Hypoalbuminemia and Inflammation as Prognostic Markers in Patients Undergoing Percutaneous Coronary Intervention

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Development of atherosclerotic cardiovascular disease is multifactorial, and several factors, such as hypertension, diabetes mellitus, smoking, and hypercholesterolemia, are included in risk prediction models and have led to major developments in medical therapy. Recently, an increasing number of novel biomarkers that predict cardiovascular events have been identified; however, use of such biomarker strategies in a cost-effective manner is restricted by the limited predictive value of the current risk-assessment models.

Hypoalbuminemia, usually used as an index of malnutrition, has been shown to be associated with worse clinical outcomes in various diseases, especially chronic kidney disease (CKD). A recent study reported the close association between hypoalbuminemia and long-term death in patients with acute myocardial infarction. Serum albumin, to a large extent, influenced by factors other than malnutrition, and it has been shown that low serum albumin levels correlate with high concentrations of acute-phase proteins, such as C-reactive protein (CRP), in malnourished CKD patients.

Inflammation also plays an important role in the progression of atherosclerosis. CRP is an exquisitely sensitive systemic marker of inflammation and tissue damage, and the recent development of high-sensitivity CRP (hs-CRP) revealed that increased hs-CRP levels, even within the range previously considered normal, strongly predict coronary events in apparently healthy individuals and in patients with established coronary artery disease (CAD). Previous studies showed that elevation of preprocedural hs-CRP levels in patients with CAD or undergoing percutaneous coronary intervention (PCI) was associated with adverse cardiac events. However, the relation between malnutrition and hs-CRP levels on clinical outcomes after PCI has not yet been investigated.

In this issue of the journal, Wada et al focus on the conventional biomarkers that are usually used for routine checking of patients, and they investigated the combined effects of preprocedural serum albumin and hs-CRP levels on clinical outcomes in 2,164 consecutive CAD patients undergoing their first PCI. The authors show an association between low serum albumin with high CRP levels with the incidence of major adverse cardiac events (MACE), including 270 deaths and 61 non-fatal myocardial infarctions during a median follow-up period of 7.5 years. This is the first report to show the synergistic adverse effect of low serum albumin and high CRP levels on the risk for long-term MACE in patients undergoing PCI.

The most important and impressive finding in the present study was that the combination of the 2 conventional biomarkers was a strong predictor of the clinical outcomes.
in patients with CAD who underwent PCI. Although the focus of studies of the various new biomarkers is likely to be the prediction of cardiovascular events after PCI, the current authors focused on conventional and easy-to-use biomarkers and elucidated the significance of the combined effect of low serum albumin and high CRP levels for prediction of clinical outcomes in CAD patients undergoing PCI. Although the mechanism by which these conventional biomarkers had a combined effect on the prediction of clinical outcome is still unclear, it is possible that several proinflammatory markers produced by various cells such as endothelial cells, smooth muscle cells, and macrophages in atherosclerotic lesions may induce CRP production and hypoalbuminemia and lead to progression of atherosclerosis (Figure).4

In the present study, patients with lower serum albumin and higher hs-CRP levels tended to have poor clinical condition, including older age, CKD, or lower body mass index, although multivariate analysis identified the combination of lower serum albumin and higher hs-CRP levels as the significant predictor for poor clinical outcome after adjusting for these poor clinical factors. Another concern is that hs-CRP may be influenced by several underlying inflammatory conditions. Also, because there were significant interactions between serum albumin and hs-CRP levels in the present study, these 2 parameters might not be independently related as a predictor for clinical outcomes in the present patient population. Based on these observations, it is possible that unknown confounding factors might have affected the present results, regardless of analytical adjustments. Further clinical multicenter studies in a large cohorts of patients are needed to strengthen the benefit of the present study.

We hope that we will be able to use the combination of preprocedural serum albumin and hs-CRP levels to predict the risk of clinical outcomes in CAD patients undergoing PCI.

Disclosures
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References