Platelet activation in the pathogenesis of obesity and vascular disease

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The pathogenesis of atherosclerotic disease is complex, and very topical, as clearly highlighted in a recent position paper of the European Society of Cardiology (ESC) Working Group on Atherosclerosis and Vascular Biology in this journal, which deals with atherosclerotic plaques and their ‘stabilisation’ per se (1).

A number of associations have been observed between lipid abnormalities, markers of metabolic syndrome and platelet activation (1–5). In recent years, many studies have explored associations for platelet activation markers to gain insights on the pathogenesis of obesity and atherosclerotic disease (6–13).

In this issue of Thrombosis and Haemostasis, Csongrádi et al. report on a large cross-sectional cohort study that explored relationships for platelet activation markers in obese subjects, including those with and without common co-morbidities for atherosclerotic disease (14). Key findings of their study were that platelet and plasma P-selectin levels, and the plasma levels of platelet microparticles, were associated with carotid intimal medial thickness and a variety of other vascular risk factors, including fasting plasma glucose, insulin levels and triglycerides (14). These observations imply that the extent of atherosclerotic disease, and the metabolic derangements associated with obesity and atherosclerotic disease, influence the generation of platelet microparticles. This possibility is supported by a recent study that showed weight loss-induced improvements in insulin resistance, among women with obesity, reduced markers of platelet activation (6).

While association studies cannot determine causation, they are important to developing new hypotheses on the pathogenesis of atherosclerotic disease. Platelet microparticles have attracted much interest both experimentally and clinically (15–19). Indeed, given their significant procoagulant activity (18, 19), their elevation in pathogenic states could contribute to the progression of vascular disease and acute thrombotic events.

Nonetheless, uncertainties remain about whether observed associations between elevated levels of platelet-derived microparticles with prothrombotic, metabolic and inflammatory parameters are correlative or causative, and how much platelet microparticle generation, and other aspects of platelet activation, contribute to the pathogenesis of atherosclerotic disease in obese individuals.

The "independent" associations that Csongrádi et al. found between platelet-derived microparticle levels with body mass index, and between soluble P-selectin and fibrinogen, and platelet P-selectin and both carotid intimal medial thickness and PAI-1 (14) provide further evidence that platelet activation is influenced by the complex metabolic and inflammatory parameters that participate in the pathogenesis of atherosclerotic disease.

Despite these advances, uncertainties still remain about whether measuring platelet activation markers has a role in diagnostic or therapeutic decision making for obese and non-obese individuals who have or do not have evidence of atherosclerotic disease. This still remains an exciting and expanding field of research.

Conflict of interest
None declared.

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References
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