Imaging of Calcifications in Human Heart

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ABSTRACT

Nowhere in the human body have implications of calcifications have been studied and demonstrated with so much zeal and zest as has been done in the case of human heart.

As autopsy after autopsy of heart attack patients revealed the presence of calcifications in the coronaries, calcium was recognized as a strong disease marker. Interests soared when it was realized that calcium could stand out on plain radiographs as well because of its density.

With this began the race to modify the methods to detect coronary calcifications such that recent revolution in CT scanning techniques and Electron-beam CT (EBCT) enabled quantitation of calcium in the coronary arteries. Gradually as 16, 32 and 64-slice scanners became available more attention was directed to coronary artery CT angiography which now has reached its state of the art status.

Coronary calcification is strongly associated with the incidence of occurrence as well as the prognosis of acute myocardial infarcts. Total calcium score reflects the extent of coronary atherosclerosis and is the most powerful predictor of subsequent or recurrent cardiac events.

Apart from the coronaries, valves of the heart, the aorta and even the pericardium can calcify. These calcifications too have adverse health impacts. Hence, this article aims at unraveling the mystery of Calcifications and Human Heart.

INTRODUCTION

I] Coronary Artery Calcifications:

With widespread reliance on autopsy to determine the cause of death, it has been understood that patients who died of coronary artery disease had 2-5 times as much calcium as those who died due to other causes.

The development of atherosclerosis in the coronary arteries is marked by the prominent presence and widespread extent of coronary calcium as it occurs exclusively in atherosclerotic arteries and is absent in the normal vessel wall. Thus, the calcification in the coronary arteries is a sure marker of the deadly coronary atherosclerosis [1].

Coronary artery disease has caused 20% of all deaths in the United States in 2004, and the cardiovascular disease mortality in women was about 460,000, more than the combined deaths from lower respiratory disease, Alzheimer's disease, accidents, and diabetes mellitus combined [2].

Thus, the atherosclerotic coronary artery disease is the number one cause of death in the western world. Hence, it is important to screen for coronary artery disease and, thereby to prevent the sequelae of myocardial infarction and sudden cardiac death.

Fluoroscopy, electron beam, and helical computed tomography can identify calcific deposits; EBCT and, to a lesser extent, double-helical CT have enhanced capability to localize coronary calcification and to detect smaller and less dense calcific deposits. When the calcium score is 0 the angiographic evidence of obstructive epicardial coronary artery involvement could be completely ruled out. With the increase in the calcium score, the presence of angiographic obstructive disease further increases [3]. By the same analogy calcium scores greater than 371, had 90% specificity in the detection of a luminal obstruction of greater than 70%. Specificity it tends to decrease with advanced patient age, but it increases with the number of calcified vessels as well as the total calcium score [4].

It is therefore not difficult to understand that higher the calcium score, the worse the prognosis [5, 6, 7]. As shown by Agatston et al., the mean calcium score for patients with a cardiovascular event was 399, as compared with a mean score of 76 in those without such an event. One study suggested that the detection of coronary calcification at EBCT was a better predictor of subsequent events than many traditional risk factors, including those evaluated in the Framingham database [8].

Although cardiac events do occur in patients with low calcium scores, their incidence is low. Intravascular ultrasonographic studies show that as many 30% of coronary plaques are devoid of calcium. In an autopsy study [9], the benefit of combined assessment of coronary artery calcification and risk factors (Framingham Risk Index) in predicting sudden cardiac death was apparent.

The left anterior descending coronary artery is the commonest to be calcified followed by the left circumflex, left main and then the right coronary artery. On plain Radiograph of chest it is seen as parallel dense lines and can be detected in upto 42% of the cases. 54% of the symptomatic population demonstrated it on fluoroscopy, which was therefore promoted as the screening modality. The threshold of calcification on spiral CT is + 90 Hounsfield units (H.U.) and that on electron beam CT is +130 H.U. [Table/Fig-1 and 2] show the typical appearance of coronary calcifications on CT scan images.

The Mechanism

Coronary calcification is composed of calcium phosphate (hydroxyapatite), which is similar to that in bone. Although initially it was believed to be the result of a degenerative process, now the evidence suggested an active process, like a response to injury which was regulated in the fashion similar to bone mineralization was the likely culprit.

The mechanism of progression of coronary atherosclerosis and plaque instability and rupture in acute coronary syndromes reveals that atherosclerotic calcification is a very organized, regulated process ehich is similar to bone formation that occurs only when other aspects of atherosclerosis are also present [10,11,12,13]. Nonhepatic Gla-containing proteins like osteocalcin, which are actively involved in the transportation of the calcium out of vessel walls, are suspected to have key roles in the pathogenesis of coronary calcification. Osteopontin and its mRNA, known to be involved in bone mineralization, have been identified in calcified atherosclerotic lesions. Calcified human atherosclerotic plaque also contains mRNA for bone morphogenetic protein-2a, a potent factor for osteoblastic differentiation, and cells that are capable of osteoblastic differentiation. These cells may be the one from which vascular calcifying cells are derived. These and other recent findings indicated that calcification is an active process and not simply a passive precipitation of calcium phosphate crystals, as once thought [14].

The coronary calcification scoring test is called as a positive scan, if it shows at least one vessel, and thus confirming the presence of atherosclerotic plaque. The greater the amount of calcification, the greater the likelihood of obstructive disease. A high calcium score may be consistent with a moderate to high risk of a cardiovascular event within the next 2 to 5 years [14].

Coronary calcification in patients with end-stage renal disease has been discovered and is believed to be a novel endocrine disorder [15].

The Coronary Tree on the CT scan

To study the health impacts of calcifications in the coronaries, Calcium scoring using EBCT has to be done. Following is the protocol for EBCT [16, 17]. No contrast is needed. 3 mm slice thickness, High resolution volume mode, 100 ms scan time, EKG gating, triggered at 80% of the RR interval, Breath hold, Supine position. The radiation exposure in this study is less than 500 mrem. The calcium score, as originally proposed by Agatston, is determined on the basis of the product of the total area of a calcified plaque and an arbitrary scoring system for those pixels with an attenuation greater than 130 Hounsfield Units (HU). A high interscan variability up to 60% has been reported.

Spiral multislice CT scores better by coupling the technique of retrospective gating with nearly isotropic volumetric imaging. Using ECG-gated volume coverage with multislice spiral CT and overlapping image reconstruction (2.5 mm collimation, 1 mm increment), an interscan variability of approximately 5–8% can be achieved.

The four main coronary arteries evaluated at CT scan are the Right Coronary Artery (RCA), the Left Main Coronary Artery (LCA), the Left Anterior Descending (LAD) artery, and the Left Circumflex (LCx) Artery.

Right Coronary Artery: The RCA arises from the anterior right coronary sinus somewhat inferior to the origin of the LCA. The RCA passes to the right and posterior to the pulmonary artery and then downward in the right atrioventricular groove toward the posterior interventricular septum.

Left Coronary Artery: The LCA arises from the left posterior coronary sinus, is 5–10 mm long, and does not vary in diameter. The LCA passes to the left of and posterior to the pulmonary trunk and bifurcates into the LAD and LCx arteries. The LAD artery passes to the left of the pulmonary trunk and turns anteriorly to course in the anterior interventricular groove toward the apex. It provides the diagonal branches (D) to the anterior free wall of the left ventricle and the septal branches to the anterior interventricular septum. The Left Circumflex Artery (LCx) courses in the left atrioventricular groove and gives off Obtuse Marginal branches (OM)to the lateral left ventricle.

[Table/Fig-1] shows the Schematic Diagram of Coronary Circulation and [Table/Fig-2] shows the Maximum Intensity Projection of Cardiac CT study showing the entire Coronary Tree in coronal oblique view. [Table/Fig-3] is the maximum intensity projection of Right Coronary Artery showing calcified plaques.
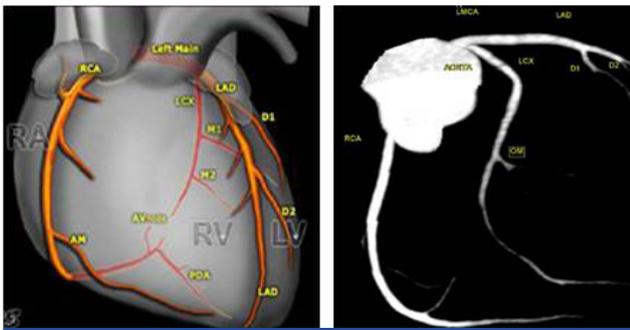
[Table/Fig-1]: Schematic Diagram of Coronary Circulation
[Table/Fig-2]: Maximum Intensity Projection of Cardiac CT study showing Coronary Tree (Coronal Oblique View)
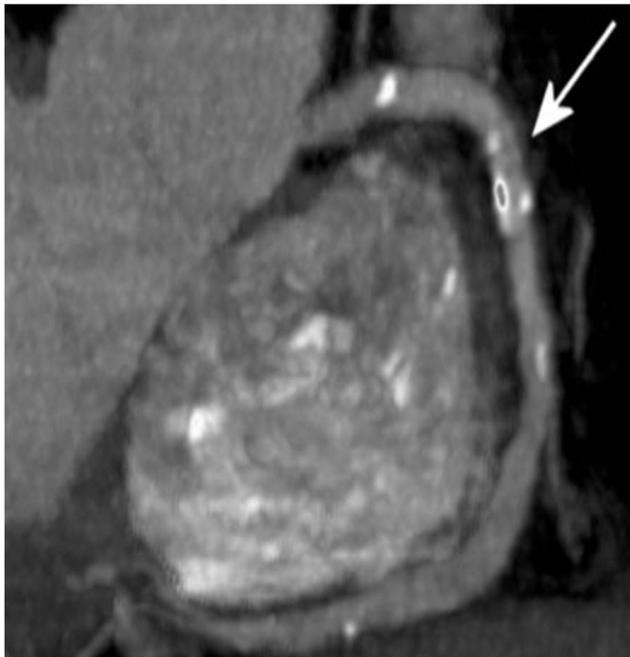
[Table/Fig-3]: Maximum intensity projection of Right Coronary Artery showing calcified plaques

On CT the Coronary calcification score [18] is given as:

- Threshold CT density > 130 HU for pixel areas > 1mm2.
- Lesion Score 1 = 130 - 199, 2 = 200 - 299, 3 = 300 - 399, 4 > 400.
- Score each region of interest by multiplying the density score and the area.
- Total coronary calcium score determined by adding up each lesion score for all sequential slices.

Absence of Detectable Coronary Artery Calcification [19 -26]

- Does not absolutely rule out the presence of atherosclerotic plaque, including unstable plaque.
- Highly unlikely in the presence of significant luminal obstructive disease.

- Observation made in the majority of patients who have had both angiographically normal coronary arteries and EBCT scanning.
- Testing is gender independent.
- May be consistent with a low risk of a cardiovascular event in the next 2-5 years.

Presence of Detectable Coronary Artery Calcification [19 -26]

- Confirms the presence of coronary atherosclerotic plaque.
- The greater the amount of calcification (i.e., calcium area or calcium score), the greater the likelihood of obstructive disease, but there is no one-to-one relation, and findings may not be site specific.
- Total amount of calcification correlates best with total amount of atherosclerotic plaque, although the true "plaque burden" is underestimated.
- A high calcium score may be consistent with moderate to high risk of a cardiovascular event within the next 2-5 year.

II] Calcification of other cardiac structures

Valvular calcification leads to haemodynamic imbalance as it causes stenosis. While Rheumatic heart disease is the commonest cause of calcified valve in case of mitral and tricuspid valves, atherosclerotic degeneration is more common in case of aortic valve.

Endocardium can get calcified in thrombosis, cardiac aneurysm as well as in endocardial fibroelastosis. Myocardium gets calcified following infarcts, aneurysms and myocarditis. Pericardial calcifications are seen in idiopathic pericarditis, rheumatoid arthritis, tuberculosis, in chronic renal failure and in post radiotherapy status. It leads to constrictive pericarditis.

Cardiac tumours like atrial myxoma, rhabdomyoma and osteosarcoma are also known to calcify.

REFERENCES

[1] O'Rourke RA, Brundage BH, Froelicher VF. American College of Cardiology/American Heart Association Expert Consensus document on electron-beam computed tomography for the diagnosis and prognosis of coronary artery disease. *Circulation.* Jul 4 2000;102(1):126-40.

[2] Rosamond W, Flegal K, Furie K, et al. Heart disease and stroke statistics--2008 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation.* Jan 29 2008;117(4):e25-146.

[3] Rumberger JA, Brundage BH, Rader DJ. Electron beam computed tomographic coronary calcium scanning: a review and guidelines for use in asymptomatic persons. *Mayo Clin Proc.* Mar 1999;74(3):243-52.

[4] Rumberger JA. Coronary artery calcification: "...empty your cup.". *Am Heart J.* May 1999;137(5):774-6.

[5] Raggi P, Khan A, Arepali C, Stillman AE. Coronary artery calcium scoring in the age of CT angiography: what is its role?. *Curr Atheroscler Rep.* Oct 2008;10(5):438-43.

[6] Ho JS, Fitzgerald SJ, Stolfus LL, Wade WA, Reinhardt DB, Barlow CE, et al. Relation of a coronary artery calcium score higher than 400 to coronary stenoses detected using multidetector computed tomography and to traditional cardiovascular risk factors. *Am J Cardiol.* May 15 2008;101(10):1444-7.

[7] Prabhakar M, Ko DT. Can coronary calcification measured by CT predict future coronary events?. *CMAJ.* Oct 25 2005; 173(9): 1034.

[8] Agatston AS, Janowitz WR, Hildner FJ, Zusmer NR, Viamonte M Jr, Detrano R. Quantification of coronary artery calcium using ultrafast computed tomography. *J Am Coll Cardiol.* Mar 15 1990; 15(4): 827-32.

[9] Taylor AJ, O'Malley PG. Self-referral of patients for electron-beam computed tomography to screen for coronary artery disease. *N Engl J Med.* Dec 31 1998;339 (27):2018-20.

[10] Ross R. The pathogenesis of atherosclerosis: a perspective for the 1990s. *Nature.* 1993;362:801-09.

[11] Fuster V, Lewis A. Connor Memorial Lecture—Mechanisms leading to myocardial infarction: insights from studies of vascular biology. Circulation. 1994;90:2126-2146. *Erratum. Circulation.* 1995; 91:256.

[12] Libby P. Molecular bases of the acute coronary syndromes. *Circulation.* 1995;91:2844-50.

[13] Falk E, Shah PK, Fuster V. Coronary plaque disruption. *Circulation.* 1995;92:657-71.

[14] Lewis Wexler, Chair, Bruce Brundage, John Crouse, Robert Detrano, Valentin Fuster, et al. John Rumberger, William Stanford, Richard White , Members; Kathryn Taubert, AHA Staff. Coronary Artery Calcification: Pathophysiology, Epidemiology, Imaging Methods, and Clinical Implications. *Circulation.* 1996;94:1175-92.

[15] Georgios Efstratiadis, Konstantinos Koskinas, Efstathios Pagourelias. Coronary calcification in patients with end-stage renal disease: a novel endocrine disorder? *Hormones.* 2007, 6(2): 120-31.

[16] Schoenhagen P, Halliburton SS, Stillman AE, et al. Noninvasive Imaging of Coronary Arteries: Current and Future Role of Multi-Detector Row CT. *Radiology.* 2004; 232:7-17.

[17] Schoepf UJ, Becker CR, Ohnesorge BM, Yucel EK. CT of Coronary Artery Disease. *Radiology.* 2004; 232:18-37.

[18] Agatston AS, Janowitz WR, Hildner FJ, Zusmer NR, Viamonte M Jr, Detrano R. Quantification of coronary artery calcium using ultrafast computed tomography. *J Am Coll Cardiol.* 1990;15:827-32.

[19] Mautner SL, Mautner GC, Froehlich J, et al, 1994 Coronary artery disease: prediction with in vitro electron beam CT. *Radiology.* 192: 625-30.

[20] Rumberger JA, Simons DB, Fitzpatrick LA, Sheedy PF, Schwartz RS, 1995 Coronary artery calcium area by electron-beam computed tomography and coronary atherosclerotic plaque area. A histopathologic correlative study. *Circulation.* 92: 2157-62.

[21] Puentes G, Detrano R, Tang W, et al, 1995 Estimation of coronary calcium mass using electron beam computed tomography: a promising approach for predicting coronary events? *Circulation.* 92: l313.

[22] Arad Y, Spadaro LA, Goodman K, Newstein D, Guerci AD, 2000 Prediction of coronary events with electron beam computed tomography. *J Am Coll Cardiol.* 36: 1253-60.

[23] Berman DS, Hachamovitch R, Shaw LJ, 2006 Roles of Nuclear Cardiology, Cardiac Computed Tomography, and Cardiac Magnetic Resonance: Assessment of Patients with Suspected Coronary Artery Disease. *J Nucl.* 47: 74-82.

[24] Taylor AJ, Merz CN, Udelson JE, 2003 34th Bethesda Conference: executive summary—can atherosclerosis imaging techniques improve the detection of patients at risk for ischaemic heart disease? *J Am Coll Cardiol.* 41: 1860-62.

[25] Pundziute G, Schuijf JD, Jukema W, et al, 2007 Prognostic Value of Multislice Computed Tomography Coronary Angiography in Patients With Known or Suspected Coronary Artery Disease. *JACC.* 49: 62-70.

[26] O'Rourke RA, Brundage BH, Froelicher VF, et al, 2000 American College of Cardiology/American Heart Association Expert Consensus Document on electron-beam computed tomography for the diagnosis and prognosis of coronary artery disease. *J Am Coll Cardiol.* 36: 326-40.

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