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REVIEW ARTICLE

The vulnerable plaque: Current concepts and future perspectives on coronary morphology, composition and wall stress imaging

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KEYWORDS
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Abstract Cardiovascular imaging plays an important role in the identification and characterization of the vulnerable plaque. A major goal is the ability to identify individuals at risk of plaque rupture and developing an acute coronary syndrome. Early recognition of rupture-prone atherosclerotic plaques may lead to the development of pharmacologic and interventional strategies to reduce acute coronary events.

We review state-of-the-art cardiovascular imaging for identification of the vulnerable plaque. There is ample evidence of a close relationship between plaque morphology and patient outcome, but molecular imaging can add significant information on tissue characterization, inflammation and subclinical thrombosis. Additionally, identifying arterial wall exposed to high shear stress may further identify rupture-prone arterial segments. These new modalities may help reduce the individual, social and economic burden of cardiovascular disease.

PALAVRAS-CHAVE
Aterosclerose;
Placa vulnerável;
Imagiologia molecular;
Síndromes coronárias agudas

A placa vulnerável: conceitos atuais e perspetivas futuras da imagiologia coronária

Resumo A imagiologia cardiovascular tem desempenhado um papel importante na identificação e caracterização da placa vulnerável. Em particular, a possibilidade de identificar os indivíduos em risco de desenvolverem rutura de placa aterosclerótica e apresentarem síndrome coronária aguda é um objetivo importante. A deteção precoce de placas ateroscleróticas predispostas a sofrer rutura pode conduzir ao desenvolvimento de estratégias de intervenção farmacológica para reduzir eventos coronários agudos.

Procuramos rever o estado da arte da imagiologia cardiovascular na identificação da placa vulnerável. A evidência apoia a existência de uma forte relação entre a morfologia da placa aterosclerótica e a evolução clínica do doente, mas a imagiologia molecular pode adicionar caracterização tecidular e avaliação da inflamação e trombose. Também a identificação de

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locais na parede arterial expostos a elevada tensão de cisalhamento pode ajudar a identificar os segmentos arteriais mais predispostos a sofrer rutura. Estas novas modalidades de imagiologia podem contribuir para reduzir a carga individual, social e económica da doença cardiovascular.

Introduction

Cardiovascular disease is the leading cause of death in the United States, Europe and most developed countries, with coronary artery disease being one of the main culprits. Atherosclerosis is recognized as the pathologic basis of this clinical entity but often remains clinically silent until narrowing of the arterial lumen becomes critical or an acute event is triggered by plaque erosion or rupture[1]; up to 60% of acute myocardial infarctions (MI) and sudden cardiac deaths occur as the first manifestation of disease.[2] Accordingly, new screening methods are needed to identify patients at greater risk. The role of various imaging modalities in this setting has been tested over the years without definitive answers being reached. However, new techniques are emerging that may increase their diagnostic yield.

Predicting individual risk for developing acute coronary syndrome (ACS) in asymptomatic patients and, ultimately, predicting the risk associated with any single atherosclerotic plaque is a major goal in cardiovascular imaging. In particular, identification of atherosclerotic plaques prone to rupture may lead to the development of pharmacologic and interventional strategies to reduce acute coronary events.

In this review we focus on the current and future perspectives of cardiovascular imaging in the prevention and timely diagnosis of ACS, by identifying the vulnerable plaque and culprit lesions. These new modalities may help to further decrease ACS mortality and reduce the individual, social and economic burden of cardiovascular disease.

Pathophysiology of the vulnerable coronary plaque and targets for imaging

The components of atherosclerotic plaques include extracellular matrix (collagen and proteoglycans), cholesterol and phospholipids, inflammatory cells (macrophages and lymphocytes) and smooth muscle cells.[3–6] Atherosclerosis primarily affects the intima but changes also occur in the media and adventitia.[7] However, there is significant heterogeneity among atherosclerotic lesions depending on the relative quantities of the different plaque components.

Inflammation plays a major role in both initiation and progression of atherosclerotic plaque. Atherosclerosis appears to be a specialized inflammatory response in which leukocyte recruitment occurs in lesion-prone areas of the arterial tree, subsequently leading to subendothelial accumulation of monocytes and lymphocytes. One of the earliest detectable cellular responses in atherosclerosis is adherence of leukocytes to the endothelium at particular anatomic sites of the artery wall.[8–10] The recruited monocytes then differentiate into macrophages that accumulate lipids using scavenger receptors, ultimately becoming foam cells. These changes at the cellular level lead to the development of the fatty streak, an early precursor of atheroma.[4]

Progression of the atherosclerotic lesion occurs when foam cells and extracellular lipid droplets accumulate to form a core region, with a covering of smooth muscle cells and collagenous matrix, the fibrous cap. At this stage, immune cells including T cells, macrophages and mast cells continuously infiltrate the lesion.[4,11,12] Many of these cells are activated and produce inflammatory cytokines that can promote plaque instability,[13,14] a characteristic of the vulnerable plaque that can lead to thrombosis and to clinical events: plaque rupture is a major cause of thrombosis.[15,16] Atherosclerotic plaques that are vulnerable to rupture have a dense inflammatory infiltrate[17] and a thin fibrous cap.[18] When plaque rupture occurs, the thrombus usually progresses to the deeper arterial layers and may lead to rapid growth of the plaque, disrupting normal blood flow.

Another mechanism responsible for coronary thrombosis is plaque erosion.[19] Eroded plaques are rich in smooth muscle cells and proteoglycans.[19] When erosion occurs, thrombus adheres to the surface of the plaque, obstructing the lumen (Figure 1).

The morphologic characteristics of atherosclerotic plaques can be targeted by invasive and non-invasive imaging modalities such as angiography, intravascular

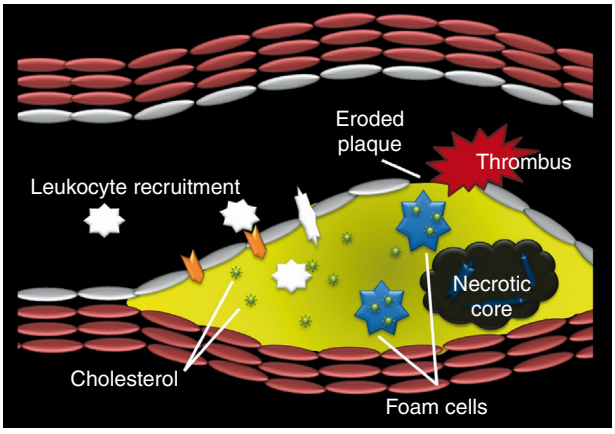

Figure 1 Schematic figure illustrating components of an eroded coronary atherosclerotic plaque with subocclusive thrombus. This type of vulnerable plaque is characterized by a thin fibrous cap, extensive leukocyte infiltration, paucity of smooth muscle cells and a large lipid core.