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The effects of obesity on lung volumes and oxygenation

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ABSTRACT

Introduction: Obesity can cause hypoxemia by decreasing lung volumes to where there is closure of lung units during normal breathing. Studies describing this phenomenon are difficult to translate into clinical practice. We wanted to determine the lung volume measurements that are associated with hypoxemia in obese patients, and explore how we could use these measurements to identify them.

Methods: We collected pulmonary function test results and arterial blood gas data on 118 patients without obstruction on pulmonary function testing. We included only patients with normal chest imaging and cardiac testing within one year of the pulmonary function test, to exclude other causes of hypoxemia.

Results: We found that as BMI increases, the mean paO_2, ERV % predicted, and ERV/TLC decrease (BMI 20-30 kg/m^2: paO_2=90±8 mmHg, ERV% predicted 112±50, ERV/TLC (%) 19.7±6.5; BMI 30-40 kg/m^2: paO_2=84±10 mmHg, ERV% predicted 84±40 ERV/TLC(%) 13.6±7.6; BMI>40 kg/m^2: paO_2 78 ±12 mmHg, ERV% predicted 64±27 ERV/TLC(%) 11.4±5.8, ANOVA p<0.001). The A-a gradient increases as BMI increases (r=0.42, p<0.001). This correlation was stronger in men (r=0.54) than in women (r=0.35). The paO_2 is lower in patients with a low ERV than in those with a normal ERV (p<0.001). In a multivariate linear regression, only the ERV/TLC predicted (%), age, and BMI were associated with oxygenation (r^2 for A-a gradient =0.28, p=0.036).

Conclusions: In obese patients without cardiopulmonary disease, oxygen levels decrease as BMI increases. This effect is associated with the obesity-related reduction in ERV and is independent of hypoventilation.

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1. Introduction

The growing obesity epidemic transforms its effects on pulmonary physiology from a theoretical consideration to a practical one. The primary clinical manifestation of these changes is an increase in exertional dyspnea. Other effects are also well established, such as its influence on breathing pattern, respiratory mechanics, and metabolic rate [1]. Hypoxemia can be another clinical manifestation of obesity, but the mechanisms behind it are not completely understood.

Obesity can potentially cause hypoxemia in three ways: first, through its association with obesity-hypoventilation syndrome, second, through co-morbid conditions such as congestive heart failure. The third is more complex. Obesity is thought to reduce the functional residual capacity (FRC) to the extent that some airways start to close, a lung volume known as the closing capacity (CC). Several studies have validated this hypothesis using complex physiologic measurements, some of which were performed while the patients were under general anesthesia [2–8]. These findings may not be applicable to awake patients sitting before you in clinic, and these physiologic measurements are available to very few clinicians.

To complicate matters further, the association between obesity and hypoxemia is inconsistent. Some studies show a mild association between the two [3,9], but others have shown no association [7,10–12]. To determine whether a particular patient's hypoxemia is secondary to obesity (when they lack the other associated conditions), the most direct method would be to compare the closing capacity (which is the sum of closing volume (CV) and residual volume) to FRC. If the FRC is lower than the CC, the A-a gradient should increase, as some lung units are closed during normal tidal breathing; if the A-a gradient increases sufficiently, the patient is

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Abbreviations

A-a gradient	alveolar-arterial gradient
BMI	body-mass index
CC	closing capacity
COPD	chronic obstructive pulmonary disease
CV	closing volume
ERV	expiratory residual volume
FEV1	forced expiratory volume in one second
FRC	functional residual capacity
paO2	arterial partial pressure of oxygen
pCO2	arterial partial pressure of carbon dioxide
TLC	total lung capacity
RV	residual volume
VC	vital capacity

hypoxemic. But measuring closing capacity is difficult and is rarely done, and the equations to predict closing capacity based on age and height have not been sufficiently standardized [13,14].

There may be a simpler way to assess for obesity-related hypoxemia. ERV is the component of FRC that decreases with obesity and increases with weight loss [15]. It is regularly measured as part of pulmonary function testing and there are accepted equations to extrapolate its predicted value [15,16]. It could be a useful tool to assess the effect of obesity on oxygenation. Therefore, we sought to determine if the relationship between obesity and hypoxemia is explained by changes in ERV.

2. Methods

This study was approved by the local institutional review board.

2.1. Patients

We screened all patients who had pulmonary function testing performed in our laboratory from 2012 to 2014. Patients met primary inclusion criteria if age >18 years, body mass index (BMI) > 20 kg/m^2, FEV_1/FVC > 0.70, residual volume (RV) < 120% predicted, and had lung volumes and arterial blood gases measured. Patients were excluded if the indications for pulmonary function testing were interstitial lung disease, systemic lupus erythematosus, sarcoidosis, pulmonary hypertension, bronchiectasis, or lung cancer.

Patients who met the primary inclusion criteria underwent chart review for secondary inclusion criteria, to exclude patients with cardiopulmonary conditions that alter closing capacity or affect oxygenation [17]. Patients were included only if they had normal cardiac testing (echocardiogram or electrocardiogram) and normal pulmonary imaging (chest computed tomography or radiograph) within one year before or after the pulmonary function tests. An echocardiogram was considered normal if there was no chamber dilatation, hypertrophy, wall motion abnormality, valvular disease, pulmonary hypertension, or pericardial disease. An electrocardiogram was considered normal if there was no chamber enlargement, conduction abnormality, or arrhythmia. All chest radiographs and tomographs were reviewed by the investigators. They were considered normal if there was no pleural effusion, bullous disease, parenchymal disease, or cardiomegaly.

2.2. Lung function measurements

Spirometry at our laboratory is performed based on ATS standards [18]. Lung volumes were measured with a single breath nitrogen washout method (Vmax, Care Fusion\BD, New Jersey, USA). Arterial blood gases were measured using a calibrated co-oximeter (ABL800 FLEX analyzer, Radiometer Medical ApS, Brønshøj, Denmark). Gases were obtained on the same day as the pulmonary function testing, while seated, and immediately before measurement of spirometry and lung volumes.

2.3. Data collected

We collected the patient age, gender, height, weight, race, and smoking history. From the pulmonary function testing we collected FEV_1, FVC, FEV_1/FVC, FRC, ERV, RV, and TLC. We also recorded the pH, pCO_2, paO_2, FiO_2, hemoglobin, and calculated bicarbonate. ERV was expressed in two ways. ERV predicted was calculated by subtracting the predicted RV from the predicted FRC [15]. We then expressed ERV as % predicted. As this ERV % predicted is dependent upon two predicted values, this calculation could double potential errors. Therefore, we also reported the absolute value of ERV in liters as a percentage of predicted TLC (ERV/TLC predicted [%]).

Calculation of predicted values: We calculated the predicted values for spirometry and lung volumes based on NHANES III standards [19]. The observed alveolar-arterial gradient of the partial pressure of oxygen (A-a Gradient) was calculated using the standard equation: [(ambient barometric pressure-47)*0.21]-(pCO_2/0.8)-paO_2 [20].

2.4. Analysis

All continuous variables are reported as mean ± standard deviation (SD) and we confirmed their normal distribution with the Kolmogorov-Smirnov test. To demonstrate the effect of obesity on spirometry, lung volumes, and arterial blood gases, we compared between 3 groups based on BMI: normal weight (20–30 kg/m^2), obese (31–40 kg/m^2), and morbidly obese (>40 kg/m^2). We used ANOVA to compare the means of the three groups.

We assessed oxygenation with two variables: arterial partial pressure of oxygen (paO_2) and the A-a gradient. We first performed univariate analysis by determining the Pearson's correlation coefficient between each of these variables with age, BMI, all spirometric variables, lung volumes, pH, and pCO_2. The correlations were also broken down by gender, and the correlation coefficients were compared using the Fischer r to z transformation. The spirometric and lung volume variables that were statistically significant for the group as a whole were entered into a stepwise multiple linear regression analysis. To explore the effects of gender, we performed an analysis of covariance (ANCOVA) on the significant variables found in the multivariate model.

For all analyses a $p \leq 0.05$ was considered significant. Analyses was performed using SPSS version 23 and Medcalc verision 15.8.

3. Results

3.1. Patient characteristics

In the years 2012–2014, 17,977 patients had pulmonary function testing. Of these, 695 patients met primary inclusion criteria. These charts were reviewed; 118 patients met secondary inclusion criteria and were included in the analysis (Table 1).

Almost two thirds of the patients were women, 18 (15%) had an arterial partial pressure of carbon dioxide (pCO_2)≥ 45 mmHg. The majority were African-American (55%). Half the patients were smokers. Twenty-six patients (22%) were not obese. The indication for pulmonary function testing was dyspnea in 46 patients, possible asthma in 22, possible COPD in 16, and cough in 15.