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Functional Status and Survival in Patients With Chronic Obstructive Pulmonary Disease Following Pulmonary Rehabilitation

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OBJECTIVES: To study functional status and survival in patients with chronic obstructive pulmonary disease (COPD) following a pulmonary rehabilitation program.

PATIENTS AND METHODS: We assessed lung function, 6-minute walk distance, Borg score for dyspnea upon completion of the 6-minute walk, workload in watts on a cycle ergometer, quality of life using the St George's Respiratory Questionnaire (SGRQ); the body-mass index, airflow obstruction, dyspnea, and exercise capacity (BODE) index; and survival.

RESULTS: One hundred five patients participated in the pulmonary rehabilitation program. The patients had a mean (SD) age of 63.9 (9.3) years, body mass index of 24.5 (4.56) kg/m^2, and forced expiratory volume in 1 second (FEV_1) of 0.91 (0.46) L. The mean distances walked in 6 minutes were 412.8 (79.4) m before the pulmonary rehabilitation program and 443.46 (81.57) m after rehabilitation. The mean workloads on the cycle ergometer before and after rehabilitation, respectively, were 47.9 (29.6) W and 77.76 (20.88) W. The mean Borg scores were 2.2 (1.37) before and 1.47 (1.37) after rehabilitation, and the SGRQ scores at the same times were 27.63 (16.02) and 25.45 (15.12). Mortality due to respiratory disease (105 months) was 19%. Cumulative survival rates at 1 year, 3 years, and 6 years were 91%, 86.7%, and 6.75%, respectively. Survival was related to an FEV_1 greater than 1.02 L (*P*=.05), a 6-minute walk distance over 448 m before rehabilitation (*P*=.04) and 454 m after rehabilitation (*P*=.05), and a workload on the cycle ergometer of over 54 W before rehabilitation (*P*=.01) and 72 W (*P*=.02) afterwards. The correlations between survival and both SGRQ and BODE scores were weaker.

CONCLUSIONS: We observed improved exercise capacity, dyspnea ratings, and, to a lesser extent, better SGRQ scores in our COPD patients following pulmonary rehabilitation. The best predictors of survival were FEV_1, the 6-minute walk distance, and the cycle ergometer workloads.

Key words: *Pulmonary rehabilitation. COPD. Survival predictors.*

Estado funcional y supervivencia de los pacientes con EPOC tras rehabilitación respiratoria

OBJETIVOS: Mostrar los resultados funcionales y la supervivencia de pacientes con enfermedad pulmonar obstructiva crónica (EPOC) tras un programa de rehabilitación respiratoria (RR).

PACIENTES Y MÉTODOS: Se evaluaron la función pulmonar, la distancia recorrida en 6 min y la disnea según la escala de Borg en la prueba de la marcha de 6 min, carga en vatios sobre cicloergómetro y calidad de vida por el St. George's Respiratory Questionnaire (SGRQ), puntuación en el índice BODE y supervivencia.

RESULTADOS: Ingresaron en el programa de RR 105 pacientes, con una edad media ± desviación estándar de 63,9 ± 9,3 años, índice de masa corporal de 24,5 ± 4,56 y volumen espiratorio forzado en el primer segundo (FEV_1) de 0,91 ± 0,46 l/s. La distancia recorrida en 6 min antes de RR fue de 412,8 ± 79,4 m, y tras RR de 443,46 ± 81,57 m. La carga en cicloergómetro fue de 47,9 ± 29,6 W pre-RR y de 77,76 ± 20,88 W post-RR. La puntuación en la escala de Borg fue de 2,2 ± 1,37 pre-RR y de 1,47 ± 1,37 post-RR, y el SGRQ de 27,63 ± 16,02 y 25,45 ± 15,12, respectivamente. La mortalidad respiratoria (105 meses) fue del 19%. La supervivencia acumulada a 1, 3 y 6 años fue del 91, el 86,7 y el 67,5%, respectivamente, y se relacionó con un valor de FEV_1 mayor de 1,02 l/s (p = 0,05), distancia recorrida en la prueba de la marcha de 6 min mayor de 448 m pre-RR (p = 0,04) y de 454 m post-RR (p = 0,05) y carga en cicloergómetro mayor de 54 W pre-RR (p = 0,01) y de 72 W post-RR (p = 0,02). La relación de la supervivencia con el SGRQ y el índice BODE fue menor.

CONCLUSIONES: La capacidad de ejercicio, la disnea y, en menor grado, la calidad de vida mejoraron con la RR en los pacientes con EPOC. Los mejores predictores de supervivencia fueron el FEV_1, la distancia recorrida en 6 min y los vatios alcanzados en el cicloergómetro.

Palabras clave: *Rehabilitación respiratoria. EPOC. Predictores de supervivencia.*

Introduction

Chronic obstructive pulmonary disease (COPD) is a leading cause of morbidity and mortality, a major social and economic burden, and a truly serious global health problem.[1] Moreover, its prevalence continues to rise in the United States of America, Europe, and Latin America.[2-4] Specific diagnosis and treatment recommendations published recently by the American Thoracic Society (ATS) and the European Respiratory Society[5] highlight the multisystemic nature of the disease. One of the systemic effects of COPD is muscle

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dysfunction, and muscle fatigue greatly limits the physical effort a patient can make.[6] Loss of muscular mass, changes in muscle fiber predominance and blood flow to the muscle, and premature lactic acidosis during exercise all result in exercise intolerance,[7] impaired health-related quality of life,[8] a high utilization of healthcare resources,[9] and low patient survival rates.[10]

Pulmonary rehabilitation has been added to the therapeutic arsenal used to manage COPD patients, and leading medical associations have published guidelines for its implementation.[1,5,11-14] Exercise training reduces perception of dyspnea and improves exercise tolerance[5-17] and peripheral muscle characteristics.[18] In turn, these effects result in improved patient health and fewer hospitalizations.[19] Survival data for COPD patients who have undergone pulmonary rehabilitation, however, are lacking.

The aim of our study was to assess functional status and survival in COPD patients following a 3-month rehabilitation program at our hospital in Uruguay.

Patients and Methods

The pulmonary rehabilitation program enrolled 105 outpatients from the department of respiratory medicine at the Centro de Asistencia del Sindicato Médico de Uruguay. All of the patients had stable COPD, were receiving medical treatment, and had no associated heart, cerebrovascular, or bone and joint diseases. Each of the participants was assessed for lung function at rest, exercise capacity, dyspnea, and quality of life before the program began and when the program ended 3 months later. The patients were followed from 1995, the year in which the program started, to December 2003 (105 months).

Lung function was assessed by pre- and postbronchodilation spirometry using a modular Collins CPL unit (Braintree, Massachusetts, USA) according to ATS recommendations.[20] Exercise capacity was measured with the 6-minute walk test and the cardiopulmonary exercise test. The 6-minute walk test was performed on a 30-m corridor in compliance with ATS guidelines.[21] Patients were asked to walk the greatest distance possible in a period of 6 minutes. The following parameters were measured at rest and at peak exercise: arterial oxygen saturation, measured with a 504DX pulse oximeter (Criticare, Waukesha, Wisconsin, USA), dyspnea on the Borg scale, heart rate, and arterial pressure. We performed 2 tests for each patient with a 30-minute interval between tests. The best results were recorded in meters.

The cardiopulmonary exercise test was a symptom-limited incremental test performed on an Ergometrics 800 cycle ergometer (Ergoline, Bitz, Germany). Ventilation, oxygen consumption, and $PaCO_2$ values were measured and maximum workloads recorded in watts. Reference values used for ventilation and heart rate were maximum voluntary ventilation and maximum heart rate.

The maximum workload value in watts was used as a measure of maximum exercise capacity.

Dyspnea and Quality of Life

Dyspnea was assessed with the Medical Research Council (MRC) Dyspnea Scale,[22] which classifies dyspnea into grades 0 to 4 depending, for example, on whether symptoms appear only with peak exercise (grade 0) or with minimum efforts such as bathing or dressing (grade 4).

From 1998 onwards we assessed health-related quality of life of patients before and after the program using the Spanish version of the St George's Respiratory Questionnaire (SGRQ),[23] a self-administered respiratory questionnaire that has 3 components, or subscales, that assess disease symptoms, activity, and impact. The maximum score of 100 indicates the worst quality of life.

Evaluation of Nutritional Status and Body-Mass Index, Airflow Obstruction, Dyspnea, and Exercise Capacity Score

We evaluated the nutritional status of patients by measuring body mass index (BMI). We also used the multidimensional index designed by Celli and colleagues[24] to evaluate COPD patients. This 10-point index, known as BODE (BMI, airflow obstruction, dyspnea, and exercise capacity) measures severity of airflow obstruction using forced expiratory volume in 1 second (FEV_1), 6-minute walk distance, BMI, and dyspnea score on the MRC scale. A higher BODE score expresses poorer performance in terms of FEV_1, 6-minute walk distance, BMI, and dyspnea.

Pulmonary Rehabilitation Program

Our department's outpatient pulmonary rehabilitation program runs for 3 months. Patients attend two 150-minute sessions a week. Among the program's goals are to help increase the patients and their families' knowledge of the disease and its management, to teach them how to use inhalers and control exacerbations, to provide them with psychosocial and nutritional support, and to exercise the patients' arms and legs. Patients perform exercises to stretch and relax different muscle groups as well as diaphragmatic and pursed-lip breathing exercises. Cycle ergometer exercises are conducted using workloads equal to 70% of the maximum workload reached in the cardiopulmonary test and are complemented with treadmill exercises, walking, stair climbing, and arm lifts with weights. Patients who experience arterial oxygen desaturation during exercise are administered oxygen during rehabilitation.

When patients join the program, they are encouraged to do daily exercise and are given a leaflet describing the different exercises they can do. Patients may also enroll on a maintenance program a year after they are discharged from the pulmonary respiration program.

Patient Survival

Survival data were collected from institutional databases, which were reviewed every 6 months. The situation of discharged patients was determined via a review of hospital records and telephone contact. Cause of death was obtained from hospital records. We were able to obtain survival data for all of the study patients.

Statistical Analysis

Anthropometric characteristics, lung function results, 6-minute walk distance, maximum workload, dyspnea ratings, and quality of life scores were all expressed as means (SD). The Student *t* test for paired data was used to determine changes in distance walked, workload, and dyspnea following pulmonary rehabilitation.

Statistical significance was established at a *P* value of less than .05.

A change of at least 4 units[25] in the SGRQ score was considered significant.

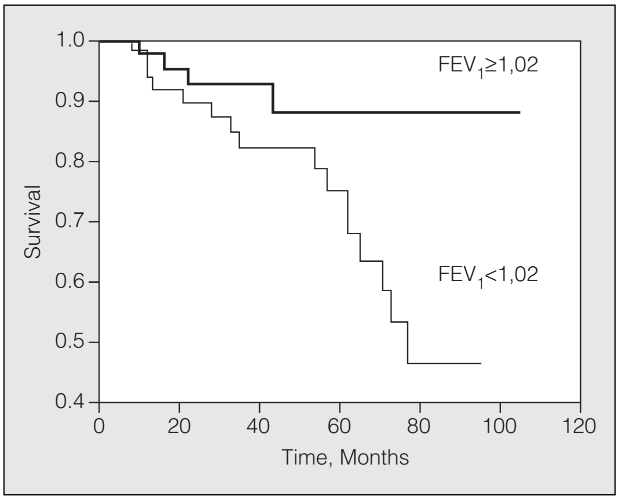

Figure 1. Correlation between lung function at rest (forced expiratory volume in 1 second [FEV_1]) and survival following a pulmonary rehabilitation program. The correlation was not statistically significant (*P*=.05, log rank test).

The mean calculated for the different variables was used as the cutoff for the Kaplan-Meier survival curves. Kaplan-Meier survival curves were constructed for the whole group and for subgroups defined by the following variables: age, sex, desaturation during exercise, 6-minute walk distance, workload, and SGRQ and BODE scores. Statistical significance was established by log-rank tests.

Results

A total of 105 patients, 81% of whom were male, enrolled in the pulmonary rehabilitation program during the period analyzed. Table 1 shows their anthropometric characteristics, lung function variables at rest and during exercise, dyspnea as measured on the MRC scale, and the BODE and SGRQ scores.

Twenty-five patients presented desaturation during the cycle ergometer test and were administered oxygen during rehabilitation. Table 2 shows the mean (SD) results obtained before and after pulmonary rehabilitation for FEV_1, 6-minute walk distance, cycle ergometer workloads, dyspnea during exercise (Borg scale), and changes in quality of life.

The clinically significant threshold of a 4-unit improvement in SGRQ total or subscale (symptoms, daily activity, and impact) scores was not reached.

The follow-up period was 105 months. Twenty patients (19%) died due to respiratory disease. Cumulative survival following pulmonary rehabilitation was 95.6% in the first year and 91%, 86.7%, 84.8%, 80.2%, and 67.5% in years 2, 3, 4, 5, and 6, respectively.

The best predictors of survival were FEV_1 at rest (Figure 1) and during exercise before and after pulmonary rehabilitation, 6-minute walk distance (Figure 2), and cycle ergometer workloads (Figure 3). Survival was or tended to be greater in patients with an FEV_1 of greater than 1.02 L/s (*P*=.05), a 6-minute walk distance over 448 m (*P*=.04), and a cycle ergometer workload over 54 W (*P*=.01) before rehabilitation. A walk distance over 454 m and a cycle ergometer workload of 72 W after rehabilitation were also correlated with greater survival.

Survival tended to be greater, though not statistically significant, in patients with higher SGRQ scores (*P*=.6) (Figure 4) and lower BODE scores (*P*=.5) (Figure 5).

The lower survival rate in patients over 70 years was not statistically significant (*P*=.08).

No correlation was observed between survival and sex, BMI, or arterial oxygen desaturation during exercise.

Discussion

The main aim of our study was to evaluate changes in lung function and survival in COPD patients who had participated in a pulmonary rehabilitation program. Our patients had advanced COPD, as is indicated by a mean

TABLE 1
Characteristics of Study Population and Lung Function Variables at Rest and During Exercise*

Characteristics	Patients (n=105)
Age, y	63.9 (9.3)
BMI, kg/m^2	24.5 (4.6)
FEV_1, L/s	0.91 (0.46)
FEV_1, %	38.35 (14.75)
6MWD, m	412.8 (79.4)
CPET, W	47.9 (29.6)
MRC grade	2.44 (0.62)
SGRQ total score†	38.18 (15.94)
SGRQ activity score†	57.98 (23.40)
SGRQ symptoms score†	30.45 (19.40)
SGRQ impact score†	28.56 (17.50)
BODE score	3.22 (1.87)

*Data are shown as means (SD). 6MWD indicates 6-minute walk distance; FEV_1, forced expiratory volume in 1 second; BMI, body mass index; MRC, Medical Research Council; CPET; cardiopulmonary exercise test; SGRQ, St George's Respiratory Questionnaire.
†Questionnaire given to 44 patients only.

TABLE 2
Lung Function Variables at Rest and During Exercise Before and After Pulmonary Rehabilitation Program*

Variables	No.	Before Rehabilitation	After Rehabilitation
FEV_1, L/s	105	0.91 (0.47)	.005 (0.47)†
6MWD, m	105	412.8 (79.4)	443.46 (81.57)‡
CPET, W	105	47.9 (29.6)	7.76 (20.88)†
Dyspnea, Borg score	105	2.00 (1.37)	1.47 (1.33)†
SGRQ total score	44	38.18 (15.94)	34.76 (15.12)
SGRQ activity score	44	57.98 (23.40)	55.77 (20.76)
SGRQ symptoms score	44	30.45 (19.40)	26.41 (19.31)§
SGRQ impact score	44	28.56 (17.50)	25.53 (15.86)

*Data are shown as means (SD). 6MWD indicates 6-minute walk distance; FEV_1, forced expiratory volume in 1 second; CPET, cardiopulmonary exercise test; SGRQ, St George's Respiratory Questionnaire.
†*P*<.01 (Student *t* test).
‡*P*<.05 (Student *t* test).
§4-unit improvement not reached after pulmonary rehabilitation.

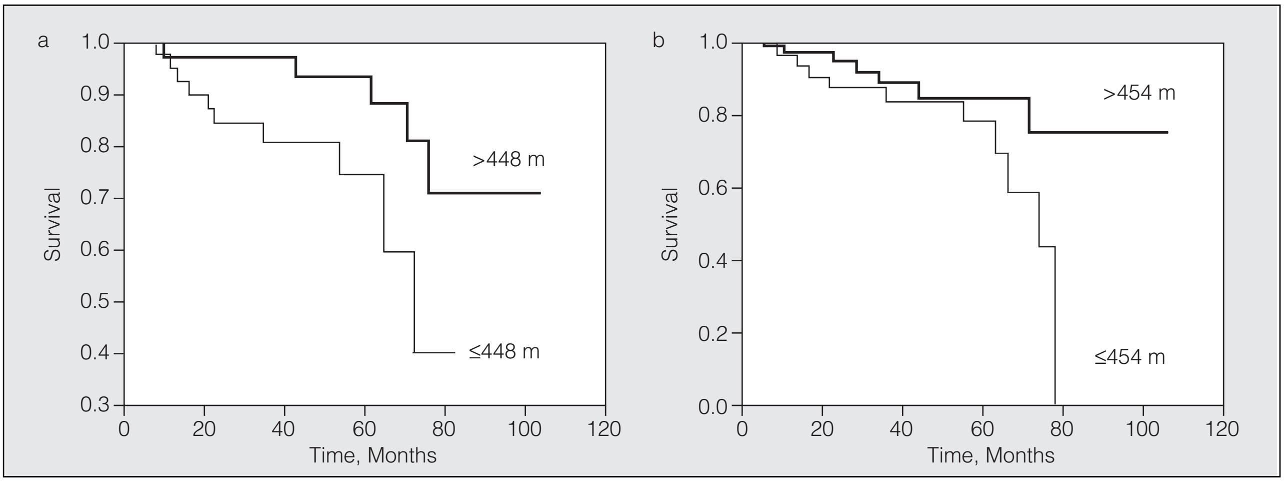

Figure 2. Correlation between survival and 6-minute walk distance before (a) and after (b) pulmonary rehabilitation. The median distance was calculated and survival rates for the 2 subgroups were compared in terms of whether the distance was greater than, less than, or equal to 448 m before pulmonary rehabilitation or greater than, less than, or equal to 454 m after pulmonary rehabilitation. Statistical significance for this correlation was *P*=.04 and *P*=.05, respectively (log rank test).

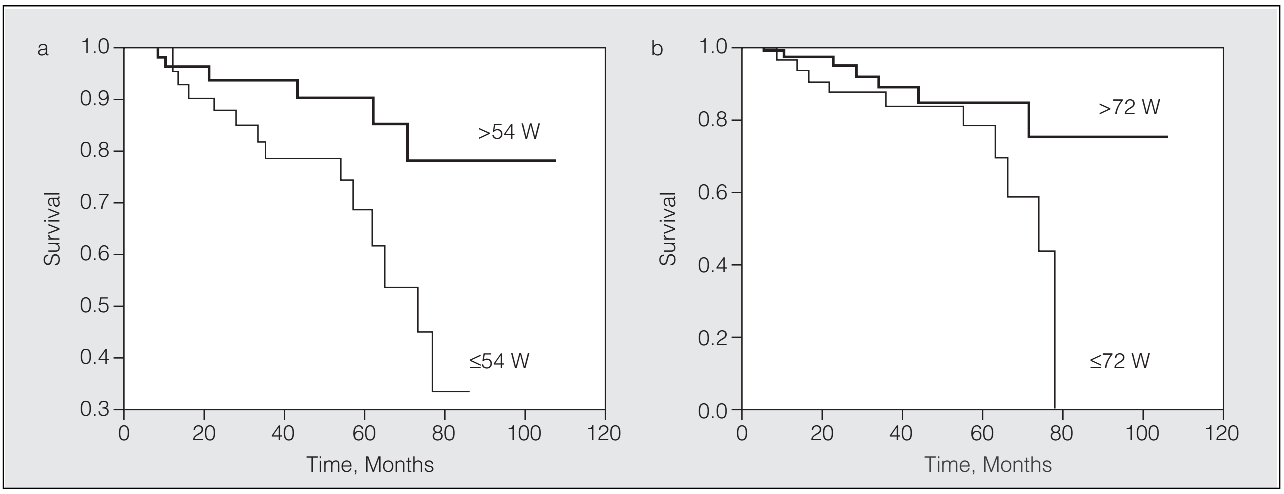

Figure 3. Correlation between survival and cardiopulmonary exercise workload before (a) and after (b) pulmonary rehabilitation. The median workload was calculated and survival rates for the 2 subgroups were compared in terms of whether the workload was greater than, less than, or equal to 54 W before pulmonary rehabilitation or greater than, less than, or equal to 72 W after pulmonary rehabilitation. Statistical significance for this correlation was *P*=.01 and *P*=.02, respectively (log rank test).

FEV_1 of 0.91 (0.46) L/s (38.35% [14.75%]). The study population was predominantly male, had normal nutritional status (BMI of 24.5 [4.6] kg/m^2) and performed well on the 6-minute walk test (412 [79.4] m). Only a small number of patients experienced desaturation during exercise. A subgroup of just 44 patients completed the SGRQ and obtained a mean score of 38.18 (15.94) points, which indicates a good quality of life. These characteristics may have influenced some of our results.

Lung function results after rehabilitation coincide with those reported by other authors,[15-17] with improvements in both dyspnea and exercise capacity as measured by 6-minute walk distance and maximum cycle ergometer workload (watts).

The improvement we observed in FEV_1 following rehabilitation was unexpected and could be related to better treatment strategies and improved inhaler techniques.

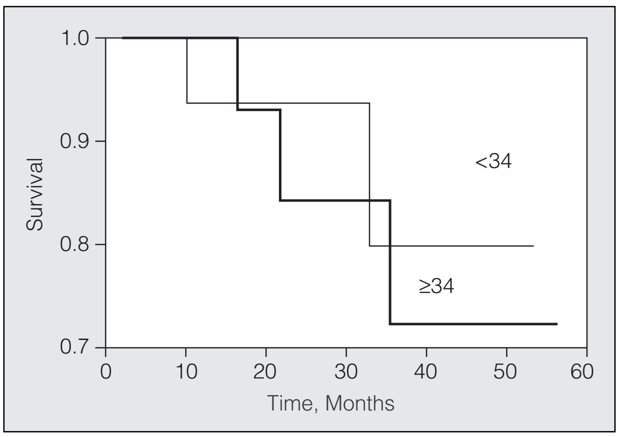

Figure 4. Correlation between survival and quality of life as measured by the St George's Respiratory Questionnaire (SRQG) in 44 patients. The median SGRQ score was calculated and the survival rates for the 2 subgroups were compared in terms of whether the score was greater than, less than, or equal to 34. The correlation was not statistically significant (*P*=.06 [log rank test]).

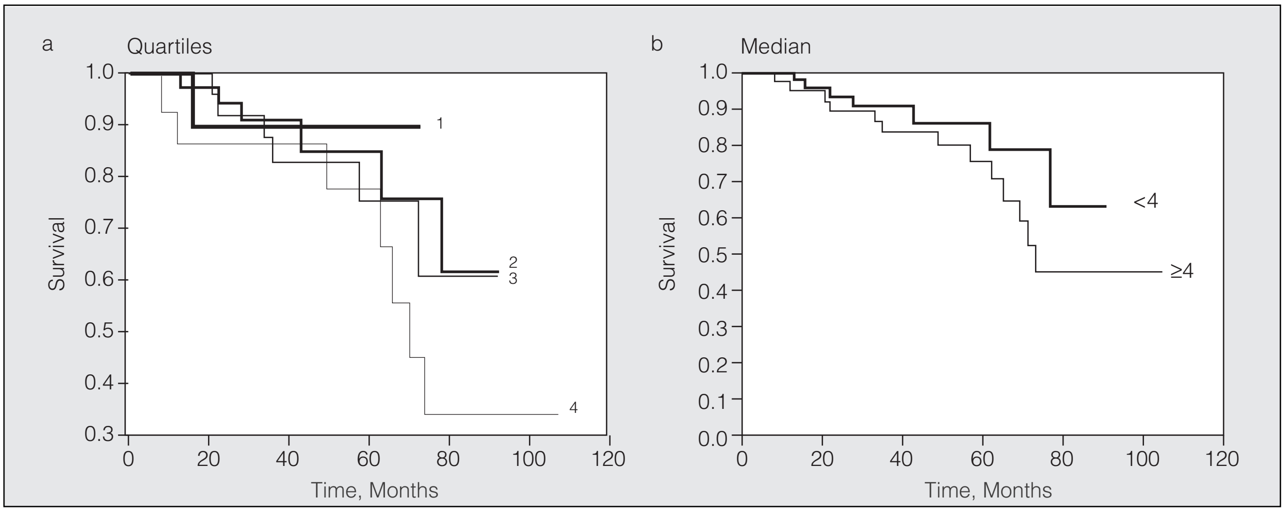

Figure 5. Correlation between survival and the score for body mass index, airflow obstruction, dyspnea, and exercise capacity (BODE). The study population was assessed using the BODE score and 2 subgroups were created (quartiles [a] and median [b]). Patients with a score higher than or equal to 4 and in upper quartiles tended to have higher survival rates. The correlation was not statistically significant (*P*=.12 for the quartile subgroup analysis and *P*=.5 for the median subgroup analysis [log rank test]).

Quality of life measurements can also be used to evaluate COPD patients[26] and significant improvements have been seen following rehabilitation.[27-29] Although the quality of life of our patients improved following pulmonary rehabilitation, this improvement did not reach the clinically significant threshold of 4 units in all the components.[25] Quality of life data were available for just 44 patients as the questionnaire was only introduced into our program in 1998.

We used a long follow-up period (105 months) and were able to obtain survival and cause of death data for all patients. Our patients were in an advanced state of the disease and our figures (FEV_1 of 38.35% [14.75%]) coincide with those reported by other studies,[30-32] although our follow-up time was longer. Gerardi and colleagues[30] and Bowen and colleagues[31] reported 3-year survival rates of 80% and 85%, respectively, whereas survival was 86.7% in our series and 77% in the Intermittent Positive Pressure Breathing Trial.[33] One more recent study reported a 3-year survival rate of 90%,[32] whereas Ries and colleagues[15] reported a 6-year survival of 61%. The rate of survival in our cohort was 67.5%.

The correlation between survival and lung function at rest and during exercise coincides with findings reported by other authors for follow-up studies of pulmonary rehabilitation patients.[30-31]

Other studies have shown that survival in COPD patients is correlated with exercise capacity as measured by oxygen consumption[32] or 6-minute walk distance.[34] Quality of life and mortality in COPD patients have also been found to be correlated[35] but this correlation was not statistically significant in our study, perhaps due to the small number of patients.

Although older age has been associated with higher mortality in COPD patients, its predictive capacity has varied from study to study.[30,32] In our study, survival in patients over 70 years tended to be worse (*P*=.08).

In contrast to other studies involving larger series of patients,[24,36] we found no link between mortality and nutritional status. The patients in those studies had poorer nutritional status than ours and a mean BMI of 24.5 (4.6).

We were unable to find a correlation between sex and desaturation during exercise with survival due to the small number of patients with these characteristics.

Even though survival rates tended to decrease when BODE score increased (using medians and quartiles to separate the patients into subgroups), the correlation was still not statistically significant. This contrasts with findings reported by Celli and colleagues[24] in a study involving 859 patients, and might be due to the smaller size of our study population. Our population was also characterized by a median BODE score of 4 and a small number of patients with a high score and in the upper quartiles because the 6-minute walk distance was greater and the BMI was maintained.

In conclusion, the patients who participated in our pulmonary rehabilitation program had advanced COPD (FEV_1 of 38.35% [14.75%]), although their exercise capacity (6-minute walk test), quality of life (SGRQ), and nutritional status (BMI) were all preserved. We observed a significant improvement in dyspnea and lung function during exercise, as well as an improvement in quality of life, although this was not statistically significant. Our follow-up of the study population over 105 months showed a 3-year survival rate of 86.7% and a 6-year survival rate of 67.5%. Cycle ergometer workloads, FEV_1, and 6-minute walk distance were all significantly correlated with survival. Survival rates tended to be lower in patients aged over 70 years, patients with lower quality of life scores, and patients with higher BODE scores, although the correlation was weak in all these cases. The statistical power of future studies could be improved by including more patients in the program.

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