



Carotid intima media thickness as an indicator of the severity of coronary artery disease: what do cardiologists need to know?

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Abstract

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 intima-media thickness (IMT). Based on the course of atherosclerosis, the classic types of lesion are intimal thickening, fatty streaks, fibrous cap, and complicated lesion. A cardiac computed tomography (CT) scan is a procedure that utilizes multiple X-ray beams from different angles to acquire high-quality, three-dimensional (3D) images of your heart, along with your great vessels and surrounding structures. Cardiac CT uses advanced CT technology, with or without intravenous (IV) contrast to better visualize your heart structure and associated blood vessels. Multi-slice CT allows for easy visualization of coronary abnormalities and can get high-resolution, 3D images of your moving heart and great vessels. MSCT angiography is an excellent tool for detecting and evaluating these variants. Because it adequately delineates the angulations or kinking of the vessel, it aids in the decision of whether or not to undergo surgical treatment and prevents misdiagnosis.

Keywords: Cardiac Imaging, Intimal Thickening, Atherosclerosis, Coronary Artery Disease

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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.

Based on the course of atherosclerosis, the classic types of lesion are intimal thickening, fatty streaks, fibrous cap, and complicated lesion. **(1).**

Early neointima, also called adaptive intimal thickening is a flow-dependent phenomenon that begins shortly after birth in all arterial beds. **(2)**

The fatty streak, or intimal xanthoma, is the first recognized lesion of atherosclerosis, and it appears as non-raised yellowish streaks containing intracellular and extracellular lipids, as well as foam cells of macrophage and or smooth muscle cell origin. **(3).**

The earliest sign of atherosclerosis is abnormal intimal Thickening. **(3).**

A 2-fold higher risk of acute myocardial infarction was associated with increased carotid intima media thickness (cIMT) measured in the common carotid artery; additionally the presence of carotid plaque was associated with a 4- to 7 fold higher risk of acute myocardial infarction depending on plaque size and stenosis.**(4)** .

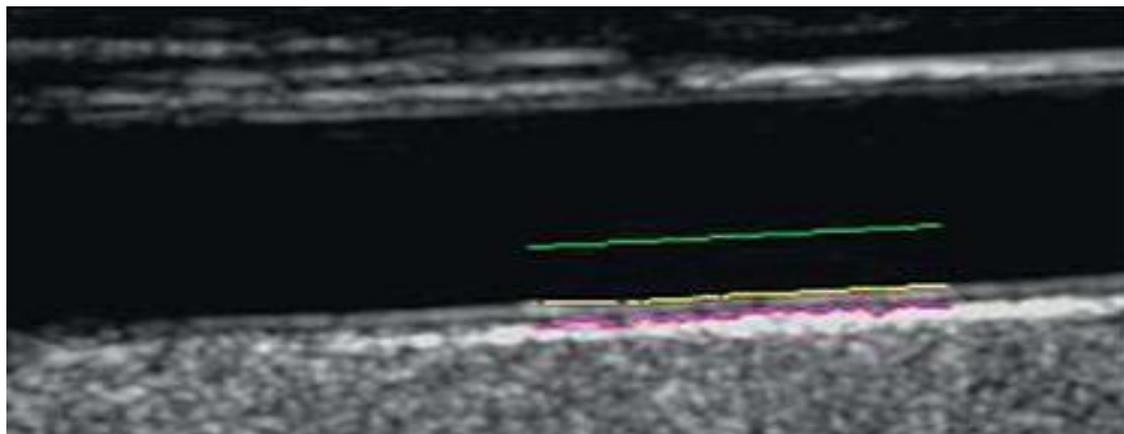


Figure (1): Intima-media thickness (IMT) definition – IMT is measured as the distance between lumen-intima (yellow line) and media-adventitia (pink line) interfaces. (5).

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.

A CIMT 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. (6).

Fate Sequences:

Plaque Calcification

Atheroma plaque calcification is another hallmark of advanced atherosclerosis. It exists as a bone-like formation within the plaque and is initiated in inflammatory regions with a local decrease in collagen fibers. The release of matrix vesicles upon the macrophage and synthetic VSMC death initiates the calcification process of the plaque. In addition, other factors, including reduced levels of mineralization inhibitors or increased osteogenic trans differentiation, contribute to the calcification process (7).

Vulnerable Plaque Atheroma plaques usually develop in branched areas where the WSS is lower. In these areas, low shear stress contributes to local endothelial dysfunction and eccentric plaque build-up. Initially, lumen narrowing is prevented by outward vessel remodeling to maintain a normal lumen and to restore shear stress distribution. However, this prolongs local, unfavorable, low-WSS conditions and aggravates eccentric plaque growth. The eccentric plaques at preserved lumen locations experience increased tensile stress on their shoulders, transforming the lesion into a rupture-prone. A plaque is considered vulnerable when the lesion shows a large necrotic core, a thin fibrous cap, and an increased inflammatory response due to the continuous exposure to the pro-atherogenic milieu. The fibrous cap separates the thrombogenic necrotic core from the circulating coagulation factors and platelets, and its thickness correlates with the vulnerability of the plaque (8) As a result of VSMC death, ECM production is reduced, and the presence of liberated matrix metalloproteinases (MMP) increases, making the fibrous cap weaker. As mentioned before, inflammation contributes to plaque development in all of the steps from initiation to plaque rupture. Indeed, in this last stage, its relevance is remarkable, as it promotes the instability of the fibrous cap. This inflammatory stage is commonly observed in the cap and shoulders of the plaque instead of a generalized inflammation. Together, the data show that, when inflammation prevails, the maintenance of the strong and rigid fibrous cap decreases, making the cap unstable and susceptible to rupture when exposed to hemodynamic forces, the most common mechanism of plaque rupture. (9).

Plaque Rupture and Thrombus Formation

When the plaque fissures or ruptures, the sub endothelial space is exposed to blood, triggering a coagulation process to cover the wound (10). Initially, platelets adhere to the sub endothelial collagen and become activated, and more platelets are then recruited and aggregated in the region in order to initiate wound

healing. Simultaneously, pro-thrombotic elements of the lipid core are released and come into contact with coagulating factors of plasma. More specifically, the tissue factor of the core reacts with factor VII of the plasma, activating the coagulation cascade that leads to thrombin production, an essential intermediate for fibrin formation (8) Fibrin is an insoluble protein that forms networks of fibrin threads and, along with platelets, covers the lesion, forming a stable and well-arranged structure. This structure is known as the thrombus (11).

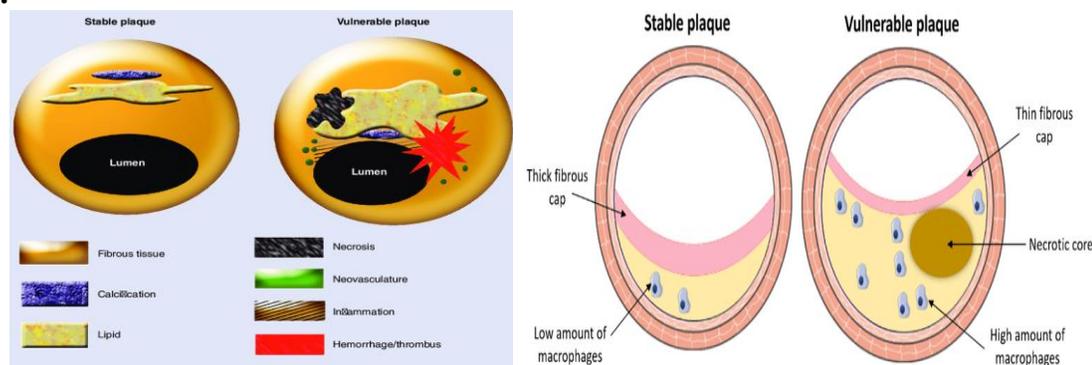


Figure (2): Graphical representation of stable and vulnerable plaque. (12)

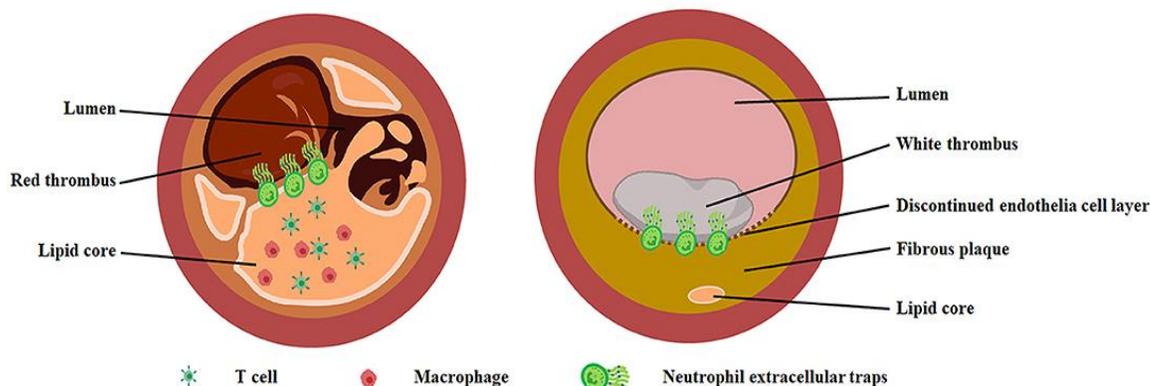


Figure (3): Pathological characteristics of plaque rupture and plaque erosion. Ruptured plaque (left image) is featured with a larger lipid core containing abundant macrophages and T cells. Red thrombus was observed in the small lumen. Eroded plaque (right image) has a large lumen with white thrombus and fibrous plaque tissue characterized by little or no lipid deposition. In particular, there is discontinuous endothelial cell layer in eroded plaque. Neutrophil extracellular traps was found at the junction of plaque tissue and thrombus in both eroded and ruptured plaque. (10)

TECHNIQUE OF CARDIAC IMAGING

A cardiac computed tomography (CT) scan is a procedure that utilizes multiple X-ray beams from different angles to acquire high-quality, three-dimensional (3D) images of your heart, along with your great vessels and surrounding structures. Cardiac CT uses advanced CT technology, with or without intravenous (IV) contrast to better visualize your heart structure and associated blood vessels. Multi-slice CT allows for easy visualization of coronary abnormalities and can get high-resolution, 3D images of your moving heart and great vessels. (13).

MSCT angiography is an excellent tool for detecting and evaluating these variants. Because it adequately delineates the angulations or kinking of the vessel, it aids in the decision of whether or not to undergo surgical treatment and prevents misdiagnosis. (14).

There are two different CT-scan procedures that can be used to assess coronary atherosclerosis. The amount of coronary artery calcification (CAC) is assessed in Agatston units and given as a CAC score on a non-

contrast CT scan (CACS). The CACS can predict the occurrence of CVD in the future. In coronary CT angiography (CCTA), contrast is frequently used to determine degree of atherosclerosis, luminal stenosis, plaque features, and plaque volume. **(15)**.

CT calcium scoring is a simpler CT scan of the heart. It doesn't provide detailed pictures of the heart or heart arteries but instead measures the amount of calcified, or hardened, plaques in the heart arteries. This is usually explained as a calcium score which provides an assessment of the number of fatty plaques in the heart arteries. Again, the more fatty plaques you have, the higher the risk of heart attacks. Unlike a CT angiogram, a calcium score doesn't involve a dye. **(16)**.

Patient preparation

Checking indications, contraindications, and explanation of the examination and obtaining informed consent. Beyond that patient preparation for cardiac CTA includes the following:

- checking contraindications for nitrates and β -blocker
- patients should take their cardiac medications as usual
- no food 3-4 hours before the scan
- no caffeine for 12 hours
- instruction on how to breathe
- an electrocardiogram signal needs to be acquired
- heart rate control
- **Premedication**

Premedication comprises the following:

- check heart rate and blood pressure before administration of medications
- administration of nitrates (400-800 μ g of sublingual nitroglycerin e.g. 1-2 sprays)
- administration of β -blocker (to target pulse of ≤ 60 bpm)
 - e.g. metoprolol 50-100 mg one hour before the exam
 - e.g. metoprolol 5mg iv followed by monitoring for 5 min repeatedly up to 15-20 m
- **Image Acquisition**

All patients were scanned 64 dual-slice General Electric GE multi-detector scanner (GE Medical Systems, Waukesha, USA®) machine passing at the following steps:

1- Scanogram.

2- Calcium score

3-C.M administration using bolus tracing technique, 70-80ml of non-ionic CM injected with rate of 5-6 ml/sec injected via dual head power injector pump together with (50ml) saline chaser bolus was used to washout contrast medium

From right side of heart

Image acquisition starting from carina till 1 cm below diaphragm (heart base). **(17)**.

Image Reconstruction

They are best observed in the systole phase if heart rate is less than 75 bpm, but they are best seen in the diastole phase if heart rate is more than 75 bpm.

Image Interpretation

Axial pictures (as source images), reconstructed images using MPR (curved and oblique), MIP, and volume rendering techniques), and axial images (as source images) were used to edit and interpret the cases.

Volume rendering (VR) technique

A 3D approach that assigns a distinct hue to each voxel's CT attenuation values, resulting in an overall image of the heart. The only genuine 3D approach is virtual reality, which gives the depth and spatial information that MIP lacks.

Maximum Intensity projection (MIP) technique

Maximum intensity projection (MIP) is a simple three-dimensional visualization tool that can be used to display computed tomographic angiography data sets. MIP images are not threshold dependent and preserve attenuation information. Thus, they often yield acceptable results even in cases in which shaded surface

display images fail because of threshold problems. MIP is particularly useful for depicting small vessels. Because MIP does not allow for differentiation between foreground and background, MIP images are best suited for displaying relatively simple anatomic situations in which superimposition of structures does not occur. MIP images should always be interpreted together with the original transaxial data set. Knowledge of display properties and artifacts is necessary for correct interpretation of MIP images and helps one create images of optimal quality, choose appropriate examination parameters, and distinguish artifacts from disease (18)

Curved Planner Reformation (CPR) Technique:

Visualization of tubular structures such as blood vessels is an important topic in medical imaging. One way to display tubular structures for diagnostic purposes is to generate longitudinal cross-sections in order to show their lumen, wall, and surrounding tissue in a curved plane. This process is called Curved Planar Reformation (CPR). We present three different methods to generate CPR images. A tube-phantom was scanned with Computed Tomography (CT) to illustrate the properties of the different CPR methods. Furthermore we introduce enhancements to these methods: thick-CPR, rotating-CPR and multi-path-CPR. (19).

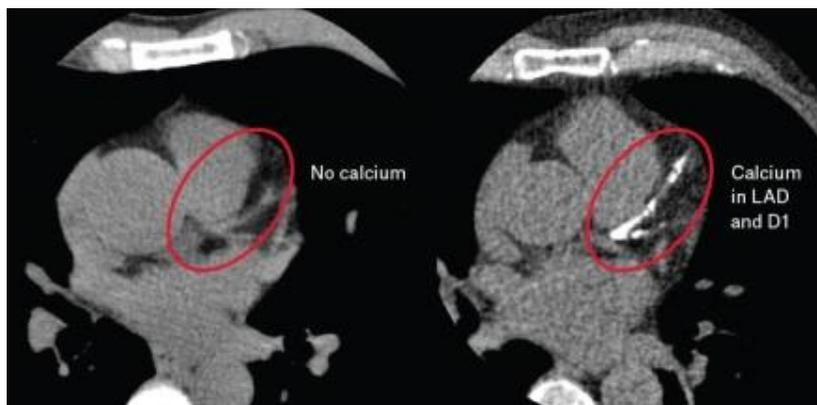


Figure (4): Coronary artery calcium in the left anterior descending (LAD) and first diagonal (D1) arteries. (20).

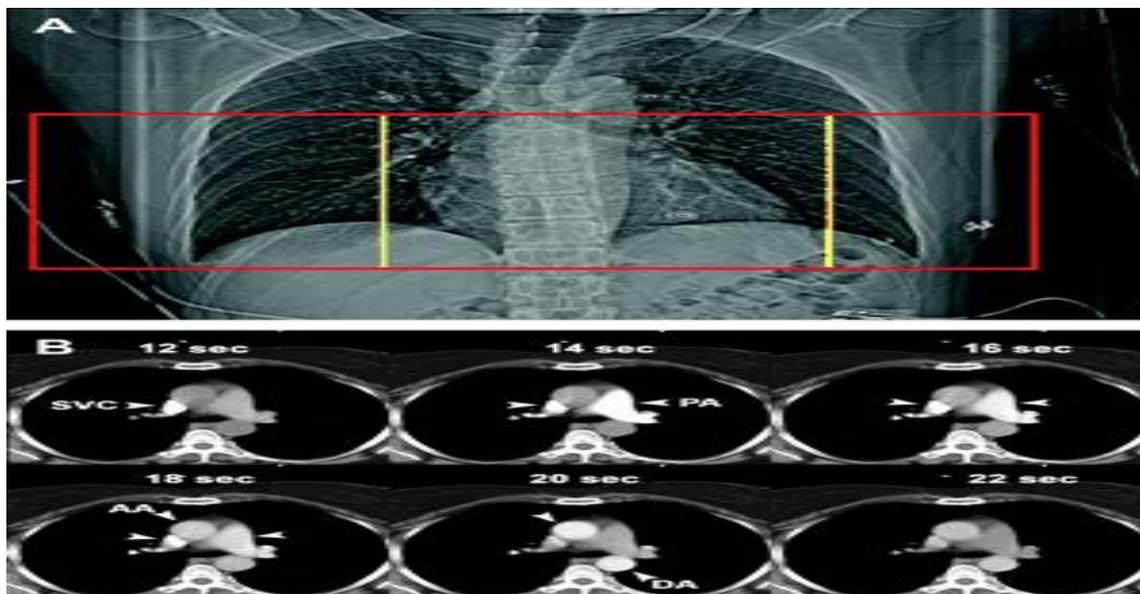


Figure (5): (A) Anteroposterior topogram showing volume coverage (field of view) required for dedicated coronary CTA (yellow box) and reading of incidental findings (red box). For coronary CTA, field of view extends from below tracheal bifurcation to base of heart. (B) Timing bolus image acquisition. Images at level

of carina are acquired every 2 s starting 10 s after injection of 20 mL of iodinated contrast material. Arrowheads show passage of contrast material through superior vena cava (SVC) at 12 s, pulmonary artery (PA) at 14 s, and ascending aorta (AA) and descending aorta (DA) at 20 s. Coronary CTA scanning was started 20 s after initiation of contrast material injection (21).

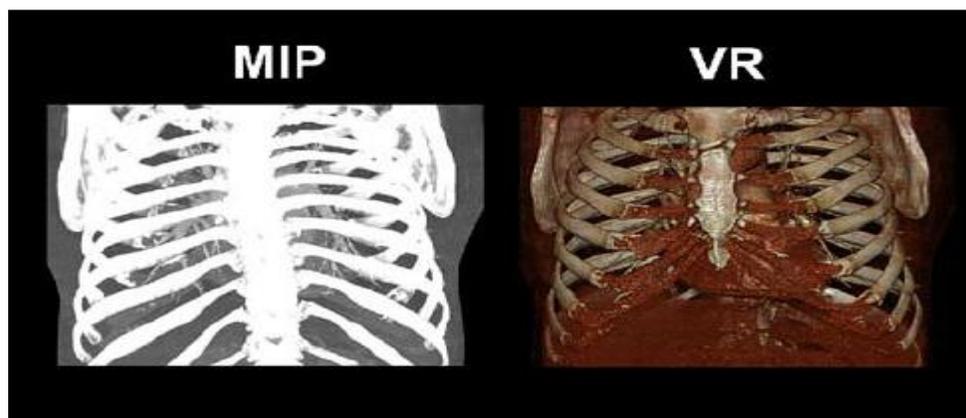


Figure (6): MIP and VR images. In MIP images, hyper intense structures are superimposed and the three-dimensional perception is lost. (18)

- **Findings:**

The presence of calcium in the coronary arteries has been shown to be a marker for atherosclerotic disease. This calcium is detectable on CT and is quantifiable using the Agatston method which adds prognostic information to available demographic and serologic risk stratification. However, CT performed for calcium scoring is not able to show non-calcified atheroma or stenosis. (22).

Coronary CT angiography (CTA) is an emerging noninvasive technique that can evaluate both calcified plaque and non-calcified plaque. Coronary CTA is able to show the lumen of the coronary arteries as well as the vessel wall, analogous to intravascular sonography. Multiple studies have shown coronary CTA to have a high negative predictive value for the detection of coronary atherosclerosis: greater than 95% for significant stenosis and approximately 90% for any plaque. Because coronary CTA uses IV contrast material, it is able to detect low-volume, non-calcified plaque that is not visible on CT performed for calcium scoring. (23).

Identification of small-volume soft plaque is the crux of coronary artery disease management. Investigators have repeatedly shown that acute coronary syndromes most frequently result from the rupture of these small plaques, which are generally not flow-limiting, do not cause stenosis, and may not be calcified. Calcification is generally a marker of plaque stability, whereas unstable plaque is characterized by a large lipid core, thin fibrous cap, and inflammation. This unstable plaque has been termed the “vulnerable plaque” and is the target of current treatment algorithms. (24).

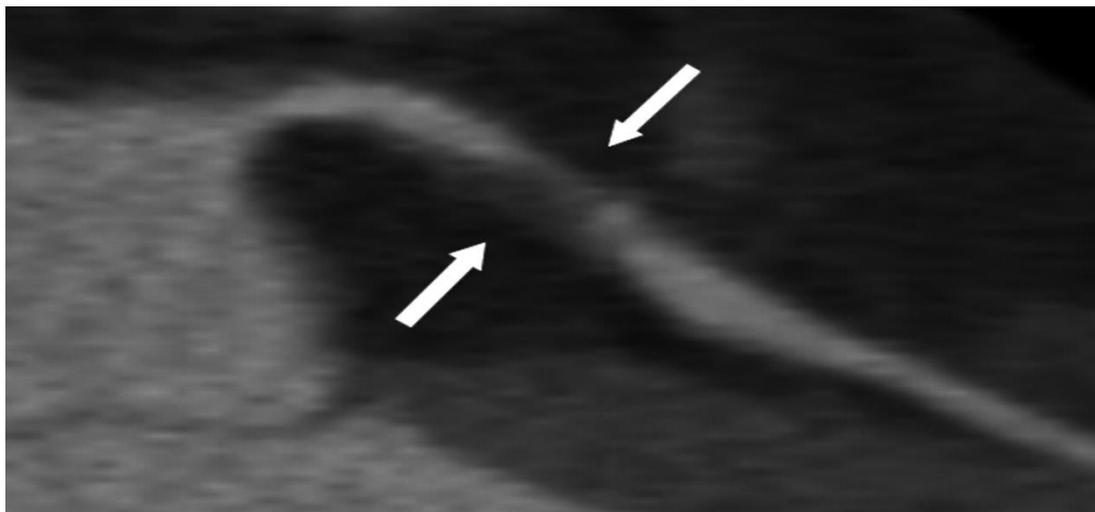


Figure (7): 52-year-old man with increased fatigue on long-distance runs. Coronary CT angiography image shows large soft plaque (between arrows) that is causing severe stenosis in the left main coronary artery. (25)

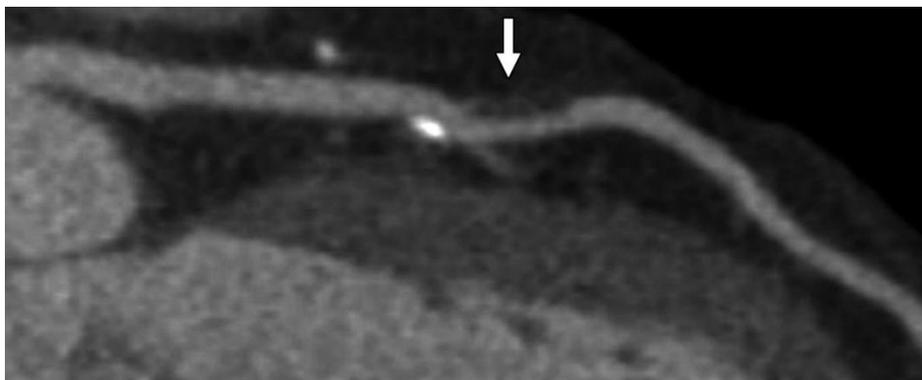


Figure (8): 56-year-old woman who presented for coronary CT angiography because of a strong family history of heart disease. Curved reformatted image from coronary CT angiography shows a large soft plaque in mid left anterior descending artery (arrow). (19).

Pitfalls of the exam:

Coronary CT angiography artifacts

These artifacts are rather widespread, and they might appear for a variety of causes. Because these abnormalities might mimic pathology or impair image quality to non -diagnostic levels, it's critical to understand them.

1-Blooming artifact :

Cause: Small high-contrast objects appear larger than they are (e.g., caused by dense calcifications, clips)

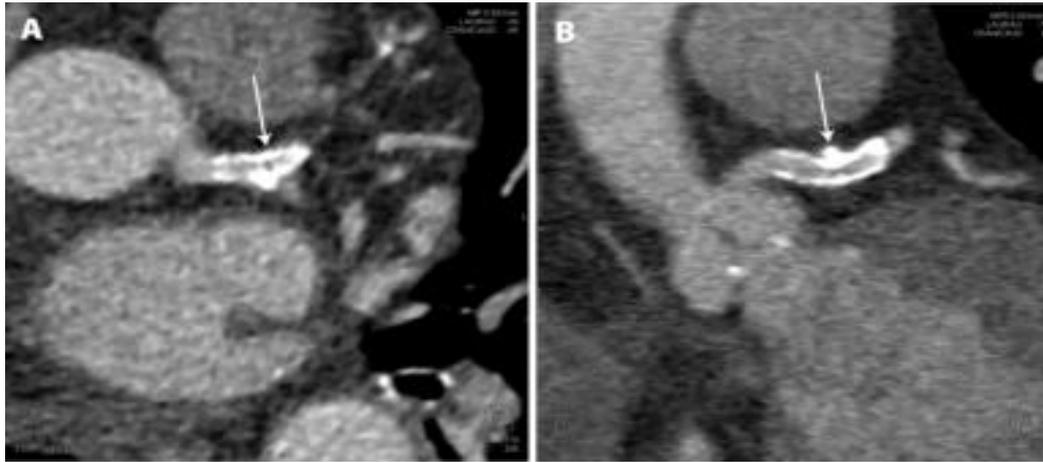


Figure (9): Axial image demonstrates Blooming artifact from the metallic struts and coronary calcium (26).

2- Blurring artifact

Cause:

- Averaging of real attenuation values in a voxel.
- Cardiac, respiratory or postural motion.

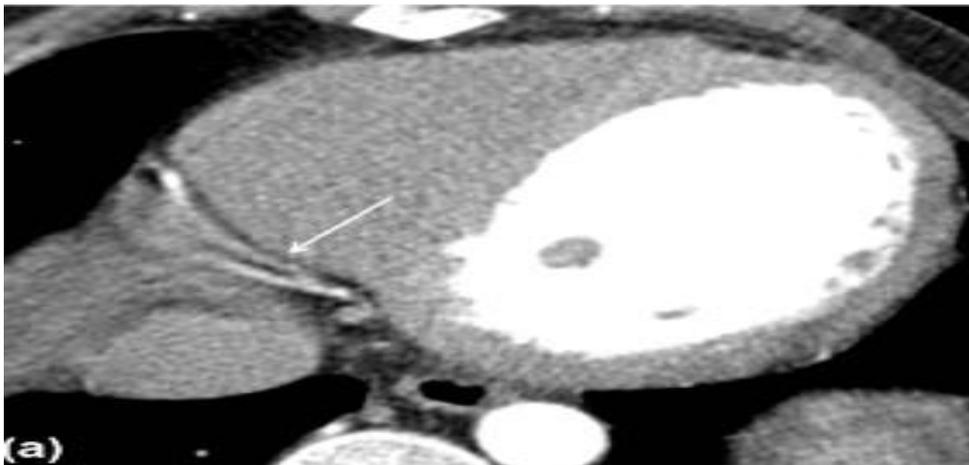


Figure (10): curved planner CT image showing blurring artifact in distal RCA. (21).

3- Streak artifact (Beam hardening) :

Cause: Metal implants or a lumen filled with a high iodine concentration
Can induce reconstruction artifacts.

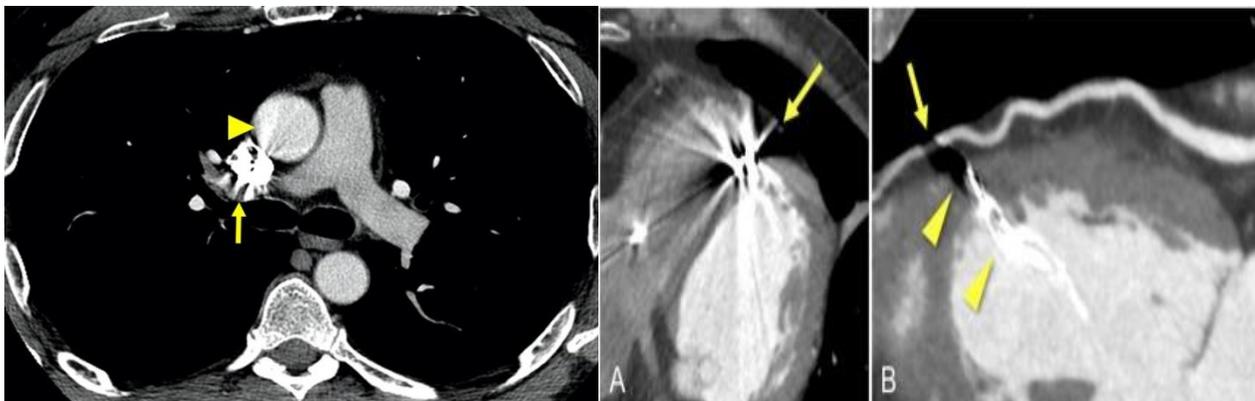


Figure (11): axial images demonstrates Streak artifact “arrows “from dense contrast meadium in SVC (1st image) and from pacemaker (A&B).(25)

4-Stairstep artifact :

Cause: Phase selection is incorrect during prospective trigger acquisition or retrospective reconstruction, resulting in tachycardia or arrhythmia.

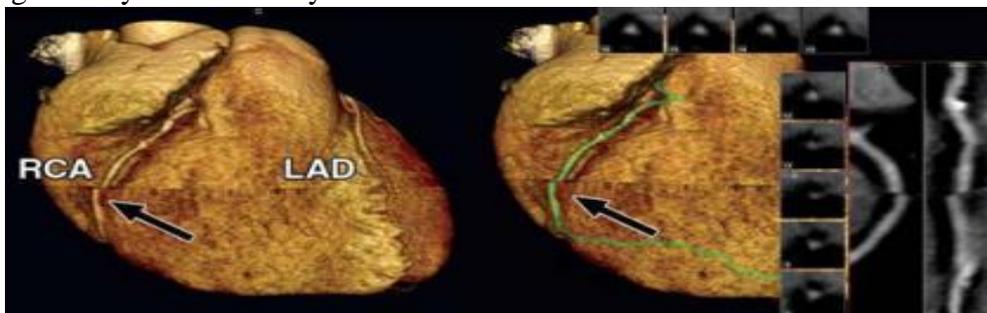


Figure (12): 3D reconstructions and central luminal line projections showing Stair step in right coronary artery (RCA) (arrows) (27)

5- Poor contrast in lumen of coronary arteries (error)

Cause: Extravasation, volume speed, timing (operator dependent), heart failure, and the Valsalva manoeuvre are all examples of technical errors in contrast administration.

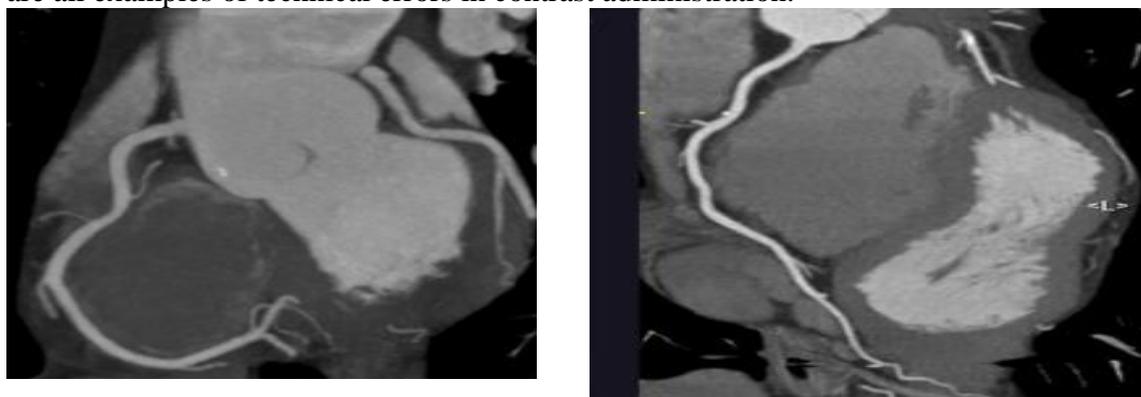


Figure (13): Curved planar CT image shows low contrast attenuation With high noise (1st image) and optimum timing with high contrast attenuation (2nd image). (28)

Technique of Carotid Duplex study

The carotid arteries show indications of atherosclerosis such as carotid intima-media thickness (CIMT), plaque, and stenosis. According to various studies, an increased CIMT which is defined as the distance between the lumen-intima and

Media-adventitia interfaces as evaluated by ultrasound, is a predictor of coronary heart disease and cerebrovascular events. (29)

B-Mode ultrasound is typically used to monitor the common carotid artery (CCA) rather than the bulb, bifurcation, or internal carotid artery for CIMT analysis. (30).



Figure (14): showing common carotid artery (CCA), internal carotid artery (ICA) and external carotid artery (ECA). (30).

Carotid ultrasound is a very safe, accessible, and reliable method of examining carotid arteries, revealing IMT, plaque presence, plaque volume, lumen narrowing, and shear stress in both the common and internal carotid arteries. This could help detect coronary artery disease early and forecast future strokes or cardiovascular events (31).

Ultrasound technology has advanced to the point that machines are now smaller and more affordable. Linear phased array probes with a fundamental frequency of at least 7 to maximum 15 MHz are used to examine carotid arteries. IMT is calculated by measuring the distance between two echogenic lines separated by an echo lucent region in the artery wall. (32)

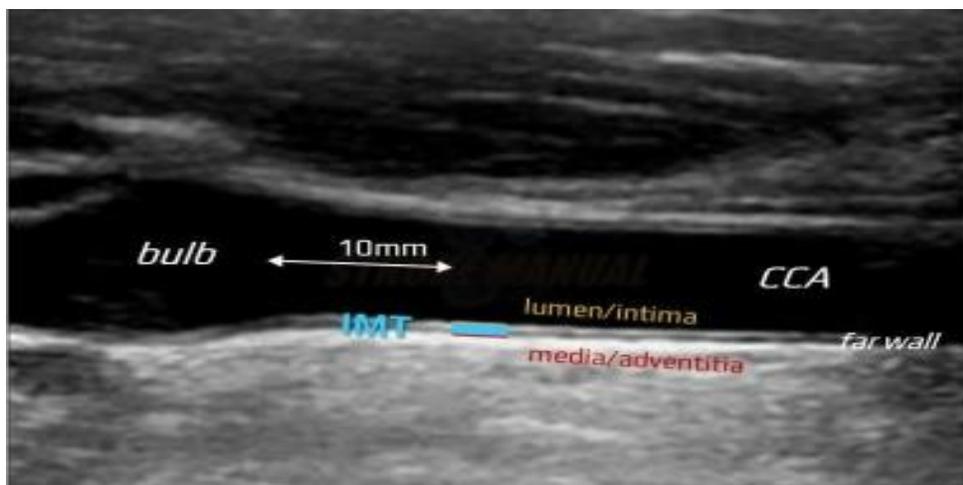


Figure (15): shows how to measure IMT. (32)

The intima-media thickness (IMT) of the carotid arteries is a non-invasive test for atherosclerosis that can help predict cardiovascular risk factors. (33).

The examination is best successful when performed in a supine position with the patient's neck slightly hyperextended and turned to the other side.

The transducer is a linear array transducer with a resolution of 5 MHz or greater. Scanning with a low frequency curvilinear array transducer may be required if the vessel is very deep. In either an anterior or posterior approach, the sternocleidomastoid muscle can be employed as an auditory Window. (34).

Image optimization:

Because potential velocity errors rise with angles above 60° the doppler angle is adjusted to be parallel to the flow and kept between 45° and 60° wherever possible. (35).

Findings:

On sonography, the carotid artery should appear patent, with adequate colour filling and no intimal thickening or plaques. The carotid intima-media thickness (CIMT) is a significant atherosclerosis risk indicator that is measured at the far wall of the common carotid artery during end diastole 1 cm before the bifurcation of the CCA at right and left side. (36).

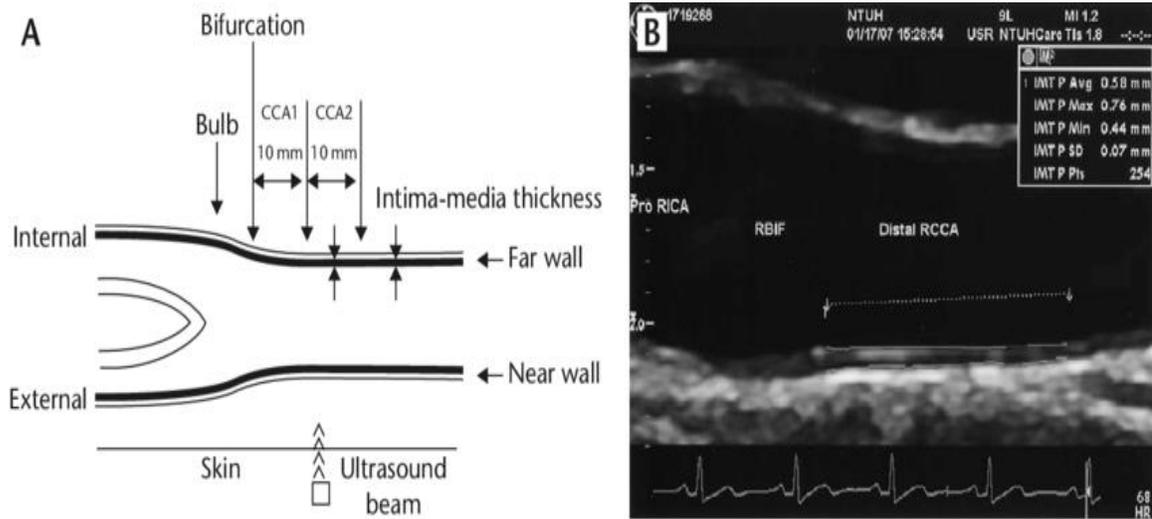


Figure (16): (A) the schematic overview of intima-media thickness (IMT) at carotid arteries and the site of measurements. (B) The real measurements of IMT at distal common carotid artery (CCA). (37).

It has age and gender-specific normal values and reference ranges.

Table (1): Common carotid artery IMT reference limit in different age groups. (38).

Age (years)	IMT reference limit in millimeter	
	Male	Female
29-18	0.47	0.47
30-39	0.62	0.59
40-49	0.72	0.67
50-59	0.80	0.70

The normal ECA waveform has a high resistance triphasic pattern with little or no diastolic flow since the ECA supplies blood to less critical regions.

The CCA, which supplies blood to both the ICA and the ECA, exhibits an intermediate waveform pattern with low resistance continuous forward diastolic flow but less than the ICA (39).

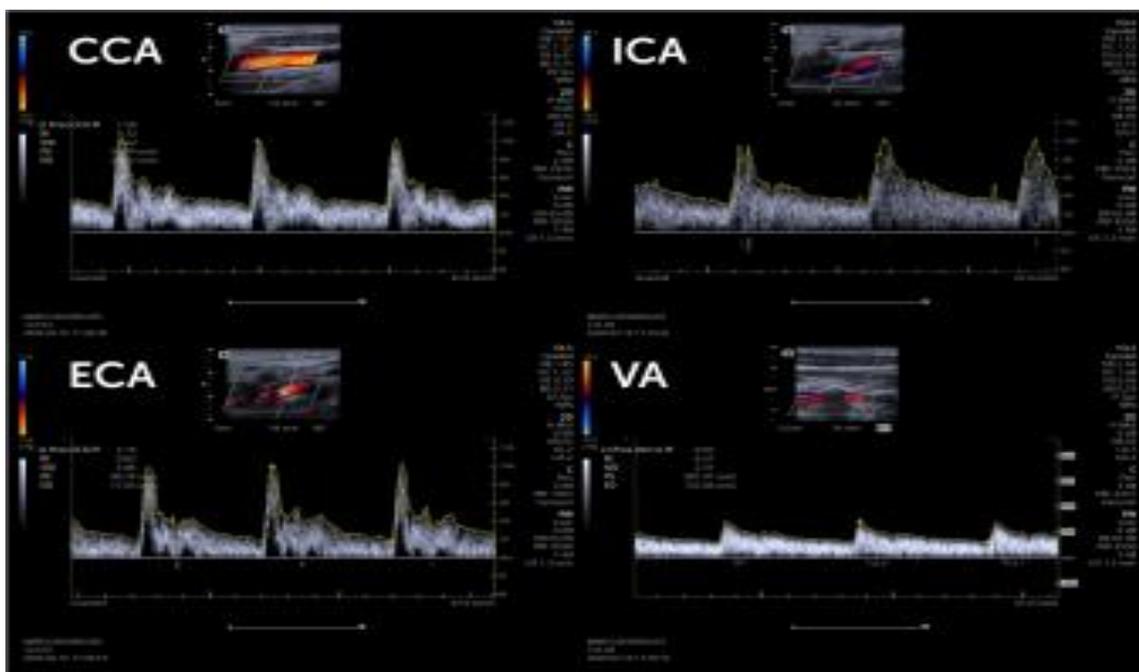


Figure (17): Normal Carotid Ultrasound Examination. (A) Common carotid artery. (B) Internal carotid artery. (C) External carotid artery. (D) Vertebral artery. (40).

Limitations of ultrasound:

The operator's expertise, the patient's habits, anatomical variations, and the tortuous route of the carotid arteries all influence ultrasound accuracy (41)

The posterior acoustic shadowing caused by calcific plaques makes greyscale imaging and Doppler sampling challenging. Another problem is that only the extra cranial cervical region of the carotid arteries may be investigated, which is limited by unfavorable anatomy (short neck) and a high carotid bifurcation; however, trans cranial Doppler may provide some additional intracranial vascular information. (42)

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