CHEST

Original Research

PULMONARY VASCULAR DISEASE

Effects of Commercial Air Travel on Patients With Pulmonary Hypertension

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Background: **Limited data are available on the effects of air travel in patients with pulmonary hypertension (PH), despite their risk of physiologic compromise. We sought to quantify the incidence and severity of hypoxemia experienced by people with PH during commercial air travel.**
Methods: **We recruited 34 participants for a prospective observational study during which cabin pressure, oxygen saturation (Spo_2), heart rate, and symptoms were documented serially at multiple predefined time points throughout commercial flights. Oxygen desaturation was defined as $Spo_2 < 85\%$.**
Results: **Median flight duration was 3.6 h (range, 1.0-7.3 h). Mean ± SD cabin pressure at cruising altitude was equivalent to the pressure 1,968 ± 371 m (6,456 ± 1,218 ft) above sea level (ASL) (maximum altitude = 2,621 m [8,600 ft] ASL). Median change in Spo_2 from sea level to cruising altitude was −4.9% (range, 2.0% to −15.8%). Nine subjects (26% [95% CI, 12%-38%]) experienced oxygen desaturation during flight (minimum Spo_2 = 74%). Thirteen subjects (38%) reported symptoms during flight, of whom five also experienced desaturations. Oxygen desaturation was associated with cabin pressures equivalent to > 1,829 m (6,000 ft) ASL, ambulation, and flight duration (all *P* values < .05).**
Conclusions: **Hypoxemia is common among people with PH traveling by air, occurring in one in four people studied. Hypoxemia was associated with lower cabin pressures, ambulation during flight, and longer flight duration. Patients with PH who will be traveling on flights of longer duration or who have a history of oxygen use, including nocturnal use only, should be evaluated for supplemental in-flight oxygen.** ***CHEST 2012; 142(4):885–892***

Abbreviations: ASL = above sea level; HR = heart rate; PH = pulmonary hypertension; Spo_2 = oxygen saturation; WHO = World Health Organization

Each year, as many as 800 million people travel by commercial aircraft worldwide.[1] To ensure passenger safety on US carriers, the Federal Aviation Administration requires that cabin pressure during flight be maintained at pressures equivalent to an altitude of ≤ 2,438 m (8,000 ft) above sea level (ASL). Passengers with chronic lung disease, however, may experience significant hypoxemia and physiologic stress resulting from changes in cabin pressure even within these mandated limits.[2] Among those with lung disease, people with pulmonary hypertension (PH) are at particularly high risk of adverse effects due to hypoxic pulmonary vasoconstriction.[3] Indeed, even modest levels of hypoxemia experienced during flight could result in further elevation of pulmonary artery pressures, thus leading to increased myocardial oxygen demand and hemodynamic compromise.

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In contrast to the wealth of data available for healthy subjects, studies on the effects of altitude in people with lung disease are relatively sparse and are particularly lacking in PH. Limited studies are small (often < 20 subjects) and focus almost exclusively on patients with COPD.[4,5] The extent to which such results can be extrapolated to other pulmonary conditions is unclear. A single study conducted among patients with restrictive lung disease suggests that they respond differently to air travel than do those with COPD.[6,7] Not only are the data in patients with lung disease limited, but most studies have relied on laboratory-based approaches employing either hypoxia challenge or hypobaric chamber testing.[4] Such controlled experimental conditions fail to reproduce the dynamic and often complex environmental changes to which passengers are exposed during commercial air travel.

To effectively advise patients with PH who anticipate air travel, health providers require a better understanding of the environmental exposures and physiologic stresses experienced by such patients during an actual flight. To address this knowledge gap, we administered a structured flight history survey among 60 patients diagnosed and treated for PH. Among those subjects, we recruited 34 subjects with prearranged travel plans to participate in a prospective observational study during which cabin pressure, oxygen saturation (Spo_2), heart rate (HR), and symptoms were assessed at multiple predefined time points during commercial flights of varying duration.

Materials and Methods

Subject Recruitment and Survey

We invited 60 patients who had an established diagnosis of PH (World Health Organization [WHO] group I or IV) to participate in a survey assessing their personal flight history and eligibility for a prospective observational study on the effects of air travel in PH. Recruitment took place at an international PH conference (June 2010). Those completing the survey were invited to enroll in the prospective study if they had prearranged travel plans on a commercial airline within the next 90 days. Exclusion criteria were a resting Spo_2 by pulse oximetry $< 90\%$ on room air or on oxygen as prescribed, resting HR > 110, inability to walk continuously for 6 min, or any history of a medical emergency occurring during air travel. All survey participants signed a written informed consent form as part of protocols approved by the institutional review board at the University of California San Francisco (IRB No. 10-00061).

Procedures and Measurements

Among 60 subjects who completed the survey, three did not have a prescheduled flight (Fig 1). Of the 57 survey participants eligible to participate in the prospective flight study, 16 declined or were unable to participate because of lack of sufficient study equipment. Two participants with Raynaud phenomenon interfering with Spo_2 readings were excluded. No subjects were precluded from participation based on the exclusion criteria noted previously. Prior to air travel, each subject was supplied with a CMS-50DL fingertip pulse oximeter (FaceLake) and a SUN-203F handheld analog altimeter (Sun Company). All eligible subjects completed a 15-min training session, during which they were instructed on how to use the equipment and then asked to perform a series of sample readings. During the training session, accuracy of the fingertip pulse oximeter was verified for each subject using a Nellcor N20P handheld pulse oximeter (Covidien-Nellcor).

Enrolled subjects were each given a flight log and instructed to perform 10 sets of recordings for Spo_2, HR, and cabin pressure (measured as equivalent altitude ASL) at different stages during the flight: (1) preboarding, (2) seated before take-off, (3) during ascent, (4) at cruising altitude, (5) 15 min after reaching cruising altitude, (6) after walking to the lavatory (performed per protocol), (7) at initial descent, (8) prior to final descent, (9) immediately after landing, and (10) at final destination. Participants were also allowed to perform up to two additional discretionary sets of readings at cruising altitude. To avoid errant Spo_2 readings, subjects were instructed to perform four replicate readings of HR and Spo_2 at 20 s intervals for each set of recordings. In addition, participants were asked to record any symptoms occurring during flight in a corresponding diary. Information on supplemental oxygen use during flight was also noted by the participants. Five of the 39 subjects enrolled did not complete the flight protocol as instructed and, thus, were excluded from further analysis (Fig 1).

Retrospective Chart Review

From the 34 subjects who completed the flight study, we requested all relevant medical records from their treating physicians after participant consent. Clinical data, including hemodynamic measurements at the time of diagnostic right-sided heart catheterization, recent echocardiographic data, and 6-min walk distance, were abstracted from each participant's medical record, when available.

Data Analysis

To calculate a single Spo_2 and HR for each flight stage for each subject, we calculated the mean of four replicate readings. If, however, the most extreme value deviated by > 1 SD from the mean, we discarded that value, and recalculated the mean based on the remaining three measurements. We defined a meaningful

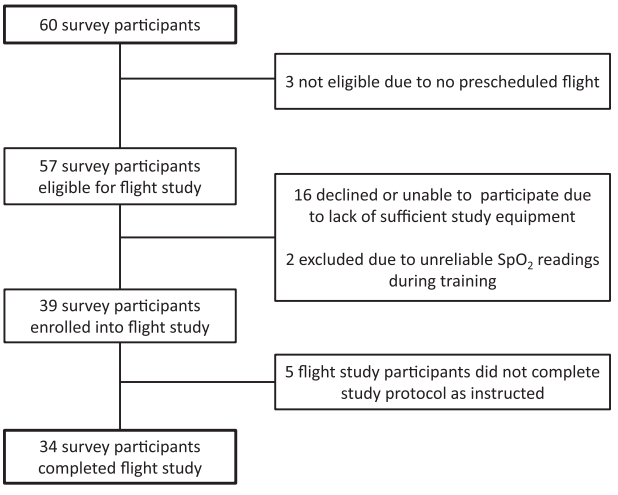

Figure 1. Flow of study enrollment. SpO_2 = oxygen saturation.

desaturation as a mean Spo_2 <85% during any stage of flight. We calculated the 95% CI for the observed proportion of participants with desaturation using the standard sample-size-based equation. Comparisons among groups for continuous variables were performed using *t* tests or a Wilcoxon rank sum test. Comparisons among groups for categorical data were performed using Fisher exact tests. Relationships among continuous variables were modeled using general estimating equations with robust SEs to account for repeated measures. All *P* values presented are for two-tailed probabilities.

Results

The demographic and clinical characteristics of the participants are shown in Table 1. The study population was predominantly female, and the majority had idiopathic pulmonary arterial hypertension. Approximately 90% of the subjects were listed as WHO functional class II-III. All the participants were receiving PH-specific therapy; nearly one-third were receiving continuous prostacyclin infusion. There were no statistically significant differences in demographics or clinical characteristics between subjects who participated in the flight study (n = 34) and those who did not (survey-only participants, n = 26).

Air travel statistics obtained by flight history survey are summarized in Table 2. The median number of round-trip flights in the previous year was two, ranging up to 12 flights. Approximately one-third of the subjects reported being evaluated for flight safety by their treating physician. There was substantial variability in what such safety evaluations entailed, and only one in 10 respondents reported having undergone an altitude simulation test. More than one-third of the subjects reported prior use of oxygen during air travel. Air travel variables for the flight study protocol participants did not differ significantly from those who completed the survey only.

Mean changes in cabin pressure and Spo_2 among the 34 who participated in the flight portion of the study are depicted in Figure 2. Median flight duration

Table 1—*Subject Characteristics*

Characteristic	Total (N = 60)	Flight Participants (n = 34)	Survey-Only Participants (n = 26)
Age, y	50 ± 13	49 ± 11	51 ± 14
Sex			
Female	48 (80)	28 (82)	20 (77)
Race/ethnicity			
White, non-Hispanic	47 (78)	30 (88)	17 (65)
Black	4 (7)	1 (3)	3 (11)
Hispanic	4 (7)	1 (3)	3 (11)
Asian	3 (5)	2 (6)	1 (4)
Other	2 (3)	0 (0)	2 (8)
Cause of pulmonary hypertension			
Idiopathic/heritable pulmonary arterial hypertension	36 (60)	21 (62)	15 (58)
Associated pulmonary arterial hypertension			
Connective tissue disease	10 (17)	6 (18)	4 (15)
Portal hypertension	1 (2)	1 (3)	0 (0)
Congenital heart disease	3 (5)	0 (0)	3 (11)
Drug induced	1 (2)	1 (3)	0 (0)
Other/unsure	4 (7)	2 (6)	2 (8)
Chronic thromboembolic pulmonary hypertension	5 (8)	3 (9)	2 (8)
WHO functional class			
Class I	5 (8)	2 (6)	3 (11)
Class II	30 (50)	16 (47)	14 (54)
Class III	24 (40)	15 (44)	9 (35)
Class IV	1 (2)	1 (3)	0 (0)
Clinical data[a]			
6-min walk distance (n = 21), m	…	453 ± 115	…
Estimated RVSP by echocardiogram (n = 22), mm Hg	…	72 ± 42	…
MPAP by right-sided heart catheterization (n = 19), mm Hg	…	49 ± 15	…
Pulmonary hypertension therapy[b]			
IV/SQ prostacyclin	16 (27)	11 (32)	5 (19)
Inhaled prostacyclin	6 (10)	5 (15)	1 (4)
Endothelin receptor antagonist	27 (46)	16 (47)	11 (44)
Phosphodiesterase-5 inhibitor	36 (61)	21 (62)	15 (60)
Combination therapy (≥ 2 classes)	30 (51)	20 (59)	10 (40)

Data are presented as No. (%) or mean ± SD. MPAP = mean pulmonary artery pressure; RVSP = right-sided ventricular systolic pressure; SQ = subcutaneous; WHO = World Health Organization.

[a]Abstracted from subjects' medical records.

[b]Not reported for one subject.

Table 2—*Flight History Survey Responses*

Characteristic	Total (N = 60)	Flight Participants (n = 34)	Survey-Only Participants (n = 26)
No. round trip flights/y[a]	2 (0-12)	2 (0-12)	2 (0-5)
Duration of flight(s), h	4 (1-10)	4 (1-10)	4 (2-9)
Evaluated for flight safety[a,b]	22 (37)	10 (29)	12 (46)
Oxygen saturation	15 (25)	6 (18)	9 (35)
Arterial blood gas	9 (15)	2 (6)	7 (27)
Predictive equation	2 (3)	1 (3)	1 (4)
Pulmonary function tests	7 (12)	2 (6)	5 (19)
Altitude simulation test	6 (10)	4 (12)	2 (8)
Not sure	1 (2)	0 (0)	1 (4)
Other	3 (5)	2 (6)	1 (4)
History of symptoms during flight[b]	29 (48)	19 (56)	10 (38)
Chest pain	11 (18)	9 (26)	2 (8)
Dyspnea	19 (32)	11 (32)	8 (32)
Light-headedness	9 (15)	6 (18)	3 (12)
Prescribed home oxygen	32 (53)	16 (47)	16 (62)
Continuous oxygen use	7 (12)	2 (6)	5 (19)
Oxygen with activity	7 (12)	2 (6)	5 (19)
Oxygen use at night	18 (30)	12 (35)	6 (23)
Liters of oxygen	3 (2-4)	3 (2-4)	2 (2-3)
Prior use of in-flight oxygen[b]	22 (37)	11 (32)	11 (42)
Compressed oxygen	11 (18)	6 (18)	5 (19)
Portable oxygen concentrator	20 (33)	9 (26)	11 (42)

Data are presented as median (range) or No. (%).

[a]Not reported for one subject.

[b]Responses not mutually exclusive.

was approximately 3.6 h (range, 1.0-7.3 h). Mean cabin pressure at cruising altitude was 1,968 ± 371 m (6,456 ± 1,218 ft) ASL, but in some cases reached as high as 2,621 m (8,600 ft) ASL. Median change in resting Spo_2 from sea level to cruising altitude was −4.9% (range, +2.0% to −15.8%). The lowest reported Spo_2 values occurred after ambulation at cruising altitude, with participants documenting Spo_2 values as low as 74%. Thirteen flight participants (38%) reported the development of symptoms during flight: six (18%), chest pressure/tightness; three (9%), increased dyspnea; four (12%), light-headedness; and two (6%), palpitations. Having any symptoms was not significantly associated with desaturation ($P = .25$).

The relationship between cabin pressure and Spo_2 is shown in Figure 3. Lower cabin pressure (higher altitude) was associated with lower Spo_2 ($r = 0.54$, $P < .0001$) but was not associated with changes in HR ($P = .28$). The minimum altitude at which oxygen desaturation occurred was 1,829 m (6,000 ft), and, on average, oxygen desaturation occurred at 1,971 ± 73 m (6,467 ± 240 ft). Nine flight participants (26% [95% CI, 12%-38%]) experienced one or more oxygen desaturation events of <85%. All desaturations were associated with higher elevation (>1,829 m [6,000 ft] ASL; $P < .001$). Oxygen desaturations occurred more frequently after ambulation (Δ in Fig 3) than at rest ($P = .01$). Six of seven subjects with desaturation after ambulation also experienced low saturations during other flight stages. No medical emergencies or complications requiring intervention were reported by any study participant.

The differences between subjects who experienced an oxygen desaturation during flight and those who did not are shown in Table 3. No statistically significant differences in subject characteristics were observed. Neither resting Spo_2 at sea level nor maximal estimated cabin altitude was predictive of desaturation during flight ($P = .75$ and .61, respectively). Seven of the nine individuals with desaturation had a history of home oxygen use ($P = .05$). Five of these seven individuals had a history of nocturnal oxygen use only and did not use oxygen during their monitored flight. Prior use of in-flight oxygen was associated with the use of oxygen during the flight ($P = .03$, not shown in table) and was also associated with a decreased likelihood of desaturation ($P = .02$). Two subjects who used in-flight oxygen reported desaturations; in both cases, however, events occurred when the flow of oxygen was interrupted (eg, running out of battery supply). Flight duration was longer among those who desaturated compared with those who did not (median, 4.0 h vs 2.5 h; $P = .03$). There was no significant association between clinical variables and desaturation during flight.

Discussion

Among people with PH, we found that hypoxemia with desaturation was relatively common during commercial air travel. Desaturations were associated

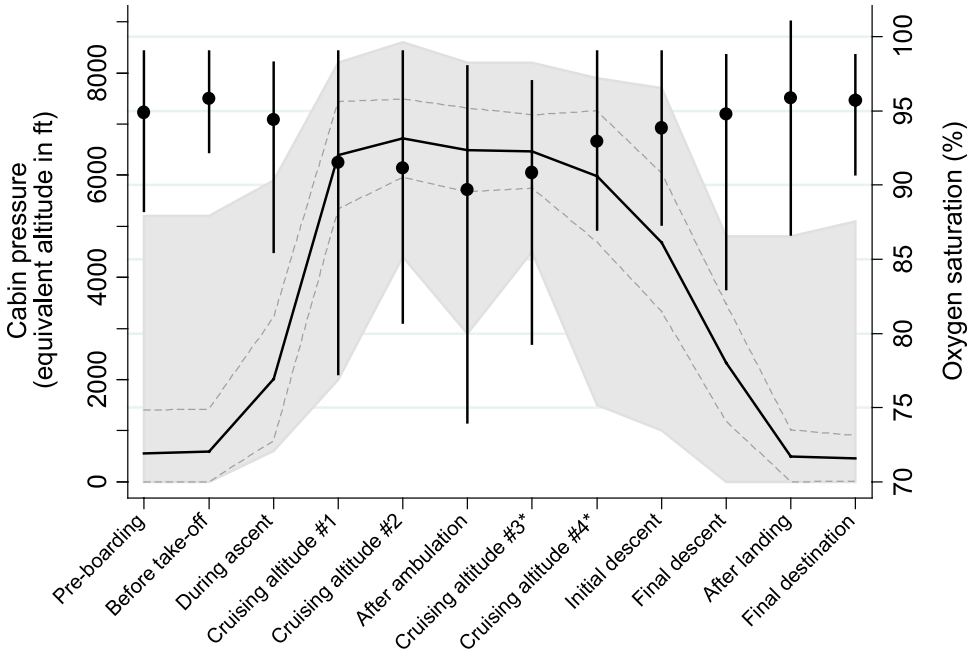

FIGURE 2. Cabin pressure and oxygen saturation measured at various time points during commercial air travel. Solid black line = mean cabin pressure (dashed gray line represents ± 1.0 SD and light gray shading represents range); ● = mean oxygen saturation (vertical bars represent range). *Optional readings.

with lower cabin pressure, ambulation, failure to use oxygen in people with home oxygen (predominantly nighttime-only users), and longer flight duration. In addition, we found that more than one-third of the participants reported symptoms during flight, including chest pressure/tightness, light-headedness, dyspnea, or palpitations. Only a minority of the participants reported being evaluated by their physician for flight safety prior to travel, and there was substantial variability in the type of safety evaluation performed. Despite these findings, all the flight participants arrived at their planned destination without any medical emergencies or complications. Overall, our results indicate that, even among selected patients with PH who choose to fly, oxygen desaturations and symptoms occur frequently and may go unrecognized by health providers.

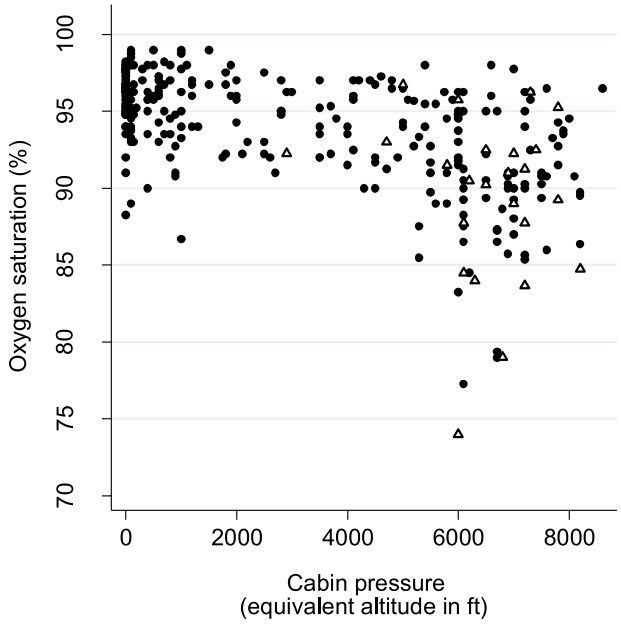

FIGURE 3. Relationship between oxygen saturation and cabin pressure during commercial air travel. ● = measurements performed at rest; Δ = measurements performed immediately after ambulation at cruising altitude.

Our results add to the existing literature on this subject in several ways. Most importantly, our study provides much needed data on the potential adverse effects of air travel among patients with PH, a condition that may be particularly vulnerable to the effects of altitude. Historically, such research has focused almost exclusively on men with COPD and has largely relied on methods to simulate altitude exposure, either by using 15.1% FIO_2 to reproduce a hypoxic environment or by using a hypobaric chamber. Such laboratory-based studies, however, are often limited in duration (< 1 h) and exclude additional stressors encountered during air travel, such as exertion, dehydration, and sleep deprivation.[8-13] Our study contributes new data about an understudied condition that affects a distinctly different patient population composed predominantly of relatively younger women. Moreover, we adopted an underused, "real-world" approach by studying patients during actual flight.

Table 3—*Factors Associated With Desaturation During Commercial Air Travel*

Subject Characteristics	Desaturation[a] (n = 9)	No Desaturation (n = 25)	*P* Value
Age, y	48 ± 3	49 ± 3	.95
Sex, female	8 (89)	20 (80)	1.00
Idiopathic PAH	6 (67)	14 (56)	.70
WHO functional class			.43
I-II	4 (44)	14 (56)	
III	4 (44)	11 (44)	
IV	1 (11)	0 (0)	
PH therapy			
IV/SC prostacyclin	5 (56)	6 (24)	.11
Inhaled prostacyclin	1 (11)	4 (16)	1.00
Endothelin receptor antagonist	4 (44)	12 (48)	1.00
Phosphodiesterase-5 inhibitor	8 (89)	13 (52)	.11
Combination therapy	7 (78)	13 (52)	.25
Flight history			
History of symptoms during flight	3 (33)	16 (64)	.14
Prior use of home oxygen	7 (78)	9 (36)	.05
Prior use of in-flight oxygen	0 (0)	11 (44)	.02
Evaluated for flight safety	3 (33)	7 (28)	1.00
Clinical data			
Resting oxygen saturation, %	95 ± 2	95 ± 3	.75
6-min walk distance,[b] m	419 ± 65	463 ± 27	.47
Right ventricular systolic pressure,[b] mm Hg	73 ± 32	71 ± 9	.94
Flight data			
Duration of flight,[c] median (range), min	240 (135-360)	150 (60-440)	.03
Symptoms during flight	5 (56)	8 (32)	.25
Oxygen use during flight	2 (22)	7 (28)	1.00
Equivalent cabin altitude at cruising altitude, altitude ± SD			
Maximum	7098 ± 817	6914 ± 731	.61
Minimum	5715 ± 409	5857 ± 504	.85
Average	6467 ± 240	6602 ± 322	.77

Data are presented as mean ± SD or No. (%), unless indicated otherwise. PAH = pulmonary arterial hypertension; PH = pulmonary hypertension. See Table 1 for expansion of other abbreviations.

[a]The oxygen saturation nadir among those with a desaturation was 81% ± 4%.

[b]Data from medical records; 6-min walk data available for 21 subjects (n = 5 and n = 16 with desaturation and without). Echocardiographic data available for 22 subjects (n = 4 and n = 18 with desaturation and without).

[c]Not reported for two subjects (n = 9 and n = 23).

Our study adds further evidence that desaturations and symptoms occur commonly during prolonged commercial flights and with associated activity. Prior research by Kelly et al[14] assessed altitude and Spo_2 among 14 patients with COPD during a commercial air flight. They reported a mean in-flight Spo_2 of 86% ± 4% but noted that desaturations were common with activity such as walking to the lavatory, with a mean nadir of 78%. We found that desaturation events occurred variably in this study population, with little association with the clinical and functional measures often used to assess the severity of PH. We observed a mean in-flight Spo_2 of 91% ± 4% while at cruising altitude and a mean nadir of 81% ± 4% in those that manifested desaturation events. The frequency and severity of oxygen desaturation was likely mitigated by the use of supplemental oxygen among some of our participants.

Our data also revealed that, although the mean altitude exposure during flight was only about 1,981 m (6,500 ft) ASL, participants were exposed to a wide range of altitudes, at times exceeding the Federal Aviation Administration limit of 2,438 m (8,000 ft) ASL (a finding also observed by Kelly et al[14]). Although lower cabin pressure (higher altitude) was associated with lower Spo_2, the strength of this relationship was not sufficient to differentiate between those who desaturated during flight and those who did not. Finally, our study provides health providers with unique insight into the travel history of a larger cohort of patients with PH, including frequency of travel, evaluation for flight safety, and type of in-flight oxygen used, which, to our knowledge, has not been reported previously.

Several limitations must be considered when interpreting our data. In our cohort, resting Spo_2 at sea level was not a good predictor of desaturation during flight, a finding that has been observed by others.[6,15,16] As with other studies, our power to detect meaningful differences was limited by our modest sample size and the availability of complete medical records (recent right-sided heart catheterization, echocardiogram, and pulmonary function testing). Although

no individual clinical factor was associated with oxygen desaturation during air travel, participants who used supplemental oxygen nocturnally and did not during air travel represented the majority of desaturation events during our study. Prior use of in-flight oxygen appeared to protect against desaturation. This observation is best explained by the fact that subjects who used oxygen during a prior flight were more likely to have used oxygen during the flight study. The lack of association between desaturation and oxygen use during flight in this study is further confounded by the fact that desaturation events recorded by two subjects using oxygen occurred specifically in settings in which oxygen delivery was temporarily interrupted. Excluding these events, the use of oxygen during flight protected against desaturation. Given the apparent benefit of oxygen among those who used it, individuals with any history of supplemental oxygen use should be evaluated for an oxygen prescription need prior to air travel.

Given the rare nature of the condition, we adopted a novel recruitment strategy by enrolling subjects at the time of an international conference on PH. As a result of this strategy, we recognize that our study cohort is only reflective of a select group of patients and may not be generalizable to all patients with PH. Despite having multiple exclusion criteria intended to maximize research participant safety, these criteria did not account for subject nonparticipation (see Fig 1), nor should they be taken as a basis to recommend against air travel for people with PH. Selection bias has the potential to skew our results insofar as patients attending a conference are likely to be less impaired than those who might not attend. Nonetheless, even in the face of such bias, we found that patients were at risk of desaturation and symptoms during the course of flight. In fact, it is worth noting that a substantial proportion of subjects studied were classified as WHO functional class III, one-third were being treated with prostacyclin infusion, and the majority were on combination PH therapies.

Conclusions

Considering the potential risks of air travel for patients with PH, we recommend that all patients with PH consult their physician prior to air travel. Based on our findings, we suggest that patients with PH who have a history of oxygen use, including nocturnal use only, be evaluated for supplemental in-flight oxygen. Furthermore, in view of the variability in aircraft cabin pressures, the statistically significant association of oxygen desaturation on longer flights, the increased likelihood of ambulation on longer flights, and the efficacy of oxygen in preventing in-flight desaturation, it is prudent to suggest that all patients with PH who will be traveling on flights of greater than 2.5 h in duration be evaluated for in-flight supplemental oxygen. Additional research is needed to assist health providers with more definitive guidance in identifying those patients with PH who are at greatest risk of developing clinically significant events during air travel and to assess their in-flight oxygen requirements.

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