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Something Old Predicting Something New.

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In this issue of *Circulation: Cardiovascular Imaging*, Yared et al study the relationship between coronary artery calcium (CAC) in middle age patients and change in CAC from early adulthood to middle age with left ventricular (LV) function, in a large asymptomatic biracial population of 5115 participants of CARDIA study (The Coronary Artery Risk Development in Young Adults). The primary findings of this study are that in middle-aged individuals, higher CAC scores were independently associated with indices of LV function, namely higher LV mass index, LV volumes, LV filling pressures, and higher left atrial volume index. Specifically, higher CAC score remained independently related to higher LV mass index, even after adjusting for baseline demographics, cardiovascular risk factors, 10-year change in risk factors, and chronic risk exposure. These findings are consistent with prior studies that have demonstrated significant associations of CAC score with high LV mass. Increase in CAC has been previously reported to be influenced by both baseline and change in cardiovascular risk factors over time. However, in a robust analysis, authors have accounted for adjusting for baseline and change in risk factor over time which helps address issues of spurious associations due to measurement error at baseline. 

Another important aspect is that the study further extends these observations to novel findings in an exploratory analysis, where they note that individuals free of CAC over 10 years of follow-up demonstrated lower LV mass and volumes, as well as better echocardiographic indices of LV systolic and diastolic function, specifically lower LV end-systolic volume, lower LV longitudinal strain, lower left atrial volume index, and lower E/e ratios. The exact mechanisms underlying LV remodeling and diastolic dysfunction remain unknown; however, association with common factors related to abnormal CAC score, including age, hypertension, inflammation, and oxidative stress have been reported. Previously, Eleid et al did not find an association between CAC score and diastolic dysfunction, however, noted an association between CAC score and left atrial volume index. Similarly, prior studies have reported positive association of CAC score with other surrogates of diastolic dysfunction including LV hypertrophy and LV filling pressures. However, the study results of the relationship between change in CAC score over time and LV remodeling are novel, compelling and provide us with important data that further highlights the prognostic use of CAC progression on LV function.

We note that left ventricle ejection fraction was not associated with CAC score or change in CAC score, but higher CAC score was associated with worse LV myocardial strain, suggesting potential effect on subclinical LV systolic impairment. This relationship has been shown previously using magnetic resonance imaging in MESA study (Multi-Ethnic Study of Atherosclerosis) cohort and has been attrib-
uted to effect of CAC on endothelial dysfunction and microembolisation related to plaque rupture.

Furthermore, the authors report racial differences in the relationship between CAC and adverse cardiac remodeling in an adjusted stratified analysis and demonstrate that change in CAC was related to higher LV mass in blacks but not in whites. Previous studies have described race-based variations in LV mass, with blacks having greater LV mass and wall thickness than whites. Race-based differences in regional LV systolic function using magnetic resonance imaging have also been reported in a cohort of asymptomatic individuals, with blacks showing the least myocardial contraction in all LV regions. We know that blacks have a higher prevalence of heart failure (HF) than people of other race/ethnic groups and notably, in a 20-year prospective study of young to middle-aged adults, incident HF before 50 years of age was 20x greater among blacks than among white subjects. The reasons for racial differences for incidence and severity of HF remain unclear and have been previously attributed to ethnic variations in prevalence of risk factors, genetic heterogeneity, and disparities in access care and treatment response. The present study results have important clinical implications in understanding the role of CAC and sub clinical atherosclerosis in the reported race-based heterogeneity in HF incidence/severity and highlights the urgent need to understand the mechanisms behind greater propensity for adverse cardiac remodeling in blacks.

CAC score has been independently associated in a with a 10-year risk of adverse cardiac outcomes including myocardial infarction and stroke. We must note that the current study results for the first time, independently link change in CAC score over time with adverse cardiac remodeling which can act as surrogate to HF but does not provide information about outcomes such as HF incidence/ severity. These myocardial changes that accompany CAC progression may be critical to explain the worsening outcomes seen with CAC progression in several large trials. CAC progression has been shown to be an independent predictor of incident coronary heart disease events in all 4 of the MESA race/ethnic groups. Other large cohort studies also demonstrate CAC progression associated with increased all-cause mortality, and certainly the potential for associated changes in the myocardium may be contributory.

The authors do highlight their results may be partially impacted by the cross-sectional nature of the analysis, and associations between CAC score and cardiac parameters detected at follow-up may have existed at baseline.

Overall, the study results remain to be of particular significance since it highlights the association of CAC score over time and subclinical LV impairment in asymptomatic middle-aged individuals and provides critical data for considering mobilization of diagnostic and therapeutic interventions/medications targeted at cardiac remodeling and risk factor modification before incidence of heart failure.

ARTICLE INFORMATION

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