Intima-media thickness: appropriate evaluation and proper measurement

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Intima-media thickness (IMT) is a marker of subclinical atherosclerosis (asymptomatic organ damage) and should be evaluated in every asymptomatic adult or hypertensive patient at moderate risk for cardiovascular disease. Intima-media thickness values of more than 0.9 mm (ESC) or over the 75th percentile (ASE) should be considered abnormal. A carotid artery ultrasound scan is the method of choice, and results are reliable, provided certain standards are followed.

Peripheral Artery Disease

Diseases of the Aorta, Peripheral Vascular Disease, Stroke

Background

Atherosclerosis most often develops gradually and slowly, starting from childhood and proceeding into adulthood with varying velocity and susceptibility to complications. The first structural change that can be detected in atherosclerosis is an increase in IMT. Intima-media thickness is an important atherosclerotic risk marker. However, this increase is not synonymous with subclinical atherosclerosis, but is related to it. Indeed, increase in IMT is also the result of nonatherosclerotic processes such as smooth muscle cell hyperplasia and fibrocellular hypertrophy leading to medial hypertrophy and compensatory arterial remodeling. Therefore This process may be an adaptive response to changes in flow, wall tension, or lumen diameter.
The uniform thickening progresses in straight arterial segments as the patient ages and

all known vascular risk factors accelerate this process. Therefore IMT is an important atherosclerotic risk marker but cannot be accepted as a risk factor and should not be subjected to treatment. (1)

I – What to evaluate and in which patients – Guidelines

Screening for multisite artery diseases is important in asymptomatic adults at moderate cardiovascular risk, as well as in hypertensive patients. (2, 3) The clinician searches for evidence of asymptomatic organ damage, which can further determine cardiovascular risk and lead to reclassification of intermediate risk patients into low or high risk categories. (4-6)

A) The European guidelines on cardiovascular disease prevention in clinical practice: SCORE chart (2012)

Who: Subjects with a 10-year risk of fatal cardiovascular disease between 1% and 5%, , i.e. those at moderate cardiovascular risk. A large proportion of asymptomatic middle-aged adults belong to this category.

What: For further cardiovascular risk assessment, these patients should be considered for IMT measurement and/or screening for atherosclerotic plaques by carotid artery ultrasound. Class of indication IIa, level of evidence B.

B) The European Society of Cardiology (ESC) / European Society of Hypertension (ESH) guidelines (2013) SCORE Chart

Who: Hypertensive individuals at moderate risk.

What: IMT measurement is advised in a search for target organ damage; asymptomatic vascular damage could be detected with ultrasound scanning of carotid arteries searching for vascular hypertrophy or asymptomatic atherosclerosis. Damage is defined as the presence of IMT >0.9 mm or plaque. The other markers of asymptomatic vascular (target organ) damage are: pulse pressure ≥ 60 mmHg, carotid-femoral pulse wave velocity > 10 m/s and ankle-brachial index < 0.9.

Why: There is evidence that asymptomatic target organ damage predicts cardiovascular death independently of SCORE. Class of indication IIa, level of evidence B.

C) The American Society of Echocardiography (ASE) (2012); Framingham Risk Score

Who: Patients at intermediate risk: 6-20% 10-year risk of myocardial infarction or coronary heart disease death without established coronary artery disease or its equivalents, those with a family history of premature cardiovascular disease in a first-degree relative, individuals younger than 60 years old with severe abnormalities in a single risk factor who otherwise would not be candidates for pharmacotherapy, and women younger than 60 years old with at least two risk factors. (7)

What: Carotid ultrasound scanning useful for refining cardiovascular disease risk assessment.

D) The ACC/AHA guidelines on the assessment of cardiovascular risk (2013)

Vascular ultrasound (IMT measurement) is not recommended for routine measurement in clinical practice for risk assessment for a first atherosclerotic cardiovascular disease event. (8) Serial studies of IMT to assess progression or regression in individual patients are not recommended. (9)

II – Intima-media thickness measurement

Examination of the carotid wall gives every clinician an opportunity to evaluate subclinical alterations in wall structure that precede and predict future cardiovascular clinical events. B-mode ultrasonography is a noninvasive, safe, easily performed, reproducible, sensitive, relatively inexpensive and widely available method for detection of early stages of atherosclerosis and is accepted as one of the best methods for evaluation of arterial wall structure.
IMT is defined as a double-line pattern visualised by echo 2D on both walls of the common carotid artery (CCA) in a longitudinal view. Two parallel lines (leading edges of two anatomical boundaries) form it: lumen-intima and media-adventitia interfaces – Fig. 1.

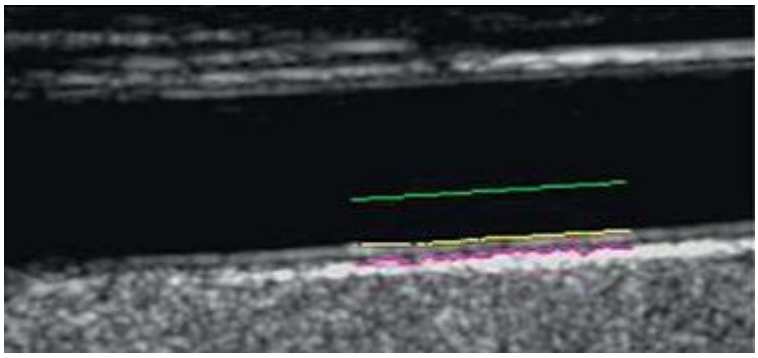

Figure 1. Intima-media thickness (IMT) definition – IMT is measured as the distance between lumen-intima (yellow line) and media-adventitia (pink line) interfaces.

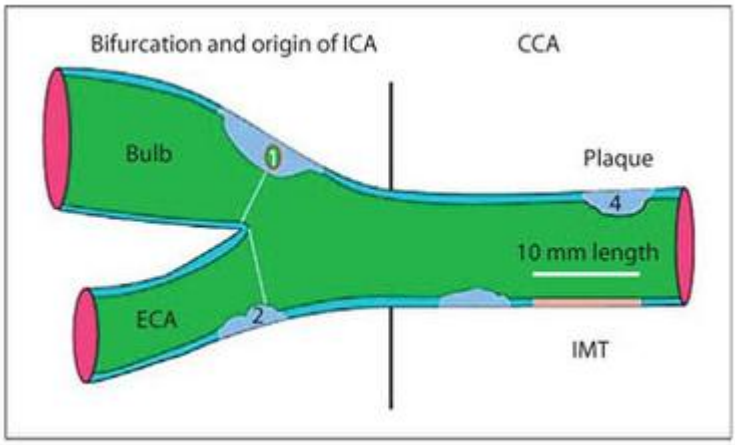

Figure 2. Proper location for IMT measurement.

III - Challenges and current recommendations for IMT measurement

One of the main problems in interpreting IMT results from clinical trials is the differences in measurement methodology. These discrepancies can refer to either one or more of these parameters: the precise definition of the investigated carotid segment, the use of mean or maximal IMT, the measurement of near and far wall or only far wall IMT, the insonation at a single or different angles, employing manual tracking or an automated software, including carotid plaques or not and uni- or bilateral measurements. (10-12)
To avoid this problem standards for IMT measurement have been developed.

Type of equipment

> High-resolution B-mode system (B-mode imaging is preferred over M-mode imaging), equipped with a linear array transducer >7 MHz with minimal compression (<10:1) and footprint of at least 3 cm.

Equipment settings

- Focus depth (30-40 mm), frame rate (>15-25 Hz) and gain settings adjusted optimally to facilitate edge detection;
- Clear 3-lead electrocardiographic signal;
- Use of a zoom function is discouraged (most of the studies relating IMT to cardiovascular events have not used zoomed images).

What to include in observation

- Inclusion of carotid bifurcation in the image plane serving as a landmark to provide accurate serial measurements;
- IMT measurement along a segment of the artery free of atherosclerotic plaque with clearly defined lumen-intima and media-adventitia interfaces (Fig. 2);
- 10-mm-in-length straight arterial segment is required;
- IMT measured in triplicate;
- The far wall of the common carotid artery is preferred. (13)

How to conduct observation

- Arterial wall segments assessed longitudinally and perpendicular to the ultrasound beam;
- Lateral probe position (best resolution for image acquisition for IMT measurement) is preferred;
- Insonation from multiple angles is not recommended;
- Horizontal position of the artery in the image sector to optimise the visualization of lumen-intima interface;
- IMT measurement at a distance of at least 5 mm below the distal end of CCA (IMT could also be measured at the carotid bifurcation and internal carotid artery bulb, but the values should be given separately).

How to measure

- Automatic or semi-automatic IMT measurement, online or offline (semi-automatic border detection program enables the reader to edit the tracked borders if necessary);
- Point-to-point measurement of IMT is not recommended;
- CCA diameter (inter-adventitial and intraluminal) should also be measured (it correlates significantly with IMT);
- IMT measured at end-diastole (R wave).

Data treatment

- IMT values averaged;
- Mean IMT values are preferred (more reproducible than maximal values; maximal IMT may reflect more advanced stages with focal thickening or plaque, or represent a sampling error);
- Increased reproducibility of IMT measurement when values from right and left CCA are combined (14); most of the data points for higher values on the left side. (15)

Equipment maintenance

- US phantom should be used every six months or year and after any system change to determine accuracy and axial and lateral resolution of transducer;
- Storage of digital images directly on digital media from the ultrasound system.

IV – Normal versus abnormal values

Normal IMT values and reference ranges are age- and sex-dependent – there is a significant steady increase in IMT with advancing age in all carotid segments (16-18) and significantly higher IMT values in men than in women – Table 1.

Table 1. Normal IMT values – median (P50), 25th and 75th percentile (P) IMT values for men and women at different age categories, separately for right (A) and left (B) CCA. (1)

A right

Age	P25	P50	P75
Men <30	0.39	0.43	0.48
Men 31-40	0.42	0.46	0.50
Men 41-50	0.46	0.50	0.57
Men >50	0.46	0.52	0.62
Women <30	0.39	0.40	0.43
Women 31-40	0.42	0.45	0.49
Women 41-50	0.44	0.48	0.53
Women >50	0.50	0.54	0.59

B left

Age	P25	P50	P75
Men <30	0.42	0.44	0.49
Men 31-40	0.44	0.47	0.57
Men 41-50	0.50	0.55	0.61
Men >50	0.53	0.61	0.70
Women <30	0.30	0.44	0.47
Women 31-40	0.44	0.47	0.51
Women 41-50	0.46	0.51	0.57
Women >50	0.52	0.59	0.64

Which IMT values should be considered as abnormal, however, is a controversial topic. The relationship of IMT with cardiovascular risk is continuous, and dichotomising this parameter (i.e. determining a threshold IMT value) would be incorrect. Nevertheless, it should be noted that in the latest ESH/ESC hypertension guidelines (2013), carotid IMT > 0.9 mm has been reconfirmed as a marker of asymptomatic organ damage, although it has been proven that in middle-aged and elderly patients the threshold values indicating high cardiovascular risk are higher. (19,20)
The American Society of Echography (ASE) task force recommends that IMT ≥ 75th percentile is considered high and indicative of increased cardiovascular risk. Values from the 25th to the 75th percentile are considered average and indicative of unchanged cardiovascular risk. Values ≤ 25th percentile are considered low and indicate lower than the expected cardiovascular risk.

There are also more conservative cut-off suggestions: IMT values ≥ age-adjusted 97.5th percentile to be defined as abnormal (and predictive of increased vascular risk). The reason is that in a large cross-sectional study, the association of CCA-IMT with vascular risk has been found to be present only for values falling in the highest quintile of the population values.

Conclusions

Intima-media thickness is accepted as a marker of subclinical atherosclerosis and IMT screening can help the clinician to reclassify a substantial proportion of intermediate cardiovascular risk patients into a lower or higher risk category. In order to implement IMT screening in our daily practice, however, we should be aware of the standards of measurement, as they are described here.

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Notes to editor

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Other resources:
E-journal article on subclinical atherosclerosis and the use of IMT as a screening tool for cardiovascular disease (2011).
A Spanish experience of carotid risk reclassification in accord with carotid intima-media thickness (2009).