Calcified Plaques in the Human Coronary Artery
— Each Calcified Plaque Is Never the Same —

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Since the introduction of percutaneous coronary intervention (PCI) into the clinical arena, the presence of coronary artery calcification (CAC) has been repeatedly reported as an important risk factor for periprocedural complications, procedural failure, revascularization, and stent thrombosis. As society is aging, the frequency of PCI for severe calcified lesions is increasing, but despite the advent of drug-eluting stents (DES), CAC has remained an unresolved issue in the field of PCI.

Several imaging modalities have been used to evaluate CAC severity. Coronary angiography has a high positive predictive value for CAC, but the sensitivity is not high. Intravascular ultrasound (IVUS) is more accurate than coronary angiography in detecting CAC, with 90–100% sensitivity and 99–100% specificity. Additionally, it can provide direct information on the circumferential, diametrical, and longitudinal distribution of CAC. However, IVUS cannot accurately measure the thickness and volume of CAC owing to its limited ability to penetrate CAC.

Figure. Case of target lesion revascularization due to regrowth of a calcified nodule (white arrowheads). PCI, percutaneous coronary intervention.
Moreover, the image resolution of IVUS is insufficient to differentiate the various CAC types observed in the pathological assessment of the human coronary artery. Therefore, few studies have examined the qualitative differences between calcified lesions and their effect on clinical outcomes.

The recent advent of optical coherence tomography (OCT) technology has allowed the in vivo classification of CAC and investigations of clinical significance. In a recent postmortem study, Saita et al classified CAC into 4 types: (1) superficial dense calcified plates, (2) deep intimal calcification, (3) scattered microcalcification, and (4) calcified nodule (CN). They validated the histological examination using OCT findings. Notably, OCT accurately distinguished CNs from other entities as high-backscattering protruding masses with an irregular surface and low-intensity areas with diffuse borders.

The concept of CN was first introduced in a postmortem study by Virmani et al.3 Described as a dense, erupтив, calcified mass with an irregular surface, it is characterized by an underlying heavily calcified plaque with a distinct nodular mass of calcium that protrudes into the lumen and causes dysfunction or loss of the overlying endothelial cells.4 The nodules are surrounded by fibrin with a non-occlusive platelet-rich “white” thrombus on top. CN is the most frequent cause of intracoronary thrombus formation resulting in the culprit lesions of acute and chronic coronary syndromes. On OCT, a CN is sometimes indistinguishable from protruding intracoronary thrombus.

Although the mechanism of CN development is unknown, it is frequently observed on the fractured underlying calcified plate. Thus, a potential hypothetical mechanism involves mechanical stress that fragments the calcium sheet, resulting in the occurrence of TLR in CN lesions. Although their data proved that MACE occurred more frequently in CN patients than in CP or SC patients and that CNs were an independent predictor of MACE, the underlying mechanisms of the higher incidence of TLR and MI were not identified. TLR occurred more frequently in CN patients despite their greater post-PCI MSA. CN was associated with a higher incidence of stent edge dissection (SED) and incomplete stent apposition (ISA), but the incidence of these findings was similar to that of TLR. SED occurred in 30% of lesions, ISA occurred in 91%, and the incidence of TLR was 7%. There was no significant difference in MSA, SED incidence, stent under-expansion, and ISA between lesions with and without MACE in each calcified plaque subtype. These data suggested that the occurrence of TLR in CN lesions was not caused by known TLR mechanisms for general lesions. Instead, unique mechanisms might influence the CN lesions. Iwai et al did not evaluate OCT imaging at the time of TLR. However, we sometimes experience cases of TLR due to progressive CN regrowth at the exact location where the CN was observed during the index PCI (Figure). Because the nodules are surrounded by fibrin with platelet-rich white thrombus on top, DES is likely insufficient to protect against restenosis in this type of lesion. Thus, their data showing a higher incidence of TLR in CN lesions make sense. Delayed reendothelialization seen after DES implantation may enhance additional thrombus attachment at the site of the original CN segment, resulting in in-stent restenosis or stent thrombosis.


