Does airway inflation stretch the bronchial mucosal membrane?

The bronchial mucosa, which consists of the airway epithelium and basement membrane, forms folds along the inner lumen of the airway wall when airway lumen size decreases during bronchoconstriction or at low lung volumes (10, 12). Epithelial folding progressively diminishes as the airway lumen expands during the distension of the lungs (12). Some years ago, James and colleagues (4, 5) described a constant relationship between airway wall area and the epithelial perimeter in guinea pig airways that were fixed at different lung volumes with and without bronchoconstriction. On the basis of these observations, they suggested that bronchial epithelial perimeter length was unaffected by lung inflation or bronchoconstriction (4, 5). The constant length of the airway epithelial perimeter under varying conditions of strain and compression was purportedly due to the inextensibility of the basement membrane that subtends the epithelium. The assumption that the epithelial perimeter of the airways does not change under differing conditions of contraction, relaxation, or lung volume has provided a basis for the use of this parameter as a marker for airway size; the epithelial perimeter can be easily determined and used to predict the size of the airway lumen in a relaxed open state. Measurements of airway perimeter have thus provided a convenient shortcut for assessing the degree of airway narrowing and smooth muscle shortening in histologic sections of airways. This approach has been used in the evaluation and modeling of the effects of diverse physiological conditions on airway narrowing and to assess the effects of pathophysiological conditions such as asthma on the structure of the airway wall (1–3, 7, 11, 13).

In this issue of the Journal of Applied Physiology, Noble and colleagues (9) challenge the concept that the bronchial mucosa is not inextensible and that the airway epithelial perimeter maintains a constant length over the physiological range of airway transmural pressures. The authors measured the distensibility of the bronchial mucosa in strips of airway mucosa dissected from pig bronchi. The mucosal strips were oscillated between fixed levels of strain to obtain stress-strain curves, and the effects of strain on epithelial length, thickness, and folding were determined. Epithelial length was not altered at modest levels of strain, but higher levels of strain resulted in significant increases in epithelial length and a slight reduction in epithelial thickness. To correlate mucosal tissue stress-strain curves with physiological pressures, airway wall stress was calculated in intact pig bronchial segments from similar anatomic locations that were fixed at transmural pressures of either 5 or 25 cmH₂O. The length of mucosal strips at a stress comparable to that measured at 25 cmH₂O was 10% greater than at a stress corresponding to a transmural pressure of 5 cmH₂O. Similarly, inflation of the bronchial segments to pressures above 10 cmH₂O resulted in lengthening of the epithelial perimeter length. The length of the epithelial perimeter of bronchial segments fixed at 25 cmH₂O was 25% greater than that of generation-matched segments fixed at 5 cmH₂O. Noble and colleagues concluded that the bronchial mucosa is not inextensible over physiological ranges of airway distension, and that inflation of an airway to 25 cmH₂O may increase the airway epithelial perimeter by as much as 25%

The study of Noble and colleagues (9) is the second recent paper to suggest that the airway mucosal membrane is not inextensible during airway inflation to physiological pressures. In 2004, McParland et al. (8) published measurements obtained on human airways and estimated that the perimeter length of the basement membrane increased by ~50% when the airways were inflated from 0 to 21 cmH₂O. The study of McParland et al. was performed on human bronchi and used a different approach than Noble et al. for the estimation of changes in the basement membrane perimeter lengths with airway inflation. Differences in methodology, species, and the anatomic origin of the airways analyzed might account for differences in the magnitude of the estimated perimeter length changes between the studies of McParland et al. and Noble et al. Furthermore, the results of both studies might be subject to question on the basis of technical issues such as fixation or the underlying assumptions used for calculations. However, the fact that both groups concluded that the bronchial mucosal membrane is distensible over physiological ranges of airway inflation suggests that the utility of this measurement as a marker of airway caliber should be reexamined and that the results of studies that depended on measurements of airway perimeter as a marker of airway size should be reassessed.

The use of the airway epithelial and basement membrane perimeters as a tool for the normalization of airway size in the morphometric analysis of airway structure is widely accepted; therefore, the implications of the question of its distensibility are significant. For example, in studies comparing the airway wall structure of normal and asthmatic subjects, these measurements have formed a basis for morphometric analyses that have documented increases in airway smooth muscle mass and airway wall thickness in the asthmatic subjects (1–3, 6, 7, 11). This increase in smooth muscle mass has been considered as a possible underlying cause of airway hyperresponsiveness. As pointed out by McParland et al. (8), if the distensibility of the airway mucosal membrane is substantial, systematic differences in fixation pressure or the state of inflation of airway samples taken from asthmatic and normal subjects could result in a marked overestimation of the increase in smooth muscle mass or wall thickness in the airways from asthmatics. This could lead to the misjudgment of the importance of such changes as an underlying mechanism for airway hyperresponsiveness in asthma.

Additional studies using alternative approaches will be required to establish the degree of distensibility of the airway mucosa and to evaluate the magnitude of this effect in airways of different species and over a range of generations. However, the observations of Noble and colleagues (9) provide a strong basis for the reassessment of our assumption that the airway epithelial perimeter length can be used as a reliable marker of airway size under all physiological conditions.

REFERENCES


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