Effect of Weight Loss on Postural Changes in Pulmonary Function in Obese Subjects: A Longitudinal Study

Mustapha Sebbane MD PhD, Moez El Kamel MD, Alice Millot MD, Boris Jung MD PhD, Sophie Lefebvre PhD, Josh Rubenovitch MD, Grégoire Mercier MD PhD, Jean-Jacques Eledjam MD PhD, Samir Jaber MD PhD, and Maurice Hayot MD PhD

BACKGROUND: Postural changes are known to affect normal lung volumes. A reduction in sitting to supine functional residual capacity (FRC) is well-described in non-obese subjects adopting a supine position. However, postural changes in lung volumes in the obese require further exploration. We aimed to longitudinally address the effects of weight loss on postural changes in lung volumes and pulmonary function in obese subjects. We tested the hypothesis that supine reduction in FRC would be absent in morbid obesity and recovered upon weight loss. METHODS: This was a prospective, observational, longitudinal study. Consecutive morbidly obese adults (N = 12, age: 44 ± 14 y, body mass index: 45 ± 5 kg/m²) enrolled in a bariatric surgery program were included. Standard pulmonary function tests and blood gas analysis were performed both before and 1 y after surgery. Pulmonary function was assessed in both the sitting and supine position using spirometry and multi-breath helium dilution. Parameters recorded before and after weight loss were compared. The main outcome measure was FRC. RESULTS: Ten subjects were retested 1 y after surgery (body mass index: 31 ± 5 kg/m²). FRC was not affected by change in posture before surgery. Supine reduction in FRC was observed after weight loss (ΔFRC: −0.6 ± 0.4 L, sitting vs supine, P = .002). Pulmonary gas exchange improved (alveolar-to-arterial oxygen partial pressure difference: −8 ± 11 mm Hg, P = .035). CONCLUSIONS: Although postural change in FRC is absent when the morbidly obese adopt a supine position, supine reduction in FRC can be recovered following gastroplasty-induced weight loss, despite residual mild to moderate obesity. This also shows that mild to moderate obesity may affect supine FRC more than morbid obesity. (Clinical-Trials.gov registration NCT02207192.) Key words: lung function; obesity; weight loss; postural change; pulmonary function test; functional residual capacity; bariatric surgery. [Respir Care 0;0(0):1–. © 0 Daedalus Enterprises]

Introduction

Obesity has become a worldwide health concern.¹ The prevalence of obese adults in the United States has risen significantly over the last decade to 32.2%, with morbid obesity increasing at even faster rates.² In Europe, while half of all adults are overweight, 10–20% of men and 15–25% of women are obese. In France, the prevalence of adult obesity has increased progressively in both men and women, from 8.6% in 1997 to 14.5% in 2009.³

Drs Sebbane, Lefebvre, Rubenovitch, and Eledjam are affiliated with the Département des Urgences, Hôpital Lapeyronie; Dr Mercier is affiliated with the Département d’Information Médicale, Hôpital Lapeyronie; Drs El Kamel, Millot, Jung, and Jaber are affiliated with the Département d’Anesthésie-Réanimation B, Hôpital St Eloi; Dr Hayot is affiliated with the Département de Physiologie Clinique, Hôpital Arnaud de Villeneuve, Centre Hospitalier Régional Universitaire Montpellier, Montpellier, France.

This study was supported by the Centre Hospitalier Régional Universitaire Montpellier. The authors have disclosed no conflicts of interest.

Correspondence: Mustapha Sebbane MD PhD, Département des Urgences, Centre Hospitalier Régional Universitaire Lapeyronie, 371, avenue du doyen Gaston Giraud, 34295 Montpellier Cedex 5, France. E-mail: m-sebbane@chu-montpellier.fr.

DOI: 10.4187/respcare.03668
The accumulation of excess body fat is the most common metabolic disorder in humans. It is a major cause of cardiac and metabolic related morbidity and mortality. Many studies have demonstrated an association between excess weight or weight gain and pulmonary dysfunction, including a reduction in lung volumes. More specifically, functional residual capacity (FRC) and expiratory reserve volume as well as, to some extent, total lung capacity (TLC) and residual volume (RV) are decreased in obesity. Both FRC and expiratory reserve volume are the most consistently reported findings, with an exponential relationship between body mass index (BMI) and either FRC or expiratory reserve volume. Weight gain also tends to be accompanied by a decrease in vital capacity (VC) and FEV₁, probably attributable to the effect of excess fat mass on chest-wall and lung compliance. Inversely, weight loss has been found to be associated with improved respiratory function.

Postural changes are known to affect normal lung volumes due to the gravitational effects of the abdominal contents on the diaphragm’s position. More specifically, a reduction in sitting to supine FRC is well-described in non-obese subjects adopting a supine position. Postural changes in lung volumes have also been studied in obesity. Although a significant supine reduction in FRC has also been reported in mild to moderate obesity, its absence has been shown in morbid obesity.6-11 Postural changes in lung volumes have also been studied in obesity.12-14 Although a significant supine reduction in FRC has been reported in mild to moderate obesity, its absence has been shown in morbid obesity.15,16 However, most studies have compared obese subjects to normal weight controls. Data from longitudinal evaluation of postural changes in lung volumes in morbidly obese individuals following weight loss is scarce.

In the present study, we longitudinally assessed the relationship between weight loss and postural changes in lung volumes. We tested the hypothesis that lack of postural change in FRC would be observed in morbid obesity, whereas supine reduction in FRC would be recovered upon weight loss. We followed morbidly obese subjects over 1 y following bariatric surgery. Changes in lung volumes and air flows were examined in both sitting and supine positions, before and after weight loss. Arterial blood gases were assessed in the sitting position to evaluate the effect of weight loss on pulmonary gas exchange.

Methods

The study was conducted from August 2005 to May 2007 in the Department of Clinical Physiology of an urban-based university hospital in Montpellier, France. The study was approved by the local ethics committee (Ethical Committee 040506, CPP Sud-Méditerranée IV, Montpellier, France) on October 26th, 2004, and subjects’ written informed consent was obtained.

Population

Sample size was based on data from a study by Benedik et al., which includes the largest series of overweight, mildly obese, and moderately obese subjects in the literature (N = 32). Sample size calculation for paired difference between supine and seated FRC indicated that 10 subjects would be required to show a mean paired difference in FRC sitting versus supine = 0.5 L, with standard deviation = 0.5, α = 0.05, and power (1 – β) = 0.8.

Twelve consecutive subjects scheduled for bariatric surgery were prospectively recruited. Subjects with respiratory and cardiac history (asthma, COPD, heart failure) were excluded. Obstructive sleep apnea was defined as an apnea-hypopnea index greater than 10, using overnight polysomnography. Subjects were 3 men and 9 women (age: 44 ± 14 y [18–61], BMI: 45 ± 5 kg/m² [40–55]). Six subjects had smoking histories (mean pack-years: 21 [8–30]), and 6 were diagnosed with obstructive sleep apnea (mean apnea-hypopnea index: 36 [30–76]).

Bariatric surgery was performed by laparoscopy under general anesthesia. Following surgery, all subjects were put on a specific weight-loss program. Pulmonary function and arterial blood gases were assessed both before and after weight loss as part of preoperative and 12-month follow-up evaluations.

Height, Body Weight, and BMI Measurements

Height (m) and body weight (kg) were routinely measured as part of preoperative and 12-month follow-up eval-
Pulmonary Function Measurements

Pulmonary function tests were performed in the sitting and then in the supine position, in accordance with the 2005 American Thoracic Society/European Respiratory Society recommendations.17,18 Dynamic and static lung volumes including TLC, FVC, FRC, RV, and expiratory reserve volume subdivisions, as well as FEV1 were measured using spirometry and the multi-breath helium dilution method. Spirometry tests were performed using automated equipment (Hyp Air compact†, Medisoft, Sorinnes, Belgium). The best value obtained from the maximum expiratory flow-volume curves was retained for FEF75%, FEF50%, and FEF25%. Results were reported as absolute and percentage of predicted values.

Arterial Blood Gas Measurements

Blood samples were withdrawn from the radial artery, with the subject at rest, sitting and breathing room air. Arterial blood gas values, including $P_{\text{a}}O_2$ and $P_{\text{a}}CO_2$, oxygen saturation ($S_aO_2$), and pH concentration were measured at the pulmonary function testing laboratory using a blood gas analyzer (Cobas B221 system, Roche Omnis, Meylan, France). Alveolar-to-arterial oxygen partial pressure difference ($P_{\text{A}-\text{a}}O_2$) was calculated as the difference between $P_{\text{A}}O_2$ and $P_{\text{a}}O_2$, with the alveolar partial pressure in oxygen ($P_{\text{A}}O_2$) obtained from the ideal alveolar gas equation.19

Statistical Analysis

The Kolmogorov-Smirnov test was performed to test normal distribution. When data were normally distributed, description of quantitative variables was presented as means and standard deviations or percentage (%), with the value range. Paired Student $t$ tests of significance were used to compare parameters recorded before and after weight loss. Non-parametric tests were performed in case of non-normal distribution. The non-parametric Spearman correlation coefficient was used to test relationships between supine reduction in FRC and BMI.

Statistical analyses were carried out using a statistical software package (StatView 5.0, SAS Institute, Cary, North Carolina). A $P < .05$ was considered as statistically significant.

Results

Two subjects were lost to follow-up. Mean baseline parameters of the 10 subjects retested 1 y after bariatric surgery did not differ from those of the 12 subjects originally included (Table 1). At 1 y follow-up, mean BMI was $31 \pm 5$ (22–37) kg/m². Mean reduction in BMI was $12.8 \pm 5.7$ kg/m², range 4.3–23.8, $P = .001$; mean reduction in body weight was $34 \pm 16$ kg (29 ± 12% of initial weight), range 13–64, $P = .001$.

Changes in Lung Volumes and Flows Before Surgery

Baseline lung volumes and expiratory flows measured before surgery are shown in Table 2. In the sitting position, most lung volumes, including VC, TLC, and RV, remained within normal ranges. Baseline FRC and expiratory reserve volume were below predicted values, with FRC and expiratory reserve volume down to 84% and 73% of predicted values, respectively.

On adopting the supine position, a significant decrease in expiratory reserve volume was observed. TLC, VC, and RV were not significantly affected by the change in posture. No significant decrease in FRC was recorded (Fig. 1). Flows were within the normal range of predicted values. FEV1, FEF50%, and FEV1/VC decreased significantly upon adopting the supine position.

Changes in Lung Volumes and Flows After Weight Loss

At 1 y follow-up, ventilatory parameters measured in the sitting position tended to improve with weight loss (Table 2, Fig. 1). VC and expiratory reserve volume significantly increased, whereas TLC, FRC, and RV were not significantly modified. Pulmonary flows also improved slightly.

On adopting the supine position, FRC and expiratory reserve volume decreased significantly when compared with sitting position values. VC, TLC, and RV decreased slightly, although the differences were not statistically sig-

---

Table 1. Characteristics of the Study Participants

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjects ($N$)</td>
<td>10</td>
</tr>
<tr>
<td>Sex ratio (M/F)</td>
<td>2/8</td>
</tr>
<tr>
<td>Age (y)</td>
<td>45 ± 15 (18–61)*</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>44 ± 4 (40–50)*</td>
</tr>
<tr>
<td>Smoking history ($n$)</td>
<td>5/10</td>
</tr>
<tr>
<td>Pack-years ($n$)</td>
<td>22 (8–30)†</td>
</tr>
<tr>
<td>Apnea-hypopnea index (events/h)</td>
<td>35 (21–76)†</td>
</tr>
<tr>
<td>Obstructive sleep apnea ($n$)</td>
<td>5/10</td>
</tr>
</tbody>
</table>

Data show baseline characteristics of the 10 morbidly obese adults tested before surgery and at 1 y follow-up.

*Values are means ± SD, with range in parentheses.
†Values are means, with range in parentheses.
M = male
F = female
BMI = body mass index
Table 2. Respiratory Parameters Measured in Both the Sitting and Supine Position, in the 10 Patients Tested Before and After Weight Loss

<table>
<thead>
<tr>
<th>Variables</th>
<th>Before Weight Loss</th>
<th>After Weight Loss</th>
<th>Before vs After Weight Loss</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Absolute Value ± SD</td>
<td>% Predicted ± SD</td>
<td>Absolute Value ± SD</td>
</tr>
<tr>
<td>TLC (L)</td>
<td>Sitting</td>
<td>5.1 ± 0.6</td>
<td>101 ± 14</td>
</tr>
<tr>
<td></td>
<td>Supine</td>
<td>5.2 ± 0.6</td>
<td>101 ± 11</td>
</tr>
<tr>
<td></td>
<td>Sitting vs supine (P)</td>
<td>.855</td>
<td>744</td>
</tr>
<tr>
<td>VC (L)</td>
<td>Sitting</td>
<td>3.4 ± 0.7</td>
<td>106 ± 15</td>
</tr>
<tr>
<td></td>
<td>Supine</td>
<td>3.3 ± 0.7</td>
<td>103 ± 15</td>
</tr>
<tr>
<td></td>
<td>Sitting vs supine (P)</td>
<td>.06</td>
<td>73</td>
</tr>
<tr>
<td>RV (L)</td>
<td>Sitting</td>
<td>1.7 ± 0.6</td>
<td>100 ± 32</td>
</tr>
<tr>
<td></td>
<td>Supine</td>
<td>1.8 ± 0.4</td>
<td>107 ± 21</td>
</tr>
<tr>
<td></td>
<td>Sitting vs supine (P)</td>
<td>.21</td>
<td>29</td>
</tr>
<tr>
<td>Expiratory reserve volume (L)</td>
<td>Sitting</td>
<td>0.7 ± 0.2</td>
<td>73 ± 20</td>
</tr>
<tr>
<td></td>
<td>Supine</td>
<td>0.37 ± 0.1</td>
<td>39 ± 15</td>
</tr>
<tr>
<td></td>
<td>Sitting vs supine (P)</td>
<td>.001</td>
<td>002</td>
</tr>
<tr>
<td>FRC (L)</td>
<td>Sitting</td>
<td>2.3 ± 0.4</td>
<td>84 ± 19</td>
</tr>
<tr>
<td></td>
<td>Supine</td>
<td>2.1 ± 0.4</td>
<td>77 ± 15</td>
</tr>
<tr>
<td></td>
<td>Sitting vs supine (P)</td>
<td>.08</td>
<td>002</td>
</tr>
<tr>
<td>FEV1 (L)</td>
<td>Sitting</td>
<td>2.69 ± 0.63</td>
<td>97 ± 12</td>
</tr>
<tr>
<td></td>
<td>Supine</td>
<td>2.48 ± 0.60</td>
<td>90 ± 14</td>
</tr>
<tr>
<td></td>
<td>Sitting vs supine (P)</td>
<td>.002</td>
<td>.044</td>
</tr>
<tr>
<td>FEV1/VC (%)</td>
<td>Sitting</td>
<td>79 ± 6</td>
<td>98 ± 8</td>
</tr>
<tr>
<td></td>
<td>Supine</td>
<td>75 ± 8</td>
<td>93 ± 11</td>
</tr>
<tr>
<td></td>
<td>Sitting vs supine (P)</td>
<td>.023</td>
<td>.58</td>
</tr>
<tr>
<td>FEF50% (L/s)</td>
<td>Sitting</td>
<td>3.6 ± 1.2</td>
<td>88 ± 27</td>
</tr>
<tr>
<td></td>
<td>Supine</td>
<td>3.2 ± 1.2</td>
<td>78 ± 27</td>
</tr>
<tr>
<td></td>
<td>Sitting vs supine (P)</td>
<td>.007</td>
<td>.001</td>
</tr>
</tbody>
</table>

Values are expressed as mean (SD) or percent of predicted values of 10 patients tested both before and 1 y after weight loss. *P < .05 indicates significant differences between parameters measured before and after weight loss or in the sitting vs supine posture.

TLC = total lung capacity
VC = vital capacity
RV = residual volume
FRC = functional residual capacity
FEF50% = forced expiratory flow at 50% of vital capacity

significant. Postural changes in TLC, FRC, and RV are depicted in Figure 1.

Forced expiratory volumes and flows decreased slightly on adopting the supine position, after weight loss (Table 2).

Postural Changes in FRC When Moving From the Sitting to Supine Position

Individual sitting to supine changes in FRC recorded in our 12 morbidly obese subjects are displayed in Figure 2. Mean difference in postural change in FRC was −0.10 ± 0.28 L (P = .098) at baseline and reached −0.6 ± 0.4 L (P = .002) at 1 y follow-up. The recovered decrease in FRC was significant (P = .002, before vs after weight loss).

No correlation was found between supine reduction in FRC and BMI (r = −0.28 (P = .43) and r = 0.27 (P = .44) before and 1 y after surgery, respectively).

Pulmonary Gas Exchange

Mean P açO2, S açO2, and pH values were within their normal ranges before surgery, and were not modified after...
weight loss (Table 3). Mean $P_{A-a}O_2$ values were within the normal range before surgery, although a slight hypoxemia was observed in 5 subjects. A return to the normal range was noted in 3/5 subjects following weight loss (data not shown). The mean $P_{A-a}O_2$ was higher in morbidly obese subjects, and returned to the normal range after 1 y, with a significant difference before and after weight loss ($\Delta P_{A-a}O_2 = -8.4 \pm 10.7$ mm Hg, $P = .035$).

Discussion

Our study is, to our knowledge, the first longitudinal study to examine the effect of weight loss on postural changes in lung volumes, when the morbidly obese become mildly to moderately obese. We specifically demonstrate that supine reduction in FRC can be recovered following gastroplasty-induced weight loss, despite resid-
Table 3. Pulmonary Gas Exchange Parameters in 10 Obese Adults Measured Prior to Bariatric Surgery and at 1 y Follow-up

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Before Weight Loss</th>
<th>After Weight Loss</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \text{P}_{\text{a}O_2} ) (mm Hg)</td>
<td>82 ± 10</td>
<td>89 ± 11</td>
<td>.11</td>
</tr>
<tr>
<td>( \text{P}_{\text{a}CO_2} ) (mm Hg)</td>
<td>36 ± 3</td>
<td>37 ± 3</td>
<td>.47</td>
</tr>
<tr>
<td>( \text{pH} )</td>
<td>7.41 ± 0.03</td>
<td>7.41 ± 0.03</td>
<td>.85</td>
</tr>
<tr>
<td>( \text{SaO}_2 ) (%)</td>
<td>96 ± 2</td>
<td>97 ± 1</td>
<td>.33</td>
</tr>
<tr>
<td>( \text{P}_{\text{A-a}O_2} ) (mm Hg)</td>
<td>23 ± 8</td>
<td>14 ± 7</td>
<td>.035</td>
</tr>
</tbody>
</table>

Values are mean ± SD. \( P < .05 \) indicates statistical significance.

\( \text{P}_{\text{a}O_2} \) = arterial partial pressure of oxygen

\( \text{P}_{\text{a}CO_2} \) = arterial partial pressure of carbon dioxide

\( \text{SaO}_2 \) = arterial oxygen saturation

\( \text{P}_{\text{A-a}O_2} \) = alveolar-to-arterial oxygen partial pressure difference

Unlike \( \text{FEV}_1 \), \( \text{VC} \) is not affected by body position before surgery. Accordingly, the \( \text{FEV}_1/\text{VC} \) ratio shows further significant decrease when adopting the supine position. This may suggest an additional effect of the supine position: reducing large airway caliber in the morbidly obese.

In our morbidly obese subjects, expiratory flows were within the normal range, with slight alterations observed in the lower volumes of vital capacity. Before surgery, a significant decline in \( \text{FEF}_{50\%} \) was observed in the supine position. \( \text{FEF}_{50\%} \) values were significantly improved following weight loss both in the sitting and supine positions. However, \( \text{FEF}_{50\%}/\text{VC} \) remained unchanged, and no significant supine reduction was recorded. This may be in favor of an improvement in lung volumes, with decreased airway obstruction after weight loss.

This longitudinal study confirms the sparse evidence in the literature of the different effects of body position on lung volumes depending on BMI range, as shown separately in the morbidly obese\(^{15,16} \) and mildly to severely obese groups.\(^{13,14,21} \)

In non-obese subjects, the decrease in \( \text{FRC} \) upon adopting the supine position is essentially attributed to the gravitational effects of the abdominal contents. The resulting relaxed diaphragm position displaces the static pressure-volume curve of the chest wall to a smaller volume, increasing the work of breathing.\(^ {15} \) Modifications of the thoraco-pulmonary compliance, especially that of the chest wall, may also be involved. Increased intrathoracic blood volume could induce a small reduction in \( \text{TLC} \) and \( \text{VC} \), and further contribute to the supine reduction in \( \text{FRC} \).\(^ {26} \)

The mechanisms responsible for the lack of supine change in \( \text{FRC} \) observed in morbidly obese subjects have not yet been clearly established. Static mechanical changes of the lung and chest wall are likely to be involved. Further thoracic compression upon assuming a supine position could be compromised, due to maximal upward displacement of the diaphragm in the upright posture. Additionally, increased chest wall stiffness resulting from fat mass deposits could affect thoracic compliance. Expiratory flow limitation with distal airway closure, causing increased air volume trapping in the distal airspaces, has also been proposed.\(^ {15,27} \) We did find slightly decreased expiratory flows suggestive of expiratory flow limitation in the distal airways in our morbidly obese subjects adopting a supine position. Recently, higher than normal intrathoracic pressure related to increased intra-abdominal pressure has been described in morbidly obese subjects at end-expiration. When changing from the seated to supine position, an increase in intrathoracic pressure combined with a decrease in intra-abdominal pressure was recorded. This resulted in pressure equilibration between the abdominal and thoracic compartment in the morbidly obese in the supine position.\(^ {28} \)

Unlike FEV\(_1\), VC is not affected by body position before surgery. Accordingly, the FEV\(_1\)/VC ratio shows further significant decrease when adopting the supine position. This may suggest an additional effect of the supine position: reducing large airway caliber in the morbidly obese.
We hypothesize that reduced chest wall stiffness following loss of chest wall fat as well as the cumulative loss of both chest and abdominal fat may be responsible for reduced intra-abdominal and intrathoracic pressures. The resulting increased transdiaphragmatic pressure and consequent cephalic shift of the diaphragm may explain the recovered decrease in FRC observed in our mild to moderately obese subjects, 1 year after bariatric surgery. Improved expiratory flows following surgically induced weight loss may also have contributed to the recovered supine fall in FRC.

Our results also confirm that improved static lung volumes associated with weight loss further contribute to improved pulmonary gas exchange. We observed improved pulmonary gas exchange after weight loss, as reflected by a significant reduction in the mean alveolar-to-arterial oxygen partial pressure difference; this is probably related to a lower ventilation-perfusion mismatch. Although not statistically significant, the combined slight changes in P_{aO_2} and P_{aCO_2} values observed after weight loss may have contributed to the reduced P_{A-aO_2}. Reduced oxygen consumption and CO2 production may also be involved. However, these parameters were not measured. Our findings corroborate previous data describing improvement in arterial oxygenation with massive weight loss (ΔBMI > 20 kg/m²). However, a review of the literature found better P_{aO_2} (by 10 mm Hg, range 1–23 mm Hg) as well as reduced P_{A-aO_2} (by −8 mm Hg, range −3 to −16 mm Hg) and P_{aCO_2} values (by −3 mm Hg, range 3 to −14 mm Hg) for a mean ΔBMI of −13 kg/m². The better gas exchange at rest described in morbidly obese women compared with men, attributed to lower waist-to-hip ratios in women, may explain the minor difference in P_{aO_2} and P_{aCO_2} values recorded before and after weight loss in our cohort (sex ratio [M/F]: 2/8).

Limitations

This study is limited by the small number of subjects, preventing further investigation such as the possible role of gender or adiposity distribution. Indeed, although the distribution of obesity can play a role in pulmonary function, the cumulative effect of overall chest wall size, rather than changes in any specific regional chest wall fat may be involved, as shown in moderately obese men. Neither the waist-to-hip ratio nor the body fat distribution was measured in our study.

Conclusions

Our longitudinal study demonstrates a lack of supine reduction in FRC when morbidly obese subjects adopt a supine position. The recovery of supine FRC reduction following gastroplasty-induced weight loss is also demonstrated, despite residual mild to moderate obesity. Furthermore, mild to moderate obesity was shown to affect supine FRC more than morbid obesity.

ACKNOWLEDGMENTS

We thank the volunteers for their participation in the research study, as well as the laboratory technicians at the pulmonary function test laboratory for their kind help and support. We are grateful to Drs Jonathan R Clarke and Julie Carr for English revisions.

REFERENCES