Sex Differences in the Association between Traditional Vascular Risk Factors and Subclinical Carotid Atherosclerosis in Taiwan

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Carotid intima–media thickness (cIMT) measured by B-mode ultrasound has been regarded as a good surrogate of subclinical carotid artery atherosclerosis since 19861). Numerous observational studies have since suggested that cIMT is predictive of many clinical cardiovascular diseases (CVDs), such as coronary heart disease and ischemic stroke. However, there were inconsistent results regarding whether cIMT can improve the prediction of CVD events beyond the traditional CVD risk factors in the general healthy populations2). Statistical significance (e.g., hazard ratios) does not provide information about the effect size or the clinical relevance3). As a result, in the American College of Cardiology and American Heart Association (2013) and European Society of Cardiology (2016) guidelines, cIMT is not recommended for routine measurement in clinical practice for CVD risk assessments.

cIMT values may differ by race/ethnicity and sex. In general, blacks have greater cIMT than whites and Hispanics, and Asians have lower cIMT than other races4). In addition, males have greater cIMT than females4). These differences indicate that the burden of atherosclerosis varies across race or sex, and thus the study of cIMT needs race/ethnicity- and sex-specific approaches. In this issue of the Journal of Atherosclerosis and Thrombosis5), Wu and colleagues examined the correlation between traditional CVD risk factors and cIMT — defined as the far-wall mean common carotid artery IMT — in 1,579 middle-to-old aged men and women in northern Taiwan. In the multivariable linear regression model, traditional CVD risk factors, including age, hypertension, fasting blood glucose, and low-density lipoprotein (LDL)/high-density lipoprotein (HDL) cholesterol ratio, were correlated with cIMT in the overall cohort. As compared with females, the mean cIMT was greater in males and per 1.0 standard deviation (SD) increases of body mass index and LDL/HDL cholesterol ratio in males resulted in 0.0971 (p=0.030) and 0.1177 (p=0.0087) SD increase in cIMT, respectively. These findings suggested that the impact of metabolic abnormalities on cIMT might be less in females than males.

The present study also revealed that the coefficients of LDL/HDL cholesterol ratio and body mass index with cIMT decreased in participants who were free of common carotid artery plaques with or without prior clinical CVD, hypertension, and diabetes. A previous study has reported that inflammation in terms of elevated C-reactive protein concentration may modify the relationship between LDL and HDL and was associated with greater cIMT6). Furthermore, high inflammation status may attenuate the association of LDL cholesterol concentrations with incident coronary heart disease in the elderly population7). Notably, the proportion of cigarette smoking in males (48%) was much higher than that in females (7.6%) in the present study, which might result in higher inflammation status in males. As compared with the females, the weaker correlations of body mass index and LDL/HDL cholesterol ratio with cIMT in the males was likely affected by the potential confounder of inflammation status.

In a previous Taiwanese study8), Su and colleagues found that the association of LDL cholesterol and body mass index with cIMT was stronger in females than in males. Their findings contradicted the
results of the present study. Shimabukuro and colleagues revealed that the component of sex difference may differ within Japan as well\(^9\). As stated in the present study, these inconsistent findings may be due to differences in the prevalence of the traditional CVD risk factors and lifestyle among different populations. Furthermore, the cross-sectional design of our study is not appropriate to translate the findings to the temporal relationship. Unexpectedly, Huang and colleagues have shown that body mass index and hypercholesterolemia were not predictive of cIMT progression in males or females in Taiwan\(^{10}\). In summary, we did not have sufficient data for determining sex-specific temporal relationship between traditional CVD risk factors and cIMT in the general populations in Taiwan, and further investigation is required.

**Conflict of Interests**

None.

**References**