Emerging biomarkers of cardiovascular risk and insulin resistance

Gordon A A Ferns
Institute for Science & Technology in Medicine, Faculty of Health, University of Keele, Staffordshire, ST4 7QB, UK
e-mail: g.a.a.ferns@istm.keele.ac.uk; Tel: +1782 554253; Fax: +1782 747319

Abstract

Immunocytochemical and morphological studies have elucidated the complex processes involved in atherogenesis. The notion of plaque instability has emerged from this work and has underscored the importance of inflammation in determining clinical complications, such as acute coronary syndrome, associated with atherosclerosis.

The use of risk 'engines' e.g. the Framingham coronary risk score, has facilitated the identification of individuals at high risk, but the constituent classical risk factors used in these algorithms do not adequately differentiate individuals at moderate risk. Because age is a major component of the equations used in these algorithms, they are not particularly useful in young people, and their applicability to non Caucasian populations has been questioned.

Biomarkers of early disease and plaque instability have therefore both been sought. Although some of these markers have been shown individually to be associated with a significant hazard ratio, no substantial improvement in discrimination has been demonstrated when they are incorporated into a risk engine. The latter has been assessed by receiver operator curve analysis, though this approach has been criticised. Other modalities, including imaging and functional assessments of vascular function are now being developed for clinical use.

Cells of the immune system have been detected within atherosclerotic lesions, and auto-antibodies directed against modified low density lipoprotein and heat shock proteins, including Hsp27 have been identified in the blood of individuals with atherosclerosis. We have found that serum Hsp27 antigen and antibody titres are associated with cardiovascular complications in individuals with glucose intolerance. Hsp27 antibody titres are also higher in patients with coronary and cerebrovascular disease.

In vitro, Hsp27 was found to reduce IL-10 by macrophages and also increased surface expression of the Toll-like receptor-4 (TLR-2) but not TLR-4, and the effect on IL-10 expression was partially blocked by TLR-2 but not TLR-4 blocking antibodies.