Role of microcalcifications in atherosclerotic plaque rupture: evolution of a longstanding paradigm

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Abstract

The longstanding paradigm describing an acute coronary event is that the culprit plaque is not calcified, or has a low amount of calcification, when compared with non-ruptured advanced lesions, which show much larger calcium scores. This notion is supported by clinical and pathological analyses that have focused on the total amount of calcification (calcified area in a whole atheroma cross section), as well as finite element studies indicating that large calcifications lead to mechanical stabilization of the atheroma. However, this paradigm has changed significantly over the past decade.

Recent research has focused on the presence of microcalcifications (μCalcs) in the atheroma, and more importantly on whether clusters of μCalcs are located in its cap. It has been shown using high-resolution μCT that μCalcs are very abundant in the lipid pools and necrotic cores of fibroatheromas, but since they are free floating they have little effect on the biomechanics of atheroma rupture. However, in Kelly-Arnold et al (2013) numerous μCalcs were also found in 35% of the fibrous caps, where they do intensify the background circumferential stress in the cap tissue. It is now known that the stress concentration factor (SCF) produced by μCalcs depends on the size and shape of the μCalcs as well as the proximity between two or more μCalcs, where the SCF can exceed a factor 5 or more. It has also been shown based on analysis of failure mechanisms that there is a minimum critical size ~ 5 μm for μCalcs to be potentially dangerous.

The vulnerability of a plaque is increased by the presence of μCalcs, which amplify the background stress in the cap. These μCalcs form as an aggregation of smaller calcified matrix vesicles. The magnitude of the background stress in the cap depends on the atheroma morphology (i.e. cap thickness, necrotic core size, location and shape of lipid core) and tissue composition (i.e. lipid core composition, residual stresses). If the cap has no μCalcs, the cap needs to thin to ~30μm to reach the rupture threshold and become prone to rupture. If a cap with very low background stress contains μCalc(s), the increase in stress concentration produced by μCalcs may not be sufficient to reach the rupture threshold. However, the presence of μCalc(s) in a cap with a background stress of about one fifth - one half the rupture threshold (a stable plaque), will produce a significant increase in local stress, which may exceed the cap rupture threshold, and thus transform a non-vulnerable plaque into a vulnerable one. In this talk, our current understanding of the role of μCalcs on plaque vulnerability and how the longstanding acute coronary event paradigm has evolved in view of thee more recent discoveries will be discussed.

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