Quality of life in severe chronic obstructive pulmonary disease: correlation with lung and muscle function


Servei de Pneumologia, Hospital Germans Trias i Pujol, Badalona. Institut Municipal d'Investigació Mèdica, Barcelona, Catalonia, Spain

Chronic obstructive pulmonary disease (COPD) patients suffer from significant impairment in quality of life (QL), but the variables related to this impairment are not well known. The aim of this study has been to identify physiological parameters related to QL in severe COPD patients undergoing long-term oxygen therapy.

**Materials and Methods.** We studied 47 COPD patients using long-term oxygen therapy (43 men/four women, 65.17 ± 8.21 years, 3.17 ± 2.61 years on oxygen). The Nottingham Health Profile (NHP) and activities of daily living (ADL) questionnaire were used to measure QL. Subjective assessment of dyspnoea was performed using a visual analogue scale. The physiological parameters determined were lung function (spirometry, arterial blood gases, lung volumes and carbon monoxide diffusing capacity), muscle function (maximum inspiratory and expiratory pressures, deltoid muscle and handgrip strength), and nutrition status (tricipital skin fold and mid-arm muscle circumference).

**Results.** High ADL (8.32 ± 6.97) and NHP scores (energy 63.3 ± 40.43, pain 35.11 ± 31.56, emotional reactions 43.03 ± 25.13, sleep 51.91 ± 32.75, social isolation 30.64 ± 26.98, physical mobility 49.73 ± 24.93) demonstrated clinically significant QL impairment in the severe COPD patients studied. Stepwise multiple regression analysis found a correlation between lung function and QL. Low FEV₁% was associated with impairment in energy, physical mobility and social isolation NHP scores and ADL score (r = -0.3, P<0.05). RV/TLC also correlated with ADL and social isolation scores (r=0.3, P<0.05). Lung function explained 39-45% of the variation in these QL dimensions. QL did not correlate with other lung function parameters, muscle function or nutrition status.

**Conclusion.** COPD patients using long-term oxygen suffer from severe QL impairment affecting not only energy and mobility but also emotional reactions, social isolation and sleep. Lung function is related to energy, mobility and social isolation dimensions, but muscle function is unrelated to QL in these patients.
referred to our university hospital for assessment of their clinical status and monitoring of oxygen use (9). All subjects from this population who had neither used long-term corticotherapy nor followed rehabilitation programmes the previous year and who were able to answer a QL questionnaire and perform lung and muscle function tests were considered suitable for the present cross-sectional study. A total of 47 patients with severe COPD (FEV₁/FVC <50%) (10,11) who had been using long-term oxygen therapy over the last 3·17 (SD 2·61) yr were enrolled in the study (43 men/four women; age: 65·17 ± 8·21 years; height: 162·47 ± 7·99 cm; weight: 68·91 ± 13·51 kg). Arterial blood analysis showed chronic respiratory insufficiency (PaO₂ <60 mmHg) in all cases.

QUALITY OF LIFE ASSESSMENT

The Spanish version of the Nottingham Health Profile (NHP) was used to measure the QL of this group (12). The NHP is a self-administered questionnaire on perceived general health that was developed in the United Kingdom and contains 38 statements pertaining to six dimensions of health (energy, pain, emotional reactions, sleep, social isolation, and physical mobility). The respondent answers 'yes' if a statement adequately reflects his/her current perception, or 'no' if otherwise (13). The NHP has proved to be valid, reproducible, and sensitive to changes over a wide range of diseases, including COPD (14,15). NHP scores were calculated as previously reported (1,12). Possible scores range from 0 (denoting absence of distress in that health dimension) to 100 (maximum distress).

A second self-administered questionnaire on activities of daily living (ADL), modified from the list of daily activities (16), was used to determine limitation in performing 11 ADL: (1) walking; (2) sitting up/down; (3) shaving/making up/comb; (4) bathing/taking showers; (5) using the toilet; (6) dressing/undressing; (7) eating; (8) climbing/descending one flight of stairs; (9) going to the street; (10) cooking own food; and (11) shopping at the supermarket. For every activity the patient was asked to choose between four possible options (no difficulty, slight difficulty, great difficulty, or impossible to do without help). The general ADL score was obtained by adding all the individual scores. Possible scores ranged from 0 (no limitation) to 33 (impossible to do any activity without help).

The questionnaires were self-administered by the patients after 15 min of relaxation in a quiet room, in all cases before the performance of lung and muscle function tests. When the patient found the questionnaire hard to read a nurse read each question aloud (23/47 patients 48.9%). In no case did the nurse give advice directly or indirectly as to how to answer. All the patients completed the questionnaires correctly.

Use of oxygen therapy was inquired about in all cases; 34/47 patients were using compressed oxygen, 10/47 were using an oxygen concentrator and 3/47 were using liquid oxygen. Most of the patients used long-term oxygen more than 15 h a day (34/47). Co-morbidity due to non-respiratory chronic diseases was reported by two patients suffering from chronic kidney failure and vascular insufficiency.

LUNG FUNCTION ASSESSMENT

Lung function measurements were performed with the patient in a clinically stable condition (no history of exacerbation the previous month) and following 15 min rest. An arterial blood sample was obtained with the patient breathing room air (Radiometer ABL, Copenhagen). Forced and slow spirometry (FEV₁, FVC, VC, FEV₁/FVC), lung volumes (RV, RV/TLC), and carbon monoxide diffusing capacity (DLCO, KCO) were assessed by a PFT Horizont spirometer (SensorMedics Corp., Torba Linda, CA, USA). Spirometric equipment was calibrated daily and checked regularly before each subject was tested, and the American Thoracic Society Guidelines for measurements were followed (17). From the actual values, we calculated the percentage of the reference for the patient's age, height, and weight using Mediterranean population reference values (18,19).

Patients were asked by a nurse to rate their usual level of dyspnoea at rest, using a visual analogue scale (VAS) (range 0 mm=no dyspnoea to 170 mm=maximum dyspnoea) (20,21).

MUSCLE FUNCTION AND NUTRITION ASSESSMENT

Respiratory and peripheral muscle function were measured after 15 min rest. Measured respiratory muscle function parameters were maximum inspiratory pressure (PImax) and maximum expiratory pressure (PEmax) (cm H₂O) and their percentage of Mediterranean population reference values (22). PImax and PEmax were measured from RV and TLC respectively, using the Black and Hyatt method (23). To obtain these values, a pressure transducer with a range of 0–300 cm H₂O (SiBelmed-163) and a rigid-tube mouthpiece (diameter 2·5 cm) were used. To overcome the learning effect, a minimum of ten manoeuvres were required until a variation of less than 5% was achieved (24). The manoeuvre was supervised by a trained technician, who manually compressed the subject's lips around the cylindrical tube to prevent possible loss of pressure as has been previously described (25).

Peripheral muscle function was measured using the strength of the deltoid muscle as previously described (left arm for right-handed patients, right arm for left-handed ones) (26). For these measurements an electronic myometer was used (Peny and Giles Ltd, Christchurch, England) (absolute values in kg). Handgrip strength of the non-dominant arm was also measured using a hand-held dynamometer (Lafayette 32528 HD) (absolute values in kg).

The skin fold of non-dominant triceps and non-dominant mid-arm muscle circumference, and their percentile in terms of Mediterranean population reference values (27) were the nutrition parameters measured. The skin fold was measured using a lipocalibrator (Holtain, Cambridge,
FIG. 1. Nottingham Health Profile dimensions. Results obtained in severe COPD patients with chronic respiratory insufficiency (means).

United Kingdom) on the posterior aspect of the triceps, midway between the olecranon process of the ulna and the acromion process of the scapula, using the standard technique (mm) (28). Mid-arm muscle circumference was measured using a millimetred tape firmly placed at the mid-point of the arm at the same point as the tricipital skin fold (cm).

STATISTICAL ANALYSIS

All the data were expressed as means and standard deviations unless specified. Pearson correlation coefficients were calculated to determine the relation between physiological variables (lung function, muscle function, nutrition), and subjective patient-based variables (NHP scores, ADL score, VAS). Stepwise regression analyses were performed using NHP and ADL scores as dependent variables and lung function, muscle function, nutrition status and VAS as independent variables. Results were considered statistically significant when $P<0.05$.

RESULTS

QUALITY OF LIFE ASSESSMENT

The mean score on the ADL questionnaire was 8.32 ± 6.97, corresponding to clinically significant difficulty in the performance of the daily activities assessed. Scores on the various dimensions of the NHP were 63.3 ± 40.3 for energy; 35.11 ± 31.56 for pain; 43.03 ± 25.13 for emotional reactions; 51.91 ± 32.75 for sleep; 30.64 ± 26.98 for social isolation; and 49.73 ± 24.93 for physical mobility (Fig. 1). All these NHP scores reflected severe limitation, considering that the mean scores for the general population of Spain are under 18 on all dimensions (30).

LUNG FUNCTION ASSESSMENT

All patients suffered from severe COPD as determined by forced spirometry: $FEV_1$ 0.91 ± 0.43; $FEV_1$% 31.79 ± 11.97; FVC 1.88 ± 0.60; FVC% 48.02 ± 13.64; $FEV_1$/FVC 48.43 ± 11.23. Arterial blood analysis showed chronic respiratory insufficiency in all cases: pH 7.38 ± 0.04; $PaO_2$ 50.25 ± 7.71; $PaCO_2$ 52.93 ± 9.12; and $\%O_2$ saturation 82.94 ± 8.81. Results for lung volumes showed high residual volumes: RV 3.87 ± 1.28; RV% 187.76 ± 61.48; RV/TLC 63.04 ± 9.19. Observed carbon monoxide diffusing capacities were low (DL$CO$% 66.38 ± 30.02), but were within the reference range when adjusted (K$CO$% 90.76 ± 38.64). Nine patients could not perform lung volume tests and/or TLC0 manoeuvres correctly, and their results were therefore not considered.

MUSCLE FUNCTION AND NUTRITION ASSESSMENT

In most cases, $P_{max}$, $P_{max}$%, skin fold of non-dominant triceps and non-dominant mid-arm muscle circumference were within the normal range (Table 1). Only in 2/47 cases (one skin fold and one mid-arm muscle circumference) were

| Table 1. Muscle function and nutrition status |
|-----------------|-----------------|-----------------|-----------------|
| $P_{max}$ (cm H$_2$O) | 29.00 | 117.00 | 60.45 |
| $P_{max}$% | 34.00 | 163.00 | 82.53 |
| $P_{max}$ (cm H$_2$O) | 40.00 | 256.00 | 150.47 |
| $P_{max}$% | 34.00 | 220.00 | 124.26 |
| DS (kg) | 6.00 | 24.80 | 14.10 |
| HS (kg) | 0.00 | 11.99 | 3.71 |
| TSF (mm) | 0.77 | 30.16 | 15.77 |
| TSF percentile | 1.00 | 99.00 | 69.28 |
| MC (cm) | 21.00 | 39.15 | 29.35 |
| MC percentile | 1.00 | 99.00 | 66.83 |

$P_{max}$=maximum inspiratory pressure; $P_{max}$=maximum expiratory pressure; DS=deltoid strength; HS=handgrip strength; TSF=tricipital skin fold; MC=mid-arm circumference.
The results obtained below the 5th percentile, showing malnutrition.

**CORRELATION BETWEEN PHYSIOLOGICAL PARAMETERS AND QUALITY OF LIFE**

Correlation between the various lung function parameters and QL scores are shown in Table 2. No significant correlations were found between QL scores and device used for long-term oxygen therapy (compressed oxygen, concentrator, liquid oxygen) or h day−1 of use (>15 h or <15 h). Significant correlations (*P<0.05) were found between years since initiating oxygen therapy and VAS, ADL scores and results on the NHP physical mobility dimension (r=0.3, Pearson correlation coefficient), suggesting that longer use of oxygen was associated with more dyspnoea, higher limitation in daily activities and mobility impairment. We found no significant correlation between arterial blood gases and VAS, ADL score or any of the NHP dimensions.

Lung function parameters (FEV1, RV/TLC) and QL were also significantly correlated. Low FEV1% was associated with limitation in daily activities and high scores on the energy, physical mobility and social isolation NHP dimensions (r=−0.3, Pearson correlation coefficient). High RV/TLC was also related to limitation in daily activities and a high social isolation score (r=0.3, Pearson correlation coefficient). No significant correlation was found between any other lung function parameter (FVC%, VC%, RV%, arterial blood gases) and QL. Carbon monoxide transfer coefficient was unrelated to QL, except for a slight correlation between KCO and the social isolation score (r=−0.3, Pearson correlation coefficient) (Table 2). No significant correlation was found between QL and muscle function parameters (Pmax, Pmax%, Pmax%, deltoid and handgrip strength) or nutritional status (tricipital skin fold and mid arm circumference).

Lung function parameters were not significantly correlated with dyspnoea (VAS), but dyspnoea, a subjective parameter, correlated significantly with QL. VAS score was related to ADL score and to scores on most NHP dimensions (energy, pain, emotional reactions and physical mobility; r=0.34 to 0.51, Pearson correlation coefficient).

Stepwise multiple regression analysis revealed that lung function explains 39−45% (model R2) of the variance for some dependent variables (energy, physical mobility, social isolation). The amount of explained variance increased when dyspnoea (VAS) was also considered as an independent variable, but only slightly (model R2: 45−69%).

**Discussion**

COPD patients using long-term oxygen suffer from severe QL impairment. Our COPD patients scored higher than 30 on all NHP dimensions, well above the general populations of Barcelona and Nottingham (13,29). The level of distress was especially high for energy (63.8), physical mobility (49.9), emotional reactions (35.1) and social isolation (30.6) and all these scores were much higher than those found in COPD patients with less severe disease (1,30). The high degree of distress found in this group of severe COPD patients cannot be explained by co-morbidity (31) because only 4.4% suffered from an associated chronic non-respiratory disease.

Our observations agree with previous studies pointing to a marked deterioration in general health in patients with severe COPD (4,8,32,33). Chronic respiratory disease, like arthritis, gastrointestinal disorders and angina, is one of the chronic diseases that have a negative impact on all dimensions of a patient's general sense of well-being (31,34−36), but the main determinants of QL impairment in COPD...
patients are not fully understood. The aim of our study was to determine which physiological variables are associated with QL in severe COPD patients on long-term oxygen, and we found significant correlations between lung function (FEV1%, RV/TLC) and QL in this group. Lower FEV1% is associated with the perception of energy loss, impairment in physical mobility and higher limitation in daily life activities, and a similar degree of correlation was found between QL dimensions and RV/TLC. Interestingly, lung function impairment was associated with the perception of social isolation in this group of severe COPD patients, an impact not previously recognized in COPD patients with less severe disease. This effect of COPD on the sociability of the patient may be related to the severity of disease or to the restriction in mobility associated with long-term oxygen.

Overall, the results of our multiple regression analysis confirmed that lung function explains almost 50% of QL variation. It is generally recognized that the score obtained on general health questionnaires partially depends on non-physiological patient-based variables, which includes psychological and sociological characteristics of the subject (37-39). Dyspnoea is a subjective parameter that, in our study, did not correlate significantly with lung function, but was related to QL (r=0.34 to 0.51), and contributed an additional 6-24% toward explaining the QL variation in the studied sample.

Lung function and dyspnoea, then, are different factors that characterize the condition of patients with COPD (40), and muscular performance is a third factor independently related to the pathophysiological condition of these patients (41). Exercise tests, respiratory pressures and peripheral muscle strength can be used to assess muscle performance, and in our study we selected PMax, PEmax and peripheral muscle force for such assessment, after considering the strong correlation between either peripheral muscle strength or Pmax and exercise capacity in COPD patients (42,43). We failed, however, to find a correlation between QL and peripheral muscle force or respiratory pressures. In COPD patients, Mahler et al. found a low but statistically significant correlation (r=0.3) between Pmax and general health status (44), but their patients had light-to-moderate obstructive disease. The differences between Mahler’s findings and ours are probably attributable to greater severity of disease in our COPD patients, suggesting that Pmax is a QL determinant only in COPD patients with light/moderate disease.

We did not find any significant correlation between nutritional status and QL. Our COPD patients showed low prevalence of severe malnutrition (only 4.2% of the patients were in the lowest 5th percentile) and this acceptable nutritional status was probably responsible for the observed absence of correlation (45,46).

We did not use respiratory disease-specific questionnaires, which have proven useful for the study of COPD patients (47-49), as valid and reliable Spanish versions of the Chronic Respiratory Disease Questionnaire and the St George’s Respiratory Questionnaire were not available when the study was performed (50,51). The NHP, however, has been used with COPD patients and has shown its accuracy in recognizing the impact of airways disease on general health (1). By using the NHP we obtained information on different aspects of daily life and a broad picture of QL changes in severe COPD, including aspects such as sociability and sleep quality.

We conclude that COPD patients using long-term oxygen suffer from a marked decrease in QL, and that this QL impairment affects not only physical dimensions, but also emotional reactions, social isolation and sleep. In these patients lung function explains almost 50% of the variability found in some QL dimensions (energy, physical mobility, social isolation), but muscle function has no impact on QL, indicating that QL is not strength-dependent in COPD patients using long-term oxygen.

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