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Emphysema and Pulmonary Impairment in Coal Miners: Quantitative Relationship with Dust Exposure and Cigarette Smoking

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Abstract. Coal miners have been shown to be at increased risk of developing chronic obstructive pulmonary diseases including emphysema. The objective of this study was to determine whether lifetime cumulative exposure to respirable coal mine dust is a significant predictor of developing emphysema at a clinically-relevant level of severity by the end of life, after controlling for cigarette smoking and other covariates. Clinically-relevant emphysema severity was determined from the association between individuals’ lung function during life (forced expiratory volume in one second, FEV 1 , as a percentage of predicted normal values) and emphysema severity at autopsy (as the proportion of lung tissue affected). In a logistic regression model, cumulative exposure to respirable coal mine dust was a statistically significant predictor of developing clinically-relevant emphysema severity, among both ever-smokers and never-smokers. The odds ratio for developing emphysema associated with FEV 1 <80% at the cohort mean cumulative coal dust exposure (87 mg/m 3 x yr) was 2.30 (1.46-3.64, 95% confidence limits), and at the cohort mean cigarette smoking (among smokers: 42 pack-years) was 1.95 (1.39-2.79).

1. Introduction
Emphysema is characterized by abnormal, permanent enlargement of the airspaces distal to the terminal bronchiole, with destruction of their walls, and it is assessed morphologically at autopsy [1] or by computerized tomography. Emphysema is classified by type and severity (as percentage of the lung tissue affected) using standardized schema [2-4]. Previous studies have shown that emphysema severity is associated with cumulative dust exposure in U.K. coal miners [5], and with coal dust lung burden in Australian and U.S. coal miners [6, 7]. Emphysema severity has also been associated with lung function deficits during life in Australian coal miners [6] and in African gold miners [8]. An
inverse relationship was observed between the emphysema severity at autopsy and FEV$_1$ in those studies [6, 8].

In this study, we quantitatively examine the relationship between emphysema severity, cumulative dust exposure, and other parameters in an autopsied population of U.S. coal miners and non-miners [7]. The effects of cumulative dust exposure and cigarette smoking on the probability of developing clinically-relevant emphysema severity were estimated in this cohort.

2. Methods

The study group consists of 722 autopsied individuals, including 616 coal miners from southern West Virginia and 106 non-miners from West Virginia and Vermont who died during 1957-1978. Characteristics of the full study population are described elsewhere [7, 9]. Briefly, data on work history, smoking, race, and age at death were obtained from medical records and questionnaire completed by next-of-kin. Cumulative dust exposures for each miner were estimated using individuals’ work history data and job-specific measurements of the airborne mean concentration of respirable coal mine dust, based on a method by Attfield and Moring [10]. Whole lung sections were prepared from sagittal slices of left lung and classified and graded by two pathologists (FHYG and VV) using standardized schema [2, 3]. Each of the 10 lung zones was graded for emphysema severity up to a maximum score of 100 for each zone, for a possible maximum score or index of 1000 for an individual’s lungs (the total emphysema severity index divided by 10 is equivalent to the percentage of the total lung tissue affected). In a subset of 116 individuals, data were available on FEV$_1$ from spirometry tests during life. A smaller subset of 65 miners had FEV$_1$ tests performed within 5 years of death, which is a criterion used in previous studies [6, 8]. The spirometry methodology in these U.S. coal miners was reported previously [11].

Clinically-relevant emphysema severity was defined in this study based on the relationship between emphysema severity at autopsy and lung function during life and on the standardized criteria for clinically-relevant pulmonary impairment. These standardized criteria include FEV$_1$ <80% of predicted normal values – approximately equal to the 5th percentile lower limit of normal [12, 13] – and FEV$_1$ <65% of predicted normal values – which has been associated with severe exertional dyspnea in U.K. coal miners [14, 15]. The emphysema severity index associated with an FEV$_1$ of either 80% or 65% of the predicted normal values was calculated from a linear regression model of the relationship between FEV$_1$ and emphysema severity index in the subset of individuals with FEV$_1$ data (n=116). Nonlinearity in this relationship was tested by the addition of a quadratic term for FEV$_1$. The emphysema severity indexes associated with an FEV$_1$ of either 80% or 65% (of predicted normal values) were used as cutoff-points for clinically-relevant emphysema, and treated as dichotomous response variables in logistic regression models. An individual was coded as a responder if his emphysema severity index was greater than these defined cut-off values.

Logistic regression models [16] of the expected proportion of responders in this cohort were used to estimate the probability of disease (i.e., emphysema severity index associated with FEV$_1$ <80% or <65%). The predictor variables in these models, which were identified in the full analysis of this cohort [9], include: cumulative exposure to respirable coal mine dust, age at death, race (white/non-white), and pack-years of smoking. The probability of developing clinically-relevant emphysema was estimated at various values of these predictor variables. Statistical tests (Wald) were performed to compare the effects of cumulative dust exposure and cigarette smoking.

3. Results

3.1. Study characteristics

The characteristics of this study population include: 85% miners; 78% ever-smokers; 72% whites; 64.6 years average age at death; 42.4 average pack-years of smoking (among smokers). For the subset of individuals for whom FEV$_1$ data were available (n=116), 98% were miners; 87% were ever-
smokers; 71% were whites; average age at death was 64 years; and average pack-years of smoking (among smokers) was 41.4 years.

3.2. Emphysema severity and FEV\textsubscript{1}

Figure 1 shows the relationship between the emphysema severity index and FEV\textsubscript{1} (p<0.0001; R\textsuperscript{2}= 0.17) among the 116 individuals with FEV\textsubscript{1} data. A quadratic term for FEV\textsubscript{1} was not significant (p=0.064). The mean emphysema severity index associated with 80% FEV\textsubscript{1} was 285, and the mean emphysema severity index associated with 65% FEV\textsubscript{1} was 392. These values were used as the cutoff-points to define clinically-relevant emphysema severity in the logistic regression models. Similar values were obtained among the 65 individuals with FEV\textsubscript{1} data within five years of death; i.e., the mean emphysema severity index associated with 80% or 65% FEV\textsubscript{1} was 277 or 383, respectively.

![Figure 1](image_url)

**Figure 1.** Relationship between emphysema severity index and forced expiratory volume in one second (FEV\textsubscript{1}) (as percentage of predicted normal values); data for 116 individuals with FEV\textsubscript{1} fit with a simple linear regression model.

3.3. Logistic regression models

Tables 1 and 2 show the logistic regression modeling results for the expected proportion of individuals developing an emphysema severity index associated with FEV\textsubscript{1} <80% or <65%, respectively, by the end of life. Cumulative exposure to respirable coal mine dust, age at death, and race are statistically significant predictors of developing either of these clinically-relevant degrees of emphysema. No significant interactions were observed, although a pack-year x age interaction was observed in the main analysis of this cohort in a weighted least squares linear regression model [9].
Table 1. Logistic Regression Model: Predictors of Emphysema Severity Associated with FEV$_1$ <80\% (of predicted normal values)$^a$

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Estimated Coefficient</th>
<th>Standard Error</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>-5.0</td>
<td>0.83</td>
<td></td>
</tr>
<tr>
<td>Cumulative exposure (mg/m$^3$ x years)</td>
<td>0.0095</td>
<td>0.0027</td>
<td>0.0004</td>
</tr>
<tr>
<td>Cigarette smoking (packs/day x years)</td>
<td>0.016</td>
<td>0.0042</td>
<td>0.0002</td>
</tr>
<tr>
<td>Age at death (years)</td>
<td>0.048</td>
<td>0.012</td>
<td>0.0001</td>
</tr>
<tr>
<td>Race (non-white)</td>
<td>0.88</td>
<td>0.28</td>
<td>0.002</td>
</tr>
</tbody>
</table>

$^a$N=342 miners and non-miners. Likelihood ratio (4 d.f.)=75.1, p<0.0001.

Table 2. Logistic Regression Model: Predictors of Emphysema Severity Associated with FEV$_1$ <65\% (of predicted normal values)$^a$

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Estimated Coefficient</th>
<th>Standard Error</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
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<tr>
<td>Cumulative exposure (mg/m$^3$ x years)</td>
<td>0.010</td>
<td>0.0027</td>
<td>0.0003</td>
</tr>
<tr>
<td>Cigarette smoking (packs/day x years)</td>
<td>0.0099</td>
<td>0.040</td>
<td>0.01</td>
</tr>
<tr>
<td>Age at death (years)</td>
<td>0.036</td>
<td>0.012</td>
<td>0.003</td>
</tr>
<tr>
<td>Race (non-white)</td>
<td>0.80</td>
<td>0.28</td>
<td>0.004</td>
</tr>
</tbody>
</table>

$^a$N=342 miners and non-miners. Likelihood ratio (4 d.f.)=56.3, p<0.0001.

Based on the model in Table 1, the odds ratios of developing emphysema associated with <80 \% FEV$_1$, for one unit of increase in either cumulative coal dust exposure or pack-years of cigarette smoking, were: 1.010 (1.004-1.015) and 1.016 (1.008-1.024), respectively (as point estimate and 95\% confidence interval, CI). For emphysema associated with <65 \% FEV$_1$ (Table 2), these odds ratios were: 1.010 (1.005-1.015) and 1.010 (1.002-1.018), respectively, for one unit of increase in either cumulative coal dust exposure or pack-years of cigarette smoking. The effects of cumulative dust exposure and cigarette smoking were not statistically significantly different at either disease response (p-values: 0.2 and 1.0, respectively).

In separate models by smoking group (ever, n=405; never, n=115), the effect of cumulative coal dust exposure (mg/m$^3$ x yr) on clinically-relevant emphysema remained statistically significant in each group (p<0.05 among ever smokers and p<0.01 among never smokers), although the coefficients for cumulative exposure were higher among never smokers. For example, in the model for emphysema associated with <65\% FEV$_1$, the coefficients (and standard errors) were: 0.0077 ($\pm$0.0031) among ever smokers, and 0.016 ($\pm$0.0057) among never smokers.

Figure 2 shows the probability of developing clinically-relevant emphysema (associated with FEV$_1$ <80\% or <65\% of predicted normal values) with increasing cumulative exposure to respirable coal mine dust, based on the models shown in Tables 1 and 2. These relationships are illustrated for either ever-smokers or never-smokers, among whites, at the cohort-average age-of-death and pack-years of smoking (among smokers). A background probability (i.e., among individuals without dust exposure) of developing these degrees of emphysema severity is predicted to be approximately 10-20\%, with the
higher levels predicted among smokers. The probability of developing either level of emphysema severity is predicted to increase with increasing cumulative exposure to respirable coal mine dust. The probability of developing emphysema associated with <80% FEV\textsubscript{1} is greater than that for developing emphysema associated with <65% FEV\textsubscript{1}, which is expected since emphysema severity of lower degree is more prevalent than emphysema of a more severe degree.

![Figure 2. Relationship between the probability of developing clinically-relevant emphysema (i.e., associated with FEV\textsubscript{1} of <80% or <65% of predicted normal values) and the cumulative exposure to respirable coal mine dust – among white never-smokers at the cohort-average age of death.]

At the cohort average cumulative dust exposure (87 mg/m\textsuperscript{3} x yr) and age of death (65 yr), the maximum likelihood estimate (MLE) of the probability of developing emphysema associated with FEV\textsubscript{1} <80% was 0.25 (95% CI: 0.18-0.34) among white never-smokers, and 0.39 (0.33-0.47) among white ever-smokers. For emphysema associated with FEV\textsubscript{1} <65%, the estimates for the same conditions were 0.22 (0.16-0.30) among never smokers, and 0.30 (0.24-0.36) among smokers. Among non-whites, the comparable estimates were nearly two-fold higher within each smoking group.

The effects of cumulative coal dust exposure and pack-years of smoking were additive (on the log odds scale) in this logistic regression model. Thus, the probability of developing clinically-relevant emphysema was higher among smokers, for a given age of death and race. The relative effects of cumulative dust exposure and cigarette smoking in this cohort can be evaluated by examining their odds ratios. The odds ratio of developing emphysema associated with FEV\textsubscript{1} <80% was 2.30 (1.46-3.64) at the cohort mean cumulative coal dust exposure (87 mg/m\textsuperscript{3} x yr), and 1.95 (1.39-2.79) at the cohort mean cigarette smoking (among smokers: 42 pack-years). For emphysema associated with FEV\textsubscript{1} <65%, the odds ratio was 2.39 (1.51-3.83) at the cohort mean cumulative coal dust exposure, and 1.52 (1.10-2.13) at the cohort mean cigarette smoking (all values as point estimate and 95% CI).
Thus, the contribution of cumulative dust exposure was greater than that of cigarette smoking at the cohort mean values, although not significantly so (p-values: 0.6 and 0.1, respectively, for emphysema associated with FEV$_1$ <80% or <65%).

4. Discussion
This study provides a clinical perspective to our earlier findings [9] based on emphysema severity as a continuous variable. The current analyses describe the quantitative relationship between FEV$_1$, emphysema severity, and cumulative dust exposure in an autopsied population of U.S. coal miners and non-miners. Results show that the probability of developing clinically-relevant emphysema severity (i.e., associated with FEV$_1$ of <80% or <65% of predicted normal values) is related to the cumulative exposure to respirable coal mine dust, cigarette smoking pack-years, age at death, and race. The higher probabilities predicted for non-whites might be attributed to unmeasured factors related to race, such as higher dust exposures than those reported in the work histories or non-occupational exposures related to cooking or heating methods used in the home. Cumulative dust exposure and cigarette smoking had similar and additive estimated effects on the probability of developing clinically-relevant emphysema.

Associations between dust exposure, emphysema severity, and pulmonary function have been observed in previous studies of miners in several countries. Ruckley et al. [5] reported that centriacinar emphysema was associated with the amount of dust retained in the lungs of U.K. coal miners who had dust-related fibrosis. Studies in living miners in the U.K. [14, 15, 17] and the U.S. [18] observed independent effects of coal dust exposure and cigarette smoking on lung function deficits, including miners with negative chest x-rays for pneumoconiosis. Leigh et al. [6] found that emphysema severity in Australian coal miners was predicted by the coal dust content in the lungs, age, and smoking; and that emphysema severity was highly negatively correlated with FEV$_1$ obtained within five years of death.

Similar relationships have been observed for other mineral dusts. In a study of South African gold miners, Hnizdo et al. [8] reported that the average FEV$_1$ was 52.0% (S.D. 19.4%) of predicted normal values among the 170 individuals with emphysema severity of 35-65% of lung tissue affected. In this analysis of U.S. coal miners, the mean FEV$_1$ was 58.1% (S.D. 15.1%) of predicted normal values among the 34 individuals with an equivalent emphysema severity of 350-650 (corresponding to 35-65% of lung tissue affected).

Differences in the spirometry and emphysema grading criteria apparently did not have a large effect. Hnizdo et al. [8] used the 1979 ATS spirometry standards and a National Centre for Occupational Health method for grading emphysema severity using whole lung sections and 20 radiating zones (summing to 100%), while the data in this study are based on FEV$_1$ prediction formulas from Miller (as reported in Rasmussen et al. [11]) and the Thurlbeck method to determine emphysema severity at autopsy [2, 3].

These consistent findings across studies suggest: (1) the emphysema severity-FEV$_1$ relationship may be broadly applicable to other dust-exposed cohorts, perhaps through a common mechanism for emphysema disease development regardless of the causative agent, and (2) the emphysema severity index is associated with lung functional deficits during life. However, it should be noted that FEV$_1$ is a relatively nonspecific test for measuring airflow limitation, as FEV$_1$ deficit can be caused by diseases such as chronic bronchitis and asthma in addition to emphysema [19]. These factors likely account for some of the variability observed in the relationship between FEV$_1$ and emphysema severity. Also, individuals’ responses to inhaled dust can vary, such that the average decrements in the emphysema index or FEV$_1$ observed in a population may not accurately portray the effects of dust exposure on the pulmonary impairment and disability in an individual miner.

In this study, cumulative coal dust exposure and cigarette smoking were each statistically significant predictors of developing clinically-relevant emphysema. These effects were additive (on the log odds scale) – indicating the need to reduce exposures to both agents in order to reduce the probability of emphysema. The odds ratios for developing clinically-relevant emphysema (i.e.,
associated with FEV$_1$ <80% or <65%) for cumulative coal dust exposure (2.30 or 2.39, respectively) were higher (although not significantly) than those for cigarette smoking (1.95 or 1.52, respectively) at the cohort mean values. It is important to note that never-smoking coal miners also had a significantly elevated probability of developing clinically-relevant emphysema severity. Reducing exposures to respirable coal mine dust, as recommended by NIOSH [20] would reduce the probability of dust-related disease including emphysema.

5. Conclusions
Cumulative exposure to respirable coal mine dust was a statistically significant predictor of the probability of clinically-relevant emphysema among both ever- and never-smokers. The observed odds ratios for developing clinically-relevant emphysema were somewhat higher for cumulative dust exposure than for cigarette smoking in this cohort.

References
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**Disclaimer**

The findings and conclusions in this paper are those of the authors and do not necessarily represent the views of the National Institute for Occupational Safety and Health.