Effect of arterial oxygen desaturation on six minute walk distance, perceived effort, and perceived breathlessness in patients with airflow limitation

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Abstract

Background The effect of exercise induced hypoxaemia in determining submaximal exercise capacity, perceived breathlessness, and perceived exertion is not known. The purpose of this study was to investigate the relation of these variables to the results of lung function tests and the degree of hypoxaemia during submaximal exercise in patients with airflow limitation.

Methods Forty two patients with chronic obstructive airways disease and 28 patients with chronic severe asthma were studied. Spirometry was performed and gas transfer (TLCO) and lung volumes were measured. Submaximal exercise capacity was assessed with a standardised six minute walk test. Arterial oxygen desaturation during the walk test was monitored by a portable pulse oximeter. Patients rated their perceived degree of respiratory impairment on a Medical Research Council (MRC) breathlessness scale before the walk. Perceived breathlessness was measured by means of a linear visual analogue scale and exertion on the Borg scale after the walk.

Results The six minute walk distance was strongly correlated (r value) with TLCO (0·68), peak expiratory flow (PEF: 0·55), forced expiratory volume in one second (FEV$_1$: 0·53), transfer coefficient KCO: 0·49), age (−0·49), and forced vital capacity (FVC: 0·48) but not with oxygen desaturation during the walk. Walk distance was also correlated with the breathlessness rating on the MRC scale (−0·52), but less strongly with perceived breathlessness (−0·35) and perceived exertion (−0·30). The prediction equation for the six minute walk distance in metres (6MD) generated by multiple regression analysis was 6MD = 387 + 29·7 (TLCO) − 3·1(age) + 0·35(PEF l/min), which accounted for 50% of the total variance in walk distance. The mean level of saturation during the walk correlated most significantly with TLCO (0·55), FEV$_1$/FVC (0·54), and PEF (0·48), but not with walk distance or with the rating on any of the analogue scales. The prediction equation produced by multiple regression analysis for the mean level of saturation during the walk was MEANSAT(%) = 1·3(TLCO) + 1·5 (baseline saturation) − 0·01(6MD) − 54.

Conclusions Oxygen desaturation during the six minute walk is not related to walk distance, nor does it determine the degree of perceived exertion or perceived breathlessness in patients with airflow limitation. Patients who consider themselves the most disabled by breathlessness have the shortest six minute walk distance but do not necessarily have appreciable desaturation.

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Among the most common symptoms in patients with respiratory diseases are breathlessness, reduced exercise capacity, and an increase in the sensation of effort taken to perform everyday tasks. Arterial oxygen desaturation is known to occur during exercise in some patients with respiratory disease.[1-7] A possible explanation for these symptoms could be arterial hypoxaemia leading to reduced oxygen delivery and acidosis resulting from anaerobic respiration; but the role of exercise induced hypoxaemia in determining submaximal exercise capacity and the degree of perceived breathlessness and perceived exertion in patients with respiratory disease is uncertain. No study has specifically examined the relation of hypoxaemia occurring during submaximal exercise to the submaximal exercise capacity and the degree of perceived breathlessness and perceived exertion.

Most studies investigating exercise induced hypoxaemia have used either cycle ergometry or treadmill walk tests.[1-7] These forms of exercise are unfamiliar to most patients, however, and extrapolation of such data to everyday activity may not be appropriate. The symptom limited six minute walk is a more familiar form of exercise for patients and more relevant to their everyday life.[8 9] We therefore chose to use the six minute walk in a group of patients with airflow limitation to determine: (1) the relation between submaximal exercise capacity and exercise induced hypoxaemia in patients with airflow limitation; (2) the relation between perceived breathlessness and effort during submaximal exercise and exercise induced hypoxaemia; and (3) the relationships between results of static lung function tests, exercise induced hypoxaemia, and submaximal exercise capacity.

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Methods

SUBJECTS

Forty two patients (30 male) with chronic obstructive airways disease and 28 patients (18 male) with chronic severe asthma were studied. None of the patients had a history of malignancy, cardiovascular or peripheral vascular disease, or locomotor problems. Patients with chronic obstructive airways disease were all ex-smokers or still smoking and had a history of chronic respiratory illness and a previously documented increase in peak expiratory flow (PEF) or forced expiratory flow in one second (FEV$_1$) of less than 10% in response to bronchodilators. Patients with chronic severe asthma had a long history of variability in lung function and 15 were having long term oral corticosteroid treatment (mean (SD) dosage 7·8 (2·8) mg prednisolone, mean duration 17·5 (9·75) years). We excluded from the study any patient who could not complete a six minute walk test or who stopped during the walk for any reason other than breathlessness or fatigue.

LUNG FUNCTION TESTS

Spirometric indices, including peak expiratory flow, FEF$_{50}$ and FEF$_{75}$, were measured with a computerised dry rolling seal spirometer (Gould Pulmograph System 2130, UK). Volumes were calibrated daily with a syringe and flow rates calibrated weekly with rotameters. Total lung capacity (TLC) and its subdivisions were calculated from measurements of thoracic gas volume made in a constant volume whole body plethysmograph (Fenyves and Gut, Switzerland). Carbon monoxide transfer capacity (TLCO) was measured by the single breath technique and the alveolar volume (VA) was calculated by helium dilution during the single breath hold. The carbon monoxide transfer coefficient (KCO) was calculated as TLCO/VA. At least three measurements were made for each lung function variable to ensure reproducibility. All patients were asked to refrain from taking any bronchodilators for at least four hours before the tests. Predicted values were obtained from regression equations given by Cotes.[10]

SIX MINUTE WALK AND VISUAL ANALOGUE SCALES

After lung function testing the patients performed two six minute walk tests along an air conditioned corridor 44 metres in length, following a standardised protocol.[8 9] Each patient was given the same instructions before the walk. An investigator followed 5–10 metres behind the patient during the walk and gave encouragement, using set phrases every 30 seconds.[11] The walks were symptom limited, so patients were allowed to stop if necessary; but they had to continue again once they were rested. After the walk the distance covered during the test was recorded in metres as the six minute distance. The second walk was performed in the same manner as the first after 30 minutes' rest. Results from the second walk only were used for analysis to allow for any learning effect.[12]

Before the walking tests patients were asked to assess their perceived respiratory impairment on the modified Medical Research Council (MRC) breathlessness scale. Patients were also told how to use a modified Borg scale and a 10 cm linear visual analogue scale before the first walk. After each walk they were asked to assess the maximum degree of perceived respiratory effort during the walk on the modified Borg scale and the maximum level of perceived breathlessness during the walk on the linear analogue scale.

OXIMETRY

Exercise induced hypoxaemia was assessed during the walk test by a pulse oximeter. A light weight (0·9 kg) portable pulse oximeter (Minolta Pulsox-7, Devilbis, Heston) was carried by the patient with a shoulder strap. The oxygen saturation was monitored by a flexible universal probe attached to a finger, and saturation readings were stored every five seconds in the memory of the oximeter. We have previously tested the readings given by this oximeter against the arterial blood gas estimations and the readings of Ohmeida Biox and Novametric oximeters on patients in the intensive care unit. We have found the results similar to those of arterial blood gas estimation down to saturations of 70%. The baseline saturation (BSAT) for five minutes before and at least five minutes after each walk was recorded. The mean saturation recorded during the walk (MEANSAT), the minimum saturation sustained for more than 10 seconds, and the mean change in saturation (that is, desatura-

Table 1 Mean (SD) values and mean (SD) percentage of predicted lung function indices, six minute walk distance, and ratings on visual analogue scale (VAS) for patients with chronic obstructive airways disease and chronic severe asthma and for the two groups together

	Chronic obstructive airways disease (n = 42)		Asthma (n = 28)		Total (n = 70)	
	Absolute value	% predicted	Absolute value	% predicted	Absolute value	% predicted
Age (years)	62·3 (9·1)	—	57·4 (12·9)	—	60·4 (10·9)	—
PEF (l/min)	164 (106)	33·8 (18·9)	224 (91)	48·2 (17·3)	188 (104)	39·6 (19·5)
FEV$_1$ (l)	1·13 (0·74)	40·3 (21·6)	1·54 (0·63)	56·7 (20·6)	1·30 (0·72)	46·9 (22·6)
FVC (l)	2·64 (1·21)	71·1 (25·6)	3·08 (1·06)	84·3 (17·9)	2·82 (1·16)	76·4 (23·6)
TLC (l)	8·02 (1·54)	137 (24)	7·25 (1·82)	125 (24)	7·71 (1·69)	132 (24)
RV (l)	5·28 (1·68)	295 (92)	3·99 (1·34)	227 (79)	4·77 (1·67)	268 (93)
TLCO (mmol/kPa/s)	5·01 (2·19)	60·4 (24·2)	8·08 (2·15)	95·3 (19·5)	6·24 (2·63)	74·3 (28·1)
KCO (mmol/kPa/l/s)	1·09 (0·47)	74·7 (30·6)	1·60 (0·35)	104 (25)	1·30 (0·50)	86·5 (30·6)
Walk distance (mm)	406 (149)	—	517 (181)	—	450 (170)	—
VAS (mm)	50 (27)	—	38 (24)	—	45 (26)	—

PEF—peak expiratory flow; FEV$_1$—forced expiratory volume in one second; FVC—forced vital capacity; TLC—total lung capacity; TLCO—carbon monoxide transfer factor; KCO—transfer coefficient.

tion) during the walk (BSAT–MEANSAT) were noted. Desaturation during the walk was also categorised according to four groups (0 = <1% desaturation; 1 = 1 – <5%; 2 = 5 – <10%; 3 = ≥10%) to permit analysis by one way analysis of variance.

STATISTICS AND ANALYSIS

All data were analysed on a microcomputer by means of the SPSS/PC+ v3·0 package of Statistical Programmes for the Social Sciences of the University of Michigan (Microsoft Corporation, Redmond, USA). Data are expressed as means, standard deviations (SD), standard errors of the estimate, and Pearson's product moment correlations for parametric and Rank correlation for non-parametric data. Graded oxygen desaturation during the walk was analysed by one way analysis of variance for parametric variables and Kruskal-Wallis analysis of variance for non-parametric variables.

Stepwise multiple regression analysis was used to determine the best predictor variables for the dependent variables distance walked in six minutes, perceived exertion (Borg scale), perceived breathlessness (visual analogue scale), and mean saturation during the walk. Scatterplots with regression lines were generated and examined for each dependent variable plotted against each predictor variable to ensure that the regression could not be improved by transformation of the data. The percentage of total variance in the dependent variable accounted for by the predictor variables is expressed as the adjusted square of the multiple correlation coefficient (r^2). To avoid collinearity, variables affected by airways obstruction (for example, PEF, FEV_1, FEF_{50}, FEF_{75}, and FEV_1/FVC) were entered into the analysis separately. A p value of less than 0·05 was taken as significant, but for correlations

only those results with a significance level of less than 0·01 are given.

Results

The mean and mean percentage predicted values of the lung function indices, six minute walk distance, and ratings on the visual analogue scales for the two groups of patients are shown in table 1. No patients were unable to complete the two walking tests. The mean (SD) baseline saturation of the whole group before the walk was 95% (2·5%). During the walk the mean saturation was 91% (6·0%) and the mean minimum saturation was 89% (8·0%).

The six minute walk distance correlated (r value) most significantly (p < 0·001) with T_{LCO} (0·68), PEF (0·55), FEV_1 (0·53), breathlessness on the MRC scale (−0·52), K_{CO} (0·49), age (−0·49), and FVC (0·48). The distance walked also correlated with all other indices of airflow limitation but to a lesser degree. A scatterplot of distance walked in relation to T_{LCO} is shown in figure 1 to show the spread of these results. There were no significant differences between the regression lines for patients with chronic obstructive airways disease and with chronic severe asthma. Baseline saturation before the walk correlated significantly with distance walked (0·32, p < 0·01), but the minimum saturation recorded during the walk was the only index of desaturation that correlated significantly with distance walked (0·28, p < 0·05; fig 2).

All the indices of desaturation during the walk were significantly intercorrelated. The strongest correlations with lung function were obtained for mean saturation during the walk, which correlated most significantly with T_{LCO} (0·55), FEV_1/FVC (0·54), and PEF (0·48), and with other indices of airflow limitation to a lesser degree, but not with any of the visual analogue scale ratings or with distance walked. A scatterplot of the mean saturation during the walk in relation to T_{LCO} and to distance walked is shown in figure 3a and b. Again there was no significant difference between the regression lines for patients with chronic obstructive airways disease and with chronic severe asthma. Baseline saturation correlated significantly with all indices of airflow obstruction (r = 0·40–0·49) and T_{LCO} (0·39).

Perceived exertion and perceived breathlessness during the walk were significantly correlated (0·65, p < 0·001) and both were correlated to the same degree with the breathlessness rating on the MRC scale and distance walked (p < 0·01). Perceived breathlessness also correlated weakly with T_{LCO} (−0·34) and FEV_1/FVC (−0·32). The MRC scale rating correlated most significantly (p < 0·001) with distance walked (−0·52) and RV/TLC (0·38), less significantly with FEV_1/FVC (−0·36) and T_{LCO} (−0·33), and to a lesser degree with other indices of airflow limitation.

When patients were divided into four groups according to the severity of their mean desaturation during the walk analysis of variance confirmed that there was no significant difference between the groups for distance
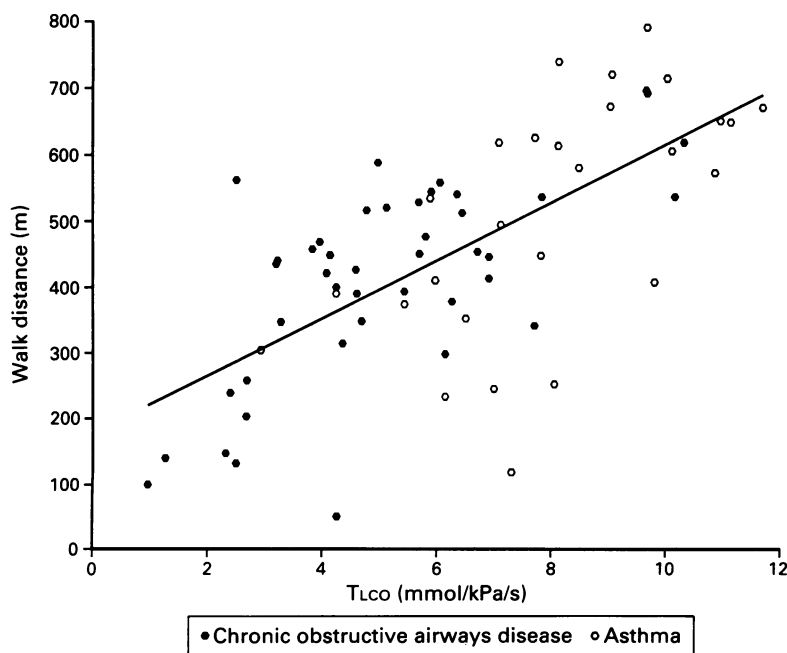

Figure 1   Scatterplot of six minute walk distance related to carbon monoxide gas transfer capacity (T_{LCO}) (r = 0·68, p < 0·001).
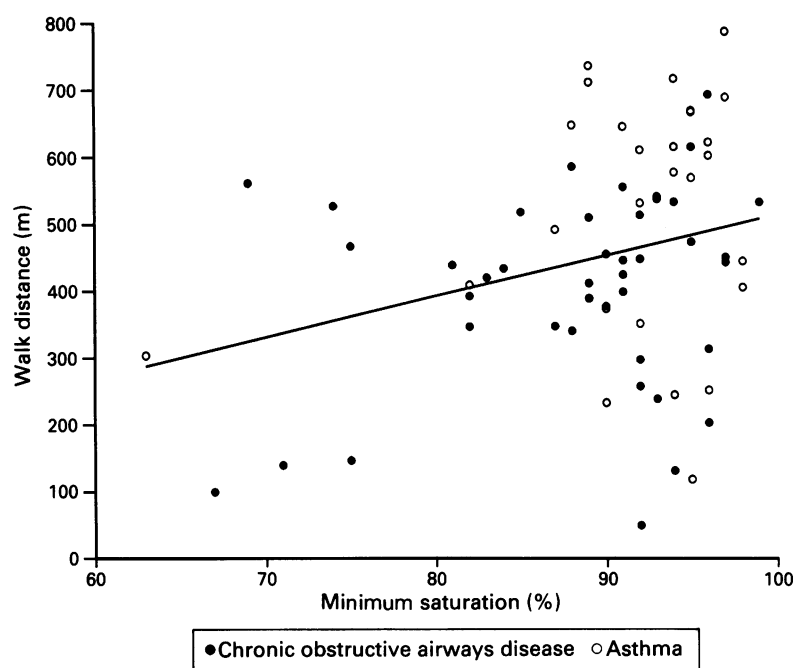
Figure 2   Scatterplot of six minute walk distance related to minimum saturation during the walk ($r = 0.28, p < 0.05$).

walked, perceived exertion, perceived breathlessness, or the MRC breathlessness rating (table 2). There were highly significant differences, however, between these four groups for all indices of lung function except TLC.

The variables that correlated significantly with distance walked were entered into a multiple regression analysis, but the MRC scale was not used as it is not clear whether breathlessness determined distance walked or vice versa. The regression equation generated by stepwise multiple regression analysis for the six minute walk distance (6MD) included TLCO, age, and PEF:

$$6MD \ (m) = 29.7(T_{LCO}) - 3.1(age) + 0.35(PEF) + 387$$
$$(r^2 = 0.50)$$

Multiple regression analysis for the variables of perceived exertion and perceived breathlessness could not account for more than 20% of the total variance in either case, the main predictor variable being distance walked. Although distance walked was not significantly correlated with mean saturation during the walk, this and also TLCO and baseline saturation (BSAT) were chosen by multiple regres-

sion analysis as the main predictor variables for the mean saturation (MEANSAT) during the walk, which together accounted for 61% of the total variance.

$$MEANSAT(\%) = 1.3(T_{LCO}) + 1.5(BSAT) - 0.01(6MD) - 54$$
$$(r^2 = 0.61)$$

Using percentage predicted values did not improve the correlations or change the predictor variables chosen by multiple regression analysis for any of the dependent variables. If data on the two diagnostic groups of patients were analysed separately the significant correlations were the same as when the two groups were analysed together.

Discussion

We have shown that changes in oxygen saturation during submaximal exercise in patients with airflow limitation is not a significant determining factor for submaximal exercise capacity or for perceived exertion or perceived breathlessness during the exercise. Self assessment by the patients of their disability according to the MRC breathlessness scale is not related to desaturation during submaximal exercise. TLCO, however, is significantly correlated with six minute walk distance, perceived breathlessness, and perceived respiratory impairment, which would suggest that oxygenation may play a part in determining these.

Although we have shown that the level of desaturation during the walk was related to the severity of impairment of lung function in terms of airflow and gas transfer, it could not be accurately predicted by any single lung function test. We did find, however, that 61% of the variability in the mean saturation during the walk could be predicted by TLCO, baseline saturation, and distance walked. This finding is supported by D'Urzo *et al*,[3] who also found that mean saturation during treadmill exercise in 38 patients with severe chronic obstructive airways disease correlated with TLCO and baseline saturation, which together accounted for 65% of the total variance.

Other studies have found that it is easier to predict patients who will not develop desaturation during exercise. Owens *et al*[2] found that a TLCO greater than 55% predicted was 100% predictive in excluding desaturation during exercise, as did Ries *et al*[5] in patients with a TLCO of over 6.78 mmol/min/kPa. In our study

Table 2   Analysis of variance between the four groups defined by change in saturation during the walk (DSAT) in relation to lung indices, six minute walk distance (6MD), and ratings on visual analogue scales (VAS), with mean (SD) values for each group (mean rank scores for Kruskal-Wallis analysis for the Borg and MRC scales)

Desaturation (%)	n	PEF*	FEV₁*	FVC*	TLC	RV*	TLCO*	KCO*	6MD	VAS	Borg	MRC
<1	28	247	1.71	3.40	7.42	3.99	8.06	1.53	512	39	33	31
		(111)	(0.75)	(1.18)	(1.28)	(0.97)	(2.04)	(0.41)	(183)	(22)		
1–<5	21	157	1.13	2.52	7.54	5.01	5.60	1.30	392	45	39	39
		(73)	(0.56)	(1.02)	(2.11)	(1.95)	(2.14)	(0.49)	(141)	(28)		
5–<10	12	163	1.09	2.54	8.34	5.19	5.06	1.01	433	57	32	40
		(92)	(0.60)	(0.85)	(1.60)	(1.52)	(2.70)	(0.45)	(178)	(26)		
≥10	9	108	0.68	2.07	8.17	6.05	3.63	0.95	418	47	37	38
		(61)	(0.42)	(1.10)	(1.82)	(1.94)	(1.43)	(0.47)	(142)	(29)		

*Highly significant difference between the DSAT groups for that variable ($p < 0.005$).
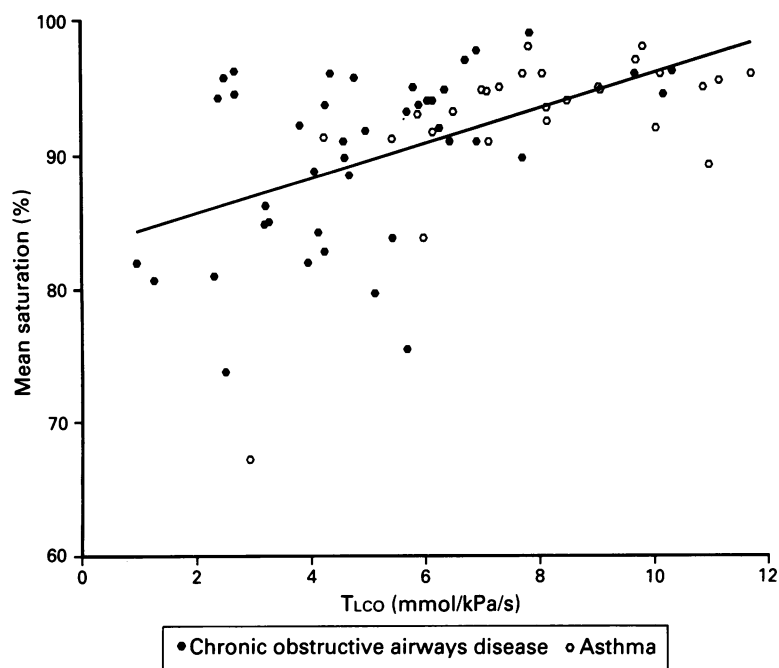Abbreviations as in table 1.

Figure 3   A—Scatterplot of carbon monoxide transfer capacity (TLCO) related to mean saturation during the walk (r = 0·55, p < 0·001).
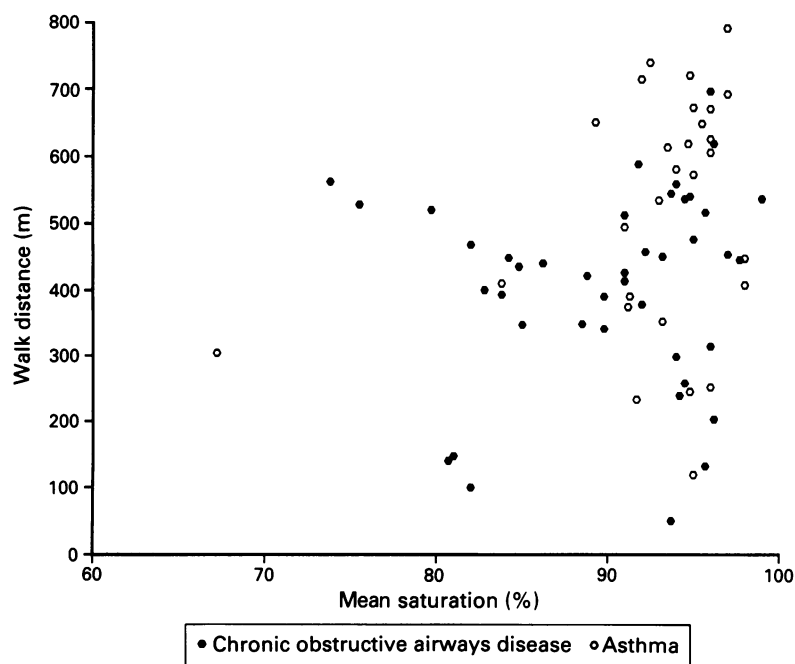

Figure 3   B—Scatterplot of six minute walk distance related to mean saturation during the walk (r = 0·23, NS).

subjects and patients with obstructive airways disease.[7][13] Both Owens et al[2] and Ries et al[5] used incremental symptom limited cycle ergometry. Cycle ergometry significantly underestimates exercise induced desaturation by comparison with treadmill walking tests at a similar level of work.[14] Indeed, step test exercise has been found to produce even greater falls in arterial oxygen tension than steady state treadmill walking in patients with chronic obstructive airways disease.[15] The symptom limited six minute walk may fall between the treadmill walking test and step test exercise in producing exercise induced arterial desaturation.

The present study used pulse oximetry as an indicator of arterial hypoxaemia. Some doubts have been cast on the accuracy of pulse oximeters in measuring desaturation during exercise[16] and on the use of finger rather than ear probes.[17] Recent reports, however, on a range of pulse oximeters show that they reliably estimate changes in arterial saturation during exercise in both normal subjects and patients with respiratory diseases,[18-20] and that finger probes are as accurate as ear probes. Obviously, some patients may have had a fall in arterial oxygen tension during submaximal exercise without an appreciable fall in arterial oxygen saturation because of the shape of the haemoglobin oxygen dissociation curve, but any desaturation detected by pulse oximetry in patients with a normal baseline saturation should represent a large fall in arterial oxygen tension.

There are few data on the effect of exercise induced hypoxaemia on the subjective sensations of breathlessness and effort. As in the present study, Jones et al[21] found a significant correlation between the grade of dyspnoea, as assessed on the old MRC breathlessness scale, and work capacity in patients with chronic airways obstruction. Some studies have found that breathlessness scores in patients with chronic obstructive airways disease are not related to chemical drives for ventilation induced by hypoxia or hypercapnia.[22][23] Lane et al,[24] however, found a reduction in breathlessness scores by preventing hypoxaemia at equivalent levels of ventilation during exercise. Despite this uncertainty about the effect of exercise induced hypoxaemia in determining respiratory sensations, some studies have shown that oxygen supplementation during exercise can improve breathlessness ratings in patients with chronic obstructive airways disease.[24][25] In the present study neither perceived breathlessness nor perceived exertion could be reliably predicted by desaturation or any variable of lung function. The fact that breathlessness and exertion were significantly correlated, and both were correlated to a similar degree with distance walked and ratings on the MRC breathlessness scale, may suggest that patients perceive breathlessness and exertion as the same sensation.

In the present study the regression equation produced by multiple regression analysis accounted for only half of the total variance in the six minute walk distance. The poor predic-

33 of 45 patients with a TLCO above 55% predicted developed some degree of desaturation during walking—seven of them more than 5% desaturation. Among the 28 patients with a TLCO of over 6·78 mmol/min/kPa 16 showed some evidence of desaturation during exercise, two of them more than 5% desaturation.

The higher prevalence of exercise induced desaturation in our study may be due to the type of exercise used and is consistent with the findings of some previous studies. Desaturation has been described even in normal subjects during unsteady state exercise. Large falls in arterial oxygen tensions may occur during simple slow stair climbing in both normal

tion of exercise capacity by indices of lung function is well known. Significant but weak correlations have been obtained between submaximal exercise capacity and FEV_1[26-28] and VC[26 28] in patients with airflow limitation. In close agreement with our results, Jones et al,[21] using multiple regression analysis in 50 men with chronic airways obstruction, found that TLco, FEV_1, and age were the main predictor variables, which together accounted for 54% of the total variance in maximum exercise capacity. Psychosocial variables, however, especially depression and patients' perception of their illness, may have a more substantial effect in determining exercise capacity than lung function.[29-31]

Although TLco, age, and indices of airflow obstruction together predict submaximal exercise capacity to some extent, patients' self ratings on the MRC breathlessness scale correlate as well with submaximal exercise capacity as most single indices of lung function. This suggests that taking an accurate history is as important as making sophisticated measurements.

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