pISSN 1975-4612 / eISSN 2005-9655

www.kse-jcu.org
http://dx.doi.org/10.4250/jcu.2016.24.2.104
EDITORIAL COMMENT J Cardiovasc Ultrasound 2016;24(2):104-105

Neutrophil-to-Lymphocyte Ratio for Risk Assessment in Coronary Artery Disease and Carotid Artery Atherosclerosis

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Two decades ago, there was an optimistic prediction that the treatment of dyslipidemia and hypertension would eliminate coronary artery disease (CAD) by the 20th century. However, cardiovascular diseases (CVD) is now the greatest single contributor (nearly one-third) to global mortality and, unfortunately, CAD still accounts for the largest proportion of CVD.[1] Furthermore, CVD is expected to dominate mortality trend over the next few decades.[2] These facts force us to consider novel effective methods of risk stratification and treatment strategies. Hence, it is not surprising that intense attention has been focusing on the search of novel biomarkers providing prognostic information in CAD patients. In this endeavor, inflammation has been a prominent target because of its importance in the development and behavior of atherosclerotic plaques. Specifically, intimal infiltration of inflammatory cells is considered one of the initial steps in the development of atherosclerosis.[3] Inflammatory cells also contribute to the development of necrotic core and the disruption of the overlying fibrous cap driven by several molecular mechanisms including the apoptosis of foam cells and the release of proinflammatory mediators and matrix metalloproteinases.[4]

Besides the detection of local inflammation in plaques, the assessment of systemic inflammation is also a relevant approach, when considering that atherosclerosis is a diffuse disease affecting various arteries of the body. Indeed, many studies have suggested that the risk of CAD is significantly associated with the levels of systemic inflammatory markers, including C-reactive protein (CRP), erythrocyte sedimentation rate, fibrinogen, and circulating adhesion molecules.[5][6] In this issue of the Journal of Cardiovascular Ultrasound, Kim et al.[7] reported an association of coronary and carotid artery atherosclerosis with the values of neutrophil-to-lymphocyte ratio (NLR), another inflammatory marker. Furthermore, these authors determined that the addition of NLR significantly improved the discrimination of the risk of significant CAD and carotid artery atherosclerosis beyond classical cardiovascular risk factors. This biomarker is attractive because it has the advantages of being readily available, inexpensive, and thus capable of being used in the daily clinical practice, compared with other indicators of systemic inflammation.

However, more data are clearly required in larger populations to determine whether NLR can be applied clinically in the management of CAD patients. What kinds of data are needed to justify the clinical use of NLR as a valuable biomarker of systemic inflammation? One of the easiest ways is to follow a well-established precedent, such as CRP. Indeed, there is extensive evidence supporting the view that CRP plays an important role in risk assessment of patients with CVD. Specifically, multiple prospective epidemiological studies have shown the clinical utility of CRP for predicting various common cardiovascular events, such as incident myocardial infarction, sudden cardiac death, stroke, and peripheral artery disease, as well as stable CAD.[8][9] There have also been numerous studies demonstrating the predictive value of CRP in diverse populations, including patients with stable angina and acute coronary syndrome and those undergoing percutaneous coronary intervention.[10-12] Furthermore, CRP has been shown to provide additive prognostic information on top of the widely accepted indicators of CVD risk, for example, at all levels of Framingham risk score and at all levels of the metabolic syndrome.[8][13] Thanks to many studies evaluating the cut-off values of CRP for predicting clinical outcomes, CRP has strong clinical appeal to physicians by allowing them to interpret CRP levels more readily.[8][14]

In this regard, it will be a long and winding road to clinical application of NLR for CVD detection and prevention. More-

• Editorials published in the Journal of Cardiovascular Ultrasound do not necessarily represent the views of JCU or the Korean Society of Echocardiography.
• Received: May 30, 2016 • Revised: May 31, 2016 • Accepted: May 31, 2016
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over, even when aforementioned data are available, we should acknowledge that these data can only support the usefulness of NLR as a risk marker rather than a risk factor. In other words, verification of the causal link between NLR and atherosclerosis is a completely different story. Against expectations, the causality has not been established for any specific mediator of systemic inflammation, including CRP, the most extensively studied one.[4)15)16)] Therefore, at least at this point in time, it is plausible that NLR, as do all other inflammatory markers, is just a marker reflecting the inflammatory process in patients with CVD, not a key element of the causal chain leading to CVD. Further research will be needed to clarify the role of NLR as a causal contributor to CVD which can pave the way for developing an inflammation-targeted treatment strategy of CVD.

In conclusion, although there are miles to go before we sleep, the study by Kim et al.[7)] in this issue of the Journal demonstrates an easy-to-perform, relatively cheap, and promising inflammatory biomarker in risk stratification of patients with suspected CAD and carotid artery atherosclerosis.

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