It’s All About the Inflammation

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Cardiovascular disease remains the number 1 killer in the developed world. Coronary artery disease is the most common form of cardiovascular disease, leading to myocardial infarction, heart failure, and death. Inflammation has been implicated as an important linchpin in the atherosclerotic process and promotion of atherogenesis. More important, atherogenesis is a diffuse disease process that often affects multiple vascular beds in a given patient. Statin medications, used as lipid-lowering drugs, have been noted to also act as an anti-inflammatory, imbuing these medications with benefits beyond lipid lowering. More importantly, anti-inflammatory drugs, such as statins and canakinumab, treat the entire vascular bed, whereas mechanical interventions, such as coronary artery stenting, treat only the segment of the epicardial coronary artery intervened on. Studies have identified markers of inflammation that are associated with coronary artery disease and outcomes. hs-CRP (high-sensitivity C-reactive protein) is a well-studied marker of inflammation, and increased hs-CRP is associated with increased incidence of coronary artery disease. In CANTOS (Canakinumab Anti-Inflammatory Thrombosis Outcome Study), canakinumab, a monoclonal antibody targeting interleukin-1B, resulted in a reduction of cardiovascular events independent of the lipid level. Taken together, these data suggest that inflammation is an important part of the atherosclerotic process and therapies that target inflammation are beneficial in terms of a reduction in cardiovascular events.

In recent years, the adipose tissue that surrounds blood vessels has been established as metabolically active and an important player in the inflammatory process of atherosclerosis. Perivascular adipose tissue is the adipose tissue that surrounds blood vessels and has an important metabolic and vasoprotective relationship with the blood vessels it surrounds. Perivascular adipose tissue secretes adipokines that act in a paracrine or vasocrine manner. In a healthy person, perivascular adipose tissue secretes adipokines that promote vasodilation and have anti-inflammatory effects. In the unhealthy state, perivascular adipose tissue secretes proinflammatory adipokines and cytokines, which affect the surrounding vasculature and promote atherosclerosis. Coronary arteries are embedded in adipose tissue referred to as pericoronary adipose tissue (PCAT). PCAT is readily measured and evaluated using computed tomography (CT). Studies have linked CT-quantified PCAT to the presence and progression of coronary plaque burden, decreased myocardial perfusion, and clinical outcomes. Thus, PCAT measured by CT is an important marker in the assessment of the coronary health in patients. This is particularly important given the increased use of coronary CT angiography (CCTA) to evaluate patients with known and suspected coronary artery disease. CCTA allows assessment of atherosclerotic overall burden and stenosis severity, the hemodynamic importance of coronary lesions using either functional flow reserve CT or stress CT, and burden of inflammation by assessing PCAT.

See Article by Kanaji et al.

Key Words: Cardiac CT ■ coronary atherosclerosis ■ inflammation ■ pericardial fat

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In this issue of the Journal of the American Heart Association (JAHA), Kanaji and colleagues assessed the relationship of PCAT attenuation and global coronary flow reserve (gCFR) in patients who have undergone urgent revascularization for non-ST-segment-elevation myocardial infarction.¹¹ The patients in this study cohort underwent CCTA before revascularization with PCAT attenuation assessment using CCTA. gCFR was assessed 30 days after revascularization with phase-contrast magnetic resonance imaging of the coronary sinus. The authors found that patients with impaired gCFR 30 days after revascularization had higher PCAT attenuation before revascularization. In a multivariate analysis, only age and mean PCAT attenuation were associated with a gCFR <1.8. This finding has several important applications. First, it links PCAT attenuation to potentially higher-risk patients who have already undergone revascularization. Second, it illustrates the limitations of local therapies, like stents, in a diffuse disease process, such as atherosclerosis. Third, it highlights the importance of therapies that improve vascular health, like statins, via anti-inflammatory pathways and suggests that PCAT metabolism may be a therapeutic target.

Of interest in this study was the lack of correlation between hs-CRP and PCAT attenuation and that PCAT attenuation was an independent predictor of gCFR and hs-CRP was not. Whether PCAT is measuring an inflammatory process not detected using hs-CRP or if it is a more sensitive measure of coronary artery inflammation needs to be investigated further.

As the authors point out in their limitations section, it is unclear if the findings in this study are associated with worse clinical outcomes. In addition, it would have been helpful if the gCFR was known before stenting to assess if those with lower mean PCAT attenuation did not have any increase in the gCFR after revascularization or if the increase in revascularization was lower compared with those with higher mean PCAT attenuation. Another limitation is that the authors did not take into consideration the extent of atherosclerosis, determined by CCTA or coronary artery calcium, or stenosis severity, as determined by CCTA on gCFR. In conclusion, this study by Kanaji and colleagues¹¹ enhances our understanding of the importance of PCAT in the inflammatory process and links the inflammatory process, as measured by PCAT attenuation, to low gCFR.

### ARTICLE INFORMATION

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**Disclosures**

None.

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