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Commentary

Adiponectin & inflammatory biomarkers in coronary artery disease

Inflammation plays a pivotal role in the initiation and progression of atherothrombosis and triggering of atherosclerotic cardiovascular disease (ASCVD). Clinical studies have demonstrated that chronic inflammation is associated with the future cardiovascular (CV) events, and the emerging biomarkers related to inflammation have been investigated to improve identification of at-risk asymptomatic patients. Conventional CV risk factors in the Framingham risk score (FRS), such as age, male sex, hypercholesterolaemia, hypertension, diabetes mellitus and smoking have been the cornerstone in the assessment of ASCVD risk for decades[1]. However, approximately one-third of low-risk individuals with 0 or 1 FRS risk factor have been known to develop ASCVD in the future[2]. Many researchers have tried to assess accurately ASCVD risk beyond FRS by identification of chronic and subclinical inflammation status. The Justification for the Use of Statins in Prevention: an Intervention Trial Evaluating Rosuvastatin (JUPITER) trial, targeted to apparently healthy persons without hyperlipidaemia but with elevated high sensitive C-reactive protein (hsCRP), demonstrated the clinical beneficial effect of rosuvastatin therapy[3]. In lines with this background, the recent 2013 American Heart Association (AHA) / American College of Cardiology (ACC) guidelines have recommended the usage of hsCRP for stratifying the high risk patients for ASCVD in addition to revising FRS to pooled cohort equation (PCE)[4]. However, the risk-stratification using hsCRP cannot go without any limitations[5]. There is a great variability in the hsCRP levels among individuals based on gender, ethnicity, *etc*[6]. Though the hsCRP levels are reported to be higher in women than in men, the association between hsCRP and ASCVD may be less in women compared with men[7]. The highest hsCRP levels were generally found in African Americans, followed by Hispanics, South Asians, Whites, and East Asians, respectively[6]. So, we need to find more specific inflammatory biomarker or multi-panel biomarkers approach for predicting ASCVD risk.

Adiponectin is an adipokine secreted specifically from the adipose tissue. Adiponectin modulates glucose metabolism and insulin resistance. Thus, adiponectin may act as a potential link between diabetes mellitus and its CV consequences. Hypoadiponectinaemia has already been shown to be associated with obesity, diabetes mellitus, insulin resistance, coronary artery disease (CAD), and heart failure[8-10]. A high serum adiponectin level is associated with favourable cardiovascular risk profiles. However, previous epidemiological studies have reported conflicting results in clinical outcomes[11,12]. Paradoxically, a high serum adiponectin level was associated with an increased mortality risk in healthy people, as well as in patients with ASCVD and heart failure, so called as 'adiponectin paradox'[13]. In this issue, Kumpatla *et al*[14] have shown the associations among inflammatory biomarkers including adiponectin and CAD in India. Though the concept of this study is not new, but it has an important clinical implication considering this clinical study conducted in India. According to this study, adiponectin and other inflammatory markers such as sE-selectin and TNF-α showed significant associations with CAD.

In western countries, many researchers have focused on the ethnic disparity between Caucasians and African Americans in the assessment of ASCVD risk. The ethnic disparities in ASCVD risk may be the result of differences in circulating adipokines and inflammatory markers. A recent study confirmed the existence of ethnic differences in adiponectin and CRP levels among Caucasians, Japanese Americans, Latinos, African Americans and native Hawaiians[15]. According to this study, Japanese Americans had

lower hsCRP and adiponectin levels compared to Caucasians. Another recent study from Korea reported that hsCRP concentrations were lower in Koreans than those reported for Caucasian population[16]. Thus, Koreans may need lower cut-off value of hsCRP for high risk group selection than Caucasians (2.0 mg/l). These findings suggest that there are variations in biomarkers such hsCRP, adiponectin, *etc*. between Asia and the other parts of the world. Recently, the inter Asian disconcordance has been paid attention. Mediators of ethnic differences in insulin resistance differed markedly depending on the ethnic groups. General adiposity explained the difference in insulin resistance between Chinese and Malays, whereas abdominal fat distribution, inflammation and unexplained factors contributed to excess insulin resistance in Asian Indians as compared with Chinese and Malays[17]. One could speculate that there might be disparities in biomarkers between East Asian and South Asian such as India. In the context of these disparities, the study by Kumpatla and group[14] should be paid more attention in Asia.

However, they did not demonstrate that adiponectin could be a better biomarker than other inflammatory biomarkers including hsCRP in the assessment of ASCVD in Indians[11]. Further, whether these biomarkers are additive to conventional risk factors in India by using advanced statistical methods such as net reclassification improvement, integrated discrimination improvement and comparing C-statics is not known. What is the cut-off point of hsCRP for Indian? Are there any differences between adiponectin and hsCRP in predicting CV events? The superiority of adiponectin over CRP in this study could just be a coincidental finding when considering small sample-sized cross-sectional study design. Therefore, it should be confirmed in prospectively designed larger sample-sized clinical study, which could compare the prognostic power of biomarkers for predicting future CV events in India.

Considering the ethnic disparities in inflammatory biomarkers, each country should try to find more reliable, reproducible, and more specific biomarker for its own people especially in Asian countries.

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