

The Linkage Between Low Pulmonary Function and Subclinical Cerebrovascular Lesion in Never-Smokers

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Cigarette smoking is known to be a risk factor for many respiratory diseases. Among them, COPD is a typical disease caused by smoking and is one of the biggest causes of respiratory illness in the general population¹). It is known that cardiovascular death increases in patients with COPD²). Several epidemiological studies have also shown the association between a low respiratory function and subclinical cerebrovascular lesions³), but none of these relationships have been shown with reference to the smoking status. Also, no research has been made to show this relationship in the Japanese population.

Seto-Yukimura and colleagues show the association between reduced pulmonary function and the subclinical cerebrovascular lesion in a Japanese population in this issue of *Journal of Atherosclerosis and Thrombosis*⁴). This relationship was observed only in the never-smokers and not in the smoking population. Causes of cerebral ischemic lesions are thought to be vascular endothelial dysfunction based on arteriosclerosis or increased blood coagulation activity^{5, 6}). Although these are caused by cigarette smoke inhalation, this study showed that lower pulmonary function is associated with the presence of subclinical cerebrovascular lesions in a population without smoking habits⁴).

Two mechanisms are assumed for this association. Firstly, even if there is no smoking habit, low pulmonary function may cause a vascular endothelial dysfunction or an enhancement of blood clotting activity. Low pulmonary function reduces physical activity. It is assumed that physical inactivity triggers systemic inflammation, resulting in a decrease in vascular endothelial function and an increase in blood coagulation. Previous study has shown that myokines such as IL-6 are produced by muscle tissue during

physical activities⁷). Myokines have been reported to have anti-inflammatory action in the whole body⁷). A decrease in physical activity may result in a decrease in myokines produced from muscle tissue. As a result, systemic inflammation may be caused⁷).

Secondly, people with decreased vascular endothelial function and/or increased blood clotting activity may have a low pulmonary function as a result of lung developmental disorder. It may be said that in people with vascular endothelial dysfunction or hypercoagulability, the development of the respiratory system including the alveoli may be impaired due to microvascular dysfunctions. Childhood asthma is thought to be one of the causes of low pulmonary function in adulthood, suggesting a relationship of lung developmental disorder in asthmatic patients⁸). However, vascular endothelial dysfunction is not clear in the pathogenesis of bronchial asthma. Also, there is no report that vascular dysfunction causes lung developmental disturbance. However, such a new perspective may be necessary to interpret the phenomenon observed in the paper by Seto-Yukimura *et al.*

Epidemiological studies cannot prove the underlying mechanisms between low pulmonary function and subclinical cerebrovascular lesions in never-smokers. Further steps are needed to solve this attractive linkage.

Disclosures

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