Vascular Ultrasound Imaging for Screening Patients at Risk for Cardiovascular Events

Application from the West to the East

Tasneem Z. Naqvi
Scottsdale, AZ, USA

Carotid intima-media thickness (IMT) has been proposed as a useful predictor of cardiovascular (CV) events in asymptomatic subjects in prospective observational studies, and has been used as a surrogate marker of efficacy in randomized therapeutic trials of statins [1]. Furthermore, meta-analyses have demonstrated incremental coronary heart disease and stroke risk prediction with IMT [2]. The evidence emerging from numerous observational, interventional, and meta-analytical studies led, at the AHA Prevention Conference V, to the recommendation of the use of "carefully performed carotid ultrasound in experienced laboratories" in asymptomatic persons >45 years of age, for further clarification of CV disease (CVD) risk over and above risk factors [3] and multisocietal development of feasible protocols for clinical use [4]. The recommendation of carotid IMT as a Class IIa test in subjects with intermediate Framingham risk scores in the Adult Treatment Panel (ATP) III 2010 prevention guidelines [5] was revoked 3 years later in the ATP IV guidelines [6] to a Class III test without any change in evidence base. The 2013 guidelines had relied on data from a single meta-analysis report that evaluated only common carotid artery IMT and ignored plaque [7]. The incremental predictive value of plaque for CV risk is far greater than that of IMT thickening [8]. In fact, evaluating IMT alone, without the inclusion of plaque assessment for the demonstration of subclinical atherosclerosis, is like looking at a coronary angiogram and ignoring coronary stenoses. This confusion in published reports of the role of IMT has resulted from methodological variations in IMT studies, leading to an incomplete evaluation of atherosclerosis; the two-dimensional (2D) nature of ultrasound that precludes the three-dimensional (3D) assessment of atherosclerosis, especially if single-angle imaging is performed; and the comprehensiveness of imaging protocols [9]. Moreover, the use of IMT only by expert personnel and measurement only by core laboratories have discouraged its routine clinical application.

CVD caused 17.3 million deaths in 2008, and 80% of these deaths were in low- and middle-income countries [10]. Of the 25 million deaths from CVD projected for 2020, 19 million are expected to be in developing countries [11]. The detection and treatment of subclinical atherosclerosis in these populations have the potential to reduce the global death toll of CVD. This fact, along with the improvement in ultrasound technology that allows for minimal user interface, suggests that the assessment of subclinical atherosclerosis by ultrasound may have reached "prime time."

The large-scale, cross-sectional study from India and North America by Bedi et al. [12] in this issue shows that the assessment of subclinical atherosclerosis by a portable, user-friendly bedside tool is feasible in large populations and that the technique of carotid ultrasound imaging and IMT assessment could be adopted by novices after an 8-hour "crash course." Nearly 1,000 subjects were recruited in two separate cohorts in India over an 8-day period, and both carotid and femoral arteries were assessed for IMT and plaque. A comparative cohort of 400 subjects from Canada and the United States was recruited in the second phase of the study, over an 8-week period by expert sonographers; risk factor profile and Framingham Risk scores were available from these subjects. The authors found a higher prevalence of plaque in the North American cohort and in a cohort from Jaipur, India (which had a less-disciplined life-style and a higher prevalence of smoking), compared with a disciplined, semi-urban population from India that led a nonsedentary life-style, practiced meditation, and refrained from cigarette smoking. Most important, the authors compared the detection of subclinical atherosclerosis in the North American cohort against the recently revised American College of Cardiology/AHA prevention guidelines [6] and found that, although the new guidelines appropriately indicated statin therapy in a larger cohort, these still missed a significant number of subjects with subclinical atherosclerosis. Thus, even in the lowest ATP risk categories, about 15% of the cohort had carotid plaque that would otherwise have been missed by the more liberal American College of Cardiology/AHA guidelines.

The study also addresses many of the concerns that exist in published reports on IMT. In addition to evaluating carotid arteries bilaterally, they examined another vascular bed in the lower extremities and proposed the incremental value of adding more vascular beds in detecting subclinical atherosclerosis. Furthermore, they performed a separate measurement of focal plaques in both vascular beds. They also developed a comprehensive method of assessing atherosclerosis and depicting it by the easy-to-understand FUster-Narula (FUN) score, a validated 3D intima-media volume measurement, in both vascular beds. Finally, the authors used this method in a U.S. population and showed a change in the appropriate allocation of CV risk by ATP III versus ATP IV risk-prediction algorithms supporting statin

The author reports no relationships that could be construed as a conflict of interest.

From the Mayo Clinic, Scottsdale, AZ, USA. Correspondence: T. Z. Naqvi (naqvi.tasneem@mayo.edu).

GLOBAL HEART

VOL. 9, NO. 4, 2014
ISSN 2211-8160/$36.00.
http://dx.doi.org/10.1016/j.gheart.2014.10.008

treatment in a larger number of subjects likely to harbor subclinical atherosclerosis. They caution that even the liberal indication for statin treatment may miss a substantial portion of patients with subclinical atherosclerosis, and they encourage re-incorporation of simple tests such as vascular ultrasound imaging in risk-assessment protocols.

All good studies have limitations and they must be discussed. Most importantly, the performance of carotid ultrasound by novices in the Indian cohort and the use of a single-angle imaging (with the clearest visualization of IMT) could have missed thicker IMT segments at other angles. The lower prevalence of plaque in the cohort from India (24%) versus the North America (42%), although attributed to the differences in risk factors, could simply have been due to their more complete detection by expert sonographers. Furthermore, the cohort from India was not a select cohort, whereas that from North America presented themselves for risk assessment and hence were more likely to have had subclinical atherosclerosis. On the other hand, the 3D technique was validated in only a small number of subjects, and 2D imaging might have underestimated the presence of subclinical atherosclerosis. Two comparable studies in a self-referred population from the United States reported a 59% prevalence of carotid plaque with comprehensive 2D imaging [13] and 78% when a 3D assessment was performed; the population was older (68.8 years) in the latter cohort [14].

The study by Bedi et al. [12] puts into perspective the weakness of a risk factor—based approach to identifying patients with subclinical atherosclerosis who are more likely to develop CV events. The study shows that vascular ultrasound imaging technology is ripe and that the previously existing barriers, such as poor resolution, cumbersome protocols, the need for off-line processing, and the need for expert sonographers, no longer exist. The question that this study does not address (and perhaps no future study might!) is whether this imaging-based approach would save more lives than the risk-based approach. We need to ponder whether treating nearly 50% of the adults on statins using a risk-scoring algorithm in the United States [15] is more appropriate versus treating only those who have subclinical atherosclerosis on the basis of a comprehensive, readily available, inexpensive, and simple screening method. This study makes a compelling argument in favor of imaging for screening.

REFERENCES

1. Crouse JR 3rd, Raichlen JS, Riley WA et al. METEOR Study Group. Effect of rosuvastatin on progression of carotid intima-media thickness in low-risk patient with subclinical atherosclerosis: the METEOR Trial. JAMA 2007;297:1344–53.
2. Lorenz MW, Schaefer C, Steinmetz H, Sitzer M. Is carotid intima media thickness useful for patient prediction of cardiovascular risk? Ten-year results from the Carotid Atherosclerosis Progression Study (CAPS). Eur Heart J 2010;31:2041–8.
3. Greenland P, Abrams J, Aurigemma GP, et al. AHA Scientific Statement Prevention Conference V: Beyond secondary prevention: identifying the high-risk patient for primary prevention: noninvasive tests of atherosclerotic burden: Writing Group III. Circulation 2000; 101:e16–22.
4. Stein JH, Korcarz CE, Hurst RT, et al. Use of carotid ultrasound to identify subclinical vascular disease and evaluate cardiovascular disease risk: a consensus statement from the American Society of Echocardiography Carotid Intima-Media Thickness Task Force. Endorsed by the Society for Vascular Medicine. J Am Soc Echocardiogr 2008;21:93–111. quiz 189—90.
5. Greenland P, Alpert JS, Beller GA, et al, American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. 2010 ACCF/AHA guideline for assessment of cardiovascular risk in asymptomatic adults: executive summary: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation 2010;122:2748–64.
6. Stone NJ, Robinson J, Lichtenstein AH, et al, American College of Cardiology/American Heart Association Task Force on Practice Guidelines. 2013 ACC/AHA Guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation 2014; 129(Suppl 2):S1–45.
7. Den Ruijter HM, Peters SA, Anderson TJ, et al. Common carotid intima-media thickness measurements in cardiovascular risk prediction: a meta-analysis. JAMA 2012;308:796–803.
8. Inaba Y, Chen JA, Bergmann SR. Carotid plaque, compared with carotid intima-media thickness, more accurately predicts coronary artery disease events: a meta-analysis. Atherosclerosis 2012;220:128–33.
9. Naqvi TZ, Lee MS. Carotid intima-media thickness and plaque in cardiovascular risk assessment. J Am Coll Cardiol Img 2014;7: 1025–38.
10. World Health Organization. Cardiovascular diseases. Available at: http://www.who.int/cardiovascular_diseases/en/. Accessed November 23, 2014.
11. Reddy SK. Cardiovascular disease in non-Western countries. N Engl J Med 2004;350:2438–40.
12. Bedi R, Nagra A, Fukumoto T, et al. Detection of subclinical atherosclerosis in peripheral arterial beds with B-mode ultrasound: a proposal for guiding the decision for medical intervention and an artifact-corrected volumetric scoring index. Glob Heart 2014;9: 367–78.
13. Naqvi TZ, Mendoza F, Rafii F, et al. High prevalence of ultrasound detected carotid atherosclerosis in subjects with low Framingham risk score: potential implications for screening for subclinical atherosclerosis. J Am Soc Echocardiogr 2010;23:809–15.
14. Sillesen H, Muntendam P, Adourian A, et al. Carotid plaque burden as a measure of subclinical atherosclerosis: comparison with other tests for subclinical arterial disease in the High Risk Plaque BioImage study. J Am Coll Cardiol Img 2012;5:681–9.
15. Pencina MJ, Navar-Boggan AM, D'Agostino RB Sr et al. . Application of new cholesterol guidelines to a population-based sample. N Engl J Med 2014;370:1422–31.