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Short review

Mechanisms of limited airway dimension with lung inflation

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Abstract

Airways distend with each inspiration, while a sigh or deep inspiration (DI) leads to a significant or a maximum distension of the airways. Distension of the airways is thought to play an important role in maintaining airway patency. Limited distension of the airways with lung inflation may be a major factor in certain lung diseases such as asthma and chronic obstructive pulmonary disease (COPD). High resolution computed tomography (HRCT) has gained wide acceptance as a diagnostic and investigational radiological tool for the evaluation of airway function. HRCT has been used to measure dynamic changes in airway caliber in vivo that are not detectable by conventional global lung measurements such as airway and lung resistance. HRCT is uniquely capable of imaging and quantifying airway size at different lung volumes. The current paper reviews the use of HRCT to examine the role of lung inflation on airway distension in animal models, and discusses potential mechanisms for limited distension of the airways with lung inflation in individuals with asthma and COPD.

Keywords: Asthma; Chronic obstructive lung disease; COPD; Deep inspiration; DI; High resolution computed tomography; HRCT

1. Introduction

Airways distend with each inspiration, while a sigh or deep inspiration (DI) leads to a significant or a maximum distension of the airways. Distension of the airways is thought to play an important role in maintaining airway patency. For example, when a healthy individual refrains from taking any DIs, airway obstruction can be induced with an inhaled spasmogen, such as methacholine or histamine. However, when DIs are performed prior to the inhalation challenge, no obstruction occurs [1,2]. Limited distension of the airways with lung inflation may be a major factor in certain lung diseases such as asthma and chronic obstructive pulmonary disease (COPD) [2–5]. This defect might result from several factors, for example, deposition of nondistensible elements such as collagen in the airway wall, airway wall oedema and increased airway smooth muscle forces, i.e. increased tone, all of which may limit airway distension with lung inflation [6]. Another factor that could affect the change in airway size with lung inflation is air trapping. Air trapping would lead to a higher residual volume (RV), and thus, a higher functional residual capacity (FRC). If the lung operates at a higher FRC, the magnitude of distension from FRC to total lung capacity (TLC) would thus be decreased, appearing as a reduced distension of the airways with lung inflation.

Conventional spirometric measurements of lung function, such as the forced expiratory volume in one second (FEV_1) and forced vital capacity (FVC), provide a single number as a gross average of the functional state of all the airways, and thus lack the ability to assess regional or individual airway variations that may be important in understanding the pathophysiological mechanisms associated with airway obstruction [7]. The ability to directly view airway responses to various stimuli, treatments and changes in lung volume would be of great advantage in our understanding of airway pathophysiology. High resolution computed tomography (HRCT) has gained wide acceptance as a diagnostic and investigational radiological tool

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for the evaluation of airway function. HRCT has been used to measure dynamic changes in airway caliber in vivo that are not detectable by conventional global lung measurements such as airway and lung resistance [8,9].

2. HRCT functional imaging

HRCT can be used to accurately and reliably measure airway luminal area and airway wall thickness in airways in vivo [10–12]. HRCT uses thin slices, high spatial frequency reconstruction algorithms, a small field of view and increased kilovoltage and milliamperage to resolve the anatomial detail of pulmonary structures as small as 200 μm in vivo [13–15]. Our laboratory was the first to demonstrate the utility of HRCT to study airway reactivity [10]. We have subsequently demonstrated that HRCT is uniquely capable of addressing questions about airway responsiveness in vivo that cannot be answered by other pulmonary measurement techniques [16–22]. A major advantage of imaging the airways using HRCT is the ability to make repeated airway luminal and airway wall thickness measurements of multiple individual airways at different lung volumes, in vivo.

The unique ability of HRCT to image airways at different lung volumes may give insight into the underlying pathophysiology of airflow limitation in lung diseases such as asthma and COPD. Previous studies have demonstrated the ability of HRCT to measure the same airway locations repeatedly at various lung volumes in dogs [23,24], sheep [21,22], and human subjects (Fig. 1) [8,9].

2.1. Airway distension

Previous studies have demonstrated that canine and ovine airways do not distend isotropically with the lung [15,17,19]. When airways were completely relaxed, airway size quickly reached a plateau at low transpulmonary pressure (Ptp), and further increases in Ptp caused negligible changes in total luminal area (Fig. 2). This observation is consistent with histological studies of the airways that show that the epithelial basement membrane is not distensible. Therefore, any changes in the composition of the airway wall, such as collagen deposition, could lead to thickening of the airway wall (i.e., remodeling), which could limit the ability of lung inflation to pull open the airways.

Moreover, the mechanism by which intrapulmonary airways are stretched during inspiration is by increased radial traction on the airways that is exerted by the surrounding lung parenchyma [25–27]. It has been proposed that edema

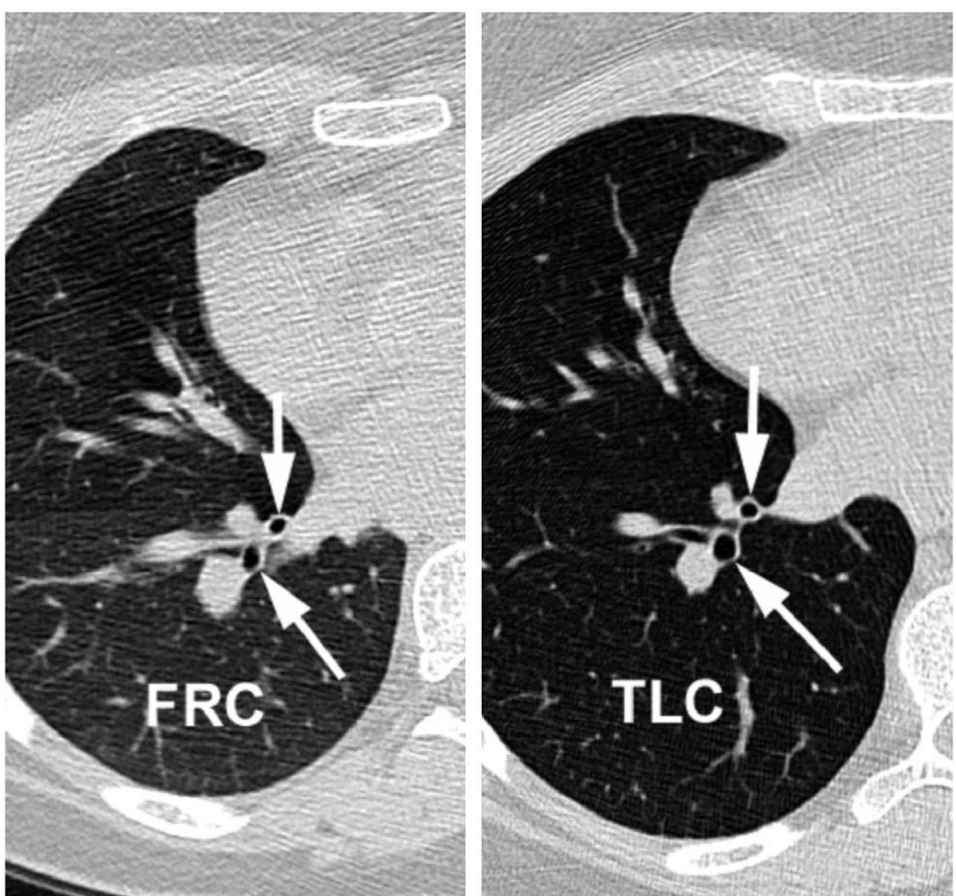

Fig. 1. Matched HRCT scans from one human subject at baseline. Images were acquired at low lung volume (FRC, left) and at high lung volume (TLC, right). The arrows show the same airways matched under both lung volumes.