Nuove acquisizioni sull'aterosclerosi: placca vulnerabile

Marina Camera

Plaque rupture vs plaque erosion

Rupture of Fibrous Cap 75-80%  Libby & Thouroux, Circulation, 2005
Superficial Erosion 20-25%

Atherothrombosis

A generalized progressive disease of large- and mid-size arteries that affects multiple vascular beds, including cerebral, coronary, and peripheral arteries.

Muller JE et al, Circulation 1989

Vulnerable Plaque

…Plaque vulnerability was defined as the susceptibility of a plaque to rupture, thus causing a clinical cardiovascular event.
Inflammation in the vessel wall is now considered to play an essential role in the *initiation, progression and final steps* of atherosclerosis, namely *plaque destabilization* and eventually plaque rupture.
Endothelial Dysfunction in Atherogenesis

The normal endothelium does not in general support binding of white blood cells

Vascular endothelium modification in atherosclerosis

Plaque formation 1 — Fatty streak
Plaque formation
2 — Fibrous cap

Activated muscle cell
Activated muscle cell

Plaque formation
3 — Lipid core

Lipid accumulation
Cell death

Vulnerable plaque
Key role of the macrophage in the degradation of the fibrous cap

Degradation of the fibrous cap
Thrombus formation

Tissue Factor expression within the plaque

Tissue Factor (TF) is one of the major determinants of the activation of coagulation cascade at site of atherosclerotic plaque rupture.

Several data indicate a positive correlation between atherosclerotic plaque thrombogenicity and Tissue Factor expression within the plaque.

V. Toschi et al, Circulation 1997

Atherothrombosis: a Immunoinflammatory, Fibroproliferative and Progressive Process

Most Myocardial Infarctions Are Caused by Low-Grade Stenoses

Vulnerable Plaque

high-risk plaque is described as thin-cap fibroatheroma (TCFA)
- lipid-rich atheromatous core
- thin fibrous cap (<65µm) with macrophage and lymphocyte infiltration (inflammation)
- decreased smooth muscle cell content
- extensive positive remodeling of the arterial wall.

Consensus of the First International Vulnerable Plaque Meeting held in Santorini in 2003.
Schaar JA et al, Eur Heart J 2004

...The primary purpose of this natural-history study was to provide prospective in vivo confirmation of the hypothesis that acute coronary syndromes arise from atheromas with certain histopathological characteristics, and that these characteristics are not necessarily dependent on the degree of angiographic stenosis at that site.

Despite continuous improvements in the catheter-based treatment of coronary artery disease (CAD), our field continues to struggle with the concept that percutaneous intervention may not prevent myocardial infarction or death in the stable patient. The main reason behind this controversial but rather accepted statement is that life-threatening coronary events arise most frequently from lesions that escape proper diagnosis and treatment. As a result, our efforts in clinical practice are almost totally consumed by the treatment of lesions that have limited impact on the natural history of atherothrombosis and CAD. Thus, it is imperative to reflect on this paradox, and do something about it....
Thrombus formation
Platelet adhesion and activation

Platelets are multifunctional cells that use elaborate molecular pathways to regulate a variety of thrombotic and inflammatory responses...

Factors released by activated human platelets

New concepts in Atherothrombosis...

Platelet contribution to vessel inflammation leading to atherogenesis and eventually to plaque rupture and thrombosis

Platelets provide the inflammatory basis for plaque formation before physically occluding the vessel by thrombosis upon plaque rupture.

A Critical Role of Platelet Adhesion in the Initiation of Atherosclerotic Lesion Formation

Seiffen Maasberg,1,4 Korbinian Brand,2 Sabine Grünert,1 Sharon Page,2 Elke Müller,1 Iris Müller,1 Wolfgang Bergmeister,3 Thomas Richter,4 Michael Lorenz,1 Rita Koch-Kosaral1 Bernhard Niewietz,1 and Meinrad Gaspoz1,4

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Circulating activated platelets exacerbate atherosclerosis in mice deficient in apolipoprotein E

Yvonne Hoos, Andrew Schmitz, Julian Barchet, Filipa Leao, Mathew Craig, Christin Magnus, and Eman Leit

Nature Medicine • Volume 5 • Number 1 • January 2009

Localized reduction of atherosclerosis in von Willebrand factor-deficient mice

Nicola Motha, Patrick Ashe, Cristina Della, Maria Eremioupolou, and Derma D. Vagner

(Blood. 2001 Sep 1;98(5):1624-1632)

Platelets induce differentiation of human CD34+ progenitor cells into foam cells and endothelial cells

Romi Beath,1 Harald Langer,3 Peter Seiler,1 Konstantinos Sofianos,1 Andrew E. May,3 Pankaj Goyal,1 Boris Benders,2 Tanja Schulzele,1 Tobias Greuel,1 Dept. of Haematology, Children’s Medical Center, University of Heidelberg,linikum, Germany 1Dept. of Internal Medicine, Children’s Medical Center, University of Heidelberg,linikum, Germany 3Dept. of Haematology, Children’s Medical Center, University of Heidelberg,linikum, Germany

the IASB Journal • 11 Express Full-Length Article
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...our results indicate that circulating activated platelets and platelet-leukocyte/monocyte aggregates promote formation of atherosclerotic lesions.
The platelet transcriptome

Affymetrix HG-U95Av2 probe set (about 12,600 genes) identified the expression of 2147 (range, 13%-17%) platelet-expressed transcripts, less than half the number (30%-50%) expected for nucleated cells.

Of these, approximately 22% collectively are involved in metabolism and receptor/signaling, with a clear overrepresentation of genes with unassigned function (32%).

De Novo Synthesis of Cyclooxygenase-1 Counteracts the Suppression of Platelet Thromboxane Biosynthesis by Aspirin
V. Evangelista et al.
Circ Res. 2006; 593-595

Activities of Platelets at the vascular interface

Platelets are multifunctional cells that use elaborate molecular pathways to regulate a variety of thrombotic and inflammatory responses
Platelets in atherothrombosis

The contribution of platelets in atherothrombosis is no more linked only to the last step of the process (thrombus formation upon plaque rupture).

Platelets play key roles since the early stage of the disease, when they contribute to endothelial and monocyte activation, leading to plaque progression.