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EDITORIAL COMMENT

Ethnic Differences in Pericoronary Adipose Tissue Attenuation

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Traditional modifiable cardiovascular risk factors such as hypertension, hyperlipidemia, smoking, and diabetes have long guided risk stratification in clinical practice. However, although these factors are associated with atherosclerosis progression, they do not capture the dynamic and complex pathophysiological processes that contribute to the development and progression of coronary artery disease, and they may lack precision when applied for risk estimation in different ethnicities.[1-3] Pericoronary adipose tissue attenuation (PCATA) quantified from coronary computed tomography angiography (CTA) is an established noninvasive imaging biomarker of coronary inflammation. Pericoronary adipose tissue (PCAT) exhibits unique pathophysiology because of its proximity to the coronary arteries and shared common blood supply with the vasa vasorum.[4] PCATA around the proximal right coronary artery (RCA) is the most standardized and reproducible measurement, and it has a strong association with future cardiovascular events.[5-7] Previous research has shown PCATA to independently predict the presence of noncalcified plaque, high-risk plaque, and incident myocardial infarction independently.[6,8,9] PCAT has largely been studied in European populations; however, variation in coronary plaque in Asian populations raises the question whether PCATA values follow a similar trend.[10,11] Smaller studies have been performed within Asian populations and demonstrate similar relationships between PCATA and coronary plaque.[12-14] Furthermore, Goeller et al[15] studied matched Asian, South East Asian, and European ethnic groups and found a higher correlation between noncalcified plaque and PCATA within the South East Asian group; however, these investigators noted that overall there was no difference in PCATA values among the groups. The literature is far from definitive when it comes to the ethnic variation in PCAT, although this remains an important area of research. Understanding this diversity may be key in tailoring this novel marker toward improving health outcomes.

In this issue of *JACC: Asia*, Nishihara et al[16] report on a multicenter study of 1,270 patients who underwent clinically indicated coronary CTA across 4 hospitals in Japan. The primary objective was to investigate the relationship between PCATA around the proximal epicardial coronary arteries and incident major cardiovascular events (MACEs), defined as cardiovascular death and acute coronary syndrome, in an East Asian population. Specifically, the study reported higher RCA PCATA values among patients who experienced MACEs vs patients without MACEs (−63.7 ± 8.9 HU vs −67.4 ± 9.1 HU; $P = 0.021$). Furthermore, high RCA PCATA, defined by a cohort-specific cutoff of >−66.6 HU) was associated with an HR of 1.555 (95% CI: 1.074-2.249; $P = 0.019$) for MACE, following adjustment for traditional risk factors and adverse coronary CTA findings. There was also a significant association with MACE with left anterior artery PCATA, left circumflex artery PCATA, and mean PCATA across all 3 epicardial vessels in multivariable analysis. Clinical utility of PCATA was assessed through comparison with the Hisayama score, a Japanese-based risk prediction model. The baseline C-statistic for the model was 0.645 (95% CI: 0.544-0.745), which marginally improved to 0.687 (95% CI: 0.602-0.772) with the addition of RCA PCATA, although the change was not statistically significant ($P = 0.208$).

Nishihara et al[16] are to be commended for this analysis, which is among the first to demonstrate the prognostic value of coronary CTA-derived PCATA in a dedicated East Asian population. Nishihara et al[16] show moderate to strong correlations of the PCATA

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measurement among the 3 major epicardial vessels, as well as excellent intraobserver and interobserver agreement. The study has several strengths, which include the large sample size, the multicenter and multivendor design, and the rigorous adjudication of MACEs.

The study places particular emphasis on the importance of considering ethnic differences in cardiovascular research. As noted by Nishihara et al,[16] previous studies involving predominantly European populations have not adequately addressed how PCATA may behave in Asian cohorts. Coronary artery disease itself has shown ethnic variation in several studies comparing Asian subpopulations. Using optical coherence tomography imaging, Nakajima et al[10] showed culprit lesions in South Asians to exhibit more features of plaque vulnerability when compared with East Asians and Caucasians. In a stable cohort undergoing coronary CTA, Ihdayhid et al[11] showed East Asians to harbor less lower-density noncalcified plaque compared with South Asian and Caucasian counterparts. These earlier findings convey the importance of recognizing distinct demographics within Asia itself. This variation in plaque burden and composition may or may not relate to PCATA, but nevertheless it raises the question of how PCATA should be used in a predominantly Asian population.

Although the present analysis does add to the literature within an East Asian population, there are important limitations. Three different computed tomography scanners were used, although the tube voltage did remain constant. Imaging characteristics have been shown to cause variation in PCATA values, and a potential solution would have been to use a scanner-specific threshold,[17,18] as reported by van Diemen et al.[19] Plaque analysis was also only qualitatively performed, and this has the potential for subjective bias and is lesion specific. This issue is of particular importance given that the study is testing the hypothesis of PCATA as a patient-level biomarker of coronary inflammation, and several automated quantitative plaque analysis platforms are currently available. Nishihara et al[16] also note the lack of a comparator group, which is a significant limitation and prevents the data from being conclusively unique to an East Asian population. Finally, this study described a cohort-specific threshold of −66.6 HU as an optimal cutoff to predict MACEs. When their data were analyzed with the more widely reported threshold of −70.1 HU, there was no evidence of association with MACEs. Interestingly, a very recent and comparative study of 1,353 Chinese patients is at odds with the current study because there was a prediction of MACEs at a threshold −70.1 HU, with the risk augmented with the use of quantitative plaque burden evaluation.[20] Therefore, it is unclear whether the prognostic value of PCATA in this demographic differs significantly from that in a predominantly European cohort. Finally, it was unfortunate that PCATA did not provide incremental predictive value beyond the Hisayama score. Thus, the clinical utility of PCATA in East Asians remains uncertain, and larger, comparative studies are needed.

This study by Nishihara et al[16] adds to the expanding literature on the prognostic value of PCATA by extending the findings to an East Asian population. Future work will need to involve larger cohorts across various Asian countries and incorporate different clinical risk scores and coronary CTA-derived quantitative plaque metrics. Critically, however, serial coronary CTA studies are also needed to assess the natural history of PCATA in this population and its response to both conventional and emerging lipid-lowering therapies.

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