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The Role of Carotid Intimal Thickness Testing and Risk Prediction for the Development of Coronary Atherosclerosis

Sirous Darabian[1], **Mehera Hormuz**[1], **Muhammad Aamir Latif**[1], **Sogol Pahlevan**[2], and **Matthew J. Budoff**[1,3]

[1]St. John cardiovascular research center, Harbor-UCLA Los Angeles Biomedical Research Institute

[2]University of California Irvine

[3]University of California Los Angeles

Abstract

Carotid Ultrasound is a safe and available non invasive diagnostic tool that provides information about the carotid arteries' characteristics and may be used for early detection of coronary artery disease as well as cardiovascular and stroke event risk stratifications. We performed a systematic search of the articles discussing carotid ultrasound in English literature, published in PubMed from the year2010 to September 2012. Generally, the studies showed that Internal carotid artery intima media thickness is a more powerful variable than common carotid artery intima media thickness. Moreover, the presence of carotid plaque and plaque volumes are more reliable and accurate estimators of coronary artery disease and risk of a stroke or cardiovascular event than intima media thickness.

Keywords

Carotid Ultrasound; Coronary Artery Disease; Risk Prediction; Intima Media Thickness

Introduction

Carotid ultrasound, a real- time imaging tool, is a readily available, inexpensive, fast, safe, and non invasive diagnostic procedure, that is becoming more popular to use by physicians. This observer dependable technique, which serves both as an early detector and a follow up tool, provides information about common carotid (CCA), bifurcation, internal (ICA) and external carotid arteries. We performed a systematic search of the articles discussing carotid ultrasound in English literature, published in PubMed from the year 2010 to September 2012 to combine the results with currently established concepts in order to understand how much carotid intima media thickness (CIMT) can be accurately utilized as a marker of atherosclerosis development in the setting of various risk factors, or as a predictor of cardiovascular (CV) and stroke events in daily clinical practice.

Corresponding Author: Matthew J. Budoff MD, FACC, Professor of Medicine, Division of Cardiology, Harbor-UCLA, 1124 W Carson Street, Torrance, CA 90502, Phone: (310) 222-4107, Fax: (310) 782-9652, mbudoff@labiomed.org.
First Author: Sirous Darabian, MD, St. John Cardiovascular Research center, Harbor-UCLA Los Angeles Biomedical Research Institute, 1124 W Carson Street, Torrance, CA 90502, Phone: (310) 222-8086, Fax: (310) 782-9652, hamashena@gmail.com

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Technical aspects

The advancement in ultrasound technology has provided smaller and less-costly machines, which may be utilized in both inpatient and outpatient settings. Fundamental frequency of at least 7 to maximum 15 MHz linear phased array probes are used for evaluating carotid arteries. Measurements of the mean and peak values of Intima-media thickness (IMT) of carotid arteries is an important part of the study and varies based on age, gender, and ethnicity. IMT is measured as the distance between two echogenic lines, separated by echo lucent space in the wall of the artery. However, the intima and media are, technically, indistinguishable by ultrasound. It is appropriate to measure thickness 3 times in the anterior, lateral and posterior plans (total of 18 measurements). Automated edge detector programs, instead of manual measurements, have made measurements faster and less variable. Based on some large population studies, normal CIMT values were defined.[1,2] CIMT above the 75th percentile of average for the age, gender and ethnicity or absolute thickness more than 1.0 mm are considered an abnormal result, and people with IMT in less than the 50th percentile are classified in the low risk group.[3] Also, in the report of the Screening for Heart Attack Prevention and Education Task Force, the 75th-percentile threshold is considered an abnormal result.[4]

More commonly, the far wall of the CCA, specifically close to the carotid bifurcation, is utilized for the measurement of the IMT. However, it could be evaluated in both far and near walls of the both CCA and ICA segments. Because of the ease of access to the CCA, measurement is much easier and the results are more reproducible. In recent years, there has been a greater interest in studying the ICA, because it seems that there is a higher correlation between findings in the ICA and CAD as well as cardiovascular and stroke events.[5] If the quartile is discrepant between the right and left carotid arteries, we may apply the higher quartile. Generally, the thickness of intima-media in the bifurcation of the carotid is higher than ICA or CCA. Typically, carotid plaques were defined as a local IMT of 1.5 mm. (range between 1.2 –1.9 mm in different studies) or as a focal thickening of greater than 50% of the surrounding area.

Recently, 3D techniques grant plaque volume measurement over a specific segment of the artery.[6] Gray scale of the arterial wall and plaque is another capability of the carotid ultrasound. In addition, lumen diameter, blood flow velocity, and sheer stress are providing more information about the patient medical condition. All these data could be obtained in the same session without additional harm to the patient.

CIMT and cardiovascular risk factors

Most of the major cardiovascular risk factors affect carotid artery wall. Based on the result of a study on 3316 Framingham offspring cohort population, CCA-IMT and ICA-IMT had similar risk factors except for total cholesterol which was not correlated to CCA-IMT. This study revealed that every year CCA-IMT increased by 0.007 mm and ICA-IMT increased by 0.037mm, and age was the strongest predictor of the both CCA-IMT and ICA-IMT. After age, gender showed a strong association with CIMT. In addition, HDL cholesterol, smoking, hypertension and diabetes had a significant relation to the IMT's of both CCA and ICA.[7] In another study on Multi-Ethnic Study of Atherosclerosis (MESA) population, it has been shown that CIMT and more specifically ICA-IMT have significant reverse correlation with both HDL cholesterol level and number of particles.[8]

CIMT and early detection of atherosclerosis

Early detection of atherosclerosis is now an important topic in medicine. It has not yet been determined that screening for subclinical atherosclerosis decreases the incidence of future

cardiovascular events, but according to the current guidelines that recommend population-based screening methods such as Framingham Risk Score (FRS)[9] and Systematic Coronary Risk Evaluation (SCORE)[10], we may consider more aggressive preventive interventions for high risk patients. Generally, compared to early detection, we may expect that diagnosis of atherosclerosis in the advanced stages would lead to higher costs and less therapeutic benefits.

Unfortunately, the office-based FRS or SCORE have limited value, and the majority of patients with acute myocardial infarction have low to intermediate scores.[11] In an attempt to enhance predictive power of FRS, many non-traditional risk factors were introduced. Among them, coronary artery calcium score, CIMT and highly sensitive C-reactive protein exhibited more acceptable results.[12] The recent American College of Cardiology Foundation– American Heart Association guidelines give carotid intima–media thickness a level IIa recommendation for cardiovascular risk evaluation (the same as the recommendation level for the ankle–brachial index and coronary-artery calcium scoring).[13] Their guidelines recommended performing CIMT studies in populations with FRS of 10–20 % without known CAD, peripheral artery disease, cerebrovascular disease, or abdominal aortic disease.

Despite a significant positive correlation between CAC and CCA-IMT, CIMT is a less sensitive test than CACS for the detection of subclinical atherosclerosis.[14] Based on a recently published meta-analysis study on 11 population- based and 27 diagnostic cohort studies, the sensitivity, specificity, and diagnostic Odds ratio of CCA-IMT for CAD were 68%, 61.5% and 3.2, in order, [15] whereas, these parameters for ICA-IMT were measured as 79%, 74.4% and 7.9, respectively. Also, the study showed that there was no significant difference between diagnostic Odds ratio of CIMT and carotid plaque for diagnosis of CAD. To explain lower specificity value of CIMT for CAD, it was proposed that thickening in carotid arteries happens earlier than in coronary arteries in the process of the atherosclerosis. Also, since arterial wall media thickness correlates with blood pressure and age, it has been proposed that this thickening of IMT is not always related to the atherosclerotic process.

CIMT and prediction of cardiovascular and stroke events

It has been established that abnormal baseline and rapid progressive CIMT are correlated to more cardiovascular and stroke events. In a meta- analysis on eight population-based cohort studies, it has been reported that CIMT was able to predict future CV events. Every 0.1 mm increase in the CIMT was associated with a 10–15% increase in the risk of myocardial infarction, and in the same line, a 13–18 % increase in stroke events.[16]

A recent published study on 3580 non-diabetic people aged 55–75 years, who were clinically free of cardiovascular disease at baseline and were followed for a median time of 12.2 years, showed that only in women, CIMT had some additional predictive value beyond traditional risk factors. The net reclassification improvement in women was 8.2% (P=0.03) for hard Coronary Heart Disease and 8.0% (P=0.06) for stroke.[17] A discrepancy between additive predictive values in older age, more specifically older men vs. younger populations who are at lower cardiovascular disease risk, have explained by this fact that prevalence of disease affects the false results of the test. Therefore, we may expect less additive predictive values for higher risk groups. In the same line, in another recently published study on total 2965 free of disease participants with a mean age of 58±10 years, ICA-IMT significantly increased the net reclassification index for both men and women, and also for both participants younger or older than 60 years old, but showed the younger group benefitting more than the older participants and women more than men. This study also suggested that despite a significant correlation between mean CCA-IMT and the risk of cardiovascular events, there is no significant additive predictive power to FRS. However, on the other hand,

this study showed that maximum ICA-IMT not only had good correlation with cardiovascular events but also significantly changed the resultant net reclassification index. Moreover, this study confirmed that carotid plaque was a significant independent predictor of cardiovascular events and had a significant net reclassification index.[18]

In an attempt to compare the predictive value of CIMT with carotid plaques, a recently published article by Meta analysis of some recent studies reported that carotid plaque had a higher diagnostic accuracy for the prediction of future myocardial infarction than that of CIMT. In addition, the negative predictive values of carotid plaque compared to CIMT for future events were higher. These facts may indicate that CIMT is a more age related process or a media layer hypertrophic response to hypertension or other risk factors but that carotid plaque, which predominantly happens at non laminar turbulent flow sites such as carotid bifurcation and the proximal part of the internal carotid artery, is representative of the atherosclerotic process. However, in advanced stages of atherosclerosis, carotid plaques may also be found in the common carotid arteries.[19]

Conclusion

Carotid ultrasound is a very safe, available and reliable method for evaluation of carotid arteries that provides information about common and internal carotid IMT, presence of plaque, plaque volume, lumen narrowing, and sheer stress. This may help us detect coronary artery disease in the early stages of disease and predict the risk of a future stroke or cardiovascular event. CIMT is correlated with most of the major cardiovascular risk factors. ICA-IMT was correlated more than CCA-IMT with CAD and enhances the predictive power of the FRS for stroke and CV events. The presence of plaque is a more powerful index than CIMT for risk stratification. Still, we need more studies to confirm that risk evaluation and early detection of CAD[20,21], based on the carotid ultrasound may help us decrease morbidity and mortality. We need to better understand the implications of progression of IMT as well.[22] Also, we need to find out how much the new modalities such as 3D ultrasound may increase the accuracy rate of the test.

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