

# The Severe Respiratory Insufficiency Questionnaire for Subjects With COPD With Long-Term Oxygen Therapy

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**BACKGROUND:** Respiratory insufficiency in COPD may present as hypoxic and/or hypercapnic respiratory failure treated with long-term oxygen therapy (LTOT) and/or noninvasive ventilation (NIV) with LTOT. The Severe Respiratory Insufficiency Questionnaire (SRI) is a tool for the assessment of health-related quality of life (HRQOL) in subjects receiving NIV. However, it remains unclear whether the SRI is also capable of assessing and discriminating HRQOL in subjects receiving LTOT. **METHODS:** Stable subjects with COPD receiving LTOT or NIV + LTOT (NIV) were prospectively recruited and completed the SRI, lung function tests, and blood gases. Confirmatory factor analysis for construct validity and internal consistency reliability were calculated. **RESULTS:** One hundred fifty-five subjects were included (113 LTOT, 42 NIV). The Cronbach  $\alpha$  coefficient of the 7 subscales ranged between 0.69 and 0.89 (LTOT) and between 0.79 and 0.93 (NIV), respectively. In both groups, confirmatory factor analysis revealed a one-factor model for the SRI summary scale; in 5 subscales, one- or 2-factor models could be established. Group differences in the SRI subsets were all  $P < .05$  (except for physical functioning) with higher scores in subjects receiving NIV. **CONCLUSIONS:** The SRI showed high reliability and validity in subjects with COPD receiving LTOT. Subjects receiving LTOT had lower SRI scores, indicating a poorer HRQOL compared with subjects with established NIV and LTOT. *Key words:* quality of life; COPD; oxygen inhalation therapy; noninvasive ventilation; chronic air flow obstruction; severe respiratory insufficiency questionnaire (SRI). [Respir Care 2016;61(9):1186–1191. © 2016 Daedalus Enterprises]

## Introduction

Evaluation of health-related quality of life (HRQOL) is an established tool in measuring the burden of disease and

the impact of treatment.<sup>1</sup> Various tools and multidimensional questionnaires (eg, 36-item Medical Outcomes Study Short Form questionnaire or St George Respiratory Ques-

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This study was conducted at the University Hospital Freiburg, Clinic for Pneumology, Germany and Klinik Schillerhöhe, Center for Pulmonology and Thoracic Surgery, Stuttgart-Gerlingen, Germany.

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tionnaire) have been established, but disease specificity is lacking in most cases. The Severe Respiratory Insufficiency Questionnaire (SRI) has been established and validated for the specific assessment of HRQOL in patients with hypercapnic respiratory failure receiving long-term noninvasive ventilation (NIV).<sup>2-7</sup> The SRI has been translated into several languages and has become the standard tool for the assessment of HRQOL in patients receiving long-term NIV.<sup>8</sup> Further details can be adapted from the homepage of the German Society of Pneumology and Mechanical Ventilation (<http://www.pneumologie.de>, Accessed March 16, 2016).

COPD is considered one of the major healthcare burdens worldwide, projected to rank fifth for disability-adjusted life years in 2030 by the World Health Organization.<sup>9</sup> Lung function impairment is poorly reversible; therefore, treatment strategies must be aimed at stabilizing the disease progression and optimizing HRQOL. In advanced COPD, hypoxemic and/or hypercapnic respiratory failure may develop and may be treated with long-term oxygen therapy (LTOT)<sup>10</sup> or NIV in conjunction with LTOT.<sup>11-13</sup> In subjects with COPD receiving NIV and LTOT, the SRI has been established and validated as a disease- and treatment-specific tool for assessment of HRQOL, showing improvements in all subsets following the establishment of NIV.<sup>2,4,7</sup>

However, the HRQOL of patients with COPD receiving LTOT due solely to hypoxemic respiratory failure has not been determined by a disease-specific questionnaire.<sup>4</sup> This observational study is aimed at evaluating HRQOL and examining the validity and reliability of the SRI questionnaire in subjects with COPD receiving LTOT compared with a matched group of subjects with COPD receiving NIV and LTOT (referred to as the NIV group in this work). This study aimed at establishing the validity and reliability of the SRI in subjects with COPD with sole hypoxemic respiratory failure. As a secondary end point, this study aimed at exploring differences in HRQOL in subjects with COPD with sole LTOT treatment compared with subjects with NIV and LTOT treatment. The null hypothesis was defined as no difference in mean scores of the SRI summary scale between both study groups.

## Methods

The study protocol was approved by the institutional ethics committee of the University of Freiburg (Freiburg, Germany) and was performed in accordance with the standards laid down in the Declaration of Helsinki. Written informed consent was obtained from all subjects before the study. The study was registered in the German Clinical Trial Register (DRKS00006067).

## QUICK LOOK

### Current knowledge

The Severe Respiratory Insufficiency Questionnaire (SRI) has been developed and validated previously for the assessment of health-related quality of life in mechanically ventilated subjects. However, it remains unclear whether subjects also suffering from sole chronic hypoxemic respiratory failure with long-term oxygen therapy (LTOT) could also be adequately assessed by the SRI.

### What this paper contributes to our knowledge

This study proved high psychometric properties (reliability and validity) of the SRI in subjects with COPD receiving LTOT. The SRI was also shown to be capable of distinguishing between subjects with COPD receiving LTOT and those receiving long-term noninvasive ventilation with the interesting finding that subjects receiving LTOT had lower SRI scores indicating a poorer health-related quality of life compared with subjects with established long-term noninvasive ventilation.

## Severe Respiratory Insufficiency Questionnaire

The SRI includes 7 subscales with 49 items covering the aspects: respiratory complaints, physical functioning, attendant symptoms and sleep, social relationships, anxiety, psychological well-being, and social functioning. All subscales can be summarized into one summary scale. Subjects were asked to report on the circumstances of the last 2 weeks.<sup>2</sup>

Ratings were done on a 5-point Likert scale with a scaling method that measures either positive or negative responses with written statements graded from “strongly agree” to “strongly disagree.” The score ranges can be reconstructed as values between 0 and 100 on each scale. Higher scores represent better HRQOL.<sup>2</sup> Although the SRI has been shown to be valid for subjects with several conditions leading to chronic hypercapnic respiratory failure,<sup>2</sup> the SRI has also been specifically validated for subjects with COPD.<sup>5</sup>

## Subjects

Subjects with stable COPD according to the Global Initiative for Chronic Obstructive Lung Disease criteria and with chronic respiratory failure were studied and recruited in 2 study centers (University Hospital Freiburg and the academic teaching hospital Klinik Schillerhöhe [Stuttgart-Gerlingen, Germany]).<sup>14</sup> All subjects had to be established

on LTOT or NIV with LTOT for  $\geq 4$  weeks before inclusion and were receiving bronchodilator medication according to current guidelines.<sup>14</sup> The group of subjects receiving NIV with LTOT are referred to as the NIV group. NIV was established with the aim to achieve normal values of  $P_{aCO_2}$  (high-intensity NIV), as described previously.<sup>15,16</sup> NIV was applied nocturnally for  $\geq 6$  h within 24 h. Exclusion criteria included LTOT and/or NIV with LTOT due to other diseases, change of medication and/or exacerbations within the last 4 weeks, malignancies, or language comprehension disorders.

### Subject Recruitment

The out-patient clinic and hospital information systems of the study centers were screened for eligible subjects. Attending subjects were directly included in the study; subjects found in the computer system were called, and, following instruction, the questionnaire was sent and returned by mail.

### Body Plethysmography and Blood Gas Sampling

Body plethysmography was performed in all participants (MasterLab, CareFusion, Hoechberg, Germany) based on current recommendations.<sup>17</sup> Only post-bronchodilation values are reported. Blood gases were collected from the arterialized earlobe (cobas b221; Roche Diagnostics, Grenzach-Wyhlen, Germany). Lung function data are reported from the last visit of the subjects in stable condition in the corresponding hospital. Blood gases for both groups were drawn from the arterialized earlobe at the individual established flow rate of oxygen before potential NIV application.

### Psychometric Properties

The SRI was validated for 2 major psychometric properties in each group. Reliability was measured using the Cronbach  $\alpha$  coefficient for assessment of each subscale and the summary scale internal consistency.<sup>1</sup> Previous studies have validated the SRI for subjects receiving NIV with various diseases and also especially in subjects with COPD receiving NIV.<sup>2,5</sup> For the LTOT group, validity was tested by scrutinizing the scale structure (construct validity); an explorative factor analysis was performed for each subscale and the SRI summary scale by using the principal components factor analysis method. Confirmatory factor analysis was performed to check the results gained by the explorative factor analysis. Further methodological details are reported in our previous study.<sup>4</sup> Retesting of validity in subjects receiving LTOT guarantees, therefore, a high consistency of results and may allow group comparisons.

### Statistics

Data analysis was performed using SAS/STAT 9 (SAS Institute, Cary, North Carolina) and Mplus (Mplus, Los Angeles, California). Sample size determination was calculated as follows: unpaired *t* test, expected difference in SRI summary scale 5 points, estimated SD of SRI summary scale 10 points, power 0.8, 2-sided type-1 error 0.05. For rejection of  $H_0$ , 100 subjects had to be included in the LTOT group and 30 subjects in the NIV group.

Statistical significance was assumed with a *P* value  $< .05$ . Normality of the data was calculated using the Kolmogorov-Smirnov test. The unpaired *t* test (normally distributed data) or Mann-Whitney rank-sum test (non-normally distributed data) was used for comparing both groups. Sex differences between groups were calculated using the Fisher exact test.

Reliability was assessed using the Cronbach  $\alpha$  coefficient to ensure that each rating scale was consistent (internal consistency) using the SAS procedure *proc corr*.<sup>18</sup> Cronbach  $\alpha > 0.7$  was assumed as high internal consistency. Validity was assessed using principal and confirmatory factor analysis by the *proc factor* procedure of SAS and Mplus, respectively.<sup>4</sup>

### Results

Demographic, lung function, and blood gas data are presented in Table 1. Neither group differed in anthropomorphic characteristics, oxygen demand, or duration of NIV or LTOT therapy. Subjects receiving NIV presented a higher degree of air-flow limitation, reduced vital capacity, and higher  $P_{aCO_2}$  values.

### Severe Respiratory Insufficiency Questionnaire Ratings

Ratings of the SRI for each SRI subscale and the summary scale are presented in Table 2 for the entire study group and for each study group, respectively. For the entire study group, the mean values of the SRI varied around the mean. The lowest values were in the subscale physical functioning, whereas the highest rating was in social relationships. In the group comparison, there were statistically higher ratings in the NIV group, except for the SRI physical functioning subscale.

### Reliability

The Cronbach  $\alpha$  exceeded 0.7 in both groups except for in the SRI attendant symptoms and sleep subscale (see Table 3), indicating high internal consistency reliability. Compared with the Cronbach  $\alpha$  of the subscales ranging from 0.69 to 0.89, the summary scale ranged even higher (0.89–0.99).

SEVERE RESPIRATORY INSUFFICIENCY QUESTIONNAIRE IN COPD

Table 1. Demographic and Lung Function Data

Characteristics	Total (N = 155)	LTOT (n = 113)	NIV (n = 42)	P (LTOT vs NIV)
Female/male sex, n	67/88	53/60	14/28	.15
Age, mean ± SD y	62.9 ± 8.1	62.6 ± 8	63.7 ± 8.3	.46
Height, mean ± SD m	1.67 ± 0.09	1.68 ± 0.09	1.7 ± 0.08	.12
Weight, mean ± SD kg	68.4 ± 17.8	67.2 ± 17.5	71.5 ± 18.4	.18
BMI, mean ± SD kg/m <sup>2</sup>	23.9 ± 5.2	23.7 ± 5.1	24.5 ± 5.6	.36
Treatment duration (LTOT + NIV), mean ± SD mo	28.3 ± 25.4	30.2 ± 25.3	22.1 ± 25.7	.13
Oxygen demand, mean ± SD L/min	2.4 ± 1	2.5 ± 0.8	2.4 ± 1.3	.77
Previous exacerbation with hospitalization, mean ± SD weeks	61.4 ± 89.3	61 ± 93.9	62.5 ± 76.5	.93
RV, mean ± SD % predicted	226.4 ± 59	221.1 ± 57.9	241 ± 60.1	.064
FVC, mean ± SD % predicted	56.7 ± 14.8	58.6 ± 15.2	51.7 ± 12.6	.01
TLC, mean ± SD % predicted	114.9 ± 18	114.5 ± 15.6	115.9 ± 23.2	.70
FEV <sub>1</sub> , mean ± SD % predicted	27.6 ± 8.5	28.4 ± 8.3	25.4 ± 8.7	.053
FEV <sub>1</sub> /FVC	36.3 ± 7.9	36.7 ± 8.1	35.3 ± 7.5	.35
pH	7.41 ± 0.03	7.42 ± 0.02	7.41 ± 0.03	.10
P <sub>aCO<sub>2</sub></sub> mm Hg	44.9 ± 6.1	43.9 ± 5.6	47.6 ± 6.7	.01
P <sub>aO<sub>2</sub></sub> mm Hg	68.8 ± 10.3	68.3 ± 9.9	70.2 ± 11.5	.33

All values are presented as mean with standard deviation.  
 BMI = body mass index  
 LTOT = long-term oxygen therapy  
 NIV = noninvasive ventilation  
 RV = residual volume  
 TLC = total lung capacity

Table 2. Severe Respiratory Insufficiency Questionnaire

Scale	Total (N = 155)		LTOT (n = 113)		NIV (n = 42)		P (LTOT vs NIV)
	Mean	SD	Mean	SD	Mean	SD	
SRI_RC	47.6	18.6	46.1	18.1	51.8	19.2	.43
SRI_PF	34.3	19.1	33.6	17.5	35.7	23.1	.30
SRI_AS	57.6	18.8	55.5	18.1	63	19.6	.01
SRI_SR	61.7	21.2	59.8	20.7	66.7	22.1	.037
SRI_AX	42.5	24.5	39.3	23.8	51.2	24.6	<.01
SRI_WB	51.4	21	49.4	19.9	56.6	23.2	.03
SRI_SF	42.4	21.7	40.6	20.9	47.2	23.1	.045
SRI_SS	48.2	16.7	46.3	15.6	53.2	18.6	.01

LTOT = long-term oxygen therapy  
 NIV = noninvasive ventilation  
 SRI = Severe Respiratory Insufficiency Questionnaire  
 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 scale

Table 3. Cronbach α Reliability

Scale	Items	Total (N = 155)		LTOT (n = 113)		NIV (n = 42)	
		n	α	n	α	n	α
SRI_RC	8	151	0.80	110	0.78	41	0.82
SRI_PF	6	154	0.80	112	0.76	42	0.87
SRI_AS	7	149	0.70	107	0.69	42	0.69
SRI_SR	6	143	0.78	105	0.76	38	0.84
SRI_AX	5	148	0.78	110	0.77	38	0.79
SRI_WB	9	148	0.87	109	0.89	39	0.87
SRI_SF	8	131	0.86	98	0.87	33	0.83
SRI_SS	7 subscales	155	0.90	113	0.89	42	0.93

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Validity

Principal confirmatory factor analysis confirmed a one-factor model for the SRI summary scale in the whole group and each subgroup, respectively. One-, 2-, and

4-factor models could be conformed in the SRI subscales in the LTOT and NIV subgroups (see Table 4). In multifactor models, it is suggested that in a subscale, 2 or 4 other subscales may contribute to the reported impairment. Further details are reported in the online

Table 4. Principal Confirmatory Factor Analysis

Scale	Total (N = 155)		LTOT (n = 113)		NIV (n = 42)	
	n	r	n	r	n	r
SRI_RC	4	0.2–0.8	4	0.18–0.74	1	
SRI_PF	2	0.69	2	0.62	1	
SRI_AS	2	0.46	1		2	0.38
SRI_SR	2	0.61	2	0.5	1	
SRI_AX	2	0.6	2	0.56	1	
SRI_WB	2	0.72	2	0.73	2	0.82
SRI_SF	2	0.85	2	0.81	2	0.79
SRI_SS	1		1	1		

LTOT = long-term oxygen therapy

NIV = noninvasive ventilation

SRI = Severe Respiratory Insufficiency Questionnaire

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 scale

supplement (see the supplementary materials at <http://www.rcjournal.com>).

## Discussion

The present study for the first time evaluated the SRI for subjects with COPD with chronic hypoxemic respiratory failure receiving LTOT. The SRI proved high reliability and validity in the LTOT subject group. In comparison with subjects with COPD receiving NIV and LTOT, subjects with sole hypoxic respiratory failure receiving LTOT exhibited a diminished HRQOL.

### Reliability

The Cronbach  $\alpha$  revealed high internal consistency reliability for all subscales in each group (.7–.93) except for the attendant symptoms and sleep subscale (.69). However, these data are comparable and even higher compared with previous studies evaluating the SRI.<sup>2,5,6,19,20</sup> A higher Cronbach  $\alpha$  coefficient in the summary scale might be due to an increased number of analyzed items, as described previously.<sup>4</sup>

### Validity

The high rate of internal correlations with a 4-factor model (respiratory complaints) and 2-factor models for the other subscales in the total study group proves that HRQOL is multidimensional and complex in its assessment.<sup>5</sup> How-

ever, these findings are consistent with the previous validation studies employing principal component factor analysis in which no subscales with a single-factor model could be established in subjects with COPD.<sup>5,19</sup>

Construct validity has repeatedly been shown to be high for the SRI when applied in subjects with chronic hypercapnic respiratory failure<sup>5,6</sup> and is now for the first time also validated with a high validity for subjects with sole hypoxic respiratory failure receiving LTOT.

### HRQOL

The total study group proved to be comparable, regarding disease severity as judged by lung function parameters and HRQOL, with the previous studies evaluating the SRI in subjects with COPD receiving NIV.<sup>4,5,21</sup> As shown in the validation study of the SRI for subjects with COPD receiving NIV<sup>5</sup> and demonstrated in this study for the NIV group, also subjects with COPD receiving LTOT achieved the lowest values in the physical functioning subscale, whereas the social relationships subscale ranked highest. However, subscale ratings were consistently lower in the LTOT group, indicating that HRQOL was more severely affected. This is surprising, since NIV application is known for more pronounced side effects, such as mouth dryness, skin irritations, or ulcers.<sup>21,22</sup> Previous reports have already demonstrated diminished HRQOL in subjects with COPD with chronic hypoxic respiratory failure that is not ameliorated by LTOT application.<sup>10</sup>

Although both groups were matched for anthropometric data, lung function parameters differed in both groups. Of note, the LTOT group had less pronounced air-flow obstruction and hyperinflation but experienced a more diminished HRQOL when compared with the NIV group. However, it may be speculative whether the extent of air-flow obstruction in this group would solely explain the diminished HRQOL or whether the effects of NIV by resting the respiratory muscles and reducing the work of breathing during NIV application may lead to an enhanced HRQOL.<sup>23</sup> Respiratory muscle function impairment is known to occur not only in subjects with COPD with hypercapnic respiratory failure but also in subjects with COPD in early disease stages,<sup>24,25</sup> and NIV application may therefore account for HRQOL benefits. It is of interest that the NIV group still presented with elevated  $P_{aCO_2}$  levels when compared with the LTOT group despite high-intensity NIV, aiming to reduce  $P_{aCO_2}$  to normal values.<sup>15,16</sup> It may be speculated that the differences between both groups could have been even more pronounced if  $P_{aCO_2}$  were completely normalized by NIV application.

### Limitations

The SRI has not been retested against other tools of HRQOL measurement (eg, the 36-item Medical Outcomes

Study Short Form questionnaire or St George Respiratory Questionnaire). However, in previous studies, the SRI has proven to be of higher specificity in evaluating HRQOL in subjects with chronic hypercapnic respiratory failure.<sup>3,21</sup>

This study does not employ a longitudinal follow-up or retest reproducibility assessment of subjects receiving LTOT or NIV. However, a longitudinal design would have been beyond the scope of this work addressing the validation of the already established SRI questionnaire in a distinct subset of subjects with COPD with sole hypoxemic respiratory failure.

The influence of comorbidities, such as arterial hypertension or cardiac insufficiency, on HRQOL in the LTOT or NIV group has not been addressed and may have influenced the results. However, this bias is true for both groups studied, and any possible confounding influence should involve both groups. Furthermore, this study was only powered for detecting differences in the SRI; further confounding variables would have greatly increased the sample size. The confounding effect of comorbidities on HRQOL in subjects with COPD with LTOT or NIV is an important question and should be subject to further studies.

### Conclusions

The SRI proved high reliability and validity in subjects with COPD with chronic hypoxemic respiratory failure receiving LTOT. Subjects receiving LTOT had lower scores in the SRI, indicating a poorer HRQOL compared with subjects with established NIV and LTOT.

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