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Economic and operational burden associated with malnutrition in chronic obstructive pulmonary disease.

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ABSTRACT

Background: Malnutrition is common in patients with chronic obstructive pulmonary disease (COPD). This study aimed to explore its association with all-cause mortality, emergency hospitalisation and subsequently healthcare costs.

Methods: A prospective cohort observational pilot study was carried out in outpatients with COPD that attended routine respiratory clinics at a large tertiary Australian hospital during 2011. Electronic hospital records and hospital coding was used to determine nutritional status and whether a patient was coded as nourished or malnourished and information on healthcare use and 1-year mortality was recorded.

Results: Eight hundred and thirty four patients with COPD attended clinics during 2011, of those 286 went on to be hospitalised during the 12 month follow-up period. Malnourished patients had a significantly higher 1-year mortality (27.7% vs. 12.1%; p = 0.001) and were hospitalised more frequently (1.11 SD 1.24 vs. 1.51 SD 1.43; p = 0.051). Only malnutrition (OR 0.36 95% CI 0.14-0.91; p = 0.032) and emergency hospitalisation rate (OR 1.58 95% CI 1.2-2.1; p = 0.001) were independently associated with 1-year mortality. Length of hospital stay was almost twice the duration in those coded for malnutrition (11.57 SD 10.93 days vs. 6.67 SD 10.2 days; p = 0.003) and at almost double the cost (AUD $23,652 SD $26,472 vs. $12,362 SD $21,865; p =0.002) than those who were well-nourished

Conclusion: Malnutrition is an independent predictor of 1-year mortality and healthcare use in patients with COPD. Malnourished patients with COPD present both an economic and operational burden.

INTRODUCTION

Disease-related malnutrition is a common problem and presents a significant clinical, economic and operational burden to healthcare systems worldwide. Malnutrition has been suggested to attribute to an increase in hospitalisation costs of 20% [1]. In patients with COPD, up to 60% of inpatients and 45% of outpatients have been found to be at risk of malnutrition [2]. According to the Australasian Nutrition Care Day Survey conducted in 56 hospitals across Australia and New Zealand, the overall prevalence of malnutrition was 32% [3]. A previous study also involving 56 hospitals, included 6150 Dutch patients and found a quarter of patients to be malnourished but less than half were identified [4]. Malnutrition is associated with several negative clinical outcomes as patients usually have prolonged convalescence from illness, increased length of hospital stay (LOS) and mortality [5 6]. Whilst the negative association between nutritional depletion and mortality in COPD is well known [7], the association between malnutrition, healthcare use and the subsequent healthcare costs associated with it in COPD patients has not been fully explored.

In Australia, COPD is ranked as having the third highest burden of disease in terms of disability-adjusted life years (DALYs) [8] and affects about 14.5% of all Australian adults above the age of 40 [9]. In 2008-2009, health expenditure directly attributed to COPD in Australia was estimated at $929 million [8] highlighting the economic burden of COPD to the Australian healthcare system. The main treatment goals of COPD are to delay disease progression and reduce the frequency of infective exacerbations [10]. Research has suggested that poor health-related quality of life is associated with the frequency of COPD exacerbations [11] and which is likely to be linked to frequent periods of hospitalisation. In 608 COPD patients hospitalised for an exacerbation in the United Kingdom, patients with a deteriorating nutritional status, indicated by unintentional weight loss exceeding 10% within the 3-6 months preceding the admission, were almost 4-times more likely to be readmitted early [12]. In addition, those patients with a body mass index (BMI) <18.5 kg/m^2 were twice as likely to die during the admission. It is likely that malnutrition is a significant driver of the large burden of COPD to healthcare systems. In the United States it has been estimated that about 88% of the total direct health expenditure attributed to COPD is associated with acute and ambulatory hospital services [13]. In Australia, inpatient hospital services account for more than half of the direct health expenditure attributed to COPD[8] but to what extent this healthcare use is driven by disease-related malnutrition is unclear. Therefore, this study explored the association between malnutrition in hospitalised COPD patients and its impact on mortality, hospital healthcare use and the subsequent healthcare costs.

METHODS

Study Subjects and Study Design

This study utilised electronic hospital records to identify all of those patients that attending the Respiratory Laboratory at Princess Alexandra Hospital for pulmonary function testing during 2011. All patients who had undertaken at least one lung function test during routine respiratory outpatient clinic attendance with a confirmed diagnosis of COPD were included. COPD patients were identified based on FEV_1/FVC <0.7 and FEV_1 <100% predicted. The nutritional status of patients was identified through the diagnosis-related group (DRG) for malnutrition recorded in the hospital records.

Demographic and clinical information such as age, gender, body mass index (BMI), lung function (%FEV_1, %DL_{CO}), and COPD disease severity according to Global Initiative for Chronic Obstructive Lung Disease (GOLD) classification [14] were collected. Additionally, malnutrition status, 1-year healthcare use and admission data (emergency and elective hospitalisation rate and subsequent duration of hospital stay (LOS) and associated costs (AUD$)) as well as 1- and 2-year mortality were collected using electronic hospital records. BMI was classified as underweight (<21kg/m^2), normal weight (21-25 kg/m^2), overweight (>25-30 kg/m^2) and obese (>30 kg/m^2) categories according to the American Thoracic Society/ European Respiratory Society Task Force

[15]. Ethical approval for the study was awarded from the hospital Human Research Ethics Committee and Governance Unit and the Queensland University of Technology (QUT) Research Ethics Unit (TPCH: HREC/13/QPCH/220, QUT: 1300000774). The reporting of this paper also conforms to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) recommendations [16]

Nutrition Assessment

In order to receive a DRG code for malnutrition, patient's nutritional status was assessed using the Subjective Global Assessment (SGA) tool [17] and was completed by a dietitian. The SGA is a validated nutrition assessment tool which involves a clinical domain: assessing weight and dietary intake changes over a period of time, nutrition impact symptoms, functional capacity and a physical assessment domain: assessing fat and muscle wasting, the presence of nutritionally-related oedema and a patient's functional capacity [17]. The SGA categorises patients into three groups, well-nourished, mild/moderately malnourished and severely malnourished. Patients diagnosed as malnourished (mild/moderately or severely malnourished) during their hospital admission were coded as such using the relevant DRG code.

Healthcare Use

Hospital admission data (frequency, LOS, type (emergency or elective)) and costs were also collected from electronic hospital records. Costs related to each hospital admission were estimated using the institution's own health economics modelling techniques which derive costs from DRG codes. All costs were recorded in Australian Dollars (AUD$).

Statistical Analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) for Windows Version 20 (SPSS Inc., Chicago, IL, USA). Continuous variables such as LOS and costs are presented as mean ± standard deviation (SD), unless otherwise stated. Categorical variables such as malnutrition status and 1-year mortality are presented as n (%). A p-value ≤ 0.05 was considered statistically significant.

Differences between two categorical variables were tested using Pearson's chi-square test. Further statistical analyses using purposeful selection with binary logistic regression were also used to predict odds ratios with the associated 95% confidence interval (95% CI) which allowed adjustment for potential confounders associated with mortality. Differences between a categorical and continuous variable were evaluated by comparing their mean ± SD using one-way ANOVA test. Interrogation of the data in this manner allowed identification of independent associations between malnutrition status, healthcare use, mortality and healthcare costs.

RESULTS

Patient Characteristics

A convenience sample of 834 unique outpatients with a confirmed diagnosis of COPD was obtained. Of those outpatients, 286 went on to experience at least one hospitalisation within a year of their test date which allowed their nutritional status to be identified (Figure 1). Characteristics of the patients included are described in Table 1. Compared to those patients that were not hospitalised (n = 548) the patients included in the study (n = 286) were significantly older (mean age 66.6 SD 11.0 years vs. 64.8 SD 11·7 years; p = 0.030) and had a significantly lower BMI (mean BMI 27.4 SD 6.6 kg/m^2 vs. 28.6 SD 7.3 kg/m^2; p = 0.016) using ANOVA analysis. No differences in lung function between the two groups were observed in terms of Forced Expiratory Volume in 1 second (FEV_1), Diffusing Capacity of the lungs for carbon monoxide (DL_{CO}), FEV_1/FVC ratio, and Residual Volume (RV). Patients coded as malnourished had a significantly lower BMI and there was a trend to be older and have a lower diffusing capacity of the lung (Table 1).

Table 1: Patient characteristics

Variables	Nourished (n 239)	Malnourished (n 47)	p-value
Male (%): Female (%)	160 (67%):79 (33%)	34 (72%):13 (28%)	0.469
Age (years)	66.1 (11.3)	69.5 (8.7)	0.054
BMI (kg/m^2)	28.2 (6.6)	23.6 (5.4)	<0.001*
FEV_1 (% predicted)	64.4 (19.6)	60.8 (20.5)	0.260
RV (% predicted)	119.1 (41.0)	123.0 (50.0)	0.691
DL_{CO} (% predicted)	64.4 (20.0)	57.4 (17.6)	0.063

*Results reported are mean (SD) using ANOVA with the exception of age (X^2); BMI = Body Mass Index; FEV_1 = Forced Expiratory Volume in 1s; RV = Residual Volume; DL_{CO} = Diffusing Capacity of the Lung for Carbon Monoxide; * $p < 0.05$.*

Malnutrition and mortality

Compared to the nourished patients, patients classified as malnourished had a significantly higher mortality rate at 1-year (27.7% vs. 12.1%; p = 0.006) and this remained the case at 2-years (40.4% vs. 18%; p = 0.001; X^2 analysis). As the malnourished patients tended to be older and have poorer pulmonary function, binary logistic regression analysis was conducted using purposeful selection adjusting for potential confounders by exploring the whole cohort of 834 outpatients. Age (p <0.001), % FEV_1 (p = 0.019), BMI (p = 0.073) and % DL_{CO} (p = 0.062) were all identified as potential confounders with p values <0.2 and adjusted for within the analysis (Table 2). Malnutrition was found to be a strong independent predictor of 1-year mortality with malnourished patients having almost three times the odds of dying within a year of their initial presentation (OR 2.93 95% CI 1.10, 7.93; p = 0.009). Other than malnutrition, the only other variable found to be significantly and independently associated with 1-year mortality was emergency hospitalisation rate. BMI, $\%FEV_1$, $\%DL_{CO}$, COPD severity and age were not associated with 1-year mortality in regression analysis.

Table 2: Binary logistic regression for predictors of 1-year mortality

Variables	Odds Ratio [95%CI]	p-value
Number of Emergency Admissions	1.55 [1.19, 8.69]	<0.001*
Malnutrition	2.93 [1.10, 7.93]	0.009*
Age	1.04 [0.99, 1.10]	0.120
BMI	0.99 [0.97, 1.02]	0.484
% DL_{CO}	0.99 [0.97, 1.02]	0.507
% FEV_1	0.98 [0.92, 1.04]	0.610
COPD disease-severity (GOLD)	0.59 [0.13, 2.67]	0.935

*BMI = Body Mass Index; FEV_1 = Forced Expiratory Volume in 1s; DL_{CO} = Diffusing Capacity of the Lung for Carbon Monoxide; * $p < 0.05$.*

Similar results were obtained when analysis of time to event was performed using cox-regression survival analysis (Figure 2). Malnutrition (OR 0.42 95% CI 0.19 to 0.91; p = 0.028) and emergency hospitalisation rate (OR 1.37 95% CI 1.15 to 1.62; p < 0.001) remained significant independent predictors of mortality.

Malnutrition and costs associated with hospitalisation

Following emergency hospital admission, malnourished patients were found to have a significantly longer LOS than nourished patients; mean LOS 11.57 SD 10.94 days vs. 6.67 SD 10.21 days; difference +4.9 SE 1.65 days 95%CI 1.65-8.15 days; p = 0.003. Similar results were also found when emergency and elective lengths of stay were combined (malnourished 22.51 SD 19.40 days vs. nourished 11.26 SD 14.67 days; difference +11.3 SE 2.48 days 95%CI 6.4-16.1 days; p<0.001). With malnourished patients remaining hospitalised for almost twice the duration as nourished patients, the resulting costs were also significantly higher in the malnourished group; mean cost $23,652 SD $26,472 vs. $12,362 SD $21,865; difference +$11,290 SE $3,618 95%CI $4,168-$18,411; p = 0.002 (Figure 3). Similar results were also found when analysing the costs associated with non-emergency admissions (malnourished $38,833 SD $25,770 vs. nourished $21,468 SD $27,747; difference +$17,365 SD $4,659 95% CI $8,195-$26,535; p<0.001).

DISCUSSION

This is the first study to evaluate the impact of malnutrition on hospitalisation, healthcare costs and mortality in patients with COPD. Malnutrition was found to be a significant and independent predictor of mortality, with malnourished patients almost three times greater odds of dying within a year. Whilst the negative association between nutritional depletion and survival in COPD is well known, previous survival analysis has shown that appropriate nutritional therapy resulting in weight gain is associated with improved survival [18]. However, it is yet to be established whether improved survival following the treatment of malnutrition is also associated with reduced healthcare use. In the current study, patients coded as malnourished during their hospital admission remained hospitalised for almost twice the duration as their nourished counterparts, at almost double the cost. Whilst previous studies have not formally diagnosed malnutrition, they have reported nutrition status, defined by various means, to be associated with increased mortality and healthcare use. In a study of patients requiring long-term oxygen therapy, a BMI <20 kg/m^2 was found to be an independent risk factor for increased mortality and hospitalisation [19]. Analysis of COPD patients from the Copenhagen City Heart Study reported BMI to be independently associated with all-cause mortality [20]. More recent retrospective cohort study involving over 300,000 COPD hospital admissions discovered obese patients to have lower in-hospital mortality and a lower risk of early readmission compared to non-obese patients [21]. The authors also found that non-obese patients had a considerably higher risk of mortality during hospitalisation and readmission within 30 days of discharge. However, full nutritional assessment and malnutrition status was not assessed.

With an increased focus on reducing the duration of hospital stay and avoidance of hospital readmission, all but the sickest patients are managed in the outpatient setting. This reduces the opportunity within which hospitalised COPD patients at nutritional risk can be identified, seen by a dietitian for nutritional assessment and the initiation and evaluation of individualised nutritional support. In order for this to occur, robust policies documenting the nutritional management of COPD patients are required. The first step is for malnourished patients to be promptly identified, either in the community or on admission. Whilst there is currently no universally accepted method for the identification of malnutrition, there are several validated nutritional screening and assessment tools available. Most nutritional screening tools involve an assessment of recent unintentional weight loss and BMI is also often recommended as a routine marker of nutritional status [22 23]. However, there is no consensus around what the BMI cut-off for nutritional risk in COPD should be, with recommendations of <20 kg/m^2 (NICE [23]) and <21 kg/m^2 (ATS/ERS [22] and BODE index [20 24]). In addition, it appears that there are currently no guidelines around the management of COPD that formally recommend routine nutritional screening and nutritional assessment. Whilst BMI has good predictive validity for survival and hospitalisation [19] and is a pragmatic measurement routinely advocated by guidelines, it is not without its limitations. Depletion of fat-free mass that is common in COPD [25] can be masked by an expansion of fat-mass impacting on the sensitivity of BMI as a marker of nutritional depletion and risk. This was highlighted in a study of 300 outpatients with COPD where a BMI <20 kg/m^2 was reported in 17% of patients but more than double (38%) had fat-free mass depletion [26]. If BMI alone is used as a method of identifying nutritional risk, a significant proportion of patients would go unidentified. Indeed, a recent review by Schols et al., [27] suggests that fat-free mass might be a better predictor of mortality in COPD patients than BMI alone. The current study found BMI to be a less sensitive predictor of survival, rather rate of emergency hospitalisation and comprehensive nutritional assessment allowing diagnosis of malnutrition had much stronger associations with poor survival.

The current findings that malnourished COPD patients experience greater emergency healthcare use and longer durations of hospital stay are consistent with previous studies in other patient groups that have reported prolonged LOS [28-30], higher rate of readmission rates[28 29], increased pressure ulcer incidence and delayed wound healing [5 31]. However, it is often thought that malnutrition is a consequence of the progressive pathophysiology associated with COPD; with those with the more severe disease having poorer respiratory function and elevated inflammatory processes contributing towards the development of malnutrition and subsequent poorer survival [7]. The current study attempted to account for this by adjusting for COPD disease severity, age and lung function, finding that only malnutrition and emergency hospitalisation rate to be independently associated with poorer survival. Due to the observational nature of the study, it is the difficult to establish exact causation between the two independent predictors and whether patients are more likely to become malnourished following recurrent bouts of emergency hospitalisation or whether those patients with malnutrition more likely to have infective exacerbations of COPD requiring hospitalisation. The aetiology of malnutrition in COPD is multi-factorial and complex and both are likely to be related. However, recent systematic review and meta-analyses have shown that if malnutrition is identified in COPD, it is amenable to treatment, resulting in significantly improved nutritional status, functional capacity and associated with improvements of quality of life [32 33]. Interestingly, the reviews found that nutritional support in stable COPD outpatients resulted in an increase in body weight of approximately 2kg and it is this level of weight gain that has previously been associated with improved survival in malnourished COPD patients [18]. Whilst the evidence base for nutritional intervention in stable (non-exacerbating) outpatients with COPD is strong, it is almost entirely based on liquid pre-prepared oral nutritional supplements (ONS). There is limited evidence demonstrating the effectiveness of other forms of nutritional intervention such as fortified meals and dietary counselling provided by a dietitian. However, this lack of evidence does not indicate a lack of effect. Also, few studies have attempted to investigate the effectiveness of nutritional support in acutely unwell hospitalised COPD patients. One reason for this is the difficulty in intervening in an acute unwell population with a relatively short length of admission. Whilst the average hospital length of stay for the nourished patients in the current study was less than a week, the malnourished patients tended to stay on average 5 days longer. Vermeeren et al., [34] found that whilst nutritional support using ONS was able to significantly increase energy and in particular protein intake during the average 9 days admission period it did not lead to any improvements above that of the control group. The authors highlight the difficulty in achieving theoretical nutritional requirements during an infective exacerbation through the normal hospital diet alone without nutritional support. It is likely that nutritional interventions need to be longer in duration for improvements to be seen with studies in stable COPD outpatients usually lasting between 8-12 weeks [33]. A previous study by Weekes et al., [35] involving stable malnourished outpatients with COPD found dietetic counselling over 6 months not only resulted in significant improvements in nutritional status and quality of life but these improvements remained at 12 months. However, further research is needed to establish whether nutritional interventions initiated promptly on admission in malnourished COPD patients, and continued for an appropriate period of time, can lead to improvements in nutritional status and reduced subsequent healthcare use and costs.

Whilst the current study involved a large enough sample size to perform regression analysis adjusting for confounders, it isn't without limitations. Although a large sample, it is from a single large tertiary hospital. Therefore extrapolation of results should be done with caution. Electronic medical record data on hospitalisation and duration of stay was only available for that hospital site and if patients were admitted to surrounding hospitals this information would not have been captured. The current sample was also limited by the fact that comprehensive nutritional assessment and the diagnosis of malnutrition was only possible in those patients admitted to hospital. Current local policy meant that routine nutritional screening was not part of outpatient clinical appointments. The prevalence of malnutrition in the 286 patients that went on to experience a hospital admission in the current study at 16%, whilst this is comparable to previous rates reported of 19%[36] and 24% [37] these studies used a BMI threshold of <20 kg/m^2. As the current study used full nutritional assessment using the Subjective Global Assessment, 16% would appear to be an underestimate of the true malnutrition prevalence. In a study that used BMI and assessment of FFM to diagnose malnutrition the prevalence was 38% [38]. It is possible patients were not documented on the electronic hospital records as malnourished, this is common in COPD and has been found to be the case in another Australian hospital [39]. However, it is felt that undiagnosed malnutrition in the current study will only have had the potential to reduce the magnitude of the current estimates and we feel the conclusions would remain unchanged.

In conclusion, disease-related malnutrition in COPD is independently associated with a significant clinical, economic and operational burden to hospitals. Malnutrition and emergency hospitalisation was also associated with poorer survival. Whilst malnutrition in COPD patients has been found to be amenable to treatment through nutritional support, the evidence is almost entirely based on stable outpatients and it is hoped future well-designed prospective nutritional intervention studies will explore the impact of early nutritional assessment and nutritional interventions on clinical and economic outcomes.

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