University Heart Journal
Vol. 20, No. 2, July 2024

EDITORIAL

Vulnerable Plaque to Vulnerable Patient: The Shifting Paradigm

University Heart Journal 2024; 20(2): 47-48
DOI: https://doi.org/10.3329/uhj.v20i2.81795

Over the past few decades, there have been significant conceptual changes in the underlying pathophysiology leading to coronary heart disease (CHD). The focus has been shifted from the "vulnerable plaque" to the "vulnerable patient," where the atheroma burden, its metabolic activity, and the individual's predisposition to vascular thrombosis play the pivotal role in CHD.

The concept of the "vulnerable plaque" has been the focus of the pathogenesis of CHD over the past decades. Vulnerable plaque morphologies include thin-cap fibroatheromas, large lipid pools, microcalcifications, and intraplaque haemorrhage.[1] The fibrous cap may rupture or erode in response to sheer stress or inflammation and may allow highly thrombogenic material to be exposed to the blood stream.[2] Based on these findings, it was thought that identifying such rupture/erosion-prone atherosclerotic plaques would enable prevention of myocardial infarction or cardiac death. Unfortunately, this hypothesis turned out to be flawed, as the positive predictive value of current imaging modalities to assess vulnerable plaque for the prediction of major adverse cardiac events (MACE) is too low for clinical relevance till now. PROSPECT study revealed plaque morphology was associated with increased hospitalization for angina but not strongly associated with myocardial infarction.[3] Given the large number of individuals with asymptomatic plaque disruption and those with obstructive coronary artery lesions, it is obvious that plaque rupture is a common phenomenon that only rarely leads to acute coronary events. Randomized clinical trials also did not find reduced risk of death or myocardial infarction with PCI of high-grade stenoses versus medical therapy in patients with stable CHD putting the "Plaque-focused" management strategy questionable.[4,5]

As the single "vulnerable plaque" hypothesis is in doubt, now the focus has been shifted to total atherosclerotic plaque burden, haemodynamics-associated biomechanical forces, local and systemic inflammation creating a prothrombotic milieu, and at last, an individual's response to all of these makes the concept of a cardiovascularly "vulnerable patient".

The concept of the coronary atherosclerotic disease burden is considered one of the main determinants for patient outcome. This concept is reinforced by the advancement of noninvasive CT coronary angiography (CTCA), which confirmed the close disease burden-adverse event risk relationship.[6] The SCOT-HEART trial revealed improved outcome in patients assigned to an anatomic versus traditional (stress testing-based) strategy attributed to the detection of nonobstructive coronary atherosclerosis and the initiation of directed prevention.[7]

In addition to plaque morphology, there is growing evidence that haemodynamic-associated biomechanical forces act in a synergistic manner to increase plaque vulnerability, promote destabilization, and produce clinical events.[8,9] The most extensively studied biomechanical forces are endothelial shear stress, plaque structural stress, and axial plaque stress.[7, 10, 11]

The coronary atherosclerotic disease activity is also an important determinant of outcome and a potential target for intervention. Inflammatory activity in fat tissue surrounding the coronary arteries has been linked to increased mortality independently of atherosclerotic disease severity and traditional risk factors.[12] Advancement in CTCA has enabled us to detect perivascular fat attenuation index (FAI), which correlates well with the degree of underlying inflammation, as well as plaque burden and disease status.[13] Inflammation plays a detrimental role in the every steps of pathogenesis of CHD. Inflammation: 1) promotes the atherosclerotic development and progression; 2) increases plaque instability and risk of rupture or erosion; and 3) facilitates a prothrombotic state.[14] Therefore, interventions targeting to decrease local and systematic inflammatory responses are associated with improved outcome.

The individual's response to atherosclerosis is a critical, modifiable factor for patient outcome. Given the widespread prevalence of atherosclerosis and evidence that plaque disruptions occur frequently without concomitant symptoms, it appears that a favourable haemostatic milieu

is necessary for permitting clinically relevant vascular thrombosis.[15] Numerous individual's factors, including age, genetics, diet, circadian changes, environmental conditions, medications, inflammatory conditions, and others, affect haemostasis.[16]

To conclude, our basic view of single, "vulnerable plaques" as a major target for intervention has evolved to a comprehensive concept of the "vulnerable patient." This evolution has guided us from treating coronary artery stenoses to controlling disease activity and modifying the risk of vascular thrombosis with a better outcome.

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