Cardiovascular disease (CVD) remains the main cause of death in developed countries. One reason for this is the difficulty associated with the early diagnosis of atherosclerotic change. Although cardiovascular risk assessment based on conventional risk factors is recommended for predicting cardiovascular risk, validation studies showed only moderate performance. Therefore, a tool with more predictive ability is necessary for identifying individuals at high risk of CVD.

The hemodynamic conditions in blood vessels lead to the development of superficial stresses near the vessel walls, and local wall shear stress (WSS) is one of the most fundamental factors influencing endothelial structure and function. There have been many evidences indicating that reduced WSS is the central factor responsible for the localization of atherosclerotic plaque formation and progression. Cell culture and experimental animal models have shown that endothelium exposed to low WSS displays an atherosclerotic phenotype with focal development of atherosclerosis and vascular remodeling. Quantitative evaluations of asymptomatic intimal plaques in 12 adult human carotid bifurcations obtained at autopsy has also indicated the key role of WSS in atherosclerotic impairment in human arteries. Similarly, comparison of detailed pulsatile hemodynamic measurements with quantitative morphologic studies of the distribution of atherosclerotic lesions in the human carotid bifurcation revealed that low mean shear stress was an important factor in the development and localization of atherosclerotic plaques. Furthermore, a recent clinical study in patients with coronary artery disease (CAD) that performed radiofrequency intravascular ultrasound (virtual histology intravascular ultrasound) and computational fluid dynamics modeling for WSS calculation in the coronary artery demonstrated that low WSS segments develop greater plaque and necrotic core progression and constrictive remodeling.

Although the direct evaluation of coronary WSS is most important to assess the risk of CAD, it is unrealistic to apply this approach to all the suspected subjects because it limited by the potential of significant adverse effects, technical difficulty, availability, and high cost. Therefore, peripheral tests are required to be applied as a non-invasive, convenient, and inexpensive surrogate for coronary WSS. Because ultrasonography meets the abovementioned conditions and carotid arteries develops atherosclerotic lesions at an early age, carotid WSS measured by ultrasound could be one of the most promising candidates.

The study by Cho KI et al in the current issue of Journal of Atherosclerosis and Thrombosis provides important new data indicating that carotid WSS, which can be evaluated relatively easily by ultrasound together with carotid intima-media thickness (IMT) and total plaque area (TPA), has a role as an early index of atherosclerosis and serves as a predictor of significant coronary atherosclerosis. In this study, they investigated the relationships between carotid WSS and the coronary artery stenosis evaluated by angiography as well as the parameters of atherosclerosis in the common carotid artery, such as IMT, TPA, and beta stiffness index. Based on the cross-sectional study in 950 patients with suspected CAD, they revealed that reduced carotid WSS was positively associated with a greater IMT and TPA and that low carotid WSS and high carotid plaque burden in the carotid arteries were significant predictors of CAD in patients with chest pain. Moreover, the receiver operating characteristics (ROC) curve analyses revealed that the predictive value (area under the curve) of carotid WSS was comparable with the Framingham Risk Score (0.632 and
0.630, respectively) and was relatively higher than that of IMT and TPA (0.548 and 0.607, respectively). These results suggest that carotid WSS has a role as an index of systemic atherosclerosis and serves as a predictor of significant coronary atherosclerosis.

However, it should be noted that the findings of this study should be confirmed in further studies. Particularly, whether the predictive ability of carotid WSS for the presence of CAD is higher than established markers, such as IMT and TPA, should be verified. A long-term follow-up study will be also required because the analysis was performed based on cross-sectional data. In addition, the subjects of this study were all Chinese patients with chest pain. Therefore, it may not be appropriate to apply their findings to non-Asian and/or asymptomatic populations.

Recently, several methods to non-invasively assess WSS and/or endothelium-dependent vasodilation in human arteries have been developed. Among them, the assessment of brachial flow-dependent, endothelium-mediated vasodilation (FMD) by vascular ultrasound, a measure of the release of nitric oxide by the endothelium due to a transient flow stimulus, would be the most widely used because it is noninvasive, repeatable, reproducible, and standardized in well-experienced laboratories. Impaired brachial FMD is widely regarded as an early and potentially reversible manifestation of vascular disease and used as a surrogate for CVD9, 10). However, its use for universal screening is not feasible because the assessment of brachial FMD is somewhat time consuming and requires a highly qualified and experienced investigator to obtain reproducible results.

As compared with brachial FMD, the clinical evidence of the utility of carotid WSS is still poor. However, future potentials of this approach as a screening tool for high-risk individuals are predicted to be high because it could be measured together with other established coronary risk markers, such as carotid IMT and TPA, in a non-invasive, convenient, and economical procedure. Therefore, it is necessary to perform further researches to confirm whether carotid WSS could be used as a reliable cardiovascular risk predictor and as an index of local endothelial function.

### Conflict of Interest

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