The health related quality of life of Greek patients with chronic obstructive pulmonary disease

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SUMMARY. Background: Chronic Obstructive Pulmonary Disease (COPD) is an advancing disease, characterized by progressive deterioration of lung function. The impact of the disease on human health is massive and it affects the health related quality of life (HRQoL) of patients in every aspect. This study assessed HRQoL of Greek patients with COPD and its association with demographic and clinical factors, and compared the findings with with those of COPD studies in other countries. In addition, the cost of pharmaceutical treatment of these patients was assessed. **Material and methods:** The study group consisted of 136 Greek patients with COPD (103 men, mean age 64.7±9.2 years, mean FEV_1 59±25.6% predicted).I Information was recorded about their demographic and clinical parameters. Their HRQoL was assessed using the Greek versions of the Medical Outcomes Study Short Form 12 (SF-12) and St George's Respiratory Questionnaire (SGRQ). **Results:** The HRQoL of Greek patients with COPD was found to be significantly lower than both that in the general population and that of patients COPD reported in other countries. Almost all the HRQoL scores were shown to be associated with gender, educational and financial status, duration of symptoms, age at onset of symptoms, pack-years of cigarettes smoked, disease stage, degree of dyspnoea, pO_2 and pCO_2 levels, numbers of medical visits and hospital admissions, participation in rehabilitation programmes, and co-morbidities, such as cardiovascular disease and diabetes mellitus (DM). The average cost of pharmaceutical treatment was assessed at 110 ± 63 € / month and was associated with the stage of the disease, the smoking habit, the degree of dyspnoea, annual numbers of medical visits and admissions and nebulizer usage. **Conclusions:** The HRQoL of Greek patients with COPD is influenced by multiple parameters, which should all be taken into consideration when their treatment is being planned. Cost-effective studies should be made on populations of Greek patients with COPD and more emphasis should be placed on rehabilitation programmes in Greece. *Pneumon 2013, 26(2):139-151.*

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a major cause of morbidity and mortality worldwide, and it is expected to rise to the third highest cause of death and the fifth highest cause of disability by 2020[1]. Smoking is the main risk factor for the disease, which progresses slowly and is characterized by impairment of lung function, airway obstruction, and finally respiratory failure[2].

The prevalence of COPD in Greece was recently estimated to be 8.4% of the population, with men suffering 2.5 times more frequently than women (men 11.6% vs women 4.8%)[3]. Prevalence was even higher (23%) in the population above 70 years[3]. According to the Hellenic Thoracic Society (HTS) mild COPD was found more often in both sexes in the Greek population (57.4% mild, 25.3% moderate και 16% severe), but 81.4% of those diagnosed with mild COPD did not know they were suffering from the disease[3]. These findings revealed the high prevalence of COPD in Greece, but did not take into consideration the smoking habit in Greece, which is among the highest worldwide[3]. COPD mortality in Greece is 6/100,000 habitants[4]. The mean hospitalization cost of COPD per patient with severe exacerbation in Greece has been estimated at 1,711€[5], but very few cost or cost-effectiveness studies have been made in Greece[5,6].

Over the past decade, more and more research on the development and validation of questionnaires has been undertaken, in an attempt to quantify the impact of COPD on the daily life and well-being of patient from their own point of view[7]. Measures of health-related quality of life (HRQoL), along with estimations of morbidity and mortality, can also be used for making medical decisions regarding treatment, because they include information on abilities, impairments, symptoms and psychological effects of the disease[8]. Because of this, HRQoL and preference-based HRQoL instruments are increasingly being used in clinical studies and for the comparison of different populations. The Medical Outcomes Study Short Form 12 (SF-12) and St George's Respiratory Questionnaire (SGRQ) are generic and disease specific HRQoL questionnaires respectively[9,10]. Both of these questionnaires have been used in a number of clinical trials in COPD.

The aim of the present study was to assess the level of HRQoL in Greek COPD patients, based on the SGRQ and SF-12 questionnaires, in order to evaluate the association between HRQoL and demographic and clinical parameters, and to compare the findings with those of studies on patients with COPD in other countries. In addition, the study aimed to explore the cost of pharmaceutical treatment and its association with the various parameters and HRQoL scales.

MATERIALS AND METHODS

Study sample

A total of 136 patients with COPD were recruited from the outpatient department of The Athens Chest Hospital "Sotiria" during the period October 2007 – February 2009. All participants agreed to take part in the study and gave their written informed consent. The study was approved by the Hospital Ethics Committee.

Study design

The study was designed as a cross-sectional estimation of scores from one dyspnoea scale, one generic HRQoL questionnaire and one HRQoL questionnaire specific to respiratory diseases in a Greek population of patients with COPD. The patients who participated were non- ex- or current smokers aged above 35 years, already diagnosed as having COPD, and who had been in a stable clinical condition, with no exacerbations or change of treatment over the preceeding 3 months. Patients with asthma, bronchiectasis, lung cancer or other active respiratory disease were excluded from the study. For all patients data were recorded about their socio-economic status, smoking history, daily dyspnoea level and clinical parameters and they completed the SGRQ and SF-12 questionnaires. All patients underwent spirometry and arterial blood gas determination. The WHO Global Initiative for Chronic Obstructive Lung Disease (GOLD) classification was used for disease staging according to post-bronchodilation FEV_1 scores[2]. HRQoL scores were compared to those documented for other populations. Cost of pharmaceutical treatment was calculated according to the quantity of medicines usually used by the patients and the current drug prices provided by the Greek National Organization for Medicines[11], and association was explored with demographic factors, clinical parameters and HRQoL scales.

HRQoL scales

In order to assess HRQoL, the following scales and questionnaires were used:

The Borg dyspnoea scale, consisting of an 11point scale, on which dyspnoea is graded from 0 (none at all) to 10 (maximum)[12].

The SGRQ for disturbances or impairment caused by

airway or parenchymal disease[13,15]. The SGRQ is a disease specific instrument with empirically weighted items. It has three components: "symptoms", measuring distress due to respiratory symptoms, "activity", measuring the effects of disturbances on mobility and physical activity, and "impacts", quantifying the psychological impact of the disease. A "total" score is also calculated from all items, providing a global estimation of the patient's respiratory health. Scores can range from 0 (no impairment) to 100 (maximum impairment) for each component. In this study the "past 3 months" version was used. SGRQ, as a disease specific questionnaire, allows comparisons between similar populations. Its wide translation and validation in different languages also enables comparisons between groups of different nationalities.

The Health Survey – SF-12, a widely used generic HRQoL questionnaire[9,15], contains 12 items divided into eight domains: physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional and mental health. These domains create a profile of the subject and two summary scores are aggregated, the physical component summary (PCS) and the mental component summary (MCS). Scores range from 0 to 100, with higher scores representing better HRQoL. In this study only the PCS and MCS results were used and correlated with other factors. As a generic questionnaire of HRQoL it allows comparison with different populations and different diseases. The standardized scoring of skills and the components in common with the more detailed SF-36 questionnaire facilitates even wider population comparisons[9,16].

Statistical analysis

Mean values and standard deviation (SD) were used to describe quantitative variables. To compare normally distributed quantitative variables between two groups and between three or more different groups, Student's t-test and ANOVA test were used, respectively. In order to control for type I errors, due to multiple comparisons, Bonferroni correction was used, by which the significance level is defined as 0.05/k (k= number of comparisons). Proportional comparison between two groups was made using Pearson's χ^2 test, and where necessary with Fisher's exact test. Linear regression analysis was used to detect association of independent factors with the scores, from which the coefficient factor (β) and standard error (SE) were derived. To control correlations between two quantitative variables, Pearson's product-moment correlation coefficient (r) was used. Correlation was considered low

when coefficient (r) was between 0.1 and 0.3, moderate when coefficient was between 0.31 and 0.5, and high when coefficient was higher than 0.5. Statistical significance was set at 0.05 and all p-values are two tailed. For the the statistical analysis, SPSS 15.0 programme was used.

RESULTS

Demographic characteristics

The demographic characteristics of the study patients are listed in Table 1. The mean age of the 136 patients (103 men) was 64.7±9.2 years, and male / female ratio 3:1. Most of the patients had primary or secondary education and the mean family monthly income was >1000€.

Clinical characteristics

The clinical characteristics of the patients are also listed in Table 1. Most (97%) of the patients were ex- or current smokers and their mean smoking history was 64±35 pack-years. Most of the patients had had respiratory symptoms for more than 5 years (mean 10±7 years) and in 35.3% symptoms had strted before the age of 49 years (mean age at symptom onset: 55.13±9.48 years). Most of the patients reported more than two non-routine medical visits in the past year, but there had been no hospital admissions in 61.8% and more than 2 in only 5%. Only 22% of the patients had normal pO_2 levels, and most of them were normocapnic. There were no underweight patients in this study, and most of them presented no or very light dyspnoea in their everydy living, according to the Borg scale. There were sufficient numbers of representatives of all COPD stages to allow for comparisons, and only 22% of the patients had no co-morbidities.

HRQoL questionnaires scores

The scores on SGRQ are shown in Table 2. The component score values covered the full range from 0 (best HRQoL) to 100 (worse HRQoL), apart from the total score (min value 6.92), which indicates that all participants have at least one aspect of their health impaired. The worst value (65.2 ± 24) appeared on the activity scale and the best (43.7 ± 22.8) on the impact scale, a result also noted in other studies[17-22]. The mean values on all scales represent bad to tolerable health status, and differ by more than 1.5 SD from the values recorded by a healthy normal population[23]. Statistical analysis revealed significant differences (p<0.001) for all SGRQ components, which indicates that Greek patients with COPD have worse HRQoL in all

TABLE 1. Demographic and clinical characteristics of the study patients with chronic obstructive pulmonary disease (n= 136).

Variable	Patients (%)	Variable	Patients (%)
Sex		Age group	
male	103 (75.7)	<60 years	46 (33.8)
female	33 (24.3)	61-70 years	45 (33.1)
		>71 years	45 (33.1)
Educational level		Monthly family income	
primary / secondary	71 (52.2)	<1000€	64 (47.1)
tertiary / postgraduate	65 (47.8)	>1000€	72 (52.9)
Smoking history		Borg dyspnoea scale	
non-smoker	4 (3)	0-1	69 (70.6)
ex-smoker	83 (61)	>1	40 (29.4)
current smoker	49 (36)		
Pack-years		pO_2 level	
<42	45 (33.1)	<60mmHg	19 (14)
42-70	46 (33.8)	60-80mmHg	87 (64)
>70	45 (33.1)	>80mmHg	30 (22)
Symptom duration		pCO_2 level	
<5 years	49 (36%)	<45mmHg	117 (86)
5-11 years	43 (31.6)	>45mmHg	19 (14)
>11 years	44 (32.4)		
Symptom onset		BMI category	
<49 years	48 (35.3)	underweight	0
49-60 years	46 (33.8)	normal	46 (33.8)
>60 years	42 (30.9)	overweight	44 (32.4)
		obesity	46 (33.8)
Medical visits		GOLD classification	
(past 12 months)	23 (16.9)	stage I	32 (24)
0	42 (30.9)	stage II	44 (32)
1-2	71 (52.2)	stage III	30 (22)
>2		stage IV	39 (22)
Admissions		Co-morbidities	
(past 12 months)	84 (61.8)	none	30 (22)
0	45 (33.1)	cardiovascular disease	62 (46)
1-2	7 (5.1)	diabetes mellitus	17 (13)
>2		depression	7 (5)
Rehabilitation programme			
yes	25 (18.4)	FEV_1% (mean±SD)	59.13±25.62
no	111 (81.6)	FVC% (mean±SD)	81.67±24.46
pO_2 (mean±SD)	71.77±10.55	FEV_1/FVC (mean±SD)	56±14
pCO_2 (mean±SD)	40.72±4.53	BMI (mean±SD)	28.22±5.44

BMI = body mass index, Gold = WHO Global Initiative for Chronic Obstructive Lung Disease scale

domains than the normal population.

Scores on the SF-12 questionnaire are shown in Table 2. The best value (45.3 ± 12.4) appeared on MCS, and the worst (40.5 ± 7.2) on PCS, which was also noted in other studies[23-25]. The mean and median rates of the study population represent tolerable to good health status for both of the components, and differ less than 1 SD from those of the general population derived from a study in Greece[9]. Statistical analysis revealed significant difference (p<0.001) for both SF-12 components, which indicates that according to SF-12 also Greek patients with COPD have worse HRQoL than the general population.

TABLE 2. SGRQ and SF-12 scores (mean±SD) in 136 patients with chronic obstructive pulmonary disease (COPD) according to GOLD classification (stage)

	Total	Stage I	Stage II	Stage III	Stage IV
Symptoms	49.50±22.58	37.0±18.9	52.3±24.3	51.5±21.2	56.8±20.6
Activity	65.25±23.95	46.0±24.3	62.6±23.4	74.1±16.8	80.8±14.1
Impacts	43.70±22.78	25.2±17.2	45.8±23.7	48.0±20.4	59.1±17.0
Total	51.31±20.91	33.5±16.8	52.0±22.0	56.7±16.2	63.7±14.7
PCS	40.5±7.2	43.1±7.4	41.2±8.1	39.4±5.8	37.8±6.0
MCS	45.3±12.4	47.8±11.3	46.8±12.9	43.6±12.9	42.1±12.2

SGRQ = St George's Respiratory Questionnaire, SF-12 = Medical Outcomes Study Short Form 12, PCS = physical components summary, MCS = mental components summary, GOLD = WHO Global Initiative for Chronic Obstructive Lung Disease scale

Correlations

All SGRQ scores were associated with educational level and monthly income (Table 3). The higher the educational level and the financial status, the better were the HRQoL scores. No associations were found with age or sex of the patients. All the SGRQ scores were also associated with duration of symptoms, the degree of dyspnoea according to the Borg dyspnoea scale, pO_2 level, and disease stage (Table 3). A high number of pack-years and a high level of pCO_2 were associated with lower scores on the activity, impact and total scales. The age at onset of symptoms and frequent non-programmed medical visits also appeared to influence some aspects of well being. After Bonferroni correction, hospital admissions appeared not to influence SGRQ scores. Patients who had participated in a rehabilitation programme in the last 2 years had better scores on the symptoms scale. Co-morbidity with another major disease such as cardiovascular disease or diabetes mellitus (DM), had a negative impact on the HRQoL of patients with COPD, but no association was found with body mass index BMI or smoking status at the time of the study. Scores on the SGRQ scales showed moderate to high association with the spirometric values of the patients (FEV_1%, FVC% and FEV_1/FVC), and as the respiratory function fails HRQoL tends to worsen. Linear regression analysis (sequential addition / ablation method) for the SGRQ scales revealed socio-economic and clinical parameters, spirometric values, co-morbidities and rehabilitation programme attendance to be independent prognostic factors for QoL.

Regarding SF-12 scores, no associations were found between PCS and demographic variables, but MCS was found to be associated with sex (women have worse scores), educational level and monthly income (Table

4). Less strong association was revealed between SF-12 scores and clinical parameters (disease severity, pCO_2 levels and dyspnoea scale) than with SGRQ scores, and no association was found between SF-12 scores and age, smoking habit, BMI, symptom duration and age of onset, pO_2 levels, cardiovascular disease, DM, medical visits and hospital admissions. Spirometric values showed weak association only with the PCS component. Linear regression analysis (sequential addition / ablation method) for SF-12 components revealed socio-economic and clinical parameters, spirometry values, co-morbidities and rehabilitation programme attendance to be independent prognostic factors for QoL.

Cost of pharmaceutical treatment

The cost of pharmaceutical treatment of the study patients was estimated at 110±63 € / month. Higher cost was associated with smoking habit, disease severity [stage I with III (p<0.001) and IV (p<0.001), and stage II with III (p=0.003) and IV (p=0.01)], medical visits [>2 visits with 0 visits (p<0.001) and with 1-2 visits (p=0.005)] and hospital admissions [0 admissions with 1-2 admissions (p=0.017) and with >2 admissions (p=0.034)], dyspnoea frequency and nebulizer usage (Table 5). No association was found between cost of regular treatment and sex, age, co-morbidities and frequency of cough / sputum / wheezing. The pharmaceutical cost was also associated with all the HRQoL scales but MCS of SF-12 (Table 5).

Comparison with other populations

The patients with COPD in this study had lower scores on the SF-12 PCS component than Greek patients with asthma and heart disease in the study of Kontodimopoulos and colleagues[9], indicative of the greater impact of COPD

TABLE 3. Associations of SGRQ scales with demographic and clinical characteristics of patients with chronic obstructive pulmonary disease (COPD) (n= 136)

		SYMPTOMS		ACTIVITY		IMPACT		TOTAL	
		Mean (SD)	P	Mean (SD)	P	Mean (SD)	P	Mean (SD)	p
Educational level	primary / secondary	55.3 (24.1)	0.001	71.4 (21.6)	0.002	51.0 (21.5)	<0.001	58.0 (19.6)	<0.001
	tertiary / postgraduate	43.2 (19.0)		58.6 (24.8)		35.8 (21.7)		43.6 (19.9)	
Monthly income	<1000€	53.7 (24.1)	0.038	70.0 (22.2)	0.030	49.0 (23.4)	0.010	56.3 (21.9)	0.007
	>1000€	**45.7 (20.6)**		**61.1 (24.8)**		39.0 (21.3)		46.6 (19.8)	
Pack-years of cigarettes	<42	46.5 (20.9)	4.421*	**56.7 (24.8)**	0.006*†	**35.3 (23.2)**	0.007*†	**43.6 (21.1)**	0.007*†
	42-70	49.3 (25.5)		66.7 (24.6)		46.2 (23.8)		52.7 (22.7)	
	>70	52.7 (21.0)		72.4 (20.0)		49.6 (18.9)		57.2 (16.5)	
Symptoms duration	<5 years	42.3 (22.6)	0.008*	51.5 (24.4)	<0.001*	34.0 (21.9)	0.001*	40.8 (20.7)	<0.001*
	5-11 years	50.3 (20.5)		73.1 (19.5)		47.9 (20.5)		56.2 (17.1)	
	>11 years	56.7 (22.5)		72.9 (20.7)		50.4 (22.6)		58.1 (20.4)	
Symptoms onset	<49 years	52.3 (20.4)	0.117*	68.3 (22.5)	0.461*	46.6 (22.5)	0.023*	54.3 (19.8)	0.071*
	49-60 years	52.0 (25.2)		65.0 (27.3)		**47.9 (24.1)**		53.6 (23.6)	
	>60 years	43.5 (21.3)		62.0 (21.7)		**35.8 (19.9)**		45.1 (18.2)	
Medical visits in past year	0	52.0 (23.8)	0.001*	60.6 (26.0)	0.193*	41.3 (26.7)	0.001*	49.1 (24.5)	0.005*
	1-2	**38.6 (20.4)**		61.8 (22.8)		34.3 (21.2)		43.4 (19.5)	
	>2	**55.1 (21.4)**		68.8 (23.7)		50.0 (20.5)		56.5 (19.2)	
Admissions	0	48.4 (21.6)	0.495*	62.9 (24.3)	0.103*	40.7 (22.0)	0.046*†	48.2 (20.4)	0.083*
	1-2	50.2 (23.8)		71.3 (21.5)		46.6 (22.7)		54.9 (20.3)	
	>2	58.7 (26.6)		66.5 (31.0)		60.8 (26.5)		62.1 (27.2)	
BORG dyspnoea score	0-1	42.8 (20.9)	<0.001	59.8 (23.9)	<0.001	37.8 (21.9)	<0.001	45.5 (20.1)	<0.001
	>1	65.7 (17.9)		78.2 (18.8)		57.8 (18.4)		65.3 (15.9)	
pO₂	<60 mmHg	56.5 (20.7)	0.003*	81.5 (15.0)	0.001*	59.6 (17.9)	<0.001*	65.8 (15.9)	<0.001*
	60-80 mmHg	52.1 (22.2)		65.4 (23.6)		45.2 (21.8)		52.6 (20.0)	
	>80 mmHg	37.6 (21.1)		54.6 (24.4)		29.2 (20.4)		38.5 19.4)	
pCO₂	<45	48.5 (22.4)	0.205	**63.4 (24.3)**	0.024	**41.5 (22.5)**	0.004	49.2 (20.9)	0.007
	>45	55.6 (23.6)		**76.7 (18.8)**		**57.4 (19.7)**		63.1 (17.3)	
GOLD classification	stage I	**37.0 (18.9)**	0.002*†	**46.0 (24.3)**	<0.001*	**25.2 (17.2)**	<0.001*	**33.5 (16.8)**	<0.001*
	stage II	52.3 (24.3)		62.6 (23.4)		45.8 (23.7)		52.0 (22.0)	
	stage III	51.5 (21.2)		74.1 (16.8)		48.0 (20.4)		**56.7 (16.2)**	
	stage IV	56.8 (20.6)		80.8 (14.1)		56.1 (17.0)		63.7 (14.7)	
Cardiovascular disease	Yes	53.2 (24.0)	0.082	**70.7 (20.7)**	0.014	**48.5 (24.4)**	0.025	**56.1 (21.5)**	0.012
	No	46.4 (20.9)		**60.6 (25.6)**		39.7 (20.7)		47.0 (19.7)	
Diabetes mellitus	Yes	52.3 (25.0)	0.582	74.3 (16.6)	0.097	**55.8 (24.5)**	0.018	**61.0 (20.2)**	0.039
	No	49.1 (22.3)		64.0 (24.6)		42.0 (22.1)		49.8 (20.7)	
Rehabilitation programme	Yes	**39.9 (22.6)**	0.018	67.7 (21.6)	0.570	43.3 (17.9)	0.922	50.5 (17.6)	0.851
	No	**51.7 (22.1)**		64.7 (24.5)		43.8 (23.8)		51.3 (21.7)	

*ANOVA, †Bonferroni correction

SGRQ = St George's Respiratory Questionnaire, GOLD = WHO Global Initiative for Chronic Obstructive Lung Disease scale

TABLE 4. Associations of components of the Medical Outcomes Study Short Form 12 (SF-12) with demographic and clinical characteristics of patients with chronic obstructive pulmonary disease (COPD) (n = 136)

| | | PCS | | MCS | |
		Mean (SD)	p	Mean (SD)	p
Sex	male	40.4 (7.3)	0.778	46.7 (12.2)	0.020
	female	40.8 (7.1)		**40.9 (12.1)**	
Educational level	primary / secondary	39.8 (7.3)	0.245	**43.1 (13.2)**	0.033
	tertian / postgraduate	41.3 (7.1)		**47.7 (11.0)**	
Monthly income	<1000	39.8 (7.4)	0.312	**43.0 (12.7)**	0.037
	>1000	41.1 (7.1)		**47.4 (11.8)**	
Symptoms duration	<5 years	**42.9 (8.2)**		48.9 (11.3)	
	5-11 years	40.2 (5.6)	**0.004***	42.8 (11.9)	**0.036*†**
	>11 years	**38.1 (6.8)**		43.8 (13.3)	
Symptoms onset	<49 years	40.4 (7.3)		43.1 (13.4)	
	49-60 years	40.5 (7.9)	0.986*	43.9 (12.0)	**0.039*†**
	>60 years	40.7 (6.6)		49.3 (10.9)	
GOLD classification	stage I	**43.1 (7.4)**		47.8 (11.3)	
	stage II	41.2 (8.1)	**0.020*†**	46.8 (12.6)	0.210*
	stage III	39.4 (5.8)		43.6 (12.9)	
	stage IV	**37.8 (6.0)**		42.1 (12.2)	
Borg dyspnoea scale	0-1	41.5 (7.1)	0.015	47.0 (12.0)	0.011
	>1	38.2 (6.9)		41.2 (12.4)	
pO2	<60 mmHg	38.2 (6.7)		38.9 (12.4)	
	60-80 mmHg	40.3 (7.0)	0.098*	46.3 (12.6)	**0.050*†**
	>80 mmHg	42.6 (7.9)		46.5 (10.7)	
pCO_2	<45 mmHg	40.7 (7.4)	0.383	**46.5 (12.2)**	0.004
	>45 mmHg	39.4 (5.6)		**37.7 (10.7)**	
Depression	Yes	40.8 (9.3)	0.914	**29.8 (8.7)**	0.001
	No	40.5 (7.1)		**46.1 (12.0)**	

*ANOVA, †Bonferroni correction

PCS = physical components summary, MCS = mental components summary, GOLD = WHO Global Initiative for Chronic Obstructive Lung Disease scale

on HRQoL. No differences were found from the patients with DM or high blood pressure in that study.

Table 6 summarizes the comparison between the HRQoL scores of the Greek patients in this study and those of patients with COPD in similar studies in other countries. In a comparison with the results from a multinational study in 13 countries[19], the Greek patients with COPD reported worse HRQoL, according to SGRQ scores in all but symptoms scale, although the Greeks had better spirometric values (Table 6). Compared with an Italian population with COPD[18], Greeks had worse scores on various SGRQ scales and specifically: the impact scale at all stages, the activity scale at stages II-IV, and the symptoms scale at stage III, and on the total scale at stages II and III. The mean age of Italian patients was 8 years older

than that of the Greeks, but their mean FEV_1 values per stage were similar to those of the Greek patients. When the Greek patients were compared with patients with COPD in Malaysia[17] worse HRQoL was recorded by the Greeks in all but the total SGRQ scale, where the Greek values were higher only at stages II and III (Table 6). It is of note that although the ages of the two groups were similar and Malaysians had greater obstruction, Greeks had worse HRQoL scores. Compared to Swedish population with COPD[26], Greek patients had also higher scores on the total SGRQ scale at stages II and III, at similar FEV_1 values and age.

In a comparison of the SF-12 scores of the COPD population with those of a Spanish population with COPD[24], the Greek patients were found to have better

TABLE 5. Associations of regular costs of pharmaceutical treatment with clinical parameters and scores on health related quality of life (HRQoL) scales in patients with chronic obstructive pulmonary disease (COPD) (n = 136)

		Mean (SD)	p
GOLD classification	stage I	**72.7 (58.8)**	**<0.001*†**
	stage II	**95 (55.1)**	
	stage III	**143.5 (62.8)**	
	stage IV	**138.1 (50.0)**	
Smoking	No	94.7 (32.5)	**<0.001***
	Current	**78.3 (65.2)**	
	Ex-	**129.4 (55.0)**	
Pack-years	<42	**96.7 (62.9)**	**0.001***
	42-70	**94.8 (60.1)**	
	>70	**138.8 (57.2)**	
Nebulizer usage	Yes	**165.7 (49.7)**	**<0.001**
	No	**89.1 (54.4)**	
Dyspnoea^	Not at all	**77.1 (60.1)**	**0.007***
	Only with chest infections	75.4 (51.8)	
	A few days a month	107.0 (54.8)	
	Several days a week	93.5 (64.2)	
	Most days a week	**129.8 (63.2)**	
Medical visits in the past year	0	**74.8 (74.1)**	**<0.001*†**
	1 – 2	**94.4 (50.3)**	
	> 2	**132.4 (55.9)**	
Admissions	0	**96.4 (61.4)**	**0.003*†**
	1 – 2	**127.9 (59.7)**	
	> 2	**157.7 (59.9)**	

	r	P	
SGRQ Symptoms score	0.24	**0.005**	
SGRQ Activity Score	0.42	**<0.001**	
SGRQ Impacts score	0.39	**<0.001**	
SGRQ Total score	0.42	**<0.001**	
SF-12, PCS	-0.42	**0.006**	
SF-12, MCS	-0.14	0.101	

^SGRQ question nr 3, *ANOVA, †Bonferroni correction
GOLD = WHO Global Initiative for Chronic Obstructive Lung Disease scale, SGRQ = St George's Respiratory Questionnaire, SF-12 = Medical Outcomes Study Short Form 12, PCS = physical components summary, MCS = mental components summary

HRQoL according to the PCS of SF-12, but worse on the MCS component, at similar age and with comparable spirometric values. Similar differences were also found in comparison with British patients[23].

DISCUSSION

Numerous predisposing factors for HRQoL impairment have been revealed in this study of Greek patients with COPD. Clinical characteristics and demographic factors may both influence the HRQoL of patients with COPD. In addition, differences were identified between the Greek study population and patients with COPD of other nationalities, indicative of the influence of sociocultural factors.

Gender appears not to play a role in perception of HRQoL impairment by COPD in the Greek population,

TABLE 6. Comparison of SGRQ and SF-12 scores (mean values ± SD) according to GOLD stage in the present Greek and other studies of chronic obstructive pulmonary disease (COPD) [association (p)].

			SGRQ scores							
	Greek study					Rutten-van Mölken et al study (13 countries)[19]	Antonelli-Incalzi et al study (Italy)[18]			
	Stage I	Stage II	Stage III	Stage IV	Total	Total	Stage I	Stage II	Stage III	Stage IV
Total	33±17	52±22	57±16	64±15	51±21	45.00±16.98 **p<0.001**	36±19 p=0.473	38±20 **p<0.001**	50±16 **p=0.040**	62±17 p=0.641
Symptoms	37±19	52±24	52±21	57±21	50±23	49.71±23.15 p=0.891	44±22 p=0.145	47±24 p=0.234	64±17 **p=0.002**	60±21 p=0.596
Activity	46±24	63±23	74±17	81±14	65±24	60.68±19.23 **p=0.018**	41±22 p=0.348	49±26 **p=0.001**	65±19 **p=0.023**	72±16 **p=0.029**
Impact	25±17	46±24	48±20	56±17	43±23	34.52±19.11 **p<0.001**	11±10 **p<0.001**	14±10 **p<0.001**	21±11 **p<0.001**	26±12 **p<0.001**

	Azarisman et al study (Malaysia)[17]					Ståhl et al study (Sweden)[26]			
	Stage I	Stage II	Stage III	Stage IV	Total	Stage I	Stage II	Stage III	Stage IV
Total	23.8±13.3 p=0.257	39.9±25.2 **p=0.049**	36.0±16.1 **P<0.001**	58.4±23.3 p=0.272	50.2±23.2 p=0.790	25±20 p=0.105	32±20 **p<0.001**	36±20 **p<0.001**	53±23 p=0.098
Symptoms					43.7±23.6 **p=0.050**				
Activity					55.1±27.9 **p=0.005**				
Impact					35.2±23.8 **p=0.016**				

	SF-12 Scores				
	Greek study	Diez et al study (Spain)[24]		Spencer et al study (UK)[23]	
	Mean (SD)	Mean (SD	p	Mean (SD)	p
PCS	40.5 (7.2)	35.9 (10.3)	**<0.001**	36 (10.0)	**<0.001**
MCS	45.3 (12.4)	48.2 (11.4)	**0.003**	50 (10.0)	**<0.001**

GOLD = WHO Global Initiative for Chronic Obstructive Lung Disease scale, SGRQ = St George's Respiratory Questionnaire, SF-12 = Medical Outcomes Study Short Form 12, PCS = physical components summary, MCS = mental components summary

as no sex-related associations was found on the disease specific questionnaire scales, in contrast with studies in other countries[20]. The generic questionnaire revealed a lower score on the MCS scale in women (p=0.02), which indicates other possible reasons than COPD for this impairment (Table 4).

Age group differences were not a strong feature in scores on the HRQoL scales, as in the studies of Antonelli-

Incalzi and colleagues and Ståhl and colleagues[18,26], apart from the 61-70 years group which recorded lower scores on most of the scales. The younger Greek patients with COPD, even though they had HRQoL statistically similar to that of the older patients, had worse general health status; they presented higher BMI, more co-morbidities, lower FEV_1 values and higher levels of dyspnoea on the Borg scale. Other studies in the Greek population have revealed less symptoms in patients below than 50 years with COPD than observed here[27].

The educational level and financial status were associated with scores on all SGRQ scales and on the SF-12 MCS (Tables 3 and 4) and were identified as independent prognostic factors for certain aspects of HRQoL impairment. For example, the less educated and poorer patients had a symptoms scale score 7.21 units lower and an activity scale 7.28 units lower than the more highly educated and wealthier patients. It is noteworthy that no socio-economic associations appeared in the Swedish population[26], and this observation in the Greek population may reflect limitations of health system access and/or treatment options, or poor information about regarding the smoking hazard.

The duration of symptoms influences scores on all scales of the SGRQ and the PCS of the SF-12 (Tables 3 and 4). Greek patients with symptoms for more than 5 years have poorer HRQoL as expressed by more symptoms, more limitation of activities, higher social impact and worse physical health. While duration of symptoms appear to play crucial role in all aspects of HRQoL, the age at onset of symptoms influences only mental status since only the score impact scale is affected (Table 3). No differences were found between former and current smokerson either of the questionnaires, but the smoking related parameter that was related with most aspects of HRQoL in was the total of cigarettes smoked, that is the pack-years (Table 3). Patients with had greater impairment of activities and impact, and a worse total SGRQ scale than patients with <42 pack-years. A history of >70 pack-years was also an independent prognostic factor for the impact and total scales.

Disease severity (i.e., stage according GOLD classification) was associated with all SGRQ scales in the Greek population, and an independent prognostic factor for the impact scale (patients at stage II had a difference of 12.77 units from those at stage I). Other studies show diversity in the factors associatied with disease stage[18,19,21,22]. On the SF-12 questionnaire, in the present study and that in Sweden, disease stage was associated only with PCS[26]. As would be expected, spirometric values were cor-

relateded with most of the HRQoL scales, and in some cases, but not all, represent an independent prognostic factor[28]. The degree of dyspnoea level according to the Borg scale was found to be correlated with all scales of both questionnaires, and an independent prognostic factor for every level and scale. It is known that degree of pnoea is one of the strongest prognostic factors regarding HRQoL[29]. pO_2 level was correlated with all SGRQ scales and pCO_2 levels with all but the symptoms scales, but arterial blood gases were not associated with any scale on the SF-12 questionnaire. Earlier studies have shown that hypoxaemia presents only low or no association with HRQoL when generic questionnaires are used, but high association with symptoms, impact and total scales of SGRQ, while hypercapnia presents marginal association with the total SGRQ scale[20,28]. in the present study hypoxaemia was revealed as an independent prognostic factor for the symptoms scale, and hypercapnia for MCS of SF-12. Patients with respiratory deficiency score 11.53 units less on the symptoms scale than those with normal pO_2, while hypercapnic patients score 9.76 and 8.07 units less on the impact scale and MCS respectively than normocapnic patients.

No relationship was found between BMI and HRQoL scales in this study. In earlier studies[29,30] underweight patients with COPD scored worse on the SGRQ scales and impaired physical functioning, role-emotional, bodily pain and general health on the SF-36 questionnaire, but in the present study there were no underweight patients. The number of unscheduled medical visits was associated with symptoms, impact and total scales and was an independent prognostic factor for the symptoms scale in this Greek population, and patients with more than two hospital admissions in the past year scored worse on all scales, but not to a statistically significant degree as in the Spanish population study[31].

Co-morbidities aggravate the HRQoL of Greek patients with COPD, and specifically, the presence of cardiovascular disease worsened the activity, impact and total SGRQ scores, while DM aggravated the impact and total scores. These findings are consistent with those in Italian patients, where co-morbidity was found to aggravate impact and total SGRQ scores[18]. The presence of depression was associated only with the MCS scale, while Okubadejo and colleagues found correlation with the total SGRQ scale. Cardiovascular diseases and depression were revealed as independent prognostic factors for the activity scale and MCS. Patients who had participated in respiratory rehabilitation programmes in the past two years had better

score on the symptoms scale but no other associations, although other studies have shown that rehabilitation programmes, in addition to improving symptoms, ameliorate stress and depression levels, increase exercise tolerance and reduce the number of exacerbations and the death risk for up to two years[17,32-35].

The cost of pharmaceutical treatment for Greek patients with COPD was associated with a variety of different clinical parameters (Table 5). Pharmaceutical treatment cost rises with progression of the disease (disease stage) and increase in frequency of dyspnoea, but is not influenced by other COPD symptoms (cough, expectoration and wheezing). Ex-smokers incur higher cost of treatment and while cost is also influenced by the number of pack-years quantity, and it can be concluded that ex-smokers have more extensive COPD lesions. Higher frequency of unscheduled medical visits and hospital admissions also increase the cost of treatment, as does use of a nebulizer for treatment. Regarding HRQoL., the cost of treatment rises as the scores on all SGRQ and PCS scales increase, although it is not associated with mental health impairment (i.e., theMCS scale), which indicates that it is the real need of treatment of COPD that raises the cost, and not psychological parameters and stress (Table 5). Most of the parameters that influence the cost of treatment are HRQoL dependent, although some, such as nebulizer use or smoking habit affect the pharmaceutical treatment cost independently.

This study has certain limitations in the possibility of extension of the results to other populations with COPD. The study was conducted on an urban Greek population and reflects the characteristics of Athenian patients with COPD, attending a major public hospital for their medical care. The design of the study thus excluded patients being treated and monitored in private doctors' offices and clinics (i.e., the wealthier patients, etc), who do not use public hospitals for their disease management. The weather conditions and ambient air pollution of Athens may also influence both the manifestations and the HRQoL of patients with chronic respiratory diseases[36].This study has also not investigated confounding factors, namely at what level one parameter is influenced directly by the presence of another parameter related to the first (such as co-morbidity and old age). Studies in the Spanish population showed that there are differences regarding sex, age, smoking habit, and educational level in the SGRQ scores of the non-COPD population and other high risk population groups[37]. These possible differences have not been taken into consideration in this study. The findings of his study,

however, present a valid picture of a large population in Greece and the conclusions can be indirectly extended to the whole COPD population. Deviations can be seen in current pharmaceutical prices, but the proportions are still valid, as are associations with pharmaceutical costs.

CONCLUSIONS

The disease specific SGRQ and the generic SF-12 questionnaires adequately reflect the HRQoL of patients with COPD in the study population, with the specific questionnaire being the more sensitive. Both of the questionnaires depict the decline in HRQoL as the clinical status aggravates, and the MSC of the SF-12 makes up for any lack that the impact scale of SGRQ might present in mental health estimation. The PCS scale appears to be weaker in COPD HRQoL estimation and for this reason a combination of the two questionnaires is proposed to be appropriate. This study emphasizes the necessity for HRQoL questionnaires for improving the management of COPD providing optimal health care for those suffering from this disease.

HRQoL, as measured with SGRQ and SF-12, was found to be lower in Greek patients with COPD than in the general population, and also compared to similar patients in other countries HRQoL, on most of the scales. This could indicate major differences in the quality of health services provided, differences in health system access, or a greater degree of impairment of the mental health of Greek patients with COPD. More studies need to be conducted to clarify the main causes of these differences.

This study has revealed many parameters that influence the HRQoL of Greek patients with COPD, including sex and socio-economic factors, and medical factors including duration of symptoms and age of onset, smoking habit and quantity of pack-years, stage of disease, degree of dyspnoea, level of arterial blood gases, and presence of co-morbidities, and care-related factors such as number of medical visits and rehabilitation programme attendance. Many of these parameters and also impaired HRQoL and influence the cost of treatment in this population. These parameters should all be taken into consideration in the disease management of COPD in Greece.

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