Carotid Intima-media Thickness And Vascular Age: You Are Only as Old as Your Arteries Look

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Because coronary heart disease (CHD) is the leading cause of death in the United States, primary prevention of cardiovascular events is a health care priority.[1] A key challenge to primary prevention efforts is identifying individuals who would be candidates for more intensive medical interventions. The Third Adult Treatment Panel of the National Cholesterol Education Program recommended using the Framingham Global Risk Assessment Model to predict risk; however, this model is very dependent on chronological age, which is a surrogate for atherosclerotic burden.[2,3] A sensitive, technically straightforward, and noninvasive marker of cardiovascular risk that can be used in the office setting would be a valuable clinical tool. Measurement of carotid intima-media thickness (CIMT) with B-mode ultrasound is a noninvasive and highly reproducible technique for quantifying atherosclerotic burden. It is a well-validated research tool, but is not used widely as a clinical tool, even though the American Heart Association Prevention Conference V concluded that CIMT "can now be considered for further clarification of CHD risk assessment."[4]

WHY LOOK AT THE NECK WHEN YOU ARE INTERESTED IN THE HEART?

As cardiologists and health care professionals, we do not simply practice "cardiac disease," we practice cardiovascular medicine, and that is what we are certified to practice by governing bodies such as the American Board of Internal Medicine. One obvious reason we should be interested in the carotid arteries is that stroke is the third leading cause of mortality in the United States and is a leading cause of disability. Another reason to look at the carotid arteries is that they provide a window to the coronary arteries. The risk factors for coronary artery disease are the same as for cerebrovascular disease, and we have known for at least 2 decades that patients with a major carotid stenosis are very likely to have a major coronary stenosis, which is why we perform preoperative assessment in people who are about to undergo carotid endarterectomies. An often unappreciated fact, however, is that the relationship between the degree of atherosclerosis in the carotid arteries and the coronary arteries is similar. That is, the relationship between the atherosclerotic burden in a carotid artery and a coronary artery is the same as between any two coronary arteries.[5] Thus, carotid atherosclerosis provides a window to the degree of coronary atherosclerosis in an individual. This is not detected using a standard carotid duplex ultrasound examination. Carotid duplex ultrasound identifies occlusive carotid lesions by identifying high-velocity Doppler signals. By the time a patient has an occlusive lesion, either in coronary or carotid arteries, there is extensive atherosclerosis burden. By examining the carotid artery wall rather than the lumen, risk prediction with carotid ultrasound identifies an earlier stage of atherosclerosis. The combined thickness of the intimal and medial layers is what is identified, measured, and used to predict risk.

Using a high-resolution B-mode ultrasound transducer, 3 segments of the carotid arteries (ie, common carotid, carotid bulb, and internal carotid) are interrogated (Figure 1). There are a wide variety of different protocols for scanning the carotid arteries. In our institutional vascular health screening program, we focus more on the far wall than the near wall. We not only look for the presence of nonocclusive plaques but specifically measure CIMT, which is an independent predictor of future cardiovascular events including heart attacks, cardiac death, and stroke.

WHY USE CIMT MEASUREMENTS CLINICALLY?

There are several advantages to using CIMT testing in a clinical setting. It is completely noninvasive, does not involve radiation, and has no known adverse biologic effects. It also identifies both minor

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J Am Soc Echocardiogr 2004;17:686-9.

0894-7317/$30.00

doi:10.1016/j.echo.2004.02.021

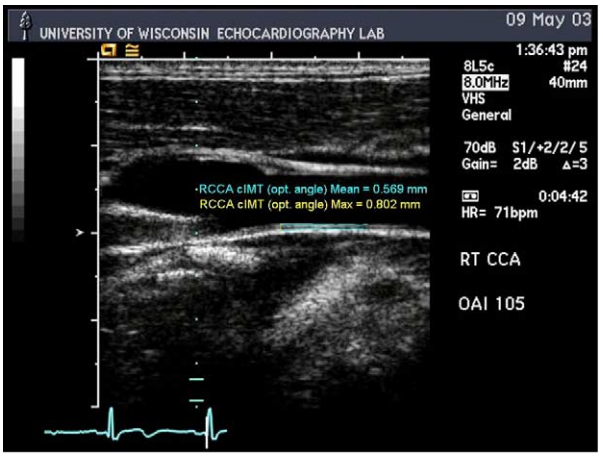

Figure 1 Normal far wall common carotid artery intima-media thickness in a 50-year-old woman.

and major stenoses, corresponding to both early and late vascular disease. A major advantage to using CIMT to predict risk is that normal values are known, which is a huge advantage over many other imaging modalities. There have been large, prospective epidemiologic studies of patients with and without atherosclerotic vascular disease that included large numbers of patients of both sexes, different races, and a wide range of ages that let us define percentiles so that we can know which values are normal, high, and low.[4,6,7] CIMT values not only predict future myocardial infarction and strokes, they provide incremental predictive power in addition to standard risk factors, which is a critical requirement for any new test. Because coronary risk factors predict events quite well, it is difficult to show additional predictive value, but CIMT is one of the few modalities that actually can show incremental predictive power.[4,6,7] Finally, The AHA Prevention Conference V recommended CIMT scanning for patients who are older than 45 years and require further clarification of their CHD risk.[4]

EVIDENCE FOR USE OF CIMT IN CLINCIAL RISK PREDICTION

There are several studies that have demonstrated that CIMT predicts future cardiovascular events.[4,7-10] For demonstration purposes, the Atherosclerosis Risk in Communities (ARIC) study will be focused on, because it has a well-defined scanning protocol and published data.[6,8,10-12] This was a study of 15,792 men and women. The people in this study at its inception were 45 to 64 years old and they were taken from 4 communities in the United States in an effort to capture a wide variety of patients in regard to race and socioeconomic level. They were followed up for 4 to 7 years (average: 5 years) and, at baseline, each patient's cardiac risk factors and CIMT were determined.[8,12] In ARIC, increasing CIMT identified prevalent cardiovascular disease including angina, myocardial infarction, stroke, transient ischemic attack, and peripheral vascular disease.[12] More importantly, the presence of increased CIMT predicted future CHD events, both for men and women.[8] As the walls of the carotid arteries became more thick, the age- and sex-adjusted incidence rates for cardiac death or myocardial infarction increased in a stepwise fashion. Of course, because this test looks at the cerebrovascular bed, it also predicts strokes, and after 7 years of follow up in ARIC, increased CIMT predicted cerebrovascular events both in men and women.[10] In multivariate analysis, after adjusting for CHD risk factors such as cholesterol levels, blood pressure, and tobacco use, the ability of CIMT to predict future coronary events remained statistically significant and had incremental predictive power both in women and men.[8]

ARIC was not the only large epidemiologic study to show this. As shown in Table, 5 studies, all of which had more than 1000 patients, have demonstrated the predictive power of CIMT measurement.[7,8,10,12-14]

USING CIMT MEASUREMENTS IN CLINICAL PRACTICE

Current guidelines recommend that if a patient has two or more risk factors for CHD, the Framingham risk algorithm should be used to determine 10-year risk of heart attack or cardiac death more precisely. To do so, a certain number of points are assigned for every risk factor the patient has including their age, total cholesterol level, whether or not they smoke, high-density lipoprotein cholesterol level, and systolic blood pressure. The points are summed and score charts are used to predict 10-year risk. One of the concerns about using the Framingham risk algorithm is it assigns the same number of points to every patient at a given age regardless of their atherosclerotic burden, which ignores great variation in plaque burden at any chronological age.[15] The rich database from the many clinical and epidemiologic trials that used CIMT provides an opportunity to adjust a patient's chronological age for their atherosclerotic burden, a concept that we like to call "vascular age."[16] For example, a 45-year-old white man who has a CIMT of 0.8 mm is at the 90th percentile.[6] One could tell the patient and referring physician that he has a CIMT of 0.8 mm, but clinical use of that number may be limited because it is difficult to understand for many patients and physicians. Instead, the patient could be told that al-

Table Selected prospective studies relating carotid intima-media thickness to increased cardiovascular events in individuals who are asymptomatic

Study	No. of patients	Sex/age (y)	Follow-up (y)	Change in CIMT	Risk ratio (95% CI), event
CHS[7]	4476	M, W/>65	6	Per 0.20-mm increase (CCA)	1.24 (1.12-1.38), MI
					1.28 (1.16-1.42), stroke
				Per 0.55-mm increase (ICA)	1.34 (1.20-1.50), MI
					1.25 (1.12-1.39), stroke
ARIC[8]	12,841	M/45-64	4-7	Per 0.19-mm increase	1.17 (1.04-1.31), CHD
		W/45-64			1.38 (1.21-1.58), CHD
ARIC[10]	14,214	M/45-64	6-9	Per 0.18-mm increase	1.21 (1.05-1.39), stroke
		W/45-64			1.36 (1.16-1.59), stroke
KIHD[14]	1257	M/40-60	3	Per 0.1-mm increase	1.11 (1.06-1.16), MI
Rotterdam[13]	1565	M, W/>55	3	Per 0.16-mm increase	1.43 (1.16-1.78), MI
					1.41 (1.25-1.82), stroke

ARIC, Atherosclerosis Risk in Communities [study]; *CCA*, common carotid artery; *CHD*, coronary heart disease; *CHS*, Cardiovascular Health Study; *CI*, confidence interval; *CIMT*, carotid intima-media thickness; *ICA*, internal carotid artery; *KIHD*, Kupio Ischemic Heart Disease; *M*, men; *MI*, myocardial infarction; *W*, women.

though he is at the 90th percentile for a 45-year-old, he is actually at the 50th percentile for a 60-year-old. In other words, his vascular age is 60 years old, the age at which an individual's CIMT represents the median CIMT value, on the basis of sex and race.[6,16]

Our institutional vascular health screening program uses the vascular age construct as part of a clinical risk prediction program and uses the standard imaging protocol from the ARIC study to scan 1-cm segments in each carotid artery, looking at the common carotid, the bulb, and the internal carotid artery. The far-wall CIMT of each of the segments is measured and averaged to define a segmental score, and the 6 segmental scores are averaged to define composite CIMT. For each patient, vascular age is estimated using a statistical model on the basis of published nomograms from ARIC using their sex, race, chronological age, and composite CIMT value.[16] In the initial group of 82 patients (45 men, 37 women), the median chronological age was 56 years old and the mean Framingham 10-year coronary risk was about 9.5%, representing middle-aged patients who were at intermediate risk for a cardiovascular event. The average CIMT was 0.806 mm and the average vascular age was about 65.5 years, an average increase in this referral population of about 9.6 years above the chronologic age.[16] In this study, substituting CIMT-derived vascular age for chronologic age also led to changes in predicted coronary risk (Figure 2). A predicted increase in coronary risk was observed in approximately 46% of patients and a reduction in predicted coronary risk was seen in 20% of patients. Of intermediate risk individuals, 36% were reclassified as higher risk and 14% were reclassified as lower risk. That is, 50% of patients at intermediate risk could be reclassified into a higher risk zone (for more aggressive therapy) or a lower risk zone (for less intensive intervention).[16] Our institutional vascular health screening program is for patients who are 40 to 70 years old and do not have known atherosclerotic vascular disease.[17] The target is patients who are at intermediate risk, and testing requires a physician's order. Some insurance companies have provided coverage for the screening, which includes measurement of the ankle-brachial index, lipid and glucose levels, and individualized counseling.

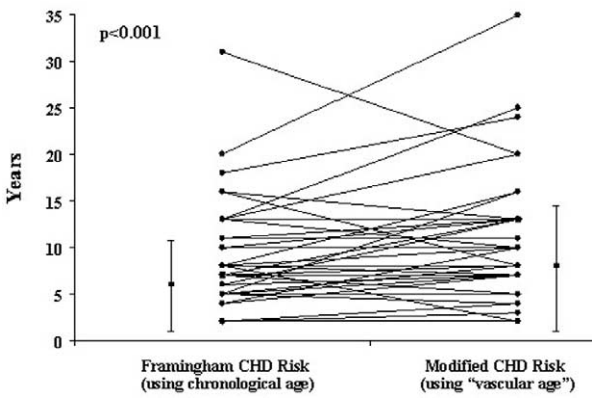

Figure 2 Change in coronary risk based on chronological and "vascular" age, using carotid intima-media thickness.

In summary, measuring CIMT using high-resolution B-mode ultrasound provides a clinical tool by which cardiovascular ultrasound can individualize risk assessment and optimize patient care. The rich research data and widespread availability of ultrasound equipment make this a tool that is ripe for widespread clinical use.[17]

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