

The modified Medical Research Council dyspnoea scale is a good indicator of health-related quality of life in patients with chronic obstructive pulmonary disease

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INTRODUCTION Health-related quality of life (HRQoL) is an important patient-centred outcome in chronic obstructive pulmonary disease (COPD). The aim of the current study is to compare the discriminative capacity of the modified Medical Research Council (mMRC) dyspnoea scale and the Global Initiative for Chronic Obstructive Lung Disease (GOLD) spirometric classification of COPD on HRQoL, as well as determine other factors that are simple and determinative of HRQoL.

METHODS In this cross-sectional observational study, a total of 328 patients with COPD were enrolled from the pulmonology outpatient clinic. HRQoL was measured using the St George's Respiratory Questionnaire (SGRQ) and the World Health Organization Quality of Life-BREF (WHOQOL-BREF). HRQoL scores were compared between the four GOLD stages and the five grades of the mMRC scale. Significant differences were determined using analysis of variance with Scheffe post-hoc test. Multiple linear regression was applied to explore the major determinants of HRQoL and exclude confounding factors.

RESULTS Significant differences were found in many more domains of the two questionnaires between mMRC grades than between GOLD stages. In the multiple linear regression model, the mMRC scale was the only factor that remained determinative of all the domains of SGRQ and WHOQOL-BREF. Patients with chronic productive cough, sleep disorders and frequent exacerbations had poorer HRQoL, as reflected by higher scores in SGRQ or lower scores in WHOQOL-BREF.

CONCLUSION The mMRC dyspnoea scale is a concise and practical tool to assess the HRQoL of patients with COPD in daily clinical practice.

Keywords: chronic obstructive pulmonary disease, Global Initiative for Chronic Obstructive Lung Disease, health-related quality of life, Medical Research Council dyspnoea scale, spirometry

INTRODUCTION

Chronic obstructive pulmonary disease (COPD), a chronic respiratory disease with high prevalence worldwide, is becoming a leading cause of mortality and morbidity.⁽¹⁾ Health-related quality of life (HRQoL) is a patient-reported outcome that is receiving increasing recognition regarding its use in patients with COPD.^(2,3) HRQoL offers an integral measurement of overall health status and the impact of disease on patients. In COPD clinical trials, HRQoL is frequently included as an endpoint to evaluate the effects of pharmacological and non-pharmacological treatments.⁽⁴⁻⁷⁾ In addition, HRQoL also predicts mortality and hospitalisation in patients with COPD.^(2,8,9) HRQoL is generally measured using validated questionnaires, either disease-specific or generic, and a comprehensive evaluation of HRQoL should enclose both disease-specific and generic instruments.⁽¹⁰⁾ However, since the application of HRQoL questionnaires in daily clinical practice is often restricted due to time constraints, a simple surrogate marker that is discriminative of HRQoL would be helpful.

A spirometric classification of COPD (Stages 1 to 4), based on forced expiratory volume in 1 second (FEV₁) percentage predicted, had been advocated by the Global Initiative for Chronic Obstructive Lung Disease (GOLD). However, the cutoff points recommended are used for the purpose of simplicity and have not been clinically validated.⁽¹⁾ Furthermore, FEV₁ is often poorly correlated with patient-centred outcomes such as HRQoL.⁽¹¹⁻¹³⁾

The modified Medical Research Council (mMRC) scale is a five-level rating scale based on the patient's perception of dyspnoea in daily activities.⁽¹⁴⁾ For patients with COPD, it is a simple and valid tool to assess disability,⁽¹⁵⁾ and has been reported to be more relevant to patients' health and psychological status than FEV₁.⁽¹⁶⁾ To the best of our knowledge, since the GOLD spirometric classification was published, no study has reported direct comparisons between these two indices to categorise patients with COPD with regard to HRQoL.

In this cross-sectional observational study, we compared the discriminative capacity of the GOLD spirometric classification

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and the mMRC dyspnoea scale with regard to HRQoL. The St George's Respiratory Questionnaire (SGRQ), a disease-specific questionnaire, and the World Health Organization Quality of Life-BREF (WHOQOL-BREF), a generic questionnaire, were used to measure HRQoL.

METHODS

A total of 328 patients were consecutively recruited from the pulmonology outpatient clinic of a teaching hospital in southern Taiwan between September 2007 and December 2009. The criteria for participation included an age of 40 years or more, and a diagnosis of COPD based on medical history and a post-bronchodilator FEV₁ to forced vital capacity (FVC) ratio (FEV₁/FVC) of < 0.7. Patients with a history of asthma, active pulmonary tuberculosis, lung cancer or pulmonary resection were excluded. All of the recruited patients were clinically stable for at least four weeks prior to recruitment, without the need for a change in treatment regimens. The protocol was approved by the local ethics committee and all participating patients signed an informed consent form.

Patient demographic data such as age, gender, body mass index (BMI), level of education and smoking status were recorded. Any history of hypertension, diabetes, cardiovascular disease and sleep disorders, which are the most commonly reported comorbid conditions in both COPD patients⁽¹⁷⁻¹⁹⁾ and the general population, was also collected based on the International Classification of Diseases, Ninth Revision, codes in the local hospital information system. Hypertension, diabetes mellitus and sleep disorders include codes 250, 401–405 and 7805, respectively. Cardiovascular disease, denoted by a history of myocardial infarction, angina pectoris, ischaemic heart disease and heart failure, was coded as 410–414 and 428. Each patient was also asked to report on any symptoms experienced that were associated with chronic bronchitis (e.g. cough with sputum expectoration for at least three months per year over a period of two consecutive years). The number of exacerbations that occurred in the patients within the previous year was also acquired. The patients were categorised by GOLD spirometric classification (with cutoff points of 80%, 50% and 30% FEV₁ percentage predicted) and mMRC grades for statistical analysis.

Spirometry measurements were carried out according to the American Thoracic Society/European Respiratory Society guidelines,⁽²⁰⁾ on the same day the quality of life questionnaires were collected, and using the HI701 spirometer (CHEST MI Inc, Tokyo, Japan). Post-bronchodilator tests were performed 15 minutes after the administration of 400 µg of salbutamol via a metred-dose inhaler with a spacer. Reference FEV₁ and FVC values were calculated as previously described.⁽²¹⁾

The degree of dyspnoea was rated as previously described in the Mahler and Wells study⁽¹⁴⁾ – Grade 0: breathless with strenuous exercise; Grade 1: short of breath when hurrying on level ground or walking up a slight hill; Grade 2: walked slower

than people of the same age on level ground, and experienced breathlessness or the need to stop to breathe when walking on level ground at their own pace; Grade 3: stop to breathe after walking about 100 yards, or after a few minutes on level ground; and Grade 4: too breathless to leave the house, or breathless when dressing or undressing. The degree of dyspnoea experienced by the patients was inquired immediately after the acquisition of patients' demographic data.

SGRQ is a disease-specific assessment tool designed to measure HRQoL in patients with asthma and COPD.⁽²²⁾ The questionnaire consists of 50 items that are classified into three domains that measure symptoms, activity limitations and the psychosocial impacts related to the disease. Each domain was scored using a preset formula that individually weighs each option. A total score, which summarises the above three domains, was also produced. Scores can range from 0 to 100, with higher scores indicating poorer health status. We utilised a translated and validated version (Taiwan/Mandarin Chinese version)⁽²³⁾ of SGRQ. WHOQOL is an international cross-culturally comparable quality of life assessment instrument developed by the World Health Organization.⁽²⁴⁾ The WHOQOL-BREF is the abbreviated version of WHOQOL; it contains 26 items that belong to four domains (Physical, Psychological, Social and Environmental). Each item is derived from five options which represent scores ranging from 1 to 5; the three negatively-worded options were positively recoded during calculation. The mean score of each domain was transformed to a 0–100 scale, with higher scores representing an improved quality of life. The Taiwan version of WHOQOL-BREF,⁽²⁵⁾ which was validated in Taiwan, was used in the present study.

Continuous variables were expressed as means and standard deviations, while categorical variables were expressed as numbers and percentages. The HRQoL scores of each domain were compared between the four stages of GOLD and the five grades of mMRC scale using analysis of variance (ANOVA). Scheffe post-hoc test was used for pairwise comparison, and multiple linear regression analysis was applied to explore the major determinants of HRQoL and exclude confounding factors. The impact of each parameter was expressed using an 'estimate' that represented the regression coefficient in continuous variables and the excess amount based on the controlled level in categorical variables. Statistical significance was established at $p < 0.05$. Data were analysed using the Statistical Package for the Social Sciences version 15 (SPSS Inc, Chicago, Illinois, USA).

RESULTS

The baseline characteristics of the 328 enrolled patients are summarised in Table I. The mean patient age was 72.1 years (range 43–99 years) and most patients were male (89%). Only 21% of the participants had a junior high school education or above. About a third (38.4%) of the patients were smokers

Table I. Baseline characteristics of patients (n = 328).

Parameter (units)	No. (%)	Parameter (units)	No. (%)
Age* (yrs)	72.1 (9.2)	Exacerbation frequency* [†]	0.97 (1.4)
Male gender	292 (89.0)	Chronic productive cough	146 (44.5)
BMI* (kg/m ²)	23.1 (4.0)	FEV ₁ /FVC percentage*	56.8 (9.3)
Education		FEV ₁ percentage predicted*	51.5 (17.4)
Elementary school and below	260 (79.3)	GOLD spirometric staging	
Junior and senior high school	52 (15.9)	GOLD 1	23 (7.0)
Junior college and above	16 (4.9)	GOLD 2	141 (43.0)
Smoking		GOLD 3	129 (39.3)
Never	39 (11.9)	GOLD 4	35 (10.7)
Ex-smoker	163 (49.7)	mMRC dyspnoea scale	
Current smoker	126 (38.4)	Grade 0	18 (5.5)
Hypertension	101 (30.8)	Grade 1	141 (43.0)
Diabetes mellitus	39 (11.9)	Grade 2	68 (20.7)
Cardiovascular disease	52 (15.9)	Grade 3	85 (25.9)
Sleep disorder	47 (14.3)	Grade 4	16 (4.9)

*Continuous variables are expressed as mean (standard deviation). [†]The number of exacerbations in the previous year.

BMI: body mass index; FEV₁/FVC: forced expiratory volume in one second to forced vital capacity ratio; GOLD: Global Initiative for Chronic Obstructive Lung Disease; mMRC: modified Medical Research Council

Table II. Scores of each domain of SGRQ and WHOQOL-BREF, stratified according to the GOLD spirometric staging.

Index	GOLD stages [Mean (SD)]				p-value
	Stage 1 (n = 23)	Stage 2 (n = 141)	Stage 3 (n = 129)	Stage 4 (n = 35)	
SGRQ					
Symptom	46.4 (19.4)	45.3 (17.9)	51.7 (18.5)	61.5 (20.3)	< 0.001
Activity	51.8 (22.8)	50.4 (20.8)	64.4 (20.7)	72.6 (22.2)	< 0.001
Impact	43.7 (17.4)	41.3 (17.3)	48.4 (15.8)	54.1 (15.6)	< 0.001
Total	46.7 (16.8)	44.8 (16.5)	54.0 (15.0)	61.0 (16.0)	< 0.001
WHOQOL-BREF					
Physical	47.5 (18.4)	46.5 (18.5)	43.9 (18.9)	33.2 (17.7)	0.002
Psychological	54.3 (20.5)	58.8 (19.3)	58.1 (19.2)	50.1 (19.2)	0.097
Social	64.1 (15.2)	64.3 (17.7)	64.2 (16.3)	60.0 (18.0)	0.588
Environmental	73.3 (14.4)	71.6 (15.7)	71.2 (14.1)	68.6 (12.7)	0.643

Significant differences between GOLD stages were found as follows: SGRQ Symptom: 1-4, 2-4; SGRQ Activity and Total: 1-4, 2-3, 2-4; SGRQ Impact: 2-3, 2-4; and in WHOQOL-BREF Physical: 1-4, 2-4, 3-4.

SD: standard deviation; SGRQ: St George's Respiratory Questionnaire; WHOQOL-BREF: World Health Organization Quality of Life (abbreviated version)

at the time the study was conducted, and about half (44.5%) of the patients suffered from chronic productive cough. The patients experienced an average of about one exacerbation within the previous year. The prevalence of hypertension, diabetes mellitus, cardiovascular disease and sleep disorders was 30.8%, 11.9%, 15.9% and 14.3%, respectively. The mean FEV₁/FVC percentage was 56.8% and mean FEV₁ percentage was 51.5%. When stratified according to GOLD stages 1 to 4, the proportion of patients was 7.0%, 43.0%, 39.3% and 10.7%, respectively. When stratified according to the mMRC scale grades 0 to 4, the proportion of patients was 5.5%, 43.0%, 20.7%, 25.9% and 4.9%, respectively.

The mean domain scores stratified according to GOLD stages are shown in Table II. Increasing GOLD stage was associated with lower HRQoL, reflected by the increasing SGRQ and decreasing WHOQOL-BREF domain scores. Significantly different scores between GOLD stages were found in all domains of SGRQ, but only in the Physical domain of WHOQOL-BREF. Post-hoc analysis showed that significant differences between GOLD stages were found mostly in SGRQ. There was significant overlap of the scores across GOLD

stages, and the major changes between consecutive stages were found to occur between GOLD stages 2 and 3.

The mean domain scores stratified according to mMRC grades are presented in Table III. An increase in mMRC grade was accompanied by a deterioration in HRQoL, evidenced by increased SGRQ and reduced WHOQOL-BREF domain scores. All domain scores differed significantly among mMRC grades, implying that the mMRC scale had a better discriminative capacity than GOLD staging in HRQoL. Post-hoc analysis showed significant differences in more domains of the two questionnaires among mMRC grades than among GOLD stages. There was much less overlap of the scores across mMRC grades, and most of the changes occurred evenly throughout all the grades.

Table IV summarises the results of the multiple linear regression analysis that evaluated each parameter's impact on SGRQ. The mMRC scale showed a strong discriminative capability in each of the domains of SGRQ ($p < 0.001$), except for mMRC grade 1 in the Symptom domain [$p = 0.008$]. Patients who experienced chronic productive cough and a higher number of exacerbations had poorer HRQoL, as reflected by the higher domain scores.

Table III. Scores of each domain of SGRQ and WHOQOL-BREF, stratified according to the grades of the mMRC scale.

Index	mMRC grades [Mean (SD)]					p-value
	Grade 0 (n = 18)	Grade 1 (n = 141)	Grade 2 (n = 68)	Grade 3 (n = 85)	Grade 4 (n = 16)	
SGRQ						
Symptom	32.4 (17.6)	44.9 (17.9)	52.0 (19.2)	57.4 (17.0)	59.3 (17.0)	< 0.001
Activity	24.0 (8.0)	46.8 (15.3)	62.8 (19.5)	75.6 (15.9)	88.4 (15.8)	< 0.001
Impact	23.7 (10.6)	38.7 (14.4)	49.2 (15.0)	55.3 (14.0)	65.0 (12.2)	< 0.001
Total	25.3 (8.3)	42.2 (12.8)	53.9 (14.3)	62.0 (12.2)	71.3 (11.4)	< 0.001
WHOQOL-BREF						
Physical	63.7 (12.4)	50.6 (15.8)	40.6 (17.8)	35.1 (18.7)	27.2 (15.8)	< 0.001
Psychological	78.4 (15.0)	59.7 (17.5)	54.4 (21.0)	52.9 (18.7)	47.1 (18.8)	< 0.001
Social	75.0 (12.9)	66.6 (17.2)	60.5 (17.4)	61.0 (16.0)	55.5 (13.7)	< 0.001
Environmental	78.7 (14.3)	72.8 (14.3)	70.5 (14.8)	69.0 (14.2)	64.3 (16.4)	0.017

Significant differences among mMRC grades were found as follows: SGRQ Symptom: 0-2, 0-3, 0-4, 1-3; SGRQ Activity and Total: all except 3-4; SGRQ Impact: all except 2-3 and 3-4; WHOQOL-BREF Physical: all except 0-1, 2-3, 2-4, 3-4; WHOQOL-BREF Psychological: 0-1, 0-2, 0-3, 0-4; and WHOQOL-BREF Social: 0-2, 0-3, 0-4.

mMRC: modified Medical Research Council; SD: standard deviation; SGRQ: St George's Respiratory Questionnaire; WHOQOL-BREF: World Health Organization Quality of Life (abbreviated version)

Table IV. Multiple linear regression to assess each parameter's impact on HRQoL as measured by SGRQ.

Parameter	Symptom			Activity			Impact			Total		
	Estimate	SE	p-value	Estimate	SE	p-value	Estimate	SE	p-value	Estimate	SE	p-value
Intercept	55.35	17.34	0.002	23.46	16.18	0.148	18.51	14.27	0.196	25.70	12.64	0.043
Age	-0.34	0.12	0.004	0.21	0.11	0.063	0.20	0.10	0.039	0.12	0.09	0.167
Male	0.61	3.96	0.879	-5.82	3.70	0.117	0.34	3.26	0.916	-1.53	2.89	0.596
BMI	-0.29	0.26	0.263	0.17	0.24	0.470	-0.08	0.21	0.694	-0.03	0.19	0.861
Education												
Primary school and below	0			0			0			0		
Junior and senior high school	-0.27	2.63	0.918	0.35	2.45	0.886	-0.21	2.16	0.922	0	1.92	1.000
Junior college and above	3.44	4.41	0.436	-7.02	4.12	0.089	-8.89	3.63	0.015	-6.28	3.22	0.052
Smoking status												
Never	0			0			0			0		
Ex-smoker	-7.45	3.87	0.055	3.78	3.61	0.297	-4.96	3.19	0.121	-2.62	2.82	0.353
Current smoker	-5.72	3.94	0.147	0.80	3.68	0.829	-3.98	3.24	0.221	-2.73	2.87	0.343
Hypertension	-0.23	2.05	0.911	-0.48	1.91	0.801	2.24	1.68	0.184	1.02	1.49	0.493
Diabetes mellitus	-2.01	3.00	0.504	-3.39	2.80	0.226	-4.24	2.47	0.087	-3.64	2.19	0.097
Cardiovascular disease	1.35	2.60	0.603	-1.91	2.42	0.432	0.70	2.14	0.742	-0.04	1.89	0.985
Sleep disorder	-0.04	2.78	0.989	1.46	2.60	0.575	0.80	2.29	0.727	0.84	2.03	0.680
Exacerbation frequency*	1.14	0.70	0.103	1.58	0.65	0.016	1.11	0.57	0.054	1.25	0.51	0.014
Chronic productive cough	11.45	1.96	< 0.001	3.55	1.82	0.053	5.06	1.61	0.002	5.59	1.43	< 0.001
FEV₁/FVC	-0.17	0.15	0.270	-0.28	0.14	0.053	-0.06	0.13	0.662	-0.14	0.11	0.204
FEV₁ percentage predicted	0.26	0.16	0.107	0.06	0.15	0.701	0.02	0.13	0.891	0.07	0.12	0.556
GOLD spirometric staging												
GOLD 1	0			0			0			0		
GOLD 2	1.69	5.28	0.749	-2.68	4.93	0.587	-4.43	4.34	0.309	-2.96	3.85	0.442
GOLD 3	7.86	7.68	0.307	3.18	7.17	0.658	-1.59	6.32	0.802	1.39	5.60	0.804
GOLD 4	16.71	10.15	0.101	4.22	9.47	0.656	-0.23	8.35	0.978	3.89	7.40	0.599
mMRC scale												
Grade 0	0			0			0			0		
Grade 1	11.53	4.29	0.008	19.40	4.00	< 0.001	14.13	3.53	< 0.001	15.32	3.13	< 0.001
Grade 2	17.53	4.66	< 0.001	32.04	4.35	< 0.001	21.80	3.83	< 0.001	24.21	3.40	< 0.001
Grade 3	22.84	4.63	< 0.001	44.97	4.32	< 0.001	28.29	3.81	< 0.001	32.55	3.38	< 0.001
Grade 4	22.16	6.18	< 0.001	53.79	5.77	< 0.001	35.39	5.09	< 0.001	38.86	4.51	< 0.001

*The number of exacerbations in the previous year.

BMI: body mass index; FEV₁/FVC: forced expiratory volume in 1 second to forced vital capacity ratio; GOLD: Global Initiative for Chronic Obstructive Lung Disease; HRQoL: health-related quality of life; mMRC: modified Medical Research Council; SE: standard error; SGRQ: St George's Respiratory Questionnaire

Age and education had sporadic or discordant effects on the Symptom and Impact domains, but not on the Activity and Total domains. These trends did not change when FEV₁/FVC, FEV₁ percentage or both were removed from the regression model.

The results of the multiple linear regression evaluating each parameter's impact on WHOQOL-BREF are reported in Table V. The discriminative capability of the mMRC scale

remained significant in each of the four domains of WHOQOL-BREF, except in mMRC grade 1 in the Social and Environmental domains. Aging had a negative effect on the Physical domain. Patients with sleep disorders had poorer HRQoL, as reflected by lower domain scores. These trends did not change when FEV₁/FVC, FEV₁ percentage, or both were removed from the regression model.

Table V. Multiple linear regression to assess each parameter's impact on HRQoL as measured by WHOQOL-BREF.

Parameter	Physical			Psychological			Social			Environmental		
	Estimate	SE	p-value	Estimate	SE	p-value	Estimate	SE	p-value	Estimate	SE	p-value
Intercept	93.97	16.29	< 0.001	73.11	19.07	< 0.001	90.34	17.50	< 0.001	70.81	15.18	< 0.001
Age	-0.51	0.11	< 0.001	-0.03	0.13	0.810	-0.21	0.12	0.078	0.13	0.10	0.212
Male	-0.90	3.72	0.808	1.44	4.36	0.742	-5.52	4.00	0.169	1.35	3.47	0.698
BMI	-0.41	0.24	0.089	-0.36	0.28	0.201	-0.14	0.26	0.603	-0.09	0.22	0.684
Education												
Primary school and below	0			0			0			0		
Junior and senior high school	5.18	2.47	0.037	5.56	2.89	0.055	2.46	2.65	0.356	3.29	2.30	0.154
Junior college and above	4.60	4.15	0.268	1.74	4.86	0.721	2.11	4.46	0.637	-0.80	3.86	0.836
Smoking status												
Never	0			0			0			0		
Ex-smoker	6.02	3.64	0.099	5.83	4.26	0.172	5.42	3.91	0.166	3.46	3.39	0.308
Current smoker	8.81	3.70	0.018	7.75	4.33	0.075	5.23	3.98	0.190	3.83	3.45	0.267
Hypertension	-0.79	1.92	0.683	0.08	2.25	0.970	-0.58	2.07	0.778	-0.79	1.79	0.658
Diabetes mellitus	2.91	2.82	0.302	1.31	3.30	0.692	0.73	3.03	0.811	2.73	2.63	0.300
Cardiovascular disease	-2.38	2.44	0.329	-0.54	2.86	0.852	0.33	2.62	0.901	1.75	2.27	0.443
Sleep disorder	-8.11	2.61	0.002	-8.93	3.06	0.004	-0.84	2.81	0.764	-5.58	2.44	0.023
Exacerbation frequency*	-0.58	0.65	0.374	-0.36	0.76	0.642	-0.66	0.70	0.347	-0.25	0.61	0.676
Chronic productive cough	-2.34	1.84	0.203	-1.82	2.15	0.399	0.14	1.97	0.945	1.63	1.71	0.342
FEV₁/FVC	0.16	0.14	0.275	0.17	0.17	0.316	0.01	0.16	0.946	0.09	0.13	0.527
FEV₁ percentage predicted	-0.03	0.15	0.856	-0.09	0.17	0.602	0.02	0.16	0.920	-0.09	0.14	0.500
GOLD spirometric staging												
GOLD 1	0			0			0			0		
GOLD 2	0.58	4.96	0.906	4.60	5.81	0.429	0.81	5.33	0.880	-3.60	4.62	0.437
GOLD 3	1.11	7.21	0.878	5.57	8.45	0.510	2.57	7.75	0.740	-3.93	6.72	0.559
GOLD 4	-7.87	9.54	0.410	-1.98	11.17	0.860	0.80	10.25	0.938	-6.40	8.89	0.472
mMRC scale												
Grade 0	0			0			0			0		
Grade 1	-9.66	4.03	0.017	-17.91	4.72	< 0.001	-8.24	4.33	0.058	-6.12	3.76	0.104
Grade 2	-17.10	4.38	< 0.001	-22.98	5.12	< 0.001	-13.67	4.70	0.004	-9.13	4.08	0.026
Grade 3	-21.70	4.35	< 0.001	-23.64	5.10	< 0.001	-13.31	4.68	0.005	-10.31	4.06	0.011
Grade 4	-25.15	5.81	< 0.001	-27.64	6.80	< 0.001	-17.16	6.24	0.006	-14.61	5.41	0.007

*The number of exacerbations in the previous year.

BMI: body mass index; FEV₁/FVC: forced expiratory volume in 1 second to forced vital capacity ratio; GOLD: Global Initiative for Chronic Obstructive Lung Disease; HRQoL: health-related quality of life; mMRC: modified Medical Research Council; SE: standard error; WHOQOL-BREF: World Health Organization Quality of Life (abbreviated version)

DISCUSSION

To the best of our knowledge, the present study is the first study to investigate the determinant factors of HRQoL in patients with COPD of all levels of severity, using both disease-specific and generic questionnaires. We found inconsistencies between the GOLD spirometric classification of COPD and HRQoL, as measured by both SGRQ and WHOQOL-BREF. We also found that the mMRC scale had better discriminative capacity than the GOLD classification in the evaluation of HRQoL, as evidenced by the results of both the ANOVA and multiple linear regression models.

Although COPD is characterised by airflow limitations, it involves several systemic components.^(1,26,27) HRQoL, a comprehensive and widely accepted measure of the impact of disease on a patient's quality of life, may help medical staff optimise treatment and help patients plan for the increasing disability associated with the disease.⁽²⁸⁾ Questionnaires such as SGRQ and WHOQOL-BREF are good tools for gauging HRQoL, but their use in clinical practice is limited due to time constraints. Spirometry provides a useful measure of the pathological changes in COPD, but poorly correlates with

some important outcomes.⁽²⁷⁾ As shown in the present study, as well as in previously published data, there is considerable heterogeneity in HRQoL impairment within each GOLD stage of severity.⁽³⁾ It has also been demonstrated that the level of dyspnoea may be a more accurate measure of the HRQoL of patients with COPD compared to measurement by categorisation of spirometry results.⁽¹²⁾

The MRC dyspnoea scale has been utilised for many years to grade disability resulting from breathlessness.^(14,29) It is short, simple to execute and can be easily performed in clinical settings. Its five consecutive questions describe patients' daily activities, and this explains why it correlates best with the SGRQ Activity and WHOQOL-BREF Physical domains, as was observed in the present study. The mMRC scale also demonstrated excellent discriminative capabilities in other domains such as the Impact, Psychological and Social domains, thus proving to be a good indicator of HRQoL.

When categorised using GOLD stages, the participants' HRQoL showed considerable variation and was not well distinguished. Nevertheless, the domain scores of SGRQ were significantly increased between stages 2 and 3; this was not

observed between other consecutive stages. Our findings are consistent with reports by Jones et al⁽³⁾, Antonelli-Incalzi et al⁽¹¹⁾ and Hajiro et al⁽¹²⁾, which found that there was dramatic deterioration of HRQoL when patients' FEV₁ dropped below 50% of the predicted normal values. The 50% predicted FEV₁ represents a critical point of HRQoL and is a likely an indicator of general health status. Therefore, therapies for COPD, either pharmacological or non-pharmacological, should be started and enforced early (before 50% FEV₁ is reached), considering the potential for irreversible impairment, which is ultimately less treatable.

It has been demonstrated that the deterioration of lung function is more prominent in the early stages of COPD (i.e. in GOLD stages 1 and 2).⁽³⁰⁾ Symptomatic patients with early COPD demonstrate rapid disease progression compared to asymptomatic patients.⁽³¹⁾ In the current study, 87.0%, 91.5%, 97.7% and 100.0% of our participants who were classified as GOLD stage 1 through 4 had mMRC grades 1, 2, 3 and 4, respectively. In other words, most patients were symptomatic and somewhat restricted in their daily activities. Compared to GOLD staging, we were able to detect the deterioration of HRQoL earlier using mMRC grading. Early detection enabled us to take appropriate and effective actions to relieve patients' symptoms, improve patients' exercise tolerance, prevent exacerbations and slow down disease progression.

The present study's multiple linear regression analysis showed that other parameters were also determining factors of HRQoL. 'Chronic productive cough', a symptom that is routinely reported in both in- and outpatient settings, had a negative effect on the HRQoL of patients with COPD. This is noteworthy because although the symptoms 'cough' and 'sputum production' were mentioned in only five of the 50 items of SGRQ, these symptoms showed extensive influence on most of the SGRQ domains. Exacerbations of COPD also showed an adverse influence on HRQoL, compatible with the findings of previous studies.^(32,33) Sleep disorders, especially sleep apnoea, are associated with increased mortality and hospitalisation of COPD patients,⁽¹⁹⁾ and in our study, sleep disorders also showed a detrimental impact on HRQoL. Aging also had a negative effect on HRQoL in the SGRQ Impact and WHOQOL-BREF Physical domains, but showed otherwise in the SGRQ Symptom domain. This discrepancy may be attributed to a blunted perception of dyspnoea in older patients with COPD.⁽³⁴⁾ Smoking status and level of education revealed sporadic and borderline effects, and may be of little significance since each of the item involves only one domain of the questionnaires. Further studies are needed to address the roles of age, smoking and level of education with regard to HRQoL.

The aim of the present study was not to abolish the importance of pulmonary function testing in the diagnosis and treatment of COPD. Instead, the study was designed to discover determinant factors of HRQoL other than lung function

and GOLD staging. Spirometry is still the cornerstone for the diagnosis of COPD, but it is not the only tool in the preliminary evaluation of disease severity. As mentioned by Hajiro et al, categorising patients according to their level of dyspnoea (e.g. using the mMRC scale) may help explain changes in HRQoL, which is often used as an endpoint in clinical trials or as a marker of treatment effects.⁽¹²⁾

There are some limitations in the present study. First, the number of participants in GOLD stages 1 and 4 were significantly lesser than those in GOLD stages 2 and 3. This unbalanced representation of patients has also been observed in the literature.^(3,11,35) In general, most patients do not seek medical treatment until they are symptomatic, and thus present with relatively bad lung function at the time of diagnosis. On the other hand, patients diagnosed with severely impaired lung function (i.e. GOLD stage 4) are frequently hospitalised due to acute exacerbation, and are thus prone to become dependent on mechanical ventilation. These patients are also more inclined to have cardiovascular events and lung cancer, which increases mortality. We postulate that these are the reasons why we had fewer patients in GOLD stages 1 and 4. Furthermore, our participants were recruited from an outpatient clinic. A thorough and well-designed survey on community populations may be able to overcome this limitation. The second limitation of our study was that most of our participants were male. This may be due to the fact that in Taiwan, a large proportion (55%–60%) of men are smokers while only a small proportion (3%–4%) of women smoke,⁽³⁶⁾ and cigarette smoking is a well-known risk factor for COPD. Although multiple linear regression analysis did not show significant difference in HRQoL between men and women with COPD, we believe that further studies with a more balanced sample of men and women are needed.

In conclusion, the mMRC dyspnoea scale is a concise and practical tool to assess the HRQoL of patients with COPD in daily clinical practice. Compared to GOLD staging, it demonstrates better discriminative validity in evaluating HRQoL and is able to detect impaired health status earlier. In addition to decreased lung function, chronic productive cough, sleep disorders and frequent exacerbations also have negative effects on HRQoL. Therefore, these factors should be taken into consideration when HRQoL is included as a measurement of patients' baseline condition or treatment effects.

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