Exacerbations as a starting point of pro-active chronic obstructive pulmonary disease management

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Summary Chronic obstructive pulmonary disease (COPD) exacerbations could represent an opportunity for pro-active COPD management rather than mere treatment if previously unknown disease is discovered; the extent of underdiagnosis and undertreatment of COPD in patients attending an emergency department (ED) with an exacerbation is not known.

During 2002, we recalled 131 COPD patients in stable conditions, 4–8 weeks after they had attended the ED or been discharged from our University Hospital (North-West of Italy). Information on diagnosis and management prior to the ED attendance were collected; spirometry and arterial blood gas analyses were performed.

One-third of patients had never been diagnosed and treated even though 83% of them had moderate-to-very-severe COPD and about 30% already had respiratory failure. Only 20% had received information on the nature of the disease and none had received a written action plan. Only 60% were receiving long-acting bronchodilators and 41% of patients with respiratory failure were receiving long-term oxygen. A substantial number of undiagnosed and untreated patients with moderate-to-very-severe COPD came to our attention through an exacerbation. This enforces the importance of exacerbations as the starting point of pro-active COPD management and of the ED as a valuable sentinel to identify this subset of patients.

Introduction

Several studies and recent expert panels have emphasized the underreporting and underrecognition of COPD. The objectives of the GOLD
The National Lung Health Education Program has suggested that primary care physicians should ensure that screening spirometry is done in patients at high risk. 

In the recent years, much attention has been paid to COPD exacerbations, their treatment and their consequences on the disease progression; however, the importance of exacerbations in becoming a point of pro-active COPD management has not been acknowledged. Emergency department (ED) attendance because of an exacerbation of respiratory symptoms could represent an opportunity to consider intervention if previously unknown disease is discovered, particularly in patient populations who underuse primary care physicians. Much recent evidence has shown that the available treatments are able to influence health-outcome measures related to quality of life, such as the severity of dyspnea, exercise capacity, and exacerbations even in the most severe patients.

The extent of previous underdiagnosis and undertreatment in moderate-to-very-severe COPD patients attending an ED because of an exacerbation of respiratory symptoms is unknown. The aims of our study were: (1) to evaluate how many COPD patients come to attention through an exacerbation requiring the ED attendance; (2) to evaluate the extent of undertreatment prior to the ED attendance; (3) to create and propose a novel approach for the management of patients with exacerbations of COPD after the discharge from the ED.

**Materials and methods**

**Patients and study design**

During 2002, 244 patients attended our ED because of increased dyspnea and sputum production. The diagnosis of exacerbation of COPD as the main cause of these symptoms and their deterioration was confirmed in 200 patients during the consequent admission to hospital or, if the patient was not hospitalized, in a subsequent specialist appointment, according to Rodriguez-Rosin.

When patients were confirmed to have suffered from COPD exacerbations, they were given a letter addressed to their GP explaining their clinical status and proposing a novel approach of ongoing pro-active management. We scheduled that the patients had to be recalled 4–8 weeks after attending the ED or after discharge from hospital, when the exacerbation had resolved, in order to answer specific questions on their clinical history, previous diagnosis, treatment, educational messages, written action plans and on whether they had undergone spirometry prior to the exacerbation requiring the ED attendance. On the same day the patients had to undergo spirometry and arterial blood gas analysis. For the purpose of the present study only patients able to reliably recall their clinical history, co-operate well during the spirometry and who had not had previous exacerbations with admission to any hospital were included; the number of excluded subjects and the specific reasons for their exclusion are reported in Fig. 1. Of the 131 eligible subjects only 13 were non-responders because they lived far away from our center.

**Classification of severity of COPD**

A Vmax 22 system (SensorMedics, Yorba Linda, CA) was used to measure lung function: forced expiratory volume in 1 s (FEV1) and forced vital capacity (FVC) were determined according to the American Thoracic Society criteria. Chronic airflow obstruction was defined as a FEV1/FVC ratio less than 70%. The severity of COPD was classified on airflow obstruction as measured by postbronchodilator FEV1; predicted values were those of the European Respiratory Society.

Blood samples were drawn from the radial artery, and gas tensions were measured by a Ciba Corning 855 gas analyzer (Ciba Corning Diagnostic, Medfield, MA). Respiratory failure was defined as a PaO2 < 60 mmHg with or without PaCO2 > 45 mmHg.

The Medical Research Council (MRC) dyspnea scale, modified according to Bestall et al., was incorporated into the questionnaire as a measure of dyspnea severity: this scale ranges from 5 to 0 and patients were considered to have dyspnea when the score was > 1.

Repeated exacerbations were defined according to Burge and Wedzicha.

**Statistical analysis**

Group characteristics and lung function data were compared by two-tailed unpaired Student’s t or χ2 tests, whichever was appropriate. A probability
value <0.05 was considered statistically significant. All values are reported as mean ±sd.

Results

Out of the 118 COPD patients included in our study (M/F 96/22; age 74 ± 11 years) 63% had been hospitalized after attending the ED, including one patient who was admitted to the intensive care unit.

At the time of our recall, all of them were in a stable condition. The main patients’ characteristics at the clinical examination and the distribution of patients by COPD severity are reported in Table 1; the majority of patients (83%) were in GOLD stage >1 and almost a half (46%) presented co-morbid conditions. The mean values of lung function and blood gas analysis parameters are reported in Table 2.

Forty-four percent of the 118 COPD patients reported that they had never undergone spirometry.

Patients without a diagnosis of COPD prior to the ED attendance

On our recall, 33 patients (28%) reported that they had never been diagnosed as having COPD prior to

**Table 1** Main patients’ characteristics.

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Without previous diagnosis</th>
<th>With previous diagnosis</th>
<th>Whole group</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n = 33)</td>
<td>(n = 85)</td>
<td>(n = 118)</td>
<td></td>
</tr>
<tr>
<td>72 ± 13</td>
<td>75 ± 8</td>
<td>74 ± 11</td>
<td></td>
</tr>
</tbody>
</table>

Smoking habit

- Persistent smokers:
  - Without previous diagnosis: 20 (60%)
  - With previous diagnosis: 29 (34%)
  - Whole group: 49 (41%)
- Past smokers:
  - Without previous diagnosis: 13 (40%)
  - With previous diagnosis: 55 (65%)
  - Whole group: 68 (58%)
- Never smokers:
  - Without previous diagnosis: 0 (0%)
  - With previous diagnosis: 1 (1%)
  - Whole group: 1 (1%)

COPD severity

- GOLD stage 1:
  - Without previous diagnosis: 6 (18%)
  - With previous diagnosis: 14 (16%)
  - Whole group: 20 (17%)
- GOLD stage 2:
  - Without previous diagnosis: 12 (36%)
  - With previous diagnosis: 20 (24%)
  - Whole group: 32 (27%)
- GOLD stage 3:
  - Without previous diagnosis: 5 (15%)
  - With previous diagnosis: 20 (24%)
  - Whole group: 25 (21%)
- GOLD stage 4:
  - Without previous diagnosis: 10 (30%)
  - With previous diagnosis: 31 (36%)
  - Whole group: 42 (35%)
- Frequent exacerbations:
  - Without previous diagnosis: 0 (0%)
  - With previous diagnosis: 20 (24%)
  - Whole group: 20 (17%)
- Respiratory failure:
  - Without previous diagnosis: 4 (12%)
  - With previous diagnosis: 29 (34%)
  - Whole group: 33 (28%)
- Co-morbid conditions:
  - Without previous diagnosis: 9 (28%)
  - With previous diagnosis: 45 (53%)
  - Whole group: 54 (46%)
the ED attendance. Eight percent of these patients had never noted any chronic respiratory symptom; 44% reported chronic cough and phlegm, 44% also suffered from dyspnea, and one patient reported only dyspnea. Fifty-two percent of patients who reported chronic respiratory symptoms to us during the recall had never reported these symptoms to their GP because they never visited their GP or consulted him for other health problems; three patients had undergone spirometry. Eighty-two percent were in GOLD stage 4; none of them reported frequent exacerbations prior to the ED attendance. Four patients had a $\text{Pa}_2 \text{O}_2 < 60 \text{mmHg}$ and none had a $\text{Pa}_2 \text{CO}_2 > 45 \text{mmHg}$ (Table 1).

### Patients with a diagnosis of COPD prior to the ED attendance

Out of the 85 patients (72%) with a previous diagnosis of COPD the diagnosis had been made by their GP for 43% of them and by a pulmonologist for the remainder. The diagnosis was based on spirometry in 75% of the patients diagnosed by a GP and in 73% of the patients seen by a specialist. On our recall, all the patients reported chronic respiratory symptoms: 49% reported chronic cough and phlegm, 48% also reported chronic dyspnea, three patients suffered only from dyspnea. Fourteen percent of these patients had never reported their chronic respiratory symptoms to their GP; 74% had undergone spirometry. Eighty-five percent of patients were in GOLD stage > 1. Twenty percent reported frequent exacerbations prior to the ED attendance. Thirty-four percent had a $\text{Pa}_2 \text{O}_2 < 60 \text{mmHg}$ and 18% had a $\text{Pa}_2 \text{CO}_2 > 45 \text{mmHg}$ (Table 1).

### Differences between patients with and without a diagnosis of COPD

No difference was found in gender, age and severity of disease between patients with a diagnosis of COPD prior to the ED attendance and those without. Among patients with a previous diagnosis there were fewer persistent smokers (34% vs. 60%, $P < 0.05$) than among those without a diagnosis. Among these patients there were more subjects with frequent exacerbations (24% vs. 0%, $P < 0.01$), more with respiratory failure (34% vs. 12%, $P < 0.05$) and more with co-morbid conditions (53% vs. 28%, $P < 0.05$) (Table 1). The mean value of $\text{Pa}_2 \text{O}_2$ was the only functional parameter which differed significantly between the two groups (Table 3).

### Management prior to the ED attendance

None of the patients who had not been diagnosed as having COPD prior to the exacerbation had received any respiratory educational information or regular treatment; none of the undiagnosed patients with respiratory failure was on long-term oxygen therapy.

Among patients with a previous diagnosis of COPD who were in stage > 1, thus requiring regular treatment according to GOLD guidelines, 21 (25%) had not received any treatment at all. The distribution of treatments by stage is shown in Fig. 2. The percentage of subjects who were not receiving any regular treatment was remarkably higher in patients with less severe COPD than in those with more advanced disease. Among the patients, 31% and 69% in stages 2 and 3–4, respectively, were receiving regular treatment with long-acting inhaled bronchodilators; and 15% and 64% of patients in stages 2 and 3–4, respectively,

### Table 2

Mean values±SD of lung function and blood gas analysis parameters in the whole group and in the different GOLD severity stages.

<table>
<thead>
<tr>
<th></th>
<th>Stage 1</th>
<th>Stage 2</th>
<th>Stage 3</th>
<th>Stage 4</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\text{FEV}_1$</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>$L$</td>
<td>1.89 ± 0.39</td>
<td>1.65 ± 0.45</td>
<td>1.11 ± 0.21</td>
<td>0.96 ± 0.45</td>
<td>1.35 ± 0.57</td>
</tr>
<tr>
<td>% pred</td>
<td>87 ± 6</td>
<td>67 ± 9</td>
<td>42 ± 5</td>
<td>38 ± 2</td>
<td>54 ± 22</td>
</tr>
<tr>
<td>$\text{FVC}$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$L$</td>
<td>3.15 ± 0.66</td>
<td>2.78 ± 0.71</td>
<td>2.16 ± 0.51</td>
<td>2.10 ± 0.76</td>
<td>2.46 ± 0.78</td>
</tr>
<tr>
<td>% pred</td>
<td>111 ± 14</td>
<td>88 ± 14</td>
<td>63 ± 13</td>
<td>63 ± 21</td>
<td>77 ± 23</td>
</tr>
<tr>
<td>$\text{FEV}_1/\text{FVC}$ (%)</td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>61 ± 6</td>
<td>60 ± 9</td>
<td>53 ± 8</td>
<td>46 ± 12</td>
<td>54 ± 13</td>
</tr>
<tr>
<td>$\text{Pa}_2 \text{O}_2$ (mmHg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>74 ± 7</td>
<td>69 ± 9</td>
<td>67 ± 4</td>
<td>57 ± 9</td>
<td>65 ± 10</td>
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<tr>
<td>$\text{Pa}_2 \text{CO}_2$ (mmHg)</td>
<td></td>
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<tr>
<td></td>
<td>37 ± 5</td>
<td>36 ± 5</td>
<td>39 ± 6</td>
<td>45 ± 6</td>
<td>40 ± 6</td>
</tr>
</tbody>
</table>
were receiving regular treatment with inhaled steroids. Ninety-three percent of patients in stage 3–4 with frequent exacerbations were receiving regular treatment with both long-acting inhaled bronchodilators and inhaled steroids. Among patients receiving other treatments—such as mucolytics, antibiotics, and theophylline—only one was receiving chronic treatment with oral steroids. Among patients with respiratory failure, 59% were not receiving long-term oxygen.

None of the patients had participated in a specific educational program although all had received some information and advice about smoking cessation. Only 20% had received information on the nature of the disease and its progression and none had received a written personal action plan.

### Discussion

The major results of our study are that: (1) a large part of patients with moderate-to-very-severe COPD, some of them already with respiratory failure, are not diagnosed and treated, and they get attention through an exacerbation requiring the ED attendance; (2) the novel approach for the ongoing pro-active management of the patients presenting at the ED with an exacerbation allows one to identify COPD and to minimize the under-diagnosis and undertreatment within the health care system.

### Under-diagnosis

About one-third of patients attending the ED of our University Hospital because of an exacerbation of COPD had never been diagnosed prior to the exacerbation even though a great majority of them were found on recall to suffer from moderate-to-very-severe COPD and a substantial part of them already had respiratory failure.

It is crucial to diagnose and treat COPD even in its more advanced stages before disability is substantial because a variable, yet quite consistent,
fraction of patients can benefit from therapy.\textsuperscript{16–18} The disease severity does not, by itself, lead more easily to the diagnosis; in fact, 80\% of our patients without a previous diagnosis were in moderate-to-very-severe GOLD stages. Our results show that patients with repeated exacerbations always received the diagnosis; they are known to have a worse health status and more frequently require medical attention than those who seldom have exacerbations.\textsuperscript{19} Similarly, the presence of comorbidity leads more easily to the diagnosis.

Besides physician-related factors, patient-related factors are also important in explaining underdiagnosis. Our study shows that underpresentation of symptoms to a physician accounts for about 50\% of missing diagnoses in patients with moderate-to-very-severe COPD. Remarkably, on our recall, only 2 patients did not report any chronic respiratory symptoms when asked specifically focused questions. So far, education has been much more actively promoted in asthma than in COPD\textsuperscript{20} even if COPD patients are usually older and frequently less skilful than those with asthma. In our study, consistent with Gorecka et al.,\textsuperscript{21} the awareness of the disease, along with simple advice about smoking cessation, significantly decreased the number of active smokers. Unfortunately, we documented that no patient at all had a written action plan, and this lack might have played a role in their utilization of the ED and made the emergency care more troublesome.

**Undertreatment**

The natural consequence of a missing diagnosis is, inevitably, no treatment. Moreover, we observed a considerable percentage of subjects not being treated even among those with a previous diagnosis of COPD. A large proportion of our patients requiring regular treatment with long-acting bronchodilators according to previous scientific evidence and to the GOLD guidelines (stage > 1) are not prescribed regular therapy. The long-acting bronchodilators were, in fact, the most underused drugs, despite the GOLD guidelines consider, as “evidence A”, bronchodilator medications to be central to the symptomatic management of COPD.\textsuperscript{3,22,23}

Almost all our patients in stage 3–4 with repeated exacerbations had been adequately treated according to the GOLD guidelines, which consider inhaled steroids along with long-acting bronchodilators appropriate for these patients. More than a half of our patients in stage 3–4 without repeated exacerbations were receiving the same treatment even though, in this case, inhaled steroids are not among the recommendations of the GOLD guidelines. Anyway, the scientific basis of this approach remains contentious.\textsuperscript{19,24–26}

Remarkably, there was a subgroup of patients with very severe COPD and respiratory failure who were not receiving long-term oxygen therapy. This omission of physicians is particularly culpable because there has long been clear evidence, recently reinforced, that long-term administration of oxygen to patients with chronic respiratory failure increases survival.\textsuperscript{26–28}

**Role of exacerbations in COPD management**

In recent years COPD exacerbations have received particular attention and complete agreement has been achieved on the importance of their prevention and prompt, aggressive treatment.\textsuperscript{29,30} The new aspect of our study is that many patients with moderate-to-very-severe COPD come to attention through an exacerbation, which can be considered a failure of COPD treatment. Thus, the ED may represent not only the setting for mere state-of-the-art treatment of exacerbation but a valuable sentinel for identifying this subset of COPD patients. Even at this time, subsequent interventions in a more appropriate and specialist setting are still useful, both for the patient’s personal health\textsuperscript{18} and for the society’s health care costs.\textsuperscript{31,32} Our study documents that this novel approach is easily feasible within the health care system in all the patients without a diagnosis of COPD prior to the ED attendance and in those who are not adequately treated. It is only required to plan a follow-up of these patients after the discharge enhancing a partnership between GPs and specialists by means of a simple letter.

**Weaknesses of the study**

Some questions may be raised about whether our observations can be generalized. However, we believe that the present data signal a poor overall functioning of the care of COPD patients and could be useful even if they are local. A recent international survey estimating the burden of COPD in the general population showed that the prevalence of the disease, underdiagnosis and undertreatment are similar in North America and in many Western European countries, Italy included.\textsuperscript{33} The last available data showed that COPD mortality was lower in Italy than in the US and similar to that of many other European countries.\textsuperscript{34}
Another methodological problem concerns the recall bias; this is inherent to population studies using short self-administered questionnaires or telephone interviews and should be low in our clinical study although not completely eliminated because many of our patients were old and/or poorly skilled. Conscious of this limitation, we considered only well co-operating patients eligible for the study. The exclusion of not co-operating patients, mainly the oldest, may have affected the results in that the real scenario is even worse than that we have depicted. Moreover, we cannot exclude that some patients had earlier “declined treatment offered” rather than being “missed from diagnosis”.

In conclusion, the clinical message of underdiagnosis and unmet need even in moderate-to-very-severe COPD and the role of exacerbations as the starting point of pro-active management are undoubtedly important and should change the medical practice. Physicians should consider that an exacerbation of COPD is a failure of management of this health problem, provide an analysis of why earlier diagnosis and treatment has failed or not been initiated, look for shortcomings in the system of care as well as in individual compliance, and initiate pro-active care.

References


