



Symptom variability over the course of the day in patients with stable COPD in Brazil: a real-world observational study

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METHODS S1

Inclusion criteria

- Age ≥ 40 years
- Diagnosis of COPD at least 1 year prior
- Post-bronchodilator FEV₁/FVC ratio < 0.70
- Smoker or former smoker with a ≥ 10 pack-year smoking history
- Stable disease (without exacerbations or changes in maintenance treatment in the last 2 months)

Exclusion criteria

- Diagnosis of sleep apnea syndrome
- Other chronic respiratory diseases or any acute or chronic condition that, in the opinion of the researcher, could limit the ability of the participant to fill out the questionnaires or participate in the study

SYMPTOM QUESTIONNAIRES

Morning symptoms were analyzed with the Early Morning Symptoms of COPD Instrument.⁽²⁷⁾ It was designed to measure three concepts of interest in patients with COPD:

1. occurrence and severity of six morning symptoms ("Did you feel any of the following symptoms this morning?: cough, wheezing, shortness of breath, chest tightness, chest congestion, or difficulty expectorating?") and general severity of symptoms ("If so, what was the intensity of the symptom: mild, moderate, intense, or very intense?"); 2. impact of those symptoms in terms of the limitation of morning activities ("To what extent did the symptoms limit your activities this morning?"); and 3. use of rescue medication ("How many inhalations of the rescue medication did you use this morning?").

Nighttime symptoms were analyzed with the Nighttime Symptoms of COPD Instrument,⁽²⁸⁾ which is based on the Early Morning Symptoms of COPD Instrument⁽²⁷⁾ and measures the following concepts of interest: 1. occurrence and severity of six nighttime symptoms and their intensity; 2. impact of these symptoms in terms of nocturnal awakenings ("Did you wake up last night because of your COPD symptoms?"; and "How many times did you wake up because of your COPD symptoms?"); and 3. use of rescue medication ("How many inhalations of the rescue medication did you use last night?").

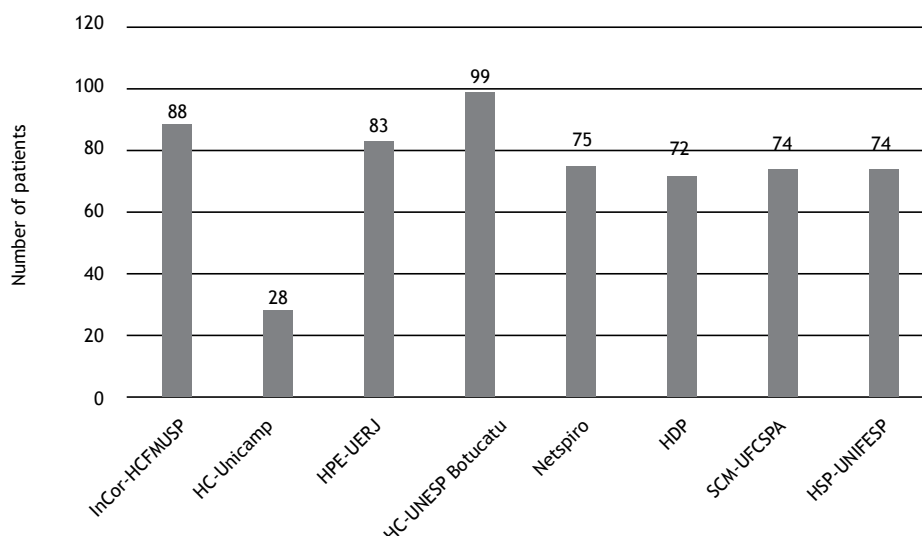


Figure S1. Number of patients evaluated at each research center. InCor-HCFMUSP: Instituto do Coração, hospital das Clínicas, Faculdade de Medicina, Universidade de São Paulo, São Paulo (SP); HC-Unicamp: Hospital das Clínicas, Universidade Estadual de Campinas, Campinas (SP); HPE-UERJ: Hospital Pedro Ernesto, Universidade Estadual do Rio de Janeiro, Rio de Janeiro (RJ); HC-UNESP Botucatu: Hospital das Clínicas de Botucatu, Universidade Estadual Paulista, Botucatu (SP); Netspiro: Clínica Médica Netspiro, São Bernardo do Campo (SP); HDP: Hospital Dia do Pulmão, Blumenau (SC); SCM-UFCSPA: Santa Casa de Misericórdia, Universidade Federal de Ciências da Saúde de Porto Alegre, Porto Alegre (RS); and HSP-UNIFESP: Hospital São Paulo, Universidade Federal de São Paulo, São Paulo (SP).

Table S1. Characteristics of patients classified as having morning and nighttime symptoms, according to definition 2.^{a,b}

Characteristics	Morning symptoms			Nighttime symptoms		
	No (n = 411)	Yes (n = 182)	p	No (n = 422)	Yes (n = 171)	p
Age, years	68.6 ± 8.8	65.8 ± 9.0	< 0.001	68.2 ± 8.9	66.5 ± 9.0	0.039
Male	227 (55.2)	82 (45.1)	0.022	231 (54.7)	78 (45.6)	0.044
BMI, kg/m ²	26.4 ± 5.2	26.4 ± 5.7	0.943	26.4 ± 5.2	26.4 ± 5.5	0.969
Active smoker	57 (13.9)	354 (86.1)	0.096	59 (14.0)	33 (19.3)	0.105
Smoking history, pack-years	51.1 ± 33.5	51.4 ± 31.5	0.907	51.0 ± 32.7	51.6 ± 33.4	0.842
Levels of physical activity			0.934			0.247
Low	158 (38.4)	75 (41.2)		157 (37.2)	76 (44.4)	
Moderate	89 (21.7)	42 (23.1)		95 (22.5)	36 (21.1)	
High	164 (39.9)	65 (35.7)		170 (40.3)	59 (34.5)	
Diagnosis of asthma	69 (16.8)	33 (18.1)	0.689	70 (16.6)	32 (18.7)	0.534
COTE index	1.1 ± 2.1	1.8 ± 2.6	< 0.001	1.1 ± 2.2	1.6 ± 2.5	0.013
mMRC scale	1.9 ± 1.0	2.5 ± 1.1	< 0.001	1.9 ± 1.0	2.5 ± 1.1	< 0.001
Spirometry						
FVC, % of predicted	71.8 ± 16.0	68.7 ± 16.9	0.029	71.5 ± 15.8	69.4 ± 17.7	0.163
FEV ₁ , % of predicted	50.5 ± 17.2	46.8 ± 18.0	0.015	49.9 ± 17.2	48.1 ± 18.3	0.248
FEV ₁ /FVC	51.5 ± 11.6	49.5 ± 10.7	0.056	51.0 ± 11.4	50.5 ± 11.3	0.581
CAT score	14.0 ± 7.1	23.2 ± 8.0	< 0.001	14.0 ± 7.1	23.6 ± 7.8	< 0.001
BODEx index	2.6 ± 1.7	3.4 ± 1.8	< 0.001	2.7 ± 1.7	3.3 ± 1.9	< 0.001
Exacerbations						
Outpatient	0.6 ± 1.1	1.5 ± 3.9	< 0.001	0.7 ± 1.1	1.4 ± 4.0	< 0.001
Inpatient	0.1 ± 0.5	0.2 ± 0.6	0.076	0.1 ± 0.4	0.2 ± 0.6	0.021
E-RS score						
Total	6.3 ± 5.8	14.9 ± 6.9	< 0.001	6.4 ± 5.9	15.1 ± 6.8	< 0.001
Breathlessness domain	4.9 ± 5.4	10.0 ± 5.8	< 0.001	4.9 ± 5.5	10.3 ± 5.6	< 0.001
Cough and sputum domain	1.0 ± 1.3	3.1 ± 2.3	< 0.001	1.1 ± 1.4	3.0 ± 2.2	< 0.001
Chest symptoms domain	0.4 ± 0.7	1.7 ± 1.5	< 0.001	0.4 ± 0.7	1.7 ± 1.5	< 0.001
Severity of morning symptoms score	1.1 ± 1.3	7.4 ± 3.9	< 0.001	1.4 ± 1.9	6.9 ± 4.5	< 0.001
Severity of nighttime symptoms score	1.2 ± 2.0	6.5 ± 4.8	< 0.001	0.8 ± 1.3	7.9 ± 3.8	< 0.001

BMI: body mass index; COTE: (COPD-specific) Comorbidity TEst; mMRC: modified Medical Research Council score; CAT: COPD Assessment Test; BODEx: Body mass index, airflow Obstruction, Dyspnea, and Exacerbations; and E-RS: EXacerbations of COPD Tool (EXACT)-Respiratory Symptoms. ^aDefinition 2: morning symptoms: at least two of the evaluated symptoms classified as being at least moderate or one symptom perceived as being at least intense; nighttime symptoms: any nocturnal awakening or at least two of the evaluated symptoms classified as being at least moderate or one symptom perceived as being at least intense. ^bValues expressed in n (%) or mean ± SD.

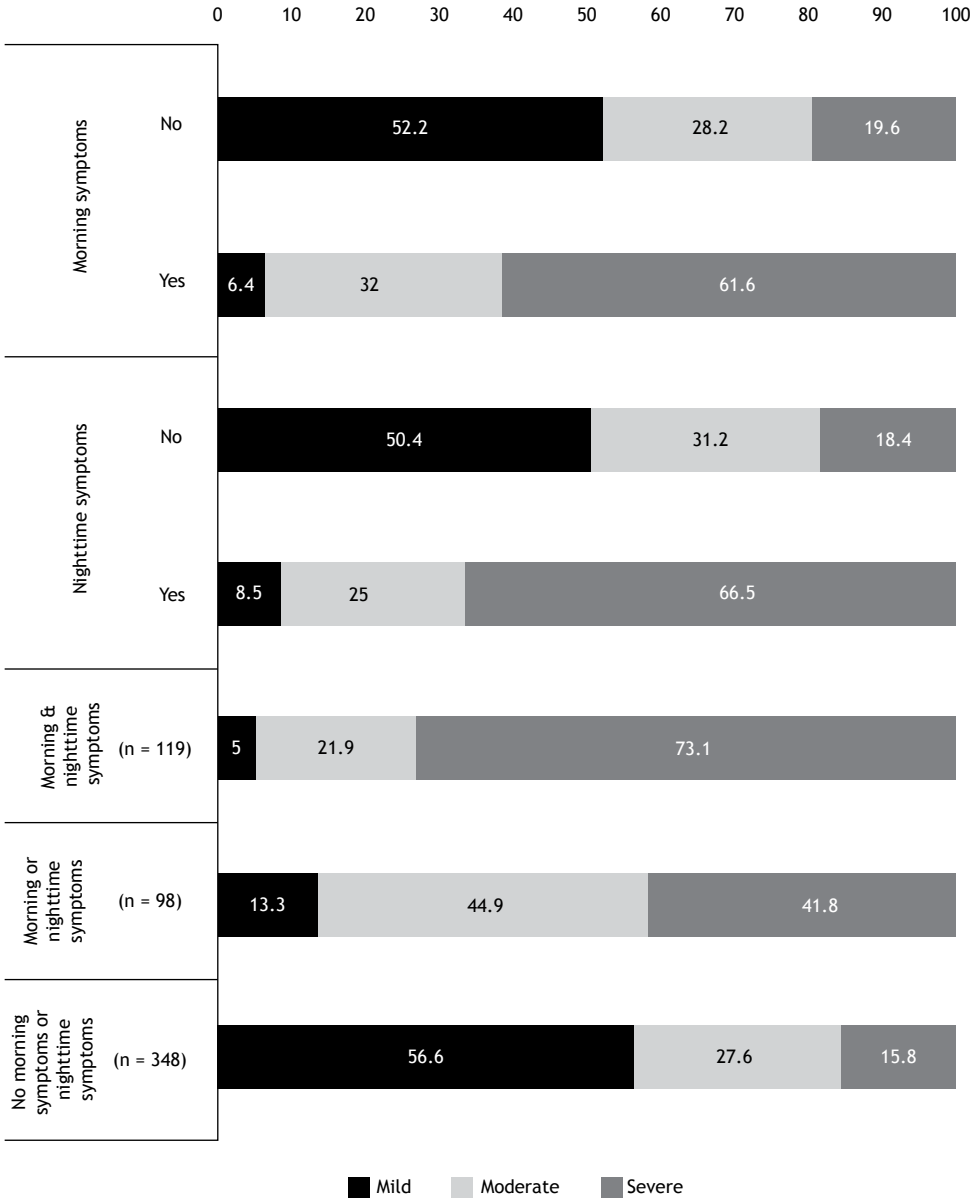


Figure S2. Associations between the intensity of daytime and nighttime symptoms and the prevalence of morning and nighttime symptoms, according to definition 2.^a

^aDefinition 2: morning symptoms: at least two of the evaluated symptoms classified as being at least moderate or one symptom perceived as being at least intense; nighttime symptoms: any nocturnal awakening or at least two of the evaluated symptoms classified as being at least moderate or one symptom perceived as being at least intense.