Letter to the Editor

Arterial microvessels – an early or late sign of atherosclerosis?

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on behalf of the
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Sir,

Hypoxia is a strong stimulus for the induction of angiogenesis. In an elegant series of experiments including in vivo labeling of hypoxic tissues, Sluimer et al (1) have demonstrated that hypoxia in advanced atherosclerotic plaques colocalized with the expression of hypoxia induced transcription factors (HIF1α, HIF2α), growth factors (VEGF) and glucose transporters (GLUT1, GLUT3) and all these microenvironmental changes were accompanied by neovascularization: the number of microvessels per mm² intima area was significantly higher in advanced than in early atherosclerotic lesions. We have previously shown that two distinctive angiogenic events occur during atherosclerosis in humans (2): in addition to ectopic plaque neovascularization we found a hyperplastic network of vasa vasorum in the arterial adventitia in early lesions of patients with active, symptomatic disease. However, the arterial adventitia is a physiologically vascularized compartment of the arterial wall and is not expected to harbor a hypoxic microenvironment. Studies based on swine models of hypercholesterolemia showed that adventitial neovascularization is not exclusively related to plaque formation; those animals presented with the highest vasa vasorum count but without any arterial wall thickening (3). The authors suggested that the main stimulus to vessel wall neovascularization might not be local hypoxia but could rather be related to the increased oxidative stress. However, Sluimer et al (1) showed that metabolically active macrophages may contribute to tissue hypoxia by oxygen exhaustion (4) and this mechanism could also contribute to hyperplasia of vasa vasorum in the arterial adventitia. Since contrast enhanced transcutaneous ultrasound is a bedside procedure that can be used to visualize both plaque (5) and adventitial microvessels (6), the two compartments
might be accessible for the diagnosis of early and late stages of preclinical atherosclerosis. A common pathogenic mechanism might eventually be targeted therapeutically.

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References


