Ambulatory pulmonary artery pressure monitoring during sleep and exercise in normal individuals and patients with COPD

D A Raeside, A Brown, K R Patel, D Welsh, A J Peacock

Background: Pulmonary hypertension is a common complication of chronic obstructive pulmonary disease (COPD) and its presence implies a poor prognosis. However, it is difficult to measure and its specific contribution to symptoms is difficult to quantify. A micromanometer tipped pulmonary artery catheter was used to measure pulmonary artery pressure (PAP) during sleep and on exercise.

Methods: Ten patients (five with COPD receiving long term oxygen therapy and five normal individuals) were studied. Pulmonary artery pressure was recorded continuously during two periods of sleep (breathing oxygen followed by air for the COPD group) and during exercise.

Results: In the COPD group PAP during sleep on oxygen was significantly lower than PAP during sleep breathing air (mean (SD) difference 9.6 (5.3) mm Hg, 95% CI 4.9 to 14.3, p=0.016). PAP during exercise was not significantly different from PAP during sleep breathing air (mean (SD) difference 0.8 (9.9) mm Hg, 95% CI –7.0 to 8.6, p=0.851). In normal individuals the group mean (SD) PAP was 15 (5.9) mm Hg for the first nocturnal period and 15 (5.7) mm Hg for the second nocturnal period. PAP during exercise was not significantly different from PAP during sleep breathing air (mean (SD) difference 3.3 (2.2) mm Hg, 95% CI 1.1 to 5.5, p=0.061).

Conclusion: In patients with COPD, PAP rose significantly during sleep to levels similar to those measured during exercise, but this could be reversed with oxygen.

Pulmonary hypertension is a common complication of chronic obstructive pulmonary disease (COPD) and, when severe, implies a poor prognosis. Because the signs and symptoms of the underlying illness can be overwhelming and accurate measurement of pulmonary hypertension requires a cardiac catheter, it is difficult to diagnose and quantify secondary pulmonary hypertension and its role in the morbidity of COPD is poorly understood. Pulmonary artery pressure (PAP) may rise during sleep or exercise in patients with COPD, but the two groups during sleep in two 4-hour periods, from midnight to 04.00 hours and from 04.00 hours to 08.00 hours. The COPD group was given continuous oxygen at their usual flow rate for the first period and remained off oxygen for the second period. Ward nursing staff were asked to confirm that the patients were asleep at the stated times. Baseline PAP values refer to those recorded while the subject was asleep breathing air as this was the state against which the effect of interventions on PAP were measured.

Written informed consent was obtained for all patients. The study was approved by the West Glasgow Hospitals University NHS Trust ethics committee.

The catheter

This has been described in detail elsewhere. Briefly, it is a 7F solid micromanometer tipped catheter (Gaeltech Ltd, Dunvegan, Isle of Skye) which can be zeroed in situ. This is carried...
out by injecting 0.4 ml of air into a luer fitting on the end of the catheter, causing a pressure of approximately 124 mm Hg to be applied to both sides of the transducer so that a high and equal pressure is applied to both its surfaces, thus restoring its zero state. This creates a calibration line which can be identified on the pressure trace. After removal from the subject the catheter tracing is checked against a known pressure using a sealed chamber and a sphygmomanometer. This value is then used in the analysis programme as a further mechanism to correct any drift which may have occurred in vivo.

Exercise testing
All patients exercised while breathing air using the Sensormedics V-Max system (Sensormedics, Yorba Linda, CA, USA) wearing an adult facemask (Hans Rudolph, Kansas City, MO, USA). The electromagnetically braked cycle ergometer was positioned in the middle of the treadmill because it is safer and can maintain a given work rate despite fluctuations in the frequency of pedalling. A steady state workload of 30 watts was chosen because it was felt to be manageable for all the patients with COPD.

Data analysis
The analysis programme (Gaelttech, Isle of Skye, UK) permits PAP tracings to be matched accurately with periods of activity. Mean pressures were derived from the recorded pressure waveform in a novel manner. Single point pressures were calculated and averaged over the period of time indicated by the observer. This method of calculation for mean pressure was employed in the initial design of the catheter because it provides a mathematical mean of all pressures. This is more accurate when information is necessarily derived from a physiological measurement such as the pressure trace. Mean PAP during sleep was measured for the middle two hours of each nocturnal period. Exercise PAP measurements were the average mean pressure recorded over 1 minute from the onset of the 4th minute of steady state exercise.

Statistics
All data are expressed as mean (SD) with 95% confidence intervals (unless otherwise stated). Statistical testing was by paired t test. A p value of <0.05 was considered to be statistically significant. Statistical analyses were carried out using the OXSTAT package for personal computers (OXSTAT II, Microsoft Corporation).

RESULTS
COPD group
Mean PAP during sleep
Group mean (SD) PAP was 60 (8.1) mm Hg during sleep breathing air and 51 (5.5) mm Hg breathing oxygen (table 2). PAP during sleep on oxygen was significantly lower than PAP during sleep on air (*p<0.05).

![Figure 1](https://example.com/fig1.png)

**Figure 1** Mean pulmonary artery pressure (PAP) in normal subjects and patients with COPD. Mean PAP for the COPD group and the control group is shown during each activity. For the COPD group PAP was significantly lower when breathing oxygen than when breathing air (*p<0.05).

### Table 1 Demographic data, lung function, and resting haemodynamics of patients with COPD and normal controls

<table>
<thead>
<tr>
<th>Parameter</th>
<th>COPD</th>
<th>Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>62 (3.9)</td>
<td>60 (11.4)</td>
</tr>
<tr>
<td>PAP (mm Hg)</td>
<td>44.4 (5.5)</td>
<td>16.2 (4.3)</td>
</tr>
<tr>
<td>PVR (Wood’s units)</td>
<td>5.5 (1.8)</td>
<td>1.6 (0.6)</td>
</tr>
<tr>
<td>Mean total pressure (mm Hg)</td>
<td>50 (5.0)</td>
<td>13.8 (6.0)</td>
</tr>
<tr>
<td>Rest</td>
<td>59.9 (10.2)</td>
<td>14.9 (5.8)</td>
</tr>
<tr>
<td>FEV1 (l)</td>
<td>0.99 (0.3)</td>
<td>2.24 (0.9)</td>
</tr>
<tr>
<td>FVC (l)</td>
<td>79 (3.4)</td>
<td>79 (3.4)</td>
</tr>
</tbody>
</table>

Rest refers to sitting at rest. Normal individuals had normal lung function. All values are mean (SD).

### Table 2 Mean (SD) pulmonary artery pressure (PAP) in mm Hg in patients with COPD and normal subjects during rest and exercise

<table>
<thead>
<tr>
<th>Group</th>
<th>PAP (mm Hg)</th>
<th>Mean (SD) difference</th>
<th>95% CI</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>COPD group</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asleep breathing air</td>
<td>59.8 (8.1)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asleep breathing oxygen</td>
<td>50.8 (5.5)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exercise</td>
<td>59.0 (10.7)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal group</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asleep breathing air</td>
<td>14.6 (5.9)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asleep breathing oxygen</td>
<td>14.6 (7.0)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exercise</td>
<td>17.0 (4.0)</td>
<td></td>
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</tr>
</tbody>
</table>

Patients were breathing oxygen during the first period of sleep and air during the second period. Normal controls were breathing air throughout. Exercise refers to steady state exercise on the cycle ergometer at 30 watts.
Mean PAP during exercise
Group mean (SD) PAP during exercise was 59.0 (10.7) mm Hg, which was not significantly different from PAP during sleep breathing air (mean (SD) difference 0.8 (8.9) mm Hg (95% CI −7.0 to 8.6), p=0.851 (table 2, fig 1). An example of an ambulatory PAP trace in a patient with COPD during rest followed by exercise, during sleep breathing air, and during sleep breathing oxygen is shown in fig 2.

Normal group
Mean PAP during exercise
Group mean (SD) PAP in the normal group was 15 (5.9) mm Hg for the first nocturnal period and 15 (5.7) mm Hg for the second nocturnal period (table 2, fig 1).

Mean PAP during exercise
Group mean (SD) PAP in the normal group during exercise was 17.0 (4.0) mm Hg (table 2), which was not significantly different from PAP during sleep breathing air (mean (SD) difference 3.3 (2.2) mm Hg (95% CI 1.1 to 5.5), p=0.061, table 2, fig 1).

Comparison between COPD and normal groups
PAP while asleep on oxygen v asleep on air for the COPD group was significantly different from asleep on air for the normal group (mean (SD) difference 7.6 (5.6) mm Hg (95% CI 2.7 to 12.5), p=0.039).

Exercise v asleep on air for both groups was significantly different (mean (SD) difference 5.0 (2.7) mm Hg (95% CI 2.3 to 7.7), p=0.034).

DISCUSSION
In this study we have shown that patients with COPD receiving LTOT tolerate invasive haemodynamic assessment, including ambulatory PAP monitoring, and can safely perform cardiopulmonary exercise testing at a low workload. The number of patients presented is small because of difficulties encountered in recruiting frail patients in respiratory failure for invasive haemodynamic monitoring but, nevertheless, we found significant changes in haemodynamics.

Previous studies of PAP in patients with COPD have shown that values are modestly increased and progression slow. However, most of these measurements have been of resting pressure which has been shown to be of relatively poor prognostic value. Furthermore, it has also been shown that even routine daily activities in patients with mild COPD and normal resting oxygen saturations are associated with reductions in oxygen saturation.

In this study we have measured PAP in a variety of situations in patients with respiratory failure receiving LTOT and the higher levels of PAP observed are therefore not surprising. Patients with COPD receiving LTOT had significantly higher levels of PAP than those of a control group when measured over 24 hours. These patients also had significantly higher PAP when the periods of sleep or exercise were excluded—that is, when performing normal daily activity breathing supplementary oxygen. We have not defined specific activities of daily living in this study so these data are not presented. When studied during sleep without oxygen, the COPD group had a further rise in PAP which was greater than that measured on exercise and which was abolished by breathing oxygen during sleep. Others have previously reported increased pulmonary vascular resistance during REM sleep and the beneficial effects of oxygen in patients with moderate pulmonary hypertension and severe COPD. However, as far as we are aware, the extent of these rises compared with those seen during other activity has not been studied.

The normal group did not show any change in PAP during sleep (which is not surprising); however, there was no significant rise in PAP during exercise which others have predicted. This is probably because the workload chosen for the exercise test (30 watts) was too low to put the pulmonary circulation of normal individuals sufficiently under stress. Furthermore, there was no variation in the PAP of this group during normal daily activity.

The number of patients with COPD in this study is small and therefore it is difficult to reach firm conclusions. However, for these individuals the rise in PAP seen during sleep may be an important contribution to the overall work facing the right heart and constitutes at least as great a haemodynamic burden as low level exercise.

In this study we have shown considerable variations in PAP during 24 hour ambulatory monitoring with normal daily activity, on exercise, and during sleep, and this may have implications for the way COPD is assessed. Measurement of PAP is difficult in ambulant patients because of the restrictions inherent in conventional cardiac catheterisation and may be unrepresentative because of the circumstances in which these are made—that is, at rest in the laboratory. Furthermore, non-invasive measurement with echocardiography in patients with COPD is often limited by the poor signal obtained. The technique of ambulatory PAP monitoring described in this paper allows the time course and extent of rises in PAP to be measured and correlated with symptoms in patients carrying out normal daily activities. Such knowledge of the pulmonary circulation under stress or during sleep in patients with COPD may be useful in assessing the contribution of pulmonary hypertension to overall morbidity and mortality. We have observed and quantified transient rises in PAP during sleep and exercise during ambulatory monitoring in the hospital environment in patients treated with LTOT. We speculate that similar increases in PAP may also be important in patients.
with milder COPD, which might have implications for future interventions.

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