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Original Article

Plaque rupture relationship to plaque composition in coronary arteries. A 320-slice CT angiographic analysis

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ABSTRACT

Background: Coronary thrombosis leading to myocardial ischemia is now recognized as a diverse process arising from plaque rupture, erosion, or calcified nodules. These vulnerable plaques may not always cause significant stenosis of the artery, and therefore be missed on an invasive catheter angiogram (ICA). The advent of multidetector computed tomography (MDCT) imaging of the walls of the coronary artery has opened a unique window to these vulnerable plaques. Differentiation of calcified plaques from soft plaques presents no challenge on CT. Further characterization of the plaque into a ruptured plaque is possible by demonstration of discontinuity of the plaque surface and contrast pooling within the plaque substance.

Purpose: To study the relation between coronary artery plaque rupture and plaque composition.

Materials and methods: 500 patients referred for coronary CT angiogram between 2008 and 2013, who had plaque thicknesses of 2 mm or more, were included in the study. The plaques were divided into totally calcified, mixed, and soft categories. The totally calcified plaques were excluded from the study as none of these showed signs of plaque rupture. A total number of 2667 mixed and soft plaques were included in the study.

Results: 52% of the total plaques were ruptured and 48% not ruptured. Of the ruptured plaques, 96.9% were mixed type and only 3.7% were soft. And of the non-ruptured plaques, 96.3% were soft and only 3.1% mixed ($p < 0.0001$).

Conclusion: This study reveals that plaque rupture is significantly associated with mixed plaques containing soft and calcific areas rather than purely soft plaques.

1. Introduction

Cardiovascular deaths account for 30% of all deaths worldwide.[1] Coronary thrombosis leading to myocardial ischemia is now recognized as a diverse process arising from rupture or erosion of atherosclerotic plaques or presence of calcified nodules within them.[2] Majority of acute coronary syndromes are caused by plaque rupture in segments with 50% or less stenosis, which are asymptomatic prior to the event.[3]

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Patients with ST elevation myocardial infarction caused by plaque rupture show a higher incidence of no-reflow, higher creatine-kinase levels, and lower ejection fractions.[4] Needless to say, that the hunt for the vulnerable plaque, which causes acute coronary syndromes, is being passionately pursued all over the world.

However, this exercise has presented significant obstacles. Animal models have led to an incomplete understanding of the progression of a stable fibroatheroma to a ruptured plaque. This is because mouse models rarely progress to plaque rupture.[5] Histologic processing of plaques in search of the vulnerable plaque has also been challenging. It requires fixation, dehydration, and some degree of decalcification before paraffin embedding to allow sectioning and thereby leads to distortion of morphology and loss of information. It also causes mechanical and physiochemical artifacts, such as shrinkage of the specimen and does not allow obtaining adjacent sections.

Coronary Computed Tomographic Angiography (CCTA) with its non-invasive cross-sectional information has seen remarkable growth in recent years. The 320-slice CTA is a new generation scanner, which can scan the whole heart in a single beat giving clear images of plaques and their morphology. Recent studies show that percent diameter stenosis determined with the use of 320-slice CCTA shows good correlation with invasive catheter angiogram (ICA) ($p < 0.0001$).[6] Differentiation of calcified from soft plaques presents no challenge on CCTA. Further characterization of the plaque into a ruptured plaque is now possible by demonstration of intraluminal contrast pooling into the plaque substance.[7]

The objective of this study is to evaluate the relationship between coronary arterial plaque rupture and plaque composition in an attempt to determine whether soft or mixed plaques are more prone to rupture.

2. Materials and methods

Between 2008 and 2013, five hundred patients with plaque thickness of 2 mm and above were included in the study. Plaques thinner than 2 mm were excluded, as it was difficult to determine presence of small calcium specks or ulcerations within them. 68% patients had chest pain with normal ECG and negative cardiac biomarkers, and hence a CCTA was ordered to rule out coronary artery disease (CAD). 32% patients were asymptomatic, but had borderline treadmill tests. CCTA was ordered to rule out CAD. 87% were men and 13% were women. 58% were hypertensives, 43% were diabetics, 41% dyslipidemics, 37% smokers, and 46% had a family history of coronary artery disease. None of the patients had had any cardiac interventions or surgery. The CCTA was performed using a 320-slice CT scanner (Aquilion One, Toshiba Medical Systems, Tokyo, Japan). Intravenous contrast used was Optiray 350 mg (Mallinckrodt, USA). Patients with heart rates more than 80 and no contraindication to beta-blockers were administered oral Metoprolol up to 100 mg to reduce the heart rate prior to the scan. A sublingual nitroglycerine tablet of 5 mg was used 10 min prior to the scan. A plain ECG gated scan was performed for calcium score followed by a contrast enhanced scan through the heart after 65 ml of intravenous contrast injection at the rate of 4.5 ml/s with a pressure injector chased by a bolus of 30 ml of normal saline at the same rate. The images were interpreted by a senior radiologist on curved reconstructions through the vessel lumen as well as the cross sections at a dedicated workstation.

The plaques were divided into totally calcified, mixed, and soft. Plaques with no calcium were considered soft, and plaques with presence of calcium within a soft component were considered mixed. Plaque rupture was identified by demonstration of discontinuity of the plaque surface and contrast pooling within the plaque substance (Figs. 1 and 2). Completely calcified plaques were excluded, as none of them revealed signs of plaque rupture. A total of 2667 mixed and soft plaques were included in the study.

2.1. *Statistical analysis*

The statistical analysis was performed per plaque and not per patient. p-Values were calculated. In all tests, differences were considered not significant when $p > 0.05$.

3. Results

52% of the total plaques were ruptured, and 48% were not ruptured. It was observed that out of the ruptured plaques, 96.9% were mixed type, and only 3.7% were soft. And of the non-ruptured plaques, 96.3% were soft, and only 3.1% were mixed ($p < 0.0001$) (Fig. 3). This demonstrated that mixed plaques were more prone to rupture than soft plaques.

4. Discussion

4.1. *Classification of atherosclerotic plaques*

Human atherosclerotic lesions are classified based on their histological composition and structure[8] (Fig. 4). The initial *Type I* lesion contains enough atherogenic lipoprotein to elicit an increase in macrophages and formation of scattered macrophage foam cells. *Type II* lesions consist primarily of layers of macrophage foam cells and lipid-laden smooth muscle cells and include lesions grossly designated as fatty streaks. *Type I* and *II* are early lesions. *Type III* is the intermediate lesion. In addition to the lipid-laden cells of *Type II*, *Type III* lesions contain scattered collections of extracellular lipid droplets and particles that disrupt the coherence of some intimal smooth muscle cells. This extracellular lipid is the immediate precursor of the larger, confluent, and more disruptive core of extracellular lipid that characterizes *Type IV* lesions. *Type IV* lesions would be visible on CCTA as soft plaques with homogeneous low-density focal thickenings of the arterial wall with a smooth convex surface towards the lumen. *Type I* lesions would be too small to be visible on CTA, and *Type II* and *III* lesions may appear as just a thin focal thickening of the wall. *Types I–IV* are clinically silent and cause no symptoms.

Beginning around the fourth decade of life, lesions that usually have a lipid core may also contain thick layers of fibrous connective tissue (*Type V* lesion) and/or fissure, hematoma, and thrombus (*Type VI* lesion). Some *Type V*