards (6).

Hematological parameters were determined on a Coulter LH 730 Haematology Analyzer (Beckman Coulter Inc., Fullerton, CA, USA). Macrocytosis was defined as a MCV of greater than 94 fl (4).

Statistical analysis

Statistical analyses were carried out using "R" version 2.9.1 (R Foundation for Statistical Computing, Vienna, Austria). Comparisons were made between COPD patients with macrocytosis (MCV ≥ 94fl) and those without macrocytosis (MCV < 94 fl). Results are reported as the mean and standard deviation for both groups and p-values come from the Mantel-Haenszel non-parametric test. Odds ratios (OR) and 95% confidence intervals (95% CI) are from logistic regression. Statistical significance was set at p<0.05.

Results

A total of 90 COPD patients (71 male) charts were retrospectively reviewed in the 12 month period. Their demographics, lung function tests and haematological parameters are shown in Table 1. Six patients were current smokers, eight were never smokers and the remaining 76 were ex-smokers (> 12 months).

Twenty-one COPD patients (23.3%) had a MCV value of ≥94 fl of whom three had a MCV >100 fl. Results of those patients in comparison with patients whose MCV was < 94 fl are shown in Table 2. It shows that there were no significant differences in BMI or dyspnea scores while FEV1 was significantly lower in those without macrocytosis.
COPD patients with macrocytosis had significantly lower red cell counts, but no significantly differences in haemoglobin, haematocrit or platelet count levels. Although macrocytosis was more common in males than in females (OR: 1.23; 95% CI: 0.38-3.93) and current smokers compared to ex or non-smokers (OR: 2.33; 95% CI: 0.57-14.74), these differences were not statistically significant.

### Table 2. Comparison of COPD patients with and without macrocytosis

<table>
<thead>
<tr>
<th></th>
<th>MCV &gt; 94 fl</th>
<th>MCV &lt; 94 fl</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI (kg/m²)</td>
<td>22.2 (3.2)</td>
<td>23.1 (3.9)</td>
<td>0.32</td>
</tr>
<tr>
<td>Age (years)</td>
<td>74.0 (8.4)</td>
<td>73.1 (10.7)</td>
<td>0.80</td>
</tr>
<tr>
<td>FEV1 (% best predicted)</td>
<td>77.6 (21.4)</td>
<td>66.0 (25.4)</td>
<td>0.03</td>
</tr>
<tr>
<td>Dyspnea score</td>
<td>1.14 (1.06)</td>
<td>1.57 (1.06)</td>
<td>0.11</td>
</tr>
<tr>
<td>Red cell count (10¹²/L)</td>
<td>4.10 (0.67)</td>
<td>4.54 (0.59)</td>
<td>0.01</td>
</tr>
<tr>
<td>Haemoglobin (g/L)</td>
<td>136 (20.0)</td>
<td>134 (15.8)</td>
<td>0.59</td>
</tr>
<tr>
<td>Haematocrit (%)</td>
<td>39.7 (5.9)</td>
<td>39.4 (4.6)</td>
<td>0.98</td>
</tr>
<tr>
<td>MCV (fl)</td>
<td>97.5 (4.9)</td>
<td>87.7 (7.5)</td>
<td>&gt;0.0001</td>
</tr>
<tr>
<td>Platelet count (10¹²/L)</td>
<td>238 (42.5)</td>
<td>250 (83.3)</td>
<td>0.58</td>
</tr>
</tbody>
</table>

Results are mean (1 SD).

### Discussion

Our study has shown that 23.3% of stable COPD patients had macrocytosis, defined as a MCV of >94 fl. This compares to a prevalence of 29% in a previous study of stable COPD patients (3). In agreement with that study we also did not find differences in BMI, smoking status, or dyspnea score between COPD patients with and without macrocytosis. In our study COPD patients without macrocytosis had significantly lower FEV1 levels and slightly, but not significantly, higher dyspnea scores. We found no significant differences in haemoglobin or haematocrit between the two groups, unlike a previous study that found statistically significant lower haemoglobin and haematocrit levels in patients with macrocytosis (4). In that study COPD patients with hypoxemia had a much higher prevalence of macrocytosis (43.75%). However, the severity of hypoxia in that study did not correlate with the erythropoietic response (4). The authors of that study hypothesised that acute erythropoietic stress occurs repeatedly in COPD as a result of frequent exacerbations leading to release of relatively immature, large red blood cells from the bone marrow, as evidenced by a significant increased number of F-cells that were significantly correlated with MCV levels.

Apart from these two recent reports describing macrocytosis in COPD patients (3,4) there have been only a few earlier reports describing this association (7-10). The earlier viewpoint was that macrocytosis in COPD was due to acidosis or CO₂ retention. Current thinking is that it is likely due to enhanced release of large red blood cells from the bone marrow as a result frequent hypoxemic exacerbations (3,4). However, other unexplored factors may also be involved in the erythropoietic response to hypoxemia and need to be explored.

A limitation of our study is that we did not measure vitamin B-12 or folate levels in our patients, deficiencies of which are a common cause of macrocytosis. Some of our patients most likely did have anaemia, as evidenced by low haemoglobin and red cell counts. However, the prevalence of macrocytosis was similar to another study where patients with haemoglobin levels of > 130 g/L were excluded (4). Excluding the 32 patients with a haemoglobin level of > 130 g/L from our study only slightly reduced the prevalence of macrocytosis from 23.3% to 18.6%. We also did not record oxygen saturation and thus some patients may have had significant hypoxia. However, none of our patients were hospitalised, all attended an outpatient pulmonary clinic. If they were severely hypoxic they would most likely have been hospitalised.

In conclusion, macrocytosis is a frequent finding in COPD patients attending an outpatient pulmonary clinic. Many haematology text books and macrocytosis review articles fail to mention COPD as being associated with macrocytosis, instead focusing on vitamin B-12 and folate deficiencies, smoking, heavy alcohol intake and certain medications. Thus physicians and laboratory scientists have to be aware that a raised MCV in COPD may be due to factors other than the usual known factors associated with macrocytosis. Further studies are required to explore the likely complex factors involved in macrocytosis in COPD.

### References


### Author contributions

Francis Wu and Mei-Wen Wu helped plan the study, collected the data and contributed to writing the article. Chin-Fu Chang helped plan the study and contributed to writing the article. Neville Pierce conducted the statistical analysis and contributed to writing the article. Rob Siebers conceived and planned the study and was the primary author. The authors have no conflicts of interest to declare.

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