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Look to Windward: Novel Applications of Vascular Ultrasound

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Epidemiologists, looking ahead, have sounded a call of warning- there is a "Tsunami" of cardiovascular disease on the horizon. The magnitude of the projected prevalence and cost of disease may be quantified in a number of ways. A recent American Heart Association policy paper projected that by 2030, 40.5% of the US population will have some form of cardiovascular disease (CVD). Between 2010 and 2030, the direct medical costs of CVD are projected to triple, from $273 billion to $818 billion. These staggering estimates have outlined the need to develop non-invasive tools to enhance CVD screening.[1]

When looking at the cost of atherosclerosis broken down by age, it is apparent that that the 65–79 year old cohort will be contributing to the highest burden of disease by 2030. This is the cohort that is presently in the mid to late 40's and though the vast majority of this population is asymptomatic, these projections compel us to ask whether we should screen and aggressively modify the projected disease course now. This belies the premise of subclinical atherosclerosis assessment- changing the projected course of disease at an individual and societal level by detecting disease early.

Atherosclerosis remains challenging and costly to screen and diagnose. The clinical standard to diagnose significant coronary atherosclerosis is an angiogram. We use an armamentarium of tools to stratify both symptomatic and asymptomatic patients such as risk scoring, CT, MRI, and nuclear imaging to determine who would benefit from this invasive procedure and/or treatment. All of these tools have limitations including cost, radiation, and limits in sensitivity and specificity. Ultrasound, which is radiation free, and relatively less expensive, may potentially overcome some of these barriers and be an additional tool for screening of subclinical atherosclerosis, enhancing the diagnostic test characteristics of our current approaches.

The Atherosclerosis Risk In Communities study (ARIC) was a large study showing the importance of carotid intimal media thickening (CIMT) and plaque presence by ultrasound for cardiovascular risk assessment. This was a 15-year prospective study of approximately 16,000 patients that found that CIMT quantification was predictive of CVD beyond traditional risk factors.[2] Of particular interest was the finding that the presence or absence of plaque was a more powerful risk stratification tool than CIMT. This important work suggested that future studies should be directed toward determining whether plaque quantification could be used to increase the accuracy of ultrasound-based CVD risk assessment.

We and others met the challenge of quantifying plaque using three- and two-dimensional methods describing this tool as a "barometer" of important CVD elsewhere.[3,4] Beyond plaque quantification, composition is now being investigated as a characteristic that may enhance the utility of peripheral plaque assessment in CVD risk stratification. It is thought that the majority of CVD events are not caused by hard stable plaques, but rather by rupture of soft, hemorrhagic plaque. Vulnerable plaque may be ulcer prone and arise due to a fragile, unstable, calcified cap. Such plaque may have a soft lipid rich core. A vulnerable plaque is thought to be neovascularized from the vasa vasorum, thus prone to hemorrhagic rupture.

Several ultrasound methods are now being investigated in the characterization of plaque vulnerability. Gray scale median (GSM) analysis is a technique used to quantify the echogenicity of plaque. A lower GSM value may signify a softer, rupture prone plaque. Could GSM characterization help identify plaque vulnerability in vascular beds, thereby identifying patients prone to CVD outcomes?

A second method of interest in ultrasound-based CVD risk detection is the use of contrast-enhanced ultrasound (CEUS). CEUS involves the injection of highly echogenic gas-filled microbubbles into the circulation so that blood flow activity may be monitored within the vessel of interest. Utilization of this technique may allow for the delineation and identification of very soft portions of plaques that cannot be imaged by conventional ultrasound due to their echolucency. CEUS may also be a valuable tool to detect neovascularization by monitoring the movement of microbubbles, which may enter the vasa vasorum and then perfuse the plaque. Quantification of this enhancement may identify rupture prone plaque, however, further correlation with outcomes is required.

Texture analysis is another emerging method that may not only provide information on the overall echolucency of a plaque, but could characterize the pattern of echolucent and echogenic areas. By taking into consideration both heterogeneity and spatial variations in pixel intensity, this method provides information about plaque composition and structure. Plaque texture analysis potentially allows for the detection of plaque morphologies predictive of vascular events. Future studies should aim to determine if plaque heterogeneity is correlated to cardiovascular outcome.

Another interesting area of work is the investigation of carotid arterial strain. Noninvasive methods to evaluate arterial stiffness in the clinical setting include carotid-femoral pulse wave velocity and local distensibility measures of superficial arteries. Early work suggests that arterial stiffness may be more closely associated with age and CVD risk factors, such as hypertension and diabetes, rather than atherosclerosis. However, clinical application of this approach as a measure of CVD risk requires further study.

As we look toward the future of vascular ultrasound, we see the emergence of complex and exciting techniques, potentially serving as new tools to screen for atherosclerosis, vulnerable plaque, and cardiac risk. The emergence of these techniques into clinical practice may provide cost-effective tools to better diagnose atherosclerosis, and navigate this "Coming Storm."

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