Research Letters

The mini nutritional assessment is associated with the perception of dyspnoea in older subjects with advanced COPD

SIR—Dyspnoea is one of the cardinal features of patients with chronic obstructive pulmonary disease (COPD), and it has been shown to be strongly associated with mortality in this population [1]. The pathophysiology of dyspnoea is related to abnormalities in ventilatory demand, respiratory muscle, breathing patterns and in blood gases [2]. However, the relationship between the level of breathlessness and lung function impairment is not obvious [3, 4]. On the other hand, dyspnoea has been shown to be affected by non-respiratory factors, such as physical disability [4], nutritional status [5] and possibly age-per-se [6], thus supporting the multifactorial origin of this symptom [2].

COPD is a respiratory disease that is associated with systemic effects [7, 8]. Agusti et al. found that underweight patients are representative of more severe COPD [7]. A high prevalence of nutritional depletion has been demonstrated in outpatient COPD [9–11], and low body weight has been associated with severity of COPD [12]. Malnutrition affects respiratory muscle strength and endurance, which in turn contributes to worsening the respiratory function [13]. Of note, dietary supplementation has been shown to reduce the severity of dyspnoea in underweight individuals with COPD [14].

The Mini Nutritional Assessment (MNA) has been proposed to evaluate the body’s nutritional status [15]. The current study aimed at investigating whether differences in nutritional status are associated with the perception of dyspnoea in individuals with COPD.

Methods

Subjects

We recruited consecutive individuals with COPD who attended the pulmonary outpatient clinic, as well as COPD inpatients at the time of discharge, in the period of April–June 2006. Patients younger than 60 years of age were excluded. Exclusion criteria were also the co-existence of malignancies or other illnesses known to alter the nutritional state. All patients were in stable condition. The study was approved by the Ethics Committee of the University of Palermo, and all patients gave written, informed consent prior to participation.

Study design

The nutritional status was evaluated through anthropometric measurements and the MNA questionnaire; the perception of dyspnoea was assessed by the Modified Medical Research Council (MMRC) Dyspnoea Scale and the degree of physical disability by the Barthel Index. Clinical and functional evaluations were performed to assess the severity of COPD [16, 17]. The number of comorbid conditions was also recorded.

Nutritional and anthropometric data: weight, height, waist and hip circumferences were measured following a standardized procedure [18]. The MNA test is an internationally validated, two-step procedure (screening for risk of malnutrition followed by global assessment of the nutritional conditions), which evaluate the overall health status of elderly subjects, by rating cognitive function, functional status, walking, balance and socio-economic status [15]. The MNA provides a total score that ranges from 0 to 30 points. According to the score achieved, patients are classified as undernourished (≤17 points), at risk of malnutrition (17.5–23.5), and well nourished (>23.5). Subjects who attained >12 points at the screening were assigned an arbitrary value of 30. To avoid inter-observer variability, the MNA evaluation was performed only by one person (GP).

The perception of dyspnoea was assessed through the MMRC Dyspnoea Scale [4] by another investigator (LM). The MMRC Dyspnoea Scale consists of five grades of physical activities that provoke dyspnoea. The Barthel Index was used to establish the degree of physical performance [19]. The final score ranges from 0 (complete dependency) to 100 (complete independence).

Data analysis

Data are presented as mean ± SD or median and range, where appropriate. Unpaired t-test or Mann–Whitney test were employed to assess differences between the two groups (‘well nourished’ versus ‘at risk of malnutrition’) for anthropometric, functional and clinical variables. An ordinal regression analysis was performed to assess independent contributors to the variance in degree of dyspnoea (MMRC score). In all analyses, P values ≤0.05 were considered statistically significant.

Results

Thirty-two individuals with COPD were enrolled (Table 1). All patients met the criteria for airflow obstruction (mean FEN/VC: 0.48; range: 0.30–0.69). Ten patients were on long-term oxygen therapy. Ten patients were current smokers (pack-year: 67 ± 29, mean ± SD) and 22 ex-smokers (73 ± 45, mean ± SD). None of the patients was free of dyspnoea (MMRC, median: 3, range: 1–4). The Barthel Index was between 29 and 100 (median: 82), with only two patients showing complete independence (100 points). The BMI resulted in 27.8 ± 3.8 kg/m², and the waist : hip
The present study shows that elderly patients with COPD with normal BMI but at risk for malnutrition complain of a higher degree of dyspnoea compared to well nourished patients with COPD. This suggests that early alterations of the nutritional status may play a significant role in the perception of symptoms in elderly individuals with COPD, and implies that the early detection of nutritional impairment should be included in the clinical assessment of the disease.

To the best of our knowledge, this is the first attempt to use the MNA in a population of patients with COPD. The MNA has been validated in different populations: Magri et al. [20] detected a significant risk of malnutrition in hospitalized patients with dementia. The MNA was also evaluated in orthopaedic patients [21], in surgical elderly patients [22] and in elderly, otherwise healthy subjects [23]. The reliability of the MNA in older patients was demonstrated by Barone et al. [24], who found that the MNA was superior than the global assessment of healthy status in identifying malnourished patients. Taken together, these studies provide evidence that the MNA can be safely used in the assessment of elderly populations.

The finding that the perception of increased dyspnoea is associated with the risk of malnutrition supports and extends previous observations on the pathogenetic role of low body weight in patients with COPD [5]. Interestingly, a more severe degree of dyspnoea has been observed in patients with COPD with lower MNA scores, even in the absence of reduced BMI. To explain the observed correlation between increased sensation of dyspnoea and the risk of malnutrition, at least two mechanisms can be proposed. First, it has been demonstrated that quadriceps endurance is reduced in patients with COPD, even in the mild stage of the disease [25]. This weakness of skeletal muscle causes a reduction in the ability to perform physical exercise, and this may, in turn, account for a greater degree of breathlessness [25, 26]. Second, the increased sensation of dyspnoea could be related to the presence of more severe emphysema. If this is the case, dyspnoea and the risk of malnutrition could share common pathogenetic mechanisms. It has been demonstrated that COPD associated with high-resolution computed tomography-documented emphysema is characterised by more severe lung function impairment, more intense airway inflammation, and, possibly, more serious systemic dysfunctioning, as compared with COPD free of HRCT-documented emphysema [27]. Therefore, nutritional alterations could be listed among the clinical manifestations of systemic inflammation in patients with COPD.

**Table 1.** Demographics and baseline lung function characteristics for all patients participating in the study. Data are expressed as mean ± SD

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>71.8 ± 6.0</th>
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<tbody>
<tr>
<td>Gender (M/F)</td>
<td>31/1</td>
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<tr>
<td>Smoking habit</td>
<td>10/22</td>
</tr>
<tr>
<td>FEV1 (% predicted)</td>
<td>47 ± 12.6</td>
</tr>
<tr>
<td>FVC (% predicted)</td>
<td>78 ± 17.5</td>
</tr>
<tr>
<td>FEV1 (L)</td>
<td>2.61 ± 0.75</td>
</tr>
<tr>
<td>FVC (L)</td>
<td>0.48 ± 0.10</td>
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The MNA score did not correlate with BMI ($r = 0.20, P = 0.27$), nor with the waist : hip ratio ($r = 0.30, P = 0.15$).

The MNA classification led to the generation of two groups: 14 patients were classified as ‘at risk of malnutrition’, and 18 regarded as ‘well nourished’. Age was not different between the two groups (at risk of malnutrition: 72 ± 5.3 years; well nourished: 71 ± 6.7 years, $P = 0.58$), nor was BMI (26.9 ± 4.1 kg/m² versus 28.5 ± 3.6 kg/m², $P = 0.29$). The FEV1% predicted was significantly lower in patients at risk of malnutrition (41 ± 10% versus 51 ± 12%, respectively; $P = 0.02$). Subjects on oxygen therapy showed lower MNA than that of individuals on pharmacological therapy (20.9 ± 3.7 versus 27.5 ± 3.9, $P<0.0001$, respectively). The number of comorbid conditions did not differ between the two groups ($P = 0.33$), nor did the total number of medications used by the patients ($P = 0.49$). Similarly, the smoking habit was not different between groups ($P = 0.69$). The Barthel Index did not differ between the at risk (74 ± 19) and well nourished (79 ± 14) patients ($P = 0.45$). The severity of dyspnoea was significantly higher in patients at risk of malnutrition than in the well nourished group (3.1 ± 0.7 versus 2.3 ± 1.0, respectively; $P = 0.02$ by Mann–Whitney test) (Figure 1). The ordinal regression analysis, in which the MMRC represented the dependent variable, and the MNA and FEV1% predicted the independent variables yielded a $P$ value of 0.01, with the MNA being the only factor that entered the model ($P = 0.05$).

**Figure 1.** Comparison of the Dyspnoea Score between the group of patients at risk of malnutrition and the group of well–nourished patients. MMRC: Modified Medical Research Council.
Early detection of nutritional impairment should be
• None of the patients was free of dyspnea. When patients
• The study shows that patients with COPD with normal
BMI but at risk for malnutrition complain of a higher
degree of dyspnea compared to well nourished patients
with COPD. This finding suggests that early alterations
in nutritional status may play a significant role in the
perception of symptoms in individuals with COPD.
• Early detection of nutritional impairment should be
included in the clinical assessment of elderly individuals
with COPD.

Key points
• Nutritional abnormalities are recognised as systemic
manifestation of COPD, but their contribution to the
occurrence of respiratory symptoms is still unclear. The
current study aimed at investigating whether differences in
nutritional status can influence the perception of dyspnea
in individuals with COPD.
• Thirty-two elderly patients with COPD underwent assess-
ment of their nutritional status through anthropometric
measurements and the MNA questionnaire; the percep-
tion of dyspnea was assessed by the MMRC Dyspnea
Scale.
• None of the patients was free of dyspnea. When patients
were classified according to the level of MNA score, the
severity of dyspnea was significantly greater in patients at
risk of malnutrition than in the well nourished group.
• The study shows that patients with COPD and normal
BMI but at risk for malnutrition may complain of a higher
degree of dyspnea compared to well nourished patients
with COPD. This finding suggests that early alterations
in nutritional status may play a significant role in the
perception of symptoms in individuals with COPD.

Conflicts of interest
None

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The aluminium content of bone, and mortality risk

SIR—Even though aluminium is the commonest metal in the earth’s crust, evolution has not conferred it with an essential biological function. The metal has been regarded as relatively biologically inert in the past. Aluminium is now considered to be a potentially toxic metal that might trigger apoptosis [1]. Aluminium poisoning may lead to three types of disorder: aluminium-induced bone disease, microcytic anaemia and encephalopathy, which is well known in patients with chronic renal failure [2–7]. Induction of progressive central nervous system diseases has also been suggested, e.g. amyotrophic lateral sclerosis, Parkinson’s disease [8, 9] and Alzheimer’s dementia [10–12].

Aluminium normally enters the body through the diet owing to its natural presence in many foods, and from leaching into food by aluminium-containing cooking utensils. The total dietary intake has been estimated at 4–9 mg Al/day [13–15], and 4% of the aluminium content of the diet is retained by intestinal absorption. This aluminium can partially be accumulated in bone—the main storage site of aluminium—for years under continuous intake conditions [16]. In the elderly, and especially in young patients with an Alzheimer-type pathology, the intestinal absorption of aluminium is increased [17, 18], thus enhancing the putative bone-tissue accumulation.

Given that aluminium is exponentially accumulated in the body with ageing [19], that aluminium is associated with neurodegenerative diseases, and that aluminium is linked to processes in the cell that eventually lead to premature cell death, the hypothesis of considering whether aluminium plays a role in the ageing process and is associated with mortality risk is warranted. This study was therefore performed in order to examine whether the aluminium content in bone in humans was associated with mortality risk.

Subjects and methods

A total of 198 patients—132 women and 66 men—with a mean age of 73 years and a range of 16–98 years were included in this study, and all characteristics are shown in Table 1. They were treated at either of the two hospitals in the county of Uppsala, and admitted to the hospitals for either arthroplasty of the hip because of osteoarthritis (n = 50), shaft fractures of the femur (n = 9) or the tibia (n = 10), or hip fracture (n = 129). Of these hip-fractures cases, 62 had a diagnosis of dementia on admission to hospital, while none of the remaining 136 participants had this diagnosis. The Ethics Committee of the Medical Faculty of Uppsala University approved the study.

During the operations on all cases, bone biopsies from the trabecular bone of the proximal femur or from the proximal tibia were taken using an aluminium-free instrument. The bone samples were immediately put in sealed polyethylene test tubes, frozen and stored at −20°C until analysis at a maximum of 6 months after the operation. Prior to analysis, after drying at 120°C for 48 h the bone samples were weighed. The bone samples were then decomposed using ultra-pure nitric acid in a quartz tube, and an internal standard (Indium), diluted with high-purity water (with a resistivity of over 18 MΩ·cm), was added. The samples were then introduced into an inductively coupled mass spectrometer (Perkin-Elmer Elan 6000) and measured for their content of aluminium (ng/g dry bone). All handling of the samples was carried out in a clean room. Quality control was assessed through use of a reference material (IAEA H-8 Animal bone) in every fifth sample, randomly distributed in the measurement series.


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Table 1. Characteristics of the participants by survival status

<table>
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<tr>
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<th>Deceased patients</th>
<th>Non-deceased patients</th>
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<tr>
<td><strong>Age</strong> (women/men)</td>
<td>82.6 (6.4)</td>
<td>65.6 (19.4)</td>
</tr>
<tr>
<td><strong>Serum creatinine</strong> (µmol/l)</td>
<td>94.8 (32.4)</td>
<td>92.0 (23.5)</td>
</tr>
<tr>
<td><strong>Aluminium ng/g dry weight of bone</strong></td>
<td>1,542 (1,458)</td>
<td>1,199 (1,551)</td>
</tr>
<tr>
<td>Log aluminium</td>
<td>6.9 (1.0)</td>
<td>6.6 (1.0)</td>
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