Pulmonary and Respiratory Medicine: Open Access

Kourlaba G, et al. J Pulm Respir Med 2017: PROA-102.

Research Article

Factors Associated with the Quality of Life of Greek Patients with Chronic Obstructive Pulmonary Disease

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Citation: Kourlaba G, Hillas G, Vassilakopoulos T, Maniadakis N (2017) Factors Associated with The Quality of Life of Greek Patients With Chronic Obstructive Pulmonary Disease. J Pulm Respir Med 2017: PROA-102.

Received Date: 25 April, 2017; **Accepted Date:** 15 May, 2017; **Published Date:** 23 May, 2017

Summary at a Glance

The factors associated with the Health-Related Quality of Life (HRQoL) of patients with COPD in Greece were evaluated. Our study revealed that older patients, and those suffering more years from COPD have worse HRQoL than their counterparts. Moreover, hospitalizations, long term oxygen therapy and emergency visits worsen patients' HRQoL.

Abstract

Background and objective: Chronic obstructive pulmonary disease (COPD) is a leading cause of disability and death worldwide, imposing a substantial socioeconomic burden. Moreover, COPD is characterized by impaired health-related quality of life (HRQoL).Since limited data are available regarding the HRQoL of COPD patients in Greece, the objective of the present study wasto assess COPD patients' HRQoL as well as the factors associated with the HRQoL of such patients in Greece.

Methods: A population-based, random-digit dialed, telephone nationwide survey was conducted to recruit patients with COPD. 351 patients were identified and completed the survey. All data were collected with a 30-minuteinterviewusing a structured questionnaire of 60 items developed to serve the purposes of this study. Data regarding demographic and lifestyle characteristics, comorbidities, disease history, breathlessness and symptoms severity, healthcare care resource consumption during the past 12 months, as well as HRQoL, measured using the Euroqol Five-Dimension Questionnaire (EQ-5D), were collected.

Results and Conclusions: The mean utility value was 0.57 indicating a moderate HRQoL. A strong negative correlation between HRQoL and age and time passed since COPD diagnosis was detected, indicating that older patients and those having been diagnosed with COPD more than 10 years have poorer HRQoL. A strong negative correlation was also detected between HRQoL and COPD Assessment Test (CAT) score and severity of breathlessness indicating that patients' HRQoL drops as the CAT score or severity of breathlessness increases. Patients who conducted visits to outpatient or emergency department of hospitals, were hospitalized at least once, was on long-term oxygen therapy and were subjected to at least one diagnostic test during the past 12 months reported poorer HRQoL compared to their counterparts. This survey indicates the great impact of COPD on patients' HRQoL and reveals the parameters that influence the HRQoL of Greek COPD patients. These parameters should be taken into consideration to achieve better management of COPD.

Keywords: Chronic obstructive pulmonary disease; Disease severity; Factors; Quality of life; EQ5D

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a leading cause of disability and death worldwide, imposing a substantial socioeconomic burden[1]. The prevalence of COPD has been found to range between 5% and 13%, worldwide[1], with the prevalence in Greecehaving been estimated at 8.4%, almost fifteen years ago [2] and 10.6% in a recently published study[3]. Moreover, the results of a study that replicated the original Confronting COPD International Survey indicate an increase of COPD prevalence across the last decade[4,5].Despite significant public health efforts aiming to prevent the burden of this disease, the World Health Organization (WHO) has predicted that COPD will become the third most common cause of death in the world by 2030 [6].COPD is characterized by impaired Health-Related Quality of Life (HRQoL)[7-11]. Moreover, there is substantial evidence declaring that poor HRQoLis associated with high levels of dyspnea [7], physical impairment[7], depression and anxiety[7], poor prognosis in terms of readmission to hospital[12] and death[13]. Acute exacerbations of COPD are important events in the natural course of disease that lead to deterioration in lung function and in HRQoL and, when complicated with acute respiratory failure, to severe short- and long-term prognosis [14,15].

HRQoL assessments may be performed using either generic or disease-specific questionnaires[16]. To the best of our knowledge, in Greece, COPD patients HRQoL has been recently estimated using the disease specific St George's Respiratory Questionnaire (SGRQ) and the generic SF-12 questionnaires in a small sample of patients and showed that the HRQoL of COPD patients was significantly lower compared to that of general population. Moreover, the factors affecting the HRQoL of such patients were identified[17]. However, nationwide data with respect toHRQoL of COPD patients in Greece are completely lacking. In this context, the objective of the present nationwide survey was to assess the COPD patients HRQoLin Greece using the EuroQol-5D (EQ-5D) questionnaire,a generic tool applicable in healthy individuals as well as in patients with specific diseases, which seems to have demonstrated validity and reliability in COPD[18].

Methods

Study Design& Population

A population-based, Random-Digit Dialled (RDD), telephone nationwide survey was conducted between 10thand 31stof July 2015 in order to recruit patients with COPD. A proportionate stratified by region, systematic sampling procedure was used to ensure a nationally representative sample of the urban/rural population based on the distribution of population as obtained from the census 2011. Based on this procedure, 362 subjects aged 40+ and having been diagnosed with COPD were identified, but 351 completed the survey (response rate=97%).Prior to completion of the survey, patients were asked to give their verbal consent since they were firstly informed by the interviewers for the purpose of the study, that all data would be confidential and anonymous and that they would be able to terminate the interview at any time. More details are presented by Kourlaba, et al. [3,19].The study protocol was not submitted to the ethical committee of any institution for approval, since the survey qualified for institutional review board exemption, as specific regulatory criteria, were met[4]: involved no medicine administration, medical devices, or biospecimen collection; respondent participation was voluntary; there was no respondent burden other than completion of the survey; the survey population was not a vulnerable population (any elderly respondents could opt out at anytime, and interviewers were trained to terminate interviews with any respondents struggling with cognitive or health issues); the survey was not conducted for litigation purposes; the survey did not collect sensitive data; there were no risks of data disclosure; and respondents could not be named or identified directly or indirectly.

Data Collection

All data were collected with the method of interview using a structured questionnaire of 60 items in Greek, specifically designed for the purposes of the study (see Appendix I).Most of questionnaire items were based on the Confronting COPD study questionnaire [4]and notably validated patient reported outcome instruments were used to elicit patients'responses.In general, data regarding socio-demographic and lifestyle characteristics, co-morbidities, disease history, symptoms and disease severity, health care resource consumption during the past 12 months as well as HRQoL were collected. To be more specific, we recorded patients' gender and age and we asked them to report their weight and height based on which, the Body Mass Index (BMI) was calculated. Then, patients were classified as normal weight (BMI<25 kg/m^2), overweight (BMI: 25-30 kg/m^2) and obese (BMI>30 kg/m^2).Moreover, smoking status such as current, ex-and non-smokers, defined using specific definitions [3,19] was recorded.Patients were additionally asked to report the duration since the time of COPD diagnosis as well as if they have been told by their physicians that they havecertain co-morbidities. The Modified Medical Research Council (mMRC) breathlessness scale was used [19] to assess patient's severity of breathlessness. In particular, patients were asked to choose which of five statements, best described their recent condition. Overall symptom severity was assessed with the COPD Assessment Test (CAT) score[20,21]. Disease exacerbations during the past year as well as GLOBAL Initiative for Obstructive Lung Disease (COLD)category were determined indirectly. More specifically, the history of exacerbations was determined using three specific criteria as listed below:

Criterion 1: In the last 12 months, have you been told by your physician that you have had worsening of your "respiratory condition"?YES

Criterion 2: In the last 12 months, have you been told by your physician that you have had acute bronchitis?YES

Criterion 3: In the last 12 months, what aspects of your "Respiratory Condition" have worsened? (cough during the daytime, cough during the night, phlegm, breathlessness or shortness of breath and fatigue, ability to perform regular activities)At least two symptoms cited [22]. Moreover, patients were classified into the 4 groups (A-D) according to an adaptation of the 2011 GOLDclassification[22], on the basis of CAT score and exacerbation history (Appendix II, Figure 1).

Patients HRQoLwas measured using the EQ-5D questionnaire that is a generic tool for measuring HRQoL, which seems to have demonstrated validity and reliability in COPD(18). Although, this instrument has never been used in COPD patients in Greece, it has been extensively used to measure HRQoL in various populations in Greece.As such, this instrument was usedso that we can compare COPD patients'HRQoL with that of other Greek populations. The five dimensions of the EQ-5D correspond to the levels of mobility, self-care, usual activities, pain/discomfort and anxiety/depression as rated by the patient (no problem, moderate problem, inability/severe problem). The European value set was used to convert the health states to the single summary EQ-5D Index[23]. Higher values correspond to better health state levels.

Finally, patients were asked about their COPD-related consultations (how often, type of physician seen, other health care professionals), hospitalizations (how many times and how many nights), emergency room visits (how many visits), lung function testing (how many spirometry tests), para-clinical tests such as chest x-ray and computed tomography (CT), use of oxygen therapy (yes/no and frequency) and medication use (checklist of specific respiratory medicines, use of over-the-counter medications, antibiotic use for respiratory infections).

Statistical Analysis

Categorical variables are presented as absolute (n) and relative frequencies (%). Continuous variables are summarized as means ± standard deviation if they were normally distributed and as median and Interquartile Range (IQR) if they wereskewed. HRQoL is presented as mean and 95% Confidence Interval (CI). The Student's-test was used to assess the association between patient's HRQoL and a binary variable (i.e. CAT score<10 vs. CAT score≥10). The One-Way Analysis of Variance (ANOVA), after testing for equality of variances wasused to evaluate the association between patients HRQoLwith categorical variables with more than 2 groups (i.e. GOLD category). Bonferroni correction was used to account for increase in typeI error due to multiple comparisons.

A Tobit regression model was employed to evaluatefactors independently associated with patients HRQoL (EQ-5D utility values). The Tobit regression model is suitablefor two reasons. First, the dependent variable, EQ-5Dutility score is censored (EQ-5D utility score: 0.074 to 1.000). Second, thedata were skewed, and many observations were at the upperlimit. In particular, factors found to be statistically significantly associated with HRQoL at a univariate level were entered in the multiple regression model. The results are presented in b-coefficients and 95% CI.

A probability value of 5% was considered as statistically significant. All statistical calculations were performed using STATA software (version 8, 2003, STATA Corp, College Station, TX, USA).

Results

Baseline characteristics

Characteristic	Mean±SD	p-value
Gender		0.124
Male	0.55 ± 0.29	
Female	0.59 ± 0.27	
Age (years)		**<0.001**
40-49	0.66 ± 0.22¶	
50-59	0.68 ± 0.24¶	
60-69	0.63 ± 0.26¶	
70+	0.45 ± 0.29	
Geographic Area		0.420
Urban	0.57 ± 0.29	
Semi-urban/rural	0.60 ± 0.27	
BMI (Kgr/m^2)		0.147
<25 (underweight/normal weight)	0.57 ± 0.29	
25.0-29.9 (overweight)	0.54 ± 0.28	
≥30.0 (obese)	0.62 ± 0.28	
Self-reported Comorbidities		0.112
None co-morbidity	0.66 ± 0.31	
At least one comorbidity	0.56 ± 0.28	
COPD duration (years since diagnosis)		**0.004**
<5	0.61 ± 0.28§	
5-10	0.59 ± 0.28§	
>10	0.50 ± 0.28	
Smoking status		0.198
Current smoker	0.61 ± 0.27	
Ex Smoker	0.55 ± 0.30	
Non-Smoker	0.55 ± 0.27	

mMRC grade		**<0.001**
Mild breathlessness (0-1)	0.70± 0.22‡†	
Moderate breathlessness (2-3)	0.50± 0.24‡	
Severe breathlessness (4)	0.12± 0.18	
CAT score		**<0.001**
<10	0.84± 0.20	
≥10	0.53± 0.27	
GOLD Category		**<0.001**
A	0.86± 0.19*#	
B	0.62± 0.23*	
D	0.47± 0.27	
Exacerbation during the last 12 months		**<0.001**
Yes	0.47± 0.28	
No	0.68± 0.25	

Table 1: Health-related Quality of Life by COPD patients' characteristics and disease severity indices.

CAT: COPD Assessment Test; GOLD: Global Initiative for Chronic Obstructive Lung Disease; mMRC scale: modified Medical Research Council breathlessness scale;BMI: Body Mass Index; COPD: Chronic obstructive pulmonary disease; SD: standard deviation

¶p<0.001 compared to patients aged>70 years, after controlling for multiple comparisons

§p<0.05 compared to patients being diagnosed with COPD more than 10 years ago after controlling for multiple comparisons

‡p<0.05 compared to severe breathlessness after controlling for multiple comparisons

†p<0.05 compared to moderate breathlessness after controlling for multiple comparisons

*p<0.05 compared to GOLD D after controlling for multiple comparisons

#p<0.05 compared to GOLD B after controlling for multiple comparisons

The mean age of patients were 65.8 years old and the majority of them was males (54.1%). The mean time passed since COPD diagnosis was 9.4 years.With respect to the grade of breathlessness, half of patients reported mild breathlessness (i.e. grades 0 & 1), while almost 9% of patients reported the highest breathlessness grade (too breathless to leave the house). As for the CAT score, thevast majority of patients wasclassified as having CAT≥10 (84%). Exacerbations during the past 12 months were detected in almost half of patients (51.7%), while by combining CAT score with the history of exacerbations during the past 12 months, it was found that almost half of patient were classified into the GOLD category D (49.9%), followed by GOLD category B (34.1%).

Quality of Life

The mean utility value was found to be 0.57±0.28 indicating a moderate HRQoL.

Resource utilization	Mean± SD	p-value
At least one visit at private office during the past 12 months		0.259
No (n = 93)	0.60 ± 0.30	
Yes (n= 258)	0.56 ± 0.28	
At least one visit athospital/health center outpatient clinicduring the past 12 months		**<0.001**
No (n=217)	0.61± 0.28	
Yes (n=134)	0.50 ± 0.28	
At least one visit athospital emergency department during the past 12 months		**<0.001**
No (n=266)	0.64 ±0.26	
Yes(n=85)	0.36 ±0.26	
At least one hospitalization during the past 12 months		**<0.001**
No (n=292)	0.62±0.26	
Yes (n=59)	0.32±0.25	
Long term oxygentherapy		**<0.001**
No (n=272)	0.64±0.25	
Yes (n=79)	0.35±0.29	
At least one lab/diagnostic test during the past 12 months		**0.009**
No (n=56)	0.66±0.28	
Yes (n=295)	0.55±0.28	

Table 2: Resource utilization during the past 12 months and health-related quality of life of COPD patients in Greece.

Considering the EQ-5D subsections, less than 10% of patients reported severe problems in all dimensions with the exception of anxiety/depression where almost one third of patients reported severe problem(Appendix II, Table 2).

Factors related to Quality of Life

A strong negative correlation between HRQoL and age was detected, while no statistically significant association was detected between HRQoL and gender, smoking habits, the presence of comorbidities and BMI status. With respect to the association between patient's age and their HRQoL, it was found that the mean (SD) utility values range between 0.67 (0.21) in patients aged 40-49 years and 0.45 (0.29) in patients aged more than 70 years.

Moreover, a strong negative relationship was detected between the time passed since COPD diagnosis and patientsHRQoL. More specifically, the mean (SD) utility values range from 0.61 (0.28) in patients suffering from COPD less than 5 years to 0.50 (0.28) in patients suffering more than 10 years (p=0.004).

Additionally, the HRQoL of patients who reported history of exacerbations of their respiratory condition during the past 12 months was statistically significantly poorer (p<0.001) compared to those who had not experienced exacerbations. Moreover, a strong correlation was detected between HRQoL and GOLD category, CAT score and severity of breathlessness. More specifically, HRQoL was found to gradually reduce as the severity of breathlessness increases, ranging from a mean utility value of 0.70 among patients with mild breathlessness to 0.12 among patients with severe breathlessness (p<0.001). With respect to GOLD category, patients in the higher-grade GOLD group (D) reported having poorer HRQoL compared to the rest patients (p<0.001) (Table 1).

A strong association was detected between patients' HRQoL and the consumption of healthcare resources during the past 12 months (Table 2). To be more specific, patients who reported visits to outpatient or emergency department of hospitals, those who were hospitalized at least once, was on long-term oxygen therapy and were subjected to at least one diagnostic test during the past 12 months reported poorer HRQoL compared to their counterparts. No difference was detected in patients HRQoL between those had at least one visit at private office or not.

Patient's age, years passed since COPD diagnosis, GOLD category, as well as visits at outpatient or emergency department of hospitals, hospitalization, long-term oxygentherapy and use of diagnostic tests during the past year were entered in the multiple Tobit regression with utility values as dependent variable. The results are presented in (Table 3).

	Adjusted
Characteristics	**b-coefficient (95% CI)**
Age (years)	
40-49	Reference
50-59	-0.002 (-0.0930.089)
60-69	0.007 (-0.0830.098)
70+	-0.057 (-0.1450.032)
Years passed since COPD diagnosis	
<5	Reference
5-10	0.007 (-0.054-0.069)
>10	**-0.067 (-0.131(-0.003))**
GOLD category	
A	Reference
B	**-0.162 (-0.244(-0.081))**
D	**-0.229 (-0.314(-0.145))**
At least one visit at hospital/health center outpatient clinic during the past 12 months	
No	Reference
Yes	0.007 (-0.0500.064)
At least one visit at hospital emergency department during the past 12 months	
No	Reference
Yes	**-0.091 (-0.170(-0.011))**
At least one hospitalization during the past 12 months	
No	Reference
Yes	**-0.114 (-0.206(-0.021))**
Long term oxygentherapy	
No	Reference
Yes	**-0.150 (-0.220(-0.079))**
At least one lab/diagnostic test during the past 12 months	
No	Reference
Yes	-0.066 (-0.1420.009)

Table 3: Association between socio-demographic, clinical characteristics, resource utilization and patients' health-related quality of life; Results from Tobitregression analysis

Among these factors, years passed since the time of diagnosis, GOLD category as well as hospitalizations, visits at emergency department of hospital and long-term use of oxygentherapy during the past 12 months were found to be independently associated with patients HRQoL(Table 3).

Discussion

The current study is a population-based, telephone nationwide survey that sought to estimate the HRQoLofCOPD patients in Greece. The survey included patients aged ≥40 years with physician-diagnosed COPD. To the best of our knowledge, this is the first study in Greece aiming to evaluate the HRQoL of COPD patients in Greece measured by EQ-5D.

Our study similarly and in line with previously conducted studies, one of which in Greek population, revealed the significant impact of COPD on patients HRQoL[10,17,24-27] Although, there are many disease-specific and generic instruments employed in studies aiming to measure COPD patients' HRQoL, EQ-5D has been widely used since it is simple to use and less time consuming(16). Comparing the findings of the present study with the results provided by other studies, it seems that Greek patients with COPD have poorer HRQoL(0.57) compared to that of COPD patients in other countries [24-27](Figure 1).

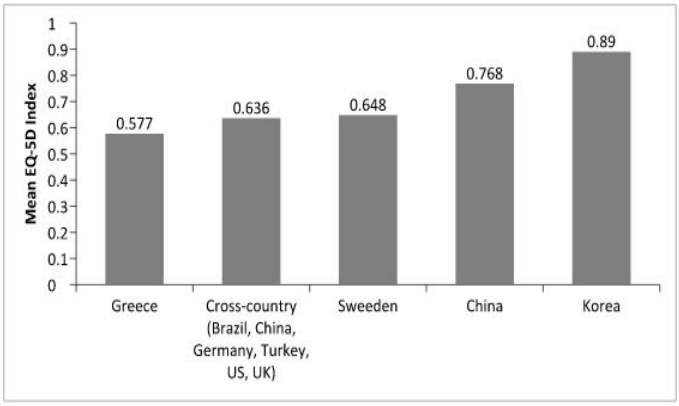

Figure 1: Health-related Quality of Life of patients with chronic obstructive pulmonary disease, as measure through EQ-5D, across countries [24-27].

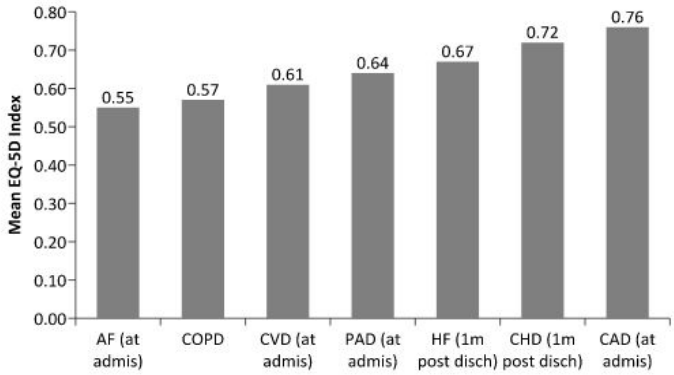

Figure 2: Health-related Quality of Life among different populations in Greece, as measured through EQ-5D.

AF: atrial fibrillation; CVD: cardiovascular; PAD: peripheral artery disease; CHD: coronary heart disease; CAD; coronary artery disease; HF: heart failure; COPD: chronic obstructive pulmonary disease.

To be more specific, in a cross-country (Brazil, China, Germany, Turkey, US and UK) cross-sectional survey conducted in a sample of COPD patients aged 45-67 years, an overall mean EQ-5D score of 0.64 was found, ranging from 0.51 in the UK to 0.80 in China[24]. A relatively high EQ-5D score (0.77) was estimated in another cross-sectional study carried out in Beijing, Guangzhou, Shanghai and Chengdu[27]. An even higher EQ-5D score (0.89) was observed in Korean COPD patients[25]. These findings confirm the results of the previously conducted study in Greece, where it was also demonstrated that Greek COPD patients have worse HRQoL compared to other COPD populations although other HRQoLinstruments (i.e. the disease specific SGRQ and the generic SF-12 questionnaires) had been used[17]. These differences in the HRQoL of COPD patients across countries could be partially explained by variations in the severity of disease and differences in local disease management, and quality of health services provided.

Moreover, comparing the utility value obtained from the present study with that of other patient populations in Greece, we found that the HRQoL of COPD outpatients in Greece (0.57±0.28) is similar to that of patients presenting in the emergency department with atrial fibrillation (0.55±0.30)(28) and significantly lower than that of patients with heart failure (0.671) and coronary heart disease (0.718) one month after their discharge date(29). These results are indicative of the greater impact of COPD on HRQoL, although it is not methodologically correct to compare data coming from different studies with different study design and sampling procedure(figure 2).

Additionally, the results of the present study indicate that patients HRQoL is strongly associated with GOLD category, severity of breathlessness, the presence of exacerbations and the years passed since disease diagnosis. To be more precise, it was found that patients HRQoL worsen gradually as breathlessness severity and GOLD category increases with the EQ-5D score reaching at very low levels for patients with severe breathlessness (0.12) and GOLD D (0.47). Moreover, it was detected that the time passed since COPD diagnosis inversely affectspatientsHRQoL revealing that patients having been diagnosed with COPD more than 10 years ago have worse HRQoL compared to the rest of patients. These findings are in agreement with previous studies reporting that HRQoL was worse for those with more severe disease [10,17,24] and those experiencing COPD symptoms for more than 5 years[17].

Moreover, gender was not found to play a role in COPD patients' HRQoL and this finding is in agreement with the results of the previously conducted study in Greece[17]. However, in other studies, females seems to have poorer HRQoL compared to males [25,27]. On the other hand, patients' age, consistently with the results of other studies, seems to inversely affect HRQoL[17,24,25,27].

Furthermore, although no difference was detected in HRQoL

of patients who conducted visits at private offices or outpatient department of hospitals compared to their counterparts, patients admitted at least once at emergency department of hospitals during the past 12 months were found to have significantly poorer HRQoL. This finding could be explained by the fact that a visit at emergency department may indicate a sudden worsen of symptoms, while outpatient visits either to private office or to outpatient department of hospitals may reflect scheduled monitoring visits. Moreover, as it was expected hospitalization and long-term use of oxygen worsen HRQoL. Although the data of the current study were obtained from a nationwide population survey with a high response rate, the limitations should be acknowledged.The majority of study limitations come from the design since it is a telephone survey and not a face-to-face survey. First of all, although a stratified systematic sample has been selected in order to ensure a representative sample, individuals without telephone service are automatically excluded[30,31], something that may violate the representativeness. Moreover, this type of surveys may suffer from poor response quality since responders can be tired of a long telephone conversation, do more things at the same time or are suspicious towards the interviewer[31]. On top of these, the GOLD category and history of exacerbations were not objectively measured and as such the results may be questionable, especially with respect to the percentage of patients experiencing exacerbations and belonging to each one of the four GOLD categories.However, the impact of these two factors on COPD patients' HRQoLis in line with the findings of other studies in which clinical examination and medical records had been used to classify patients into GOLD category and into those with and without exacerbations.

To sum up, this survey demonstrates the great impact of COPD on patients' HRQoL in Greece, as measured by the generic instrument EQ-5D. Moreover, this study provides data regarding the determinants of COPD patients' HRQoL indicating that older patients, those suffering more years from COPD, patients with severe disease as well as hospitalizations, long term oxygentherapy and emergency visits worsen patients HRQoL. These parameters should be taken into consideration in order to achieve better disease management and to formulate appropriate policies.

Acknowledgments

Authors would like to thank Hellenic Thoracic Society that sponsored this study.

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