Functional variables associated with the clinical grade of dyspnoea in coal miners with pneumoconiosis and mild bronchial obstruction

T T Bauer, G Schultze-Werninghaus, J Kollmeier, A Weber, R Eibel, B Lemke, E-W Schmidt

Abstract

Objectives—Dyspnoea is a common symptom in coal miners with pneumoconiosis. Among others, gas exchange disturbances due to airway obstruction or mismatch between ventilation and perfusion may be underlying mechanisms. The validation of dyspnoea by the degree of airway obstruction is controversial, because the extent of airway obstruction often does not correlate with the clinical grade of breathlessness.

Methods—The association was investigated between breathlessness (self reported, on a six point scale) and indices of submaximal spiroergometry in 66 coal workers with radiographically confirmed pneumoconiosis (International Labour Organisation (ILO) grade of profusion ≥ 1/0, mean (SD) age 64 (5.5) years, mean (SD) forced expired volume in 1 second (FEV₁) 77.5 (22.9) % predicted).

Results—The clinical degree of breathlessness was independently associated with minute ventilation/oxygen consumption (VE/VO₂) ratio (β = 0.423, 95% confidence interval (95% CI) 0.18 to 0.67, p=0.001) and smoking (β = 0.318, 95% CI 0.21 to 1.79, p=0.014) in a multiple linear regression analysis. The VE/VO₂ ratio (β = 0.556, 95% CI 0.20 to 0.90, p=0.003) was also the best predictor of breathlessness when only coal miners with airway obstruction (FEV₁ < 80% predicted) were analyzed.

Conclusion—The VE/VO₂ ratio as a measurement of mismatch between ventilation and perfusion predicted the clinical grade of breathlessness better than measurements of bronchial obstruction at rest in coal workers with pneumoconiosis. (Occup Environ Med 2001;58:794–799)

Keywords: coal workers’ pneumoconiosis; bronchial obstruction; ventilation

Main messages

• The VE/VO₂ ratio during exercise is associated with the self reported degree of breathlessness in coal workers with pneumoconiosis.
• A higher VE/VO₂ ratio is found in patients with more exertional dyspnoea.
• Self reported dyspnoea is better described by the VE/VO₂ ratio during submaximal exercise testing with a steady state protocol than by the FEV₁.
• A higher VE/VO₂ ratio was not found among smokers although they reported higher levels of dyspnoea than non-smokers.
• The VE/VO₂ ratio may therefore be an interesting variable possibly to assess respiratory disability independent from smoking.

Policy implications

• Exercise testing should be included in the evaluation of respiratory disability in coal miners with pneumoconiosis.
• The VE/VO₂ ratio should be assessed during a submaximal steady state protocol—for example, 50 W.
• Mismatch between ventilation and perfusion should be considered in coal miners with mild bronchial obstruction and unexpectedly high self reported dyspnoea.

Pneumoconiosis is still a major cause of disability worldwide despite a decreasing incidence in Western countries.¹ Underground coal workers are exposed to dust consisting of coal particles and free silica eventually resulting in coal workers pneumoconiosis.² ³ The disease is characterised by ventilation defects and dyspnoea. The verification and measurement of breathlessness is a cornerstone for the identification of clinically important occupational lung damage. ¹

However, the correlation of functional variables obtained at rest—for example, forced expired volume in 1 second (FEV₁)—with the clinical grade of dyspnoea is generally poor.⁴ ⁶ Various approaches have been made to improve the prediction of exertional dyspnoea from pulmonary function tests and to provide an independent measure of dyspnoea. Cotes et al identified a reduced diffusing capacity and forced vital capacity (FVC) as predictors,⁷ but also hypothesised that measurements of ventilation standardised for oxygen uptake during submaximal exercise may improve the predictive power.⁸

The objective of this study was therefore to describe the association between the degree of
Methods

Coal miners were selected from a cohort investigated for compensation benefits in our institute between 1 December 1994 and 30 June 1997. All coal miners received compensation benefits at that time and data were obtained during a scheduled follow up visit. All patients with symptoms of chronic bronchitis and radiologically confirmed pneumoconiosis were asked to participate in this study.

Chronic bronchitis was defined as the presence of productive cough for 3 months in each of 2 successive years. Chronic bronchitis with airflow obstruction was assumed in the presence of a FEV₁ ≤ 80% of the predicted value.

Radiologically confirmed pneumoconiosis was defined as profusion for small opacities of at least 1/0 with or without large opacities (A, B) according to the guidelines of the International Labour Organisation, Geneva.9

Exclusion criteria were the following: (a) denied informed consent, (b) clinically apparent or history of congestive heart failure, ventricular arrhythmia, or severe arterial hypertension (systolic pressure at rest ≥ 180 mm Hg or diastolic pressure ≥ 110 mm Hg), (c) severe physical or mental disability, (d) airflow obstruction stage II or worse (FEV₁ ≤ 50% predicted)10, (e) large opacities (International Labour Organisation (ILO) classification C) on the chest radiograph, and (f) oral corticosteroid medication during the preceding 4 weeks.

Chronic medication allowed during the study included theophylline, inhaled β-2-adrenergic drugs, and inhaled corticosteroids. Written informed consent was obtained from all subjects. The study was approved by the ethics committee of the Ruhr-University, Bochum.

QUESTIONNAIRE

Respiratory symptoms were assessed by a questionnaire adapted from the British Medical Research Council (BMRC) questionnaire on respiratory symptoms and smoking habits.11 Smoking habits were grouped as non-smokers and smokers (ex-smokers and current smokers) and a full occupational history was obtained. In the questionnaire the frequency of cough (0=none, 1=in frequent (<3 weeks/year in the preceding 2 consecutive years), 2=frequent (daily), 3=frequent cough attacks, and 4=frequent cough with dyspnœa or dyspnœa attacks) and phlegm (0=none, 1=in frequent (<3 weeks/year in the preceding 2 consecutive years), 2=frequent (daily), and 3=frequent with dyspnœa attacks) was obtained. Exer- tional dyspnœa was graded by a set of six questions about different levels of dyspnœa during walking on slight hills, level ground, or rest.11 0=no dyspnœa, 1=dyspnœa during fast walking on level ground, walking up hill, or climbing stairs, 2=dyspnœa during regularly paced walking on flat ground, 3=dyspnœa during slow walking on flat ground requiring occasional stops, 4=dyspnœa during rest or during dressing, and 5=dyspnœa level 0–4 with occasional attacks of breathlessness.

CHEST RADIOGRAPHY

Routine posterior-anterior chest radiographs were obtained and evaluated separately by two expert radiologists according to the 1980 ILO classification.7 The profusion score was converted to numerical numbers from 0 to 9 according to increasing density of small opacities (0/0=0, 0/1=1, 1/0=2, etc). Numbers assigned by each rater were compared by an independent third person and the mean was used when the scores differed by one step (5 v 6; 2/1 v 2/2 resulted in a score of 5.5). The radiographs were reassessed by both raters under the same conditions in cases of discordance ≥ two steps (5 v 7; 2/1 v 2/3). If discordance persisted, a third radiologist was consulted and an agreement was reached among the three of them.

PULMONARY FUNCTION

Spirometry and body plethysmography were performed with a Jaeger IV device (jaeger IV, Würzburg, Germany). For spirometry the trial with the highest FEV₁ was selected and data were compared with reference values.12 The variables assessed were: resistance (Rₐ), intrathoracic gas volume (ITGV), residual volume as a % of total lung capacity (RV∕TLC), FEV₁, and forced and inspiratory vital capacity (FVC, IVC). Diffusing capacity for CO (T̄CO₃) was measured by a single breath method (Pneumotest Alveotest, Jaeger, Würzburg, Germany) and compared with reference values.13 Arterial capillary blood was drawn from the hyperaemic ear lobe with a heparinised capillary at rest and during steady state exercise (after 4 minutes). Hyperaemia was induced by a rubefacient (nicoboxil/nonivamid, Finalgon) and ensured visually. This method may underestimate arterial CO₂ tension (PaCO₂), but arterial catheterisation was not permitted for ethical reasons. Samples were immediately analysed in a blood gas analyser (AVL 995-S automatic blood gas system, AVL Graz, Austria), that performed calibration cycles every 2 hours.

EXERCISE TESTING

Spiroergometry was performed on an electro-magnetically braked bicycle in 30 degrees upright body position. The gas exchange was measured by breath (MedGraphics, CPX/D, Minneapolis, USA). Subjects breathed through a mouthpiece with a dead space volume of 20 ml with a nose clip in place. Daily maintenance of the system included gas analyser calibration with a precision gas mixture and volume calibration with a 3 litre syringe before each exercise test. Heart rate was calculated by R-R intervals with the highest signal amplitude of a 12 lead configuration. Arterial blood pressure was measured by a sphygmomanometer at rest and during exercise. All exercise tests were performed between 0900 and 1200 and the exercise protocol...
Table 1 Demographic and clinical characteristics of coal miners eligible for the study and those included during the study period (Student’s t test for continuous variables and χ² test for frequencies, exact p values are given)

<table>
<thead>
<tr>
<th></th>
<th>Coal miners included (n=66)</th>
<th>Coal miners not included (n=94)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y, mean (SD))</td>
<td>64 (5.5)</td>
<td>66 (6.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI (kg/m², mean (SD))</td>
<td>26.1 (2.7)</td>
<td>26.1 (3.7)</td>
<td>0.063</td>
</tr>
<tr>
<td>FEV₁ (% predicted, mean (SD))</td>
<td>77.5 (22.9)</td>
<td>75.2 (26.4)</td>
<td>0.429</td>
</tr>
<tr>
<td>Duration of work underground (y, mean (SD))</td>
<td>25.8 (9.2)</td>
<td>26.0 (9.2)</td>
<td>0.720</td>
</tr>
<tr>
<td>Smoking (n (%))</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-smokers</td>
<td>8/66 (12)</td>
<td>15/94 (16)</td>
<td>0.495*</td>
</tr>
<tr>
<td>Smokers</td>
<td>58/66 (88)</td>
<td>79/94 (84)</td>
<td></td>
</tr>
</tbody>
</table>

*p Value calculated with χ² test.

...results of blood gas analysis before and during exercise were compared by paired Student’s t test.

For describing the degree of dyspnoea by functional variables, a multiple linear regression analysis was used. The variable was tested for normal distribution by Kolmogorov-Smirnov test before the procedure to test for normal distribution. A stepwise forward model was used to give transparency of variable selection and to reduce the risk of overfitting the data. The following variables were investigated in connection with the clinical grade of breathlessness: age, smoking history, FEV₁, FEV₁/FVC, T.LCO, VE/VO₂ ratio, and arterial end tidal PCO₂ difference, P(a-ET)CO₂ (positive or negative). The VE/VO₂ ratio was not included in the multivariate analysis because of its close physiological and mathematical correlation to the VE/VO₂ ratio. Results of this analysis are reported as the standardised β coefficient, the 95% confidence interval (95% CI), and the level of significance. The standardised β coefficient is the regression coefficient for change in the dependent variable per unit change in the predictor variable. This allows the direct comparison of the effect in a multivariable model.

All data were processed with SPSS version 8.01 on a Windows 98 operating system. Comparisons were regarded as significant with p<0.05 (all two tailed). Exact levels of significance are reported.

Results

DESCRIPTION OF THE POPULATION

A total of 160 coal miners were investigated and 66/160 were included in this study (41%). Seventy three coal miners denied informed consent for this extended investigation (73/160, 46%) and 21 had at least one exclusion criterion (21/160, 13%). Table 1 compares the clinical characteristics of coal miners eligible for the study and those included. Coal miners included were on average 2 years younger than those not included (p<0.001). No other significant differences were found for this comparison. A total of 58/66 (88%) coal miners were smokers or ex-smokers and the median values according to the grading obtained by the questionnaire for dyspnoea, frequency of cough, and phlegm were 2 IQR 1, 1 IQR 2, and 1 IQR 2, respectively.

Coal miners included in the study had the following radiographic scores according to ILO classification 1980: 1/0 (5/66, 8%), 1/1 (16/66, 24%), 1/2 (9/66, 14%), 2/1 (17/66, 26%), 2/2 (13/66, 20%), 2/3 (3/66, 5%), 3/2 (3/66, 5%), p/p (9/66, 13%), p/q (26/66, 39%), q/p (3/66, 5%), q/q (14/66, 21%), q/r (11/66, 17%), r/q (1/66, 2%), r/r (2/66, 3%). The frequency of large opacities was 15/66 for ILO classification A (23%) and 23/66 for ILO classification B (35%). Radiographic signs of emphysema were present in 30/66 (46%) radiographs.

Results of the pulmonary function tests, blood gas analyses, and spirometry were summarised in table 2. Overall 12/66 (18%) exercise tests could not be included in this study for the following reasons: early ending of
ASSOCIATION OF THE DEGREE OF BREATHELESSNESS WITH FUNCTIONAL VARIABLES

The results of the multiple linear regression for the 54 coal miners who could be included in this analysis are shown in table 3. The degree of dyspnoea as assessed by the questionnaire was positively associated with \( \text{VE/VO}_2 \) (\( \beta = 0.423, 95\% \text{ CI} 0.18 \text{ to } 0.67, p=0.001 \)). This indicates that a higher degree of breathlessness on the self reported scale is strongly associated with an increased \( \text{VE/VO}_2 \) during constant 50 W exercise (fig 1). Also, a positive relation between smoking and the degree of breathlessness (\( \beta = 0.318, 95\% \text{ CI} 0.21 \text{ to } 1.71, p=0.014 \)) could be established in this multivariable analysis. Smokers or ex-smokers reported higher dyspnoea scores than non-smokers (2 IQR 1 \( \geq \) 2 IQR 1, \( p=0.036 \), fig 2). By contrast, the \( \text{VE/VO}_2 \) ratio was not significantly different when smokers and ex-smokers (34.9 (7.8)) were compared with non-smokers (35.0 (11.9), \( p=0.979 \)). However, the number of non-smokers was low in this cohort (n=8) and formal interaction analysis to test for independency of effects was not undertaken.

SUBANALYSIS FOR COAL MINERS WITH AND WITHOUT AIRWAY OBSTRUCTION

Smoking had to be removed from the independent variable list when the multiple regression analysis was repeated for coal miners with and without airway obstruction, because all smokers had airway obstruction according to the definition. The degree of breathlessness was also positively associated with \( \text{VE/VO}_2 \) (\( \beta = 0.556, 95\% \text{ CI} 0.20 \text{ to } 0.90, p=0.003 \)) in the subgroup of coal miners with airway obstruction. The \( T_\text{CO} \) (\( \beta = -0.571, 95\% \text{ CI} -0.95 \text{ to } -0.20, p=0.004 \)) was the single best predictor of the degree of breathlessness when coal miners without airway obstruction were studied exclusively.

Discussion

The main results of this study were: (1) The \( \text{VE/VO}_2 \) ratio during steady state exercise was associated with breathlessness in coal miners with pneumoconiosis, whereas FEV, or FEV/FVC were not. (2) The association between breathlessness and the \( \text{VE/VO}_2 \) ratio was strongest in coal miners with pneumoconiosis.
and airway obstruction (FEV₁ < 80% of predicted). (3) Smoking was associated with a higher degree of breathlessness but not with the VE/VO₂ ratio during steady state exercise in the population studied.

Dyspnoea is a subjective sensation with a complex pathophysiological basis. Among the contributors that have been discussed are diaphragmatic fatigue,27 physiological signalling,28 and most commonly bronchial obstruction. Obstructive airway disease as measured by pulmonary function tests remains the basis for grading respiratory disability in patients with pneumoconiosis, although more complex methods have been proposed.29 However, measurements of pulmonary function tests are only poorly associated with the clinical degree of breathlessness. This has been verified for normal subjects,30 patients with COPD,31 silicosis,1 and coal workers’ pneumoconiosis.32 Our results corroborate these negative findings because neither FEV₁ nor FEV₁/FVC were significantly associated with the dyspnoea score in multivariate analyses.

In our study, with a submaximal 50 W steady state protocol to minimise bias by the subject’s effort, we found a strong association between the clinical grade of breathlessness and the VE/VO₂ ratio during stable exercise. The VE/VO₂ ratio measures gas exchange efficiency and is also a measure of uneven ventilation/perfusion (VA/Q).23 The VE/VO₂ ratio is influenced by the anaerobic threshold and is highest at rest and decreases during exercise in healthy subjects until the anaerobic threshold is reached but remains increased in patients with uneven VA/Q.23 We did not include a maximal work rate test because we considered this to be of limited information in a compensation process due to the strong dependency on motivation for this variable. Therefore, we could not exactly define the exercise modality (aerobic or anaerobic) at the steady state level. However, we think that this is unimportant for our study because we consider it of limited value to differentiate between the aetiologies of dyspnoea at the 50 W level. Also, the end tidal PCO₂ difference (P(a-ET)CO₂) remained positive during exercise indicating decreased CO₂ clearance from the alveoli, most likely due to uneven VA/Q.23 Voluntary hyperventilation may also result in a high VE/VO₂ ratio during exercise but is accompanied by corresponding changes in PaCO₂.23 However, we did not find any decrease in capillary PaCO₂ during exercise which may rule this possibility out confidently. We may therefore conclude that the clinical degree of breathlessness correlates better with measurements of uneven VA/Q during exercise, than with measurements of airway obstruction at rest in coal workers with pneumoconiosis. However, future studies should make an attempt to confirm this finding by other measurements of uneven VA/Q such as the multiple inert gas elimination technique.27

The second important result of this study was that the VE/VO₂ ratio remained the best predictor of self rated breathlessness even in coal workers with airway obstruction. In our study we used a submaximal exercise protocol with breathing patterns that resemble daily activities better than the forced manoeuvre necessary to measure FEV₁. Airway obstruction also contributes to uneven VA/Q23 and our finding may therefore indicate that it is probably the degree of VA/Q mismatch that causes dyspnoea in this population rather than bronchial obstruction.

The TₐCO remained the best predictor of breathlessness in the multivariate analysis in the population with pneumoconiosis without airway obstruction thus corroborating previous findings.27,28 A decreased TₐCO correlates well with the functional impairment due to emphysema,27 which was also a frequent finding in our population with pneumoconiosis.28–30

As expected, smoking was related to a higher degree of self reported breathlessness in our study. However, it is noteworthy that smoking and the VE/VO₂ ratio during exercise were independently associated with dyspnoea. Smoking also did not contribute to the level of the VE/VO₂ ratio when smokers and non-smokers were compared. This indicates that measurements of the VE/VO₂ ratio may be helpful to differentiate between dyspnoea attributable to smoking or pneumoconiosis. However, these data have to be interpreted with caution because only a few coal miners were non-smokers in our study and therefore a formal interaction analysis could not be performed in our statistical model.

There are limitations to this study that deserve consideration. The participation rate in our study was 41% of the initially approached subjects. This was not unexpected because the study protocol required an exercise test which imposes an additional burden on the patients. As older and sicker patients are more likely to decline the participation of this study our sample may have been selected in that way. However, special care was taken to document this possible bias and at least the lack of a significant difference in FEV₁ between the study group and the group of subjects declining participation indicated that this bias may have been minimal.

All coal miners were investigated during the compensation process and it might be argued that they tried to overestimate their exertional disability. This limitation, however, applies only to the average level of the dyspnoea score but not to associations found in this study. Up to date there are no objective measures of dyspnoea and all self rated scores are subject to this limitation in a study on coal miners.

In conclusion, we found that self rated breathlessness was approximated best by the VE/VO₂ ratio measured during steady state submaximal exercise, even in coal miners with airway obstruction. These results suggest that measurement of uneven VA/Q may be a better predictor of dyspnoea than measurements of airway obstruction in coal miners with mild to moderate pneumoconiosis. Smoking also contributed to a higher degree of breathlessness but did not affect the VE/VO₂ levels. This may
Table 4 Abbreviations used in alphabetical order

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>BMRC</td>
<td>British Medical Research Council</td>
</tr>
<tr>
<td>CB</td>
<td>Chronic bronchitis</td>
</tr>
<tr>
<td>COPD</td>
<td>Chronic obstructive pulmonary disease</td>
</tr>
<tr>
<td>TcO2</td>
<td>Diffusing capacity for CO</td>
</tr>
<tr>
<td>FEV1</td>
<td>Forced expiratory flow in 1 second</td>
</tr>
<tr>
<td>FVC</td>
<td>Forced vital capacity</td>
</tr>
<tr>
<td>HR</td>
<td>Heart rate</td>
</tr>
<tr>
<td>ILO</td>
<td>International Labour Office</td>
</tr>
<tr>
<td>ITGV</td>
<td>Intrathoracic gas volume</td>
</tr>
<tr>
<td>IVC</td>
<td>Inspiratory vital capacity</td>
</tr>
<tr>
<td>P(a-A)O2</td>
<td>Alveolar-arterial PaO2 difference</td>
</tr>
<tr>
<td>P(a-ET)CO2</td>
<td>Arterio-endothelial PCO2 difference</td>
</tr>
<tr>
<td>PaCO2</td>
<td>Partial arterial pressure for CO2</td>
</tr>
<tr>
<td>PaCO2%</td>
<td>Partial arterial pressure for CO, % of predicted</td>
</tr>
<tr>
<td>PaO2</td>
<td>Arterial oxygen tension</td>
</tr>
<tr>
<td>Rt</td>
<td>Airway resistance</td>
</tr>
<tr>
<td>% Predicted</td>
<td>Percent of predicted</td>
</tr>
<tr>
<td>Pco2</td>
<td>End-expiratory CO2 partial pressure</td>
</tr>
<tr>
<td>PexO2</td>
<td>End-expiratory O2 partial pressure</td>
</tr>
<tr>
<td>PFT</td>
<td>Pulmonary function test</td>
</tr>
<tr>
<td>RER</td>
<td>Respiratory exchange ratio</td>
</tr>
<tr>
<td>RV/% TLC</td>
<td>Residual volume in % total lung capacity</td>
</tr>
<tr>
<td>TLC</td>
<td>Total lung capacity</td>
</tr>
<tr>
<td>VA/Q</td>
<td>Ventilation or perfusion ratio</td>
</tr>
<tr>
<td>VCO2</td>
<td>CO2 output</td>
</tr>
<tr>
<td>VE</td>
<td>Minute ventilation</td>
</tr>
<tr>
<td>VE/VO2</td>
<td>Ventilatory equivalent for O2</td>
</tr>
<tr>
<td>VE/CO2</td>
<td>Ventilatory equivalent for CO2</td>
</tr>
<tr>
<td>VO2</td>
<td>Oxygen uptake</td>
</tr>
</tbody>
</table>

indicate that the VE/VO2 ratio may bear discriminant potential for dyspnoea attributable to either smoking or pneumoconiosis.

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