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10ème CONGRESS OF AMIWIT

LABORATORY OF RESEARCH ON DIABETES

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GUIDELINES AND STANDARDS

Recommendations for the Assessment of Carotid Arterial Plaque by Ultrasound for the Characterization of Atherosclerosis and Evaluation of Cardiovascular Risk: From the American Society of Echocardiography

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- Background
- Rationale
- Methods
- Definition of plaque
- Clinically significant carotid arterial plaque or CIMT
- Quantification methods
- Application of carotid arterial plaque imaging in clinical practice
- Conclusion

BACKGROUND

- Atherosclerotic cardiovascular disease (CVD) remains the leading global cause of morbidity and mortality
- Ultrasound imaging of the carotid artery has the ability to provide a unique "window" into the identification of a patient's underlying cardiovascular risk.
- The presence and degree of atherosclerosis, as defined by plaque presence detected in the carotid arterial system, has been used to estimate and classify or reclassify an individual's cardiovascular risk.
- Beyond overall risk stratification, carotid atherosclerosis is also a known predictor of other CVD events, such as stroke resulting from luminal vessel stenosis and plaque rupture

RATIONALE

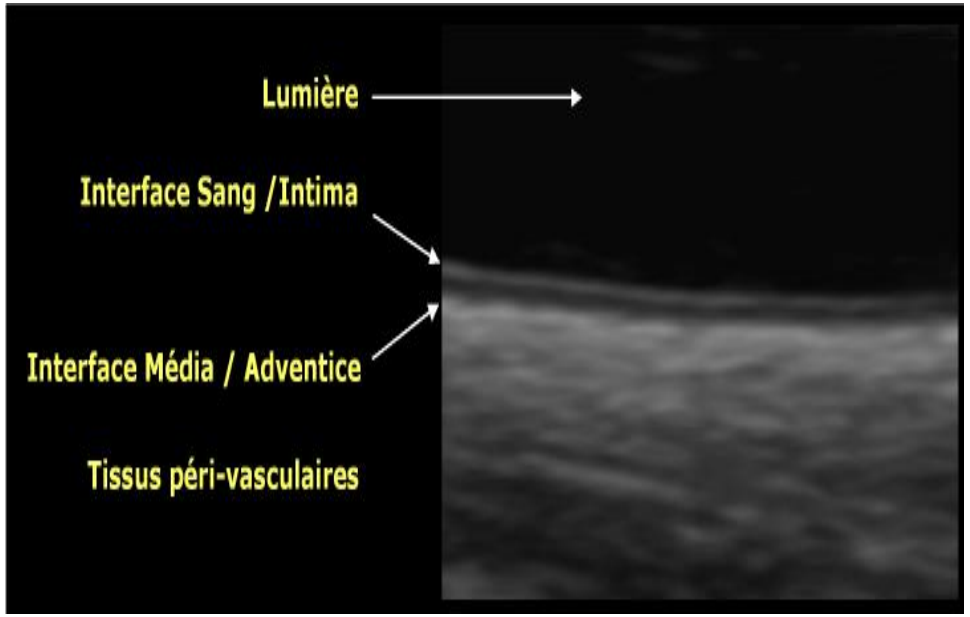
- Several methods have been used to assess risk for CVD using carotid ultrasound, including the following two distinct approaches:

  - Measurement of carotid intima-media thickness (CIMT)

  - Assessment of carotid arterial plaque.

RATIONALE

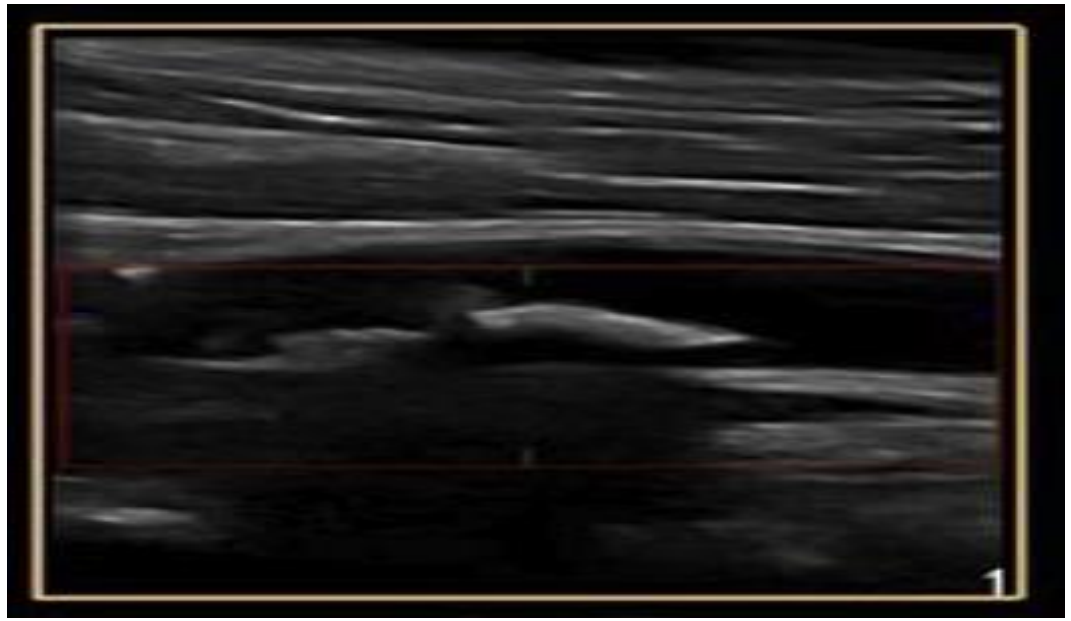
- Measurement of carotid intima-media thickness (CIMT):



  - Identifies areas of increased carotid artery wall thickness

  - Easily accessible imaging biomarker for the classification of cardiovascular risk for individuals

RATIONALE



- Assessment of carotid arterial plaque:
  - It is now recognized that the assessment of carotid arterial plaque provides even greater risk stratification
  - Carotid plaque, a sub-intimal process, may be more reflective of atherosclerosis, as it correlates with overall atherosclerotic burden in the coronary vascular bed

METHODS

- This consensus statement provides recommendations for the **2- and 3-dimensional quantification of carotid arterial plaque by ultrasound** for the basis of CVD risk stratification.

- Role of **ultrasound enhancing agents (UEA)** for assessment of intraplaque neovascularization and composition analysis

DEFINITION OF PLAQUE –,PROTUBERANT AND DIFFUSE

- Carotid arterial atherosclerosis is thought to develop beneath the intimal layer in the sub-intima.
- In contrast, the medial layer is subject to non-atherosclerotic medial hypertrophy commonly induced by aging and hypertension.
- Carotid plaque, on the other hand, represents the atherosclerotic process itself, and starts in the intimal layer and **has thus been shown to predict CVD events better than CIMT.**
- It can be difficult to discern medial thickening from diffuse atherosclerotic plaque.
- Though some atherosclerotic plaques are discrete lesions that can be easily distinguished from the surrounding wall, plaque can also be eccentric and spread over the surface of the wall, appearing indistinct from the media. In such cases it is difficult to determine whether there is simply medial thickening present or eccentric, diffuse plaque.

DEFINITION OF PLAQUE –PROTUBERANT AND DIFFUSE

- Arbitrary definitions to define the presence of diffuse plaque beyond a certain CIMT threshold have been proposed.

- Adding to this complexity is the debate as to whether the transition from increased CIMT to plaque formation is a continuous process, or if CIMT and plaque are truly separate phenotypes.

- A commonly reported threshold value to define diffuse plaque is
    - **CIMT value greater than 1.5 mm or a focal intimal medial thickening of greater than 50%of the surrounding area**

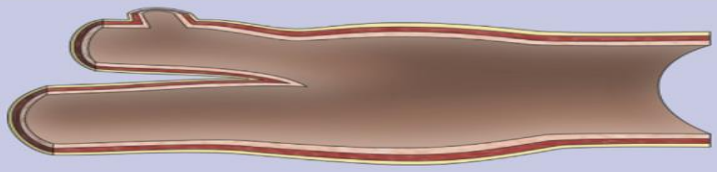
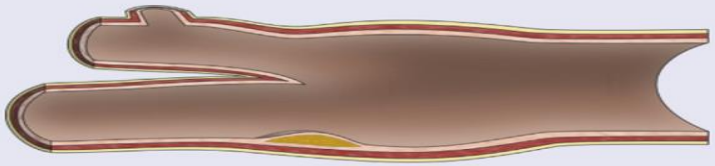
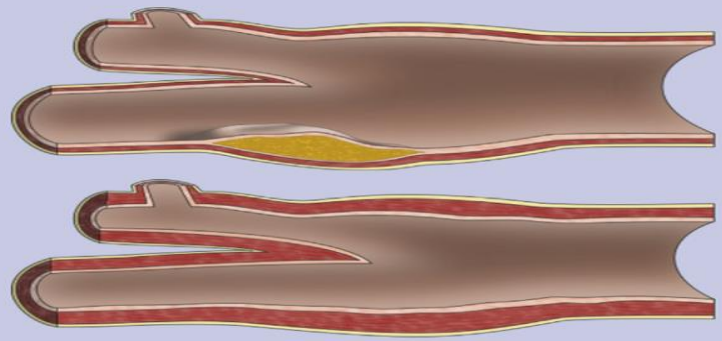
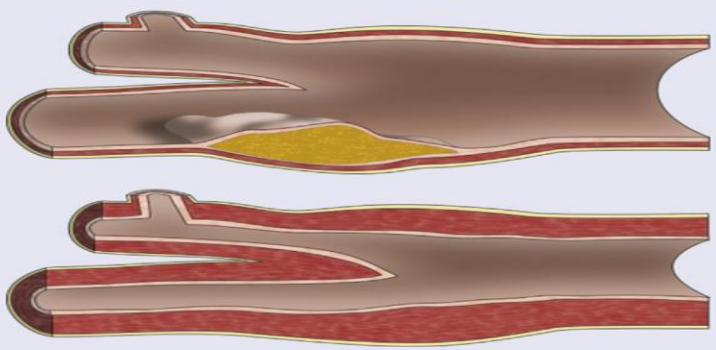
- However, confusion occurs because ultrasound resolution now allows for the visualization of distinct protuberant plaque lesions that could be smaller than this threshold value.

DEFINITION OF PLAQUE – PROTUBERANT AND DIFFUSE

- Recommendation 1: carotid arterial plaque is defined in one of the following 2 ways:
    - 1) any focal thickening thought to be atherosclerotic in origin and encroaching into the lumen of any segment of the carotid artery (protuberant-type plaque)
    - 2) in the case of diffuse vessel wall atherosclerosis, when carotid intima-media thickness (CIMT) measures 1.5 mm in any segment of the carotid artery (diffuse-type plaque).

•Recommendation2: evaluation of both protuberant and diffuse types of carotid arterial plaque for cardiovascular risk stratification and the serial assessment of atherosclerosis.

•Recommendation 3: that first, the carotid arterial wall be visually scanned for the presence of protuberant plaque, and if absent, then carotid intima-media thickness (CIMT) measurement be performed to identify the presence of diffuse plaque (defined as CIMT 1.5 mm).

Grade	Plaque Type		Plaque Thickness
0		No plaque	IMT < 1.5 mm
I		Protuberant (Focal thickening of vessel wall)	< 1.5 mm
II		Protuberant or Diffuse (Vessel wall thickened throughout; (CIMT ≥1.5 mm)	1.5 – 2.4 mm
III		Protuberant or Diffuse (CIMT ≥ 2.5 mm)	≥ 2.5 mm

CLINICALLY SIGNIFICANT CAROTID ARTERIAL PLAQUE OR CIMT

- CIMT 1.5 mm is considered a clinically significant lesion for patients less than 65 years of age.

- The thickness of a carotid arterial plaque lesion, whether it is protuberant or diffuse, was chosen as the initial measure to define plaque because of its widespread availability and because this variable can be measured in both protuberant or types of plaque lesions

- Such lesions may be focal or diffuse wall calcification layered in a concentric or eccentric manner and may represent atherosclerotic processes.

- The grading system does not reflect the degree of vessel occlusion

QUANTIFICATION METHODS

- **Highly variable approach, was to quantifying plaque using a visual plaque score** :

which evaluated and reported the total number of plaques or affected segments occurring anywhere in the common carotid artery (CCA), carotid bulb, or internal carotid artery (ICA) in any wall (near, far, lateral).

- **2-dimensional (2D)** quantification techniques such as the maximal plaque height or thickness.

- **The plaque score is a semi-quantitative approach where the total number of sites containing plaque along the CCA, carotid bulb, and ICA are visualized and summed**. This approach varies greatly among studies **- some investigators count plaque lesions in any visualized segment, whereas others count only the lesions seen in easily identified segments such as the distal first centimeter (cm) of the CCA, bulb, and proximal ICA**.

QUANTIFICATION METHODS

- ASE recommend that if a plaque score is being calculated, then lesions limited to the distal 1 cm of the CCA, bulb, and proximal 1 cm of the ICA

- Clinical studies have shown an association between plaque score and incident CVD. In the Three-city study of 5895 individuals (aged 65-85 years) free of CVD

- An important advantage of the plaque score is its ease of performance and lack of need for advanced quantification software.

- Disadvantages. The plaque score is a semi-quantitative method that simply counts the number of lesions.

QUANTIFICATION METHODS

Two-dimensional Plaque Quantification

- Cross-sectional (transverse) sweeps to evaluate for the presence of plaque are made
- And then once a plaque lesion is identified, Electronic calipers are placed beginning along the origin of the plaque at the vessel wall, into the lumen along the most protuberant aspect of that particular plaque.
- The maximum plaque height or thickness among all identified plaque lesions, visualized in both the right and the left carotid arteries, is then reported.

QUANTIFICATION METHODS

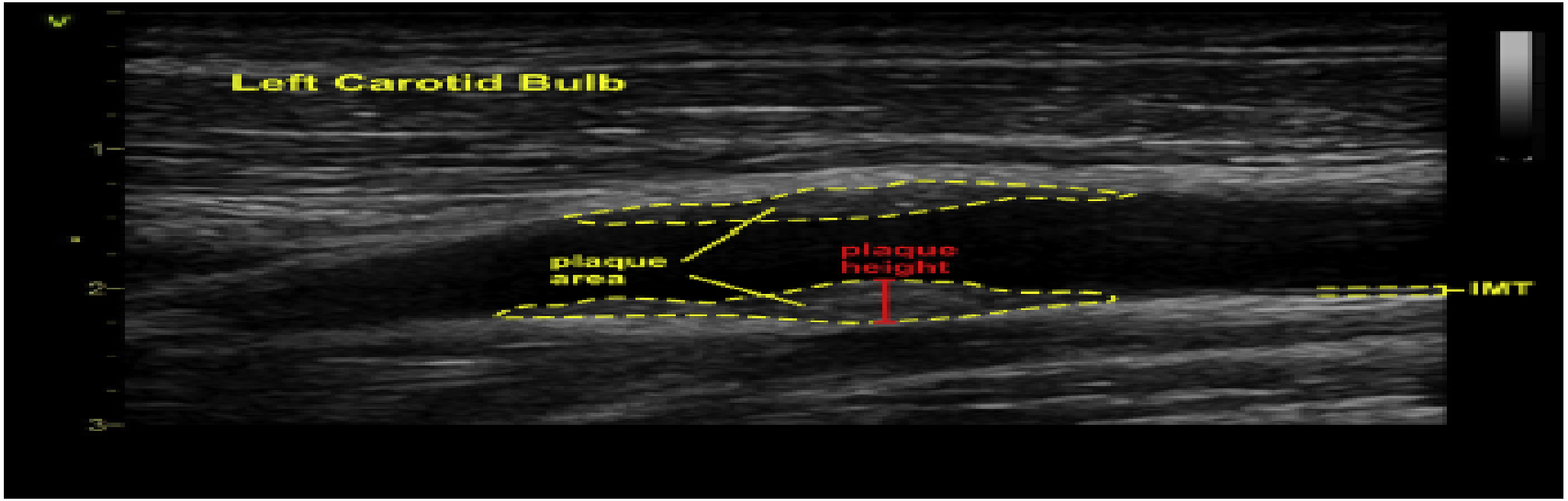
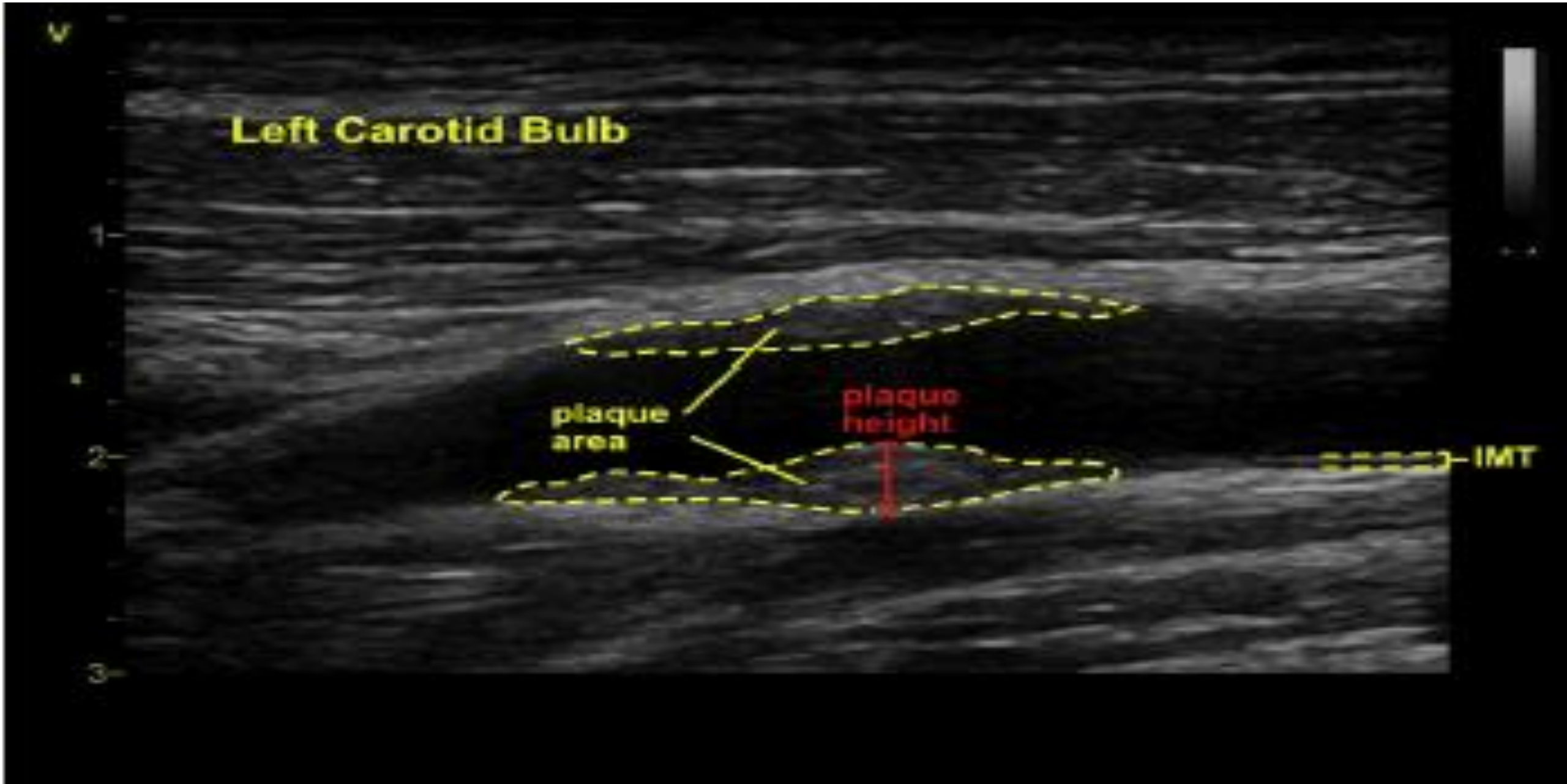


Figure 2 2D methods of plaque assessment. Two-dimensional methods of quantifying arterial plaque, including plaque area and plaque height. Intimal–medial thickening is also shown for demonstration but is suggested to be measured in the absence of plaque. As demonstrated in this figure, plaque thickness is measured beginning from the adventitial plane (same plane as where CIMT begins). It is recognized that in some cases the plaque may be mostly intimal, appear distinct from the underlying medial layer, and not extend fully to the medial–adventitial border, however the measurement should still begin from this medial–adventitial plane for the purposes of standardization.

QUANTIFICATION METHODS



QUANTIFICATION METHODS

Two-dimensional Plaque Quantification

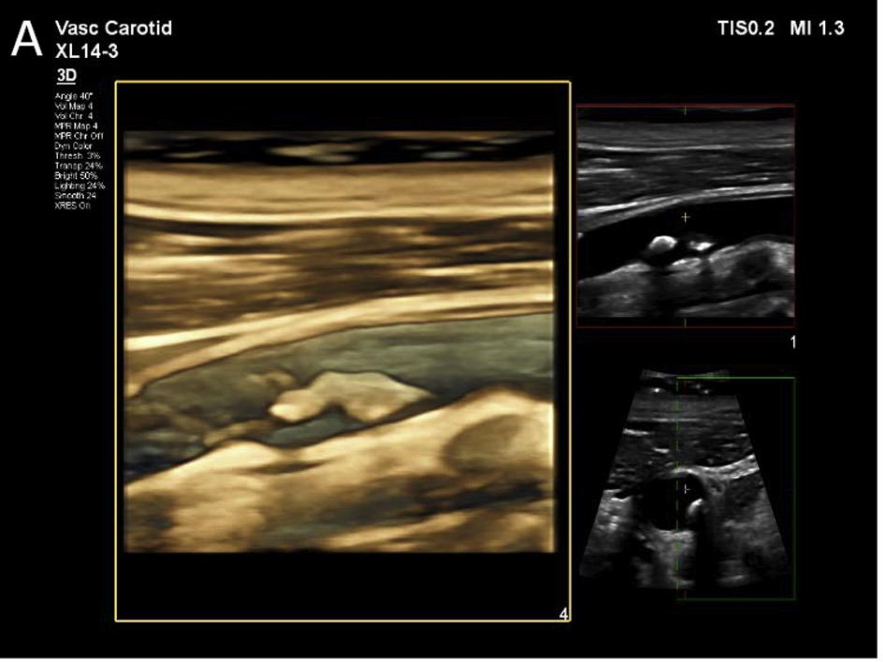
- Advantages:
  - Using maximum plaque thickness
  - very simple to perform using a standard 2D linear probe.
  - It is usually easy to visualize the largest plaque from any segment of the right and left common carotid arteries, and then one only needs to measure the height of the largest plaque.

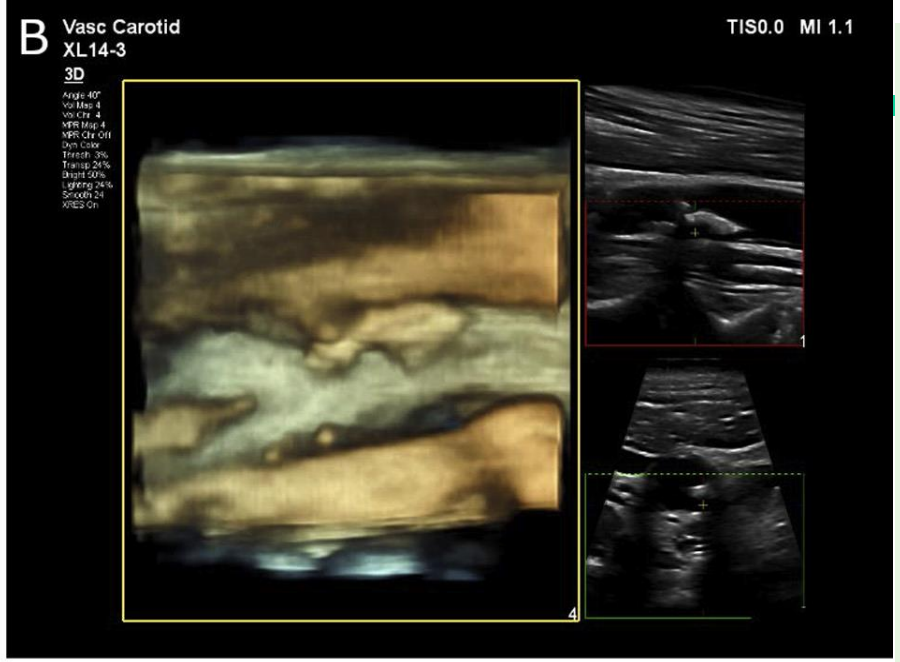
- Disadvantages:
  - The maximal plaque height may be out of plane andunderestimated, or overestimated if scanning is not performed through the center of the artery.
  - Thickness may not truly reflect the burden of disease, (protuberant, diffuse)

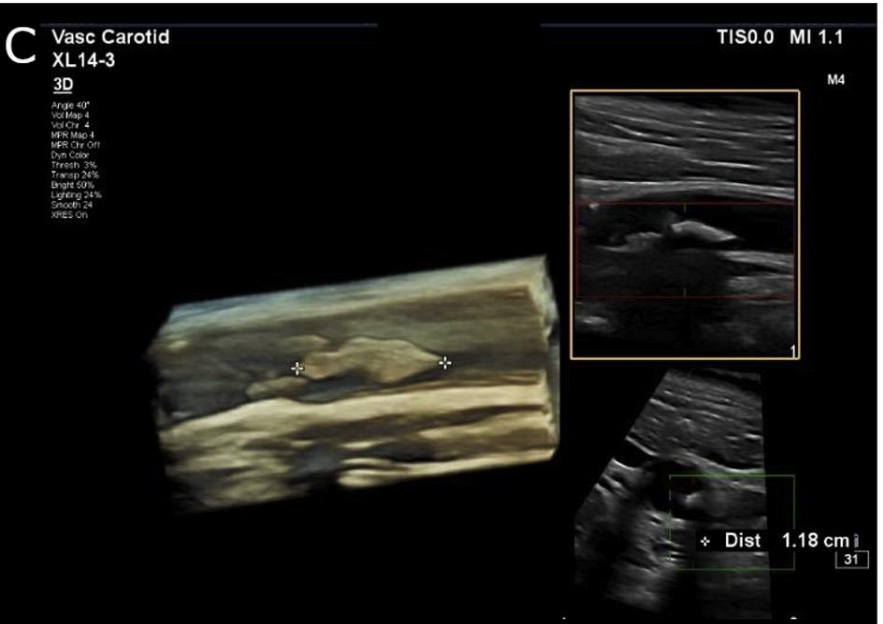
QUANTIFICATION METHODS

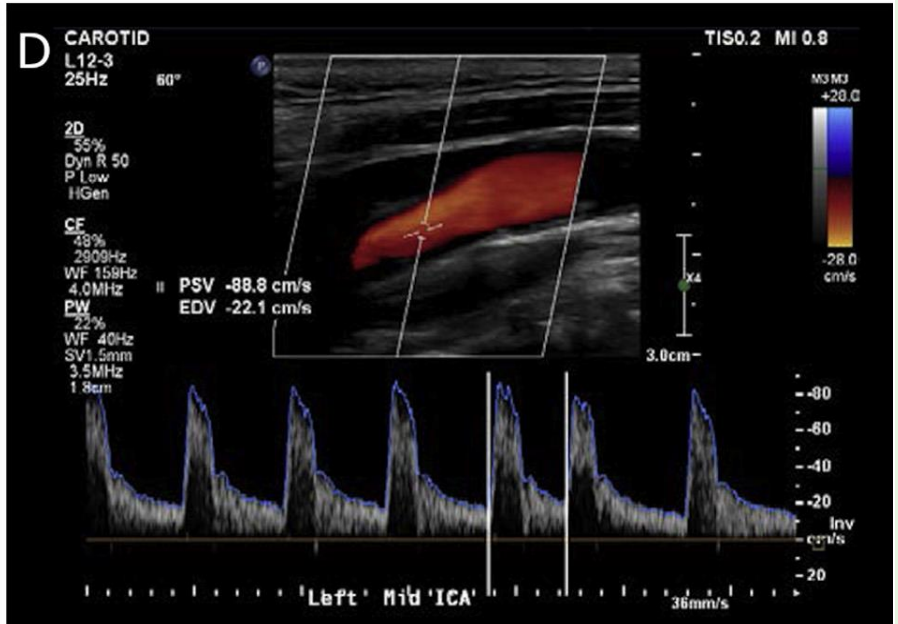
Three-dimensional Plaque Quantification

- The main advantage of 3D quantification is the ability to measure a specific lesion in all planes.
- 3D ultrasound allows for complete visualization of the plaque geometry and surface, allowing for the differentiation between ulceration and gaps between contiguous plaques:
    - Plaque **ulceration** and surface irregularity are known contributors to plaque **vulnerability** and are strongly associated with the presence of **rupture,** it used to detect changes in the progression and regression of ulceration over a mean observation period
    - Plaque **hemorrhage**, a large lipid core, reduced fibrous tissue, and overall **instability**
- Inform cardiovascular risk stratification is required before a recommendation can be made.
- Provides an opportunity to follow the disease process over time,

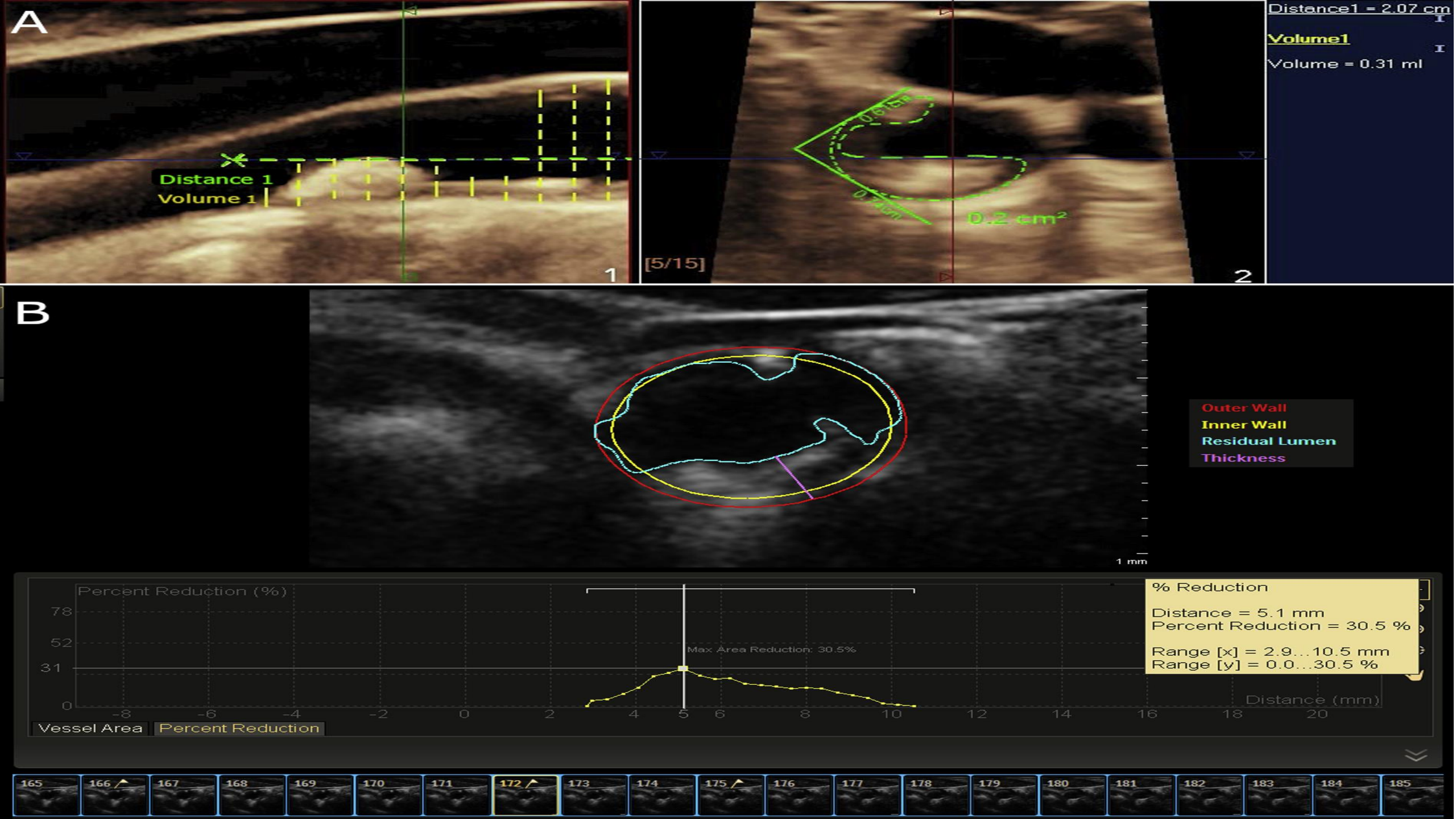


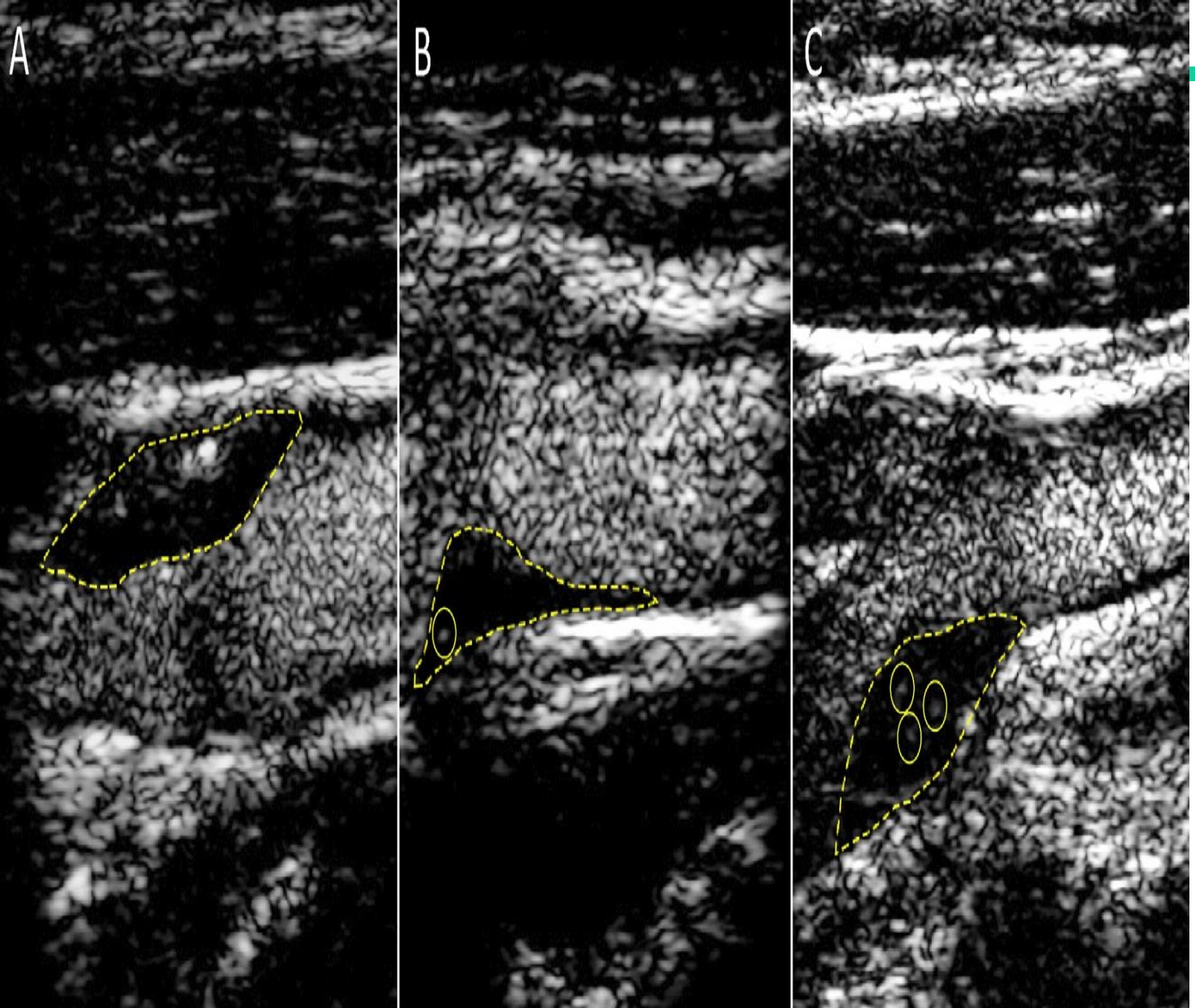






3D plaque acquisition. Three-dimensional imaging of the carotid artery, providing plaque lesion morphology. **A-C:** Images acquired by a matrix array vascular probe of the left carotid artery. **D:** The protocol was preceded by a two-dimensional image and Doppler velocity assessment that suggested 40% stenosis. The three-dimensional images demonstrated the complexity of the arterial plaque, not appreciated by two-dimensional imaging. Three-dimensional imaging may explain why the velocities were lower than expected, by detailing the complexity of the plaque and identifying additional flow channels through the body of the lesion not visualized by two-dimensional imaging. The degree of protuberance seen by three-dimensional imaging was also not appreciated by twodimensional imaging alone.


A
Distance 1
Volume 1
1
[5/15]
0.2 cm²
2
Distance1 = 2.07 cm
Volume1
Volume = 0.31 ml
B
Outer Wall
Inner Wall
Residual Lumen
Thickness
1 mm
Percent Reduction (%)
78
52
31
0
Max Area Reduction: 30.5%
% Reduction
Distance = 5.1 mm
Percent Reduction = 30.5 %
Range [x] = 2.9...10.5 mm
Range [y] = 0.0...30.5 %
Distance (mm)
-8 -6 -4 -2 0 2 4 5 6 8 10 12 14 16 18 20
Vessel Area
Percent Reduction
165 166 167 168 169 170 171 172 173 174 175 176 177 178 179 180 181 182 183 184 185



Contrast-enhanced carotid ultrasound for the detection of plaque neovascularization. Adapted from Mantella et al.60 with permission. Carotid intraplaque neovascularization scoring method. Representative contrast-enhanced ultrasound images of carotid plaques. (A) demonstrates a plaque score of 0, no visible microbubbles within the plaque; (B) demonstrates a plaque score of 1, minimal microbubbles confined to peri-adventitial area; (C) demonstrates a plaque score of 2, microbubbles present throughout the plaque core. The yellow dotted line outlines the plaque lesion. Yellow circles depict intraplaque contrast microbubbles.

Table 1 Comparison of multi-modality imaging techniques for the assessment of arterial plaque

Modality	Advantages	Disadvantages	Developing Techniques
Ultrasound	• Widely available • Non-invasive • Portable • Low cost • Identification of ulceration, intraplaque hemorrhage • 2D and 3D quantification	• Operator dependent • Technical challenges ◦ Acoustic shadowing from calcification ◦ Vessel tortuosity	• UEA • GSM analysis • 3D lumen assessment
Multidector Computer Tomography (MDCT)	• Image from aortic arch to distal cervical vessels • Identification of plaque ulceration, intraplaque hemorrhage • Identification and quantification of calcification • Quantification of plaque volume	• Radiation exposure • Iodinated contrast exposure • Blooming artifact from calcification	• 3D lumen geometry for shear stress
Magnetic Resonance Imaging (MR)	• Image from aortic arch to distal cervical vessels • High soft tissue contrast • High resolution • High reproducibility • Identification of plaque ulceration, intraplaque hemorrhage	• Low availability • High cost • Long procedure time • Multiple sequences and protocols • Not portable • Complex training • Safety requirements	• 3D based techniques • Molecular MRI
Fluoro-deoxyglucose Positron Emission Tomography (^{18}FDG PET)	• Direct imaging of plaque inflammation	• Lacks anatomic precision • Limited spatial resolution • Non-specific uptake by surrounding tissues • Cost, lack of portability, complex training needs	• Co-registration with CT and MRI • Novel molecular PET tracers

2D, two-dimensional; *3D*, three-dimensional; *CT*, computed tomography; *FDG*, fluorodeoxyglucose; *GSM*, grayscale median; *MRI*, magnetic resonance imaging; *PET*, positron emission tomography; *UEA*, ultrasound enhancing agent.

APPLICATION OF CAROTID ARTERIAL PLAQUE IMAGING IN CLINICAL PRACTICE

Primary prevention/asymptomatic

- The 2016 European Society of Cardiology Guidelines on Cardiovascular Disease Prevention have included plaque detection as a modifier in cardiovascular risk assessment (class IIb, level B) after the initial assessment has been performed using established risk scores.

- The same recommendation (class IIb, level B) is given for coronary calcium scoring. A risk modifier is likely to have reclassification potential.

- The 2019 American Heart Association/American College of Cardiology guidelines and Canadian Guidelines for the Management of Dyslipidemia for the Prevention of in the Adult have only included coronary calcium scoring but not carotid plaque imaging as a risk modifier.

APPLICATION OF CAROTID ARTERIAL PLAQUE IMAGING IN CLINICAL PRACTICE

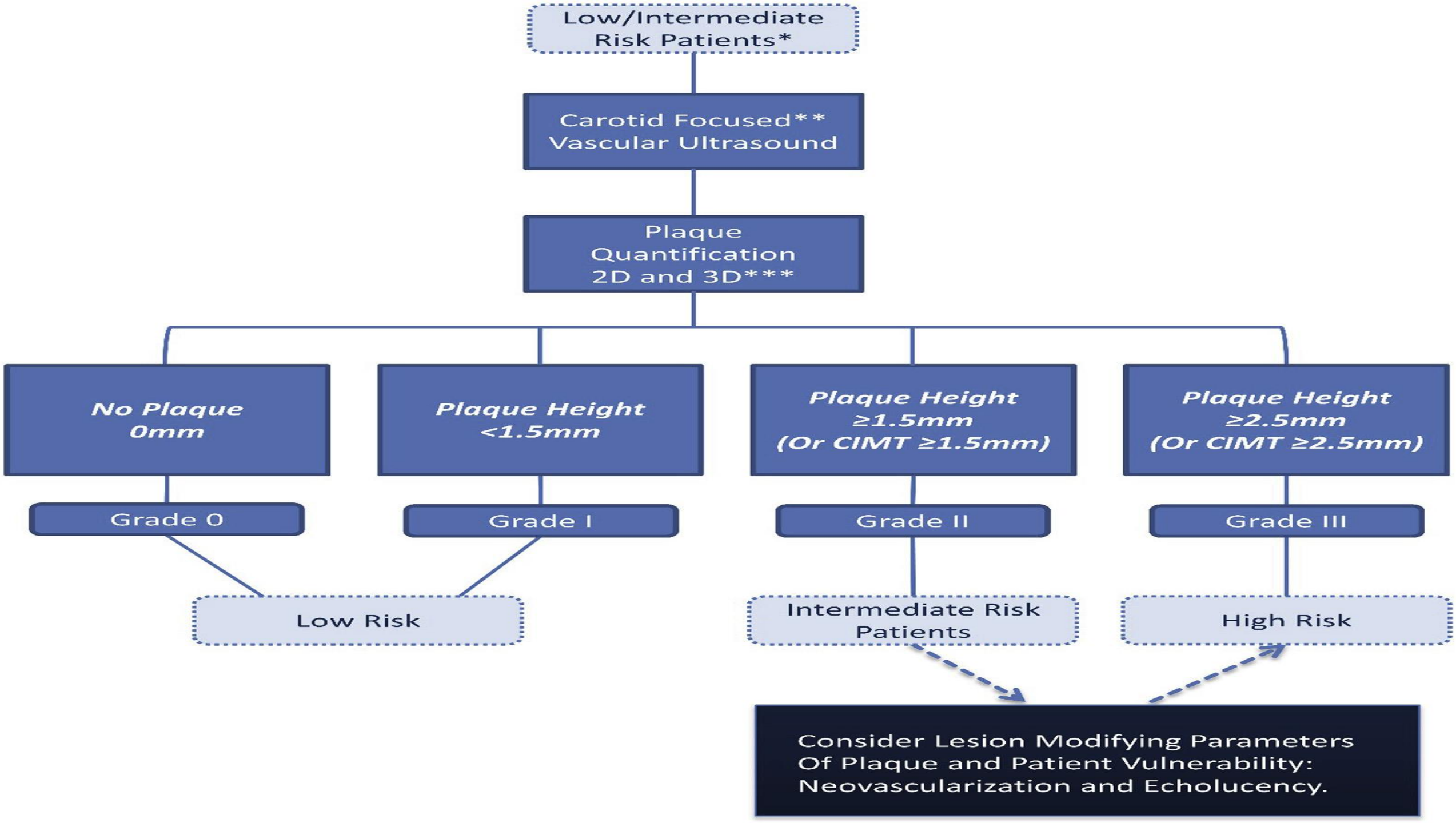
Symptoms suspicious of coronary artery disease, but normal non-invasive tests

- Recent studies suggest that carotid plaque imaging in **patients with normal stress tests provides improved prognostic information: patients without plaque have an excellent prognosis, where as patients with a normal imaging test for myocardial ischemia, but atherosclerotic plaques in the carotid artery, may benefit from more aggressive medical treatment**.

- The combination of carotid plaque assessment with stress testing is a promising area offering enhanced risk stratification.

- Further multicenter confirmation will allow for consideration of practice recommendations in the future.

- The writing panel calls for further development and study of application tools for the integration of carotid plaque assessment into existing risk stratification algorithms and testing.


Low/Intermediate Risk Patients*
Carotid Focused** Vascular Ultrasound
Plaque Quantification 2D and 3D***
No Plaque 0mm
Plaque Height <1.5mm
Plaque Height ≥1.5mm (Or CIMT ≥1.5mm)
Plaque Height ≥2.5mm (Or CIMT ≥2.5mm)
Grade 0
Grade I
Grade II
Grade III
Low Risk
Intermediate Risk Patients
High Risk
Consider Lesion Modifying Parameters Of Plaque and Patient Vulnerability: Neovascularization and Echolucency.

CONCLUSION

- US carotid evaluation is waidly avaible
- Using 2D and 3D to mesure CIMT and evaluate (composition) plaque is important to stratificate the cardio vascular risck
- Carotid plaque burden was shown to predict future major CVD events similarly to coronary calcium score and much better than traditional risk factors.
- Primary prevention before any vascular event stroke (stenose carotid) or coronary

THANK YOU