



Health-related quality of life in COPD patients with chronic respiratory failure

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ABSTRACT: The Mageri Respiratory Failure (MRF-28) and Severe Respiratory Insufficiency (SRI) questionnaires were recently developed to assess health-related quality of life (HRQoL) in patients with chronic respiratory failure, although not exclusively in chronic obstructive pulmonary disease (COPD) patients. The aim of the present study was to investigate whether the MRF-28 and SRI are reliable and valid HRQoL questionnaires in COPD patients with chronic hypercapnic respiratory failure (CHRF).

In total, 72 COPD patients with CHRF underwent pulmonary function and exercise testing, and completed the MRF-28, the SRI, the Chronic Respiratory Questionnaire (CRQ), the Hospital Anxiety and Depression Scale, the Groningen Activity and Restriction Scale and two dyspnoea indexes.

Physical domain scores of the questionnaires correlated with exercise tolerance, dyspnoea and daily activities, while psychological domains correlated strongly with anxiety and depression. Anxiety scores accounted for 51 and 56% of the total explained variance in total CRQ and SRI scores, respectively. The emphasis of the MRF-28 was restrictions in activities of daily living (52% of total variance).

In conclusion, the present study showed that the Mageri Respiratory Failure and Severe Respiratory Insufficiency questionnaires were reliable and valid questionnaires in chronic obstructive pulmonary disease patients with chronic hypercapnic respiratory failure. While the emphasis in the Mageri Respiratory Failure questionnaire is on activities of daily living, the Severe Respiratory Insufficiency questionnaire, like the Chronic Respiratory Questionnaire, is more related to anxiety and depression.

KEYWORDS: Chronic obstructive pulmonary disease, quality of life, respiratory insufficiency

Chronic obstructive pulmonary disease (COPD) is a leading cause of morbidity and mortality worldwide [1]. As COPD is a progressive disease, the number of COPD patients with severe disease and chronic respiratory failure will increase in the coming years. It has been shown that patients with chronic respiratory failure have poor survival. A 5-yr mortality of 70–100% was reported [2]. Survival rates are difficult to improve once patients have become respiratory insufficient. Despite treatment with long-term oxygen or home mechanical ventilation (HMV), median survival was still only 3 yrs [3].

Although survival rates are difficult to improve, therapeutic interventions in severe COPD might nevertheless improve health-related quality of life (HRQoL) [4, 5]. The Chronic Respiratory

Questionnaire (CRQ) is a widely used disease-specific questionnaire that has been shown to be reliable, valid and responsive in COPD patients [6]. It has also been used in more severe patients [7–9]. However, it was not designed for patients with chronic respiratory failure and might not include items specifically important for these patients. Therefore, a need was felt for questionnaires specific for patients with respiratory failure [10]. The Mageri Respiratory Failure (MRF-28) and Severe Respiratory Insufficiency (SRI) questionnaires were developed especially for these patients [11, 12]. Both questionnaires contain items on problems that patients with chronic respiratory failure experience. However, both questionnaires were developed in a group of patients with respiratory failure of different origin, already treated with HMV for a longer period. Reliability and validity of the MRF-28 and

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SRI have not been investigated in a homogeneous group of patients with COPD who actually suffer from chronic respiratory failure.

The purpose of the present study was to determine whether the MRF-28 and SRI are reliable and valid HRQoL questionnaires in COPD patients with chronic hypercapnic respiratory failure (CHRF). Therefore, the following were evaluated: 1) reliability of the three questionnaires, by methods including assessing reproducibility; 2) concurrent validity, by comparing SRI and MRF-28 scores with CRQ scores; 3) construct validity of the three questionnaires, by correlating the scores with relevant physiological parameters, dyspnoea ratings and psychological status, in COPD patients with CHRF.

METHODS

Patients

All participants were in a stable condition, out of rehabilitation for ≥ 18 months and treated with medication and long-term oxygen if necessary. None of the participants was or had been on long-term ventilation. Inclusion criteria were Global Initiative for Chronic Obstructive Lung Disease stage III or IV [13] COPD with CHRF, defined as forced expiratory volume in one second (FEV₁) $< 50\%$ predicted and arterial carbon dioxide tension (P_{a,CO_2}) > 6.0 kPa (45 mmHg), while breathing room air at rest [14]. Exclusion criteria were cardiac or musculoskeletal diseases limiting exercise performance, or obstructive sleep apnoea syndrome (apnoea/hypopnoea index ≥ 10 episodes·h⁻¹). Details are given in the online supplementary information.

The study was approved by the local Medical Ethical Committee (University Medical Center Groningen, Groningen, the Netherlands). All participants gave written informed consent.

Measurements

Patients underwent pulmonary function testing [15–17], maximal incremental cycle ergometry and a test of 6-min walking distance (6MWD) [18, 19]. HRQoL was measured by the MRF-28 [11], the SRI [12] and the CRQ [6]. The MRF-28 contains three subscales related to daily activities, cognition and invalidity, and a total score with additional items related to fatigue, depression and problems with treatment. MRF-28 scores range 0–100; higher scores indicate worse HRQoL [11]. The SRI contains seven subscales related to respiratory complaints, physical functioning, attendant symptoms and sleep, social relationships, anxiety, psychological well-being and social functioning, and a summary scale. SRI scores range 0–100; higher scores indicate better HRQoL [12].

Dyspnoea was assessed with the Medical Research Council (MRC) scale [20] and the Baseline Dyspnoea Index (BDI) [21, 22]. Activities of daily living were assessed by the Groningen Activity and Restriction Scale (GARS) [23], and mood state by the Hospital Anxiety and Depression Scale (HADS) [24]. Additional information about the tests and questionnaires is presented in the online supplementary information.

Study design

Tests were performed on three different days. On day 1, the CRQ was administered first. Patients completed the MRF-28,

SRI, MRC, BDI, HADS and GARS by themselves in random order. The 6MWD and cycle ergometry were performed on two different days, to allow the patients to rest sufficiently. Pulmonary function testing was performed ≥ 3 h before or after an exercise test. After 12 weeks, the tests were repeated in a similar order.

Analysis and statistics

Reliability was assessed by internal consistency, distribution of the scores and test–retest reproducibility. Internal consistency was determined by Cronbach's α -coefficient. Test–retest reproducibility was approximated by intraclass correlation coefficients (ICC) in the 23 patients who completed the questionnaires for a second time after 12 weeks and who had no exacerbations in those 12 weeks [25]. Reproducibility could not be tested in the 36 patients who did have an exacerbation, in seven patients whose therapy was changed, in three patients who withdrew, or in three patients who died during the 12-week period.

To evaluate construct validity of the questionnaires, the present authors investigated whether the HRQoL scores correlated with other measures that assessed the same construct [26]. Physical domains should correlate with related physical parameters, while psychological domains should correlate with psychological parameters. The construct was further scrutinised by backward multiple regression analysis, identifying patterns in parameters that could best explain the variance in the questionnaires' total scores. Variables entered in the backward model were chosen on the basis of existing literature together with a value of $p < 0.10$ in the univariate regression analyses. Since strong correlations were found between the HADS anxiety and HADS depression scores ($r = 0.69$) and between the GARS score and the 6MWD ($r = 0.77$), only one variable of these respective parameters was entered. For the final model, the following were chosen as independent variables: sex; exacerbation frequency during the previous year; FEV₁; GARS scores; lactate at rest; HADS anxiety score; and BDI score. Exacerbation frequency was divided by the median into two categories (few (≤ 3) versus frequent (> 3) exacerbations·yr⁻¹). The dependent variables were MRF-28, SRI and CRQ total scores. For all analyses, a p -value < 0.01 was considered significant.

RESULTS

Patients

Baseline measurements were performed in 86 patients. In total, 14 patients were excluded from the analyses: nine patients were not hypercapnic, three had an apnoea/hypopnoea index ≥ 10 , one had an FEV₁ $> 50\%$ pred and one patient was unable to complete the questionnaires. Therefore, a total of 72 patients were included in the present study (table 1). All patients were hypercapnic as per protocol. In addition, 31 were also hypoxaemic (arterial oxygen tension < 8.0 kPa (60 mmHg) on room air at rest) and 33 patients were on long-term oxygen therapy. No significant differences were found in pulmonary function, exercise tolerance or any of the questionnaire scores between the patients who were and were not hypoxaemic, except for a significantly lower pH and higher P_{a,CO_2} in the hypoxaemic patients. All patients were treated with inhaled β_2 -agonists or anticholinergic medication; 60 patients used

inhaled corticosteroids; and 33 patients were treated with oral corticosteroids. No significant differences were found in any of the questionnaire scores between the patients who were and were not on steroids (inhaled and/or oral).

Reliability

Scores were obtained over a large range for the MRF-28, SRI and CRQ (table 2 and fig. 1). The MRF-28 cognition domain showed obvious floor and ceiling effects, with 11 (15%) patients scoring the maximum (worst) possible score, and 19 (26%) patients scoring the minimal (best) possible score. Floor and ceiling effects were also observed for the daily activities and invalidity domain. For the CRQ and SRI, no obvious floor and ceiling effects were observed.

Internal consistency of the MRF-28 was high for the daily activity domain but lower for the cognition and invalidity domains (table 2). Internal consistency of the CRQ was high for

all domains, while for the SRI it was high for all domains except for the attendant symptoms and sleep domain, for which a lower value was obtained (0.66). Test-retest reproducibility was good for the MRF-28, SRI and CRQ (ICC values of 0.92, 0.81 and 0.87, respectively).

Validity

Concurrent validity

The MRF-28 and SRI total scores correlated significantly with all CRQ domains (table 3). The best correlations for both questionnaires were found with the CRQ fatigue domain. The anxiety and well-being domains of the SRI correlated highest with the CRQ emotion domain. The MRF-28 cognition domain did not correlate with any of the CRQ domains. The SRI attendant symptoms and sleep domain did not correlate with the CRQ dyspnoea domain.

Construct validity

The physical domains of the questionnaires, which are the MRF-28 daily activities domain, the SRI physical functioning domain and the CRQ dyspnoea domain, correlated strongly with GARS ($r=0.75$, $r=0.86$ and $r=0.42$, respectively) and with dyspnoea scores and the 6-min walking distance. The highest correlations with these physical parameters were found for the SRI domain. Emotional domains, which are the SRI anxiety and psychological well-being domains and the CRQ emotion and mastery domains, correlated strongly with both HADS anxiety and depression. The highest correlations were found for the SRI psychological well-being domain.

Only the MRF-28 daily activities and invalidity domains and three SRI domains correlated weakly to moderately with pulmonary function parameters; none of the CRQ domains did. The MRF-28 invalidity domain contains questions on effort and social activities. It correlated moderately both with physical and psychological parameters. However, no MRF-28 domain correlated as strongly with mood state as the psychological domains of the other questionnaires. The cognition domain did not correlate with any parameters at all, including arterial blood gases. Overall, the SRI contains domains that correlated most strongly both with physical and psychological parameters. Interestingly, several domains of the SRI correlated with bicarbonate levels (table 4).

Determinants of HRQoL

Of the variance in the MRF-28 total score, 66% was explained by sex, GARS score, HADS anxiety score and BDI. The largest part (52%) of the variance in the MRF-28 total score was explained by the GARS score. Of the total variance in the SRI summary score, 72% was explained by HADS anxiety, GARS and exacerbation frequency. The largest part (56%) of the total explained variance was attributable to the HADS anxiety score. Of the total variance in the CRQ total score, 63% was explained by sex, lactate at rest, HADS anxiety and BDI scores, with the largest part (51%) explained by HADS anxiety score (table 5).

To strengthen the conclusions based on the present model with seven variables, the model was tested with only GARS and HADS anxiety included. For the CRQ and SRI, this model was again dominated by the HADS anxiety, while for the MRF-28 it was dominated by the GARS.

TABLE 1 Patient characteristics

Sex M/F n	39/33
Age yrs	62±8.6
Treatment n[#]	
Long-term oxygen	33
Oral steroids	33
Inhaled steroids	60
Exacerbations·yr⁻¹	4.0±3.2
BMI kg·m⁻²	27.1±6.2
FEV₁ L	0.80±0.31
FEV₁ % pred	30±11
VC L	2.60±0.77
FEV₁/VC %	31±9
TLC % pred	125±18
RV % TLC	64.8±8.4
P_{I,max} kPa	5.3±2.1
pH[†]	7.39±0.03
P_{a,O₂} kPa[‡]	8.1±1.2
P_{a,CO₂} kPa[‡]	6.8±0.6
HCO₃⁻ mmol·L^{-1†}	28.8±2.4
BE mmol·L^{-1†}	4.1±2.0
6MWD m	284±119
GARS score	42±11
HADS depression	7.5±5
HADS anxiety	7.2±4
BDI total score	3.6±1.8
MRC	3.5±0.9

Data are presented as mean±SD, unless otherwise stated. M: male; F: female; BMI: body mass index; FEV₁: forced expiratory volume in one second; % pred: % predicted; VC: vital capacity; TLC: total lung capacity; RV: residual volume; P_{I,max}: maximal inspiratory pressure; P_{a,O₂}: arterial oxygen tension; P_{a,CO₂}: arterial carbon dioxide tension; HCO₃⁻: bicarbonate; BE: base excess; 6MWD: 6-min walking distance; GARS: Groningen Activity and Restriction Scale (scores range from best (18) to worst (72)); HADS: Hospital Anxiety and Depression Scale (separate scores for anxiety and depression; scores range from best (0) to worst (21)); BDI: baseline dyspnoea index (scores range from best (12) to worst (0)); MRC: Medical Research Council dyspnoea scale (scores range from best (1) to worst (5)). [#]: some patients received a combination of treatments; [†]: while breathing room air.

TABLE 2 Maugeri Respiratory Failure (MRF-28), Severe Respiratory Insufficiency (SRI) and Chronic Respiratory Questionnaire (CRQ) scores and internal consistency

	Score range	Items n	Minimum score n [#]	Maximum score n [#]	Mean ± SD score	α-coefficient [†]
MRF-28						
Daily activities	0–100	11	3	6	60.6 ± 28.9	0.83
Cognition	0–100	4	19	11	44.1 ± 35.2	0.69
Invalidity	0–100	5	4	15	63.1 ± 29.6	0.60
Total	0–100	27	0	0	55.5 ± 22.0	
SRI						
Respiratory complaints	0–100	8	0	0	46.7 ± 15.5	0.73
Physical functioning	0–100	6	0	0	38.5 ± 18.5	0.73
Attendant symptoms and sleep	0–100	7	0	0	59.7 ± 16.9	0.66
Social relationships	0–100	6	0	0	63.2 ± 18.0	0.78
Anxiety	0–100	5	1	0	48.2 ± 19.8	0.70
Well-being	0–100	9	0	0	57.0 ± 18.3	0.84
Social functioning	0–100	8	1	0	46.2 ± 17.5	0.73
Summary score	0–100	49	0	0	51.3 ± 13.6	
CRQ						
Dyspnoea	5–35	5	1	0	16.2 ± 5.5	0.73
Fatigue	4–28	4	1	0	13.8 ± 4.9	0.82
Emotion	7–49	7	1	0	30.3 ± 7.7	0.78
Mastery	4–28	4	1	0	17.6 ± 5.4	0.80
Total	20–140	20	0	0	78.1 ± 19.3	

[#]: number of patients; [†]: Cronbach's α-coefficient for internal consistency.

DISCUSSION

The present study shows for the first time that the recently developed MRF-28 and SRI are reliable and valid HRQoL questionnaires in a homogeneous group of COPD patients with CHRF. Overall, the MRF-28 total score was more related to activities of daily living and less to psychological functioning. The SRI total score, like the CRQ total score, was most strongly related to anxiety and depression. In addition, the SRI total score was also substantially related to daily activity level.

From the present study, two results advocate the use of the MRF-28 and/or SRI in addition to or instead of the CRQ in patients with chronic respiratory failure. First, the MRF-28 and SRI contain items on specific problems that patients with CHRF might encounter that are not included in the CRQ. Secondly, the present study showed that construct validity was slightly better for the MRF-28 and especially the SRI compared with the CRQ in these patients. The version of the CRQ used in the present study necessitates an interviewer, while the MRF-28 and SRI are self-administered. The MRF-28 might be more attractive in the practical sense as it contains 28 items and took the patients ~10 min to complete, while the SRI contains 49 items and takes 20 min to complete. However, as answer possibilities were clearly indicated, both questionnaires were easy for the patients to complete.

The importance of addressing the care for patients with end-stage COPD is increasingly recognised [27]. Once a chronic respiratory failure develops, a patient often becomes limited by specific symptoms and complaints that negatively influence HRQoL [28]. Patients might experience severe breathlessness during minimal effort or even at rest. High carbon dioxide

levels might cause headaches or concentration problems. These problems reduce the ability to perform the activities of daily living. Social relationships and activities become problematic and patients might become depressed or anxious.

A good HRQoL questionnaire should include all the items that are considered to be important for HRQoL in these patients [10]. Since the CRQ was not designed for patients with respiratory failure, it was felt that a HRQoL questionnaire that included items that were complaint and symptom specific for patients with chronic respiratory failure was needed [10]. However, the MRF-28 and SRI were designed for a mixed group of patients with chronic respiratory failure, not exclusively in patients with COPD [11, 12]. The present study investigated these questionnaires in a homogeneous group of COPD patients with CHRF and concluded that, in the future, the MRF-28 and SRI could probably be added to or even substitute the CRQ in the assessment of HRQoL in COPD patients with C(H)RF.

The MRF-28 and SRI add the following items that are considered to be important in these patients. The MRF-28 adds the cognition domain, which contains four items on the effects of impaired memory, attention and concentration on daily living. It has been shown that neurophysiological functioning is impaired in COPD patients, especially in patients who were hypoxaemic [29]. In the present study's hypercapnic COPD patients, 74% answered "true" to at least one and 56% to at least two out of four questions of the cognition domain. Thus, cognitive problems are frequently encountered by patients with CHRF. However, no relationship was found with resting blood gases, although the cognition

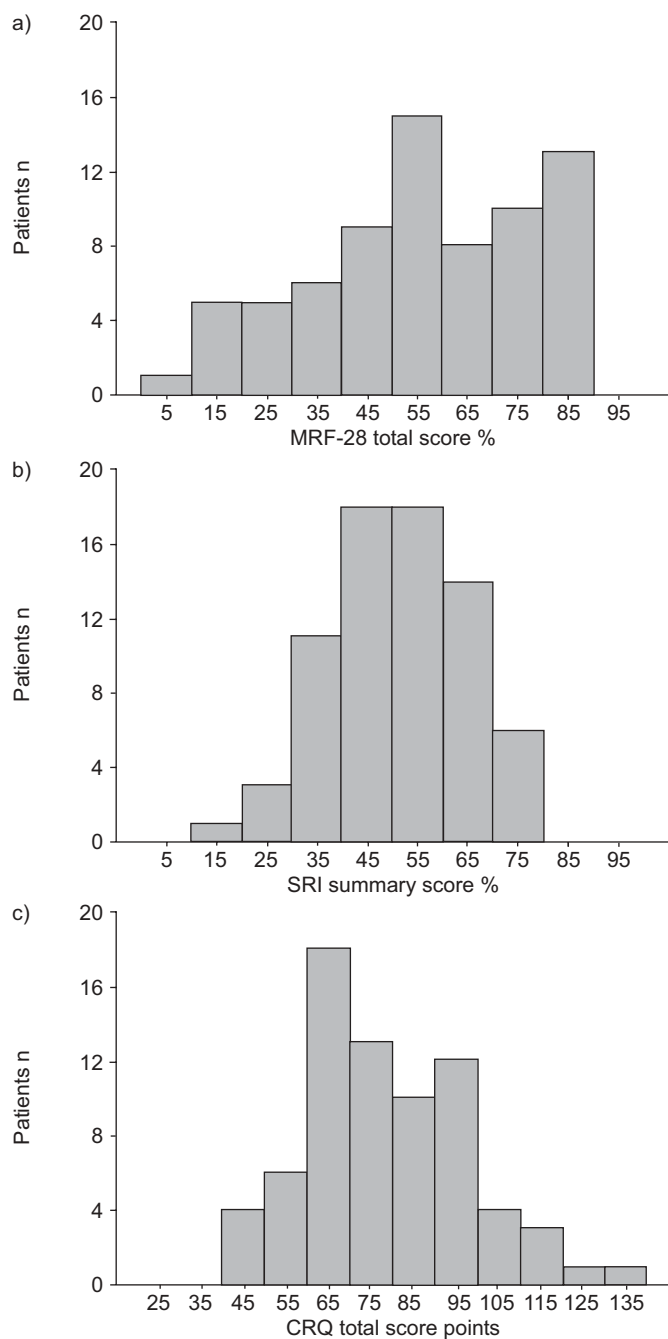


FIGURE 1. Variation in total scores of the questionnaires. MRF-28: Maugeri Respiratory Failure; SRI: Severe Respiratory Insufficiency; CRQ: Chronic Respiratory Questionnaire.

domain is very short and probably too limited to find such a relationship. In addition, an obvious floor and ceiling effect was observed for this domain (table 2). These limitations advocate the addition of more items in the cognition domain.

The SRI physical functioning domains correlated with bicarbonate levels, the most robust parameter for the severity of CHRf. As only the SRI seemed to be able to pick up the influence of bicarbonate levels on physical functioning and social activities, the current authors advocate the use of the SRI

TABLE 3 Spearman's rank correlations between Maugeri Respiratory Failure (MRF-28), Severe Respiratory Insufficiency (SRI) and Chronic Respiratory Questionnaire (CRQ) scores

	CRQ				
	Dyspnoea	Fatigue	Emotion	Mastery	Total
MRF-28					
Daily activities	-0.44	-0.51	-0.33	-0.25	-0.45
Cognition					
Invalidity	-0.44	-0.49	-0.45	-0.41	-0.54
Total	-0.52	-0.61	-0.49	-0.36	-0.60
SRI					
Respiratory complaints	0.57	0.59	0.40	0.34	0.54
Physical functioning	0.46	0.61	0.47	0.42	0.59
Attendant symptoms and sleep		0.39	0.38	0.27	0.39
Social relationships	0.44	0.57	0.59	0.45	0.63
Anxiety	0.35	0.57	0.65	0.60	0.67
Well-being	0.38	0.60	0.79	0.70	0.79
Social functioning	0.42	0.57	0.51	0.41	0.60
Summary score	0.53	0.74	0.73	0.62	0.81

Only significant correlations ($p < 0.01$) are shown.

in intervention studies aimed at improving the degree of respiratory failure. This is in line with a previous study that showed a high correlation between a reduction in bicarbonate level following establishment of HMV and an increase in the SRI summary scale [30].

The construct validity was better for the MRF-28 and SRI than for the CRQ in the present patient group. MRF-28 and especially the SRI scores correlated more strongly with other measures that assessed the same construct. Compared with the CRQ dyspnoea and fatigue domains, the MRF-28 daily activity domain and SRI physical functioning domain correlated more strongly with daily activities, dyspnoea and exercise tolerance. In addition, the SRI psychological domains correlated more strongly with mood state, compared with the respective CRQ domains. The MRF-28 contains no psychological domain. The invalidity domain contains items on feelings of invalidity, effort and social activities. Therefore, it was also unsurprising that correlations with psychological parameters were only moderate.

The MRF-28, SRI and CRQ emphasise different aspects of HRQoL. For the CRQ, anxiety accounted for a large part of the total explained variance in total score. This is in line with the study of HAJIRO *et al.* [31], which found that HADS anxiety, next to BDI scores, accounted for a large percentage of variance in CRQ. For the SRI, as for the CRQ, anxiety also accounted for a large part of the total variance in the summary scale. In addition, for the SRI, restrictions in activities of daily living accounted for a substantial part (13%). However, in the MRF-28, the emphasis was on restrictions in the degree of activities of daily living. HADS anxiety, on the contrary, explained only 5% of the total variance in MRF-28 score. As mood state was

TABLE 4 Spearman's rank correlations between physiological parameters and Mageri Respiratory Failure (MRF-28), Severe Respiratory Insufficiency (SRI) and Chronic Respiratory Questionnaire (CRQ) scores

	MRF-28				SRI								CRQ				
	Daily	Cog	Inv	Total	RC	PF	AS	SR	AX	WB	SF	SS	Dys	Fat	Em	Mas	Total
Exacerbations	0.36		0.30	0.40	0.37	0.43		0.43	0.35		0.45	0.46	0.35	0.33	0.31	0.27	0.37
FEV1 % pred	0.27		0.40	0.33		0.33			0.26	0.27	0.26	0.27					
VC L	0.39		0.27	0.30		0.27	0.33			0.28	0.35	0.32	0.28				0.26
RV % TLC																	
P_{I,max} kPa	0.34					0.26					0.25						
V'O_{2,max} mL·min⁻¹·kg⁻¹	0.31		0.40	0.26		0.38					0.25						
6MWD m	0.53		0.50	0.50	0.38	0.60		0.48	0.29	0.25	0.58	0.49	0.33	0.39	0.30	0.23	0.36
P_{a,O₂} kPa																	
P_{a,CO₂} kPa																	
pH		0.27															
HCO₃⁻ mmol·L⁻¹								0.32									
Lactate mmol·L⁻¹#		0.24		0.26		0.30		0.33		0.29	0.36	0.30		0.26	0.36	0.29	0.33
GARS	0.75		0.59	0.70	0.49	0.86		0.53	0.40	0.36	0.66	0.65	0.42	0.52	0.39	0.33	0.47
HADS depression	0.52		0.48	0.57	0.41	0.54	0.26	0.61	0.54	0.68	0.58	0.68	0.29	0.61	0.60	0.56	0.65
HADS anxiety	0.43		0.56	0.56	0.50	0.51	0.39	0.56	0.69	0.79	0.54	0.75	0.30	0.54	0.75	0.72	0.74
BDI	0.67		0.58	0.68	0.57	0.67		0.43	0.41	0.40	0.51	0.59	0.53	0.63	0.40	0.32	0.54
MRC	0.49		0.50	0.47	0.43	0.59		0.30	0.26		0.43	0.41	0.41	0.33			0.27

Only significant correlations (p<0.01) are shown. Daily: daily activities; Cog: cognition; Inv: invalidity; RC: respiratory complaints; PF: physical functioning; AS: attendant symptoms and sleep; SR: social relationships; AX: anxiety; WB: psychological well-being; SF: social functioning; SS: summary score; Dys: dyspnoea; Fat: fatigue; Em: emotion; Mas: mastery; FEV1: forced expiratory volume in one second; % pred: % predicted; VC: vital capacity; RV: residual volume; TLC: total lung capacity; P_{I,max}: maximal inspiratory pressure; V'O_{2,max}: maximal oxygen uptake during cycle ergometry; 6MWD: 6-min walking distance; P_{a,O₂}: arterial oxygen tension; P_{a,CO₂}: arterial carbon dioxide tension; HCO₃⁻: bicarbonate; GARS: Groningen Activity and Restriction Scale; HADS: Hospital Anxiety and Depression Scale; BDI: baseline dyspnoea index; MRC: Medical Research Council dyspnoea scale. #: from arterial blood sample.

shown to have substantial effects on HRQoL in patients with CHRF [32], the under-representation of psychological aspects is a disadvantage of the MRF-28. Therefore, the present authors

recommend using the MRF-28 in addition to the SRI and not as a substitute. Now that the reliability and validity of the two new questionnaires have been evaluated in a homogeneous

TABLE 5 Backward multiple regression analyses

	MRF-28 total score %		SRI total score %		CRQ total score points	
	B	R ²	B	R ²	B	R ²
GARS points#	0.7 (0.3–1.1)	0.52	-0.4 (-0.6– -0.3)	0.13		
HADS anxiety points[†]	1.2 (0.3–2.1)	0.05	-1.7 (-2.2– -1.2)	0.56	-2.3 (-3.0– -1.5)	0.51
BDI points[‡]	-4.1 (-6.4– -1.7)	0.08			2.5 (0.7–4.2)	0.06
Sex female[§]	6.0 (0.8–12.7)	0.01			-8.6 (-14.6– -2.5)	0.03
Frequent exacerbations[‡]			-4.9 (-8.7– -1.1)	0.03		
Lactate mmol·L⁻¹					-6.7 (-12.0– -1.4)	0.03
Cumulative R²		0.66		0.72		0.63

The following were included as independent variables in the models: sex, exacerbation frequency, forced expiratory volume in one second (% predicted), lactate, Groningen Activity and Restriction Scale (GARS) score, Hospital Anxiety and Depression Scale (HADS) anxiety score and baseline dyspnoea index (BDI). Only variables that were included in the final models are shown. MRF-28: Mageri Respiratory Failure; SRI: Severe Respiratory Insufficiency; CRQ: Chronic Respiratory Questionnaire; B: unstandardised regression coefficient (95% confidence interval), indicating predicted increase in questionnaire total scores for 1 unit increase in the given variable; R²: proportion of explained variance for independent variables included in the backward model. Scores from best to worst: #: 18–72 points; †: 0–21 points; ‡: 12–0 points; §: 0= male, 1= female; ‡: 0=few exacerbations (≤3 exacerbations·yr⁻¹), 1=frequent exacerbations (>3 exacerbations·yr⁻¹).

group of COPD patients with CHRF not on mechanical ventilation, the responsiveness of the different questionnaires should be evaluated in intervention studies, e.g. on pulmonary rehabilitation and HMV.

The MRF-28 and SRI are not yet widely used, which makes it difficult to compare the present scores with previous studies. Somewhat higher MRF-28 scores (indicating worse HRQoL) were found compared with those of CARONE *et al.* [11]. This can be explained by the fact that the current patients had more severe airflow obstruction. JANSSENS *et al.* [33] investigated the MRF-28 in a group of patients treated with HMV, but only 15% of patients included had COPD. CLINI *et al.* [34] used the MRF-28 as an outcome measure in their study on HMV in COPD; however, they mentioned only change in scores and not absolute scores. Recently, CARONE *et al.* [5] showed that pulmonary rehabilitation increases MRF-28 scores in COPD patients with chronic respiratory failure. Scores were comparable except for a better (lower) cognition domain score in the present study, which might be explained by a lower age in the present patients. The SRI scores were comparable with the scores found by WINDISCH *et al.* [12].

In conclusion, to include the most extensive measurement of health-related quality of life in chronic obstructive pulmonary disease patients with chronic hypercapnic respiratory failure, the present authors recommend using the Severe Respiratory Insufficiency questionnaire. The emphasis in the Mageri Respiratory Failure questionnaire is mostly on restrictions in activities of daily living, but it underscores the importance of psychological aspects in these patients. However, the Mageri Respiratory Failure questionnaire adds the cognition domain, with which prevalent and relevant problems in these patients are addressed. Therefore, the addition of this domain might be a reason to add the Mageri Respiratory Failure questionnaire into intervention studies.

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