CHEST™

Ventilation/Perfusion Distribution Abnormalities In Morbidly Obese Subjects Before and After Bariatric Surgery

Eva Rivas, MD; Ebymar Arismendi, MD; Alvar Agustí, MD; Marcelo Sanchez, MD; Salvadora Delgado, MD; Concepción Gistau, MsC; Peter D. Wagner, MD; and Roberto Rodriguez-Roisin, MD

BACKGROUND: Obesity is a global and growing public health problem. Bariatric surgery (BS) is indicated in patients with morbid obesity. To our knowledge, the effects of morbid obesity and BS on ventilation/perfusion ($\dot{V}_A/\dot{Q}$) ratio distributions using the multiple inert gas elimination technique have never before been explored.

METHODS: We compared respiratory and inert gas ($\dot{V}_A/\dot{Q}$ ratio distributions) pulmonary gas exchange, breathing both ambient air and 100% oxygen, in 19 morbidly obese women (BMI, 45 kg/m^2), both before and 1 year after BS, and in eight normal-weight, never smoker, age-matched, healthy women.

RESULTS: Before BS, morbidly obese individuals had reduced arterial P_{O_2} (76 ± 2 mm Hg) and an increased alveolar-arterial P_{O_2} difference (27 ± 2 mm Hg) caused by small amounts of shunt (4.3% ± 1.1% of cardiac output), along with abnormally broadly unimodal blood flow dispersion (0.83 ± 0.06). During 100% oxygen breathing, shunt increased twofold in parallel with a reduction of blood flow to low $\dot{V}_A/\dot{Q}$ units, suggesting the development of reabsorption atelectasis without reversion of hypoxic pulmonary vasoconstriction. After BS, body weight was reduced significantly (BMI, 31 kg/m^2), and pulmonary gas exchange abnormalities were decreased.

CONCLUSIONS: Morbid obesity is associated with mild to moderate shunt and $\dot{V}_A/\dot{Q}$ imbalance. These abnormalities are reduced after BS. CHEST 2015; 147(4):1127-1134

Manuscript received July 16, 2014; revision accepted September 15, 2014; originally published Online First October 9, 2014.

ABBREVIATIONS: A-aP_{O_2} = alveolar-arterial P_{O_2} difference; BS = bariatric surgery; D_{LCO} = diffusing capacity of the lung for carbon monoxide; ERV = expiratory reserve volume; Log SDQ = dispersion of blood flow distribution; Log SDV = dispersion of alveolar ventilation distribution; MIGET = multiple inert gas elimination technique; $\dot{Q}t$ = cardiac output; $\dot{V}_A/\dot{Q}$ = ventilation/perfusion

AFFILIATIONS: From Servei d'Anestesiologia (Dr Rivas); Institut d'investigacions Biomèdiques August Pi i Sunyer (IDIBAPS) and Fundació Clínic per a la Recerca Biomédica (FCRB) (Drs Rivas, Arismendi, Agustí, Sanchez, Delgado, and Rodriguez-Roisin); Servei de Pneumologia (Institut Clínic del Tòrax [ICT]) (Drs Agustí and Rodriguez-Roisin and Ms Gistau); CIBER Enfermedades Respiratorias (CIBERES) (Drs Arismendi, Agustí, and Rodriguez-Roisin and Ms Gistau); Centre de Diagnòstic per la Imatge (CDI) (Dr Sanchez); Servei de Cirurgia Gastrointestinal (Dr Delgado), Hospital Clínic, Universitat de Barcelona, Barcelona, Spain; and the Department of Medicine (Dr Wagner), University of California, San Diego (UCSD), San Diego, CA.

Part of this study has been presented in abstract form at the American Thoracic Society Annual Meeting, May 21, 2014, San Diego CA.

FUNDING/SUPPORT: This study was funded by the Fondo de Investigación Sanitaria (FIS) PI 080311, CIBERES, the Generalitat de Catalunya [2014SGR661], and a grant-in-aid from Almirall.

CORRESPONDENCE TO: Roberto Rodriguez-Roisin, MD, Servei Pneumologia (Institut del Tòrax), Hospital Clínic, Villarroel 170, 08036-Barcelona, Spain; e-mail: rororo@clinic.ub.es

DOI: 10.1378/chest.14-1749

Obesity has become a global and rising public health challenge, affecting millions of adults and children. Current estimates indicate that > 12% of the world population is obese, as defined by a BMI > 30 kg/m^2, and that this figure is on the rise.[1,2] Bariatric surgery (BS) causes a significant and sustained reduction of BMI, with minor morbidity and mortality, in morbidly obese subjects.[3,4]

Many previous studies have investigated the effects of obesity on lung function. The excess adipose tissue in the abdomen and around the rib cage reduces functional residual capacity, as shown by a marked decrease in the expiratory reserve volume (ERV).[5] In addition, a widened alveolar-arterial P_{O_2} difference ($A\text{-}aP_{O_2}$) is frequently reported in morbidly obese subjects.[6] However, to our knowledge, except for radioactive measurements of regional ventilation/perfusion ($\dot{V}_A/\dot{Q}$) distributions in a few obese subjects,[7] the effects of obesity on $\dot{V}_A/\dot{Q}$ relationships and the potential influence of BS have not before been reported.

We hypothesized that (1) morbid obesity is associated with abnormal $\dot{V}_A/\dot{Q}$ ratio distributions and (2) BS reduces them. To test this hypothesis, we used the multiple inert gas elimination technique (MIGET) in morbidly obese individuals, before and after BS, breathing ambient air and 100% oxygen to further explore the pulmonary vascular response. The results of this study have been reported previously in abstract form.[8]

Materials and Methods

Participants, Study Design, and Ethics

Morbidly obese BS candidates (BMI ≥ 40 kg/m^2 or ≥ 35 kg/m^2, with obesity-related comorbidities) were recruited prospectively and studied 24 h prior to and 1 year after BS (median, 51 weeks). Exclusion criteria were the presence of moderate to severe sleep apnea[9] (by polysomnography) and other chronic respiratory (asthma, COPD, bronchiectasis), cardiovascular, and/or mental illnesses. Normal-weight, sex- and age-matched never smokers were enrolled and served as control subjects. Obese subjects and control subjects were studied while seated at rest, during ambient air and 100% oxygen breathing (30 min each), in random order, after they had refrained from any medication during the prior 24 h. One hundred percent oxygen breathing, inert gas, and hemodynamic measurements were not determined in control individuals. All participants signed informed consent. The study was approved by the ethics committee of the Hospital Clínic (Protocol 2008/4015).

Measurements

Lung Function: Forced spirometry (before and after bronchodilation), static lung volumes by body plethysmography, and single-breath diffusing capacity of the lung for carbon monoxide (D_{LCO}) (Master Screen Body; Jaeger, CareFusion) were determined before and after BS according to international guidelines. Reference values were those of a Mediterranean population.[10-12]

Respiratory Gas Exchange: Arterial and mixed venous blood sample gases were analyzed in duplicate for pH, P_{O_2}, and P_{CO_2} (Ciba Corning 800), and $A\text{-}aP_{O_2}$ values were calculated using a standard formula.[13] Oxygen uptake and CO_2 production were calculated from mixed expired fractions of oxygen and CO_2 (Medical Graphics Corporation), respectively. Minute ventilation was measured using a Wright spirometer and corrected to body temperature and pressure saturated (Respirometer MK8; BOC Healthcare).

Hemodynamic Measurements: Heart rate and systemic and pulmonary arterial pressures were continuously monitored (HP 1001A-1006A monitor; Hewlett-Packard Company) as previously described.[13] Systemic and pulmonary vascular resistances were calculated according to standard formulae.

$\dot{V}_A/\dot{Q}$ Distributions: The MIGET was used to estimate the distributions of $\dot{V}_A/\dot{Q}$ ratios within the 24 h prior to surgery, as reported previously.[13,14] To calculate these, we used arterial, mixed venous, and mixed expired inert gas concentrations, and cardiac output ($\dot{Q}t$) determined by thermodilution, in obese patients with Pa_{O_2} < 80 mm Hg (range, 55-79 mm Hg; n = 13), whereas they were estimated without mixed venous sampling, and $\dot{Q}t$ was determined by bioimpedance (PhysioFlow; Manatec Biomedical), as described previously[15] in those with normal Pa_{O_2} (range, 82-97 mm Hg; n = 6).

Circulating Inflammatory Biomarkers: Serum samples were obtained by centrifugation of venous blood and were stored at −80°C until analysis. C-reactive protein was quantified using an immunoturbidimetry method (Advia Chemistry; Siemens AG) and leptin, adiponectin, soluble tumor necrosis factor-receptor 1, and IL-8 serum levels were measured using an enzyme-linked immunosorbent assay (Diagnostics Biochem Canada Inc, US BIOLOGIC, IBL International, and Anogen), respectively.

Statistical Analysis

Results are presented as mean ± SE, median, or percentage, as appropriate. To compare obese and control subjects, we used the unpaired Student *t* test (or the Mann-Whitney test for nonnormally distributed data) and the χ^2 test. Obese individuals before and after surgery were compared using the paired Student *t* test (or the Wilcoxon test for nonnormally distributed data) and the McNemar test. Pearson and Spearman tests were used, as appropriate, to explore bivariate correlations among variables of interest. A *P* value < .05 was considered statistically significant.

Results

Characterization of Participants

We studied 19 middle-aged, morbidly obese women (17 never smokers and two former smokers) and eight normal-weight, never smoker, healthy women. Table 1 presents their main demographic, serum biomarker, and lung function values at recruitment. As expected, both BMI and waist circumference were greater in obese than in control subjects. The prevalence of arterial hypertension (42% vs 0%), diabetes mellitus (26% vs 0%), and metabolic syndrome (37% vs 0%) ($P < .05$ each) was also higher in obese participants. The apnea/hypopnea index in obese individuals was 10 ± 2/h. All serum biomarker concentrations except adiponectin were significantly higher in obese than in control individuals (Table 1).