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Predictors of hospital admission and mortality in patients with chronic obstructive pulmonary disease

AM Yohannes
Manchester Royal Infirmary, Manchester, UK

MJ Connolly
University of Manchester, Manchester UK

Introduction

Hospital readmission rates for COPD patients are high, with two-week readmission rates of 22% being recorded in one study of patients with acute exacerbation of chronic obstructive pulmonary disease (AECOPD).[1] In a separate study, patients admitted with $PaCO_2 \geq 50$ mm Hg had a readmission rate of 40% at six months.[2] There are no agreed clinical evidence factors that determine readmission. A few studies have reported that readmission is associated with an individual's inability to cope with the disease, and that anxiety and socioeconomic status are important variables. [3-5] Others argue that readmission relates to severity of lung function abnormality, changes in atmospheric pollution, and impaired quality of life (QoL). [6-9]

In the United Kingdom 81 500 people aged above 65 years died of COPD between 1990 and 1992. [10] During severe AECOPD, inpatient mortality is estimated at between 11% and 14%, [2,11] and this figure is even higher in those patients admitted to the intensive care unit.[12] Inpatient mortality is associated with elevated $PaCO_2$, low bodymass index and low maximal inspiratory mouth pressure.[11,13-14] Conversely, epidemiological studies consistently report that low baseline forced expiratory volume in one second (FEV_1) is the most powerful mortality predictor,[15-18] and that mortality is associated with age.[15,16]

A review of predictors of mortality and hospital admissions is timely, as the morbidity of COPD is projected to increase in the next two decades and COPD-related health-care expenditure is exponentially rising in both Europe and the United States.[19-21]

This review explores the risk factors that may be associated with AECOPD, duration of admission, episodes of readmission and mortality. We have also explored the management of AECOPD and the outcome of rehabilitation programmes for this patient group.

For the review, potentially relevant studies were extracted by searching English-language articles (Medline 1976–2000 and Cinahl 1982–2000). This was complemented by hand-searching of articles reviewed in bibliographies of papers identified as above. The following search terms were used: chronic obstructive pulmonary disease (COPD), hospitalization and mortality. Studies that did not include the term COPD plus either 'mortality' or 'hospitalization' were excluded.

Acute exacerbation and hospital admission

AECOPD is common in elderly patients and costly to treat. An individual may commonly experience one to four mild or severe exacerbations per annum. [22] Severe exacerbations are a frequent cause of hospital admission. Symptoms may include breathlessness, purulent sputum and increased sputum volume. Bacterial respiratory infection is a major cause of admission and commonly reported pathogens [23, 24] in sputum culture may include *Haemophilus influenzae, Streptococcus pneumoniae*, *Staphylococcus aureus, Pseudomonas aerugionsa* and *Moraxella catarrhalis*.

Recent meta-analysis of randomized controlled trials in the use of antibiotics in this situation identified a small but clinically significant benefit of antibiotic use. [25] The British Thoracic Society

Address for correspondence to: AM Yohannes, Manchester School of Physiotherapy Manchester M13 9WL, UK.

guidelines for management of COPD [26] state that patients presenting with two or more of the above-mentioned symptoms of AECOPD should be treated with antibiotics. This guideline challenged the blanket approach which had been used in clinical practice, and suggested a more rigorous investigation that might help physicians to prescribe appropriate antibiotics in order to reduce the emergence of drug-resistant pathogens.

In one UK study, over 10% of all hospital admissions of elderly patients were due to relatively minor COPD exacerbations in individuals who were disabled by respiratory impairment, and for every 1000 elderly patients on a general practitioner list there were 700 GP consultations for AECOPD per year. [27]

Risk factors associated with hospital admission

Chronic mucus hypersecretion (CMH) may be associated with admission episodes in elderly COPD patients. Vestbo *et al.* ,[28] in a longitudinal study, demonstrated that, in patients with CMH, FEV_1 declined at a mean rate of 22.8ml per annum and, after adjusting for FEV_1, relative risk of subsequent hospitalization was approximately 2.5 times that of non-CMH patients, in whom FEV_1 decline was only 12.6ml p.a. In contrast, a previous longitudinal study reported little effect of CMH on COPD prognosis.[29]

Collet *et al.*[30] has suggested the potential benefits of an immunostimulating agent in improving the immune mechanism and possibly the severity of respiratory events that may lead to hospital admission. Conversely, Niewoehner *et al.*[31] investigated the effects of systemic glucocortocoids in AECOPD patients. They showed that glucocorticoids had modest benefit in reducing length of stay and that the benefit was partially maintained for six months.

Recent findings by Bhowmik *et al.*[32] showed that sputum inflammatory markers in the stable state (raised baseline sputum cytokine levels) are good predictors of future episodes of exacerbation. In addition, Kessler *et al.* [33] identified pulmonary hypertension as an independent predictor of hospital readmission.

Repeated exacerbations are associated with loss of self-esteem and decrease in physical activities, in turn leading to impaired quality of life.[7,8] Geraci *et al.* [34] examined the prevalence of in-hospital complications of three chronic conditions: congestive cardiac failure, diabetes and COPD. There was no statistically significant difference in the prevalence rate of complications (15.7%, 14.8% and 13.1%) between the three conditions. The most frequent cause of inpatient complication for COPD patients was theophylline toxicity. Other factors that related to inpatient complications were patient characteristics such as age and presence of co-morbid diseases. For each condition, complications lead to an increased length of stay.

Recently, Dewan and associates,[35] in an elegant study, showed that, after AECOPD, treatment failure defined as 'return visit for persistent respiratory symptoms that required a change of antibiotic in under four weeks', was associated with low FEV_1 (< 35% predicted), use of home oxygen therapy and frequency of exacerbations. In a separate study, recovery from AECOPD was prolonged in those identified with increased dyspnoea and upper respiratory tract infection at the onset of exacerbation. [36] Others have shown that longer *duration* of hospitalization relates to high $PaCO_2$ levels and to antibiotic treatment begun prior to admission.[37]

Sin and Tu [38] investigated short-term versus longer-term hospital stay in elderly patients with AECOPD. Early discharge (less than four days of hospital stay) was associated with a high relapse rate (39% readmission and 45% mortality rate within two weeks) and also increased health-care usage compared to those who stayed longer than four days in hospital.

Cigarette smoking

Elderly COPD subjects who remain active smokers have more rapid deterioration in lung function than ex-smokers.[39,40] Furthermore, continued smoking is associated with impaired QoL and with high health-care resource usage in COPD patients. [41] In one study, it was reported that smoking tended to have a greater impact (more FEV_1 decline) in women[39] than in men. Active smoking has been related to episodes of exacerbations and increased drug prescription.[42] The British Thoracic Society guidelines emphasize [43] the benefits of smoking cessation in reducing health-care usage and averting the spiral of lung function decline. Health-care professionals should play an active role in encouraging smokers to stop, and provide them with appropriate support

and help. A recent editorial review[44] highlighted the benefits of smoking cessation for elderly COPD patients. Smoking cessation programmes should include the provision of advice and education on successful quitting, nicotine replacement therapy, the regular monitoring of the patient's condition and medium-term and long-term support.

Atmospheric pollution and seasonal variation

It is well-recognized[9,45–47] that 'black smoke', smog and exposure to airborne particles and to ozone are causes of emergency hospital admission and GP visits for elderly patients with COPD. Seasonal variations and climatic changes may affect patients' perception of their well-being. Vilkman *et al.*[48] have shown excess hospital admission and relapses of exacerbations in the winter, compared to summer, months. However, perhaps surprisingly, no difference was observed in the seasonal variation in the use of emergency medical services for elderly asthmatic and COPD patients.[49]

Current initiatives to reduce hospitalization

In a controlled study, Gravil *et al.*[50] examined the benefits of a 'hospital-to-home' service for AECOPD patients. AECOPD patients, after formal hospital assessment, were released to be cared for by nurses at home. There was a reduction in treatment costs, number of exacerbations and hospital admissions, and over 80% of subjects were satisfied with the service and happy to be treated at home. Some, though not all, previous studies[51–54] of similar initiatives have demonstrated not only reduced hospitalization but also improved quality of life and sense of well-being, self-esteem and social interaction. A hospital-based intervention study by Tougaard *et al.*[55] claimed that teaching COPD patients about their illness reduces the health-care costs by increasing patients' knowledge of disease and hence their ability to manage themselves.

Clini *et al.*[56] examined the benefits of an intensive home-care programme in three groups of COPD patients with chronic hypercapnia who were randomly allocated to home mechanical ventilation and long-term oxygen therapy (LTOT) *or* LTOT only, *or* control (normal standard treatment). The findings suggested a reduction in subsequent hospital admission in the two 'treated' groups compared to the control group.

Table 1. *Risk factors associated with hospital admission in COPD*

Low FEV_1
Chronic mucus hyper-secretion
Atmospheric air pollution
Flu outbreaks or epidemics
Clinical anxiety
Physical disability
Severity of respiratory impairment
Age
Co-morbid illness
Impaired quality of life

Table 2. *Risk factors associated with mortality in COPD*

Low FEV_1
Age
Low body-mass index
Pulmonary hypertension
Low PaO_2
High $PaCO_2$
Smoking status
Co-morbid illness

Table 1 summarizes the factors recognized to be associated with hospital admission in COPD. A multimodal approach to tackle the problem is clearly needed.

Predictors of mortality in COPD

In England and Wales in the past decade, the number of deaths from COPD has been increasing.[57] Several studies have identified factors associated with mortality in COPD patients (Table 2). Differences in methodology, socioeconomic status of subjects and availability of health-care resources make it difficult to extrapolate from these studies. However, they may act as a platform to identify potential at-risk patients and plan appropriate treatment strategies.

Connors *et al.*[2] examined survival rates in a six-month period after severe AECOPD, and found death was associated with severity of exacerbation, low bodymass index and co-morbid factors, such as presence of corpulmonale and congestive cardiac failure. In longitudinal studies in elderly COPD populations, mortality seems to be associated with smoking status and physical disability.[58–60] Other studies have shown death

rate from COPD to be associated with defects in carbon monoxide transfer,[61] clinical depression and difficulty in coping with the disease,[62] and with cognitive impairment.[63] There also appears to be an unusual inverse association with total serum cholesterol.[64]

Long-term oxygen therapy and survival

Long-term domiciliary oxygen therapy (LTOT) improves survival in COPD patients with chronic hypoxaemia.[65,66] However, in the Nocturnal Oxygen Therapy Trial,[65] mean patient age was 65 years, and the Medical Research Council[66] studied only COPD patients aged < 70 years. In both studies, subjects were predominantly men. The evidence-base for the benefits of LTOT in elderly COPD patients is not known, and research in this area would be valuable. Furthermore, others have been unable to demonstrate the benefits of LTOT in prolonging survival in moderately hypoxaemic COPD patients.[67] Storm[68] investigated the causes of mortality in COPD patients receiving LTOT. Increased mortality was associated with use of oral corticosteroids, poor physical performance and female gender. Others identified the significance of pulmonary artery pressure greater than 30 mm Hg as a prognostic factor for survival in patients receiving LTOT.[69] In this study neither FEV_1 nor degree of hypoxaemia or hypercapnia were mortality predictors. Earlier studies[70,71] have also reported that pulmonary hypertension is a strong predictor of mortality. In the advanced stage of COPD, the presence of hypercapnoea carries a poor prognosis. Zielinski *et al.*[72] investigated the cause of death in elderly LTOT patients and found (not surprisingly) that the majority died from acute or chronic respiratory failure. The survival rate in COPD patients (Table 3) with chronic respiratory failure is generally poor (five-year survival estimated at 27%)[73] This emphasizes the importance of smoking cessation, the only intervention known to limit progression to respiratory failure in COPD.

Socioeconomic status and mortality

Prescot and Vestbo[74] observed that the mortality impact of socioeconomic status on individuals with COPD is enormous and second only to cigarette smoking. The death rate in those with low socioeconomic status was twice that of those in higher social classes. In old age, the impact of COPD is very considerable, as the combination of disease and relative poverty leads to social isolation and an inability to participate in social activities. This in turn may contribute to the high prevalence of depressive symptoms reported in this patient group.[75,76]

In a community survey not exclusive to COPD patients, House *et al.*[77] showed that passive solitary activities (watching television, listening to radio and reading) seem to relate to higher mortality compared to physically active pastimes in old age. Sedentary lifestyle, loneliness and passive solitary activities are a common scenario for many elderly COPD patients.

Co-morbid factors associated with mortality in COPD

Incalzi *et al.*[78] have confirmed that the diseases commonly associated with COPD include hypertension, diabetes mellitus and ischaemic heart disease. Death in this patient group was predicted by ECG signs of right ventricular hypertrophy and

Table 3. *Survival analysis in COPD patients*

Studies	Number	Mean age	Gender M/F	Mean FEV1 in litres	Duration of follow up	Percentage mortality
Gray-Donald *et al.* 1996[14]	348	63	237/ 111	0.71	5 years	47%
Traver *et al.* 1976[16]	200	59	178/22	–	15 years	88%
Vestbo *et al.* 1998[17]	487	67	267/220	–	5 years	45%
Yohannes *et al.* 2000[59]	137	73	69/68	0.89	1 year	16%
Ashutosh *et al.* 1997[62]	16	62	16	0.75	4 years	44%
Oswald-Mamsor *et al.* 1995[69]	84	63	75 / 9	0.83	5 years	48%
Keller *et al.* 1985[70]	87	63	71/16	0.94	3 years	45%
Costello *et al.* 1997[73]	85	68	61/24	0.73	5 years	73%

myocardial infarction or ischaemia, and by chronic renal failure. In addition Lynn *et al.*[79] has shown that nearly 40% of patients with advanced COPD have three or more co-morbidities. A case-controlled study by Cappel and Nadler[80] investigated acute upper gastrointestinal bleeding with and without COPD, and confirmed a higher death rate in COPD sufferers. This bi-directional effect of co-morbid disease on mortality confirms the clinical impression of practitioners.

Comparison of death from asthma and COPD

Cydulka and associates,[22] in an eight-year observational study, compared hospital usage, length of stay and inpatient mortality in elderly COPD sufferers and asthmatics. Elderly COPD patients were twice as likely to die during hospitalization, had longer lengths of stay and higher health care usage. Similar findings were observed in a twenty-year longitudinal study.[81,82] One possible explanation for these differences might be the pathological process of the disease, that is, asthma has reversible characteristics, while COPD is irreversible and, in the presence of continued smoking, is progressive in nature. Keistinen *et al.*[81] suggest that thorough investigations of 'COPD' patients admitted at the first hospitalization or before, should take place, to plan appropriate treatment strategies and in particular to identify reversibility.

Do pulmonary rehabilitation programmes reduce morbidity and mortality?

Recent randomized controlled trials (mean age 62–68 years) have demonstrated the benefits of pulmonary rehabilitation (PR) programmes in improving exercise capacity and quality of life in COPD patients. The benefits of PR may be sustainable for up to 12 months.[83–85] There was no difference in survival or hospital admission between the rehabilitated group compared with the controls,[84,85] but a slight reduction in the length of hospital stay in favour of the rehabilitated group. One would assume that if rehabilitation improves general well-being, then this improvement should be translated to a reduction in morbidity, if not mortality. The absence of such a relationship is puzzling, and further study is worthy of consideration.

Conclusion

AECOPD is a major cause of hospital admission and high health-care usage in elderly patients. Factors associated with hospital admission and mortality in elderly COPD patients are complex and may be physiological, social or environmental. To reduce the health-care expenditure, morbidity and mortality of COPD patients, self-management, education and pulmonary rehabilitation programmes (particularly including smoking-cessation strategies) are essential. Furthermore, early identification of risk factors may help health-care providers, patients and carers in planning appropriate treatment. Finally, discharge planning should include attempts to prevent future episodes of exacerbation and admission by planning follow-up visits, lifestyle management and activity levels, identifying an early-warning system of the signs of exacerbation and providing the support required at home .

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