Dyspnea is associated with overall symptom burden in patients with chronic respiratory insufficiency

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Research note

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Abstract

Objective

Patients with chronic respiratory insufficiency suffer from many symptoms together with dyspnea. We evaluated the association of dyspnea with other symptoms in patients with chronic respiratory insufficiency due to chronic obstructive pulmonary disease or interstitial lung disease.

Results

This retrospective study included 101 patients. Dyspnea was assessed with modified Medical Research Council dyspnea questionnaire (mMRC) and other symptoms with Edmonton Symptom Assessment System (ESAS) and Depression Scale (DEPS). Patients with mMRC 4 (most severe dyspnea) compared to those with mMRC 0–3 reported higher median (IQR) symptom scores on ESAS in e.g. dry mouth (7.0 (4.0–8.0) vs. 3.0 (1.0–6.0), P < 0.001), tiredness (6.0 (3.0–7.0) vs. 3.0 (1.0–5.0), P < 0.001) and anxiety (3.0 (0.0-5.5) vs. 1.0 (0.0–3.0), P = 0.007). Patients with mMRC 4 were more likely to reach the DEPS threshold for depression compared to those with mMRC 0–3 (42.1% vs. 20.8%, P = 0.028). In conclusion, patients with chronic respiratory insufficiency need comprehensive symptom screening with relevant treatment, as they suffer from many severe symptoms worsening with increased dyspnea.

Introduction

Respiratory insufficiency in chronic obstructive pulmonary disease (COPD) or interstitial lung disease (ILD) is a marker of advanced disease and impaired life-expectancy. Patients with advanced COPD or ILD typically suffer from severe dyspnea,[1–3] which increases with approaching death and is associated with impaired quality of life.[4–6] In addition to dyspnea, patients with COPD and ILD suffer frequently from other symptoms, such as fatigue, weight loss, depression and anxiety, further impairing their quality of life.[7] Centers managing chronic respiratory insufficiency in patients with COPD or ILD commonly screen for dyspnea as a target of therapy. However, assessment of other symptoms and their association with increasing dyspnea would be important in order to offer more comprehensive treatment for these patients.

Our aim was to assess how dyspnea on exercise is associated with overall symptom burden in patients with chronic respiratory insufficiency due to COPD or ILD.

Materials And Methods

This was a retrospective study performed in patients with chronic respiratory insufficiency visiting the respiratory insufficiency clinic of Tampere University Hospital between 1.10.2016 and 31.10.2017. All the patients with chronic respiratory insufficiency due to COPD or ILD, who had filled in the modified Medical Research Council (mMRC) dyspnea questionnaire during the routine visits, were included. Patients'

clinical characteristics, diagnoses, mMRC dyspnea scores, Edmonton Symptom Assessment System (ESAS), and Depression Scale (DEPS) were collected from medical records. The Charlson comorbidity index (CCI) was calculated for each patient.[8, 9]

Questionnaires

The mMRC questionnaire asks patients to self-report dyspnea in daily activities. The scale varies from 0 to 4: 0 for “I only get breathless with strenuous exercise”, 1 for “I get short of breath when hurrying on the level or up a slight hill”, 2 for “I walk slower than people of the same age on the level because of breathlessness or have to stop for breath when walking at my own pace on the level”, 3 for “I stop for breath after walking about 100 meters or after a few minutes on the level” and 4 for “I am too breathless to leave the house”.[10, 11]

ESAS is used for assessing symptoms in many advanced disease.[12, 13] Patients rate different symptoms on a numeric rating scale from 0 (no symptoms) to 10 (the worst possible symptoms).[14, 15] We used a modified version with 12 questions covering 11 symptoms and general well-being (0 for the best possible well-being and 10 for the worst possible well-being). The cut-off point for each symptom to be categorized as moderate or severe was ≥ 4.[16–18]

The DEPS is a validated, self-assessed screening tool for depression consisting of 10 questions and provides a total score varying from 1 to 30 points.[19] The suggested cut-offs for depressive symptoms and clinical depression are ≥ 9 and ≥ 12, respectively.[20]

Statistical analysis

The five-step mMRC scale was converted to two-step scale by comparing scores 0–3 and 4 to sort out the group with most difficult dyspnea. Comparisons of different groups were performed by Mann-Whitney U test for continuous variables as the distributions were non-normal based on visual estimation, and Pearson’s chi-square or Fisher’s exact tests for categorical variables. Statistical significance was set as $P < 0.05$. Analyses were performed with IBM SPSS Statistics version 26.0. (IBM Corp, Armonk, NY).

Results

During the follow-up time, 128 patients with COPD or ILD and chronic respiratory insufficiency visited the clinic. The mMRC questionnaire was available in 101 patients, among whom ESAS and DEPS questionnaires were available in 98 and 91 patients, respectively. Reasons for the missing mMRC, ESAS or DEPS questionnaires were unwillingness to answer the questionnaire, inability to complete the questionnaire and technical or unknown reasons.

The patient characteristics are shown in Table 1.

Table 1
Patient characteristics according to the modified Medical Research Council (mMRC) dyspnea scale category.

	All patients	mMRC 0–3	mMRC 4	P value*
Total, n	101	55	46	0.801
Male, n (%)	65 (64.4)	36 (65.5)	29 (63.0)	0.141
Age, years, median (IQR)	75.0 (70.0–81.0)	74.0 (69.0–80.0)	75.5 (71.0-81.5)	0.001
BMI, kg/m^2, median (IQR)	24.5 (21.1–29.3)	27.0 (22.5–33.2)	23.3 (19.3–27.7)	0.104
Smoking status, n (%)				0.366
Never-smoker	9 (8.9)	3 (5.5)	6 (13.0)	0.008
Ex-smoker	89 (88.1)	48 (87.3)	40 (87.0)	0.003
Smoker	4 (4.0)	4 (7.3)	0 (0.0)	0.789
Disease causing the chronic respiratory insufficiency, n (%)	89 (88.1)	47 (85.5)	42 (91.3)	< 0.001
COPD	12 (11.9)	8 (14.5)	4 (8.7)	0.098
Interstitial lung disease	0.90 (0.60–1.25)	0.98 (0.68–1.48)	0.72 (0.46–1.1)	
FEV_1	31.0 (23.0-48.5)	34.0 (27.0–54.0)	25.5 (19.0-44.3)	
Liters, median (IQR)	2.0 (0.0–2.0)	2.0 (0.0–2.0)	2.0 (0.0–2.0)	
% of predicted, median (IQR)	38 (37.6)	9 (16.4)	29 (63.0)	
Charlson Comorbidity Index, median (IQR)	48 (47.5)	22 (40.0)	26 (56.5)	
Need for help with ADL, n (%)				
Died before 31.12.2018, n (%)				

* Between the patients in categories mMRC 0–3 and mMRC 4

BMI, body mass index; ADL, activities of daily living; COPD, chronic obstructive pulmonary disease; FEV_1, forced expiratory volume in one second; IQR, interquartile range

Most (75.2%) of the patients with COPD suffered from severe or very severe COPD.[21] Patients in mMRC category 4 were more likely to need help in activities of daily living and had lower FEV_1 and BMI than those scoring 0–3 in mMRC. The treatment for respiratory insufficiency was oxygen therapy in 81 (80.2%), noninvasive ventilation (NIV) in 10 (9.9%), and both in six (5.9%) patients. Four patients (4.0%) refused to use NIV or oxygen therapy despite chronic respiratory insufficiency. Of the patients, 29 (28.7%) died during the following year after the visit in the clinic.

The symptom severities measured by ESAS in the two mMRC categories are shown in Table 2.

Table 2
Median scores and proportion of patients with at least moderate symptoms (≥ 4 points) in Edmonton Symptom Assessment System (ESAS) questionnaire according to modified Medical Research Council (mMRC) dyspnea scale category.

	All	mMRC 0–3	mMRC 4	P value*
	(n = 98)	(n = 55)	(n = 43)	
ESAS scores†				
Pain at rest				
median (IQR)	0.0 (0.0–3.0)	0.0 (0.0–3.0)	2.0 (0.0–4.0)	0.063
≥ 4, %	21.9	17.0	27.9	0.198
Pain on movement				
median (IQR)	2.0 (0.0–6.0)	2.0 (0.0–4.0)	5.0 (0.0–6.0)	0.068
≥ 4, %	41.7	30.2	55.8	0.011
Tiredness				
median (IQR)	3.0 (2.0–6.0)	3.0 (1.0–5.0)	6.0 (3.0–7.0)	< 0.001
≥ 4, %	49.0	32.1	69.8	< 0.001
Shortness of breath				
median (IQR)	6.0 (3.0–8.0)	4.0 (2.0–6.0)	8.0 (6.0–9.0)	< 0.001
≥ 4, %	72.2	57.4	90.7	< 0.001
Loss of appetite				
median (IQR)	1.0 (0.0–5.0)	1.0 (0.0–3.0)	3.0 (0.0–6.0)	0.001
≥ 4, %	28.9	14.8	46.5	0.001
Nausea				
median (IQR)	0.0 (0.0–1.0)	0.0 (0.0-0.3)	0.0 (0.0–2.0)	0.027
≥ 4, %	6.2	3.7	9.3	0.255
Dry mouth				
median (IQR)	5.0 (2.0–7.0)	3.0 (1.0–6.0)	7.0 (4.0–8.0)	< 0.001
≥ 4, %	60.2	47.3	76.7	0.003
Constipation				
median (IQR)	1.0 (0.0–4.0)	1.0 (0.0–3.0)	2.0 (0.0–6.0)	0.072

	All	mMRC 0–3	mMRC 4	P value*
≥ 4, %	28.9	18.5	41.9	0.012
Depression				
median (IQR)	1.0 (0.0–4.0)	1.0 (0.0–3.0)	2.0 (0.0–5.0)	0.120
≥ 4, %	30.2	22.2	40.5	0.053
Anxiety				
median (IQR)	1.0 (0.0-4.8)	1.0 (0.0–3.0)	3.0 (0.0-5.5)	0.007
≥ 4, %	32.3	22.2	45.2	0.017
Insomnia				
median (IQR)	2.0 (0.0–4.0)	2.0 (0.0–3.0)	3.0 (1.0–7.0)	0.027
≥ 4, %	28.1	18.9	39.5	0.025
Well-being				
median (IQR)	4.0 (3.0–5.0)	3.0 (2.0–5.0)	5.0 (4.0–6.0)	< 0.001
Total score median (IQR)	34.0 (21.0-51.5)	24.0 (15.8–34.8)	44.0 (34.0–63.0)	< 0.001

*Between the patients in categories mMRC 0–3 and mMRC 4

†Data missing in 3 patients: *inability to fill in the questionnaire (2), unwillingness to answer the questionnaire (1)*

IQR, interquartile range

In the total study population, shortness of breath and dry mouth were the most severe symptoms. Compared to patients with mMRC 0–3, those with mMRC 4 reported significantly higher median score in dry mouth, tiredness, loss of appetite, constipation, anxiety, insomnia and impaired well-being. Patients with mMRC 4 reached the threshold for moderate or severe symptom (≥ 4) in shortness of breath, pain on movement, tiredness, and dry mouth more often than patients scoring 0–3 in mMRC. The total ESAS score was also higher in patients in mMRC category 4.

The scores of DEPS in the two mMRC categories are shown in Table 3.

Table 3
Median scores and proportion of patients with at least 9 or 12 points in Depression Scale (DEPS) questionnaire according to modified Medical Research Council (mMRC) dyspnea scale category.

	All	mMRC 0–3	mMRC 4	P value*
	(n = 91)	(n = 53)	(n = 38)	
DEPS score, median (IQR)†	8.0 (3.0–14.0)	6.0 (2.5–10.5)	9.5 (4.8–18.5)	0.025
DEPS ≥ 9 points, n (%)	41 (40.6)	20 (37.7)	21 (55.3)	0.097
DEPS ≥ 12 points, n (%)	27 (26.7)	11 (20.8)	16 (42.1)	0.028

* Between patients in categories mMRC 0–3 and mMRC 4

† Data missing in 10 patients: *inability to complete in the questionnaire (2), unwillingness to answer DEPS questionnaire (3), technical or unknown reason (5)*

IQR, interquartile range

As compared to patients scoring 0–3 in mMRC, those in mMRC category 4 had higher median DEPS scores and more often reached the threshold for clinical depression.

Discussion

We identified a high symptom burden among patients with chronic respiratory insufficiency due to COPD or ILD. Patients with more severe dyspnea and scoring 4 in mMRC had more severe symptoms of pain on movement, tiredness, loss of appetite and dry mouth in addition to impaired well-being measured with ESAS compared to those with mMRC 0–3. Also depression measured with DEPS was more common in patients with mMRC 4 than in patients with mMRC 0–3.

Our finding that patients with chronic respiratory insufficiency suffer from many symptoms in addition to dyspnea is in line with previous studies.[22, 23] There are also earlier studies showing that symptoms are worse in those patients with COPD or ILD who suffer from more severe dyspnea,[1, 24] but this is the first study to assess this specifically in patients with chronic respiratory insufficiency. Many of the symptoms found in this study, such as fatigue, loss of appetite and tiredness, may be consequences of an advanced disease.[25] On the other hand, some of the symptoms, e.g. dry mouth, could be directly associated with dyspnea as a result of mouth breathing and higher frequency of breathing, but also the airflow of oxygen therapy or NIV and used medication, i.e. inhaled anticholinergics, may provoke dryness of mouth.

Scoring at least 12 points in DEPS questionnaire, the cut-off for depression,[20] was significantly more common in patients with mMRC score 4 than in those with mMRC score 0–3. This is in line with previous studies that have focused on the same relation from the opposite perspective and showed higher levels of dyspnea and other symptoms in patients with COPD suffering from anxiety and depression.[26, 27]

Dyspnea has also been associated with higher depression scores in patients with ILD.[28] In a previous study on an unselected population of patients with chronic respiratory insufficiency, one third of the patients suffered from depressive symptoms and a quarter from depression,[29] being less than in the current study focusing only on patients with COPD or ILD causing their respiratory insufficiency. The patients with mMRC score 4 have, by definition, restricted ability to leave home or take part in activities, which may lead to social exclusion and depression. This further underlines the importance of screening depression in patients with chronic respiratory failure due to pulmonary disease to find out those patients, who will benefit from therapy of depression.

Conclusions

In patients with chronic respiratory insufficiency due to pulmonary disease increasing dyspnea is associated with higher overall symptom burden, especially symptoms of pain on movement, tiredness, loss of appetite, dry mouth, anxiety, depression and insomnia. These patients therefore need a comprehensive symptom screening and management including psychosocial support and early integrated palliative care.

Limitations

Due to the retrospective nature of the study, there were some questionnaire data missing, and this probably biased the sample to those with less severe symptoms. This may have underestimated the total symptom burden of the patient sample. Medical treatment of the underlying pulmonary disease and treatment of chronic respiratory insufficiency may affect the relationship between dyspnea and other symptoms, but we were not able to assess this effect in our cross-sectional setting. Further long-term follow-up studies would provide more information on how the relationship between dyspnea and other symptoms develop during the course of the disease.

Abbreviations

ESAS, Edmonton Symptom Assessment System; mMRC, modified Medical Research Council dyspnea questionnaire; DEPS, Depression Scale; IQR, interquartile range; NIV, noninvasive ventilation; COPD, chronic obstructive pulmonary disease; ILD, interstitial lung disease; ADL, activities of daily living; CCI, Charlson comorbidity index; BMI, body mass index; FEV_1, forced expiratory volume in one second; CPAP, continuous positive airway pressure

Declarations

Ethics approval and consent to participate

This study was approved by the Regional Ethics Committee of Tampere University Hospital, Finland (approval code R15180 / December 1, 2015). The informed consent was not obtained due to the nature of the retrospective study based on medical records.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interest.

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Author’s contributions

All authors (HAR, SL-K, JTL, LL) participated in the study design, data analysis literature search, manuscript preparation and approved the final manuscript. HR carried out the data collection.

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