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REVIEW

Clinical impact of Intima-Media Thickness measurement

Miguel Rodrigues[1]

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Abstract

The Intima-Media Thickness (IMT) as measured by ultrasonography of carotid arteries is an acknowledged non-invasive method for assessing the impact of vascular risk factors and the progression of cardiovascular disease. The average of the far wall IMT of the common carotid artery (CIMT) from right and left sides is most frequently used. It correlates well with histology and it is a precursor phenotype of early atherosclerosis.

Its increase is associated with vascular risk factors. Systematic reviews have quantified this risk, showing that an increase of 0.1 mm in the CIMT is associated with an increased relative risk of 8% of myocardial infarction and 12% of stroke.

The evaluation of this parameter is simple, fast, and inexpensive, when integrated into a routine cervical artery ultrasound examination. However, CIMT also has applications in clinical research as an important study outcome, and then a standard measurement protocol should be applied to avoid information and measurement biases. The main consensus statements, both from Europe and North America, outline the technical conditions for IMT assessment and favor the use of automated edge detection software.

The relation between CIMT and vascular risk factors or vascular events has been extensively reported. Nevertheless, the implications of CIMT change observed in repeated measurements are not so thoroughly established in the available follow-up studies.

The CIMT is an attractive method of measuring target organ damage. However, it will remain a structural evaluation only, a static photograph that does not capture the complex interplay between vessel inflammation and thrombogenic processes.

Keywords: Carotid atherosclerosis, Intima-media thickness, IMT, CIMT, Cardiovascular risk assessment

[1]Neurology Department, Hospital Garcia de Orta, Almada, Portugal

Correspondence: Miguel Rodrigues
Neurology Department, Hospital Garcia de Orta
Av Torrado da Silva, Pragal, 2801-951 Almada, Portugal
Email: mig.rodrigues69@gmail.com

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Introduction

Atherosclerosis associated diseases are one of the most important contributors for the global burden of disease worldwide. Atherosclerotic vessel changes start very early in life, but its progression rate varies between subjects, according to intrinsic non-modifiable and modifiable or environmental factors [1, 2]. Risk scores, combining risk factors present at the individual level, can predict the probability of cardiovascular events, but methods that are able to directly measure the impact of atherosclerotic processes on vessels are interesting alternatives. Several methods access subclinical atherosclerosis, and carotid Intima-Media Thickness (IMT) measurement is one of the most attractive methods, allowing direct visualization of the vessel wall [2]. Although the IMT can be easily measured in other vessels like the femoral or radial arteries, most literature supports carotid artery IMT as the most reliable and better correlated with vascular risk factors.

Carotid Intima-Media Thickness measurement

After the seminal work by Pignolli et al. [3] that showed the good correlation between ultrasound image and histology of the common carotid artery wall, sonographic image of the vessel wall became increasingly popular. The IMT is a double layer structure defined by the distance between the interface of the anechoic lumen and echogenic intima, and another interface between the hypoechoic media and echogenic adventitia [4]. As this structure is typically thinner than 1.0 millimeters in the common carotid artery of normal subjects, strict protocols and standards of measurement apply when evaluating this complex.

European and North-American consensus on Intima-Media Thickness measurement

Pursuing comparable and consistent methodology on IMT measurement, expert consensus were produced in Europe and North America [4, 5]. These consensus define precise parameters concerning recommended equipment and imaging protocol (**Table 1**).

The European Consensus also establishes clear definitions for both carotid IMT and atherosclerotic plaques [4]. IMT is defined as a double-line pattern visualized by ultrasound on both walls of the common carotid artery in a longitudinal image of the vessel. Two parallel lines form it: the lumen-intima interface, and the media-adventitia interface. Plaque is a focal structure encroaching into the arterial lumen, at least 0.5 mm or 50% thicker than the surrounding IMT value, or which thickness is exceeding 1.5 mm, measured from the intima-lumen interface to the media-adventitia interface.

Which Carotid Intima-Media Thickness to use?

Several studies showed that far wall IMT measurement is more reliable, contrasting with near wall IMT which is more dependent on technical issues [4]. Common carotid artery IMT (CIMT) is easier to access and more influenced by vascular risk factors than bulb or internal carotid IMT. The later are more difficult to display, depending on technical issues and operator experience. Twenty seven percent of the IMT variability at the common carotid level is explained by classical vascular risk factors, whereas bulb and internal carotid IMT variability is less influenced by those factors (11% and 8%, respectively) [6]. When considering just CIMT, the maximal point value reflects more advanced stages of atherosclerosis. Mean IMT is less susceptible to outlier measurements and therefore more reliable. One sided values can be used to report the highest mean IMT found or one can choose to display values separately for the left and right side, but it is correct to calculate an average mean IMT from both sides to produce only one IMT for each individual [4].

Manual versus semi-automated edge detection measurement

Information available from several follow-up and population-based studies used manual IMT measurement, but semi-automated software is becoming more popular as some ultrasound equipments already have built-in software solutions. Manual measurement implies that the operator draws the limits of the IMT based on his visual assessment of the interface lumen-intima and media-adventicia, possibly aided by enhancing the quality or increasing the size of the image. In semi-automated measurement the software defines the limits of the IMT on a pre-specified segment chosen by the operator. In this method further adjustments can be made by the operator [7].

Manual IMT has the advantage of being universally available and is inexpensive, but requires rigorous quality control and can be time consuming. Semi-automated edge detection software has the great advantage of providing in a quick single assessment the mean and maximal value of more than a hundred point evaluations. Nevertheless, the quality of the data depends on the accuracy of the built-in or offline software used, and if the operator has to override the software frequently, it can also be time consuming and unreliable. The financial cost of the software can also limit the availability of this method, but newer ultrasound equipments should already have the necessary software packages by default [4, 7].

Reference values for Carotid Intima-Media Thickness

There is no consensual established cut-off to define increased carotid IMT, so two approaches can be used. A conservative approach is to considerer all CIMT above 0.9 mm as an indicator of increased future cardiovascular risk, which is not consensual among all follow-up studies[8]. Other approach is to produce age- and gender-specific reference values like those established for the French population [9] and make use of the 75th percentile as a cut-off value [5]. The first approach, being immediately available,

Table 1. Standard equipment and imaging parameters.

Instrumentation and display	Imaging of the vessel wall
State-of-the-art ultrasound system Digital image acquisition and storage, preferably DICOM Phantom scans every 6 months and after any system changes Semiannual routine preventive maintenance Transducer Linear array Minimal compression (<10:1) Fundamental frequency ≥7 MHz Footprint ≥3 cm Display Depth 4 cm Single focal zone Frame rate ≥25 Hz High dynamic range Clear 3-lead electrocardiographic signal Annotate images to describe segments, angles, and other findings Carefully adhere to predefined scanning protocol	Longitudinal view with parallel vessel walls, with good visualization of both walls Optimal diameter should be obtained during diastole IMT measured in the far wall, in a 10 mm segment at least 5 mm from bifurcation Plaques should not be included in the IMT segment Lateral probe position Acquisition in the center of the screen Automated edge detection methods are preferable, as are less operator dependent

IMT= Intima-Media Thickness

is the most attractive, but as reference values differ among countries and ethnic groups [10], a fixed predetermined cut-off is probably inadequate for several populations.

Relation between increased Carotid Intima-Media Thickness and established risk factors and vascular disease

It is clearly demonstrated in single- and multi-country studies that when any number of traditional cardiovascular risk factors increase, so does the CIMT [9, 10].

CIMT has been extensively correlated with traditional cardiovascular risk factors, like aging, male gender, hypertension, body mass index (BMI), LDL and HDL cholesterol, diabetes, smoking, and also with emerging risk factors like inflammation and atherosclerotic changes in other organs: brain, heart, kidneys, lower limb arteries, and brachial artery [11].

Clinical significance of Carotid Intima-Media Thickness

CIMT can be used in several clinical settings: as a population cardiovascular risk marker, as a surrogate endpoint in clinical trials, and as a clinical decision and risk stratification tool for individual patients.

Regarding the use as a population risk marker, a first meta-analysis combining cross-sectional data from studies available until 2006 showed that for each 0.1 mm increase in IMT, the risk of stroke rises 15% (Hazard Ratio - HR 1.15; 95% CI 1.12-1.17) and the risk of myocardial infarction increases 18% (HR 1.18; 95% CI 1.16-1.21) [12]. In 2012 the same authors revised these numbers using additional studies, decreasing the risk estimate of stroke for each 0.1 mm to 12% (HR 1.12; 95% CI 1.10-1.15) and for myocardial infarction to 8% (HR 1.08; 95% CI 1.05-1.10) [13]. Moreover, it is stated in the same publication that when using the Framingham Risk Score with the CIMT more than 90% of the subjects, with or without previous vascular events, did not change Framingham Risk Score classification. For those classified as being at an intermediate risk score, the added information of the CIMT measurements presented a slightly higher score value, reclassifying more than 20% of the subjects in the higher risk category, while 4.6% lowered risk category [13]. Meanwhile, CIMT progression in repeated measurements from follow-up studies available so far did not predict future cardiovascular events in the general population [14]. As a population risk marker, the evidence is that CIMT measurement in the general population does not significantly modify the risk profile, so it should not be done routinely [13]. Still, this CIMT increase over time is documented in several subpopulations, like tobacco users, hypertensive, diabetic, hiperlipidemic, obese, and metabolic syndrome populations [15], subjects with rheumatic disease [16], HIV-infected patients [17], or people with periodontal disease [18]. Other areas like inflammatory bowel disease [19] or assessment of the Ideal Cardiovascular Health (American Heart Association) in adolescents [20] are promising but require further research.

As a surrogate endpoint in clinical trials, the interventions were evaluated for its ability to modify CIMT rate progression and the agreement between this modification and the mortality and morbidity trials. Several statins (simvastatin, atorvastatin, fluvastatin, lovastatin, rosuvasta-

tin), using high dosages for periods ranging from 12 to 48 months, proved to modify CIMT rate progression, which was also in agreement with mortality and morbidity trials [21, 22]. Non-statin lipid lowering drugs (torcetrapib, ezetimibe, niacin, fibrates, and acyl–coenzyme A: cholesterol acyltransferase inhibitors) failed to produce results both in CIMT progression and mortality and morbidity trials [22]. In respect to antihypertensive therapy, numerous drugs (verapamil, amlodipine, nifedipine, lacidipine, doxazosine, metoprolol, enalapril, lisinopril, fosinopril, quinapril, ramipril, trandolapril, losartan, telmisartan, candesartan, irbesartan) were able to achieve convincing effects on CIMT progression and mortality and morbidity trials in primary prevention of cardiovascular effects [22, 23], while ramipril versus placebo and losartan versus atenolol did not shown agreement between ultrasound results and mortality and morbidity trials [22]. In diabetic patients, quite a few drugs, like glucose-lowering drugs, antiplatelet drugs (aspirin, ticlopidine, cilostazol), completed trials showing change on CIMT progression rate [24-26].

Regarding the use of CIMT in clinical decision and risk stratification at the individual level, in 2006 the Screening for Heart Attack Prevention and Education (SHAPE) algorithm included IMT measurement above the 50th percentile or the presence of carotid plaques as an useful test for atherosclerosis in apparently healthy individuals (men above 45 years-old or women above 55 years-old) to set lower LDL targets for intervention [2]. Some years later the Society of Atherosclerosis Imaging and Prevention did an expert panel evaluation of 33 scenarios where CIMT could be used, and found a single measurement to be appropriate to determine coronary heart disease (CHD) risk in the following settings: intermediate risk subjects, metabolic syndrome patients, diabetics without known CHD, people with a family history of premature CHD with calculated intermediate risk, and those with a known coronary artery calcium score of zero and calculated risk between 11 and 20% [27]. Serial IMT imaging was not considered appropriate, with the so far available studies, for monitoring of CHD risk status, due to lack of evidence on technical success of serial IMT in clinical settings and insufficient reliable data on anticipated progression rates.

Conclusion

IMT of the common carotid artery is widely used, even if the strict technical requirements for its measurement are not always met. A few recent reviews on the subject cast some shadows on CIMT usefulness, especially in the setting of repeated assessment in follow-up studies, which was not yet soundly associated with cardiovascular disease risk progression. Regardless, the papers published on CIMT measurement in Pubmed on various clinical settings are now over 2,400, and increasing, with 80% having been issued on the last 10 years, as this review is being written.

Leaving the discussion of risk prediction aside, CIMT is a proven method to evaluate subclinical atherosclerosis. However, it is only the reflection of a moment in time, a static image that cannot tell the interplay of present structural wall changes and complex dynamic processes like vessel inflammation or thrombosis, which in the end will determine the occurrence of cardiovascular events.

Abbreviations

BMI: Body mass index; CHD: Coronary heart disease; CIMT: Common carotid artery Intima-Media Thickness; IMT: Intima-Media Thickness

Competing interests

The authors declare no conflict of interest.

References

1. Goldstein LB, Bushnell CD, Adams RJ, Appel LJ, Braun LT, Chaturvedi S, et al. Guidelines for the primary prevention of stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 2011; 42(2):517-84.
2. Naghavi M, Falk E, Hecht HS, Jamieson MJ, Kaul S, Berman D, et al. From vulnerable plaque to vulnerable patient--Part III: Executive summary of the Screening for Heart Attack Prevention and Education (SHAPE) Task Force report. Am J Cardiol 2006; 98(2A):2H-15H.
3. Pignoli P, Tremoli E, Poli A, Oreste P, Paoletti R. Intimal plus medial thickness of the arterial wall: a direct measurement with ultrasound imaging. Circulation 1986; 74(6):1399-406.
4. Touboul PJ, Hennerici MG, Meairs S, Adams H, Amarenco P, Bornstein N, et al. Mannheim carotid intima-media thickness and plaque consensus (2004-2006-2011). An update on behalf of the advisory board of the 3rd, 4th and 5th watching the risk symposia, at the 13th, 15th and 20th European Stroke Conferences, Mannheim, Germany, 2004, Brussels, Belgium, 2006, and Hamburg, Germany, 2011. Cerebrovasc Dis 2012; 34(4):290-6.
5. Stein JH, Korcarz CE, Hurst RT, Lonn E, Kendall CB, Mohler ER, 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(2):93-111.
6. Polak JF, Person SD, Wei GS, Godreau A, Jacobs DR, Jr., Harrington A, et al. Segment-specific associations of carotid intima-media thickness with cardiovascular risk factors: the Coronary Artery Risk Development in Young Adults (CARDIA) study. Stroke 2010; 41(1):9-15.
7. Bots ML, Sutton-Tyrrell K. Lessons from the past and promises for the future for carotid intima-media thickness. J Am Coll Cardiol 2012; 60(17):1599-604.
8. Mancia G, Fagard R, Narkiewicz K, Redon J, Zanchetti A, Bohm M, et al. 2013 ESH/ESC Guidelines for the management of arterial hypertension: The Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). J Hypertens 2013; 31(7):1281-357.
9. Touboul PJ, Labreuche J, Vicaut E, Belliard JP, Cohen S, Kownator S, et al. Country-based reference values and impact of cardiovascular risk factors on carotid intima-media thickness in a French population: the 'Paroi Arterielle et Risque Cardio-Vasculaire' (PARC) Study. Cerebrovasc Dis 2009; 27(4):361-7.
10. Touboul PJ, Vicaut E, Labreuche J, Acevedo M, Torres V, Ramirez-Martinez J, et al. Common carotid artery intima-media thickness: the Cardiovascular Risk Factor Multiple Evaluation in Latin America (CARMELA) study results. Cerebrovasc Dis 2011; 31(1):43-50.

11. Peters SA, Grobbee DE, Bots ML. Carotid intima-media thickness: a suitable alternative for cardiovascular risk as outcome? Eur J Cardiovasc Prev Rehabil 2011; 18(2):167-74.
12. Lorenz MW, Markus HS, Bots ML, Rosvall M, Sitzer M. Prediction of clinical cardiovascular events with carotid intima-media thickness: a systematic review and meta-analysis. Circulation 2007; 115(4):459-67.
13. Den Ruijter HM, Peters SA, Anderson TJ, Britton AR, Dekker JM, Eijkemans MJ, et al. Common carotid intima-media thickness measurements in cardiovascular risk prediction: a meta-analysis. JAMA 2012; 308(8):796-803.
14. Lorenz MW, Polak JF, Kavousi M, Mathiesen EB, Volzke H, Tuomainen TP, et al. Carotid intima-media thickness progression to predict cardiovascular events in the general population (the PROG-IMT collaborative project): a meta-analysis of individual participant data. Lancet 2012; 379(9831):2053-62.
15. Hurst RT, Ng DW, Kendall C, Khandheria B. Clinical use of carotid intima-media thickness: review of the literature. J Am Soc Echocardiogr 2007; 20(7):907-14.
16. Tyrrell PN, Beyene J, Feldman BM, McCrindle BW, Silverman ED, Bradley TJ. Rheumatic disease and carotid intima-media thickness: a systematic review and meta-analysis. Arterioscler Thromb Vasc Biol 2010; 30(5):1014-26.
17. Longenecker CT, Hoit BD. Imaging atherosclerosis in HIV: carotid intima-media thickness and beyond. Transl Res 2012; 159(3):127-39.
18. Beck JD, Elter JR, Heiss G, Couper D, Mauriello SM, Offenbacher S. Relationship of periodontal disease to carotid artery intima-media wall thickness: the atherosclerosis risk in communities (ARIC) study. Arterioscler Thromb Vasc Biol 2001; 21(11):1816-22.
19. Theocharidou E, Gossios TD, Giouleme O, Athyros VG, Karagiannis A. Carotid Intima-Media Thickness in Patients With Inflammatory Bowel Disease: A Systematic Review. Angiology 2013.
20. Pahkala K, Hietalampi H, Laitinen TT, Viikari JS, Ronnemaa T, Niinikoski H, et al. Ideal cardiovascular health in adolescence: effect of lifestyle intervention and association with vascular intima-media thickness and elasticity (the Special Turku Coronary Risk Factor Intervention Project for Children [STRIP] study). Circulation 2013; 127(21):2088-96.
21. Riccioni G. Statins and carotid intima-media thickness reduction: an up-to-date review. Curr Med Chem 2009; 16(14):1799-805.
22. Peters SA, den Ruijter HM, Grobbee DE, Bots ML. Results from a carotid intima-media thickness trial as a decision tool for launching a large-scale morbidity and mortality trial. Circ Cardiovasc Imaging 2013; 6(1):20-5.
23. Riccioni G. The effect of antihypertensive drugs on carotid intima media thickness: an up-to-date review. Curr Med Chem 2009; 16(8):988-96.
24. Yokoyama H, Katakami N, Yamasaki Y. Recent advances of intervention to inhibit progression of carotid intima-media thickness in patients with type 2 diabetes mellitus. Stroke 2006; 37(9):2420-7.
25. Mita T, Watada H, Shimizu T, Tamura Y, Sato F, Watanabe T, et al. Nateglinide reduces carotid intima-media thickening in type 2 diabetic patients under good glycemic control. Arterioscler Thromb Vasc Biol 2007; 27(11):2456-62.
26. Stocker DJ, Taylor AJ, Langley RW, Jezior MR, Vigersky RA. A randomized trial of the effects of rosiglitazone and metformin on inflammation and subclinical atherosclerosis in patients with type 2 diabetes. Am Heart J 2007; 153(3):445 e1-6.
27. Appropriate use criteria for carotid intima media thickness testing. Atherosclerosis 2011; 214(1):43-6.