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Pneumothorax after air travel in lymphangioleiomyomatosis, idiopathic pulmonary fibrosis, and sarcoidosis

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Abstract

Background: The prevalence of pneumothorax associated with travel in interstitial lung diseases is unknown. In lymphangioleiomyomatosis, where pneumothorax is common, patients are often concerned about the occurrence of a life-threatening event during air travel. The aim of this study was to determine the prevalence of pneumothorax associated with air travel in patients with lymphangioleiomyomatosis, idiopathic pulmonary fibrosis (IPF), and sarcoidosis. **Methods:** Records and imaging studies of 449 patients traveling to NIH were reviewed. **Results:** 449 patients traveled 1,232 times: 299 by airplane (816 trips) and 150 by land (416 trips). Sixteen of 281 lymphangioleiomyomatosis patients arrived with a pneumothorax. In five, the diagnosis was made by chest roentgenogram, and in 11 by computed tomography scans only. Of the 16 patients, 14 traveled by airplane and two by land. Seven of the 16, one of whom traveled by train, had a new pneumothorax; nine had chronic pneumothoraces. A new pneumothorax was more likely in patients with large cysts and more severe disease. The frequency of a new pneumothorax for lymphangioleiomyomatosis patients who traveled by airplane was 2.9 % (1.1 per 100 flights) and by ground transportation, 1.3 % (0.5 per 100 trips). No IPF (n=76) or sarcoidosis (n=92) patients presented with a pneumothorax. **Conclusions:** In interstitial lung diseases with a high prevalence of spontaneous pneumothorax there is a relatively low risk of pneumothorax following air travel. In lymphangioleiomyomatosis, the presence of a pneumothorax associated with air travel may be related to the high incidence of pneumothorax and not to travel itself.

Key words: Pneumothorax; air travel; interstitial lung diseases

ABBREVIATION LIST:

ANOVA, analysis of variance

CT, computed tomography

DL_{CO}, diffusion capacity for carbon monoxide

FEV₁, forced expiratory volume in the first second

FRC, functional residual capacity

FVC, forced vital capacity

FEV₁/FVC, ratio between FEV₁ and FVC

IPF, idiopathic pulmonary fibrosis

LAM, lymphangioleiomyomatosis

NHLBI, National Heart, Lung, and Blood Institute

NIH, National Institutes of Health

RV, residual volume

RV/TLC, ratio between RV and TLC

SEM, standard error of the mean

TLC, total lung capacity

Introduction

A concern of patients with cystic or bullous lung diseases, especially those associated with spontaneous pneumothorax, is its occurrence during air travel, which could be life-threatening¹. Frequently, because of fear of pneumothorax, patients are reluctant to travel, especially by airplane, which may have a substantial impact on quality of life. Because cabins of commercial aircraft are pressurized only to a barometric pressure equivalent to an altitude of 1,524 to 2,438 meters, during the airplane's ascent the cabin pressure falls, and according to Boyle's law, gas expands within body cavities including lung cysts or non-functioning bullae¹. This change in volume poses a potential risk of pneumothorax for patients with interstitial lung diseases.

Few data are available regarding the prevalence of pneumothorax associated with traveling in patients with interstitial lung diseases. In the case of lymphangioleiomyomatosis (LAM), a disorder affecting women characterized by cystic lung destruction, lymphatic abnormalities, and abdominal tumors (e.g., angiomyolipomas)²⁻⁶, registry data indicate that 4.8% of patients with a history of pneumothorax, experienced one episode related to air travel⁶. A mail survey of 276 LAM patients who traveled by plane 454 times revealed ten events of pneumothorax, eight of which were confirmed by chest roentgenogram⁷. Five of the ten patients had symptoms suggestive of pneumothorax prior to the flights; overall, the incidence of pneumothorax was 2.2 per 100 flights and 4 per 100 patients.

Since 1995, patients with interstitial lung diseases, including LAM, idiopathic pulmonary fibrosis (IPF), and sarcoidosis, traveled to NIH to participate in research studies. The majority of patients traveled by airplane, from within the USA, Canada, and other parts of the world. Patients had chest roentgenograms on admission and most had a computed tomography scan of the thorax on the following day. The purpose of our study was to determine the prevalence of pneumothorax associated with travel in patients with LAM, IPF and sarcoidosis.

Material and Methods

Study Population. The population comprised 281 subjects with LAM (NHLBI Protocol 95-H-0186), 76 patients with IPF (NHLBI Protocols 99-H-0056, 99-H-0068, and 04-H-0211), and 92 patients with sarcoidosis (NHLBI Protocols 82-H-0032, 96-H-0100 and 06-H-0072), who were admitted to the NIH Clinical Research Center, a research hospital where patients are enrolled in research protocols. Protocols allowed us to perform CT scans and chest roentgenograms and publish findings. The chair of the Institutional Review Board (IRB) indicated that additional consent was not required since patients were aware that imaging data would be used for research purposes. Patients travelled to NIH Clinical Research Center between 1999 and 2008. Patient participation was approved by the IRB of the National Heart, Lung, and Blood Institute; written consent was obtained from all subjects.

Study design. Records were reviewed to determine whether there was evidence (chest roentgenogram and/or computed tomography scan) of a pneumothorax. Information was collected regarding mode of travel, grade of disease severity, lung cyst size (computed tomography scan), lung function, and history of pneumothorax and pleurodesis.

Chest Roentgenograms and Computed Tomography (CT) Scans. Radiologic studies were reviewed by a radiologist and a pulmonologist, who were both blinded to subject travel status. For LAM and IPF patients, the severity of lung disease and cyst size were graded semi-quantitatively by CT scans, as previously described^{8,9}. Patients who had one to ten cysts were placed in the category of minimal disease (grade 0). If more than ten cysts were identified, the lungs were divided in three zones (upper, middle, and lower). The extent of involvement in each of the zones was graded according to the percentage of the volume judged abnormal using the following scale: grade I <30% abnormal lung, grade II = 30–60% abnormal, grade III >60% abnormal. CT scans were also assigned scores according to the average cyst size, with size I <0.5 cm, size II = 0.5–1.0 cm, and

size III >1.0 cm. For sarcoidosis, the roentgenologic severity of disease was graded, as is common, from 0-IV¹⁰.

Pulmonary Function Tests. Lung volumes, flow rates and single-breath diffusing capacity for carbon monoxide (DL_{CO}) were measured (SensorMedics Vmax 229, Yorba Linda, CA, USA), according to the American Thoracic Society recommendations¹¹⁻¹³.

Statistical methods. Rate of lung function decline over time for patients with LAM, in whom serial lung function data obtained throughout several years were available, was calculated as previously reported¹⁴. Because in LAM the most useful pulmonary function tests in assessing disease severity and progression are the FEV₁ and DL_{CO}¹⁴, data analysis is restricted to these two parameters. Student's t-test was employed to compare data sets. Analysis of variance (ANOVA) was employed to evaluate lung function data for groups of study subjects. All p-values reported are two-sided and data are shown as means ± SEM.

Results

Demographics. Clinical and physiologic characteristics of the 449 patients are shown in Table 1. All LAM patients were female; 240 were Caucasian, 18 Asian American, 17 African American, four Hispanic, and two from the Pacific Islands. The diagnosis of LAM was established by tissue biopsy in 169 patients and computed tomography findings in 112 patients. One hundred forty patients had a history of pneumothorax and 122 had undergone pleurodesis.

Twenty three of the IPF patients were female and 53 were males. Sixty-seven were Caucasian, four Hispanic, four Asian and two African-American. The diagnosis of IPF was made by biopsy in 62 patients and in 14 by clinical and radiographic data. No patient had a past history of pneumothorax.

Fifty six of the 92 patients with sarcoidosis were male and 36 female. Thirty seven patients were Caucasian, one Hispanic, and 54 were African-American. The diagnosis of sarcoidosis was made by lung, lymph node or skin biopsy in 88 patients and by clinical and radiologic data in four. No patient had a prior history of pneumothorax.

Mode of travel. The 449 patients traveled to the NIH 1,232 times; 299 patients traveled by airplane for a total of 816 trips; 200 travelled by ground for a total of 416 trips. Of the 816 flights, nine were from Europe, eleven from Central and South America, four from the Middle East, six from the Pacific Islands, six from Alaska, 62 from Canada, and 718 from within the USA.

The 281 LAM patients traveled to the NIH 742 times: 77 patients by ground for a total of 206 trips, and 204 by airplane for a total of 536 flights. For the patients with IPF, there were a total of 248 trips; 47 of the 76 patients traveled by airplane (159 trips) and 29 by ground (89 trips). For the sarcoidosis cohort there was a total of 242 visits; 48 traveled by airplane (121 trips) and 44 chose ground travel (121 trips). There was no significant difference in lung function between those who traveled by ground and those who chose air transportation.

Severity of lung disease

Lymphangiomyomatosis. Pulmonary function tests are shown in Table 1. Severe disease by computed tomography (CT scan grade III) was present in 80 patients; 61 had moderate disease (CT scan grade II), 125 had mild disease (CT scan grade I), and 15 had minimal disease (CT scan grade 0); 43 patients had large cysts, 126 had moderate cyst size lesions, and 112 had small cysts.

Idiopathic pulmonary fibrosis. Lung function data are shown on Table 1. CT scans showed that 15 patients had CT scan grade III disease, 25 had grade II disease, 33 had grade I disease and three had grade 0 disease. Fifteen of the 76 patients had lung cysts larger than 1 cm in diameter.

Sarcoidosis. Lung function data are shown in Table 1. Radiologic data showed that 14 patients had stage IV sarcoidosis, 24 had stage III, 28 stage II, 17 stage I, and nine had stage 0¹⁰.

Prevalence of pneumothorax.

Lymphangiomyomatosis. Sixteen patients were diagnosed with a pneumothorax: five by chest roentgenograms and 11 by CT scans only. Of the 16 patients diagnosed with pneumothorax, 14 had traveled by airplane, and two by ground transportation. In nine of the 16 patients the pneumothorax preceded the study-visits. Seven patients, one of whom traveled by car, had evidence of a pneumothorax that was not present at the previous visit. The six patients who traveled by airplane had flights averaging $3,092 \pm 845$ miles, respectively, from Pakistan, Ecuador, Alaska, California, Texas and Idaho. In three of the seven patients the diagnosis was made by chest roentgenogram and in the remaining four by CT scan. In no patient could we ascertain whether the pneumothorax occurred during the trip; patients did not relate respiratory symptoms that suggested the presence of a pneumothorax. Based on these data, we estimated that the frequency of a new pneumothorax, potentially related to flying, in a LAM population of 204 patients was 2.9 % (6/204). Pneumothorax was observed in 1.1% of 536 flights. For the 77 patients who traveled by car or train the corresponding figure was 1.3 % (1/77). Pneumothorax was observed in 0.5% of 206 ground trips. Three of the seven patients with a new pneumothorax required subsequent pleurodesis. In three of the remaining patients, the pneumothorax resolved spontaneously and, in the other patient, was not treated and it became chronic.

Of the nine patients with chronic pneumothorax, eight traveled by airplane. We reviewed their CT scans (mean 3.2 ± 0.5 CT scans per patient), before and after enrollment in the current study. We found that the pneumothoraces had been present for 2.2 ± 0.3 years prior to enrollment (Table 2). We estimated the volume of the pneumothoraces, assuming that they were ellipsoidal in shape and found that during 4.4 ± 0.4 years of follow-up, the pneumothoraces did not increased significantly (82 ± 40 to 107 ± 52 cm³, $p=0.702$).

IPF and Sarcoidosis. No patient with IPF or sarcoidosis had a pneumothorax at the time of admission to the NIH Clinical Research Center.

Characteristics of the LAM patients with pneumothorax. A history of pneumothorax was present in 15 of the 16 patients; 14 had prior pleurodesis. (see Table 2). There was a trend for FEV₁ to be lower in patients who presented with a pneumothorax (acute and chronic) (62±6%) and patients with a history of pneumothorax (66±2%) than in those without a history of pneumothorax (75±2 %). However, as shown in Figure 1 only the difference in FEV₁ between those who had a pneumothorax and those who never had one, was statistically significant (p<0.01, by ANOVA). There were no differences in DL_{CO} among the three patients' groups (Figure 1). The rate of FEV₁ decline tended to be greater (121±21 ml per year) in patients with pneumothorax than that in patients without pneumothorax (80±7 ml per year), but the difference was not statistically significant. Fourteen of the sixteen patients with pneumothorax had predominantly size III cysts (Table 2).

Discussion

In this retrospective study of 449 patients with interstitial lung diseases who traveled to NIH from within the USA, Canada and other parts of the world, we found evidence of recent pneumothorax potentially associated with travel only in patients with LAM. Among 281 LAM patients, seven had evidence of a new pneumothorax. However, because pre-travel radiologic imaging was not available and none of the seven patients with a pneumothorax experienced symptoms of dyspnea or chest pain during or after travel, it was not possible to determine whether or not the pneumothorax occurred prior to or during travelling, i.e., a relationship between the development of the pneumothorax and travel could not be established. A second limitation of our study is that a selection bias may have occurred because patients with more severe disease, potentially at a greater risk of developing a pneumothorax may have avoided enrollment into our protocols. However, the patients whom we identified with pneumothorax had degrees of lung disease severity ranging from minimal to severe (see Table 2).

Assuming that the pneumothoraces were caused by the air travel, the frequency of such an event was low: 1.1 per hundred flights and 2.9 per hundred patients. A common denominator among these patients was a history of pneumothorax; fifteen patients had a history of pneumothorax confirming that a history of pneumothorax appears to be a risk for subsequent pneumothorax ¹⁵.

The fact that many of our patients had prior pleurodesis may have lowered the risk for pneumothorax and influenced our results. However, Chu et al ³, found that 19 of 24 patients with pneumothorax had prior pleurodesis. Also, Almoosa et al ¹⁵, found that chemical and surgical pleurodesis, although reducing the recurrence of pneumothorax was still associated with a recurrence rate of 27 and 32 % respectively.

In contrast with the patients with LAM, none of the patients with IPF or sarcoidosis presented with pneumothorax. This may reflect the fact that compared to LAM, spontaneous pneumothorax is uncommon in IPF and sarcoidosis. Indeed, McCloud et al. ¹⁶ reported a 7.4% prevalence of pneumothorax in 95 patients with IPF, while in patients with sarcoidosis, pneumothorax occurred in only 2.5-2.7% of the patients ¹⁷⁻¹⁹.

Our study is important because it is the first conducted in patients with interstitial lung diseases in which the frequency of pneumothorax associated with traveling, especially flying, included the review of chest X-Rays and CT scans. We are not aware of prior publications where the prevalence of pneumothorax during air travel has been radiologically evaluated either in sarcoidosis or IPF. Further, a prior publication ⁷ addressing this issue in LAM patients, was a mail survey not an actual review of chest X-rays and CT scans.

Our data may be helpful to patients who are considering air travel and assist physicians in counseling such patients. Indeed, we believe that patients with LAM may safely travel by airplane provided that they have no clinical or radiologic evidence of pneumothorax or a history of recent pneumothorax. The relatively low risk of pneumothorax associated with air travel may be even lower

in those patients with small lung cysts, mild disease, and no history of prior pneumothorax. In addition, the possibility that the association between flying and development of a pneumothorax may be coincidental can not be discounted. That is, patients with a history of recurrent pneumothorax are more likely to have them, regardless of travelling by any route or not travelling at all.

In agreement with prior observations⁹, we found that LAM patients who had pneumothoraces tend to have lower FEV₁, and a CT scan pattern consisting of larger cysts scattered throughout relatively normal lung parenchyma. This suggests that presence of larger cysts predisposes both to pneumothorax and greater rates of FEV₁ decline. However, the possibility that a lower FEV₁ be directly related to the pneumothorax can not be excluded.

Finally, an interesting finding of our study is the observation that the size of chronic loculated pneumothoraces did not seem to increase progressively with air travel. This is consistent with the report by Currie et al.²⁰ of two patients with chronic pneumothoraces who were stable for at least one year. Although these are limited data, they do suggest that the presence of a chronic stable pneumothorax in patients with LAM may not pose additional risks for air travel. Further follow-up with additional patients is warranted. A different situation would be that of a patient with a recent pneumothorax. The complete resolution of a pneumothorax for at least a week prior to flying is recommended¹. In patients with LAM, however, our study shows that the presence, or the complete absence, of a pneumothorax can not be ascertained by a chest roentgenogram. It is imperative, as illustrated by the report of Pollock-BarZiv et al.⁷, that patients with symptoms suspicious for pneumothorax undergo appropriate radiologic testing before being approved for air travel. This may require a CT scan of the thorax.

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Figure legend

Figure 1. Percent predicted FEV₁ and DL_{CO}, in LAM patients without a history of pneumothorax (white columns), patients who had prior pneumothorax (crosshatched columns) and patients who presented with pneumothorax (black columns). Patients presenting with a pneumothorax had significantly lower FEV₁ (* p<0.01 by ANOVA) than patients who never had a pneumothorax.

Table 1. Clinical and physiologic data of 449 patients with interstitial lung diseases*

	LAM	IPF	Sarcoidosis
Number	281	76	92
Age (years)	47.7±0.6	62.7±1.1	47.9±0.9
Female/Male	281/0	23/53	36/56
TLC (%)	96.1±0.9	71.5±2.1	86.0±1.5
FRC (%)	98.8±1.4	69.5±2.2	79.8±1.8
RV (%)	114.9 ±2.1	70.1±2.4	86.3±2.4
RV/TLC (%)	50.0±1.0	33.9±0.8	31.7±0.7
FVC (%)	86.3 ±1.1	73.9±2.3	89.0±1.8
FEV ₁ (liters)	70.5±1.6	85.2±2.4	91.9±2.2
FEV ₁ /FVC (%)	60.0±1.0	82.6±0.8	77.2±0.9
DL _{CO} (%)	66.6±1.5	58.2±2.4	73.7±2.2
Ground trips	206	89	121
Air trips	536	159	121
Pneumothorax	16	0	0

* Data are presented as means±SEM. Pulmonary function data, except RV/TLC and FEV₁/FVC ratios, are shown as percent-predicted values. Abbreviations used are: LAM, lymphangioliomyomatosis; IPF, idiopathic pulmonary fibrosis; TLC, total lung capacity; FRC, functional residual capacity; RV, residual volume; RV/TLC, ratio between RV and TLC; FVC, forced vital capacity; FEV₁, forced expiratory volume in the first second; FEV₁/FVC, ratio of FEV₁ to FVC; DL_{CO}, diffusion capacity for carbon monoxide.

Table 2. Characteristics of 16 LAM patients with pneumothorax *

Patient	CT score	Cyst size	Prior pneumothorax /pleurodesis	Type of pneumothorax (duration/years)	Mode of travel	Oxygen use
1	3	III	yes/yes	chronic (3)	train	yes
2	1	II	yes/yes	chronic (3.5)	airplane	no
3	1	III	yes/yes	new	airplane	no
4	2	III	yes/yes	chronic (2)	airplane	yes
5	0	III	yes/yes	new	airplane	no
6	1	III	yes/yes	chronic (4)	airplane	no
7	1	III	yes/yes	chronic (2)	airplane	no
8	2	III	yes/yes	chronic (2)	airplane	yes
9	0	III	yes/yes	new	airplane	no
10	1	III	yes/yes	new	car	no
11	2	III	yes/yes	new	airplane	yes
12	1	III	yes/yes	new	airplane	yes
13	1	III	yes/yes	chronic (2.5)	airplane	no
14	3	III	yes/yes	new	airplane	yes
15	1	III	yes/no	chronic (1)	airplane	no
16	1	II	no/no	chronic (1)	airplane	no

* CT scan –grade 0, one to ten lung cysts; grade I <30% abnormal lung; grade II = 30–60% abnormal; grade III >60% abnormal. Average cyst size: I <0.5 cm, II = 0.5–1.0 cm, III >1.0 cm. The duration of chronic pneumothoraces before patients traveled to the NIH is shown within brackets. Abbreviations: CT, computed tomography.

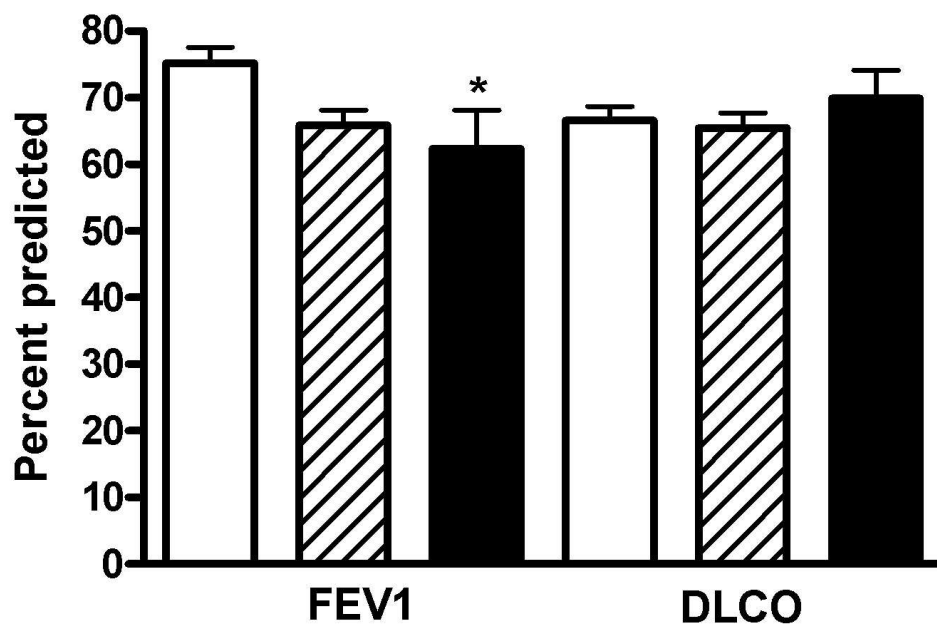


Figure 1. Percent predicted FEV1 and DLCO, in LAM patients without a history of pneumothorax (white columns), patients who had prior pneumothorax (crosshatched columns) and patients who presented with pneumothorax (black columns). Patients presenting with a pneumothorax had significantly lower FEV1 (* $p < 0.01$ by ANOVA) than patients who never had a pneumothorax.
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