Original Article

TANAFFOS

Effect of COPD on Health-Related Quality of Life; Results from the BOLD Study in Iran

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Background: Chronic obstructive pulmonary disease (COPD) has been the third leading cause of morbidity and the sixth leading cause of mortality in 2020. This chronic disease usually impairs health status and is an independent predictor of morbidity and mortality. The main objective of this study was to assess health-Related quality of life (HRQL) in a large sample of participants with and without COPD.

Materials and Methods: The present study was based on the data obtained from the population-based BOLD study in Iran. The sampling frame in this study included the whole population of 31 provinces of Iran. Participants were recruited using a stratified cluster sampling strategy with proportional allocations within strata. All the participants were requested to fill the Short Form 12 (SF-12) Health Survey Questionnaire, an abbreviated version of the SF-36.

Results: A total of 1062 subjects, including 479 (45%) males and 583 (54.7%) females, were enrolled in the study. The mean age of the participants was 40±15.04 years. The overall COPD prevalence based on the post-bronchodilator spirometry functional criteria was 5.0%. The mean PCS- 12 and MCS- 12 for all the subjects were 66.61±22.72 and 60.79±23.52, respectively. The mean scores of PCS and MCS were significantly lower in patients with COPD than those without COPD (P<0.001).

Conclusion: The findings of this study demonstrated that COPD, female gender, and an age above 40 years influenced HRQL, especially the physical dimension, as shown by the SF-12 instrument.

Key words: Chronic obstructive pulmonary disease; Epidemiology; Health-related quality of life; Iran

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is characterized with limited airflow, which is not fully reversible, and an accelerated decline in lung function. The disease is a leading cause of morbidity and mortality worldwide (1, 2). The disease has been proven to be the third leading cause of morbidity and the sixth leading cause of mortality in 2020 (3).

As a respiratory disease, COPD causes a range of extrapulmonary sequels, such as nutritional abnormalities, systemic inflammation, elevation in the metabolic rate, a gradual and significant weight loss, and muscular

deterioration, as well as defects in other organs (4). These conditions usually impair health status, which is an independent predictor of morbidity and mortality (5, 6). It has been proven that some factors, such as concomitant comorbidities, low levels of physical activity, decreased lung function, and gender, have negative effects on the health status of COPD patients (7, 8). On the contrary, pharmacological interventions and physical activity have been revealed to positively affect the health status (9, 10).

A number of reliable and rational instruments have been designed to divulge the specific aspects of COPD (11, 12). These instruments have been developed over the last decades. Among these standardized tools, the Short Form 12 Health Survey Questionnaire (SF-12) has been designed to assess the overall health status. Using this instrument, it is possible to recognize the factors influencing the health status of COPD patients and then compare it with that of the general population.

To our knowledge, a few studies have investigated health-related quality of life (HRQL) in COPD patients. Janson et al. (13), based on the data from the international Burden of Obstructive Lung Disease (BOLD) study, found that subjects with COPD had lower scores on the physical and mental health components compared to people without COPD, which is a momentous finding. The Epidemiologic Study of COPD in Spain (EPI-SCAN) has highlighted the impaired health status in people with undiagnosed COPD (14). The Latin American Project for the Investigation of Obstructive Lung Disease (PLATINO) study has found that for COPD patients, the scores of HRQL in males were significantly higher than in females (8).

The major purpose of the BOLD study is to ascertain the global burden of COPD and its risk factors (15). The BOLD study includes questionnaires on the prevalence and risk factors of COPD, tobacco smoking, economic aspects, HRQL (suing SF12), and the standardized measurement of pulmonary function (11).

Previous analyses on the BOLD study's results in Iran have concentrated on the prevalence and risk factors (3, 16, 17) of COPD and tobacco smoking. (18) The main objective of this study was to gather information on HRQL from a large number of participants with and without COPD. Our secondary objective was to assess the impact of COPD on the health status of adults aged ≥40 years and to identify the determinants of the health status in people with COPD.

MATERIALS AND METHODS
Population and Sampling Strategy

The present study was based on the data obtained from the population-based BOLD study in Iran, which was published elsewhere (19). We used the same sampling protocol consistently throughout the study. The sampling frame in this study included the whole population of 31 provinces of Iran, encompassing an estimated population of nearly 78 million.

Sample Size

Regarding a design effect of 1.5, the prevalence of 50%, and a response rate of 90%, the total sample size was calculated as 1152. Participants were recruited from both sexes and among those aged between 18-39 and >40 years. The present analysis included data from 10 sites in five main provinces.

Sampling Plan

This study followed a stratified cluster sampling strategy with proportional allocations within strata. The target population comprised all noninstitutionalized inhabitants of different Iranian provinces in 2015, who were categorized into the age groups of 18–39 and over 40 years.

The stratification of the subjects was performed according to 31 provinces of Iran. Proportional to the number of households in 31 provinces, the appropriate number of clusters is weighted according to each province. The decision about the number of clusters is based on total sample size, mean household members, and logistical facilities for subject enumeration, transport, and examination.

For each cluster, a team of three members (one male and one female aged <28 years as interviewers dressed in white medical clothes and a driver) referred to the target household specified through the aforementioned random cluster selection. The process continued in a clockwise direction until the selection of ten neighbor households in a

systematic manner in the indexed household, if there was more than one person, the interviewers were advised to use the Kish method to choose the right participant(s) (20).

The interviewers attended a central training course according to the BOLD project. They were articulate, able to accurately and easily read the questions out loud, and were able to follow required instructions. Formal medical training was not necessary, and in fact, it could result in less accurate responses to the questionnaire.

Study Tool

The study tool included a questionnaire covering respiratory symptoms, health status, limitations in performing activities, and potential risk factors of COPD such as tobacco smoking, occupational risk factors, and biomass exposure. Pre- and post-bronchodilator spirometry tests were also performed to record 1- and 6-s FEVs (i.e., FEV_1 and FEV_6, respectively) and FVC.

Questionnaires

The main questionnaire included the one developed from preexisting validated questionnaires used in multinational studies (21). This questionnaire obtained information about respiratory symptoms, exposure to potential risk factors (e.g., smoking, occupational hazards, respiratory problems, comorbidities, etc.), health-care utilization, medication use, restrictions in doing activities, and health status. All participants completed the Short Form 12 (SF-12) Health Survey Questionnaire, an abbreviated version of the SF-36 (22). These 12 items explain more than 90% of the variance of physical and mental components of the SF-36. From these questions, two scores can be calculated: the physical (PCS-12) and the mental (MCS-12) component summary, using a value of 50 with a standard deviation of 10 as the reference values. Scores range from 0 to 100, with higher scores representing better HRQL. A score >60 is regarded as high HRQL, 40–60 as normal, and <40 as impaired (low) HRQL.

Spirometry

As a single most important test in this study, spirometry was performed before and after the administration of 200 mg (two puffs) of salbutamol. For quality control and methodological homogeneity, all teams were required to use the 2120 In2itive Vitalograph

Spirometer, which was chosen because it provides acceptable degrees of accuracy, robustness, portability, and ease of storage. It can be used easily in the field and where there is no electric power available. The 2120 In2itive Vitalograph Spirometer has been approved by the National Research Institute of Tuberculosis and Lung Diseases, Tehran, Iran as it meets predetermined performance criteria related to measurement reliability, suitability for field use, and ease of data access. Proper training for the interviewers and ongoing quality control were considered to perform consistent and high-quality measurements over time.

Chronic Obstructive Pulmonary Disease Definition

The definitions of COPD were as follows: 1) spirometry: post-bronchodilator FEV1/FVC ratio <70%; 2) prior medical diagnosis: an affirmative response to: "Have you ever had chronic bronchitis, emphysema, or COPD confirmed by a doctor?"; and 3) clinical definition: a positive criterion for the standard definition of chronic bronchitis. These definitions, as widely used standards, allowed comparison with other published studies without the need for the reference values (15).

Statistical Analysis

All statistical analyses were done using SPSS 21 software. The statistical significance level was considered as P<0.05. For describing continuous variables, the mean ± standard deviation (SD) was used, and qualitative variables were described using frequency and percent. The Chi-square test was used to compare COPD status among the categories of the qualitative variables of sex, education, smoking status, body mass index (BMI), and also the presence or absence of comorbidities. The student t-test was used to compare the means of age and quality of life sub-scales' scores regarding COPD status and also to compare PCS-12 and MCS-12 scores between males and females.

RESULTS

A total of 1062 subjects, including 479 (45%) males and 583 (54.7%) females were enrolled in this study. The mean age and mean BMI for the participants were 40±15.04 years and 29.01±12.25 kg/m², respectively. Out of all the

participants, 111 (10.4%) patients, including 57 (51.4%) males and 54 (48.6%) females, had clinical COPD. The overall COPD prevalence defined by the post-bronchodilator spirometry functional criteria was 5.0%. Data for demographic features and comorbid conditions according to the COPD status have been presented in Table 1. There were significant differences in the education level (P<0.001) and smoking status (P<0.001) between subjects with and without COPD. Amongst comorbid conditions, heart failure and hypertension were significantly more prevalent in patients with COPD compared with non-COPD subjects (P<0.001).

Table 1. Socio- demographic and clinical characteristics of patients

	Total	No COPD	COPD	p-value
	n = 1062	n =951	n =111	
Age (SD); year		39.28(15.05)	46.26(13.42)	<0.001
Sex				0.19
Female	583(54.9)	529(55.6)	54(48.6)	
Male	479(45.1)	422(44.4)	57(51.4)	
Educational level				<0.001
Uneducated or basic	409(38.8)	342(36.3)	67(60.4)	
High school	359(34.1)	332(35.2)	27(24.3)	
University	285(27.1)	268(28.5)	17(15.3)	
Smoking status				<0.001
Never smoker	889(84.3)	809(85.8)	80(72.1)	
Current smoker	102(9.7)	79(8.4)	23(20.7)	
Ex- smoker	63(6.0)	55(5.8)	8(7.2)	
Body mass index (kg/m²)				0.24
Normal (18.5 ≤ BMI < 25)	113(20.6)	103(21.7)	10(13.3)	
Overweight (25 ≤ BMI < 30)	244(44.4)	207(43.7)	37(49.3)	
Obese (BMI > 30)	192(35.0)	164(34.6)	28(37.3)	
Comorbid conditions:				
Heart failure	138(13.1)	106(11.2)	32(29.4)	<0.001
Blood pressure	177(16.8)	140(14.8)	37(33.6)	<0.001
Stroke	10(0.9)	10(1.1)	0(0.0)	0.61
Lung Cancer	5(0.5)	5(0.5)	0(0.0)	1.00
Diabetes	117(11.1)	98(10.4)	19(17.3)	0.37

Abbreviations: COPD, chronic obstructive pulmonary disease; SD, standard deviation

The mean total PCS-12 and MCS-12 scores were obtained 66.61±22.72 and 60.79±23.52, respectively. Both of these scores were significantly lower in COPD patients compared with people without COPD (P<0.001). In addition, SF-12-derived scores were compared according to

the COPD status. For all eight dimensions (questions), the mean scores were lower in COPD patients than non-COPD subjects (all P values < 0.05). Details have been presented in Table 2.

The PCS-12 and MCS-12 scores were categorized into three levels of low, normal, and high. At all the three levels, mean PCS and MCS scores were lower in COPD patients compared to non-COPD individuals (P<0.001, Table 2). The physical and mental domains were compared regarding the COPD status and two age groups (<40 and ≥40 years). Among those older than 40 years old, more people had low and normal PCS scores compared to the subjects under 40 years of age in both COPD and non-COPD groups. Additionally, among COPD patients, most people at all three levels of MCS scores were under the age of 40 years while in non-COPD individuals, most people at the three levels of MSC aged over 40 years (Figure 1 A-D).

Table 2. Quality of life in participants

	Without COPD	With COPD	P- value
SF-12 questionnaire	Mean (SD)	Mean (SD)	
PCS-12	68.87(21.48)	47.16(23.96)	<0.001
MCS-12	62.20(23.14)	48.75(23.45)	<0.001
SF-12 scales			
Physical functioning	77.39(34.85)	53.18(39.65)	<0.001
Role physical	80.29(27.39)	61.81(31.35)	<0.001
Bodily pain	76.29(32.73)	49.31(37.16)	<0.001
General health	45.94(24.22)	28.83(21.37)	<0.001
Vitality	49.89(33.93)	39.41(32.78)	0.002
Social functioning	73.68(31.91)	59.23(33.69)	<0.001
Emotional role	68.55(31.49)	56.59(35.20)	<0.001
Mental health	43.59(31.41)	59.90(32.73)	<0.001
Physical domain (n =1040)	Number (%)	Number (%)	
Low	103(11.1)	39(36.1)	<0.001
Normal	187(20.1)	37(34.3)	
High	642(68.9)	32(29.6)	
Mental domain (n =1040)			
Low	177(18.8)	46(41.8)	<0.001
Normal	224(23.8)	37(33.6)	
High	541(57.4)	27(24.5)	

Abbreviation: COPD, chronic obstructive pulmonary disease; Physical component summary, PCS; Mental component summary, MCS; Domain, Low: <40; normal: 40-60; high: >60

The PCS and MCS scores were also compared between males and females, showing significant differences between the two sexes in both scores (P<0.001). Regarding the COPD status, in both COPD and non-COPD individuals, the mean scores of PCS sub-scales were higher in males than females, and these differences were significant (all P values <0.05) except for the general health score in COPD patients (P=0.61) Comparing the sub-scales

of MCS, the mean scores were not significantly different between males and females with COPD. For non-COPD participants; however, the mean scores of vitality (P<0.001), social functioning (P<0.001), and emotional role (P<0.001) were higher in males than in females while the mental health score was higher in females (P=0.001, Figure 2 A-D).
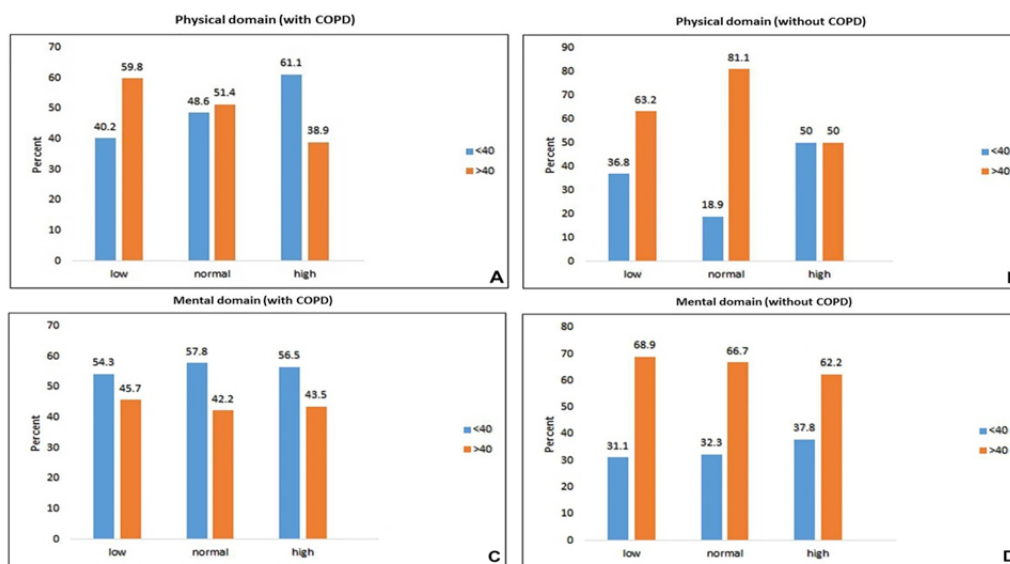

Figure 1 (A-D). Differences in the physical and mental domain according to COPD condition and age (<40, >40 years)
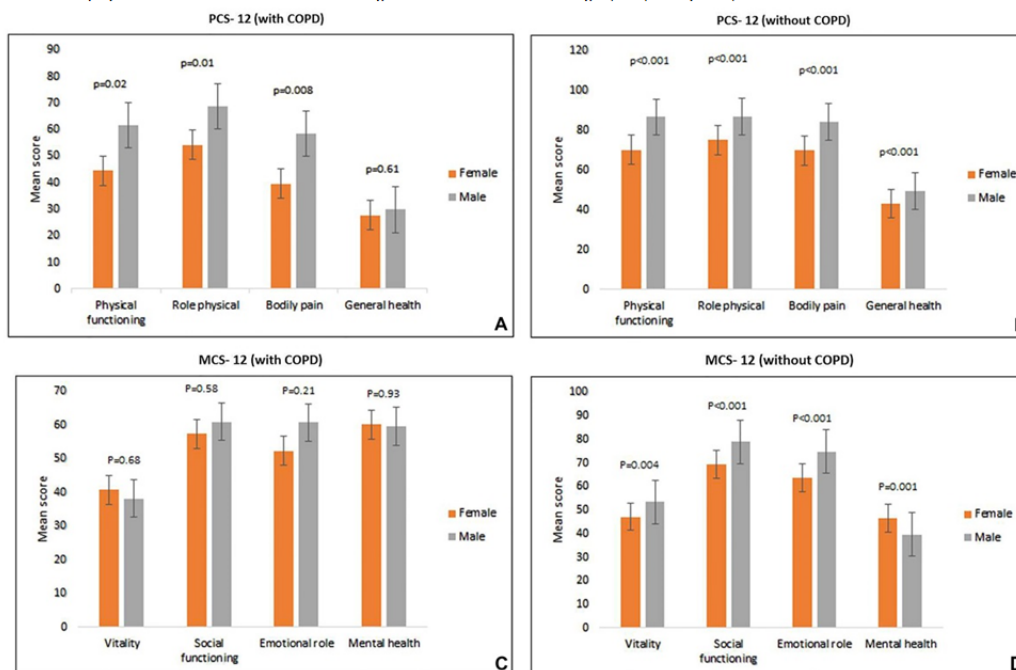

Figure 2 (A-D). Mean scores of the physical component summary (PCS-12) and the mental component summary (MCS-12) according to the sex in patients with and without COPD

DISCUSSION

One of the main goals of our study was to investigate the impact of COPD on HRQL. Participants with COPD were proved to have a decline in daily physical activity; therefore, it was essential to assess a link between COPD, as a chronic condition, and HRQL in the general population. The main finding of this study implies that COPD is an important determinant of the health status, and that physical and mental aspects of HRQL are both significantly affected by COPD. These findings are in line with those of other similar studies (8, 23, 24).

In our study, the physical domain (including general health, physical functioning, and physical role and vitality) and also the mental domain (encompassing mental health, emotional role, social functioning, and bodily pain) were poor in participants with COPD compared to individuals without COPD. Lower scores for SF-12 components in patients with COPD have been also reported by others (24, 25).

In this analysis, all participants with relevant clinical symptoms and/or a ratio of FEV1/FVC of <0.7 after bronchodilation were included in the COPD group. In other studies, respiratory symptoms were reported to be independently and negatively related to both PCS and MCS (26). In recent years, the respiratory symptoms of dyspnea, chronic cough, chronic phlegm, and wheeze have been accentuated to be associated with COPD. In a longitudinal analysis on the data from the SAPALDIA study, authors concluded that the presence of respiratory symptoms was of critical importance in predicting long-term clinical outcomes in subjects with COPD, (27) approving the hypothesis that a more severity of respiratory symptoms indicates a worse prognosis in COPD, independent of the airflow limitation level (28).

In the present study, females with COPD in terms of mean PCS had lower scores than males. Although there are only a few population-based studies on HRQL in men and women with COPD, this was a replication of the findings of similar studies (8, 26, 29).

In a study by De Torres et al. who used the Saint George's Respiratory Questionnaire (SGRQ), they revealed that women had lower scores than men at younger ages and earlier stages of the disease (30). In another study on matched men and women with COPD, the same authors reported that compared with men, women had lower scores in all SGRQ domains, suggesting that for a similar degree of physiological impairment, women experienced worse health status (31). In a study by Antonelli-Incalzi et al. who assessed health status based on the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria, females with COPD represented a worse disease-specific health status (32). The increasing trend of COPD prevalence among females seems to affect their health status greater than expected, highlighting the necessity of providing them with gender-specific care. Regarding COPD, the health care system should not ignore the importance of providing medical treatments, as well as designing programs, strategies, or policies targeting women to prevent disease exacerbation in this population.

In summary, findings from this study demonstrated the impacts of COPD, female gender, and an age older than 40 years on HRQL, especially in physical domains, as shown by the SF-12 instrument. Moreover, our results highlighted that both physical and mental dimensions of subjects with chronic respiratory diseases should be managed in clinical practice.

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