Air travel in women with lymphangioleiomyomatosis

Stacey Pollock-BarZiv, Marsha M Cohen, Gregory P Downey, Simon R Johnson, Eugene Sullivan, Francis X McCormack

Background and objective: The safety of air travel in patients with pneumothorax-prone pulmonary diseases, such as lymphangioleiomyomatosis (LAM), has not been studied to any great extent. A questionnaire-based evaluation of air travel in patients with LAM was conducted to determine experiences aboard commercial aircraft.

Methods: A survey was sent to women listed in the US LAM Foundation registry (n = 389) and the UK LAM Action registry (n = 59) to assess air travel, including problems occurring during flight. Women reporting a pneumothorax in flight were followed up to ascertain further details about the incident.

Results: 327 (73%) women completed the survey. 308 women answered the travel section, of whom 276 (90%) had “ever” travelled by aeroplane for a total of 454 flights. 95 (35%) women had been advised by their doctor to avoid air travel. Adverse events reported included shortness of breath (14%), pneumothorax (2%, 8/10 confirmed by chest radiograph), nausea or dizziness (8%), chest pain (12%), unusual fatigue (11%), oxygen desaturation (8%), headache (9%), blue hands (2%), haemoptysis (0.4%) and anxiety (22%). 5 of 10 patients with pneumothorax had symptoms that began before the flight: 2 occurred during cruising altitude, 2 soon after landing and 1 not known. The main symptoms were severe chest pain and shortness of breath.

Discussion and conclusion: Adverse effects occurred during air travel in patients with LAM, particularly dyspnoea and chest pain. Hypoxaemia and pneumothorax were reported. The decision to travel should be individualised; patients with unexplained shortness of breath or chest pain before scheduled flights should not board. Patients with borderline oxygen saturations on the ground should be evaluated for supplemental oxygen therapy during flight. Although many women had been advised not to travel by air, most travelled without the occurrence of serious adverse effects.

Pulmonary lymphangioleiomyomatosis (LAM) is a progressive lung disease that affects young women, and is characterised by diffuse proliferation of abnormal smooth-muscle cells and cystic destruction of the lung parenchyma. LAM occurs in about 30% of women with neurocutaneous syndrome, tuberous sclerosis (TSC) and also in those without heritable disease (sporadic LAM). Clinically, LAM is characterised by progressive dyspnoea with exertion, fatigue, pneumothorax (in as many as 70% of patients), chronic cough, wheezing and chest pain, chylothorax, and an obstructive or mixed restrictive and obstructive pattern on pulmonary function tests. The rate of advancement varies considerably; however, as the disease progresses, patients often require supplemental oxygen. No definitive treatment for LAM currently exists, and lung transplantation remains the only therapeutic option for patients with advanced disease.

The exact prevalence of LAM is not known. In the UK, a minimum prevalence of 1/373 000 women aged 16–65 years was reported, and the minimal prevalence rate worldwide is estimated at 2.6 cases per 1 million women. The incidence of TSC LAM is currently estimated at about 30–40% of women with TSC; TSC occurs as 1/6000 births, suggesting there may be as many as 8000–10 000 women with TSC LAM in North America, and almost 250 000 worldwide.

Rajjoub et al reported on a 21-year-old woman who experienced acute, severe dyspnoea during air travel, requiring immediate transport to hospital where a chest radiograph disclosed a pneumothorax. Further anecdotal reports suggest air travel may predispose patients with LAM to pneumothorax. (Dr McCormack, US LAM Foundation, personal communication, 2003). Therefore, doctors are often asked about the risk to patients when flying. Despite this, there has been little study on the safety of commercial air travel in patients with LAM. During flight, the cabin pressure is generally adjusted to be equivalent to that at an altitude of 1524–2438 m (5000–8000 feet) above sea level, which typically results in a 40% decrease in arterial oxygen pressure (PaO2), from 95 to about 56 mm Hg (from 12.7 to about 7.5 kPa) in healthy people. Clinically significant hypoxia may occur in some patients with reduced baseline PaO2 at sea level. Further, given the sinusoidal shape of the oxyhaemoglobin saturation curve, these individuals may experience precipitous declines in their oxygen levels during flight. The falling PaO2 with increasing altitude may in turn result in several physiological adaptations, including hyperventilation, pulmonary vasoconstriction, altered ventilation/perfusion matching and increased sympathetic tone.

The British Thoracic Society has published recommendations for passengers with respiratory disease planning air travel (http://www.brit-thoracic.org.uk/page246.html). They note that physiological compensations for acute hypoxaemia at rest include mild to moderate hyperventilation and a moderate tachycardia. In those with pulmonary disease, these compensatory mechanisms may be insufficient to offset the risk of hypoxaemia and concurrent adverse effects, especially during air travel. Similarly, the Canadian and American Thoracic Societies have published guidelines for air travel for patients with chronic obstructive pulmonary disease. Both warn of the risks of altitude-related hypoxaemia and provide recommendations for pre-travel assessment. Nonetheless, patients with chronic obstructive pulmonary disease with arterial

Abbreviations: LAM, lymphangioleiomyomatosis; PaO2, arterial oxygen pressure; TSC, tuberous sclerosis

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walking along the aisle) led to severe hypoxaemia in 13 of the
15 patients. The availability of in-flight oxygen may help to alleviate
problems with hypoxaemia in flight. Many commercial airlines
offer in-flight oxygen to passengers, but some smaller airlines
do not. There is usually a substantial fee for oxygen for each in-
flight segment and there are often restrictions on the type of
aircraft that will accommodate the oxygen cylinders. New
Federal Aviation Authority regulations allow certain portable
oxygen concentrators but these are expensive and not yet
practical for most travellers. These factors may limit the
accessibility of air travel to patients with lung disease.

In addition to the risk of hypoxaemia, patients with cystic
lung diseases such as LAM may be particularly vulnerable to
other flight-related complications such as pneumothorax.
During ascent, there is a decrease in cabin pressure and a
consequent increase in the volume of gases contained in closed
body cavities, such as within non-communicating airspaces in
the lungs of patients with LAM. Pressure fluxes during ascent and descent pose the greatest risk for expansion of an existing pneumothorax and, in theory, for the occurrence of a new pneumothorax. The British Thoracic Society air travel guidelines for those with a history of pneumothorax were updated in 2004 (http://www.brit-thoracic.org.uk/page246.html), and include the following recommendations:

- Minimum 1 week after full radiographic resolution on chest x-ray prior to air travel
- Minimum of 2 weeks prior to air travel for traumatic pneumothorax or thoracic surgery
- Patients with current closed pneumothorax should not travel by commercial air
- Risk of recurrence is higher in those with coexisting lung disease up to a year, particularly in those not undergoing surgical treatment of the initial pneumothorax.

Patients with LAM may be at increased risk for pneumothorax in general. Almoosa et al. reported that 66% of patients had at least one spontaneous pneumothorax, and 77% of those had at least one subsequent pneumothorax. Although anecdotal reports of in-flight pneumothorax have led many doctors to advise patients not to fly, no published guidelines exist for air travel in women with LAM (US LAM Foundation, personal communication). Moreover, excess costs and limited access to medical assistance and supplemental oxygen are potential barriers to air travel in these women. To better understand the experiences of air travel and the occurrence of in-flight adverse events, we surveyed a large population of women with LAM.

METHODS

After institutional research ethics board approval was obtained from the University of Toronto and the Trent Multicentre Research Ethics Committee, a survey was mailed to all women registered with the US LAM Foundation (n = 389) and women in the UK LAM Action registry (n = 59) in 2002–3. The US LAM Foundation promotes support, research and awareness of this disease, as well as the procurement of LAM tissue for research. Like the LAM Foundation, the UK LAM database has information on all patients with LAM who complete registration. Patients with all severities of disease are included. Women who were waitlisted for transplant or transplant recipients were excluded as they were surveyed separately. To increase response rate, non-respondents were sent a second survey within 6 weeks, followed a month later by a postcard reminder and a third mailing.

The survey included a letter summarising the study, and women were told that by returning the survey they were providing informed consent to participate. Potential identifying information on the surveys was removed and completed anonymised surveys were sent to the researchers for analyses. Respondents were asked to provide demographic data, time since LAM diagnosis, medical history, use of drugs including progesterone and the use of supplemental oxygen. Participants were provided with a list and asked to check any medical conditions that had been diagnosed and treated. Also, women were asked to rate their degree of shortness of breath on a 1–7 scale, where 1 indicated never short of breath and 7 indicated short of breath all the time (dyspnoea score).

Respondents were also asked to provide detailed information about air travel experiences between 2000 and the fall of 2003, and flights before 2000. Women who did not travel by air were asked to provide detailed information about reasons for not flying (eg, no reason to fly, health professional advice, fear of flying).

Women who had travelled at least once by air were asked to indicate the year of flight, whether the flight duration was greater or lesser than 4 h, and whether or not they had used supplemental oxygen in flight. They were further asked if they experienced symptoms in flight including shortness of breath, unusual fatigue, chest pain, pneumothorax, headache, anxiety, drop in oxygen saturation, difficulty using the in-flight restroom or no symptoms, and whether each of these symptoms existed before getting on the flight. Finally, women who had flown were asked to indicate how they felt about flying again in the future, and under what circumstances they would fly again (eg, with the use of supplemental oxygen, with the provision of medical assistance, on flights of a certain time duration).

Women who reported the occurrence of a pneumothorax in flight were sent a follow-up survey by mail to obtain detailed information regarding the event, including the following questions:

1. Were there any symptoms to suggest that the pneumothorax actually occurred prior to boarding the flight (eg, carrying luggage, etc)?
2. What were the symptoms of the pneumothorax?
3. If you can tell, did the pneumothorax occur during ascent, descent or at cruising altitude?
4. Did you have a chest x-ray or other examination to verify the presence of the pneumothorax?
5. Were you hospitalised?
6. How was the pneumothorax treated?
7. How many pneumothoraces had you experienced prior to the in-flight event?
8. Do you have reactive airway disease/asthma?

Data analysis

Respondent characteristics and background data were reported descriptively using frequencies, central tendency, standard error and percentages. The frequency and percentage of adverse events occurring on flights were also calculated. The risk of pneumothorax during flight was estimated by using the number of women reporting at least one pneumothorax in flight and the estimated number of flights as denominators. All
RESULTS
We received 327 completed surveys (response rate 73%), of which 308 (94%) had complete information on air travel. The mean age of respondents was 46.6 years (table 1). Of the 327 women who completed the survey, 209 (63%) reported at least one pneumothorax in their lifetime. Among respondents, 276 (90%) women indicated that they had flown by commercial aircraft for a total of 454 flights. There was a wide range in dyspnoea scores for both women who flew (mean score 4.2) and those who did not fly (mean score 4.8); however, women who did not fly had slightly worse scores overall (p = 0.02; table 1).

Of the 32 women who indicated that they never flew, eight women had no reason to fly, one followed advice of a health professional not to fly, one was afraid of flying, one did not fly because of fear of LAM complications, three said “other” and 18 women provided no reason. Of the women who never flew, 19 (59%) had a history of pneumothorax although it is not known if this factor contributed to their avoidance of air travel. A total of 97 (35%) respondents in the total group had been advised by their health professional to avoid air travel, of whom 77 (79%) had had a prior pneumothorax.

When asked about flying again in the future, 168 (61%) said yes, without hesitation; 43 (16%) said yes, with supplemental oxygen; 11 (4%) said yes, with oxygen and medical support; 29 (11%) said not unless it was an emergency; and 17 (6%) said absolutely not.

Use of supplemental oxygen
The use of supplemental oxygen increased over time, with 4% of the respondents using oxygen on flights before 1997, and 27% using oxygen on flights between 2000 and 2003. The lack of availability of supplemental oxygen was a deterrent to flying in 22 (9%) women; an additional 23 (10%) indicated that the cost of supplemental oxygen restricted them from flying as much as they would like (fees for supplemental oxygen on domestic US flights range from US$75 to US$150 per flight segment).

Adverse events during flight
Whereas 68.5% of the flights were uneventful with no adverse effects, several women experienced some adverse effect of LAM occurring during air travel was shortness of breath, events that could be attributed to hypoxaemia also occurred during flights, with variable frequency. For example, on all flights, 8% of women reported a drop in oxygen saturation assessed by personal oximeters. Other reported adverse events included chest pain (12%), fatigue or lethargy (11%) and headache (9%). Interestingly, anxiety was the most common adverse effect of flying, reported by women during 22% of flights. Women reporting no adverse effects were significantly less likely to have been evaluated for a lung transplant (\(\chi^2 = 5.5, \text{df} = 1, p = 0.025\)), but we found no differences in chronological age or age at diagnosis.

Pneumothorax
Pneumothorax occurred in 10 women during flight (table 2); mean and median age at the time was 34.5 (range 24–49) years, with two women in their mid-20s, five women in their 30s and two in their 40s. Eight of the 10 women had had at least one prior pneumothorax. Five women experienced a pneumothorax on a flight between 2001 and fall 2003, and five on flights before 2001 (four confirmed by chest x ray in each group). One woman developed a pneumothorax on two separate flights.

Based on these results, the estimate of the risk of a pneumothorax in flight was 2.2% (10 pneumothoraces during 454 flights), and risk estimate of pneumothorax per woman flying was 4% (10 women with pneumothoraces among 276 women who flew).

Follow-up of women with in-flight pneumothoraces
We surveyed 9 of the 10 women (excluding one woman for whom we had no contact information but had some details regarding the pneumothorax incident from the original survey) and received detailed information regarding the event from eight of them (table 3). Eight of the 10 pneumothoraces had been documented by chest x ray. Eight of these women had had a least one previous pneumothorax before the pneumothorax in flight. None knew they had LAM before boarding the flight in which the pneumothorax occurred; all had flown safely before. Four of the women indicated that they also had reactive airway disease or asthma. Five women indicated that they had symptoms that may have suggested the presence of a pneumothorax before boarding the flight, including unusual shortness of breath (n = 5), chest pain (n = 2), burning (n = 1), unusual fatigue (n = 2) and difficulty walking (n = 1). Further, one of these women stated that she was also pregnant during the flight, and had unusual sharp chest pain the morning of the flight (before boarding).

Four women developed symptoms consistent with pneumothorax while in flight or soon after landing. Two women explained that they began to feel symptoms while at cruising.
supplemental oxygen for patients with marginal oxygen saturations before boarding and good clinical health at the time of travel are reasonable prerequisites for safe air travel. Results of prior studies would suggest that symptoms related to reduced blood oxygen content at high altitude would lead to considerable risk of symptoms in patients with hypoxaemia travelling by air. However, medical emergencies during flight in this group were rare, and may have been mitigated by the frequent use of supplemental oxygen during flight.

We observed that anxiety regarding flying is common. Anxiety may exacerbate symptoms of breathlessness, chest pain and nausea, and is extremely important to consider before travel. Reports of anxiety may have been reflective of a generalised fear of flying or in response to being aware of the increased risk of adverse effects due to LAM. Anxiolytics may be considered for women at risk for disabling anxiety during commercial air travel.

In 2001, the US Federal Aviation Authority issued a ruling requiring the inclusion of bronchodilator inhalers and non-narcotic analgesics in medical kits on flights by April 2004. Although these agents may be useful, supplemental oxygen is the cornerstone of treatment for a patient with hypoxaemia who becomes symptomatic during flight. The provision of supplemental oxygen must be arranged before flight. Suspected pneumothorax during flight should be treated with high-flow oxygen by nasal cannula. Unfortunately, definitive medical care including drainage of the pleural space is generally not available before landing. Tension pneumothorax, or pneumothorax occurring in a patient with exhausted pulmonary reserves, can be life threatening. Diversion to the closest airport with medical care should be considered if severe shortness of breath does not resolve with simple interventions such as oxygen or bronchodilator therapy.

It is generally advised in the literature that individuals who have a medical condition that is adversely affected by hypoxia or changes in pressure avoid air travel. A simple test to assess a person’s fitness for air travel is to check his or her ability to walk 46 m (150 feet) without severe dyspnoea or chest pain. However, results were not correlated with disease severity at the time of flight, or with outcome. Recent research has focused on preflight assessment of patients to predict those at risk to develop adverse consequences. Methods include assessment in a hypobaric chamber where arterial blood gas tensions are reactive airway disease, Y/N

**DISCUSSION**

To date, this study is the largest air travel survey of women with LAM, and provides some revealing, albeit retrospective, data on the experiences of air travel in women with LAM. It should be noted, however, that women who were waitlisted for or who had undergone lung transplantation for end-stage disease were excluded from this study, therefore findings may not generalise to women with more advanced disease. Nonetheless, the group of women who travelled by air had, on average, better dyspnoea scores than those who did not, and there was a wide range in values of dyspnoea scores for both women who flew and those who did not. Therefore, the participants include women with LAM who had differing severities of disease, thereby affirming the generalisability of our results.

Although hypoxaemia-related problems such as dyspnoea and chest pain occurred during air travel in women with LAM, these results yield an approximate risk of 2% for pneumothorax. Although the risk of pneumothorax is small, it is more likely in women with a history of pneumothorax, and occurred most frequently in women aged 30–39 years. Interestingly, circumstantial evidence suggested that pneumothorax may have occurred before boarding in half of the cases. Ironically, our data indicate that most of the pneumothoraces occurred in women who did not know they had LAM, and counselling patients with known LAM on the safety of air travel on the basis of these data must be done with caution.

Importantly, adverse events plausibly related to hypoxaemia commonly occurred in women who flew. Women with LAM reported chest pain, fatigue or lethargy, nausea and vomiting, headache and a drop in oxygen saturation during flight. However, these factors alone may not necessarily prevent a patient wishing to travel from doing so. The availability of supplemental oxygen for patients with marginal oxygen saturations before boarding and good clinical health at the time of travel are reasonable prerequisites for safe air travel. Results of prior studies would suggest that symptoms related to reduced blood oxygen content at high altitude would lead to considerable risk of symptoms in patients with hypoxaemia travelling by air. However, medical emergencies during flight in this group were rare, and may have been mitigated by the frequent use of supplemental oxygen during flight.

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**Table 3** Characteristics of women who experienced pneumothoraces in flight (n = 10)

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (years)</th>
<th>Age (years) at Ptx in flight</th>
<th>Prior Ptx, Y/N (n)</th>
<th>Symptoms*</th>
<th>Main symptoms</th>
<th>Treatment</th>
<th>Reactive airway disease, Y/N</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (NR)</td>
<td>39</td>
<td>24</td>
<td>Y (2)</td>
<td>Cruising</td>
<td>Sharp pain, SOB</td>
<td>Chest tube/pleurodesis</td>
<td>Y</td>
</tr>
<tr>
<td>2</td>
<td>29</td>
<td>27</td>
<td>Y (&gt;5)</td>
<td>Soon after landing</td>
<td>Chest pain</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>3</td>
<td>30</td>
<td>28</td>
<td>N</td>
<td>Before</td>
<td>SOB</td>
<td>Chest tubes</td>
<td>N</td>
</tr>
<tr>
<td>4</td>
<td>32</td>
<td>30</td>
<td>Y (1)</td>
<td>Before</td>
<td>Sharp pain, burning, SOB</td>
<td>Hospitalised for observation (also pregnant)</td>
<td>N</td>
</tr>
<tr>
<td>5</td>
<td>36</td>
<td>34</td>
<td>Y (1)</td>
<td>Before</td>
<td>SOB, fatigue</td>
<td>Chest tube</td>
<td>Y</td>
</tr>
<tr>
<td>6</td>
<td>40</td>
<td>35</td>
<td>Y (5)</td>
<td>Before</td>
<td>Chest pain, SOB, nausea, unusual fatigue</td>
<td>Chest tube</td>
<td>NA</td>
</tr>
<tr>
<td>7</td>
<td>56</td>
<td>35</td>
<td>Y (3)</td>
<td>Severe pain soon after landing</td>
<td>Severe chest pain, pressure</td>
<td>Chest tube, pleurectomy</td>
<td>N</td>
</tr>
<tr>
<td>8</td>
<td>52</td>
<td>49</td>
<td>Y (1)</td>
<td>Before</td>
<td>SOB, unusual fatigue</td>
<td>Pleurodesis with talc</td>
<td>Y</td>
</tr>
<tr>
<td>9</td>
<td>50</td>
<td>48</td>
<td>N</td>
<td>Cruising</td>
<td>Sudden sharp pain, followed by pain on inspiration, SOB</td>
<td>Chest pain, SOB</td>
<td>NA</td>
</tr>
<tr>
<td>10 UK</td>
<td>42</td>
<td>35</td>
<td>Y (&gt;2)</td>
<td>NA</td>
<td></td>
<td>Chest pain, SOB</td>
<td>NA</td>
</tr>
</tbody>
</table>

N, no; NA, non respondent; Ptx, pneumothorax; SOB, shortness of breath; Y, yes.

*Symptoms include before boarding, during ascent, at cruising altitude or during descent.
The use of supplemental oxygen during air travel has increased over time. This may in part reflect the progressive nature of the disease, but probably represents increasing recognition of the need for in-flight oxygen and better accessibility. An increase in this percentage could mean that patients with more severe disease are now flying (and using oxygen), whereas such patients may not have flown in the past. Unfortunately, accessibility to and the cost of oxygen was a major barrier to travel in this group of women with LAM. Arranging for the use of supplemental oxygen can be difficult, and even if done in advance, adds to the stress of air travel. The ability to board aircraft with personal oxygen devices would greatly simplify air travel for all patients who require supplemental oxygen while travelling. In 2004, the Federal Aviation Authority released a proposal facilitating the use of certain portable oxygen concentrator devices onboard aircraft, thereby considerably simplifying advanced planning for patients who require supplemental oxygen.

Although this is the largest survey regarding the risk of air travel in women with LAM, the retrospective and cross-sectional nature of this study warrants caution in interpretation. A potential limitation is that we were looking at the incidence of pneumothorax only among patients who flew. There may be important differences between those who flew and those who chose not to. For example, it is possible that more severely ill patients did not fly, and that if they did, their risk might be greater. However, although results are dependent on recollection of experiences, recall of major medical events such as a pneumothorax in flight is likely to be reliable. Moreover, the rarity of the disease complicates the performance of large prospective studies on the experiences of patients with LAM who travel by air, and patient survey reports are the only data that are currently available for making recommendations.

Although the current data do not allow for the identification of individual patients with LAM who may be at increased risk of pneumothorax during flying, patients with LAM should be advised that the presence of any clinical symptoms such as unusual chest pain or shortness of breath before flight should preclude flying. Almost all patients who experienced a pneumothorax in flight had a history of pneumothorax, but as two thirds of patients with LAM experience a pneumothorax at some point in their disease course, this is not a discriminat-
ing feature when assessing risk of pneumothorax during flight. Advanced cystic disease with limited pulmonary reserves may enhance the health consequences of pneumothorax during flight, and should be considered in the risk–benefit analysis before flying. Patients with borderline oxygen saturations on the ground should be evaluated for supplemental oxygen before flying. Patients with borderline oxygen saturations on flight, and should be considered in the risk–benefit analysis at some point in their disease course, this is not a discriminat-

CONCLUSION

Although many women had been advised not to travel by air, most travelled without the occurrence of serious adverse effects. Results of this study provide preliminary information for patients with LAM and healthcare providers advising them; however, a prospective study is warranted on patients at various stages of the disease choosing to fly.

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