Management of Chronic Obstructive Pulmonary Disease Patients after Hospitalization for Acute Exacerbation

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Background

Acute exacerbations of chronic obstructive pulmonary disease (COPD) are a frequent cause of emergency department visits and hospitalizations. In the United States there was an average of 0.6 million emergency department visits per year for acute exacerbations from 1993 to 2005 [1] resulting in more than 500,000 hospitalizations per year [2].

An exacerbation of COPD is defined by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) as a change in the patient’s ‘baseline dyspnea, cough, and/or sputum that is beyond day-to-day variations, is acute in onset, and may warrant a change in regular medication’ [3]. The management in emergency departments of patients experiencing an acute exacerbation varies despite guideline-recommended care [1]. There is even more uncertainty regarding the management of COPD patients in primary care [4, 5]. Several risk factors for relapse after acute exacerbations have been identified. These include the number of previous exacerbations, the use of home oxygen, low lung function, FEV₁ <35%, the absence of a primary caregiver and the choice of oral therapy [6–16].

The question remains: how should a patient with COPD be managed after hospitalization or emergency department visit for an acute exacerbation?
The objective of this study was to review the literature regarding the follow-up of patients with exacerbations, the use and value of spirometry in their further management, the potential benefit of home monitoring, the value of long-term oxygen therapy, the value of self-management programs including the use of action plans, the potential benefit of noninvasive ventilation as well as the value of early rehabilitation.

Follow-Up

The COPD guidelines published by GOLD recommend a follow-up visit 4–6 weeks after hospitalization for COPD including an assessment of the patient’s ability to cope in his usual environment, a reassessment of inhaler technique, measurement of FEV\textsubscript{1} and an assessment of the need for long-term oxygen therapy [3].

Up to one third of the patients presenting at the emergency department with an acute exacerbation are newly diagnosed with COPD [17]. After an emergency department visit for an exacerbation of COPD there is a 21–28% relapse rate during the first 2 weeks after discharge [13, 18]. In the study conducted by Murata et al. [13] the relapse rate leveled off within the first 14 days after discharge. Patients with asthma were also included in this study while patients with an exacerbation requiring hospitalization were excluded [13]. In the prospective multicenter study by Kim et al. [18] only patients with acute exacerbations of COPD were included. Patients requiring hospitalization were also excluded. Patients who showed a high risk of relapse needing urgent attention had a history of prior emergency care utilization [18]. Patients who frequently use emergency care services more often lack a primary caregiver than those who use emergency services less frequently [15]. On the other hand, in a different study, COPD patients with intensified access to primary care showed a trend toward higher readmission rates than the control group, although the study was not powered for subgroup analysis according to disease categories [19].

In other studies, relapse was defined as an event occurring within a maximum period of 4 weeks [7, 9, 20, 21].

It has also been shown that exacerbations are not random events but that the risk of recurrence is greatest within the 8 weeks following the initial event [22]. If, as recommended by the GOLD guidelines, a patient is seen for follow-up 4–6 weeks after an exacerbation, the primary caregiver misses out on more than 20% of the relapses which occur within this time period (fig. 1). The question remains whether a follow-up earlier after discharge could reduce the high relapse (or re-exacerbation) rate.

In the study by Casas et al. [23] patients were recruited after hospitalization for an acute exacerbation of COPD and either assigned to standard care or to an integrated care intervention. Patients in the integrated care group were thoroughly assessed at discharge in terms of their respiratory disease, comorbidities and their social support. These patients were also educated on self-management and they had access to a specialized nurse via call center. No regular follow-up was scheduled. The aforementioned measures reduced the rehospitalization rate for the period of 1 year but had no influence on mortality [23].

Hermiz et al. [24] conducted a study, randomizing patients after hospitalization for an acute exacerbation to a control group receiving standard care and an intervention group. Patients in the intervention group were visited by a nurse within 1 week after discharge, were educated on disease management and received a care plan. This intervention did not reduce the number of emergency department visits or hospital admissions [24]. Table 1 sums up the characteristics of the mentioned studies.

To the best of our knowledge there is no study comparing the relapse rate of COPD patients after hospitalization for an acute exacerbation with differences in timing or frequency of follow-up visits as the sole intervention.

Table 1 sums up the characteristics of the mentioned studies.
The GOLD guidelines recommend spirometry with measurement of FEV₁ 4–6 weeks after hospitalization for an acute exacerbation of COPD [3].

In patients with moderate to severe COPD a low level of lung function has been shown to be an independent risk factor for exacerbation and hospitalization. In the study by Niewoehner et al. [25] the percentage of predicted FEV₁ was predictive of exacerbations and hospitalization within a 6-month period [25]. However, the use of spirometry for monitoring disease or modifying therapy according to spirometric results has not yet been evaluated in randomized controlled trials [26].

The spirometry results obtained 4–6 weeks after an acute exacerbation might help to identify patients who are at higher risk of relapse or rehospitalization, but there are no data regarding the benefit of therapeutic interventions based upon these results.

### Table 1. Overview of studies regarding relapse after COPD exacerbation

<table>
<thead>
<tr>
<th>Study</th>
<th>Characteristics of patients included</th>
<th>Number of patients/ED visits or hospitalizations</th>
<th>Length of follow-up</th>
<th>Relapse rate</th>
<th>Definition of relapse</th>
</tr>
</thead>
<tbody>
<tr>
<td>Murata et al. [14]</td>
<td>Patients visiting ED for exacerbation</td>
<td>496/868 ED visits</td>
<td>14 days</td>
<td>28.1%</td>
<td>Unscheduled visit to ED for respiratory symptoms</td>
</tr>
<tr>
<td>Kim et al. [18]</td>
<td>Patients visiting ED for exacerbation</td>
<td>151/151 ED visits</td>
<td>14 days</td>
<td>21%</td>
<td>Unscheduled visit to physician for worsening of COPD symptoms</td>
</tr>
<tr>
<td>Tsai et al. [15]</td>
<td>Patients visiting ED for worsening of COPD symptoms</td>
<td>388/1,009 ED visits</td>
<td>1 year</td>
<td>21% in 14 days</td>
<td>Unscheduled visit to ED for worsening of COPD symptoms</td>
</tr>
<tr>
<td>Weinberger et al. [19]</td>
<td>Patients hospitalized with congestive heart failure, diabetes mellitus, COPD</td>
<td>583 with COPD/583 hospitalizations</td>
<td>6 months</td>
<td>Not powered for subgroup of COPD patients</td>
<td>Readmission</td>
</tr>
<tr>
<td>Adams et al. [7]</td>
<td>ED visits for COPD exacerbation</td>
<td>172/362 ED visits</td>
<td>14 days</td>
<td>22%</td>
<td>Return visit to ED with persistent or worsening symptoms</td>
</tr>
<tr>
<td>Dewan et al. [9]</td>
<td>Outpatients with COPD exacerbation</td>
<td>228/232 exacerbations</td>
<td>4 weeks (failure to respond)/24 months</td>
<td>14.7% failure-to-respond rate</td>
<td>Persistence or worsening of COPD symptoms</td>
</tr>
<tr>
<td>Aaron et al. [20]</td>
<td>Patients visiting ED for COPD exacerbation</td>
<td>147/147 exacerbations</td>
<td>30 days</td>
<td>27%</td>
<td>Unscheduled visit to physician’s office or ED because of worsening COPD symptoms</td>
</tr>
<tr>
<td>Niewoehner et al. [21]</td>
<td>Patients hospitalized for COPD exacerbation</td>
<td>271</td>
<td>6 months</td>
<td>30-day treatment failure rate of 27%</td>
<td>Treatment failure (readmission, death, intubation)</td>
</tr>
<tr>
<td>Casas et al. [23]</td>
<td>Patients hospitalized for COPD exacerbation</td>
<td>155/155 hospitalizations</td>
<td>12 months</td>
<td>31 vs. 49% readmission rate</td>
<td>Readmission</td>
</tr>
<tr>
<td>Hermiz et al. [24]</td>
<td>Patients hospitalized for COPD exacerbation</td>
<td>177/177 hospitalizations</td>
<td>3 months</td>
<td>24 vs. 18% hospitalization</td>
<td>Frequency of patients’ presentation and admission to hospital</td>
</tr>
</tbody>
</table>

ED = Emergency department.

### Spirometry

A variety of studies have evaluated the benefits of patient education and the use of action plans in the management of patients with COPD. The study designs vary greatly regarding the choice of intervention and follow-up times.

For their study Bourbeau et al. [27] recruited patients who had been hospitalized for an acute exacerbation during the previous year. Patients were only included if the time period between exacerbation and inclusion was at least 4 weeks. The interventions included patient education, an individualized action plan and exercise. The hospital admission rate for exacerbations and the emergency department visits were significantly reduced in the intervention group within the 12-month follow-up period [27]. In the study by Coultais et al. [28] patients received education in the form of problem-based learning and an individually tailored action plan. These measures did not result in fewer hospitalizations or emergency department visits.
visits within a 6-month follow-up period [28]. No change in the hospitalization rate within 1 year of follow-up was seen in stable COPD patients selected by general practitioners who were assigned to a care plan [29]. In contrast to the first-mentioned study by Bourbeau et al. [27], the studies by Coulta et al. [28] and Martin et al. [29] did not include any form of exercise in the intervention groups. However, a study by Monninkhuf [30], for which patients from an outpatient pulmonary clinic were recruited and randomized to a self-management intervention group that included education and a fitness program or to a control group, failed to show a positive effect on the number of exacerbations in the intervention group. The number of hospitalizations or emergency department visits was not reported. In the study by Rea et al. [31], stable COPD patients were recruited and the intervention group was assigned a care plan, action plan, regular check-ups and pulmonary rehabilitation. These patients showed a lower hospital admission rate compared to their pretrial rate. However, when compared to the control group, the hospital admission rate did not decrease significantly [31].

Owing to the great heterogeneity of interventions and different follow-up periods, it is difficult to make specific recommendations. Self-management interventions for patients with COPD that focus on educating them on the disease and the skills needed to guide their health behavior might be associated with a reduction in hospital admissions, but there is insufficient information to specify detailed measures [32]. Data on self-management interventions directly following hospitalizations for an acute exacerbation of COPD, not including rehabilitative programs, are lacking.

The review of action plans in the management of COPD in the Cochrane Database includes 3 studies and concludes that the use of action plans shows no effect on health care utilization but does have a positive effect on the self-initiation of antibiotics and/or oral steroids [33]. The studies included in the Cochrane review are based on stable COPD patients recruited either from outpatient clinics or from general practitioner surgeries [33–35]. There is no literature regarding the use of action plans directly following hospitalization for an exacerbation of COPD and its potential benefit in reducing readmission or relapse, especially its effect on the high acute relapse rates.

Use of Home Monitoring

Few studies have evaluated the benefits of home monitoring in patients with COPD and its effect on relapse rates, quality of life and health care costs. Vitacca et al. [36] conducted a telemedicine study in patients needing mechanical ventilation or long-term oxygen therapy. Patients randomized to the intervention group received a pulse oximetry device and had scheduled telemonitoring appointments as the main measures. In patients with COPD a reduction in the hospitalization rate was shown within a 1-year follow-up period [36]. In the study by Casas et al. [23] patients discharged after an acute exacerbation were randomized to usual care or an intervention group that included self-management strategies, a care plan and scheduled telemedicine contacts with a specialized nurse. Patients in the intervention group were less likely to be hospitalized within a 1-year follow-up period [23]. There is no information available regarding patients being discharged after an acute exacerbation and the value of different forms of home monitoring, e.g. symptom diary, pulse oximetry measurements or frequent peak flow measurements.

Long-Term Oxygen Therapy

Clinical guidelines recommend an assessment of the need for long-time oxygen therapy 4–6 weeks after an exacerbation [3], as studies have shown a survival benefit for severely hypoxemic patients with COPD [37, 38] and a reduction in the number of hospitalizations [39]. If a patient is medically unstable at the time of oxygen therapy initiation, a reevaluation is recommended 1–3 months later [40]. As most patients start their domiciliary oxygen therapy immediately after hospitalization [39], the recommended reevaluation could be included in the aforementioned follow-up 4–6 weeks after an exacerbation, provided that medical stability has been achieved. Oba et al. [41] concluded in their cross-sectional study that most patients were prescribed long-term oxygen therapy when clinically unstable, and that a significant proportion of these patients remained on this therapy without a reassessment. Close to 60% of patients who were adequately reevaluated were taken off the oxygen therapy [41]. Normoxemic emphysema patients and COPD patients with only moderate hypoxemia do not benefit from long-term oxygen therapy [42, 43]. Guyatt et al. [44] conducted a randomized trial of strategies for assessing the eligibility for long-term oxygen therapy, in order to restrict this
therapy to those who benefit. A reassessment of the patients after 2 months of clinical stability resulted in a significant reduction of patients eligible for oxygen therapy and therefore in a reduction of costs without raising mortality [44]. To assess patients 4–6 weeks after an exacerbation for their need for long-time oxygen therapy might be too early as clinical stability has not been reached. The value of continuous oxygen therapy commenced immediately after exacerbation and its effect on the early relapse rate has not been studied.

Noninvasive Ventilation

Patients benefit from positive-pressure ventilation for acute respiratory failure secondary to an exacerbation of COPD [45]. In chronic COPD patients, noninvasive ventilation might result in a reduction of hospitalizations but has not been shown to reduce mortality [46, 47]. Patients with a recent exacerbation that were offered domiciliary noninvasive ventilation benefited by attaining a reduction in readmissions [48]; however, controlled randomized studies are missing [49]. The results of the studies mentioned are summarized in table 2. The value of subsequent domiciliary noninvasive ventilation in patients that have recently been hospitalized for an exacerbation and have received noninvasive ventilation during hospitalization has to be elucidated.

Early Rehabilitation

Rehabilitation that started within a few days of hospital admission for an acute exacerbation has been shown to cause an increase in exercise capacity [50–52]. The hospital readmission rate decreased when respiratory rehabilitation was started while the patient was still in hospital for an acute exacerbation, or immediately after discharge, if a supervised exercise program was continued for 6 weeks to 6 months [53–55]. A meta-analysis of randomized controlled trials showed that patients benefit from respiratory rehabilitation after an acute exacerbation of COPD by attaining an improvement in their quality of life and their exercise capacity. A reduction in hospital readmissions and mortality has also been shown [56].

Conclusions

The COPD guidelines published by GOLD recommend a follow-up visit 4–6 weeks after hospitalization for an acute exacerbation to assess the patients’ coping ability, FEV1, inhaler technique, understanding of treatment and their need for long-term oxygen therapy [3]. There is a paucity of literature regarding the follow-up of patients after hospitalization for an acute exacerbation of COPD. Several interventions have been studied to reduce the high relapse rate in these patients. In their systematic review of the chronic care model in COPD management, Adams et al. [57] conclude that patients who received at least 2 chronic-care-model components had lower hospitalization rates, but they also ‘highlight the need for well-designed trials’ [57]. Rehabilitation is recommended after an acute exacerbation because it has been shown to reduce the rehospitalization rate and improves exercise capacity and quality of life [56]. However, the availability of rehabilitation poses a problem for many patients in different health care systems.

<table>
<thead>
<tr>
<th>Study</th>
<th>Characteristics of patients included</th>
<th>Number of patients</th>
<th>Intervention</th>
<th>Follow-up</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tuggey et al. [48]</td>
<td>Patients with recent exacerbation who tolerated NIV and responded well to it</td>
<td>13</td>
<td>Provision of domiciliary NIV service</td>
<td>1 year</td>
<td>Reduction in readmissions and hospital costs</td>
</tr>
<tr>
<td>Clini et al. [47]</td>
<td>Patients with stable COPD, hypercapnic during &gt;6 months of LTOT</td>
<td>90</td>
<td>Randomization to NIV plus LTOT vs. LTOT</td>
<td>2 years</td>
<td>Survival and hospitalization similar, dyspnea and health-related quality of life better in NIV group</td>
</tr>
<tr>
<td>Casanova et al. [46]</td>
<td>Patients with stable severe COPD</td>
<td>52</td>
<td>Randomization to NIV plus standard care vs. standard care</td>
<td>1 year</td>
<td>Survival and exacerbations similar, dyspnea better in NIV group</td>
</tr>
</tbody>
</table>

NIV = Noninvasive ventilation; LTOT = long-term oxygen therapy.
Although COPD and its exacerbations are common and present a major financial burden for most health care systems, there is little information on how to manage patients after hospitalization for COPD in order to optimize care and lower the relapse rates. The data currently available do not allow clear recommendations to be made regarding all the components of a care plan, but they strongly indicate that rehabilitation should be included.

References
Continuous or nocturnal oxygen therapy in