Thrombus formation followed by disruption of atherosclerotic plaques leads to major clinical complications such as acute coronary syndromes and ischemic stroke. Although the process of thrombus formation is regulated by many factors, such as vascular wall thrombogenicity, local hemorheology, and the activity of blood coagulation and the fibrinolysis system, the thrombogenicity of atherosclerotic plaque plays the most important role in the progression of atherothrombosis after plaque disruption. Tissue factor (TF), also known as thromboplastin, is the key initiator of the coagulation cascade. Under normal physiological conditions, TF is expressed only at extravascular sites and perivascularly in the adventitial layer of blood vessels. Following arterial plaque disruption, various factors, such as cytokines, growth factors, and TF-containing microparticles, are released into the blood, leading to rapid initiation of coagulation, platelet aggregation, and, ultimately, thrombus formation with vessel occlusion.

**Figure.** Positron emission tomography (PET) imaging using [18F]-fluorodeoxyglucose ([18F]-FDG) for the detection of macrophage-derived inflammation, tissue factor (TF) expression, and thrombus formation in atherosclerotic plaque. [18F]-FDG accumulation in the vessel wall reflects the severity of atherosclerotic plaque inflammation, and [18F]-FDG uptake closely correlates with plaque macrophage content. In the inflammatory environment of atherosclerotic plaques, TF is present at high levels, especially in macrophages/foam cells of the necrotic core. NF-κB activation induced by the plaque inflammation accelerates TF expression in the atherosclerotic plaques, whereas inhibition of NF-κB significantly reduces TF expression in cultured plaque tissues. On plaque rupture, highly procoagulant material, including TF-containing microparticles, is released into the blood, leading to rapid initiation of coagulation, platelet aggregation, and, ultimately, thrombus formation with vessel occlusion.

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and biogenic amines, can induce TF expression and activity in endothelial cells, vascular smooth muscle cells (SMCs), and monocytes/macrophages in the atherosclerotic plaque, leading to thrombus formation. Based on these observations, one can conclude that TF expression is probably a crucial determinant of thrombogenicity in atherosclerotic plaques.

The most important clinical implication of the current study is whether PET imaging using \(^{18}\)F-FDG is useful clinically, especially for the detection of vulnerable coronary, carotid and cerebral atherosclerotic plaques that can cause thrombus formation. This issue needs to be elucidated because thrombi induced mechanically by a balloon catheter are not identical to those that follow spontaneous plaque rupture in human atherothrombosis. Some clinical studies in a retrospective series of patients with cancer who underwent PET scanning have suggested that \(^{18}\)F-FDG PET can identify patients at risk for future cardiovascular events. Prospective clinical studies are needed to confirm the predictive value of \(^{18}\)F-FDG PET for cardiovascular events in patients with non-cardiovascular diseases, and to assess the effects of medical treatment after cardiovascular events, such as acute coronary syndromes or ischemic stroke. Hopefully, we will be able to use \(^{18}\)F-FDG PET to assess the thrombotic risk of atherosclerotic plaques in patients with cardiovascular diseases.

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