Sleep desaturation and its relationship to lung function, exercise and quality of life in LAM

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KEYWORDS
Lymphangioleiomyomatosis (LAM); Polysomnography; Sleep hypoxaemia; Six-minute walk test; Lung function test

Summary
Background: Lymphangioleiomyomatosis (LAM) is characterised by progressive airway obstruction and hypoxaemia in young women. Although sleep may trigger hypoxaemia in patients with airway obstruction, it has not been previously investigated in patients with LAM.

Methods: Consecutive women with lung biopsy proven LAM and absence of hypoxaemia while awake were evaluated with pulmonary function test, echocardiography, 6-min walk test, overnight full polysomnography, and Short Form 36 health-related quality-of-life questionnaire.

Results: Twenty-five patients with (mean ± SD) age 45 ± 10 years, SpO₂ awake 95% ± 2, forced expiratory volume in the first second (median—interquartile) FEV₁(% predicted) 77 (47—90) and carbonic monoxide diffusion capacity, DLCO (%) 55 (34—74) were evaluated. Six-minute walk test distance and minimum SpO₂ (median—interquartile) were, respectively, 447 m (411—503) and 90% (82—94). Median—interquartile apnoea—hypopnoea index was in the normal range 2 (1—5). Fourteen patients (56%) had nocturnal hypoxaemia (10% total sleep time with SpO₂ < 90%), and the median sleep time spent with SpO₂ < 90% was 136 (13—201) min. Sleep time spent with SpO₂ < 90% correlated with the residual volume/total lung capacity ratio (r s = 0.5, p: 0.02), DLCO (r s = −0.7, p: 0.001), FEV₁ (r s = −0.6, p: 0.002). Multivariate linear regression model showed that RV/TLC ratio was the most important functional variable related to sleep hypoxaemia.

Conclusion: Significant hypoxaemia during sleep is common in LAM patients with normal SpO₂ while awake, especially among those with some degree of hyperinflation in lung function tests.
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Introduction

Lymphangioleiomyomatosis (LAM) is a rare and fatal interstitial lung disease, with an over world incidence ranging from 1 to 2.5 cases in 1 million. Although the aetiology is not completely understood, LAM is associated with tuberous sclerosis complex (TSC) 2 gene loss of heterozygosis and consequently loss in the balance between hamartin/tuberin, proteins synthesised by TSC-1/TSC-2 and extremely important in the regulation of cellular proliferation and apoptosis. LAM occurs almost exclusively in women of childbearing age, sometimes with mild symptoms as dry cough and wheezing which may lead to incorrect diagnosis of asthma or COPD in no smoking women. The most typical clinical findings, however, are dyspnoea and recurrent spontaneous pneumothorax. Hypoxaemia during exercise represents one of the first functional impairments in patients with LAM. In addition to physical exercise, sleep may also trigger hypoxaemia. For instance, patients with chronic obstructive pulmonary disease (COPD) with similar pulmonary functional impairments (i.e., hyperinflation and reduced DLCO) may experience hypoxaemia during sleep. Nocturnal hypoxaemia may be associated with sleep efficiency decline, quality-of-life impairments, and development of pulmonary hypertension. Nonetheless, to the best of our knowledge, sleep has not been previously investigated in patients with LAM.

The aim of this study was to evaluate sleep and nocturnal desaturation in patients with LAM and its relation to functional capacity, exercise, and quality-of-life variables in an outpatient population with LAM. We also evaluated nocturnal desaturation and its relation to pulmonary hypertension.

Methods

Study population

Consecutive women with LAM attending the Pulmonary Division of the Hospital das Clinicas, University of Sao Paulo, Brazil, were prospectively screened from January 2005 to May 2008. Eligible subjects had (1) a diagnosis of LAM confirmed by surgical lung biopsy reviewed by pathologists with pulmonary expertise from the Department of Pathology of the University of Sao Paulo Medical School and (2) clinical stability for at least 4 weeks, defined by the absence of hospitalisation, antibiotic use, or increase in dyspnoea. Patients using oxygen due to resting hypoxia (arterial oxygen saturation <90%), presence of chylothorax, or pneumothorax were excluded. Medications and general treatment were not modified during the protocol evaluation that was performed within an interval no longer than 8 weeks. Patients who failed to perform all functional evaluations were further excluded. Written informed consent was obtained from all subjects, and the Institutional Review Board approved the study “Estudo da função pulmonar, sono, exercício e qualidade de vida de pacientes com linfangioleiomiomatose pulmonar” number: 2645.0.015.000-05.

Pulmonary function test (PFT)

Lung volumes, flow rates, and DLCO were measured using a computerised system — Collins Plus Pulmonary Function Testing Systems (Warren E. Collins, Inc., Braintree, MA, USA) according to international guidelines recommendations. Post-bronchodilator volumes were registered. Percentages of predicted values were derived from standard equations. All tests were done in the same respiratory physiology laboratory under a barometric pressure around 695 mm Hg. Baseline dyspnoea index was used to evaluate resting dyspnoea.

Six-minute walk test (6MWT)

Six-minute walk tests (6MWT) were conducted in a 50-m long flat straight corridor in the outpatient clinic of Hospital das Clinicas by a respiratory therapist trained in basic life support. Every patient performed the test according to the ATS recommendations. No supplemental oxygen was used. Distance in metres, continuous oxygen saturation level, ΔSpO2 (Δ: initial SpO2 – final SpO2), and Borg index (limbs and dyspnoea) were registered. Predicted distances were calculated according to reference equations for healthy adults.

Polysonomography

All participants underwent a standard overnight polysomnography (EMBLA; Flaga hf. Medical Devices, Reykjavik, Iceland), including electroencephalography, electrooculography, electromyography, oximetry, nasal thermistor, a cannula for airflow and ribcage and abdominal belts to detect breathing movements as previously described. Apnoea was defined as complete cessation of airflow for at least 10 s. Hypopnoea was defined as a decrease to less than 70% of baseline on either inductance plethysmography channel or nasal cannula airflow, for 10 s or longer and associated with 4% desaturation or more. The apnoea–hypopnoea index (AHI) was calculated as the total number of respiratory events (apnoeas plus hypopnoeas) per hour of sleep. The AHI cut-off for no obstructive sleep apnoea (OSA), mild to moderate OSA, and severe OSA was, respectively, less than 5, 5—15, and more than 15 events per hour of sleep. Other measures included the magnitude of nocturnal oxygen desaturations, expressed by minimum nocturnal SpO2 and total time with SpO2 less than 90% (time SpO2 <90%). Clinically relevant nocturnal desaturation was defined as a fall in SpO2 below 90% for at least 10% of total sleep time.
Echocardiography

Echocardiographic images were obtained in the para-sternal long-axis and short-axis, the apical long-axis, and the apical 4-chamber view, according to current standards, by personnel blinded to the results of the polysomnography and PFT. Left atrial diameter (LAD), left ventricle (LV) end-diastolic internal dimension (LVEDD), LV end-systolic internal dimension, interventricular septal thickness (IVST), and LV posterior wall thickness (LVPWT) were determined from M-mode measurements. In addition, we obtained the LV ejection fraction and LV mass measurements. Echocardiography was performed according to the Brazilian Society of Cardiology Guidelines.\(^{25}\) Ejection fraction lower than 65% and systolic arterial pulmonary pressure higher than 40 mm Hg were considered abnormal.

Questionnaires

Each subject completed the Short Form 36 (SF-36)\(^ {26,27}\) questionnaire measuring generic health-related quality of life (HRQL); the baseline dyspnoea and Borg index (BDI) measuring basal and exercise shortness of breath, respectively,\(^ {20,28}\) Epworth Sleepiness Score\(^ {29}\) and Berlin\(^ {30}\) measuring excessive daytime somnolence and risk to OSA, respectively.

Analysis

Continuous variables are presented as mean (SD) or median/interquartile range (IQR), and categorical variables are presented as frequency (percentage) except where stated. To investigate the possible association between oxygen desaturation during sleep and functional variables determined while awake, Spearman correlation coefficients were calculated between time \(\text{SpO}_2 < 90\%\) on PSG with functional parameters while awake, including PFT and 6MWT variables. Differences across groups were compared using the Wilcoxon Rank Sum test where distribution was skewed. Stepwise multiple logistic regressions were used to select the significant predictors for oxygen desaturation. Model assumptions were assessed by residual plots. Data were analysed with statistical software (SPSS 14.0; SPSS; Chicago IL). All \(p\) values are two-tailed, and values <0.05 are considered statistically significant.

Results

Demographic and functional characteristics of the population

Thirty women were initially evaluated. Five were excluded because they did not fulfil biopsy review criteria \((n = 2)\), were using continuous oxygen therapy due to awake hypoxaemia \((n = 1)\), and failed to perform all tests \((n = 2)\). Therefore, a total of 25 patients completed the protocol (Fig. 1). The time lag between LAM diagnosis and study evaluation was 2.6 ± 0.8 years. The demographic and functional variables, including pulmonary function test and 6MWT of the population studied are presented in Table 1. At the time of the study, all but three patients were being treated with anti-hormonal therapy (GnRH analogue), which lead to a state of chemical menopause. Patients did not have hypoxaemia while awake (Table 1), due to the study design, and the baseline dyspnoea index was in the normal range [median: 25–75%, interquartile: 3 (2–4)]. As expected, pulmonary function tests revealed an obstructive pattern with reductions in predicted \(\text{FEV}_1\) and \(\text{DL}_{CO}\). At the end of the 6MWT, median/IQR Borg dyspnoea was 3 (2–4.5), and 11 patients had developed \(\text{SpO}_2 < 90\%\) (mean ± SD − minimal 6MWT \(\text{SpO}_2\) 77 ± 7%).

![Figure 1: Awaken stage.](https://example.com/figure1.png)
Polysomnography findings are summarised in Table 2. Generally, sleep efficiency, median apnoea—hypopnoea index (AHI), and AHI in REM were in the normal range. Four patients had an AHI $>5$ events/h (mean $\pm$ SD — AHI $10.2 \pm 4.9$). Despite the absence of hypoxaemia awake and the absence of significant sleep apnoea disorder, patients frequently had oxygen desaturation (Table 2). While ventilation and oxygen saturation remained stable during most of the slow wave sleep phase (S3–S4), desaturation was much more common during REM sleep, with irregular ventilatory pattern, especially during clusters of eye movements. Figs. 1–5 represent the most common polysomnography pattern observed among this set of patients with LAM. Based on oxygen saturation, patients were stratified into nondesaturators and desaturators during sleep (Table 3). Nondesaturators and desaturators were similar regarding age and BMI and had a slightly lower SpO2 while awake with no statistical significance. In contrast, desaturators had significantly lower FEV1, DLCO, final SpO2 in 6MWT, and a higher RV/TLC ratio.

### Table 1: Baseline patient characteristics of the population studied.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Median (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>45 (35–60)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>24 (19–35)</td>
</tr>
<tr>
<td>FEV1 (% predicted)</td>
<td>77 (47–90)</td>
</tr>
<tr>
<td>FVC (% predicted)</td>
<td>87 (76–99)</td>
</tr>
<tr>
<td>FEV1/FVC (% predicted)</td>
<td>77 (52–82)</td>
</tr>
<tr>
<td>RV/TLC (% predicted)</td>
<td>102 (92–137)</td>
</tr>
<tr>
<td>DLCO (mL/min/mm Hg) (% predicted)</td>
<td>55 (34–74)</td>
</tr>
<tr>
<td>Awaken resting SpO2 (%)</td>
<td>95 (94–96)</td>
</tr>
<tr>
<td>Distance walked 6MWT (m)</td>
<td>447 (411–503)</td>
</tr>
<tr>
<td>Distance walked 6MWT (% predicted)</td>
<td>72 (62–81)</td>
</tr>
<tr>
<td>Minimum SpO2, 6MWT (%)</td>
<td>90 (82–94)</td>
</tr>
<tr>
<td>Baseline dyspnoea index</td>
<td>3 (2–4)</td>
</tr>
</tbody>
</table>

BM1: body mass index; FEV1: forced expiratory volume in one second; FVC: forced vital capacity; FEV1/FVC: ratio between FEV1 and FVC; RV: residual volume (L); TLC: total lung capacity (L); RV/TLC: ratio between RV and TLC; DLCO: diffusion capacity for carbon monoxide (mL/min/mm Hg); 6MWT: 6-minute walk test; and SpO2: transcutaneous oxygen haemoglobin saturation.

### Table 2: Sleep characteristics in the population studied (n = 25).

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Median (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total time of sleep (min)</td>
<td>402 (356–432)</td>
</tr>
<tr>
<td>Sleep efficiency (%)</td>
<td>87 (81–90)</td>
</tr>
<tr>
<td>Sleep latency (min)</td>
<td>13 (5–19)</td>
</tr>
<tr>
<td>REM latency (min)</td>
<td>115 (75–169)</td>
</tr>
<tr>
<td>S1 + S2 (%)</td>
<td>63 (53–81)</td>
</tr>
<tr>
<td>S3 + S4 (%)</td>
<td>14 (6–20)</td>
</tr>
<tr>
<td>REM (%)</td>
<td>17 (10–19)</td>
</tr>
<tr>
<td>Apnoea index (events/h)</td>
<td>2 (1–5)</td>
</tr>
<tr>
<td>Apnoea – REM (events/h)</td>
<td>3 (1–15)</td>
</tr>
<tr>
<td>Minimum SpO2 (%)</td>
<td>83 (81–88)</td>
</tr>
<tr>
<td>% Time SpO2 $&lt;90%$ (%)</td>
<td>31.2 (0–60.2)</td>
</tr>
<tr>
<td>Time SpO2 $&lt;90%$ (min)</td>
<td>136 (13–201)</td>
</tr>
</tbody>
</table>

S1 + S2: superficial sleep stages; S3 + S4: slow wave sleep stages; REM: rapid eye movement stage; and time SpO2 $<90\%$: time of sleep with SpO2 less than 90%.

### Polysomnography

### Table 3: Multivariate analysis showing that nocturnal hypoxaemia correlation to RV/TLC ratio was the most important one.

### Discussion

This is the first study that systematically evaluated sleep in patients with LAM. Our study conveys several novel findings. First, 56% of the patients had significant nocturnal hypoxaemia during sleep despite normal oxygen saturation while awake. Second, despite the menopause induced by GnRH analogue treatment, obstructive sleep apnoea was not common among patients with LAM. Third, nocturnal hypoxaemia did not correlate with demographic characteristics or awaken SpO2.

Lastly, nocturnal hypoxaemia correlated with pulmonary function variables, including FEV1, RV/TLC, DLCO, and minimum SpO2 on 6MWT. Multivariate analysis showed that nocturnal hypoxaemia correlation to RV/TLC ratio was the most important one.

These findings indicate that nocturnal desaturation is a much more common problem in clinical practice than...
would have been supposed by current outpatient management based only on resting PFT and oximetry. The strength of it is that we consecutively screened an entire LAM outpatient clinic population with resting, exercise, and nocturnal oximetry. The majority of patients were not in an advanced disease stage, and we looked for possible earlier predictor variables of functional deterioration. Patients had mild obstructive ventilatory disturbance and moderate impairment in DLCO, and none of them had severe obstructive sleep apnoea (OSA). Because the GnRH analogue induced menopause could be responsible for increasing sleep apnoea, OSA was a concern for us during the design of study.\textsuperscript{31} This finding ensured us about the safety of anti-hormonal treatment in not increasing the incidence of OSA.

LAM is structurally characterised by gradual replacement of lung parenchyma by thin wall cysts, which functionally leads to progressive obstruction, diffusion impairment and finally hyperinflation detected in lung function tests. Our set of patients had mild to moderate obstructive and diffusion disorder, without rest hypoxaemia, and nocturnal hypoxaemia was mainly detected during irregular ventilation presented in REM sleep. There are several mechanisms underlying nonapnoeic oxygen desaturation during sleep that may explain why patients with LAM and without rest hypoxaemia desaturate during sleep. They include impairments in: functional residual capacity, ventilatory responses to hypoxia and hypercapnia, respiratory mechanical effectiveness, arousal responses, respiratory muscle fatigue, chemical respiratory

Figure 2  S3–S4 regular ventilation.

Figure 3  REM — hypoventilation.
drive, upper airway resistance and also in the position of baseline saturation values on the oxyhaemoglobin dissociation curve. Among the functional variables evaluated, the RV/TLC ratio was the main variable related to nocturnal sleep desaturation. For instance, hyperinflation may be directly related to the impairment in the ventilation to perfusion ratio that occurs during recumbence in sleep in this set of patients. It may also intensify hypoventilation, because tonus is reduced and auxiliary respiratory muscles are inactivated. Although, we did not measure exhaled CO2, and therefore were not able to conclude that hypoventilation was the main phenomenon related to nocturnal sleep desaturation, the respiratory pattern (Figs. 1–4) observed during polysomnography suggests that hypoventilation might be an important concern in women with LAM during sleep.

Since sleep had not been properly evaluated in LAM, and pulmonary function test results in LAM are very similar to those of COPD, we may infer that there may be some common physiologic mechanisms. COPD patients desaturate during sleep even in the absence of OSA, and one of the most important mechanisms is hypoventilation. Several studies have shown that recurrent transient hypoxaemia during sleep is frequent in patients with COPD. Nocturnal hypoxaemia is particularly marked in patients with “blue and bloated” clinical phenotype and frequently occurs during REM sleep. The measurement of minute ventilation with a pneumotachograph and oxygen saturation with pulse oximetry in a group of patients with severe

Figure 4  Transitional ventilatory pattern: S2–REM.

Figure 5  Hypnogram.
COPD demonstrated a nearly 20% lower SpO2 during non-REM sleep and 40% lower oxygenation during REM sleep than during the awake state, primarily due to reduced tidal volume.\(^{36,37}\)

Tidal volume small reductions, with little or no change in breathing frequency, are present from wakefulness to NREM sleep reducing alveolar ventilation. This phenomenon leads to a mild increase in arterial CO2 tension of \(NREM\) sleep reducing alveolar ventilation. This phenomenon breathing frequency, are present from wakefulness to volume.\(^{36,37}\) than during the awake state, primarily due to reduced tidal volume.\(^{36,37}\) REM sleep and 40% lower oxygenation during REM sleep Therefore, desaturation during sleep may represent an important predictor of severity and influence on patients with COPD and pulmonary hypertension and \textit{cor pulmonale} are commonly seen in this set of patients.\(^{40}\)

According to analysis of the questionnaires, we found that patients with nocturnal desaturation had more limitations in physical and emotional domains than the ones who did not. Impairments in quality of life related to health efficiency found in our group of patients (88%), despite the fact that they did or did not desaturate during sleep. In addition, chronic hypoxaemia has been associated with development of pulmonary hypertension, mainly through enhancement of prevascular resistance (potassium channel blockage and intracellular calcium influx) and misbalance in serotonin and endothelin actions.\(^{39}\)

### Table 3

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Desaturators ((n = 14))</th>
<th>Nondesaturators ((n = 11))</th>
<th>(p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>45 (42–55)</td>
<td>45 (36–53)</td>
<td>0.18</td>
</tr>
<tr>
<td>BMI (kg/m(^2))</td>
<td>23 (20–28)</td>
<td>23 (23–25)</td>
<td>0.75</td>
</tr>
<tr>
<td>MNSpO2 (%)</td>
<td>80 (76–83)</td>
<td>90 (85–90)</td>
<td>0.04</td>
</tr>
<tr>
<td>FEV(_1) (L)</td>
<td>1.3 (0.8–1.9)</td>
<td>2.4 (2.2–2.7)</td>
<td>0.02</td>
</tr>
<tr>
<td>FVC (L)</td>
<td>2.5 (2–2.9)</td>
<td>3.2 (2.6–3.8)</td>
<td>0.14</td>
</tr>
<tr>
<td>TLC (L)</td>
<td>5.0 (4.1–5.9)</td>
<td>4.9 (4–5.7)</td>
<td>0.35</td>
</tr>
<tr>
<td>RV (L)</td>
<td>2.3 (1.6–3.2)</td>
<td>1.5 (1.1–2.0)</td>
<td>0.17</td>
</tr>
<tr>
<td>RV/TLC</td>
<td>0.4 (0.40–0.60)</td>
<td>0.3 (0.29–0.34)</td>
<td>0.04</td>
</tr>
<tr>
<td>DL(_{co}) (mL/min/mm Hg)</td>
<td>9.2 (4.6–13.3)</td>
<td>18 (16–20)</td>
<td>0.03</td>
</tr>
<tr>
<td>Awake SpO(_2) (%)(^{a})</td>
<td>94 ± 2</td>
<td>97 ± 1</td>
<td>0.17</td>
</tr>
<tr>
<td>Apnoea index (events/h)</td>
<td>2.7 (1.3–6.7)</td>
<td>1.5 (0.7–7)</td>
<td>0.27</td>
</tr>
<tr>
<td>Minimum saturation 6MWT(^{a})</td>
<td>80 ± 8</td>
<td>93 ± 4</td>
<td>0.018(^{a})</td>
</tr>
<tr>
<td>Distance (m)</td>
<td>463 (353–503)</td>
<td>460 (420–541)</td>
<td>0.74</td>
</tr>
</tbody>
</table>

\(MNS: \) minimum nocturnal saturation; \(BMI: \) body mass index; \(FEV\(_1\): \) forced expiratory volume in one second; \(FVC: \) forced vital capacity; \(RV: \) residual volume; \(TLC: \) total lung capacity; \(RV/TLC: \) ratio between \(RV\) and \(TLC\); \(DL_{co}: \) diffusion capacity for carbon monoxide (mL/min/mm Hg); and \(\text{time SpO}_2 < 90\%: \) time of sleep with \(\text{SpO}_2\) less than 90%.

Data are expressed as Median (IQR).

\(^{a}\) Mean ± SD.

### Table 4

<table>
<thead>
<tr>
<th>Measure</th>
<th>MNS</th>
<th>Time SpO(_2) &lt; 90%</th>
</tr>
</thead>
<tbody>
<tr>
<td>(%) FEV(_1)</td>
<td>0.6 ((p = 0.02))</td>
<td>-0.6 ((p = 0.002))</td>
</tr>
<tr>
<td>(%) RV/TLC</td>
<td>-0.5 ((p = 0.02))</td>
<td>0.5 ((p = 0.02))</td>
</tr>
<tr>
<td>(%) DL(_{co})</td>
<td>0.7 ((p = 0.0001))</td>
<td>-0.7 ((p = 0.001))</td>
</tr>
<tr>
<td>Minimum</td>
<td>-0.7 ((p = 0.0001))</td>
<td>0.6 ((p = 0.02))</td>
</tr>
</tbody>
</table>

\(r_s: \) Spearman correlation coefficient.

\(p < 0.05\) Wilcoxon test; \(MNS: \) minimum nocturnal saturation; \(FEV\(_1\): \) forced expiratory volume in one second in litres; \(DL_{co}: \) diffusion capacity for carbon monoxide (mL/min/mm Hg); \(RV/TLC: \) ratio between residual volume in litres and total lung capacity in litres; \(6MWT: \) 6-min walk test; \(\text{SpO}_2: \) haemoglobin oxygen saturation; and \(\text{time SpO}_2 < 90\%: \) time of sleep with \(\text{SpO}_2\) less than 90%.

\(R^2 = 0.512; \) \(p = 0.022.\)

\(DL_{co}: \) diffusion capacity for carbon monoxide (mL/min/mm Hg); \(FEV\(_1\): \) forced expiratory volume in one second in litres; \(RV/TLC: \) ratio between residual volume in litres and total lung capacity in litres; \(MNS: \) minimum nocturnal saturation; \(6MWT: \) 6-min walk test; and \(\text{SpO}_2: \) transcutaneous oxygen haemoglobin saturation.
status are certainly multifactorial, and probably architectural sleep disturbance and other variables not evaluated may influence health perceptions. However, there might be a direct relation between HRQOL impairment and nocturnal hypoxaemia, although not precisely demonstrated in other obstructive populations (COPD), which should make us pay great attention to this association in patients with LAM.

Our study has limitations that warrant discussion. First, it is possible that because of our sample size and mild functional impairments pulmonary hypertension was not observed and therefore no association with nocturnal hypoxaemia could be observed. Second, we do not have data about arterial blood gas either in rest or in exercise, which would have helped us evaluate respiratory functional status. Third, although we believe that hypoventilation was the main mechanism leading to nocturnal hypoxaemia, CO2 levels were not measured during sleep, and so we are not able to confirm this hypothesis. However, the ventilatory pattern detected during REM versus NREM sleep may lead us to hypothesise that this could be an important mechanism associated with sleep desaturation.

In conclusion, in a survey of a LAM outpatient population, isolated nocturnal desaturation was very common and was present in more than half of patients. Hyperinflation was the main functional characteristic related to nocturnal sleep hypoxaemia. HRQOL impairment was more frequent among desaturators; physical and emotional roles were the most disturbed domains. Desaturation was more intense during sleep than during 6MWT, and patients with nocturnal desaturation did not have impaired sleep efficiency. Therefore, to stratify LAM severity and understand its progression, we believe that nocturnal oxygen desaturation during sleep must be investigated and ruled out in all patients with LAM.

Ethical approval

The study was approved by the InCor/Hospital das Clinicas ethics board.

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Conflict of interest

The authors have no financial or other potential conflicts of interest to disclose.

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