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MICROVASCULAR HYPERPERMEABILITY IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE AIRWAYS

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Chronic obstructive pulmonary disease (COPD) is characterized by an abnormal inflammatory response of the lungs. Previously, an elevation of the albumin concentration in the sputum of COPD patients was reported.[1] This may suggest that the airway microvascular permeability is increased in COPD airways, because the albumin comes from the vasculature via endothelial contraction at post-capillary venule lesions. However, the quantification of sputum samples has some limitations such as contamination by saliva. In this report, we first quantified the albumin concentration of the airway lumen in COPD subjects using a new direct technique for collecting airway epithelial lining fluid (ELF).[2]

Eighteen non-treated peripheral-typed lung cancer patients who received bronchoscopic examination for the diagnosis were recruited after approval from the Wakayama Medical University Ethics Committee and with the written informed consent of the patients. The age was 70.4±2.0 yrs (mean±SEM). Eight patients were current-smokers, seven ex-smokers and three non-smokers. Five patients were not COPD, four were at risk (Stage 0), six were moderate (Stage II) and three severe (Stage III) according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) classification of the severity of COPD.[3] ELF was collected with a microsampling probe under bronchoscopy at the main or intermediate bronchus of the tumor-absent side. The albumin concentration in the extracted ELF was measured and

normalized by the values in the serum.

The normalized airway albumin values showed a strong correlation with the forced expiratory volume in one second % of predicted (%FEV_1) values (r= -0.727, p= 0.0006) (Fig.1). There was no significant difference in the airway albumin values according to the smoking status (non-smoker; 1.21±0.29, ex-smoker; 1.23±0.28, current smoker; 1.14±0.28 (%), values were mean±SEM) or aging. These data suggest that an increase in airway microvascular permeability may be involved in the inflammatory and subsequent obstruction process of COPD. The precise mechanism of the microvascular hyperpermeability observed in COPD has not been well characterized. Recently, we have reported that oxidative and nitrosative stress is exaggerated in COPD airways.[4][5] Reactive oxygen/nitrogen species such as superoxide anion and peroxynitrite may participate in the microvascular hyperpermeability of COPD airways.

At present, some airway/pulmonary cells including epithelial cells, neutrophils, and macrophages are considered therapeutic targets for future COPD therapy. In addition to these cells, the airway microvasculature may also be a target in the treatment for COPD. Further, the airway albumin values may be a good marker of the therapy's efficacy for COPD.

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Figure Legend

Fig.1

Relationship between normalized airway albumin and forced expiratory volume in one second % of predicted (%FEV_1). Normalized airway albumin values are calculated as values of epithelial lining fluid / values of serum.

Fig. 1