Requiem for the ‘vulnerable plaque’

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myocardial infarction (STEMI), the survivors may develop more heart failure in the long term.

We contend that we currently find ourselves amidst a shift in disease manifestations of atherosclerosis due to altered demographics, attendant changes in risk factor profiles, efforts to control tobacco abuse, and the increased prevalence of statin treatment. Myocardial infarction has ‘gone global’, not only affecting predominantly middle-aged Caucasian males in higher socioeconomic strata, and no longer associates mainly with cigarette smoking, hypertension, and high low-density lipoprotein (LDL). Women, non-Caucasians, younger individuals, and those with obesity, insulin resistance or frank diabetes, and high triglycerides and low high-density lipoprotein (HDL) represent an increasing proportion of our patients with ACS. We also now find ourselves in the midst of a transition in the presentation of ACS, with STEMI on the wane and non-ST segment elevation myocardial infarction (NSTEMI) rising.¹¹ While much of the increase in NSTEMI might result from the introduction of ever more sensitive troponin assays, shifting ACS previously classified as ‘unstable angina’ to NSTEMI, the decline in STEMI, and rise in NSTEMI began before the use of such assays. The temporal decline in STEMI incidence accompanies a substantial decline in stroke incidence and case fatality.¹²,¹³ These findings strengthen our proposition regarding a transition in the pathological mechanisms and presentations of the acute complications of atherosclerotic disease.

Concomitant with this trend from STEMI dominance towards NSTEMI, statin use has risen.¹⁴ While the temporal coincidence of a shift in ACS pathogenesis and the penetration of statin therapy do not prove causality, substantial evidence supports such a relationship. Animal studies show that lipid-lowering and/or statin treatment can reinforce the fibrous cap, decrease the lipid pool, and reduce inflammation.¹⁵ Human imaging studies buttress the notion that statin therapy reduces the lipid content of plaques and augments the proportion of the plaque composed of fibrous tissue, a characteristic associated with resistance to rupture.¹⁶,¹⁷ Studies on retrieved atherosclerotic plaque specimens in the Athero-Express collection have shown a time-dependent shift in the morphology of human atherosclerotic plaques over the last dozen years or so. Plaques obtained from more recent patients with symptomatic carotid artery disease reveal significantly more fibrous, non-inflammatory characteristics.¹⁸ Although obtaining plaque

Table I  Challenges to the ‘vulnerable plaque’ concept

- Thin-capped, lipid-rich atheromata are not solitary, rather often multiple, and affect several arterial beds in the same individual.
- Thin-capped, lipid-rich atheromata most often persist for years without causing a clinical event.
- The risk profile and demographics of acute coronary syndrome patients are shifting worldwide (global burden, younger patients, more women, more insulin resistance/diabetes, more hypertriglyceridaemia, and less low-density lipoprotein excess).
- Statin treatment and other preventive measures have begun to modify atherosclerotic disease.
- ST segment elevation myocardial infarction wanes as non-ST segment elevation myocardial infarction waxes.
- Plaque rupture declines as a cause of acute coronary syndromes while superficial erosion appears on the rise.
- Plaques underlying cerebrovascular events reveal more stable fibrous characteristics compared with 10 years ago.

Figure 1  Contrasts between superficial erosion and fibrous cap rupture as causes of arterial thrombosis. LDL, low-density lipoprotein.