Guest Column

Unstable or High Risk Plaque: How Do We Approach It?

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Vulnerable Plaque: Issue of Nomenclature

Every year, >1 million people in the United States and >19 million others worldwide experience a sudden cardiac event (acute coronary syndrome and / or sudden cardiac death) resulting in > 450 000 deaths annually in the United States. A large portion of this population has no prior symptoms [1]. This is due to non flow limiting vulnerable/unstable plaques rupturing and setting up the cascade of thrombosis producing subtotal or total occlusion and leading to Acute Coronary Syndrome (ACS).

The term 'vulnerable' plaque was coined by Muller and colleagues, to describe a plaque that by becoming disrupted has a high likelihood of starting the adverse cascade [2,3]. There is disagreement over the meaning of this term, and several terms like high risk plaque, culprit plaque and unstable plaque have been used interchangeably to indicate the same pathological lesion.

The term 'unstable plaque' basically connotes an unstable clinical situation. It should therefore, be used only when vulnerable plaque has already initiated the clinical cascade of ACS. Because the term also has well-accepted clinical usage to describe unstable angina pectoris, confusion between the clinical syndrome and plaque is inevitable. Therefore it is proposed that the term 'unstable' be reserved for the clinical syndrome and not for the plaque. The term 'culprit plaque' indicates that the clinical syndrome has set in and the plaque has played causative role. The classical 'vulnerable plaque' has certain well defined histopathology namely a thin fibrous cap, extensive macrophage infiltration, paucity of smooth muscle cells, large lipid and calcified nodule which are likely as a result of repetitive plaque rupture and healing, causing shrinkage of vessel lumen with consecutive high grade coronary stenosis [4].

The correct terminology should be 'high risk plaque' because it would encompass all varieties of histopathologic plaques that are likely to disrupt. In the literature, the most widely used terminology is 'vulnerable plaque' and for the sake of avoiding confusion we would use the same term in this article.

The results from recent studies have proposed the following histopathologic and clinical criteria for the definition of vulnerable plaque.

Major Criteria

1. Active Inflammation (monocyte/macrophage infiltration) [5]: Plaques with active inflammation may be identified by extensive macrophage accumulation. Possible intravascular diagnostic techniques include thermography (measurement of plaque temperature), contrast-enhanced (CE) MRI, and fluorodeoxyglucose positron emission tomography. It has recently been shown that optical coherence tomography (OCT) reflects the macrophage content of the fibrous cap.
2. A thin cap with a large lipid care [6]: These plaques have a cap thickness of <100 μm and a lipid core accounting for >40% of the plaque's total volume. Possible diagnostic techniques include OCT, intravascular ultrasonography (IVUS), MRI, angioscopy, near infrared (NIR) spectroscopy and radiofrequency IVUS analysis.
3. Endothelial Denudation with Superficial Platelet Aggregation [4]: These plaques are characterized by superficial erosion and platelet aggregation or fibrin deposition. Possible intravascular diagnostic techniques include angioscopy with dye and OCT. Noninvasive options include platelet/fibrin-targeted single photon emission computed tomography and MRI.
4. Fissured/Injured Plaque [4]: Plaque with a fissured cap that did not result in occlusive thrombi may be prone to subsequent thrombosis. Possible diagnostic techniques include OCT, IVUS, angioscopy and MRI. Fissured coronary plaques can be found in up to 25% of patients with CAD who died of non-cardiac causes [7].

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5. Severe Stenosis : On the surface of plaques with severe stenosis, shear stress imposes a significant risk of thrombosis and sudden occlusion. The current standard technique is resonance angiography. Noninvasive options include multislice CT and magnetic resonance angiography with or without a contrast agent.

Minor Criteria

1. Superficial Calcified Nodules [4]: These plaques have a calcified nodule within or very close to their cap and this structure protrudes through and can rupture the cap. This event may or may not be associated with severe coronary calcification and a high calcium score.
2. Yellow Colour (on Angioscopy) [8]: Yellow plaques, particularly glistening ones may indicate a large lipid core and thin fibrous cap, suggesting a high risk of rupture. However, because plaques in different stages can be yellow and because not all lipid-laden plaques are destined to rupture or undergo thrombosis, this criterion may lack sufficient specificity.
3. Intraplaque Hemorrhage [4]: Extravasation of red blood cells or iron accumulation in plaque may represent plaque instability. Possible diagnostic technique include NIR spectroscopy, tissue Doppler methods and MRI.
4. Endothelial Dysfunction [9]: Vulnerable plaques have sites of active inflammation and oxidative stress and are likely to be associated with impaired endothelial function. Possible diagnostic techniques are endothelium-dependent coronary artery dilatation and measurement of flow-mediated dilatation by brachial artery ultrasonography.
5. Expansive (positive) Remodeling: Many of the nonstenotic lesions undergo "expansive," "positive," or "outward" remodelling i.e. compensatory enlargement before compromising significantly on the vascular lumen. As the luminal area was not affected, this phenomenon was considered as positive remodelling. Several studies have suggested that such remodelling is a potential surrogate marker of plaque vulnerability [10]. IVUS was used in these studies to evaluate remodelling in coronary arteries.

Relation to the AHA classification of atherosclerotic lesions

The AHA classification [11], which is based on histologic features rather than functional significance, divides plaques into six types with increasing complexity.

1. Type I: initial changes
2. Type II: fatty streak
3. Type III: pre atheroma
4. Type IV: atheroma
5. Type V: fibroatheroma
6. Type VI: complicated plaque

Most vulnerable plaque exhibit a Type IV or Type V histologic appearance.

Diagnosing the vulnerable plaque:

Rupture of vulnerable plaques is the main cause of ACS. Identification of vulnerable plaque is therefore important to enable the development of treatment modalities to stabilize such plaque.

Invasive Modalities

Coronary Angiography

Coronary angiography has been the gold standard to assess the severity of luminal narrowing. Studies have shown that the culprit lesion prior to an MI has been, in 48-78% of all cases, a stenosis smaller than 50% [12,13]. 70% of acute coronary occlusions are in areas that were previously angiographically normal [14]. Angiography therefore, has a low discriminatory power to identify vulnerable plaque.

Angiogscopy

Intracoronary angioscopy offers direct visualization of the plaque surface and intraluminal structures like tears and thrombi. It allows assessment of the colour of the plaque and thrombus with higher sensitivity compared to angiography [15]. In a 12 month follow up of 157 patients with stable angina, ACS occurred more frequently in patients with yellow plaques than in those with white plaques [16]. Limitations of Angioscopy are difficulty to perform, invasive, limited part of vessel can be investigated and to enable clear visualization of the vessel wall, the vessel has to be occluded and the remaining blood flushed away with saline, thereby potentially inducing ischemia.

Intravascular Ultrasound (IVUS)

IVUS provides some insight into the composition of coronary plaque. In IVUS images lipid depositions are echolucent and detected with sensitivity between 78-95% and specificity of 30% [17]. Plaque calcification, characterized by a bright echo signal with distal shadows can be detected with a sensitivity of 86% [18]. Ruptured plaque is characterized by an echolucent area within the plaque and a tear of the thin fibrous plaque. It can be confirmed by injecting contrast medium and seeing filling of the plaque cavity on IVUS. Potential of ultrasound radiofrequency signal analysis for tissue characterization has been studied. It offers better tissue characterization with improved differentiation of