EDITORIAL

Revisiting carotid imaging: integrating atherosclerosis, the adventitia, and perivascular adipose tissue

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Arteriosclerosis, and specifically atherosclerosis, is the underlying pathophysiologic disease process that causes most clinical cardiovascular events, such as myocardial infarction and ischemic stroke. Risk factors for atherosclerosis and cardiovascular events are well described, and are the focus of primordial and primary prevention strategies. Nonetheless, established risk factors account for less than 50% of the extent and severity of atherosclerosis,[1] and while they are associated with incident cardiovascular events, they fail to identify a large number of people at risk of cardiovascular events, while incorrectly identifying others who are not at risk.[2]

It has been proposed that a noninvasive assessment of the burden of atherosclerosis (ie, direct visualization and quantification of the underlying disease process) may assist in better prediction of incident cardiovascular events and be of relevance in targeted prevention strategies. Probably the most well-established of these measures is carotid intima-media thickness (IMT). Originally described in 1986 by Pignoli et al,[3] carotid IMT measured by high-resolution ultrasound is higher in people with established cardiovascular disease, predicts incident cardiovascular events independent of established cardiovascular risk factors, and responds to risk factor reduction.[4] However, making clinical treatment decisions based on carotid IMT, for example, risk factor reduction in moderate-risk patients, remains controversial.

Alternate and complementary measures exist. One proposed complementary measure is carotid extra-medial thickness (EMT), which is also derived from high-resolution carotid ultrasound. Carotid EMT was originally developed with the intention of, at least partially, capturing the variation in arterial adventitial structure,[1] given an emerging body of evidence from experimental studies at the time that highlighted the role of the adventitia in the development and progression of atherosclerosis.

A major challenge of imaging the arterial adventitia by ultrasound is the poor delineation of the external interface. Carotid EMT bypasses this by measuring from the arterial media-adventitia interface through to the jugular lumen at a site where the 2 vessels run alongside one another. But in doing so, carotid EMT accordingly includes other distinct physical components, specifically interstitial tissue, the entire venous wall, and perhaps most notably, perivascular adipose tissue. With the exception of the perivascular adipose tissue, these nonadventitial components are unlikely to be affected by cardiovascular risk factors or atherosclerosis, and indeed after adjustment for whole-body adiposity, for example, body mass index (BMI), as a proxy for perivascular adiposity,[5] the variation in carotid EMT appears to be predominantly due to differences in carotid adventitial thickness.[6] Without adjustment, it is not clear whether adventitial thickness or perivascular adipose tissue is the greatest contributor to variation in carotid EMT, although a postmortem case report has provided some evidence that perivascular adipose tissue is the major contributor to the absolute thickness of the measure in an adult with obesity.[7] Accordingly, carotid EMT has gained some traction as both a measure of adventitial structure, providing mechanistic insight into the likely role of the adventitia in arteriosclerosis, and also as a measure of perivascular adiposity.[8]

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Key findings that have leveraged the technique include those that describe the potential role of the adventitia in fibroelastic remodeling of the intima and media,[9,10] the association of carotid EMT with nonmodifiable cardiovascular risk factors,[1] and the association of carotid EMT with the severity and complexity of coronary artery disease.[11] Yet, available evidence suggests that carotid EMT is not associated with incident clinical cardiovascular events in high-risk individuals,[12] although this is derived from a post hoc analysis of a single study.

In this issue of *Kardiologia Polska* (*Kardiol Pol*, *Polish Heart Journal*), Haberka et al,[13] sought to address a key question regarding the value of carotid EMT, as well as carotid IMT, carotid stenosis, and PATIMA—a combined index of vascular health and perivascular adipose tissue—for predicting coronary revascularization in patients scheduled for coronary angiography as part of their clinical care. All 322 participants (men, 64%) were considered to be at high risk of clinical cardiovascular disease: all had hypertension and hypercholesterolemia, half had obesity, and one-third had diabetes. Ultrasound analysis of vascular health was undertaken prior to coronary angiography, during which the decision on whether or not to revascularize was made by the independent treating interventional cardiologist based on European Society of Cardiology guidelines. Coronary angiography revealed that 71% of patients had coronary artery disease (≥50% stenosis), and revascularization was performed in 49% of patients, on the basis of European clinical guidelines. Carotid IMT, PATIMA, and carotid stenosis were all greater in individuals who were revascularized, while carotid EMT and the number of cardiovascular risk factors did not differ between groups. The receiver operating characteristic (ROC) curve analysis revealed similar results, although the ratio of carotid EMT to BMI, which was not compared between groups, predicted subsequent coronary revascularization. The area under the ROC curve was modest, similar to that for carotid stenosis, and slightly greater than that for carotid IMT. Carotid stenosis and carotid IMT had the highest sensitivity, while the ratio of carotid EMT to BMI had the highest specificity. Although collectively no measure performed well enough for clinically meaningful stratification, they may still play an important role in prediction, but there remain important evidence gaps. How far in advance can these markers be used to "predict" the incidence of cardiovascular events or a clinically indicated coronary intervention? And does the relative predictive value of these markers differ in people of different ages and different disease stages? The latter is particularly relevant when extending these measures into childhood and adolescence, during which the earliest functional and physical manifestations of arteriosclerosis develop in select vessels.[14]

Identifying or developing methods for assessing arteriosclerosis much earlier in life, and which are useful in predicting lifetime risk, monitoring the efficacy of prevention strategies, and guiding clinical decisions will potentially have a central role in more holistic approaches across the life course to cardiovascular disease prevention. Thus far, the best evidence supports a potential role for carotid IMT and pulse-wave velocity in adulthood. Whether carotid EMT will gain significance within this context is unknown. However, both carotid EMT and the PATIMA index, measures that combine vascular health and perivascular adiposity, may be particularly attractive in younger people in whom there are challenges for accurately assessing lifetime risk.

ARTICLE INFORMATION

CONFLICT OF INTEREST None declared.

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