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STATE-OF-THE-ART PAPERS

Lessons From the Past and Promises for the Future for Carotid Intima-Media Thickness

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Carotid intima-media thickness (CIMT) measurements have been used in cardiovascular research for more than 2 decades. There is a wealth of evidence showing that CIMT can be assessed in a reproducible manner and that increased CIMT relates to unfavorable risk factor levels and atherosclerosis elsewhere in the arterial system and to the risk of vascular events. Change in CIMT over time can be readily assessed, and trials showed that the rate of change is modifiable by treatment. Several issues important for the cardiovascular research community and its application in clinical practice are still outstanding. Promising future areas for CIMT measurements are: 1) application in studies among children and adolescents; 2) use of CIMT trials positioned decisively before the start of a morbidity and mortality trial; and 3) the use of CIMT measurement in risk stratification in those with an intermediate 10-year risk estimate. (J Am Coll Cardiol 2012;60:1599–604) © 2012 by the American College of Cardiology Foundation

Carotid intima-media thickness (CIMT) measurements have been applied in cardiovascular (CV) research for more than 2 decades. There is a wealth of evidence showing that CIMT can be assessed in a reproducible manner (1), that increased CIMT relates to unfavorable levels of risk factors and atherosclerosis elsewhere in the arterial system (2), and that it shows a consistent and gradual relation to risk of vascular events (3). Change in CIMT over time can be readily assessed, and trials have indicated that this rate of change can be modified by treatment (4–6). Finally, the American Heart Association has endorsed that measures of CIMT provide incremental prognostic information over and above that provided by a traditional risk factor assessment in those with an intermediate risk estimate based on the Framingham score (7).

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The purpose of this report is to address outstanding issues dealing predominantly with choices of how to measure CIMT and to point toward promising future areas for CIMT measurements in research and clinical practice. For information on technical aspects in the assessment of CIMT, such as equipment, angles of insonation, electrocardiogram triggering, and gain settings, we refer to existing reviews (8,9).

Measurement Issues

What is CIMT? A characteristic B mode image of the arterial wall is composed of 2 parallel echogenic lines separated by a hypoechoic space (Fig. 1). The distance between the 2 lines reflects the intima-media thickness, a combined measure of the intima and media layers of the arterial wall (8). A thickened CIMT measurement does not lead directly to the occurrence of a myocardial infarction or stroke. The measurement merely reflects what is going on in the vasculature of an individual (10). Similarly, the rate of change in CIMT over time is a reflection of how the development of atherosclerosis is altered over time. As such, a CIMT measurement at 1 time point and a measurement of the rate of change in CIMT over time are both reflections of CV risk.

Measured CIMT can be used in studies as a primary outcome or as a risk factor. For example, cohort studies such as the ARIC (Atherosclerosis Risk In Communities) study (11,12), the Cardiovascular Health Study (13), and the Rotterdam Study (14) started with reports dealing with how risk factors related to CIMT level (CIMT as outcome), whereas later reports published the relation of CIMT level

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Abbreviations and Acronyms

BIF = carotid bifurcation

CCA = common carotid artery

CIMT = carotid intima-media thickness

CV = cardiovascular

ICA = internal carotid artery

with future CV events (CIMT as determinant) (11–14). Similarly, rate of change in CIMT over time has been used as an outcome in intervention studies (5,6,15) and cohort studies (16,17) as well as a determinant (rate of change in relation to events) (18).

Not all CIMTs are the same. At present there is great diversity in the choice of ultrasound protocols used to acquire B-mode ultrasound images from which CIMT can be measured. The simplest protocol takes a single image from the far wall of the common carotid in just 1 of the 2 carotid arteries. The most extensive protocol is where CIMT images are obtained from both the near and the far walls of the common carotid artery (CCA), the carotid bifurcation (BIF or Bulb), and the internal carotid artery (ICA), at different angles of insonation (from 1 to 5) and both the left and right carotid artery (19). Thus, at a single ultrasound visit, one may obtain up to $2 \times 3 \times 5 \times 2 = 60$ separate images from which CIMT can be measured. Therefore, there is not 1 "CIMT," and when evaluating the measure, one must be clear about exactly what images were incorporated into the measurement.

The most frequently reported CIMT measure is an average of the far wall of the CCA from both right and left sides. Studies that collect information beyond the CCA provide specific CIMT measures for the CCA, BIF (Bulb), and ICA. When CIMT measurements are averaged, some focus on the average of all measures (mean average), and some focus on only the maximum values for each segment (mean maximum). When plaques are present in a segment, the maximum value is by definition at the maximum height of the plaque. Thus, mean maximum measures can be viewed as more heavily weighted toward plaque.

The importance of acknowledging that not all CIMT measurements are the same comes from the observations that each specific CIMT has its own specific mean value, reproducibility, completeness rate during assessment, rate of change over time, and relation with future CV events (1,9,20). Finally, for intervention studies, the susceptibility to drug treatment varies by carotid segment, and it is often impossible to predict which segment will show the strongest intervention effect (21,22).

Which CIMT measurement is the best? Clearly, the final choice for a CIMT measurement depends heavily on your research question(s) and how the characteristics of that specific CIMT measurement suit that purpose. We touch upon several opinions.

What is the best: near versus far wall? In vitro experiments showed that the far wall CIMT most accurately reflects the true thickness of the wall and that the near wall is an approximation of the thickness, a fact that is based on the properties of ultrasound waves (4). Yet, the near wall CIMT can be measured as reproducibly as the far wall CIMT and might still carry valuable information that is specific to the participant under study. In some studies the combined near and far wall CIMT was the best predictor

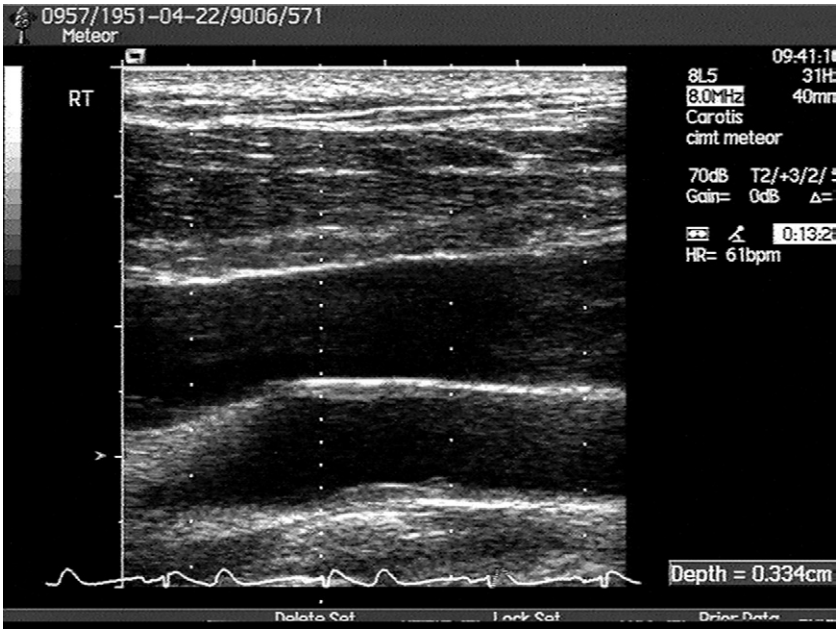

Figure 1 **Characteristic B-Mode Image of Distal Common Carotid Artery**

Interfaces of the near and far wall carotid intima media thickness from a B-mode ultrasound image. The **dotted vertical line** represents the location of the tip of the flow divider.