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Editorial

Vitamin D and Chronic Obstructive Pulmonary Disease: Biomarker Related to Outcomes

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Chronic obstructive pulmonary disease (COPD), a heterogeneous disease, is a leading cause of high morbidity and mortality.[1,2] In patients with COPD, predictive factors, such as acute exacerbation, lung function decline, and death are very important because they are closely related to prognosis. Because these risk factors are different for each COPD patients, it is necessary to analyze clinical phenotypes and subgroups for tailored precision treatment. Therefore, many studies have been conducted to analyze these clinical phenotypes of COPD and to develop biomarkers that can represent each phenotype.

Vitamin D is well known as a nutrient that plays an important role in balancing between calcium and phosphorous in our body and has received much attention in the recent years. Vitamin D is not only a nutrient, but also has a function with immunomodulation and anti-inflammation and protection against infection.[3] Vitamin D deficiency is relatively common in patients with COPD, and many studies have found that vitamin D deficiency is associated with frequent exacerbation and lung function declines.[3,4] Randomized controlled trials (RCTs) showed that vitamin D supplementation reduced the rate of COPD exacerbation in patients with vitamin D deficiency.[5] However, the association between COPD clinical outcomes and vitamin D levels remains controversial, therefore, vitamin D is not yet considered as a representative biomarker for COPD phenotypes.

Serum fibrinogen is a coagulation factor, that is also an inflammatory marker. Fibrinogen is a major acute-phase reactant and level of serum fibrinogen is increased in chronic systemic inflammatory diseases.[6,7] COPD is a disease characterized by systemic inflammation, therefore, serum markers, such as fibrinogen and C-reactive protein (CRP), were considered as candidates for COPD biomarkers. Several studies showed the results that higher levels of fibrinogen were strongly correlated with the disease severity, exacerbation, and mortality.[6,8,9] In 2015, the United States Food and Drug Administration (FDA) approved plasma fibrinogen as the only COPD biomarker based on clinical evidence.

Although the relationship between vitamin D and fibrinogen has not been clearly elucidated, vitamin D plays an immune modulation role, therefore, it can be associated with pro-

inflammatory markers such as white blood cell, CRP, interleukin-6, and fibrinogen. In particular, neutrophils are frequently elevated in patients with COPD, and other pro-inflammatory markers are also increased. Vitamin D has been reported to inhibit matrix metallopeptidase 9 (MMP9), a well-known neutrophil derived elastase, and MMP9 is strongly correlated markers of fibrinogen.[10,11] As a result, vitamin D is thought to have a role in immune modulation and inhibition of airway remodeling, and may be correlated with other pro-inflammatory markers.

In this issue of the journal, Hyun et al.[12] focused on demonstrating the clinical phenotype and the COPD biomarker with a combination of fibrinogen, which has been proven to be useful as a COPD biomarker, and vitamin D, which is considered a candidate for COPD biomarker. These findings not only demonstrate that the combination of the two serum markers is a more representative biomarker for severe COPD but also raised the value of vitamin D as a more useful indicator as a biomarker. In other words, this study is meaningful in that the two indicators of vitamin D and fibrinogen are emphasized as more valuable biomarkers than other previous studies. Needless to say, further studies are required to demonstrate causality and researchers have to investigate more. For example, we should prove that the COPD outcome will be improved when vitamin D is supplied in patients with high plasma fibrinogen and vitamin D deficiency. In addition, studies exploring the underlying mechanism should be conducted. If such results are obtained, they will be clinically useful, providing strong evidence of the correlation between vitamin D and COPD clinical outcome.

COPD is a chronic airway disease, a very complex disease. Nevertheless, COPD is broadly defined by spirometry, and more innovative and clinically useful biomarkers have not yet been demonstrated. Clinically, COPD is manifested by a variety of phenotypes, and the clinical courses are diverse depending on the phenotype. The development of useful biomarkers is important, as well as analysis of phenotypes and subgroups in COPD. In particular, it is imperative to develop biomarkers that predict the development of COPD, rapid lung function decline, exacerbation, and death. Based on such biomarkers, it is possible to precisely evaluate disease prevention, drug targets development, and therapeutic effect monitoring. As in this study, potential biomarkers that still lack value as a biomarker and still controversial about the correlation with clinical outcomes can be combined into a more valuable biomarker according to the phenotypes. Moreover, these approaches may help identify pathogenesis in COPD. Researchers should pay more attention to COPD and conduct many studies based on large-scale cohorts.

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