RESPIRATORY MEDICINE (1998) **92**, 772–776

Vital prognosis after hospitalization for COPD: A study of a random population sample

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Study aim: To examine survival after admission due to chronic obstructive pulmonary disease (COPD) in a population sample over a time span of 15 years.
Design: Linkage between a prospective population cohort and register information on hospitalization and mortality.
Setting: The Copenhagen City Heart Study (CCHS).
Participants: A total of 267 men and 220 women who had participated in the CCHS and who were hospitalized with a discharge diagnosis of COPD (ICD-8 491-2).
Main results: The crude 5-yr survival rate after a COPD admission was 45% (37% for men and 52% for women). Mortality risk increased with age and with decreasing forced expiratory volume in 1 s (FEV_1)% predicted; for subjects with an FEV_1 $\leq$40% at the CCHS survey, 5-yr survival after subsequent hospitalization was only 28%. Smoking and presence of chronic mucus hypersecretion at the examination in CCHS were not strongly associated with prognosis. Survival after admission due to COPD did not change significantly over time.
Conclusion: Compared to previous studies of COPD patients, the present study indicates that prognosis after hospital admission remains virtually unchanged over the last decades. FEV_1 is still the strongest predictor of survival in this patient group.

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Introduction

Knowledge on prognosis in chronic obstructive pulmonary disease (COPD) is mainly derived from studies of carefully selected patient groups followed by observant clinicians (1–8). These studies have all shown prognosis to be related to age (1,5,6), forced expiratory volume in 1 s (FEV_1) (1–7) and other lung function indices (1,5,6). Some studies have also shown a prognostic value in markers of cardiac involvement (3,4,8). Depending on severity of disease, 5-yr mortality rates have varied from 20 to 50%. Whereas these studies have been valuable in demonstrating the remarkably strong predictive value of FEV_1 and other variables, they all potentially have limited value due to the fact that they represent selected groups of patients. Only the Tucson study has looked at subjects from a sample of the general population (9). Also, virtually all studies published have predominantly included men and surprisingly little is known about the prognosis of female COPD patients. Finally, a growing disadvantage with many of the above cited studies is the fact that they are old. More widespread use of long-term oxygen therapy and perhaps the growing use of inhaled steroids in this patient group may have improved prognosis.

The aim of this study was to make use of a nationwide register of all admissions to somatic hospital wards by linking it with information from an ongoing epidemiologic survey with information on smoking habits, self-reported health including respiratory symptoms, and lung function for the purpose of examining vital prognosis after admission due to COPD.

Received 8 August 1997 and accepted in revised form 2 January 1998.
Supported by: The National Union against Lung Diseases, The Danish Heart Foundation, and The Danish Medical Research Council.
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Subjects and Methods

POPULATION

The study population comprised a random, age-stratified sample of 19 327 subjects out of 87 172 aged 20 years or

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more, living in a defined area around Rigshospitalet in Copenhagen, Denmark in 1976. In 1976–1978, The Copenhagen City Heart Study (CCHS) examined 14 223 subjects (response rate 73·6%); a detailed description of the study procedure has been published previously (10). Recordings of FEV_1 and forced vital capacity (FVC) were made on an electronic spirometer (Monaghan N 403, Littleton, CO, U.S.A.), which was calibrated daily. As a criterion for correct performance, at least two measurements differing by less than 5% from each other had to be produced. The largest volume was used in the analyses. FEV_1% predicted was calculated using predicted values for FEV_1 based on the following equations, derived from never-smokers with a daily consumption of alcohol of less than five drinks who did not suffer from asthma, diabetes mellitus or heart disease, and had no pulmonary symptoms (11):

Women: FEV_1 (ml) = 410 − 27·6 × age (years) + 21·2 × height (cm)

Men: FEV_1 (ml) = −469 − 35·2 × age (years) + 32·0 × height (cm)

Respiratory symptoms were assessed using questions from the British Medical Research Council questionnaire (12). Chronic mucus hypersecretion was considered present when cough and sputum had lasted at least 3 months for more than 1 yr.

Different measures of smoking were used. All subjects reported whether they were current smokers, ex-smokers or never-smokers, their present amount and type of tobacco smoked (cigarette = 1 g, cheroot = 3 g and cigar = 5 g), smoking history, and if they inhaled at present. In the analyses presented here, pack-years and inhalation (yes/no) was used together with the following categorization: never-smokers, ex-smokers, light smokers reporting 1–14 g daily; medium smokers reporting 15–24 g daily; and heavy smokers reporting 25+ g daily.

HOSPITALIZATION AND FOLLOW UP

Information on time of hospitalization and diagnoses on discharge in the period from the survey to 31 December 1992 was obtained from the National Patient Register administered by the National Board of Health. This nationwide register, established in 1977, contains all admissions to somatic hospital wards. Diagnoses are classified at discharge by hospital doctors, in the study period according to the International Classification of Disease, eight revision (13). In this study, only the first main diagnosis was used and only hospitalizations of 24 h duration or longer were included. Hospitalizations were classified as caused by COPD for ICD-8 diagnosis codes 491-2. No information on smoking, symptoms or lung function from the time of hospitalization was available. The follow-up concerning vital status covers the period from the hospital admission to 9 January 1995.

TABLE 1. Hospitalization during follow-up according to gender, age and level of FEV_1

	Sex (M/F)	Admitted because of COPD M/F (10^{-5} person-years)
FEV_1		
80+% predicted	3772/4798	41/45 (0·20/0·16)
60–79% predicted	1910/2124	77/73 (0·81/0·66)
40/59% predicted	537/512	77/64 (3·28/2·42)
− 39% predicted	166/97	65/31 (11·50/7·26)
Age		
20/49 yr	2460/2835	5/8 (0·033/0·045)
50–59 yr	2013/2791	35/41 (0·33/0·25)
60/69 yr	1580/1657	111/97 (1·63/1·10)
70+ yr	458/429	116/74 (8·12/4·14)

STATISTICAL METHODS

When comparing continuous and dichotomous variables between groups, *t*-tests and chi-square tests were used. Survival after hospital admission was compared using Kaplan-Meier plots and was further analysed using a multivariate Cox Regression model (14,15). Time from first hospitalization due to COPD and 5 yr later was used as time variable. Regression coefficients were estimated by the maximum partial likelihood method as suggested by Cox.

Results

During follow-up after the 1976–1978 survey, 267 men (4·1%) and 220 women (2·9%) were hospitalized for COPD. Hospitalization was evenly distributed over time after the first survey in the Copenhagen City Heart Study. As shown in Table 1, admission was strongly associated with FEV_1 and age in both men and women. The mean age at the time of first registered admission due to COPD was 68·3 yr for men and 66·0 yr for women (P=0·003) and mean FEV_1% predicted at the CCHS survey was 56·9% for men and 63·5% for women (P>0·001).

PREDICTORS OF SUBSEQUENT SURVIVAL

The association between lung function and survival is shown in Fig. 1. Patients with an FEV_1 of 80+% predicted at the preceding examination in CCHS had a 5-yr survival after hospital admission of 60%; for subjects with an FEV_1

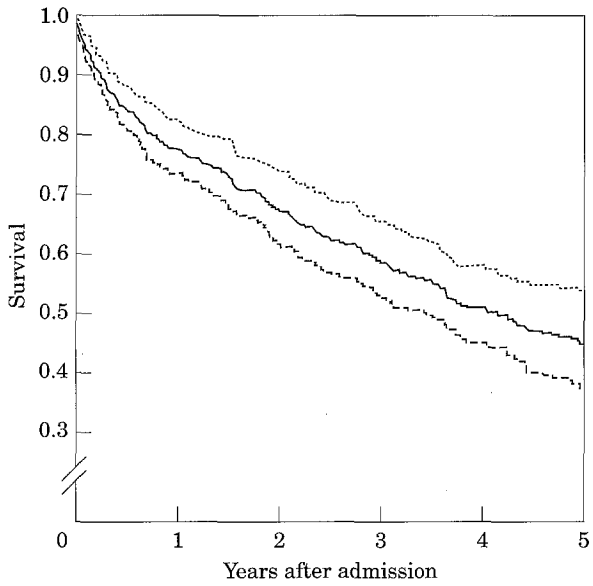

FIG. 1. Survival after COPD admission. ——, all; · · · ·, women; – – –, men.

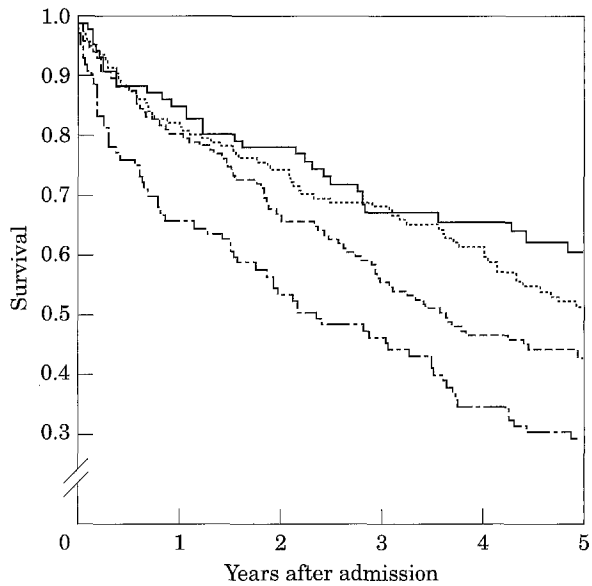

FIG. 2. Survival after COPD admission according to level of FEV_1 at the Copenhagen City Heart Study survey. ——, 80+% predicted; · · · ·, 60–79% predicted; – – –, 40–59% predicted; –·–·, – 39% predicted.

of 60–79%, 40–59% and less than 40%, 5-yr survival was 50, 42 and 28%, respectively. Smoking was not strongly associated with prognosis. Although there was a trend towards poorer prognosis with increasing daily consumption and with number of pack-years, the only smoking variable significantly associated with mortality was inhalation relative risk [(RR)=1·51 (1·19–1·92)] compared to non-inhalers after controlling for age and gender. There were no interactions between gender and smoking variables examined. Presence of chronic mucus hypersecretion at the examination in CCHS had no significant impact on survival within the first 5 yr after hospital admission.

As shown in Fig. 2, the 5-yr survival differed between men and women. The crude 5-yr survival rate after a COPD admission was 45 (37% for men and 52% for women). The gender difference in prognosis after hospitalization was examined using a Cox Regression model. The mortality risk increased with age (RR 1·64 per decade, 95% confidence interval 1·43–1·87) and with decreasing FEV_1% predicted; compared to subjects with an $FEV_1 \geq 80\%$, RR was 1·18 (0·83–1·68), 1·65 (1·17–2·34) and 2·17 (1·50–3·14) for those with an FEV_1 of 60–79, 40–59 and <40% predicted, respectively. After adjusting for age at the time of admission and FEV_1 at the preceding examination in CCHS, men still had a significantly increased risk [RR=1·31 (1·04–1·64)] compared to women. Further adjusting for smoking category or number of pack-years did not affect this gender difference, whereas inclusion of tobacco smoke inhalation in the Cox model weakened the difference [RR=1·18 (0·91–1·52)].

A total of 82 subjects with subsequent COPD hospitalization had answered affirmatively to the question 'Do you have asthma?'. These subjects had a slightly more favourable prognosis with a mortality risk of 0·70 (0·51–0·95) compared to non-asthmatics after adjusting for age, gender and FEV_1 in a Cox model. Separate from their COPD admission, the other 88 subjects had been admitted to hospital and discharged with a diagnosis of asthma (ICD-8 493) at some time during follow-up. An admission coded as 'asthma' did not change prognosis significantly [RR=0·79 (0·59–1·07)].

CHANGES IN PROGNOSIS OVER TIME

In order to examine possible trends in prognosis over time, follow-up after the CCHS survey was divided into two periods. First, 125 admissions during the initial 5 yr of follow-up after the CCHS survey was excluded because of the obvious risk of bias, as the authors had no way of ascertaining that these admission were first admissions. The subsequent follow-up was divided into Period 1 covering 6–10 yr after the CCHS survey, and Period 2 covering 11–15 yr after the CCHS survey. As shown in Fig. 3, there was a tendency towards a poorer prognosis in Period 2 for women, whereas no difference was seen in men. Some of this difference may be due to a difference in mean age at time of hospitalization, which rose from 66·4 yr in Period 1 to 69·6 yr in Period 2.

Discussion

In this random population sample, the crude 50yr survival after ad mission due to COPD was found to be 45%, primarily dependent on lung function. Survival was not markedly better than reported previously and did not improve over the period under observation. In fact, these findings do not differ from those of Boushy *et al.* from 1973 (1). In their follow-up of 663 patients with COPD, 5-yr survival varied from 67% for those with FEV_1 >1·14 l to 56% in those with FEV_1 0·75–1·14 l and 20% in those with

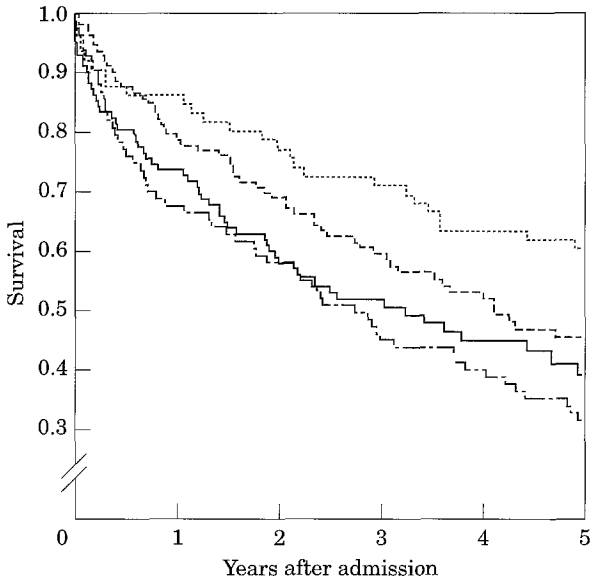

FIG. 3. Survival after COPD admission according to time period. Survival is shown for each gender; Period 1 approximately covers the calendar period 1981–1986 and Period 2 covers 1987–1992. · · · ·, women, Period 1; – – –, women, Period 2; ——, men, Period 1; –·–·, men, Period 2.

FEV_1 <0·75 l. This poor prognosis is somewhat surprising since earlier patient series have been collected at specialized departments thus selecting more severely ill COPD patients. It is, however, possible that hospitalization occurs at a relatively late stage of the disease and because of this, little can be done to alter the subsequent course of the disease significantly. It is possible that more rigorous attempts of smoking cessation in this patient group could improve prognosis, and long-term oxygen therapy could also have this effect. Especially in the beginning of the authors, observation period, long-term oxygen therapy was not used extensively in Denmark.

Women were significantly younger than men at the time of hospitalization, and it is difficult to imagine that this is due to some spurious bias in the design. Furthermore, women had better lung function at the CCHS survey prior to hospitalization. These differences could be interpreted in several ways. It is possible that women seek care earlier in the course of their COPD than men, and that the differences in age and FEV_1 are merely reflections of increased use of medical care. On the other hand, women who develop COPD may do so more rapidly than men. This has been suggested by previous analyses in the authors' cohort (16) in which the crude FEV_1 decline in smoking females was almost similar to that of smoking males in spite of their obvious differences in lung volume and where women were hospitalized more often than men because of COPD (17). Similar findings indicating a higher susceptibility to smoking among women have been reported from other population studies (18–20). If women develop COPD more rapidly than men, they may experience worsening of lung function at an earlier stage and this could, to some extent, explain the higher FEV_1 in women. Also, comparison of FEV_1% predicted between men and women should be made with caution since reference values for the two genders may differ. The observed better vital prognosis in women than in men after admission most likely favours women seeking care earlier in the course of their lung disease.

Interestingly, prognosis in subjects with self-reported asthma and subjects who had also been admitted because of asthma was more favourable than in those who had been admitted solely for COPD. In general, subjects with self-reported asthma have an increased mortality (21). In patients hospitalized with COPD, however, self-reported asthma and hospital admission classified as asthma may indicate beneficial features such as a higher degree of reversibility. This would be in accordance with findings of Burrows *et al.* (9) who found a much better survival in subjects with asthma and asthmatic bronchitis than in patients with irreversible and emphysematous COPD. The present authors do not think that prognosis was better as a result of asthmatics being misclassified as COPD on admission. From clinical experience, the opposite situation seems much more likely.

The major disadvantage of the present study is the fact that several of the examined characteristics were recorded at the CCHS survey which, in most cases, took place years before hospitalization. Also, there is a limited range of variables of interest as the epidemiological survey included more than 10 000 subjects. Study size alone precluded measurements of arterial blood gases and pulmonary artery pressure, which have been reported to have significant prognostic value in previous studies. In spite of these shortcomings, FEV_1 recorded at the CCHS survey was a strong predictor of subsequent survival. Other potential prognostic indicators such as smoking and chronic mucus hypersecretion played no major role in the present study. Both have a strong predictive value concerning hospitalization for COPD (16,22), and the present negative findings may be due to the fact that they were recorded at the CCHS study. However, predictors of hospitalization may not necessarily be predictors of subsequent prognosis as, for example, smoking may have played its role in reducing FEV_1which would thus include the effects of smoking. The same could, to some extent, be said for chronic mucus hypersecretion, although a previous analysis on data from CCHS showed an association between chronic mucus hypersecretion and death from COPD related to infection (23). Usually, epidemiological studies rely on firmly established baseline data and often less clearly defined end-points. In the present study, the opposite seems to be the case. The exact time of hospitalization may not represent exactly the same degree of severity of disease influencing the starting point of survival analysis (24). In contrast to this, the present study end-point is well-defined and, in general, the authors believe that this register linkage nested in a prospective cohort study will yield less biased results than follow-up of patient materials from selected hospital departments. From these findings, it does not seem that vital prognosis after COPD hospitalization is more favourable than what has been described in previous, more selected, patient materials.

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