Coronary Artery Calcification: Etiology, Pathophysiology, Evaluation and Clinical Application

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Abstract:

In both the general population and individuals with coronary artery disease, coronary artery calcification (CAC) is a risk factor for poor outcomes. CAC pathophysiology, risk factors, and progression all have clinical implications. Medical therapy has not been effective in controlling CAC. Patients with coronary calcification have a worse event-free survival rate after both percutaneous coronary intervention (PCI) and bypass graft surgery. Despite the fact that drug-eluting stents and devices for plaque modification have improved results in calcified arteries, adverse event rates remain substantial. To improve the dismal prognosis of CAC patients, novel pharmacologic and device-based therapies are required.

Keywords: Calcification**,** CAC, Calcium, PCI

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Introduction:

Calcium is the most abundant mineral in the human body. Although most calcium is found in teeth and bone, only around 1% gets dissolved in the bloodstream. Calcium can deposit in numerous regions of the human body as it matures. Arterial calcium formation is linked to vascular injury, inflammation, and healing ***(1)***.

Calcification happens extremely early in the development of atherosclerosis; however, it can only be recognized when the amount grows and imaging modalities are used. In both men and women, this buildup normally happens after the age of 40. In all patients with proven coronary artery disease, coronary calcification is present ***(2)***.

Noncontrast, electrocardiographic (ECG)-gated cardiac electron beam computerized tomography (EBCT) or multidetector computed tomography (MDCT) is the most commonly used method for assessing coronary artery calcium. Coronary calcium score is not a predictor of plaque vulnerability, but it is correlated with plaque burden. Nevertheless, it provides information about the patient's risk for cardiovascular disease and aids in directing therapies to stop coronary artery disease ***(3, 4)***.

Etiology

The prevalence of coronary artery calcification is higher in men than in women and rises with age. In addition, there is a higher chance of developing coronary artery calcification in those who have metabolic syndrome, dyslipidemia, tobacco use, hypertension, chronic renal disease, and a high baseline C-reactive protein level. It should be mentioned that there are two primary categories of coronary artery calcification: medial and intimal. There is a correlation between hypertension, dyslipidemia, tobacco use, advanced age, and intimal artery calcification. However, renal illness is linked to medial calcification***(5)***.

Epidemiology

The occurrence of coronary artery calcification is contingent upon both gender and age. Sixty-seven percent of women and ninety percent of males over 70 have it ***(5)***.

Pathophysiology

It is commonly known that aberrant vasomotor response, decreased myocardial perfusion, and overall poor vascular compliance are caused by coronary calcification. Numerous hypotheses have been put out regarding how coronary artery calcification develops. The complete mechanism is currently unknown, though. Apoptotic bodies, activation of bone formation, calcium-phosphorus imbalance, and the function of vascular smooth muscle cells are some of the mechanisms that have been proposed. However, it is recognized that the development of fatty streaks can trigger calcification in the coronary arteries as early as the second decade of life. Young adult lesions analyzed in a lab have shown crystalline calcium to aggregate with lipid particles. Moreover, complicated lesions and older persons had higher concentrations of calcific deposits ***(6-8)***.

Evaluation

Despite not having any particular clinical symptoms, coronary artery calcification has a major impact on prognosis. It has the ability to reclassify patients into more accurate categories and independently predict future cardiovascular events ***(7)***.

Computed Tomography

The invention of the electron-beam CT (EBCT) scanner in the 1980s allowed for the diagnosis of coronary artery calcification by CT scanning. This resulted from the CT scanner's noticeably faster speed. Heart activity may be stopped for a sufficient amount of time to identify calcification in the coronary arteries because to the superior speed. Moreover, the advancement of the multi-detector CT scan has made it possible to get images even more quickly ***(9)***.

The assessment of coronary artery calcium scoring by computed tomography (CT) provides a quick, reliable, and reasonably priced method to ascertain the degree and existence of coronary calcification. Patients do not require any special preparation or intravenous access prior to the test. Usually, prospective electrocardiogram triggering is used to get scans during diastole. The Agatston score is used to quantify the degree of calcification following image acquisition. Multiplying the calcification area by the matching density yields the Agaston score ***(5)***.

According to the Framingham risk score, the American College of Cardiology/American Heart Association currently recommends class IIa indication for coronary artery calcium scanning in asymptomatic patients with intermediate-risk (10% to 20%) 10-year risk of cardiac events and in asymptomatic individuals 40 years of age or older with diabetes mellitus. According to the Framingham risk score, people with a low (10% or less) or high (20% or more) 10-year risk of cardiac events are generally not advised to have their CAC measured***(9)***.

Grading of coronary artery disease (based on total calcium score) no evidence of CAD: 0 calcium score ***(10)***

- minimal: 1-10
- mild: 11-100
- moderate: 101-400
- severe: >400

Electron Beam Computed Tomography

One type of computed tomography (CT) is called electron beam computed tomography (EBCT), where the source of X-ray photons is rotated without the need for a mechanical spin of the X-ray tube. This alternative design was specifically created to improve the visualization of cardiac structures, which move constantly and complete a cycle of movement with every beating***(11)***.

The X-ray source-point moves around an object to be scanned in a circle in space, just like in traditional CT technology. However, in EBT, the imaging circle is only partially encircled by the huge, stationary X-ray tube. The X-ray source point and the electron-beam focus point are electronically swept along a tungsten anode within the tube, creating a sizable circular arc on its inner surface, as opposed to the tube itself being moved. This motion can be very fast ***(12)***.

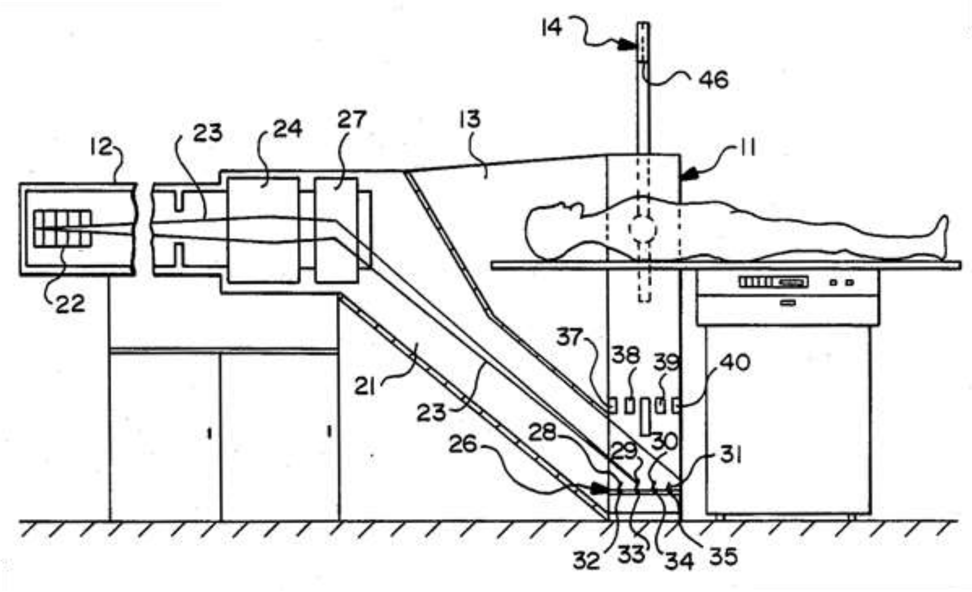

Fig. (1): Three Dimensional Scanned Projection Radiography Using High Speed Computed Tomographic Scanning System" ***(13)***.

Figure (1) showing a cutaway view of an electron beam computerized tomography system is seen in the patent illustration. 22. electron cannon, 23. Electron beam, 24. focus coil, 27. beam bending coil, 28-31. Target rings, 14. detector array, 11. Scan tube are the components. At the target rings, the electron beam generates x-rays, which radiate through the patient to the detector at the opposite end of the scan tube ***(12)***.

Electron beam CT was unable to compete with faster advancements in multidetector CT imager technology and was rendered obsolete by the 2020s ***(14)***.

Clinical Application

The unique method known as computed tomography angiography, or CT angiography, allows one to see venous and artery channels across the entire body. X-ray contrast agent is used to create a contrast of the vascular system; however, unlike conventional angiography, it does not have to be put directly in the vessel system to be seen; instead, it can be injected into a vein in the arm. Following the brief wait required for the contrast agent to pass the region of interest (ROI), which typically lasts only a few seconds, the capture sequence is either initiated manually or automatically ***(15)***.

Intra-Vascular Ultrasound

The primary applications of intravascular ultrasonography (IVUS) in interventional cardiology include characterization of lesion shape, quantification of plaque burden, guidance of stent sizing, evaluation of stent expansion, and identification of procedural problems. An image from inside an artery can be obtained using a specialized catheter and ultrasound-based technology, providing cross-sectional views that show the vessel from all angles. Many of the drawbacks of angiography, which creates a 2-dimensional lumenogram of a 3-dimensional structure using x-ray technology, are addressed by this approach. IVUS offers the evaluation from inside the vessel as opposed to angiography, which evaluates the vessel from the outside***(16).***

The inner tunica intima, the muscular tunica medium, and the outer tunica adventitia are the three layers of the arterial wall that can be identified and distinguished using intravascular ultrasonography of a coronary artery. The grayscale cross-sectional image of the smooth muscle cells that make up the tunica media appears dark and does not reflect ultrasound waves, making identification simple. IVUS-assisted intravascular imaging describes and measures plaque. IVUS evaluation is able to differentiate between neointimal growth, lipid accumulation, and calcified plaque. IVUS makes it possible to identify calcified plaque that an angiography alone could miss***(17).*** IVUS is essential for determining the mechanism of stent failure and directing the proper course of treatment when evaluating stent failure due to stent thrombosis or in-stent restenosis***(18).***

Technique

A manual or automatic pullback can be used to perform an IVUS examination of a vessel. By creating a longitudinal profile, automated pullback enables length measurements that are helpful in determining the proper stent length to choose. The process of selecting a stent diameter involves first identifying and measuring the proximal and distal references. IVUS can evaluate the minimal stent area (MSA) after stent implantation. This is a prognostic sign that is directly linked to the probability of stent-related events in the future ***(19).***

Clinical Significance

IVUS can be used to check the left major coronary arteries, guide revascularization, and assess the seriousness of lesions. Using IVUS frequently results in a modification to the PCI approach ***(20).*** Clinical evidence from meta-analyses and multicenter randomized studies has repeatedly shown that using IVUS can lower the incidence of adverse clinical events***(17,21).***

IVUS evaluation after PCI can use the post-intervention cross-sectional area to identify restenosis predictions. The United States continues to have poor IVUS utilization even after several decades of research demonstrating its benefits and use***(22).***

In the cardiac catheterization laboratory, IVUS is a crucial auxiliary tool that helps guide percutaneous coronary procedures and assess the shape of the plaque. In order to maximize clinical results when using IVUS, image interpretation is a critical ability. When an all-comers population and individuals with lengthy lesions receive stent implantation (28 mm stent placed), the use of IVUS has been linked to better clinical outcomes***(21).***

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