Bronchoscopic Lung Volume Reduction by Histoacryl

Thesis
Submitted for Partial fulfillment of MD Degree in Chest Diseases

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List of abbreviations

- 6MWT Six minutes walking test.
- ABG Arterial blood gas.
- AMP Adenosine monophosphate.
- ATS American Thoracic Society.
- BLVR Bronchoscopic lung volume reduction
- BMI Body mass index.
- BODE Body mass index, obstructive degree, dyspnea grade and exercise capacity.
- BP Blood pressure.
- BTS British Thoracic Society.
- CF Cystic fibrosis.
- CLE Centeri-lobular emphysema
- COPD Chronic obstructive pulmonary disease.
- CPET Cardiopulmonary exercise test.
- CT Computed tomography.
- CXR Chest X ray.
- DLCO Diffusion lung capacity for carbon monoxide.
- EBV Endobronchial valve.
- ECG Electrocardiogram.
- ERS European Respiratory Society.
- FEV_1 Forced expiratory volume in first second.
- FVC Forced vital capacity.
- GOLD Global Initiative for Chronic Obstructive Lung Disease.
- HD High dose.
- HDACs Histone deacetylases.
- HLA Human leukocyte antigen.
- HRCT High resolution computed tomography.
- ICU Intensive care unit.
- IM Intramuscular.
- IPF Idiopathic pulmonary fibrosis.
- ISHLT International Society for Heart & Lung Transplantation
- IU International unit.
- IV Intravenous.
- KCO The transfer coefficient.
- Kpa Kilo Pascal.

- L Litter.
- LD Low dose.
- LVR Lung volume reduction.
- LVRS Lung volume reduction surgery.
- M Meter.
- Mg Milligram.
- Min Minutes.
- Ml Milliliter
- MmHg Millimeter mercury.
- MRCD Medical Research Council Dyspnea.
- NETT National Emphysema Treatment Trial.
- NO Number .
- PA Poster anterior view.
- PaCO2 Partial pressure of carbon dioxide in arterial blood.
- PaO2 Partial pressure of oxygen in arterial blood.
- PC Personal computer.
- P_E max Maximum expiratory pressure.
- PFT Pulmonary function test.
- PLE Panlobular emphysema .
- R Correlation coefficient.
- RV Residual volume.
- S Second.
- SaO_2: Oxygen saturation in arterial blood.
- SD Standard deviation.
- SPSS Statistical Package for Social Science.
- TLCO Carbon monoxide transfer factor.
- TNFα Tumor necrosis factor alpha.
- UNOS United Network for Organ Sharing.
- US United State.
- VATS Video assisted thoracoscopy.
- V_A/Q Ventilation/perfusion ratio.

Introduction

Emphysema is defined pathologically as the presence of permanent enlargement of the airspaces distal to the terminal bronchioles, accompanied by destruction of their walls without obvious fibrosis**.** Emphysema, or destruction of the gas exchanging surfaces of the lung (alveoli), is a pathological term that is often (but incorrectly) used clinically and describes only one of several structural abnormalities present in patients with COPD ***(Hashimoto et al, 2014).***

Emphysema is commonly associated with bullae which are large non-ventilated air-containing intrapulmonary spaces of their walls formed by compressed and attenuated lung tissue. Bullae impart mechanical impediment to the ventilation of adjacent lung parenchyma, increase the residual volume (RV) and RV/total lung capacity ratio and also impair the function of the inspiratory muscles especially the diaphragm. These effects alone may cause symptoms even without the further complications of rupture, infection, etc… ***(Krishnamohan et al, 2014).***

Some studies have indicated that lung volume reduction surgery (LVRS) ameliorates dyspnea, increases exercise capacity, improves lung function, enhances health-related quality-of-life measures, and reduces mortality in selected patients with advanced emphysematous bullae. Although beneficial to many emphysema patients, LVRS is associated with an operative mortality rate of 4 to 7%, a morbidity rate of 30 to 50%, and an average hospital stay of 10 to 14 days ***(Zahid et al, 2011).***

The development of less invasive and less morbid approaches to lung volume reduction would represent a substantial advance in the treatment of emphysematous bullae. Several bronchoscopic procedures designed to reduce lung volume in patients with emphysema are under development. These include one-way valves, or bronchial occlusive devices to collapse emphysematous regions of lung and bronchial fenestration with bypass stents to improve expiratory flow ***(Murphy et al, 2014).***

Shah and Herth (2014) reported that bronchoscopic injection of autologous blood in emphysematous bulla will decrease the bulla in size and improve dyspnea.

Moreover***, Hartman et al, 2014*** proved that biological lung volume reduction can be safe and produce benefits in appropriately selected patients with advanced heterogeneous emphysema.

Aim of the work

The aim of this work is to evaluate the safety and efficacy of bronchoscopic lung volume reduction using adhesive material (histoacryl blue) in patients with emphysema and emphysematous bullae.

Review of LiteRatuRe

Chapter (1)

(Emphysema)

The word emphysema is derived from Greek and means "to blow into," hence "air containing" or "inflated". Although "voluminous lungs" and lungs "turgid particularly from air" were described respectively by ***Bonet in 1679 and Morgagni in 1769*** the first description of enlarged airspaces in emphysema in the human, together with illustrations, was furnished by ***Matthew Baillie in 1807*** who not only clearly recognized and illustrated emphysema, but also pointed out its essentially destructive character ***(Vestbo J., 2013*)*.***

Laennec, 1821 recognized that air trapping and increased collateral ventilation were features of emphysematous lungs, and that the peripheral airways were the primary site of obstruction in emphysema. Furthermore, he noted that air spaces enlarged with increasing age, and he distinguished these changes from emphysema ***(Valipour A et al., 2014).***

Assessment of COPD

Determine the severity of the disease, its impact on the patient's health status and the risk of future events (for example exacerbations) to guide therapy. Consider the following aspects of the disease separately:

- current level of patient's symptoms
- severity of the spirometric abnormality
- frequency of exacerbations
- presence of comorbidities.

COPD Assessment Test (CAT): An 8-item measure of health status impairment in COPD .

Breathlessness Measurement using the Modified British Medical Research Council (mMRC) Questionnaire: relates well to other measures of health status and predicts future mortality risk.(**GOLD ,2013)**

Table (1): Modified Medical Research Council Questionnaire for Assessing the Severity of Breathlessness

PLEASE TICK IN THE BOX THAT APPLIES TO YOU (ONE BOX ONLY)	
mMRC Grade 0. I only get breathless with strenuous exercise.	☐
mMRC Grade 1. I get short of breath when hurrying on the level or walking up a slight hill.	☐
mMRC Grade 2. I walk slower than people of the same age on the level because of breathlessness, or I have to stop for breath when walking on my own pace on the level.	☐
mMRC Grade 3. I stop for breath after walking about 100 meters or after a few minutes on the level.	☐
mMRC Grade 4. I am too breathless to leave the house or I am breathless when dressing or undressing.	☐

Table (2): Classification of Severity of Airflow Limitation in COPD

(Based on Post-Bronchodilator FEV1)

In patients with $FEV_1/FVC < 0.70$:	
Mild GOLD 1:	$FEV_1 \geq 80\%$ predicted
Moderate GOLD 2:	$50\% \leq FEV_1 < 80\%$ predicted
Severe GOLD 3:	$30\% \leq FEV_1 < 50\%$ predicted
Very Severe GOLD 4:	$FEV_1 < 30\%$ predicted

(GOLD ,2013)

Assessment of COPD

- ✓ Assess symptoms
- ✓ Assess degree of airflow limitation using spirometry
- ✓ Assess risk of exacerbations

Use history of exacerbations and spirometry.

Two exacerbations or more within the last year or an FEV1 < 50 % of predicted value are indicators of high risk

Combined Assessment of COPD

- Assess symptoms
- Assess degree of airflow limitation using spirometry
- Assess risk of exacerbations

Combine these assessments for the purpose of improving management of COPD(**GOLD ,2013).**

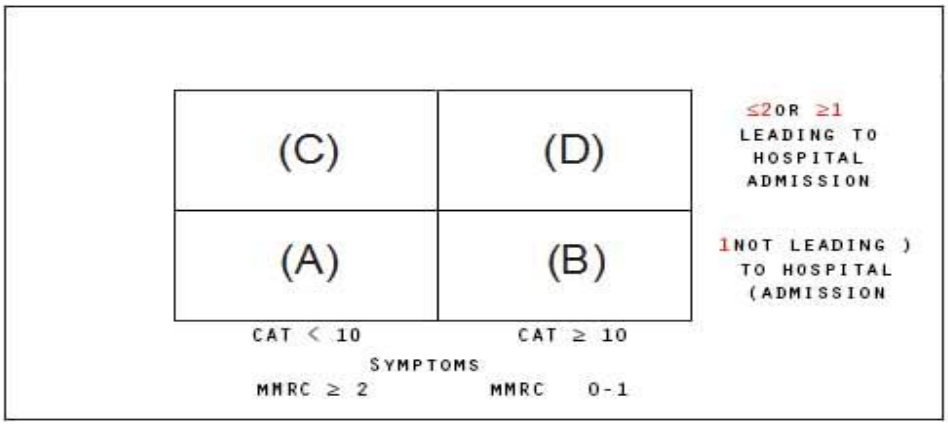

Figure (1): *Assessment Using Symptoms, Breathlessness, Spirometric Classification and Risk of Exacerbations* (**GOLD ,2013)**

Pathogenesis

Anatomy of respiratory system:

The bronchioles or bronchioli are the passageways by which air passes through the nose or mouth to the alveoli (air sacs) of the lungs, in which branches no longer contain cartilage or glands in their submucosa. They are branches of the bronchi, and are part of the conducting zone of the respiratory system. The bronchioles divide further into smaller terminal bronchioles which are still in the conducting zone and these then divide into the smaller respiratory bronchioles which mark the beginning of the respiratory region. ***(Merck., 1997).***

Structure:

A pulmonary lobule is the portion of the lung ventilated by one bronchiole. Bronchioles are approximately 1mm or less in diameter and their walls consist of ciliated cuboidal epithelium and a layer of smooth muscle. Bronchioles divide into even smaller bronchioles, called terminal, which are 0.5mm or less in diameter. Terminal bronchioles in turn divide into smaller respiratory bronchioles which divide into alveolar ducts. Terminal bronchioles mark the end of