Health-related Quality of Life and Mortality in Male Patients with Chronic Obstructive Pulmonary Disease

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To assess whether generic and specific health-related quality of life (HRQL) are independently associated with total and specific mortality in patients with chronic obstructive pulmonary disease (COPD), we followed until 1999 a cohort of 321 male patients with COPD, recruited in 1993–1994 at outpatient respiratory clinics. Baseline characteristics recorded under stable clinical conditions included forced spirometry, arterial blood gas tensions, dyspnea scales, 11 comorbid conditions, St. George's Respiratory Questionnaire (SGRQ), and SF-36 Health Survey. Vital status was assessed through reinterviews, the Mortality Register, and clinical records. Subjects who died (106) were older (69.8 versus 62.5 years) ($p < 0.001$), had lower body mass index (BMI) (25.4 versus 27.1) ($p < 0.01$), were more impaired in the clinical characteristics studied (%FEV_1, 34.0 versus 51.0) ($p < 0.001$), and had long-term oxygen therapy more frequently (31% versus 7%) ($p < 0.001$). Survival was shorter when worse HRQL was reported. SGRQ total and SF-36 physical summary scores were independently associated with total and respiratory mortality in Cox models, including age, FEV_1, and BMI. The total mortality-standardized hazard ratios for both HRQL measures were 1.3, whereas those for FEV_1 were 1.6. HRQL measures provide independent and relevant information on the health status of male patients with COPD. Their use should be considered for a more thorough evaluation and staging of patients with COPD.

Keywords: lung diseases, obstructive; COPD; health-related quality of life; mortality; Spain

The use of health-related quality of life (HRQL) measures in chronic obstructive pulmonary disease (COPD) has currently achieved widespread acceptance. Most clinical and therapeutic research on COPD involves the use of different types of HRQL instruments. However, the relationship between HRQL and the physiologic components of the disease as well as its role in the natural course of COPD is not well-understood.

Generic and respiratory-specific HRQL measures have been associated with disease severity among patients with COPD (1–3) and with their use of resources and rehospitalization rate (4). HRQL measures are probably also important for the survival of these patients. Two generic HRQL measures were associated with the survival of patients with COPD in two clinical trials (5, 6). These associations were independent of other clinical markers of severity, suggesting that deterioration in HRQL is an independent risk factor leading to death. However, the fact that these studies had used only generic measures of HRQL and assessed all-cause mortality did not allow establishing that the reported associations were related directly to COPD. We are aware of only one study that measured both specific HRQL and specific mortality in a trial of pulmonary rehabilitation; this study found no association between HRQL and mortality after adjustment for other relevant variables. Unfortunately the study included a small number of respiratory deaths (26 deaths) (7).

The main objective of this study was to assess the independent contribution of HRQL, through both generic and specific HRQL instruments, to all-cause and cause-specific mortality in patients with COPD after controlling for clinically relevant predictors of mortality.

METHODS

Between April 1993 and July 1994, 321 male patients with COPD were consecutively recruited in outpatient respiratory clinics and reinterviewed from July 1999 to February 2000. Details on the patients' evaluation at entry have been reported elsewhere (2, 8). In short, inclusion criteria at entry were chronic airflow impairment (percentage of $FEV_1 < 80\%$ and $FEV_1/FVC < 0.7$), with a change in FEV_1 less than 200 ml and 15% in the bronchodilator test, and clinical stability in the preceding month. Information was collected by trained nurses on forced spirometry using standard techniques (9), dyspnea (10-point visual analog scale) (10), presence of any of the 11 comorbid conditions, sociodemographic variables (age, social class according to occupation, years of formal education), HRQL (the Spanish versions of St. George's Respiratory Questionnaire [SGRQ]) (11, 12), and SF-36 Health Survey (SF-36) (13, 14). SGRQ contains 50 items that can be divided into three dimensions (symptoms, activity, and impacts), and their scores range from 0 to 100 (worst status). The SF-36, with eight scales, scoring 0 to 100 (best health), can be summarized into two component summary scores: physical (PCS-36) and mental (MCS-36). Arterial blood gas tensions were collected, if available, during the 6 months before enrollment from the patients' medical record.

Vital status was assessed through reinterviews, by linkage with the Mortality Register, and by the review of clinical records. The closing date was November 30, 1999. The underlying causes of death were taken from death certificates at the Mortality Register and coded using the International Classification of Diseases, Ninth Edition (ICD-9). If no death certificate could be accessed (n = 13 patients), additional information was obtained from clinical records and family interviews. The study protocol was approved by the institution's ethical committee, and informed consent was signed by target patients.

Baseline differences of patients according to their vital status at follow-up were tested using the Fisher's exact test for proportions, *t* test, or Mann–Whitney U test, as appropriate. To avoid multiple comparisons T^2-Hotelling was performed to test the hypothesis that scores of dimensions in SGRQ and those for SF-36 component summaries

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TABLE 1. BASELINE CHARACTERISTICS OF THE COHORT OF PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE ACCORDING TO VITAL STATUS IN NOVEMBER 1999

	Alive (*n* = 197)	Dead (*n* = 106)	p Value
Age, yr	62.5 (9.1)*	69.8 (8.8)	< 0.001
BMI, kg/m^2	27.1 (4.9)	25.4 (4.2)	0.003
Years of education	5.0 [6.0]*	6.0 [7.0]	0.682
Social class			0.774
I–III	39 (19.8%)*	20 (19.2%)	
IVa	123 (62.4%)	62 (59.6%)	
IVb–V	35 (17.8%)	22 (21.2%)	
Number of chronic conditions	2 [2.0]	2 [2.0]	0.656
Current-smoker	75 (43.1%)	23 (25.3%)	0.017
Dyspnea (VAS)	3.1 (2.4)	3.8 (2.7)	0.033
FEV_1, % over predicted	51.0 [30.5]	34.0 [22.0]	< 0.001
FEV_1, L	1.5 [1.0]	1.0 [0.7]	0.07
FEV_1/FVC	0.54 (0.13)	0.45 (0.13)	< 0.001
FEV_1 postbronchodilator, L	1.6 [1.0]	1.0 [0.7]	< 0.001
Pa_{O_2}, mm Hg	71.7 (11.3)	66.2 (13.8)	0.002
Pa_{CO_2}, mm Hg	41.0 [5.5]	42.8 [9.9]	0.025
ATS staging			< 0.001
I (50–80% predicted FEV_1)	103 (52.3%)	23 (21.7%)	
II (35–49% predicted FEV_1)	43 (21.8%)	28 (26.4%)	
III (< 35% predicted FEV_1)	51 (25.9%)	55 (51.9%)	
Long-term oxygen therapy	12 (7.1%)	26 (31.0%)	< 0.001

Definition of abbreviations: ATS = American Thoracic Society; BMI = body mass index; VAS = visual analogue scale, from 0 (no shortness of breath) to 10 (maximum shortness of breath).

* Mean (SD); median [interquartile range]; number (%).

were different by vital status. When significant differences were observed, *post hoc* comparisons were performed to ascertain which dimension or component summary contributed to significance. Kaplan–Meier survival curves and log-rank tests were performed after stratifying by tertiles of baseline HRQL results and COPD stages according to the American Thoracic Society (ATS) (15).

Semiparametric Cox models were used to assess the association between baseline PCS-36 and MCS-36, and SGRQ total scores and survival time. Different analyses were performed by all-causes and by specific causes for the total follow-up period and for 3-year follow-up. This latest analysis was done to overcome the time dilution effect with a variable changing over time. Deaths were classified as due to respiratory causes (ICD-9 codes 460–519) or other causes (all other ICD-9 codes).

In the final models, to have all hazard ratios (HR) indicating increase in mortality, we changed the sign of FEV_1 and SF-36 scores. To facilitate comparisons, the estimated HR were standardized by multiplying the β coefficient by the standard deviation of the variable. The analyses were performed using S+ (16), and Egret (17) packages.

Further details are available in the online data supplement.

RESULTS

Three hundred and twelve men (97% of those eligible), with a mean age of 65.0 years (SD 9.7) and a mean percentage of predicted FEV_1 of 44.5 (SD 17.8) at baseline contributed a mean follow-up time of 4.8 years (SD 1.8). Vital status at the closing date was ascertained for 303 men (94.4%). Nine persons were alive but were lost to follow-up at some time before the closing date and censored at that time. One hundred and six (33.0%) patients had died by the end of follow-up. Persons lost to follow-up (n = 18) were similar to those followed, although none of the former had long-term oxygen therapy (LTOT) (p = 0.08).

Baseline characteristics of patients according to vital status are shown in Table 1. Subjects who died during follow-up were older, had a lower body mass index (BMI), were more impaired in all clinical characteristics studied, had LTOT more frequently, and were less likely to be current-smokers. There were no differences according to years of education, social class, or presence of chronic comorbid conditions.

There were differences in HRQL scores at baseline according to vital status (Table 2). *Post hoc* comparisons showed differences for all SGRQ dimensions, whereas only PCS-36 contributed to the significance in SF-36. It was not possible to compare all SF-36 scales at once due to non-normal distribution of their scores; nonparametric tests yielded statistically significant differences for three scales according to vital status (physical functioning, social functioning, and emotional role).

Forty-eight of 106 deaths corresponded to respiratory causes. The distribution of specific causes of death was as follows: COPD (ICD-9 codes 490–496), 38 deaths (35.8%); other respiratory causes (ICD-9 codes 460–489, 497–519), 10 deaths (9.4%); cardiovascular diseases (ICD-9 codes 390–459), 18 deaths (17.0%); lung cancer (ICD-9 code 162), 9 deaths (8.5%); other cancers (ICD-9 codes 140–239, except 162), 13 deaths (12.3%); all other causes, 12 deaths (11.3%); unknown, 6 deaths.

Mortality was closely related to FEV_1 ($p < 0.001$). According to the Kaplan–Meier survival curves (Figure 1), after 4 years of follow-up, those with severe COPD (ATS stage III) showed a 60% survival (95% confidence interval [CI]: 51–70%), those in stage II 73% (95% CI: 63–84%), and those with mild COPD (stage I) 89% (95% CI: 84–95%). In relation to HRQL, survival was shorter in those patients with worse HRQL scores, differences between tertiles being statistically significant for SGRQ total score (log-rank test, $p < 0.001$) (Figure 2) and marginally significant for PCS-36 ($p = 0.053$) (Figure 3). For MCS-36, differences in survival were small and nonsignificant.

Both SGRQ total and PCS-36 scores were independently associated with mortality after adjustment for age, FEV_1, and BMI (Table 3). Similar results were obtained using postbronchodilator FEV_1 instead of basal FEV_1. None of the remaining variables, including dyspnea, cough, education, and chronic conditions were associated with mortality in the multivariate model. In the final adjusted model, a worsening of 1 SD in either the SGRQ total or PCS-36 scores was associated with a 30% increase

TABLE 2. MEAN (STANDARD DEVIATION) OF HEALTH-RELATED QUALITY OF LIFE MEASURES AT BASELINE ACCORDING TO VITAL STATUS IN NOVEMBER 1999

	Alive (*n* = 197)	Dead (*n* = 106)	p Value
St. George's Respiratory Questionnaire			< 0.001*
Symptoms	43.4 (21.7)	51.0 (20.7)	0.006†
Activity	48.5 (25.8)	64.0 (24.9)	< 0.001†
Impact	33.8 (22.6)	41.5 (22.3)	0.012†
Total	39.9 (21.3)	49.9 (20.6)	< 0.001‡
SF-36			0.03§
Physical component summary (PCS-36)	40.6 (9.5)	37.1 (9.2)	0.006†
Mental component summary (MCS-36)	51.0 (10.9)	49.1 (12.5)	0.78†
SF-36 scales			
Physical functioning	62.1 (24.9)	45.4 (28.5)	< 0.001‖
Role physical	69.2 (40.6)	61.1 (41.9)	0.090‖
Bodily pain	64.1 (32.1)	68.5 (30.6)	0.297‖
General health	43.6 (19.9)	39.0 (18.6)	0.058‖
Vitality	60.3 (23.9)	53.6 (27.3)	0.0504‖
Social functioning	85.3 (20.3)	76.5 (24.7)	0.002‖
Emotional role	78.8 (37.8)	69.2 (42.3)	0.027‖
Mental health	71.8 (21.3)	71.9 (22.1)	0.93‖

* Global T^2-Hotelling.

† *Post hoc* comparisons.

‡ Student's *t* test.

§ Global T^2-Hotelling for component summaries.

‖ Mann–Whitney U test.

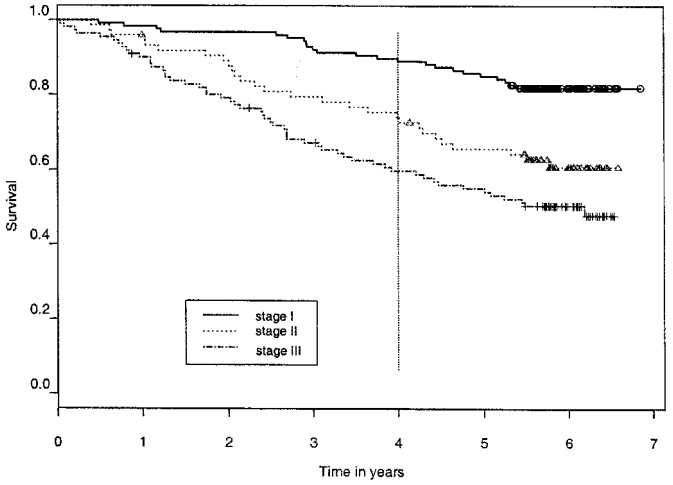

Figure 1. Kaplan–Meier survival curves according to ATS staging.

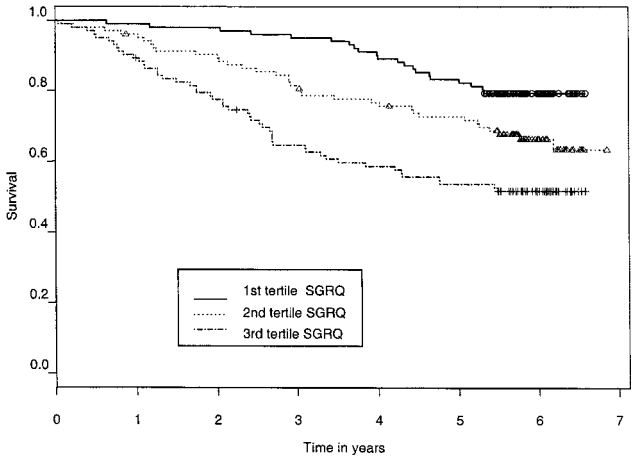

Figure 2. Kaplan–Meier survival curves according to tertiles of SGRQ total score.

in total mortality, whereas the corresponding increase for 1 SD of change in FEV_1 was about 60%. Similar results for both SGRQ and PCS-36 were obtained when only mortality due to respiratory diseases was considered, but the association between SGRQ total score and mortality was of marginal significance. In contrast, the association between FEV_1 and respiratory mortality almost doubled. Neither HRQL nor FEV_1 was associated with nonrespiratory mortality (Table 3). MCS-36 scores did not show statistical association with mortality in the multivariate analysis.

An analysis was conducted in a subsample of 213 patients with COPD for whom Pa_{O_2} information was available. Previous models with SGRQ and PCS-36 were expanded with Pa_{O_2}, and both total SGRQ and PCS-36 remained significantly associated with all-cause and respiratory mortality, whereas Pa_{O_2} (HR for all-cause mortality = 0.98 [95%CI: 0.96–0.997] and HR for respiratory mortality = 0.96 [95%CI: 0.94–0.99]) captured a significant portion of the FEV_1-explained variability.

To determine if the association between baseline HRQL and mortality was stronger at an earlier time point, a subsequent model was restricted to 3-year follow-up data. This period included 61 deaths, of which 31 were due to respiratory diseases. The association between HRQL measures and 3-year all-cause and respiratory mortality increased for both SGRQ total (HR for 1 SD = 1.61 and 1.92, respectively) and PCS-36 (HR for 1 SD = 1.46 and 1.62, respectively) scores, whereas the corresponding associations for FEV_1 remained similar for all-cause mortality (HR for 1 SD = 1.59–1.72) and decreased slightly for respiratory mortality (HR for 1 SD = 1.73–1.90). All HR, except FEV_1, in the model assessing the association between respiratory mortality and SGRQ were statistically significant (Table 4). Neither the HRQL scores nor the covariates showed any statistical association with nonrespiratory causes of mortality.

DISCUSSION

To our knowledge this is the first study reporting that both generic and specific baseline HRQL scores are independently associated with both all-cause and respiratory mortality of patients with COPD after adjustment for other relevant clinical and physiopathologic variables. These results provide further support to the notion that health status, as perceived by the patient, is associated with the natural course of COPD, independent of the biologic variables.

General HRQL measures have been previously reported as being independently associated with all-cause mortality in patients with COPD (5, 6). In contrast, no relationship between specific HRQL and respiratory mortality was found by Gerardi and coworkers (7) in a cohort mainly including patients with COPD. Because this latter study was the only one that included specific measures for both HRQL and cause of death, its results could be taken as indicating that the previously reported positive associations between HRQL and total mortality were not directly relevant to the COPD disease itself. However, the study included a small number of respiratory deaths (26), and the cohort was composed of patients with COPD (87%) and patients without COPD who were followed for a period of up to 5 years after a rehabilitation program.

Our results provide a different picture by showing that HRQL scores, both generic and respiratory-specific, were consistently associated with mortality. This association was stronger with respiratory than with nonrespiratory mortality, suggesting that this relationship is specific. According to our results, every four points increase in the SGRQ total score, a figure that has been suggested as clinically relevant (11), is associated with an increased risk of global mortality of 5.1% (95% CI: 0.97–9.4%).

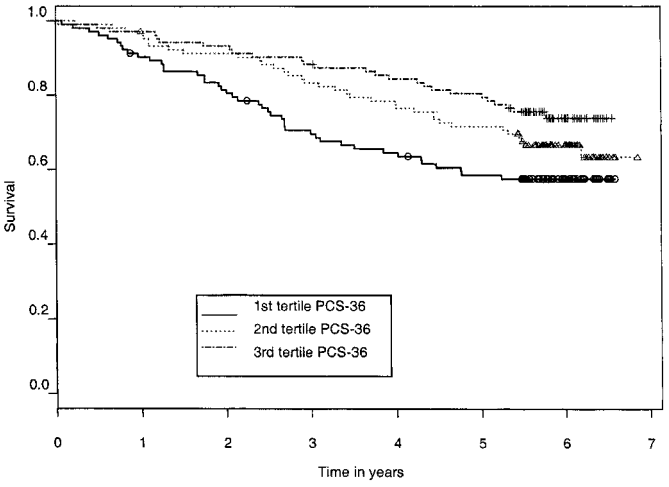

Figure 3. Kaplan–Meier survival curves according to tertiles of the physical component summary score of SF-36 (PCS-36).

TABLE 3. ADJUSTED ASSOCIATION (COX MODELS) BETWEEN BASELINE HEALTH-RELATED QUALITY OF LIFE AND COMPLETE FOLLOW-UP (MEAN: 4.8 YEARS) MORTALITY BY DIFFERENT MORTALITY EVENTS

	All-Cause Mortality		Respiratory Causes Mortality*		Nonrespiratory Causes Mortality†	
	Standard HR‡	HR (*95% CI*)	Standard HR	HR (*95% CI*)	Standard HR	HR (*95% CI*)
SGRQ	1.30	1.01 (1.00–1.02)	1.36	1.01 (1.00–1.03)	1.17	1.01 (0.99–1.02)
Age	1.76	1.06 (1.03–1.09)	1.59	1.05 (1.01–1.09)	1.98	1.07 (1.04–1.11)
FEV_1§	1.60	2.06 (1.32–3.20)	2.32	3.64 (1.72–7.69)	1.25	1.40 (0.77–2.55)
BMI	0.81	0.96 (0.91–1.01)	0.69	0.92 (0.86–0.99)	0.86	0.97 (0.90–1.04)
R^2‖		0.23		0.18		0.09
PCS-36	1.32	1.03 (1.01–1.05)	1.40	1.03 (1.02–1.07)	1.24	1.02 (0.99–1.05)
Age	1.80	1.06 (1.04–1.09)	1.65	1.05 (1.01–1.09)	2.02	1.07 (1.04–1.12)
FEV_1§	1.64	2.14 (1.38–3.31)	2.38	3.77 (1.80–7.91)	1.24	1.40 (0.78–2.51)
BMI	0.80	0.95 (0.91–1.00)	0.68	0.92 (0.86–0.99)	0.85	0.97 (0.90–1.04)
R^2‖		0.23		0.175		0.09

Definition of abbreviations: BMI = body mass index; CI = confidence interval; HR = hazard ratio; HRQL = health-related quality of life; PCS-36 = physical component summary of SF-36; SGRQ = St. George's Respiratory Questionnaire.

* ICD-9 codes: 460–519.

† ICD-9 codes: all others not included in 460–519.

‡ Standard HR: standardized hazard ratios are given for a change of 1 SD in the corresponding variable (SGRQ = 21.36; PCS-36 = 10.08; age = 9.69; FEV_1 = 0.653; BMI = 4.69).

§ FEV_1 sign has been changed to facilitate interpretation.

‖ Calculated according to Nagelkerke (30).

Moreover, at 3-year follow-up the increase in risk for respiratory mortality associated with an addition of four points in the SGRQ was 12.9% (95% CI: 4.5–22%). Thus, our findings substantiate the claim that a four-point increase should be considered as clinically relevant. These results suggest that, similar to what is done with FEV_1 (the strongest predictor of mortality in patients with COPD, also in our study), HRQL scores should be used for staging and monitoring patients with COPD.

It is important to note that the mental component summary score of SF-36 (MCS-36) was not associated with mortality, whereas some of the scales reflecting mental health (emotional role, social functioning) did show a statistically significant association in the univariate analysis. This observation further contributes to the debate about the way in which SF-36 component summary scores were constructed (18) and highlights the need to take both the summary component and the scale scores into account when assessing mental health status.

The independence of the HRQL association with mortality found in the present study is based on the wide range of variables included in the adjusted model. Only BMI and FEV_1 were retained in the final Cox models, but other relevant variables like dyspnea, cough, and sputum were also tested. Although Pa_{O_2} could only be analyzed in a subsample of 213 patients with COPD, for these subjects in the model expanded with Pa_{O_2}, both total SGRQ and PCS-36 remained significantly associated with all-cause and respiratory mortality. Thus, in no case was the association between HRQL and mortality accounted for by any of these other explored variables. As in a previous study assessing treatment compliance (19), the administration of LTOT in our cohort was associated with mortality, but we did not include it in the multivariate model. Because there is strong evidence, based on randomized controlled trials, that LTOT increases survival in patients with COPD (20), the most likely explanation for its association with mortality is that LTOT behaves as a marker of severity, which in our study was already controlled for by FEV_1.

In accordance with what was expected, HRQL measures, both generic and specific, were more strongly associated with all-cause and respiratory mortality with a shorter length of follow-up (3 years). However, no major change was observed in FEV_1 HR, probably supporting the survivor bias effect reported by Anthonisen and coworkers (5). The problem with a shorter follow-up period is the smaller number of events (deaths) observed, which may lead to a decrease in statistical power.

It may be speculated that some other factors not included in our models could explain the independent effect of HRQL, the response in a timed walking test being one of these variables. In fact, the response to the 12-minute walking test after a rehabilitation program was the most powerful predictor of death in the study reported by Gerardi and coworkers (7). As a consequence, we cannot elucidate whether the difference between the results of this study and our own is a consequence of the absence of a walking test in our model. An alternative reasoning is that both specific HRQL and walking distance are part of the same construct, as was suggested in a factor analysis of the study of Wegner and coworkers (21) in a sample of patients with COPD. Supporting this idea would be the fact that, when SGRQ total score was substituted by its three dimension scores in the final models for all-cause and respiratory mortality, only the HR for activity showed a CI not including unity, both at complete and

TABLE 4. ADJUSTED COX MODELS BETWEEN BASELINE HEALTH-RELATED QUALITY OF LIFE AND 3-YEAR TOTAL AND RESPIRATORY MORTALITY

	All-Cause Mortality		Respiratory Causes Mortality*	
	Standard HR†	HR (*95% CI*)	Standard HR	HR (*95% CI*)
SGRQ	1.61	1.02 (1.01–1.04)	1.92	1.03 (1.01–1.05)
FEV_1‡	1.59	2.04 (1.12–3.70)	1.73	2.32 (0.95–5.66)
Model adjusted by age and BMI				
PCS-36	1.46	1.04 (1.01–1.07)	1.62	1.05 (1.01–1.09)
FEV_1‡	1.72	2.29 (1.25–4.18)	1.90	2.68 (1.07–6.72)
Model adjusted by age and BMI				

Definition of abbreviations: BMI = body mass index; CI = confidence interval; HR = hazard ratio; PCS-36 = physical component summary of SF-36; SGRQ = St. George's Respiratory Questionnaire.

* ICD-9 codes: 460–519.

† Standard HR: standardized hazard ratios are given for a change of 1 SD in the corresponding variable.

‡ FEV_1 sign has been changed to facilitate interpretation.

3-year follow-up. In a recent study by Engström and coworkers (22) the SGRQ activity score was most strongly associated with FEV_1.

Comorbidity is also a relevant potential confounder in this type of study because it may be associated with both HRQL and mortality. We have previously reported (2) that comorbidity may modify the specific HRQL in patients with COPD. Antonelli and coworkers (23) showed that comorbidities like chronic renal failure or electrocardiogram signs of myocardial ischemia were associated with mortality in patients with COPD. In our data there was no relationship between comorbidity and mortality, and although we used a standard list to assess self-reported chronic conditions, it may not have been specific enough to include the type of severe comorbidity studied by Antonelli and coworkers.

Several other characteristics of the present study deserve attention because they may have limited the validity of our results. First, it is important to note that we studied a cohort consisting of only male patients with COPD. Women were not included because in our country the proportion of women with COPD treated at the outpatient clinics where the cohort was recruited was very low, reflecting a relatively late beginning of smoking among women. A recent study of COPD admissions, in the same hospitals where our cohort was recruited, showed that only 8% of patients with COPD admissions were women (24). The experiences of men and women suffering from COPD and asthma seem to be different, with women reporting a worse HRQL than that of men (4, 25). On the other hand, although sex was not found to be associated with mortality in any of the previous studies referred to previously (5–7), the relationship between HRQL and mortality could be different for women, and a replication of the present study in a cohort involving both sexes is needed. Second, in prognostic studies it has been recommended that a representative and a well-defined sample of patients at a similar point in the course of the disease be included (26). In our study we achieved a wide spectrum of disease severity through a systematic recruitment of patients diagnosed with the disease. The adjustment by age and FEV_1 should have partially accounted for the effect of disease duration. Furthermore, a restricted model including only the patients with COPD at ATS stages II and III yielded almost identical HR for both the SGRQ total and the PCS-36 score. Third, another potential limitation is the validity of the cause of death in death certificates, as previously pointed out by other authors (27). The Catalan Register of Mortality is managed following standards of quality (28). Unfortunately, no data are available about the validity of certificates of death caused by COPD. A high percentage of deaths in our study was due to COPD; however, this cause was probably underestimated because multiple causes of death were not taken into account (29). Finally, it may be argued that baseline predictors were taken over a long period of time, without taking into account changes occurring during follow-up. Nevertheless, it was reassuring that our results in a model truncated at 3 years of follow-up provided consistent results, with even larger coefficients for HRQL.

In summary, our results have shown that HRQL, both generic and specific, are independent risk factors of respiratory and all-causes mortality. This is evidence that HRQL is a valid measure of disease activity in patients with COPD not shown by studied variables. Up to now, FEV_1 has been considered the cornerstone measure to gauge patients with COPD. Our results highlight the importance of HRQL in the evaluation of the severity of the disease in patients with COPD and support the view that HRQL should be considered, in addition to lung function, to more properly assess patients with COPD.

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