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High prevalence of respiratory symptoms during air travel in patients with COPD

Anne Edvardsen [a,*], Aina Akerø [b], Jon A. Hardie [c], Morten Ryg [a], Tomas M.L. Eagan [c], Ole H. Skjønsberg [b], Per S. Bakke [c]

[a] Department of Respiratory Physiology, Glittreklinikken AS, Pb 104 Åneby, 1485 Hakadal, Norway
[b] Department of Pulmonary Medicine, Oslo University Hospital, University of Oslo, Kirkeveien 166, 0450 Oslo, Norway
[c] Department of Thoracic Medicine, Haukeland University Hospital, 5021 Bergen, Norway

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KEYWORDS
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Summary
Objective: The reduced pressure in aircraft cabins may cause severe hypoxemia and respiratory distress in patients with chronic obstructive pulmonary disease (COPD). The primary objective of this study was to determine the prevalence of in-flight symptoms in COPD patients and non-COPD subjects, and evaluate associations between these symptoms and pre-flight variables.
Methods: In a cross-sectional study of 391 COPD patients and 184 non-COPD subjects, we recorded lung function, blood gas values, exercise capacity, air travel habits and in-flight symptoms.
Results: Fifty-four percent of the COPD patients had travelled by air the last two years. Hypoxia-related symptoms during air travel were experienced in 25% of the COPD patients and 9% of the non-COPD subjects ($p < 0.001$). After adjusting for smoking status, age and gender, the odds ratio for COPD patients to experience dyspnea or air hunger was 6.6 (95% CI 2.5–17.3, $p < 0.001$) compared to non-COPD subjects. In the COPD patients, in-flight dyspnea or air hunger was strongly associated with pre-flight score on the Medical Research Council (MRC) Dyspnea scale ($p < 0.001$).
Conclusion: COPD patients had significantly increased risk of in-flight dyspnea or air hunger compared to non-COPD subjects. In COPD patients these symptoms were strongly associated with pre-flight MRC Dyspnea score.

* Corresponding author. Tel.: +47 67058289; fax: +47 67075344.
E-mail address: anne.edvardsen@glittreklinikken.no (A. Edvardsen).

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Introduction

Commercial airlines transport nearly two billion passengers every year.[1] At maximal cruising altitude, the cabin pressure is allowed to decrease to the equivalent of 2438 m altitude. This may cause a significant decrease in arterial oxygen tension (PaO_2) in patients with respiratory disease, such as chronic obstructive pulmonary disease (COPD).[1–6]

Previous literature has focused on hypoxemia during air travel,[4,7–11] whereas data on in-flight *symptoms* are limited. Two studies report symptoms in 18% of patients with respiratory disease during air travel.[12,13] These studies lack comparison with healthy subjects. Moreover, it is not known whether the occurrence of in-flight symptoms can be predicted on the basis of pre-flight examination of the patient.

Here we report a study on unselected, well characterized COPD patients and a group of subjects without COPD. The primary objectives were to determine the prevalence and kind of symptoms during air travel in COPD patients and in a community sample, and to assess whether sea-level values of lung function, arterial blood gases, exercise dyspnea, walking distance or desaturation during exercise were related to in-flight symptoms. Secondary aim was to determine air travel habits.

Methods

Study design

The present cross-sectional survey included 433 COPD patients and 233 subjects without COPD from the Bergen COPD Cohort Study (BCCS). The patients were recruited through outpatient clinics from several hospitals in Western Norway, and from three private specialist practices in Bergen (Norway).[14] The control subjects were among earlier participants of a large general population survey from the same area.[15]

All COPD patients had a smoking history of at least 10 pack-years, post-bronchodilator $FEV_1/FVC<0.7$, and $FEV_1<80\%$ predicted. The BCCS baseline visit in 2006 included clinical examination, Medical Research Council (MRC) Dyspnea scale[16] scoring, arterial blood gas sampling, pulse oximetry, and lung function testing. The COPD patients also performed a 6-min walk test (6MWT).[17] At the one-year follow-up visit, we collected questionnaire data on air travel habits and symptoms experienced during air travel within the previous two years. Of the eligible subjects, 575 (86%) completed the questionnaire and were included in the further analyses.

Written informed consent was obtained from all participants. The study was approved by The Regional Committee for Medical Research Ethics.

Questionnaire

The questionnaire included questions on air travel habits, reasons for not flying (if applicable), number and duration of flights within the last two years, pre-flight physician consultation, and in-flight symptoms. Unscheduled use of in-flight oxygen and healthcare within 48 h post-flight were registered. Symptoms were classified as hypoxia related (dyspnea, dizziness, headache, chest pain, air hunger, cough, fainting, palpitations) or hypoxia unrelated (ear pressure, sinus pressure, swollen legs). Wording of the questionnaire and alternatives for answering are given in the Online supplement.

Pulmonary function testing, blood gas measurement and functional walking test

Methods for spirometry and arterial blood gas measurements were performed as previously described.[14] Diffusing capacity of the lung (*D*L,CO) and total lung volumes were measured according to standardised criteria (SensorMedics V_{max} Encore, VIASYS Healthcare Respiratory Technologies, Yorba Linda, USA).[18,19] Reference values were based on equations from the European Community for Coal and Steel, or post-bronchodilator values from Johannessen et al.[20,21] Dyspnea during the 6MWT was measured with the Borg CR10 scale.[17,22] Data for *D*L,CO, blood gases, MRC Dyspnea scale, and 6MWT were missing in 123 (21%), 40 (7%), 33 (6%), 37 (9%) subjects, respectively.

Statistical analysis

Chi-squared tests, two sample *t*-tests and Mann Whitney tests were applied as appropriate. For identifying factors associated with prevalence of symptoms, a logistic regression model was used. Adjustment was made for smoking, age, and gender. A significance level of 5% was considered as statistically significant. The analysis was performed with SPSS version 16 (SPSS Inc., Chicago, IL, USA).

Results

Population characteristics, entire study group

Of the 575 subjects who completed the flight outcome questionnaire, there were 391 COPD patients and 184 non-COPD subjects (Fig. 1). The COPD group included significantly more men, and had a higher mean age (Table 1). According to the GOLD classification, 189 (48%), 141 (36%), and 61 (16%) of the COPD patients were in GOLD stages II, III, and IV, respectively.[23]

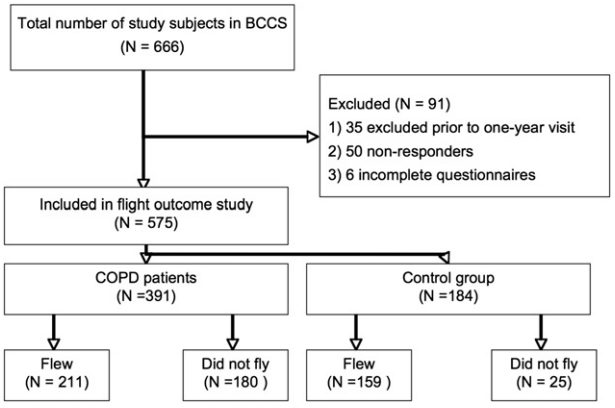

Figure 1 Flow chart of the subject selection. BCCS; Bergen COPD Cohort Study.[14]

Table 1 Characteristics of study population.

	COPD patients	Subjects without COPD	*p*-value
	$n = 391$	$n = 184$	
Sex, M/F	237/154	94/90	0.031
Age, yrs	62.9 (6.8)	53.8 (8.4)	<0.001
BMI, kg/m^2	25.5 (5.6)	26.0 (3.7)	0.196
Smoking habits			<0.001
Never	0	31 (17)	
Former	222 (57)	20 (11)	
Current	169 (43)	133 (72)	
FEV_1, % of predicted	48.9 (14.1)	102.9 (9.4)	<0.001
FEV_1/FVC	0.46 (0.11)	0.79 (0.05)	<0.001
*D*L,CO, % of predicted	58.5 (18.5)	84.0 (11.0)	<0.001
RV/TLC, %	45.2 (10.3)	27.9 (6.8)	<0.001
Blood gases and pulse oximetry			
Pa,O_2, kPa	9.3 (1.1)	10.8 (1.1)	<0.001
Pa,CO_2, kPa	5.3 (0.6)	5.2 (0.4)	<0.001
Sp,O_2, %	95.0 (1.2)	97.5 (2.7)	<0.001
Six-minute walk test			
Distance, m	432 (106)	–	–
End exercise Sp,O_2, %	91.0 (5.8)	–	–
Dyspnea, Borg CR10	4.2 (3.0)	–	–

Data are presented as n (%), mean (SD). FEV_1%predicted: post-bronchodilator forced expiratory volume in 1 s in percent of predicted; FVC: forced vital capacity; *D*L,CO: diffusing capacity of the lung for carbon monoxide; TLC: total lung capacity; RV: residual volume; Pa,O_2: arterial partial pressure of oxygen; Pa,CO_2: arterial partial pressure of carbon dioxide; Sp,O_2: arterial oxygen saturation by pulse oximetry.

COPD patients who did not fly the previous two years

Forty-six percent of the COPD patients did not travel by air, compared to 13.6% of those without COPD ($p < 0.001$). The COPD patients who did not fly were older, had more reduced lung function, lower PaO_2, a more pronounced exercise desaturation and a shorter 6-min walking distance than those who flew (Table 2).

Of the 180 COPD patients who did not fly, 143 (79.4%) had no reason to travel by air during the previous two years, 16 (8.9%) did not dare to fly due to their lung disease, 16 (8.9%) stated other reasons (general fear of flying, economy, and hypersensitivity to perfume), and 5 (2.8%) were advised by a physician or other health professionals not to fly. As for the subjects without COPD, one patient (4.0%) did not fly due to fear of flying, and 24 (96.0%) reported no reason to fly.

Characteristics of COPD and non-COPD subjects who flew

Two-hundred eleven (54.0%) of the COPD patients and 159 (86.4%) of those without COPD flew during the previous two years ($p < 0.001$) (Fig. 2). During this period, 82.5% of the COPD patients had two or more flights, with a most common duration of 3–6 h (Fig. 2). The COPD patients travelled less frequently than those without COPD (median number 2–4 flights vs. more than 4 flights, respectively, $p < 0.001$).

The COPD group had higher mean age and pre-flight MRC Dyspnea score, and significantly lower FEV_1% predicted, *D*L,CO% predicted, Pa,O_2 and Sp,O_2 than the non-COPD subjects (Table 2).

Symptoms

Symptoms during air travel were more frequently experienced in the COPD group (28.4%) than the non-COPD group (16.4%) (OR = 2.0, 95% CI 1.2–3.4, $p < 0.001$) (Fig. 3). One or more hypoxia related symptoms were reported by 52 (24.6%) of the COPD patients and by 14 (8.8%) of the non-COPD subjects (OR = 3.4, 95% CI 1.8–6.4, $p < 0.001$) (Fig. 3). The most frequent hypoxia related symptoms in the COPD group were dyspnea and air hunger, which were significantly higher in the COPD than in the group without COPD ($p < 0.001$) (Table 3). There was no significant difference between the groups with regard to symptoms that were not hypoxia related; ear pressure, sinus pressure, and swollen legs (OR = 0.7, 95% CI 0.3–1.6) (Fig. 3).

After adjustment for confounders (smoking status, age, and gender), patients with COPD had a more than 3-fold higher risk of experiencing hypoxia related symptoms than those without COPD (OR = 3.3, 95% CI 1.6–6.7). For the respiratory symptoms, dyspnea or air hunger, the risk was nearly 7-fold higher (OR = 6.6, 95% CI 2.5–17.3).

Associations between pre-flight parameters and in-flight symptoms

Only the MRC Dyspnea score and exercise Sp,O_2 showed a significant relationship to in-flight dyspnea and air hunger

Table 2 Comparison of COPD patients who flew and did not fly and subjects without COPD who flew.

	COPD patients $n = 391$			Subjects without COPD $n = 184$	
	Flew $n = 211$	Did not fly $n = 180$	P[1)]	Flew $n = 159$	P[2)]
Sex, M/F	124/87	113/67	0.419	80/79	0.106
Age, yrs	61.9 (6.7)	63.9 (6.7)	<0.01	53.6 (8.6)	<0.001
FEV_1,% of predicted	51.6 (12.6)	45.7 (15.2)	<0.01	103.0 (9.2)	<0.001
*D*L,CO, % of predicted	61.4 (17.9)	54.7 (18.6)	0.001	84.3 (11.0)	<0.001
RV/TLC, %	43.1 (9.2)	47.8 (11.0)	<0.001	27.6 (6.8)	<0.001
Blood gases and pulse oximetry					
Pa,O_2, kPa	9.5 (1.0)	9.1 (1.3)	<0.001	10.8 (1.2)	<0.001
Sp,O_2, %	95.5 (2.3)	94.3 (3.0)	<0.001	97.5 (1.2)	<0.001
Six-minute walk test					
Distance, m	459 (99)	401 (106)	<0.001	–	
End Sp,O_2, %	92.0 (4.7)	89.9 (6.6)	<0.001	–	
MRC Dyspnea scale	$n = 194$	$n = 167$	<0.001	$n = 157$	<0.001
Stage 0	35 (18)	24 (14)		132 (84)	
Stage 1	87 (45)	42 (25)		24 (15)	
Stage 2	52 (27)	58 (35)		0	
Stage 3	14 (7)	22 (13)		1 (1)	
Stage 4	6 (3)	2 (1)		0	

Data are presented as n (%) or mean (SD). FEV_1%predicted: forced expiratory volume in 1 s in percent of predicted; *D*L,CO: diffusing capacity of the lung for carbon monoxide; TLC: total lung capacity; RV: residual volume; Pa,O_2: arterial partial pressure of oxygen; Sp,O_2: arterial oxygen saturation by pulse oximetry; MRC: modified Medical Research Council. -:test not performed. p[1)] = between COPD patients who flew and did not fly; p[2)] = between COPD patients who flew and subjects without COPD who flew.

in COPD patients (Table 4). As for *D*L,CO and walking distance, there was a non-significant tendency towards a relationship. A logistic regression model including age, gender, MRC Dyspnea score, exercise desaturation, walking distance, and *D*L,CO was used to study associations between pre-flight variables and symptoms during air travel in patients with COPD. The risk for experiencing dyspnea and air hunger during flight was significantly related to the MRC Dyspnea score. Level 2 or higher on the MRC Dyspnea scale gave an OR 4.8 (95% CI 1.2—19.3) for in-flight dyspnea and air hunger compared to MRC Dyspnea score 0. The OR for experiencing in-flight dyspnea and air hunger was 0.93 (95% CI 0.87—0.99) per year increase in age. No other statistically significant associations were found.

Use of in-flight oxygen and healthcare before and after the flight

Before planning to travel by air, twenty-three (5.9%) of the COPD patients had consulted a physician, while two (1.1%) of those without COPD had a pre-flight physician consultation ($p = 0.007$). Fourteen of the twenty-three COPD patients were advised not to travel. Nine of those patients travelled despite the physicians' advice, and five of them experienced hypoxia related symptoms. Eleven of the 391 COPD patients were on long-term oxygen therapy (LTOT). Two of them flew, both with supplementary oxygen, and none of them reported symptoms during air travel. Two of the 209 patients without LTOT needed unscheduled use of

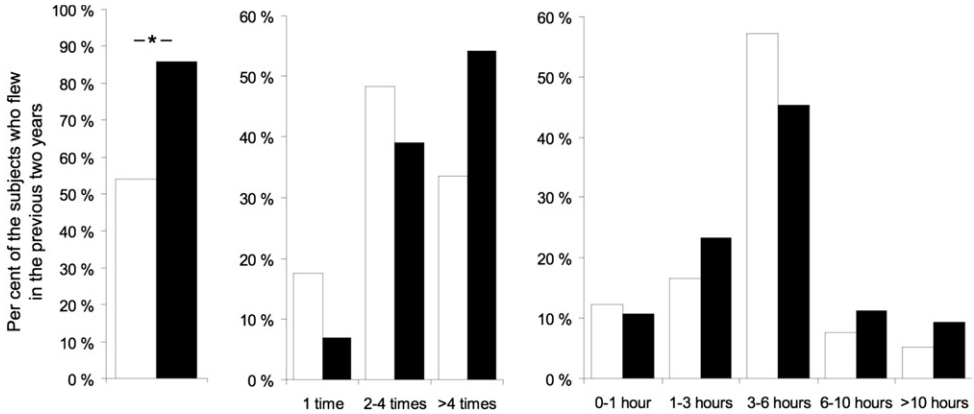

Figure 2 Frequency and duration of flights in COPD patients and subjects without COPD. □: COPD patients, ■: subjects without COPD. *:$p < 0.001$.

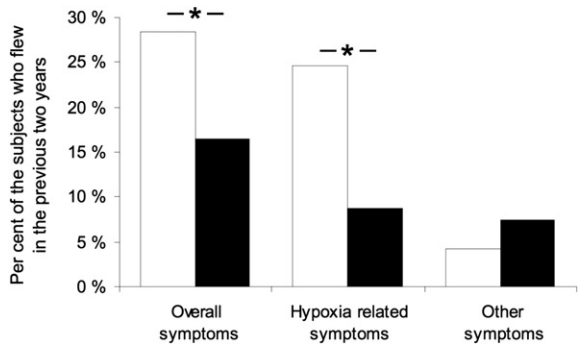

Figure 3 Reported symptoms in COPD patients and subjects without COPD. Values are given in percent of each group. Overall symptoms: all symptoms reported. Hypoxia related symptoms: dyspnea, dizziness, headache, chest pain, air hunger, cough, fainting, and palpitations. Other symptoms (the most frequent; ear pressure, sinus pressure, swollen legs). □: COPD patients, ■: subjects without COPD. *:$p < 0.001$.

supplementary oxygen during flight. The pre-flight Pa,O_2 in these patients were 9.6 kPa and 8.3 kPa, and their FEV_1% pred were 52% and 30%, respectively.

In the time span of 48 h after air travel, nine (4.3%) COPD patients needed unscheduled healthcare, of these, four (1.9%) were hospitalized. Four of the nine patients had hypoxia related symptoms during flight. One of the subjects without COPD was hospitalized after air travel, but the subject in question did not report any symptoms during flight.

Discussion

More than fifty percent of an unselected, western COPD population had travelled by air during the previous two years. One fourth of them experienced hypoxia related symptoms during air travel, compared to nine percent of individuals without COPD. The risk of experiencing dyspnea or air hunger was almost seven times higher in the COPD group than in those without COPD. In patients with COPD, there was a strong association between in-flight dyspnea or air hunger and sea-level MRC Dyspnea score. Desaturation during 6MWT was also related to in-flight symptoms.

In 1991 and 1993 two studies from USA and Britain reported that 44% and 35% of the COPD patients had travelled by air.[12,24] In the present study, 54% of the COPD patients had travelled by air, most of them more than once during the previous two years. Taking into account the high and increasing prevalence of COPD, the number of flight passengers suffering from this disease is considerable and likely to increase further.[25]

To our knowledge, this is the first flight outcome study that compares COPD patients with non-COPD subjects. Our data show a 3-fold increase in hypoxia related symptoms, and a near 7-fold increase in dyspnea and air hunger. Altogether, one fourth of the COPD patients experienced hypoxia related symptoms during flight. We acknowledge that symptoms classified as hypoxia related may have other causes than hypobaric hypoxia. However, the occurrence of other air travel related symptoms like ear pressure, sinus pressure, and swollen legs did not differ between the groups, indicating that the COPD patients were not more prone to report symptoms in general.

Although the COPD population in the present study had a milder disease than in the study by Coker et al, the prevalence of in-flight symptoms was higher. This discrepancy can probably be explained by difference in patient selection.[13] The patients in Coker's study either used supplementary oxygen during flight or, according to a respiratory specialist assessment, were not expected to develop in-flight hypoxemia. Thus, it seems reasonable to assume that the prevalence of symptoms presented in the current study is more representative for an unselected population of flight passengers with COPD.

The difference in symptom prevalence between the COPD and the non-COPD group might have been influenced by difference in age, gender and smoking habits. Correcting for these parameters, however, did not influence the outcome variables significantly.

In previous studies, the majority of COPD patients reporting in-flight symptoms had severe hypoxemia during subsequent testing with Hypoxia-altitude simulation test (HAST).[7,11] Thus, it seems reasonable to assume that the symptomatic patients in the current study suffered from hypoxemia, and that pre-flight testing would have resulted in the use of supplementary oxygen. It should be noted, however, that patients may become severely hypoxemic during hypobaric and normobaric hypoxia without experiencing symptoms.[4,5,7,10,26] Nine patients needed healthcare after arrival, and almost half of those patients had symptoms during flight. It is worth noting that a large proportion of those who travelled against the advice of their physician experienced in-flight symptoms.

There are various methods for predicting in-flight hypoxemia, but as far as we know, prediction of in-flight symptoms

Table 3 Hypoxia related symptoms in COPD patients and subjects without COPD.

	COPD patients $n = 211$	Subjects without COPD $n = 159$	p
Dyspnea	31 (14.7)	2 (1.3)	<0.001
Air hunger	24 (11.4)	4 (2.5)	0.001
Cough	10 (4.7)	3 (1.9)	0.140
Headache	10 (4.7)	6 (3.8)	0.651
Dizziness	8 (3.8)	1 (0.6)	0.084
Palpitations	5 (2.4)	2 (1.3)	0.703
Chest pain	3 (1.4)	0 (0.0)	0.263
Fainting	1 (0.5)	1 (0.6)	~1

Data are presented as n (%).

Table 4 Characteristics of COPD patients who had or did not have dyspnea and air hunger, $n = 211$.

	n	Had dyspnea and air hunger $n = 44$	n	Did not have dyspnea and air hunger $n = 167$	p
Sex, M/F	44	22/22	167	102/65	0.228
Age, yrs	44	61.2 (6.8)	167	62.1 (6.7)	0.885
FEV_1, % of predicted	44	46.2 (13.1)	167	48.9 (12.3)	0.197
*D*L,CO, % of predicted	38	56.8 (15.0)	151	62.5 (18.4)	0.077
RV/TLC, %	37	46.9 (7.5)	144	45.2 (7.9)	0.258
Blood gases and pulse oximetry					
Pa,O_2, kPa	42	9.4 (1.0)	162	9.5 (1.0)	0.746
Sp,O_2, %	42	95.4 (2.4)	157	95.5 (2.3)	0.688
6 min walk test	41		147		
Distance, m		435 (102)		466 (97)	0.077
End exercise Sp,O_2, %		90.7 (5.9)		92.4 (4.3)	0.039
MRC Dyspnea scale	43		151		0.001
Stage 0		3 (7)		32 (21)	
Stage 1		13 (30)		74 (49)	
Stage 2		18 (42)		34 (23)	
Stage 3		5 (12)		9 (6)	
Stage 4		4 (9)		2 (1)	

Data are presented as n (%), and mean (SD). FEV_1% predicted: forced expiratory volume in 1 s in percent of predicted; *D*L,CO: diffusing capacity of the lung for carbon monoxide; TLC: total lung capacity; RV: residual volume; Pa,O_2: partial pressure of oxygen; Sp,O_2: arterial oxygen saturation; MRC: modified Medical Research Council.

has not previously been studied.[2,3,27] Whereas lung function is only weakly correlated with in-flight hypoxemia, exercise related variables may give useful information for pre-flight assessment.[4,10,28] We evaluated the association between these variables and the occurrence of in-flight symptoms. The MRC Dyspnea score at sea-level was strongly associated with in-flight dyspnea and air hunger. This is an interesting and not previously described observation, which may be clinically useful. Desaturation during a 6MWT also showed a significant relationship with in-flight dyspnea and air hunger and corroborates earlier observations of associations between exercise desaturation and in-flight hypoxemia.[28] Inclusion of both MRC Dyspnea score and exercise desaturation may possibly be valuable in pre-flight evaluation algorithms.

It would have been of interest to establish whether in-flight symptoms were associated with development of hypoxemia during HAST, but hypoxic challenge testing was not performed. In addition, the current study has some other limitations. The time between the measurements and air travel could have been up to one year, and possible worsening of the lung disease may have influenced the results. In addition, the severity of the symptoms was not recorded. Also, the design of the study may give recall bias, which might result in under-reporting of symptoms. On the other hand, a design where the participants are asked to record respiratory distress during actual flights might lead to increased symptom awareness, and thereby over-reporting of symptoms. Although age and gender differences between subjects with and without COPD were corrected for in the analyses, these differences could conceivably have influenced the results.

In conclusion, a large proportion of patients with moderate to severe COPD travel by air. One fourth of them reported hypoxia related symptoms during air travel. The COPD patients had a near 7-fold higher risk of experiencing dyspnea or air hunger than those without COPD. The symptoms were strongly associated with MRC Dyspnea score, and an association between exercise desaturation during a 6MWT was also observed. The high prevalence of symptoms seems to justify pre-flight evaluation of COPD patients. The optimal algorithm for this evaluation remains to be established, but our results indicate that a symptom-based approach in the pre-flight evaluation might be useful.

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Conflict of Interest Statement

None.

Supplementary data

The supplementary data associated with this article can be found in the on-line version at doi:10.1016/j.rmed.2010.10.006.

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