8-1-2013

Barometer in the storm--carotid artery plaque quantified by three-dimensional ultrasound

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To the clinician treating cardiovascular disease, carotid ultrasound is an exciting and practical imaging biomarker, vigorously being explored and implemented for use in cardiac disease detection and risk stratification. Given that the rise of cardiac risk factors has been likened to a coming tsunami, a call of warning has been raised by epidemiologists for the need to develop cost effective diagnostic tools for primary and secondary prevention. Carotid ultrasound stands out among other modalities as a relatively inexpensive and safe tool in our growing armamentarium of stratification approaches. However, recently there has been some debate, questioning the true potential of carotid ultrasound given the emerging evidence that carotid intimal medial thickening (CIMT) may not be as predictive of disease as previously thought. Several recent studies and meta-analyses now make it evident that the true potential of carotid scanning may lie in the assessment of a phenomenon other than CIMT—we should, in fact, be measuring carotid artery plaque.

Compared with CIMT, carotid artery plaque may be a truer barometer of disease elsewhere in the vascular tree, including the coronary arteries. Plaque has a stronger association than CIMT with coronary atherosclerosis because the two represent biologically distinct phenomenon. CIMT is mainly a result of hypertensive thickening of smooth muscles in the media layer, but atherosclerosis is, in fact, a subintimal process. Thus plaque volume and area, which represent focal increases in arterial wall thickness, are more likely to represent regions of atherosclerosis rather than medial hypertrophy. This has been supported by several studies, including the ARIC trial, which did not quantify carotid plaque, but simply noted its presence or absence, and showed that the addition of plaque to CIMT significantly improved risk prediction. This and subsequent studies called for methods of quantifying plaque to further improve risk prediction.

Earlier methods of plaque quantification used two-dimensional techniques including plaque area and plaque score. These studies were found to be quite promising, though it was realized that we were quantifying a three-dimensional (3D) structure using two-dimensional (2D) techniques. For example, 2D carotid plaque area was initially validated by Spence and colleagues as a strong predictor of stroke, death or myocardial infarction. Even after adjustment for traditional risk factors and treatment, patients in the top quartile of plaque burden carried 3.5 times the risk of those in the lowest quartile. Other investigators used a plaque score in which the maximal plaque thickness was measured (in mm) in a single plane as a line drawn from the intima to the maximal point of protuberance into the lumen, and added for all four segments of the carotid artery. The plaque score was significant as an independent predictor for coronary artery disease after adjustment for cardiovascular risk factors, sex and age.

A new era: Like all things in ultrasound these days, three-dimensional ultrasound has emerged as an exciting technique to visualize plaque in the carotid arteries. Being well versed in three-dimensional echocardiography, some groups, like ours, have translated a three-dimensional quantification template from the heart to the carotid artery. And unlike other uses of 3D ultrasound, which simply allow for better visualization of a particular lesion, in this instance 3D quantification confers highly useful clinical risk information affecting patient outcomes. We have used a rapid, automated, single sweep method of quantifying carotid artery plaque using commercially available, three-dimensional ultrasound techniques. In this protocol, the entire volume of the carotid bulb is visually scanned for the presence of plaque. Scanning in this manner allows for simultaneous visualization of the vessel in short axis, long axis and sagittal views in all possible planes. This avoids the pitfalls of a 2D assessment where the plaque may be out of plane and not visualized in the long axis or short axis acquired.

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Is 3D carotid ultrasound ready for clinical application? In general, carotid plaque quantification by ultrasound is a rapid, inexpensive, safe technique with the potential to serve as a cardiac risk stratification tool. In the hands of experts, 3D total plaque volume assessment is also used to assess the response to investigational treatment. At the current time, 3D quantification methods are on the horizon for clinical application, though long-term study is lacking and we are still in the process of coming to a consensus regarding standardization of measurements. Especially intriguing is the question of what long-term impact low amounts of plaque may have on cardiac risk. Would these patients benefit from intensive medical management? Who should be screened? Analysis of plaque texture, use of contrast, assessment of plaque calcification and synergism with other imaging, plasma, or genetic biomarkers are all important areas requiring greater study. As the image resolution and precision of the software continue to improve and become easier to use, we are very excited about the immense potential of three-dimensional carotid ultrasound plaque quantification for detection, prevention, and treatment of the cardiovascular epidemic. In the face of this coming storm, we need all the warning that we can get. Dr. Amer Johri posts about cardiovascular health on Twitter. Follow him at @amerjohri.