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Determinants of self-reported adherence to inhaler therapy in patients with chronic obstructive pulmonary disease

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ABSTRACT

Background: Adherence to therapy is crucial for COPD patients, since non-adherence leads to worse quality of life, increased health-care expenditure and poor clinical outcome. The aim of this study was to identify the main determinants of suboptimal adherence to therapy in a cohort of COPD patients.

Methods: General information (age, BMI, smoking, comorbidities, education, life style), lung function, exacerbations, symptoms and COPD treatment were collected. Adherence to therapy was assessed by self-reported 4-item Morisky Medication Adherence Scale (MMAS-4), and was related to anthropometric, socio/economic and health status data, obtained by questionnaires (COPD Assessment Test, CAT; Treatment Satisfaction Questionnaire, HRQoL; Katz Index of Independence of Daily Living Activities, Lawton Instrumental Activities of Daily Living Scale).

Results: 136 COPD patients were studied (age 72±8 yrs; 73.5% men; BMI 28.5±7.4 kg/m^2; FEV_1 53.5±19.0 % predicted). Nearly half of the patients (46.3%) had suboptimal adherence to therapy (score >0) and, as compared to those with optimal adherence, had higher prevalence of women and coronary artery disease, heavier smoking history and worse CCQ overall score. The results of multivariate analysis showed that the determinants of suboptimal adherence were female sex (OR 4.339, 95%CI 1.509-12.474, p=0.006), amount of pack/years smoked (OR 1.947, 95%CI 1.141-3.323, p=0.015), higher CCQ overall score (OR 3.318, 95%CI 1.050-9.892, p=0.049) and higher education (OR 2.758, 95%CI 1.083-7.022, p=0.033). Adherence was better in patients assuming triple inhaler therapy.

Conclusions: Suboptimal adherence is frequent among COPD patients, particularly in women, heavy smokers and subjects with high educational level. Interventions to improve adherence should be especially addressed to patients with these characteristics.

Key words: COPD; therapy adherence; inhaler therapy; lung function.

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Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a common, preventable and treatable disease which affects 384 million people worldwide [1] whose prevalence will increase in incoming years due to smoking habits and aging, so that in 2030 it is expected to become the fourth leading cause of death [2].

According to the Global Initiative for Obstructive Lung Disease (GOLD), the goals of COPD treatment are to prevent lung function deterioration, to alleviate symptoms, and to treat exacerbations [1]. Smoking cessation is a crucial component of therapy for patients who still smoke. Pharmacologic therapy has been shown to significantly improve lung function [3], to decrease lung hyperinflation [4], to mitigate symptoms, to reduce exacerbations and hospitalizations, and to improve exercise tolerance and health-related quality of life [5,6]. With respect to pharmacological therapy, inhaled medications have many advantages over oral medications, being able to reach quickly and directly the internal lumen of the airways, allowing low dosage and minimizing the side effects. Unfortunately, many COPD patients use inhalers incorrectly; over 50% of patients struggle to use a metered-dose inhaler properly, with consequent lack of perceived benefit and intentional discontinuation of therapy [7]. Poor medication adherence can cause negative health outcomes, such as worsening of symptoms and exercise tolerance, increased frequency and severity of exacerbations, or even death [8,9]. The most common type of non-adherence in patients with COPD is the underuse of the medicaments, mainly due to low understanding about their illness, confusion about medications in polypharmacy regimens, forgetfulness, lack of faith in treating physician [10], lack of perceived benefits from the treatment [11] and concerning about side effects from the medications [12]. A poor instruction to the correct use of an inhaler device can also be a possible cause.

The aim of the study was to identify the main determinants of low adherence to therapy in a cohort of COPD patients, focusing on patients' sociodemographic conditions (*i.e.* age, gender, marital status and educational level), disease severity, smoking habits, perceived benefit from the medication, presence of comorbidities and polypharmacy.

Methods

The study was conducted on consecutive COPD outpatients attending the Respiratory Clinic of Città della Salute e della Scienza in Turin (Italy) and outpatients' clinics in the geographic area of Turin, in the period from February to June 2017. The inclusion criteria were: documented diagnosis of COPD requiring regular treatment according to GOLD guidelines [1], no exacerbations in the last month.

All COPD patients performed a baseline post-bronchodilator spirometry according to American Thoracic Society (ATS)/European Respiratory Society (ERS) standardization [13]. Forced Expiratory Volume in 1 second (FEV_1) and Forced Vital Capacity were assessed in accordance with the latest GOLD guidelines [14]. Patients were categorized according to ABCD GOLD grouping, based on symptoms, exacerbations and lung function. Questionnaires were administrated through a face to face structured interview, performed by an investigator who was trained to understand the purpose and the meaning of the study, who was familiar with the contents and skilled with recruitment interview techniques. Prior to answering the questionnaires, each patient was explained the intention of the study and asked to sign an informed consent. Data collection included: gender, age, BMI, smoking habits, educational level, life style, current COPD pharmacological treatment, comorbidities, spirometry, history of exacerbations in the last year, self-reported physical activity (0=none, 1=light, 2=moderate-vigorous). Comorbidities were recorded on the basis of prior diagnosis and current treatment for: coronary artery disease (CAD), hypertension, diabetes, Asthma-COPD Overlap Syndrome (ACOS). All the patients were administered the following questionnaires: COPD Assessment Test (CAT) [15], COPD Clinical Questionnaire (CCQ) [16], 4-item Morisky Medication Adherence Scale (MMAS-4) [17], Abbreviated Treatment Satisfaction Questionnaire-9 (TSQM-9) [18], Health-Related Quality of Life Questionnaire (HRQoL) [19], Katz Index of Independence of Activities of Daily Living (ADL) [20] and Lawton Instrumental Activities of Daily Living Scale (IADL) [21]. The study was approved by local ethical committee (n. CS2/458) and all patients gave their informed consent to participate in the study.

COPD assessment test

CAT measures the impact of COPD on a person's life, including symptoms (cough, sputum, shortness of breath, chest tightness), confidence and activity. The total CAT score is calculated by summing the points for each of the 8 questions and ranges from zero to 40. The CAT score was classified into four groups of mild (<10), moderate (10-20), severe (21-30) and very severe (>30) [15].

COPD clinical questionnaire

CCQ consists of ten questions distributed in three domains: symptoms (dyspnoea, cough, and phlegm), mental state (feeling depressed and concerned about breathing), and functional state (limitations in different activities of daily life due to the lung disease). The questions regard the previous week and use a seven-point scale from zero to six. The total score is calculated from the sum of each item divided by ten (= number of items). The total CCQ score varies between 0 (very good health status) to 6 (extremely poor health status). The score was classified as follows: 0-2.0, good health; 2.1-4.0, fair health and 4.1-6.0, poor health [16].

4-item Morisky medication adherence scale

MMAS-4 evaluates the self-reported adherence to therapy. MMAS-4 consists of four items with a scoring scheme of "Yes" = 1 and "No" = 0. A total = 0 indicated optimal adherence.

Abbreviated treatment satisfaction questionnaire for medication

TSQM-9 is a reliable and valid instrument to assess patients' satisfaction with medication, providing scores on three scales (effectiveness, convenience and global satisfaction). TSQM scores have a range of 0 to 100, with higher scores indicating higher satisfaction [18].

Health-related quality of life questionnaire

HRQoL evaluates patient's quality of life. It consists of three modules that investigate recent pain, depression, anxiety, sleeplessness, vitality, and the cause, duration, and severity of current activity limitation an individual may have in his or her life. Module 1 (Health Days Core Module) and Module 3 (Healthy Days Symptoms Module) have a range of 0 to 100, with higher scores indicating better quality of life. Module 2 (Activity Limitations Module), scored 0 to 1, indicates absence or presence of current activity limitation by health problems [19].

Activities of daily living

The Katz Index of Independence of ADL, is the most appropriate instrument to assess functional status as a measurement of the ability to perform independently activities of daily living. This tool is typically used to detect problems in performing activities of

daily living and to plan care accordingly. The Index ranks adequacy of performance in six functions: bathing, dressing, toileting, transferring, continence, and feeding. Patients are scored yes/no for independence in each of the six functions. A score of 6 indicates full function, 4 indicates moderate impairment, and 2 or less indicates severe functional impairment [20].

Instrumental activities of daily living scale

IADL is an appropriate instrument to assess independent living skills. These skills, which include telephoning, shopping, food preparation, housekeeping, laundering, use of transportation, use of medicine and financial behaviour, are considered more complex than the basic activities of daily living explored by the Katz Index of ADL. This instrument is most useful for identifying how a person is functioning in that moment, and for detecting improvement or deterioration over time. There are eight domains of function measured with the IADL scale. Women are scored on all 8 areas of function; historically, for men, the areas of food preparation, housekeeping, and laundering are excluded. Patients are scored according to their highest level of functioning in-each-category, with a range from 0 (low function, dependent) to 8 (high function, independent) for women, and from 0 to 5 for men [21].

Statistical analyses

Since this was a descriptive study, no formal statistical hypotheses were set and the sample size corresponded to the number of patients who attended the clinics in the study period. Continuous variables were expressed as mean and standard deviation (SD), while categorical variables were expressed as frequencies and percentages. When appropriate, Chi square, Fisher's exact test, and one-way ANOVA test were used to test for associations.

A univariate analysis was carried out to identify associations with adherence to COPD medications. According to their responses to the MMAS-4, patients were categorized into two groups: those with optimal adherence (negative response to all items) or those with suboptimal adherence (any positive response). Odds ratios (ORs),95% Confidence Intervals (96% CIs) and interquartile ranges were reported.

A final multivariate model was developed based on clinical discussion and statistical selection procedures. Model selection was performed using an automatic approach based on the Akaike Information Criteria (AIC) method [22]. Given the large number of covariates, a genetic algorithm was employed to explore the candidate set of models. Model goodness of fit was computed with reference to the Brier score (the closer to 0, the better) and the Somers' Dxy Index, indicating the capability of the model to discriminate. To deal with the optimism in model accuracy evaluations induced by the use of the same data source for training and testing purposes, goodness of fit indexes was computed using bootstrap [23].

The significance level was set at $p<0.05$. All statistical analyses were performed using R ver. 3.5.0.

Results

General and clinical characteristics of COPD patients

A cohort of 136 COPD patients (73.5% men and 26.5% women) was studied. General and clinical characteristics of all patients are reported in Table 1. According to GOLD ABCD classification, 30 patients (22.1%) were in GOLD A, 54 (39.3%) in GOLD B, 7 (5.7%) in GOLD C and 45 (32.9%) in GOLD D. As expected, spirometry was more impaired in group C and D compared to A and B (Table 1).

Regarding COPD therapy, 106 patients (77.9%) assumed LAMA [16 (11.8%) as monotherapy], 83 patients (61%) assumed ICS/LABA [71 (52%) associated with LAMA], 33 patients (24%) assumed the combination LABA/LAMA [14 (10%) as a single device], 3 patients (2%) assumed LABA alone. Most of the 71 patients treated with combined ICS/LAMA/LABA were in GOLD group C and D. The prevalence of patients on oxygen therapy was significantly higher in GOLD D patients (73.3%), compared to GOLD A (36.7%), B (42.6%) and C (28.6%). Physical activity was significantly reduced in patients with GOLD B and D, *i.e.* those with more severe symptoms. Self-reported adherence to inhaler therapy was optimal in 73 out of 136 COPD patients (53.7%), and suboptimal in 63 (46.3), with the highest prevalence of optimally adherent patients among GOLD C and the lowest among GOLD D patients (Table 1). Fifty-one patients (37.5%) referred no exacerbation in the last year, 41 (30.1%) had 1 exacerbation, 36 (26.5%) had 2 exacerbations, 4 (2.9%) had 3 exacerbations and 4 (2.9%) had 4 exacerbations. As expected, the number of annual exacerbations was higher in group C and D as compared to A and B ($p<0.001$). Most patients (91.2%) had at least 1 comorbidity and most (89.7%) received multiple pharmacological treatments (Table 1). Among comorbidities, the most frequent was hypertension (78.6%), followed by diabetes (20%), CAD (12.9%) and ACOS (8.6%).

Determinants of adherence to COPD therapy - Univariate analyses

The characteristics associated with suboptimal adherence to COPD therapy are reported in Supplemental Table S1. All collected variables were evaluated for their potential association with adherence to medical therapy by performing a univariate analysis (Table 2). Adherence was inversely related to cigarette pack/years, (OR 1.55, 95% CI 1.01-2.40, $p=0.048$), and to CCQ overall score (OR 2.03, 95% CI 1.016-4.27, $p=0.049$), showing a trend toward significance with respect to gender, presence of CAD, GOLD stages, educational level, CAT score, CCQ symptoms and CCQ functional state. No significant association was observed between adherence and the following variables: age, marital status, physical activity, CCQ mental state, TSQM score (effectiveness, convenience and global satisfaction), HRQoL, oxygen therapy, presence of at least 1 comorbidity, polypharmacy, ADL and IADL score. The prevalence of optimal adherence was significantly higher in patients treated with multiple inhalation therapy, *i.e.* combined ICS/LAMA/LABA (64.8% *versus* 41.5%, $p=0.018$). As regards the device, the most frequent was Respimat, used by 94 pts, followed by Spray (32), Diskus (31), Breezhaler (27), Ellipta (24) and Genuair (10). At the time the investigation was done the association of 3 drugs in a single inhaler was not yet available. No significant influence of the type of device on adherence was found.

Determinants of adherence to COPD therapy - Multivariate analyses

In Table 3, the results of the multivariate analysis are given. Cigarette pack/years, CCQ overall score, CCQ (mental state and overall score), gender, presence of CAD, GOLD stages and educational level entered into the model, explaining 25.6% of the variance of adherence (Nagelkerke R^2 =0.256, indicating a good fit). In particular, the risk for suboptimal adherence was higher in females (OR 4.339, 95% CI 1.509-12.474, $p=0.006$), and increased proportionally to each pack/year unit (OR 1.947, 95% CI 1.141-3.323, $p=0.015$). The risk was higher in GOLD A vs GOLD B (OR 4.090, 95% CI 1.121-14.927, $p=0.033$), in patients with higher CCQ overall score (OR 3.318, 95% CI 1.050-9.892, $p=0.049$) and in those with higher educational level (OR 2.758, 95% CI 1.083-7.022, $p=0.033$).

Discussion

The main finding in our cohort of COPD patients is that adherence to therapy was suboptimal in nearly half of the patients. The major factors adversely affecting adherence were: female gender, amount of smoking (pack/year), mild COPD stage with less symptoms, high educational level and overall worse health status. Non-adherence to medical therapies is a growing issue, particularly in COPD, so that the World Health Organization (WHO), defined it as "a new pharmacological problem" [7]. Adherence to medical therapy is often suboptimal when patients are on long-term pharmacotherapy using repeat prescriptions. A study published by the WHO estimated a 50% or less adherence in COPD patients on long-term pharmacotherapy [10] supporting our finding. Detecting adherence is not easy and several approaches have been proposed, such as self-reported questionnaires, pharmacy refill methods and electronic monitoring (smart-inhaler). Electronic audio recording devices, compared to other approaches, can objectively quantify adherence to inhaler therapy [24], however their use involves a knowledge of technology that may be difficult to acquire by old COPD patients. In the clinical setting, a helpful approach is to use self-reported questionnaires because they are easy to use, fast and inexpensive. In the present study, adherence to COPD therapy was investigated through the administration of the MMAS-4, a self-reported validated questionnaire which can be easily integrated into the medical visit [17]. Other questionnaires have been administered in order to explore symptoms, health status, patients' satisfaction with medication, quality of life and functional status and to evaluate their relationship with adherence. Our analysis showed that the determinants of suboptimal adherence to COPD therapy were mostly related to sociodemographic/socioeconomic status, *i.e.* gender, smoking habits, health status and educational level.

Table 1. Characteristics of the sample stratified by ABCD GOLD grouping.

	A	B	C	D	Overall	*p*
n	30	54	7	45	136	
Age, mean, (SD)	71 (8)	72 (9)	70 (5)	72 (8)	72 (8)	0.898
Gender, male (%)	28 (93.3)	38 (70.4)	5 (71.4)	29 (64.4)	100 (73.5)	0.041
Married, yes (%)	21 (70.0)	37 (68.5)	5 (71.4)	33 (73.3)	96 (70.6)	0.963
BMI, mean, (SD)	27.7 (4.6)	30.8 (9.5)	26.4 (1.8)	26.5 (5.8)	28.5 (7.4)	0.021
Smoking, n (%)						
Current smokers	8 (25.8)	11 (20.0)	1 (12.5)	12 (26.1)	32 (22.9)	
Ex-smokers	23 (74.2)	43 (78.2)	6 (75.0)	32 (69.6)	104 (74.3)	
Never smokers	0 (0)	1 (1.8)	1 (12.5)	2 (4.3)	4 (2.9)	
Pack/year, mean, (SD)	55.4 (51.7)	58.3 (39.9)	42.6 (33.1)	60.3 (33.4)	57.5 (40.4)	0.741
Education, low (%)	24 80.0)	33 (61.1)	7 (100.0)	31 (68.9)	95 (69.9)	0.091
Presence of at least 1 comorbidity, yes (%)	30 (100.0)	48 (88.9)	6 (85.7)	40 (88.9)	124 (91.2)	0.283
Presence of CAD, yes (%)	2 (6.7)	6 (11.1)	0 (0.0)	10 (22.2)	18 (13.2)	0.134
Polypharmacy, yes (%)	29 (96.7)	46 (85.2)	6 (85.7)	41 (91.1)	122 (89.7)	0.394
ICS+LAMA+LABA	9 (30)	27 (50)	6 (85.7)	29 (64.4)	71 (52.2)	0.008
Exacerbations, mean, (SD)	0.35 (0.49)	0.42 (0.49)	1.88 (0.64)	2.11 (0.74)	1.04 (1.01)	<0.001
FEV_1, mean, (SD)	1.68 (0.75)	1.43 (0.55)	1.14 (0.17)	1.13 (0.45)	1.38 (0.59)	0.001
FEV_1 perc, mean, (SD)	62.8 (25.6)	54.8 (16.6)	46.3 (11.6)	47.0 (14.3)	53.5 (19.0)	0.004
FEV_1/FVC, mean, (SD)	56.6 (12.2)	55.13 (17.07)	45.83 (11.65)	47.20 (13.81)	52.01 (15.74)	0.081
Inhaler adherence (%)						0.054
Optimal	17 (56.7)	32 (59.3)	6 (85.7)	18 (40.0)	73 (53.7)	
Suboptimal	13 (36.7)	22 (37.0)	1 (14.3)	27 (40.0)	63 (46.3)	
Physical activity (%)						0.018
None	15 (50.0)	43 (79.6)	3 (42.9)	36 (80.0)	97 (71.3)	
Light	13 (3.3)	10 (18.5)	4 (57.1)	9 (20.0)	36 (26.5)	
Moderate/vigorous	2 (6.7)	1 (1.9)	0 (0.0)	0 (0.0)	3 (2.2)	
CAT, mean, (SD)	4.80 (3.18)	18.61 (5.49)	6.14 (1.77)	20.67 (7.17)	15.60 (8.58)	<0.001
CCQ						
Overall score, mean, (SD)	1.54 (0.62)	2.80 (0.91)	1.56 (0.80)	3.32 (0.98)	2.63 (1.12)	<0.001
Symptom, mean, (SD)	1.81 (0.71)	2.67 (0.94)	1.77 (0.88)	3.09 (1.22)	2.57 (1.11)	<0.001
Functional state, mean, (SD)	1.49 (0.82)	3.12 (1.26)	1.67 (0.81)	3.80 (1.18)	2.91 (1.43)	<0.001
Mental state, mean, (SD)	1.15 (1.10)	2.32 (1.87)	1.07 (0.93)	2.70 (1.65)	2.12 (1.72)	<0.001
TSQM-9						
Effectiveness, mean, (SD)	74.40 (13.61)	68.49 (15.14)	71.43 (10.34)	65.93 (14.39)	69.10 (14.56)	0.093
Convenience, mean, (SD)	86.20 (18.69)	81.72 (17.01)	89.86 (7.40)	78.51 (15.63)	82.07 (16.79)	0.146
Global satisfaction, mean, (SD)	76.00 (10.73)	72.94 (14.07)	78.00 (10.38)	68.66 (14.23)	72.46 (13.51)	0.074
ADL score, mean, (SD)	5.93 (0.37)	5.81 (0.75)	6.00 (0.00)	5.51 (1.32)	5.75 (0.92)	0.175
IADL, mean, (SD)	4.97 (1.25)	5.13 (1.37)	5.86 (1.46)	4.78 (1.76)	5.01 (1.50)	0.298

Data presented as mean ± standard deviation or as count (%); BMI, body mass index; CAD, coronary artery disease; FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity; CAT, COPD assessment test; CCQ, COPD clinical questionnaire; TSQM, abbreviated treatment satisfaction questionnaire-9; ADL, activities of daily living; IADL, instrumental activities of daily living scale.

Patients' adherence to COPD therapy was lower among women compared to men. This is in good agreement with other studies, which have shown that women are more likely to intentionally interrupt therapy [25,26]. Given the higher prevalence of depression among women with COPD reported in previous papers [25-28], we speculate that depression played a role in the lower adherence in women, found in our study. Another relevant factor related to suboptimal adherence to therapy in our COPD patients was heavy smoking, in agreement with previous findings [25,29]. Smokers are per se non-adherent to the medical advice of stopping smoking, and thus are expected to be less adherent to the treatment advice. Actually, smoking, particularly current smoking seems to have a negative impact on patient's perceptions of illness and therapy, which are critical to adherence [25,29].

Symptoms were also relevant to adherence but only in mild stages of the disease. Actually, patients in GOLD A with fewer symptoms were at higher risk of suboptimal adherence than patients in GOLD B. Likely, the poor perception of the disease

Table 2. Univariate ORs and 95%CI for suboptimal versus optimal adherence to COPD therapy. For continuous variables, ORs represent the increase or reduction of risk for a difference reported in column Diff (which also corresponds to the interquartile range).

	Diff	OR	95%CI		*p*
Age	11	0.980	0.619	1.552	0.932
Gender - female:male		1.933	0.893	4.186	0.094
Married - no:yes		1.421	0.678	2.979	0.352
Pack/year	45	1.553	1.005	2.401	0.048
Education - high:low		2.027	0.964	4.265	0.063
Presence of at least 1 comorbidity - no:yes		0.813	0.245	2.700	0.735
Presence of CAD – yes:no		2.627	0.924	7.474	0.07
Polypharmacy - no:yes		1.624	0.532	4.963	0.395
GOLD - A:B		1.112	0.451	2.745	0.817
GOLD - C:B		0.242	0.027	2.156	0.204
GOLD - D:B		2.182	0.974	4.887	0.058
Physical activity - light vs none		1.078	0.501	2.320	0.848
Physical activity - moderate/vigorous *vs* none		2.409	0.211	27.461	0.479
CAT 13	1.559	0.921	2.636	0.098	
CCQ					
Overall score	1.6	2.030	1.016	4.272	0.049
Symptom	1.2	1.404	0.963	2.048	0.078
Functional state	2.2	1.600	0.940	2.724	0.083
Mental state	2.5	1.360	0.828	2.233	0.225
TSQM-9					
Effectiveness	18.38	0.730	0.471	1.130	0.158
Convenience	29	0.794	0.441	1.429	0.442
Global satisfaction	17	0.764	0.495	1.180	0.225
ADL score	6	1.171	0.129	10.654	0.889
ADL score	0.25	1.035	0.976	1.097	0.249

CAD, coronary artery disease; CAT, COPD assessment test; CCQ, COPD clinical questionnaire; TSQM, abbreviated treatment satisfaction questionnaire-9; ADL, activities of daily living; IADL, instrumental activities of daily living scale.

Table 3. Multivariate ORs for suboptimal *versus* optimal adherence to COPD therapy.

	Diff	OR	95%CI		*p*
Gender - female:male		4.339	1.509	12.474	0.006
Pack/year	46.5	1.947	1.141	3.323	0.015
GOLD - A:B		4.090	1.121	14.927	0.033
GOLD - C:B		0.859	0.079	9.381	0.901
GOLD - D:B		1.604	0.595	4.328	0.351
CCQ - mental state	2.5	0.551	0.214	1.415	0.215
CCQ - overall score	1.6	3.318	1.050	9.892	0.049
CAD - yes:no		2.609	0.671	10.139	0.166
Education - high:low		2.758	1.083	7.022	0.033

Scaled Brier score = 0.199 (range between 0 and 1 with 0 indicating a perfect model); Somers DXY = 0.596 (range between 0 and 1, the further from zero the better); Nagelkerke R2= 0.256 (0.2-0.4 indicating good fit); CAD, coronary artery disease; CAT, COPD assessment test; CCQ, COPD clinical questionnaire; TSQM, abbreviated treatment satisfaction questionnaire-9; ADL, activities of daily living; IADL, instrumental activities of daily living scale.

(*i.e.*, lack of clinical symptoms) may induce some patients to take therapy episodically, rather than daily [30]. A statistical significance was found for health status (CCQ overall score) as determinant of suboptimal adherence. These results are consistent with those reported in other populations showing that patients with suboptimal adherence have worse health status, as compared with those with optimal adherence [31]. This supports the role of pharmacologic COPD therapy in controlling symptoms and in improving exercise tolerance.

An interesting finding of this study is that patients with higher educational level had worse adherence to COPD therapy, indicating that scholar education does not imply better awareness of the disease. A plausible explanation is that patients with lower educational level had more trust in physicians' advice. Although the influence of COPD treatment on adherence was not a major issue of this study, we found that optimal adherence was significantly more prevalent among patients treated with combined ICS/LAMA/LABA, who had more severe disease (group C and D). Previous evidence suggests that triple therapy is the most effective treatment in moderate/severe symptomatic patients with COPD at risk of exacerbations [32]. Noteworthy, at the time of the study a single device providing the three medications was not yet available. However, no significant influence of the type of device on adherence was found.

Strengths and limitations

A key strength of our study consists in the evaluation of sociodemographic factors and of the subjective perception of health status as determinants of adherence to therapy in patients with COPD, a topic poorly studied so far. These determinants were assessed by means of well-validated, fast and inexpensive self-reported questionnaires, which can be easily integrated into the medical visit.

The major limitation of this study is the small number of patients.

Another limitation is that the data obtained by self-reported questionnaires were not supported by objective measures of adherence, such as pharmacy refill methods and electronic monitoring. However, the usefulness of the Morisky Medication Adherence Scale [17] has been validated by clinicians and health professionals for different chronic conditions across several countries, by comparing the results with other measures of adherence such as prescription claims records, serum drug concentrations, or pharmacologic effects [33,34]. Finally, treatment satisfaction for medication derived from TSQM questionnaire was not adjusted for adequacy of the drug intake (*i.e.*, errors in inhaler technique).

Conclusions

In conclusion, suboptimal adherence to therapy is frequent among COPD patients, and is favoured by female gender, smoking habits, and high educational level. Interventions to improve adherence should be tailored to the specific modifiable factors, such as cigarette smoking, especially addressed to women and subjects with higher educational level, through periodic counselling and medical advice.

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