

Davos 2015

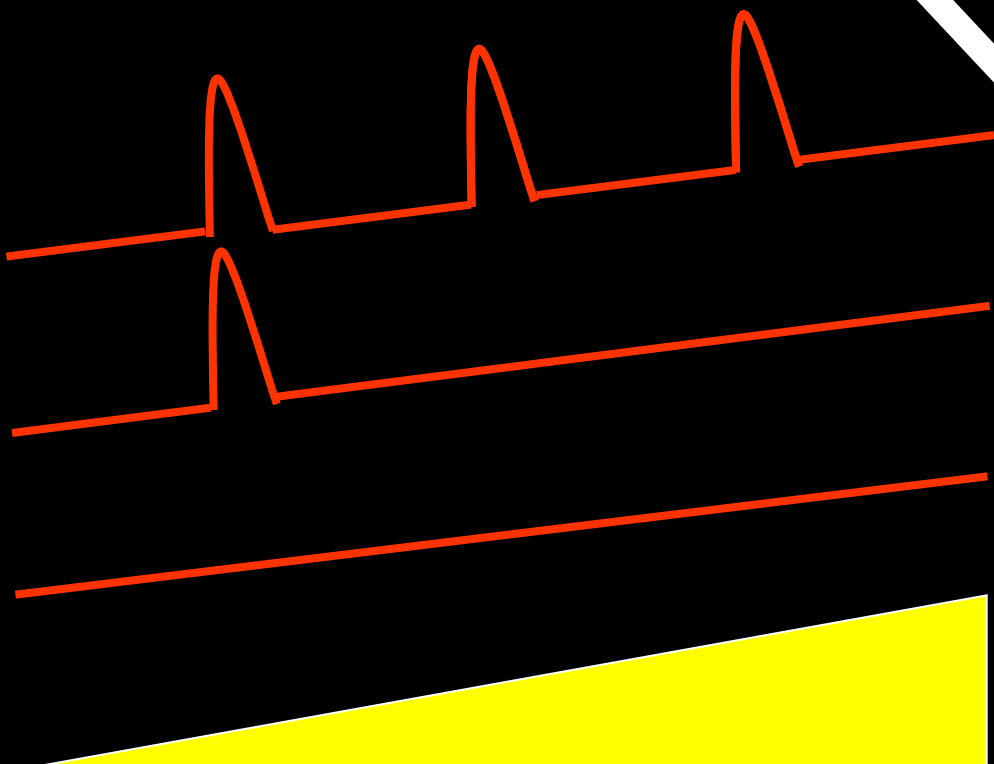
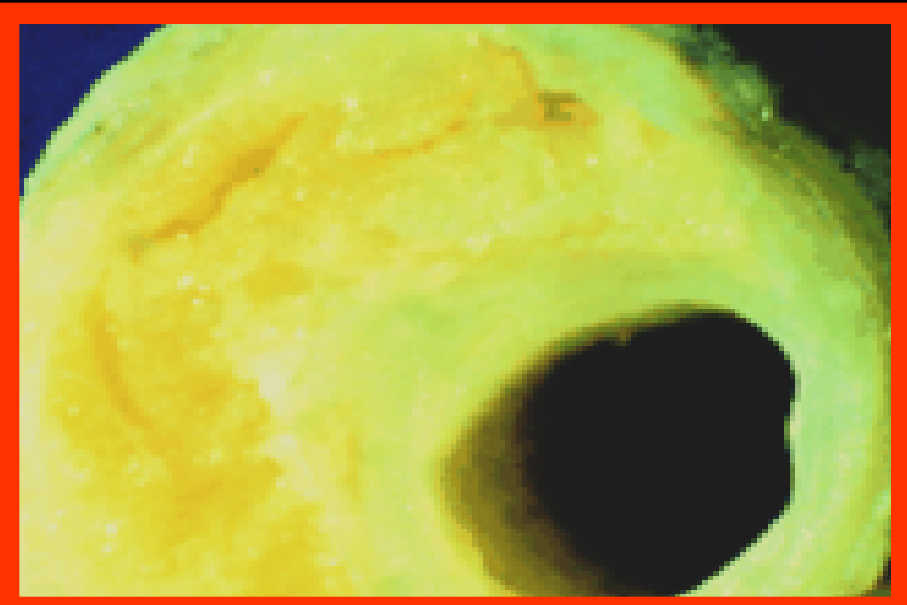
Mechanisms of ACS: the clinical perspective

Filippo Crea
Institute of Cardiology
Catholic University of the Sacred Heart
Rome, Italy



No conflict of interest to declare

Why?



C-reactive protein

Berk et al, AJC 1990

Liuzzo et al, NEJM 1994

Neutrophils

Finerman et al, JACC 1990

Biassucci et al, JACC 1994

Monocytes

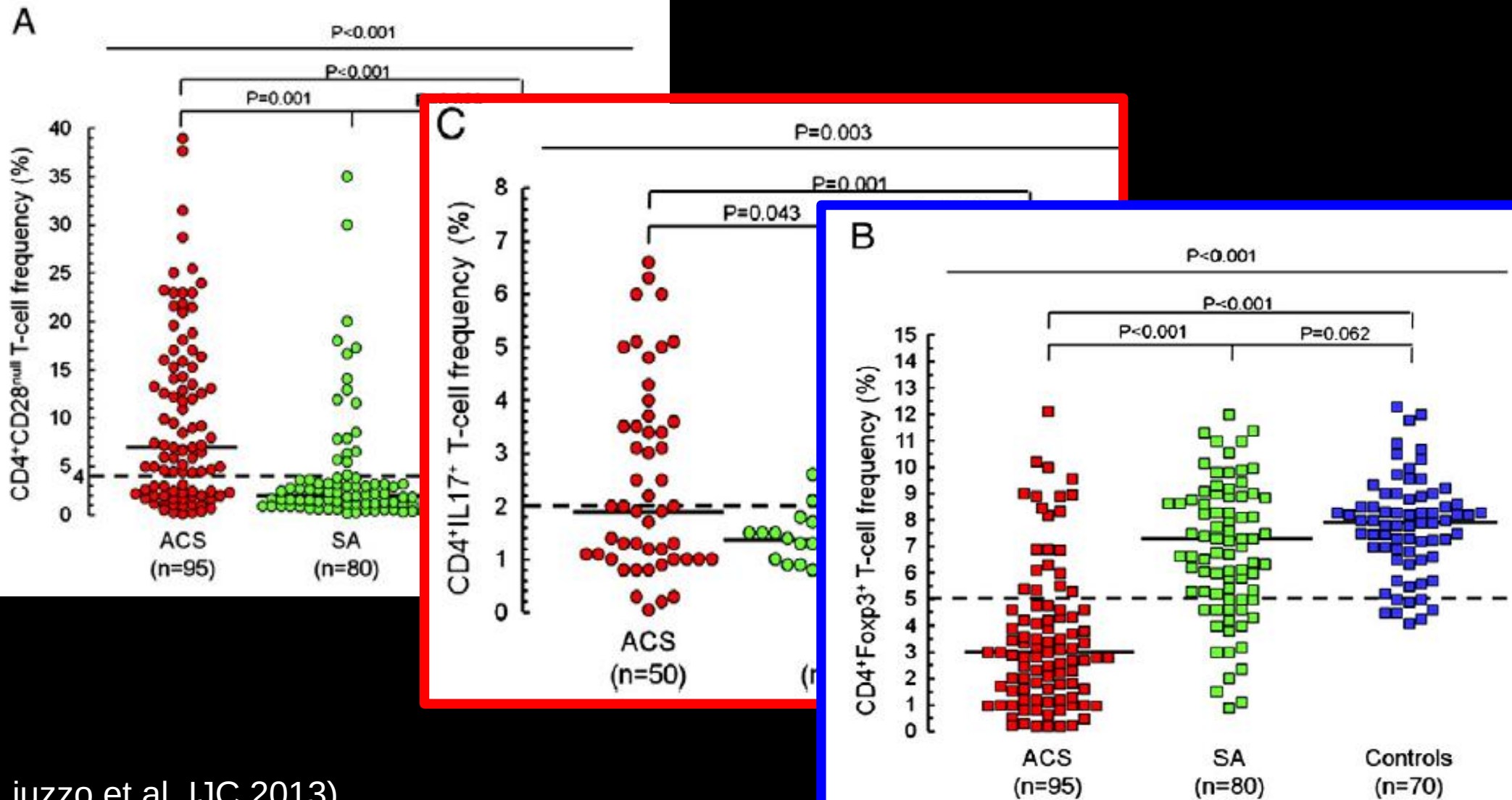
Mazzone et al, Circulation 1993

Lymphocytes

Serneri et al, Circulation 1992



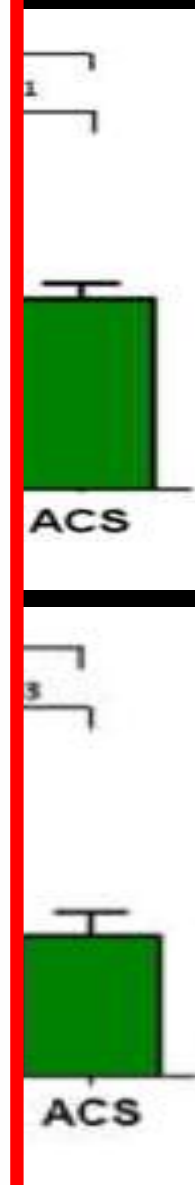
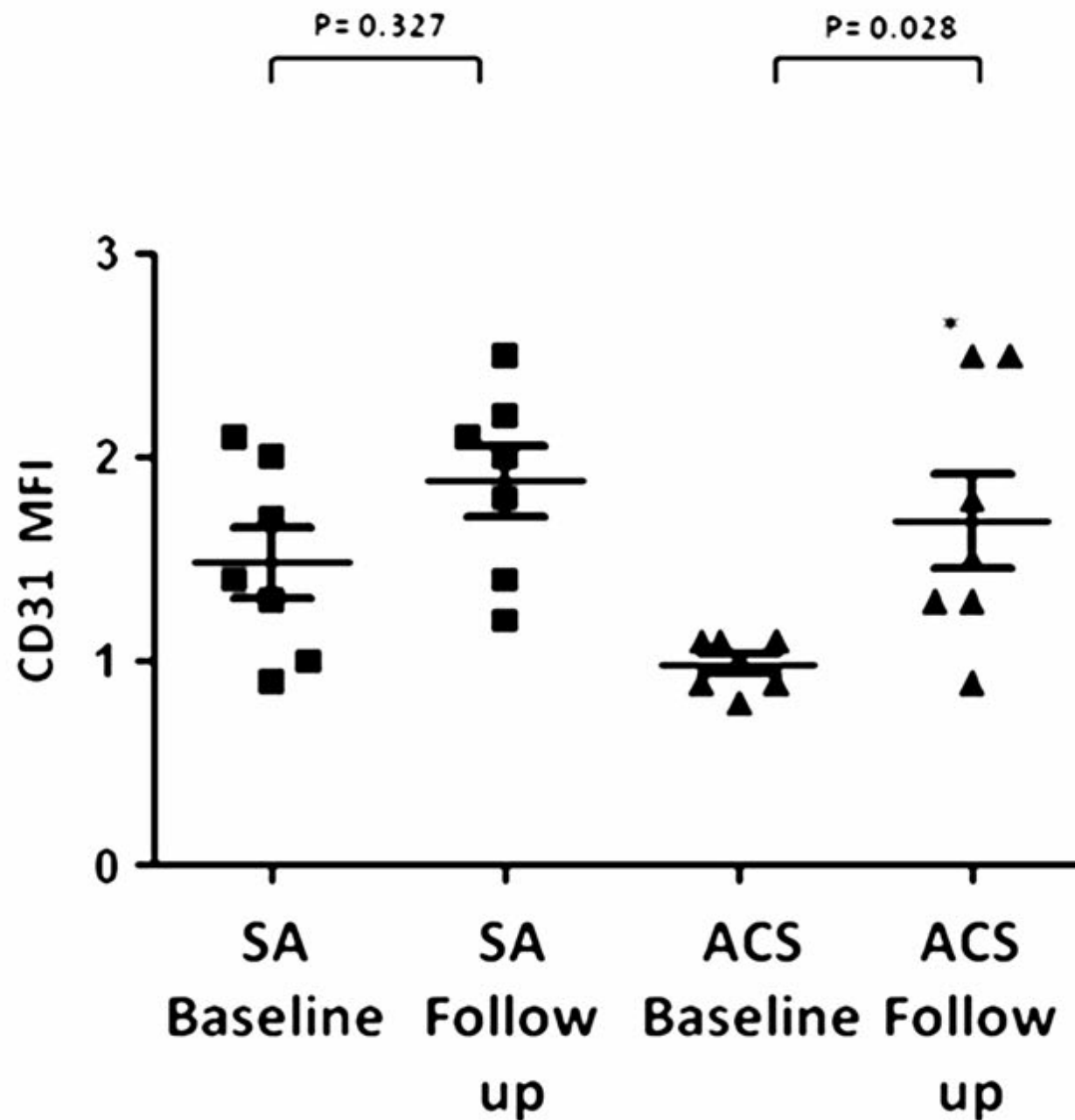
Dysregulation of T cell subsets in ACS



CD3

tion

CD4⁺ CD28^{null} T Cells

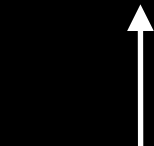


iol 2014)

Auto-antigens

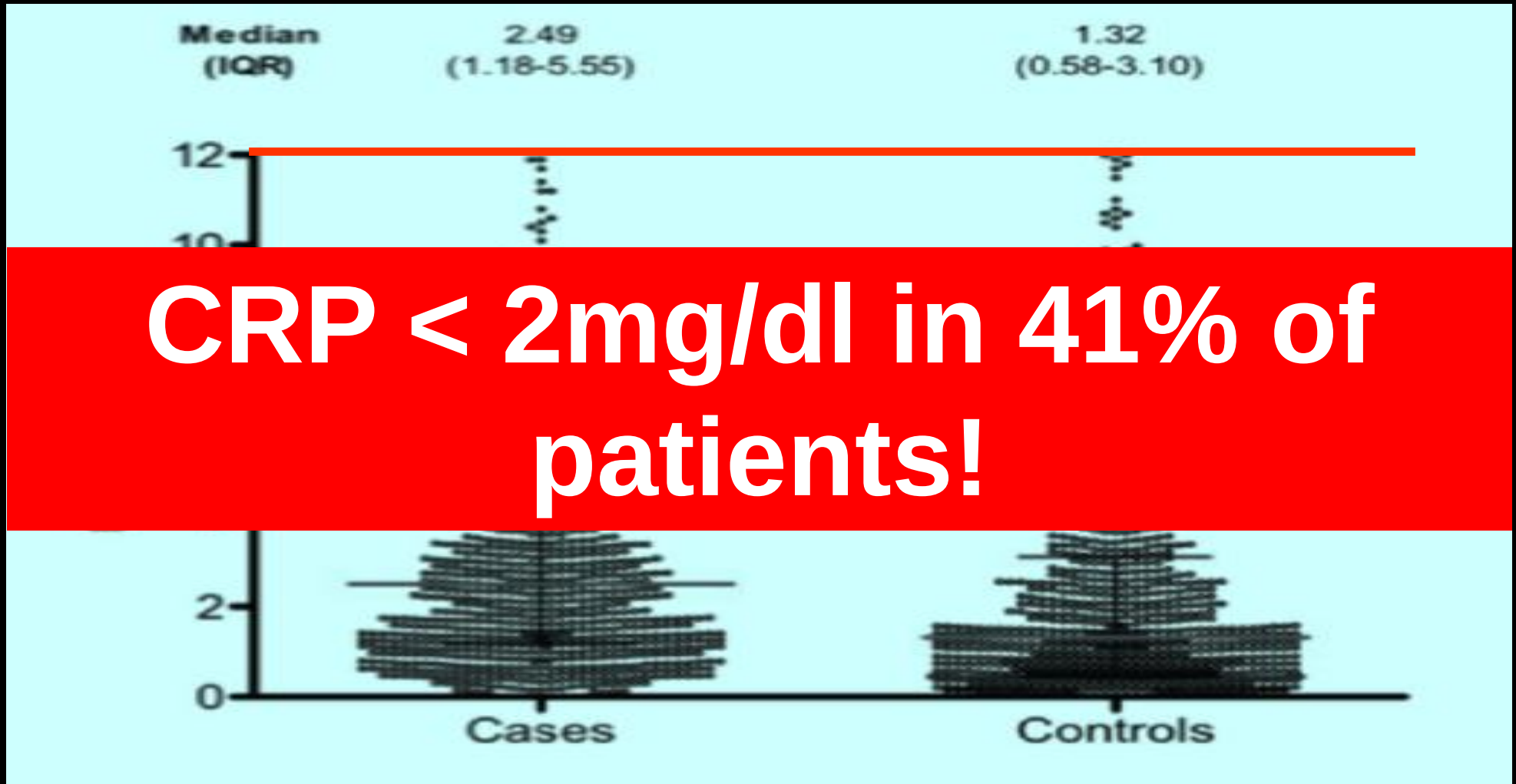


**Obstructive ATS
with adaptive
immunity
activation**

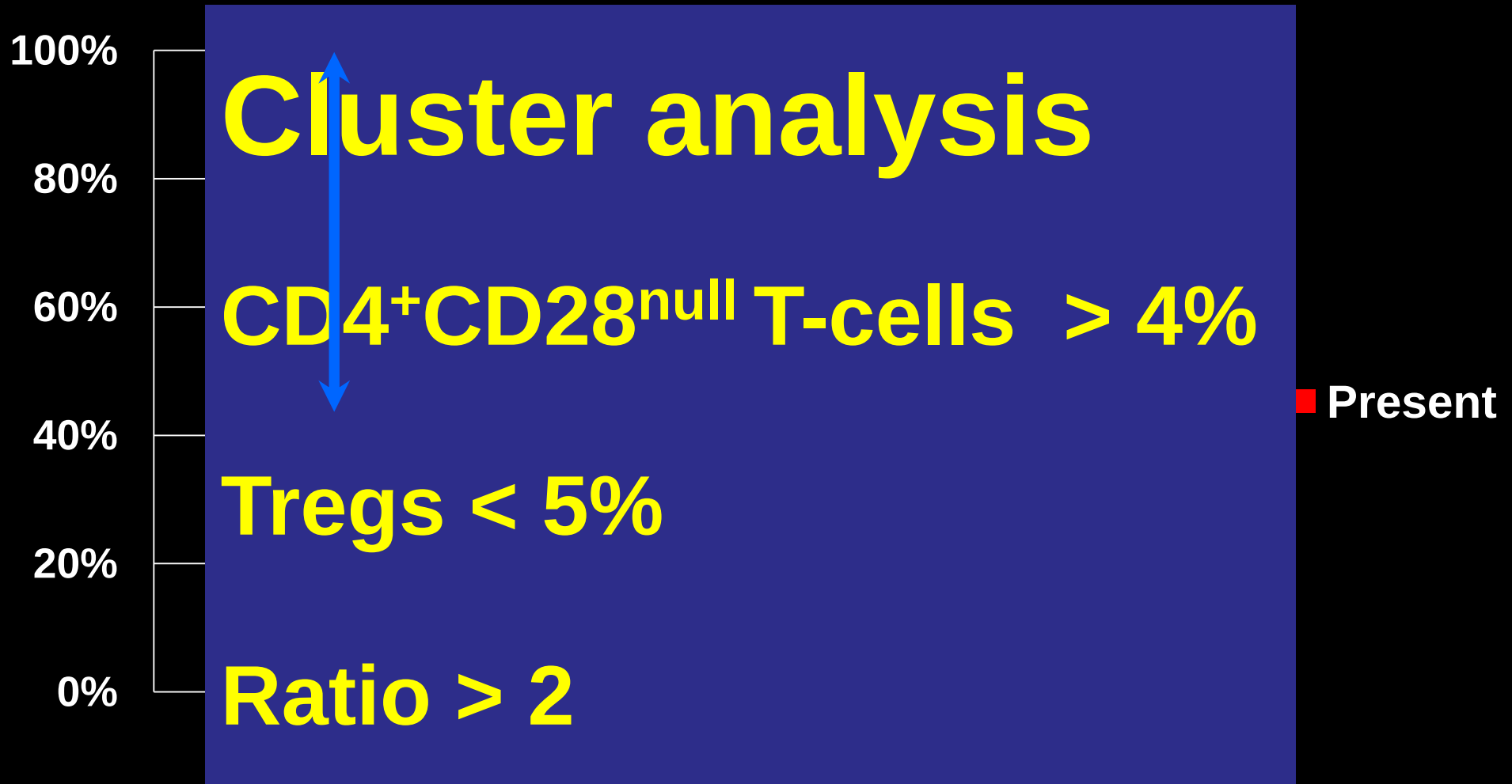


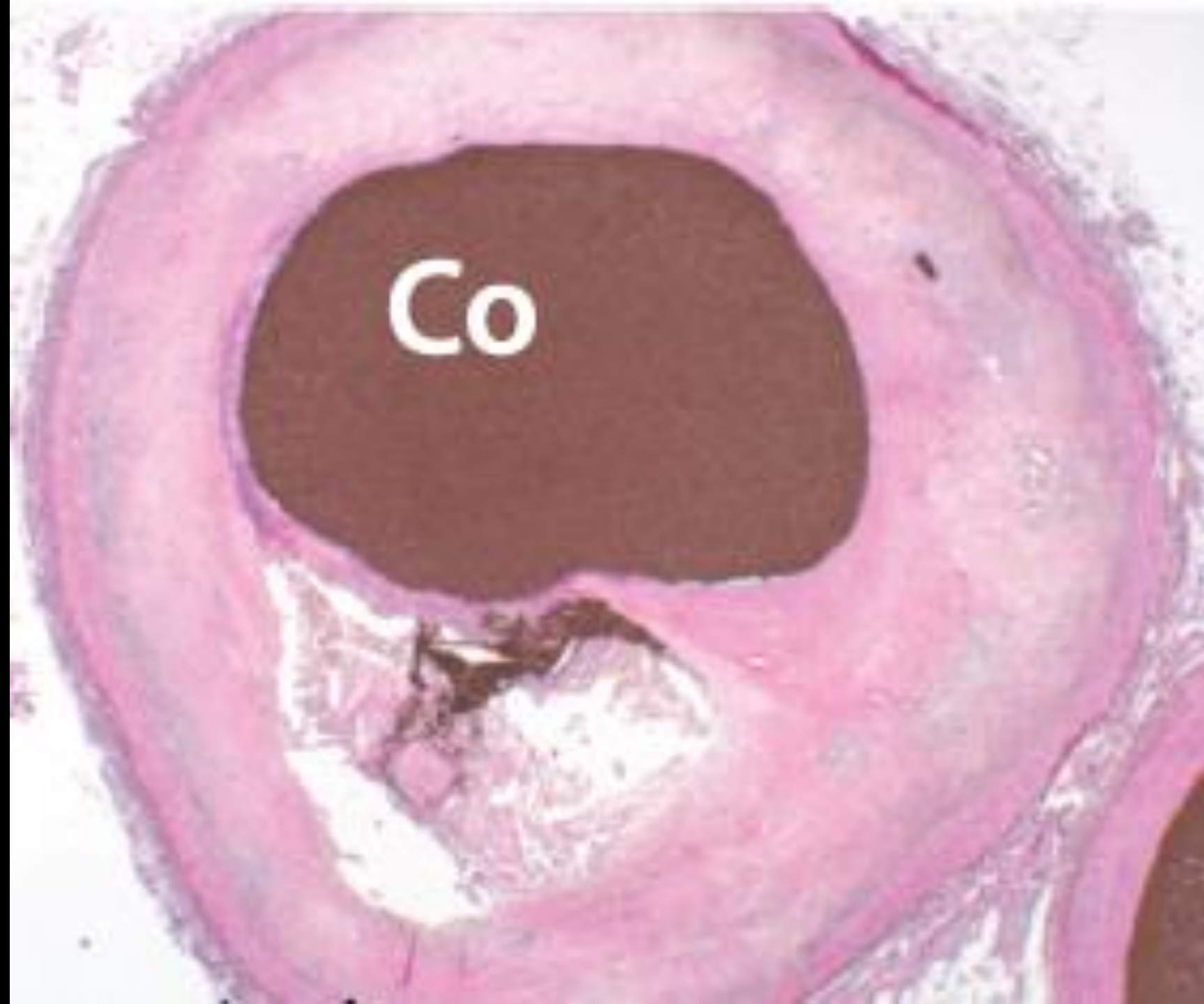
**Infectious
agents**

Association between inflammation and CV events



Cluster analysis according to T cell subsets and their ratio





Mechanical triggers of plaque fissure: stress

80

Mechanisms of stress-induced ACS associated to plaque fissure

- Hypertension
- Constriction of epicardial coronary arteries
- Increase of coronary microvascular resistance
- Platelet activation and hypercoagulability

Stress

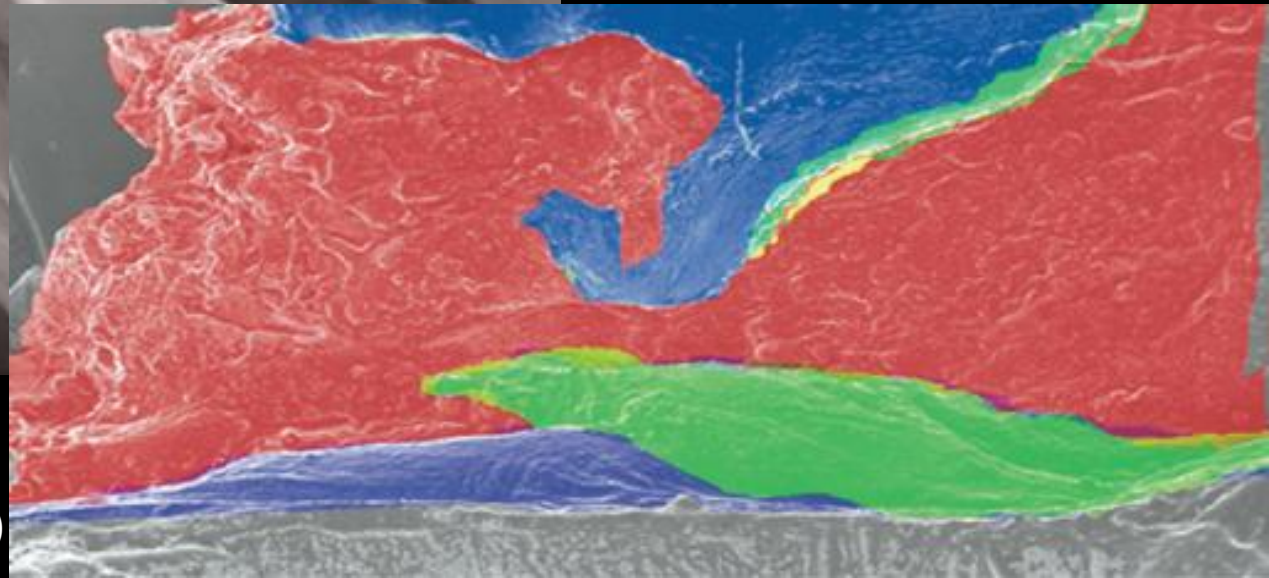
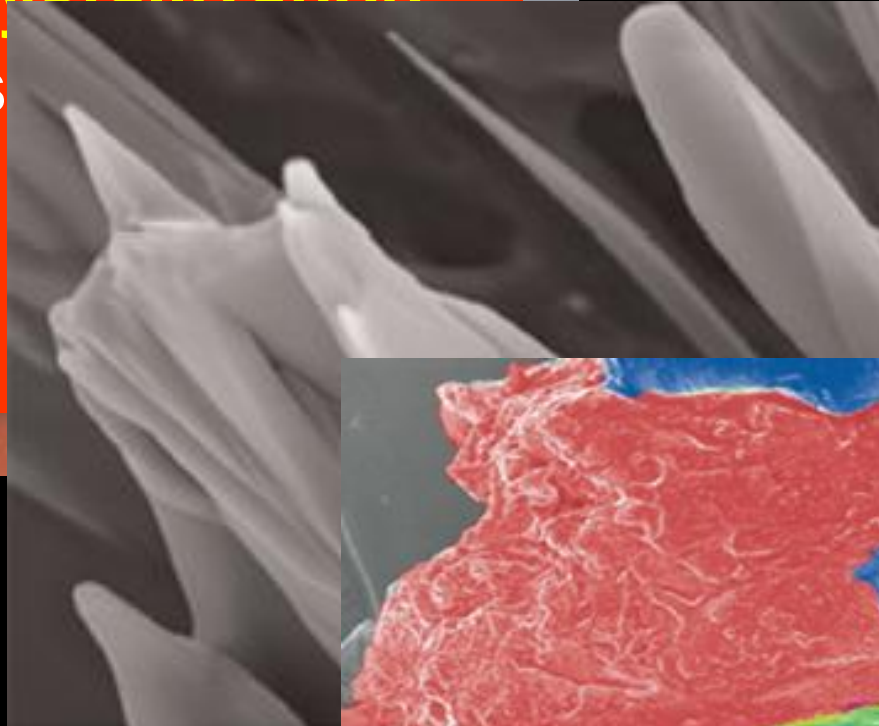
Rest

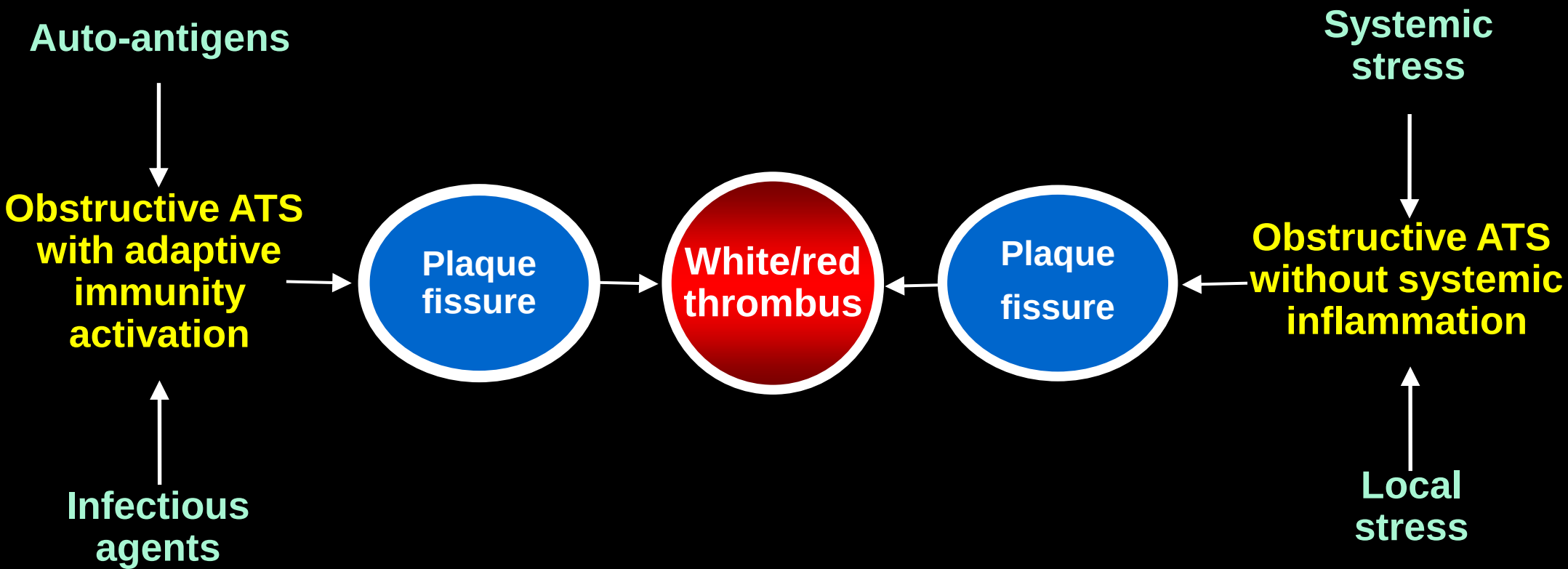
(Burke et al, JAMA 1999)

Mechanical triggers of plaque fissure: cholesterol crystals

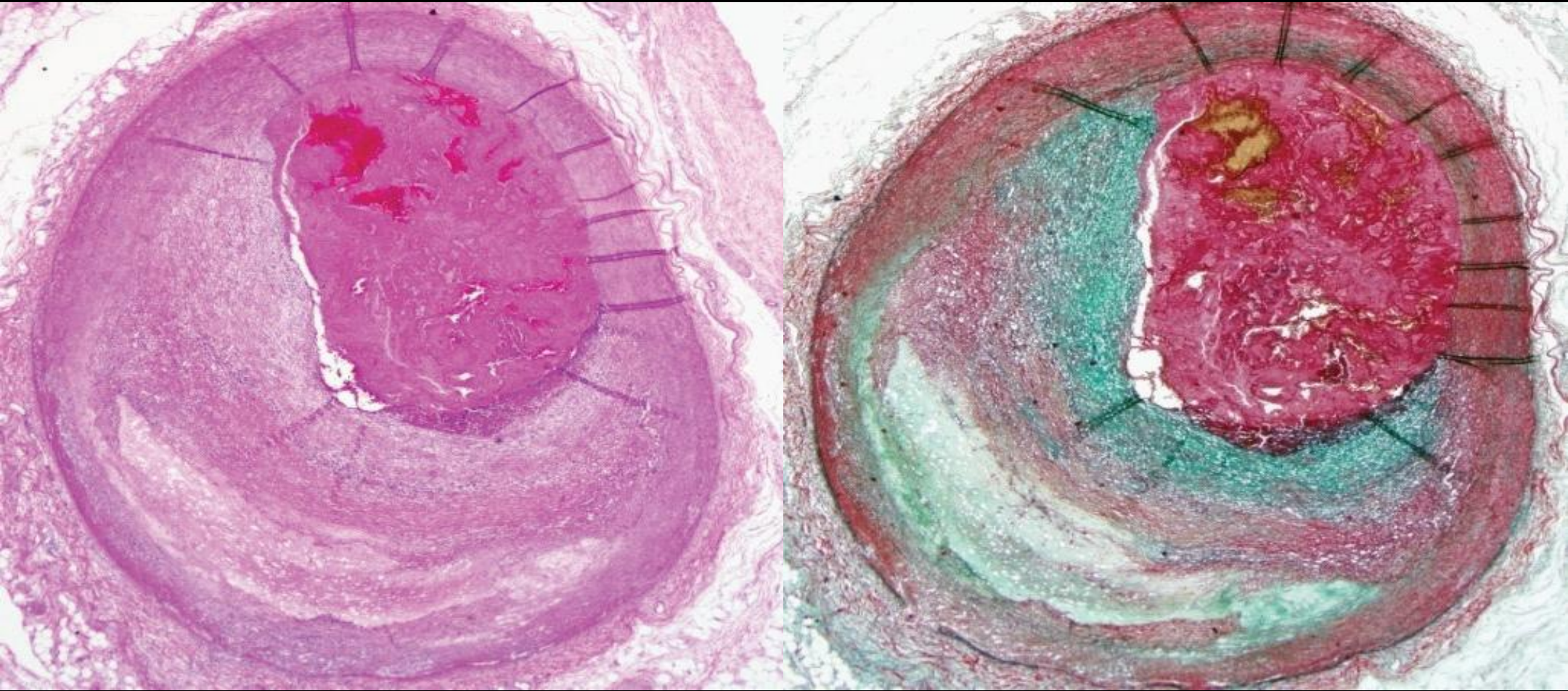
Factors affecting cholesterol crystallization

- Cholesterol saturation
- Hydration
- Temperature
- pH



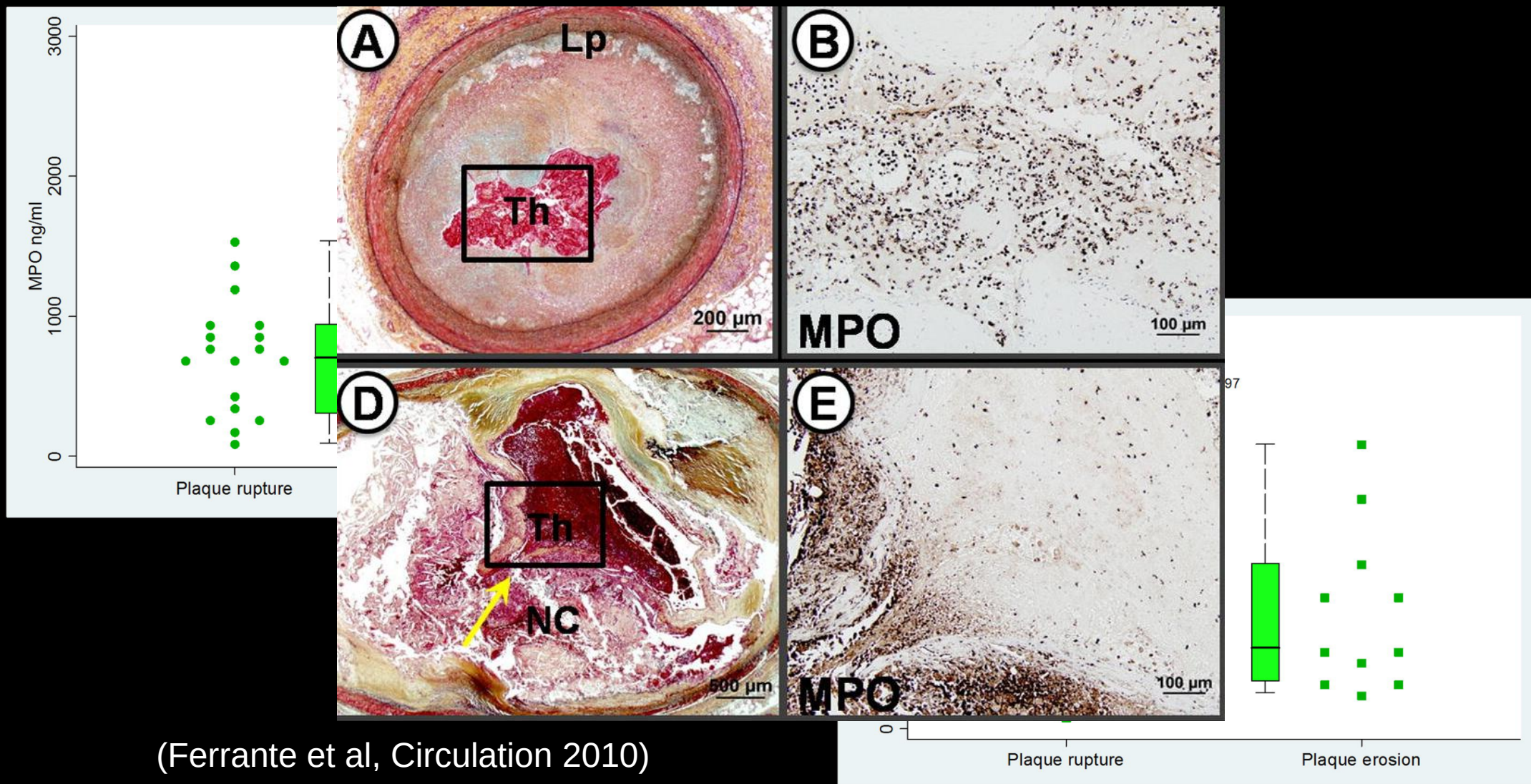


Plaque erosion

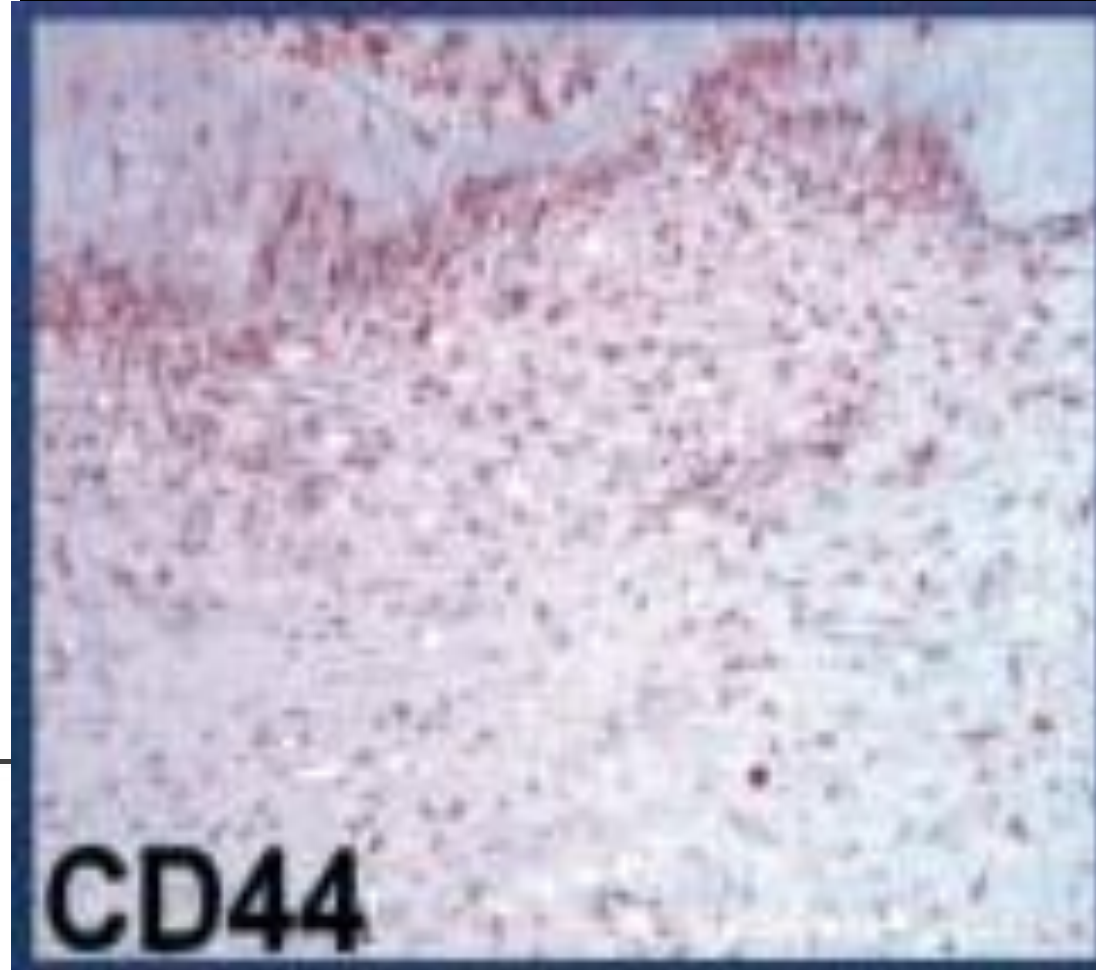
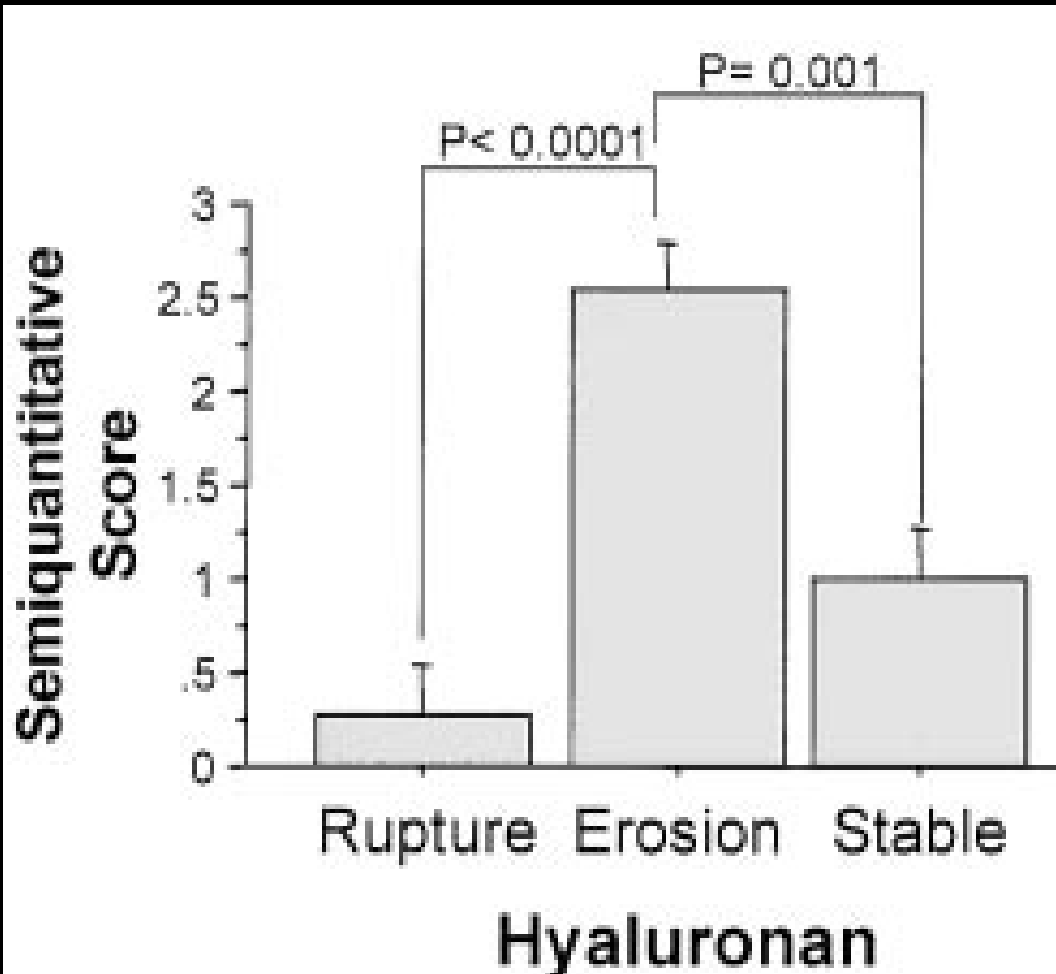


(Fog Bentzon et al, Circ Res 2014)

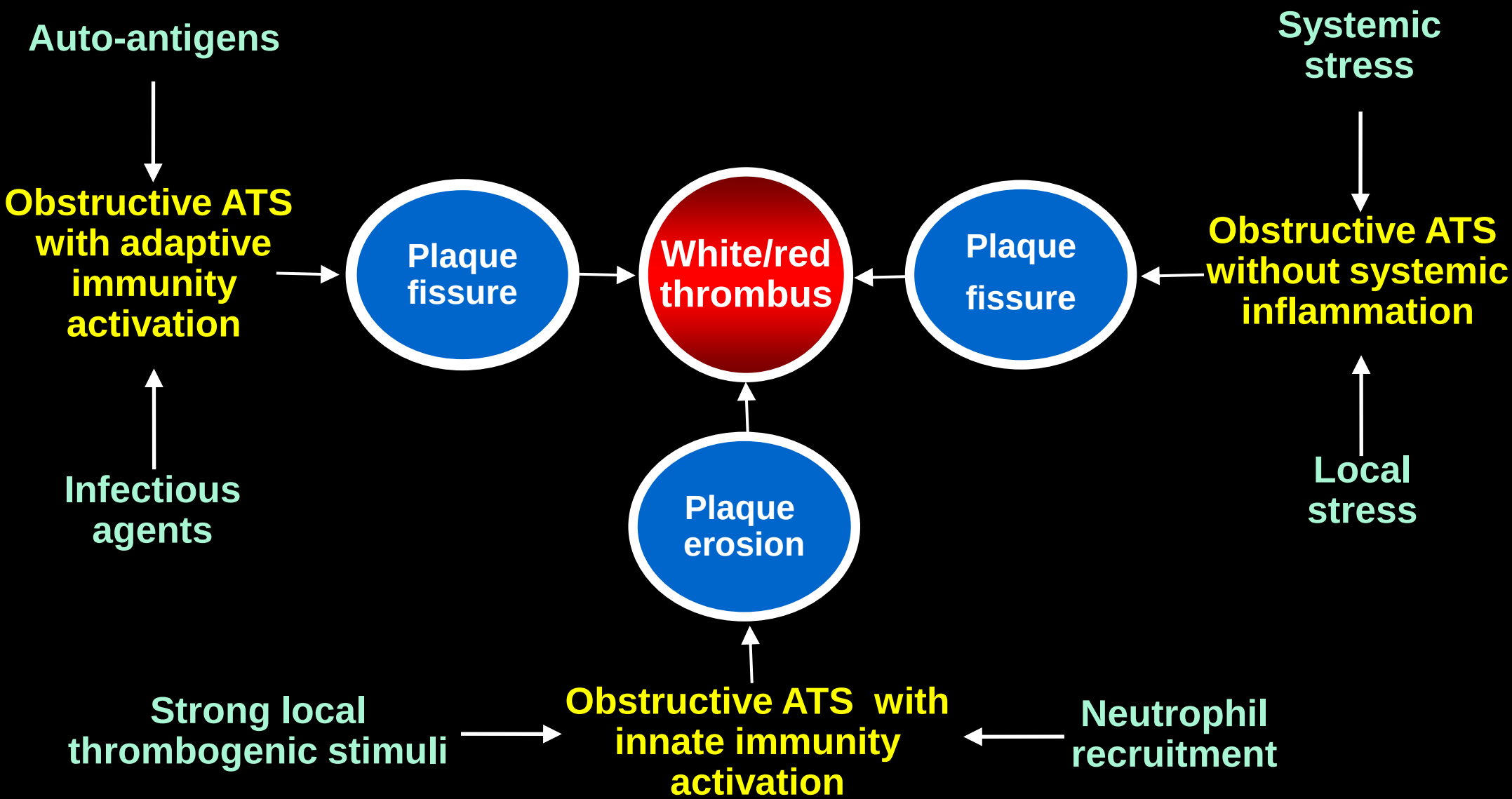
Myeloperoxidase is Associated with Coronary Plaque Erosion



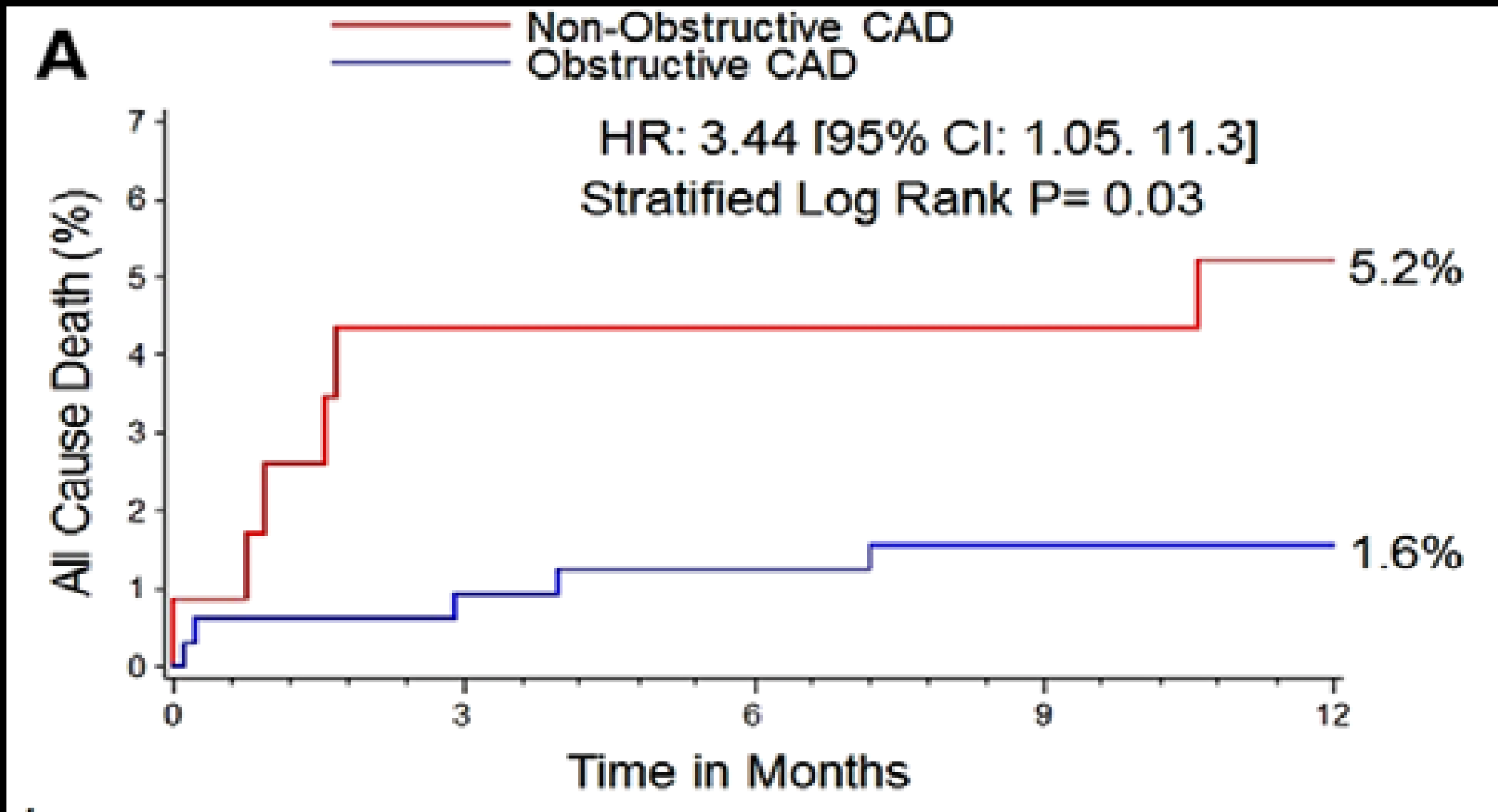
Differential accumulation of hyaluronan expressing CD44 in culprit lesions



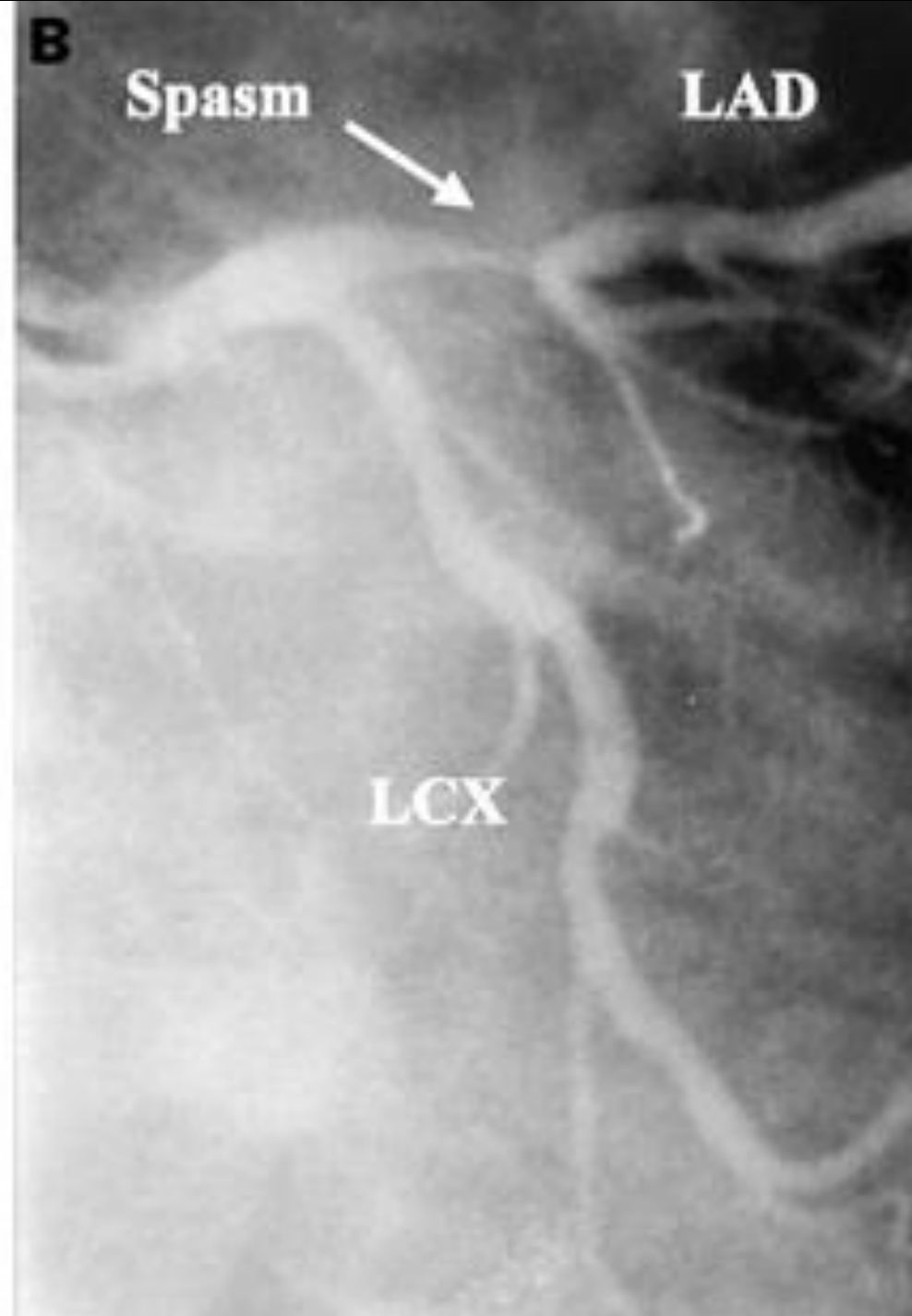
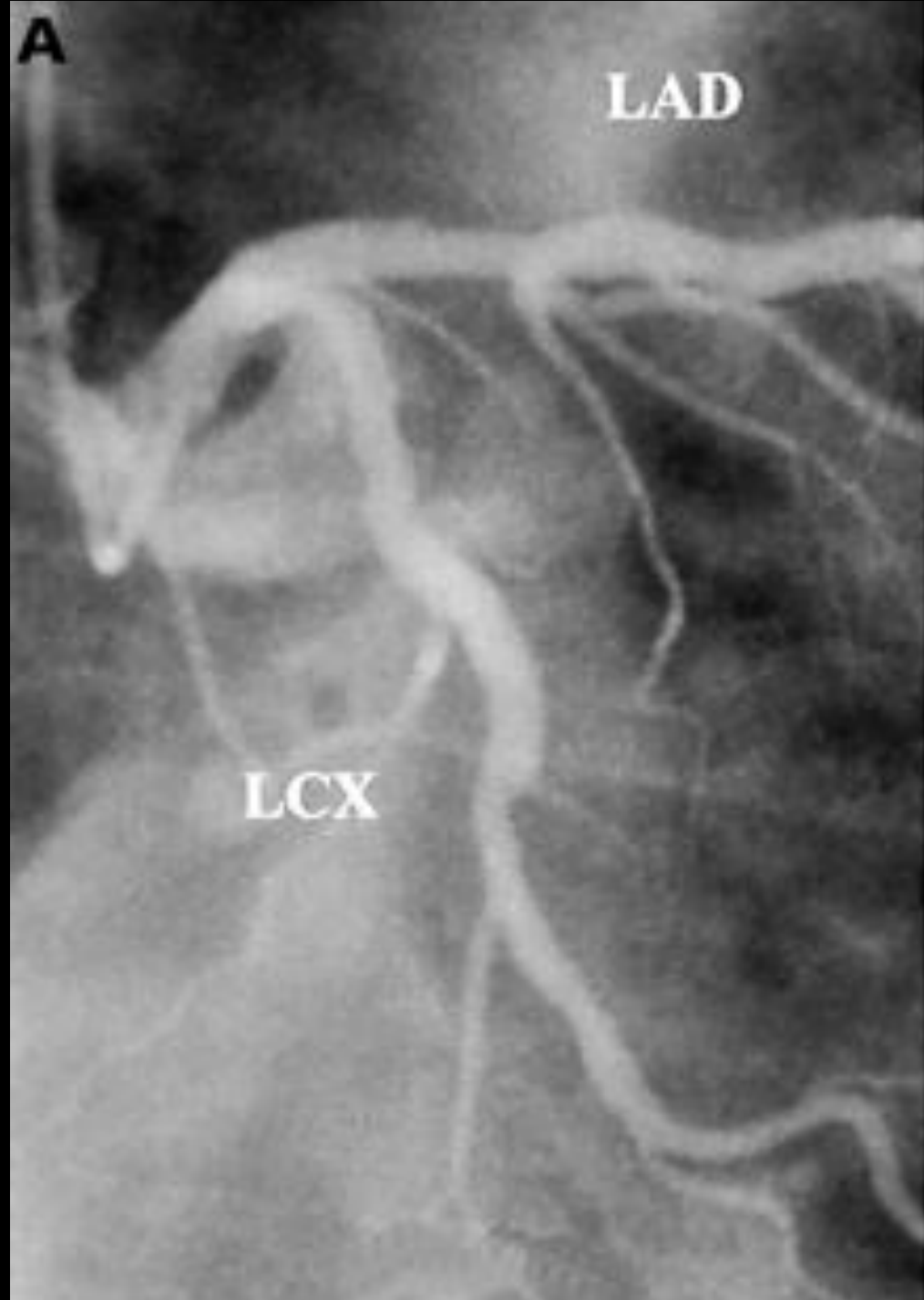
(Kolodgie et al, ATVB 2002)

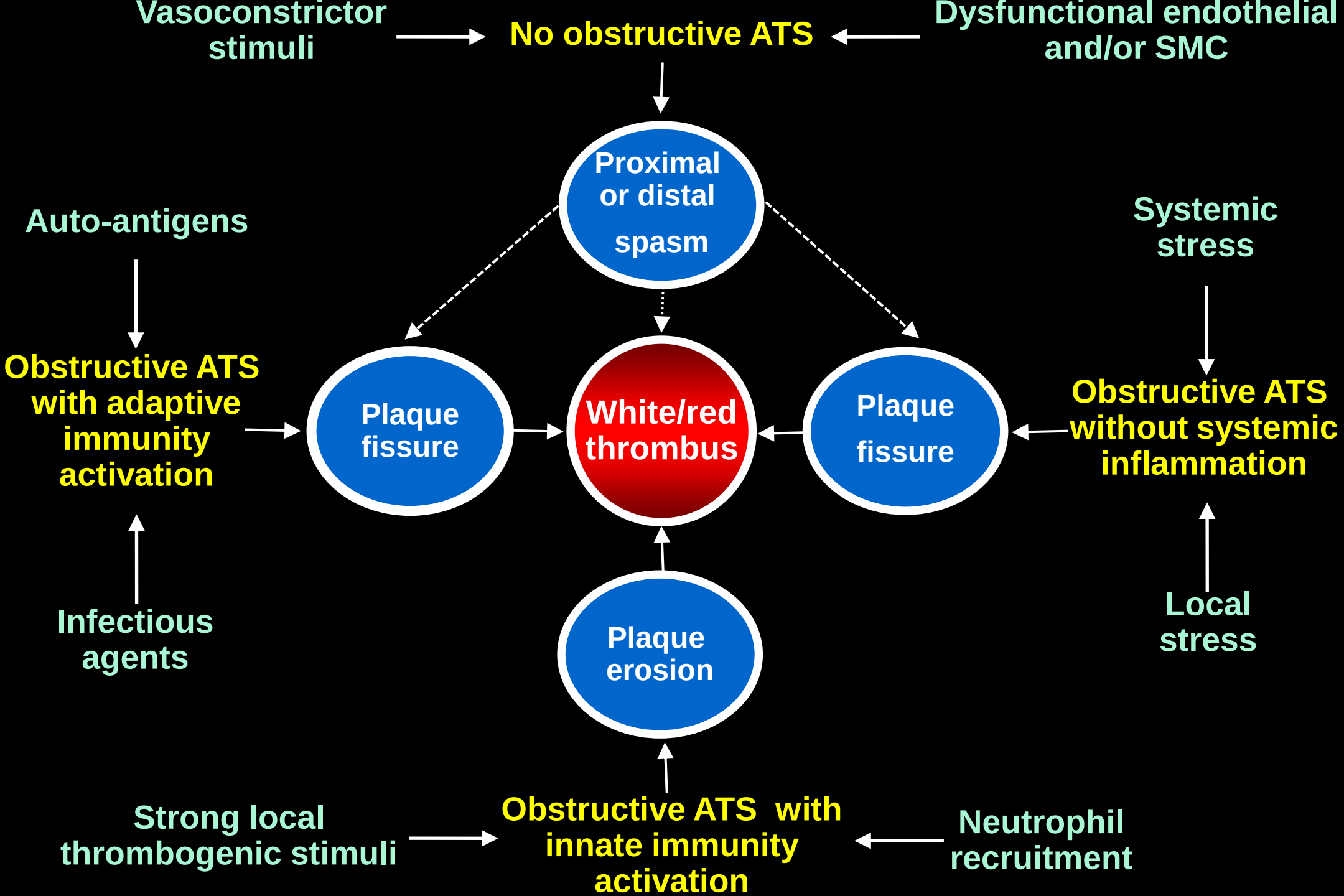


Mortality of patients with NSTEMI and non-obstructive CAD in ACUTITY (n=2442; 8.8% MINOCA)

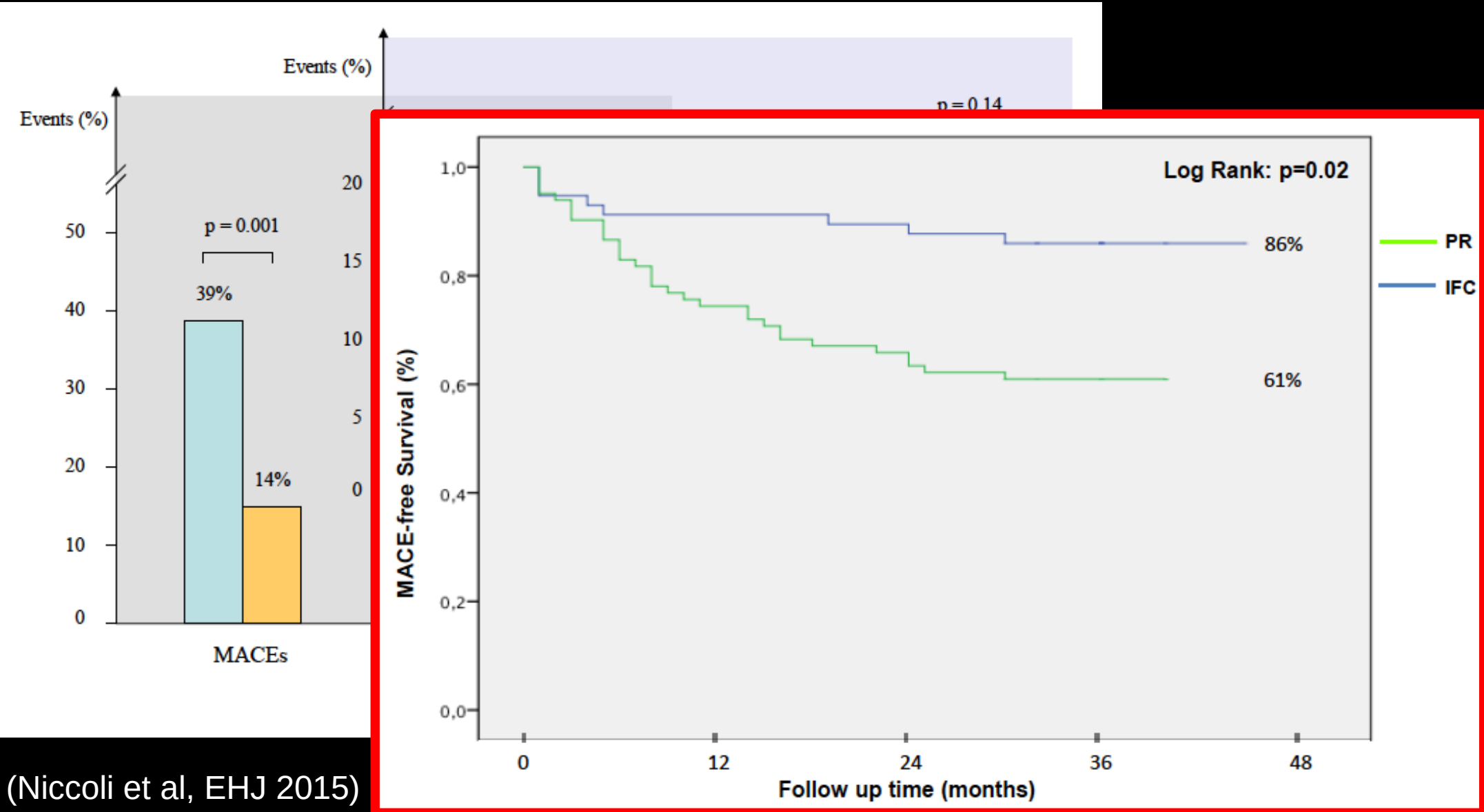


(Planer et al, Circ Cardiovasc Interv 2014))

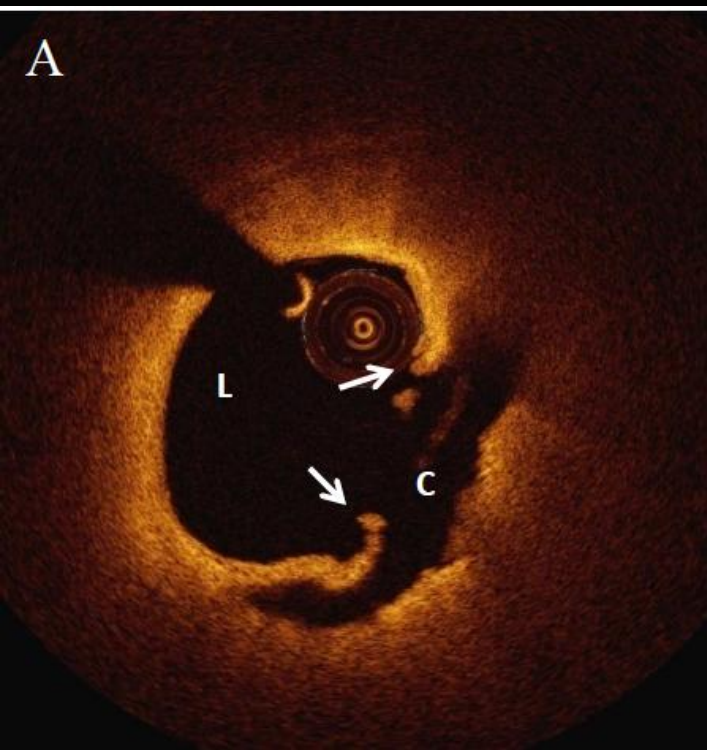




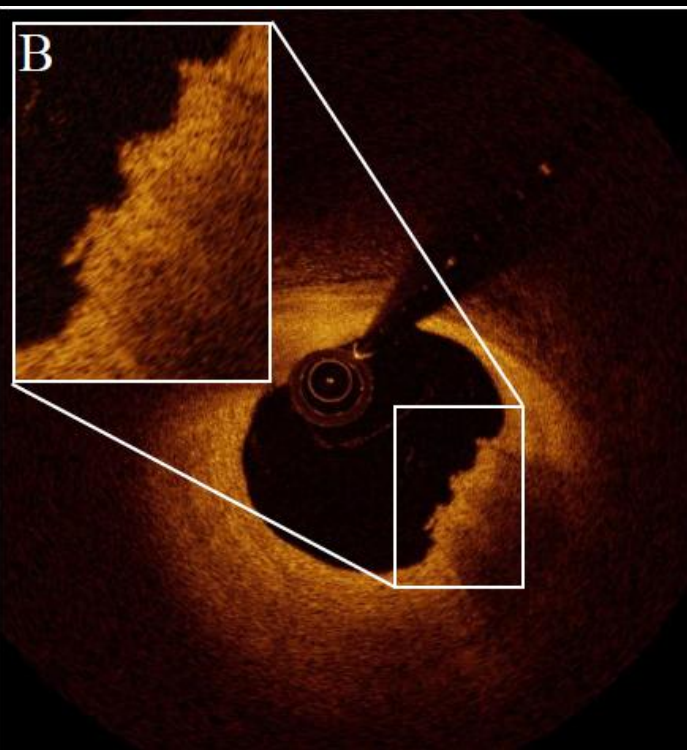
Plaque rupture and erosion assessed by OCT portend a different outcome in ACS (n=139)



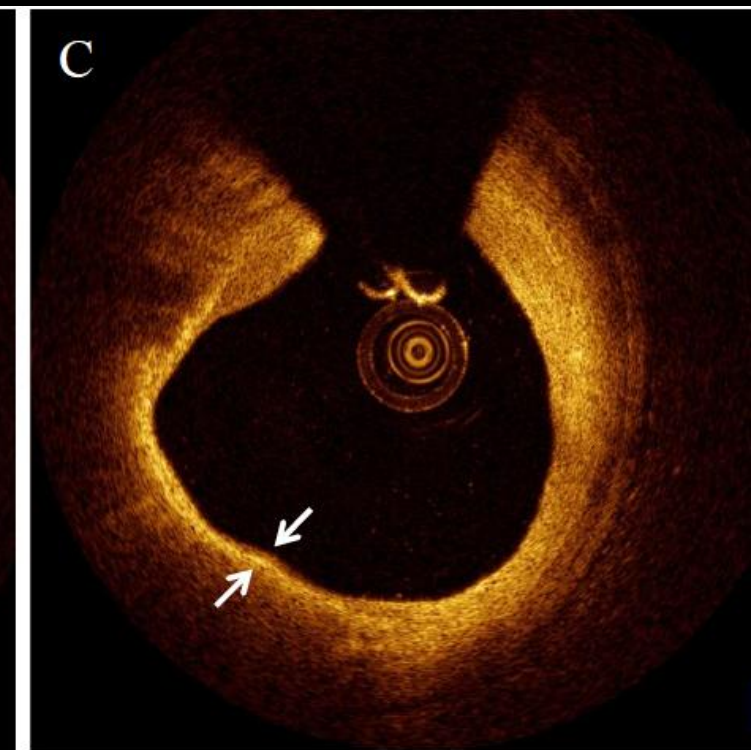
Rupture



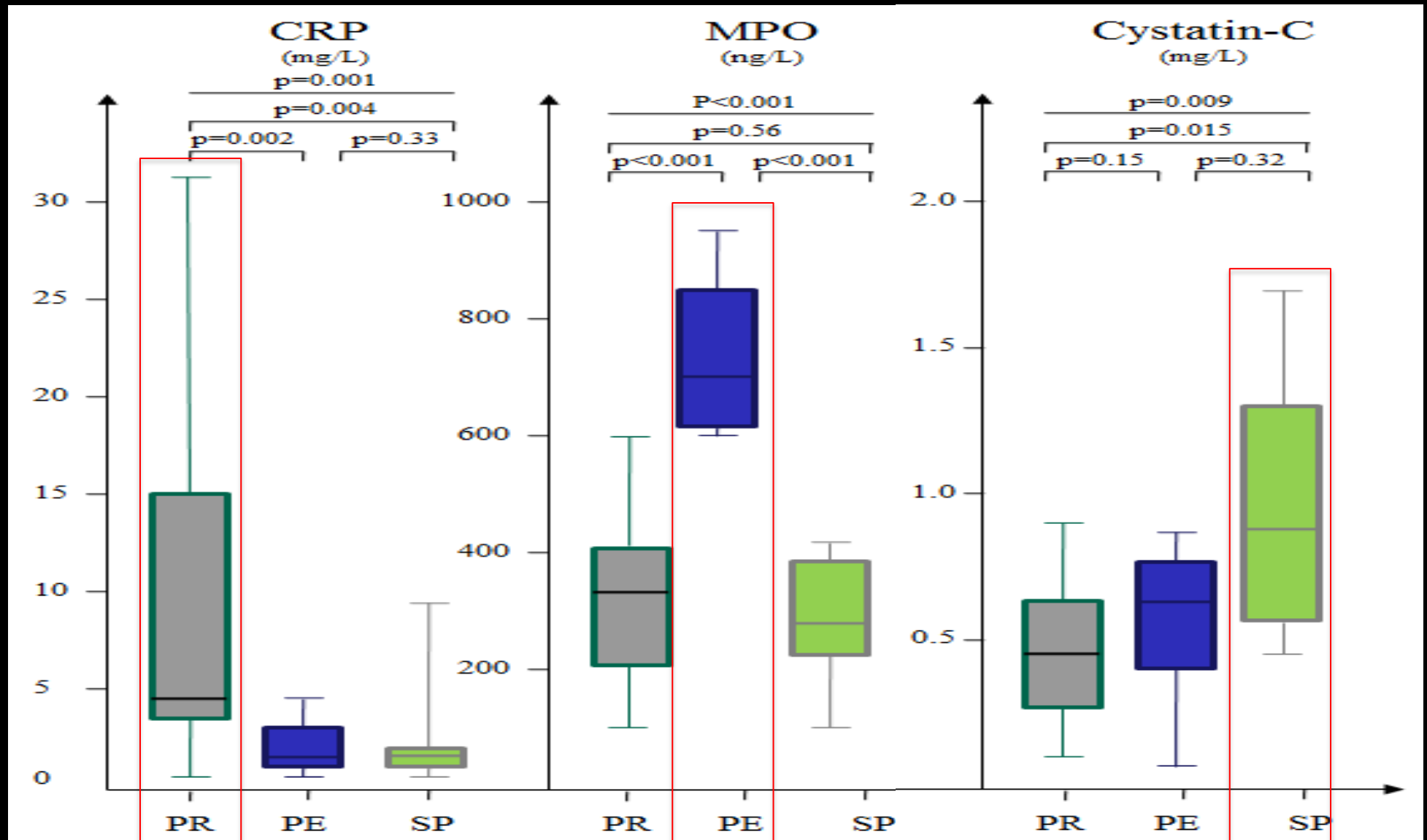
Erosion



Smooth plaque



Morpho-functional correlations in NSTE-ACS



(Niccoli et al, IJC 2014)

Targeting the mechanisms of ACS

Plaque fissure with inflammation

- Methotrexate, IL-1 β antagonists, Treg expansion, Vaccines

Plaque fissure without inflammation

- Colchicine

Plaque erosion

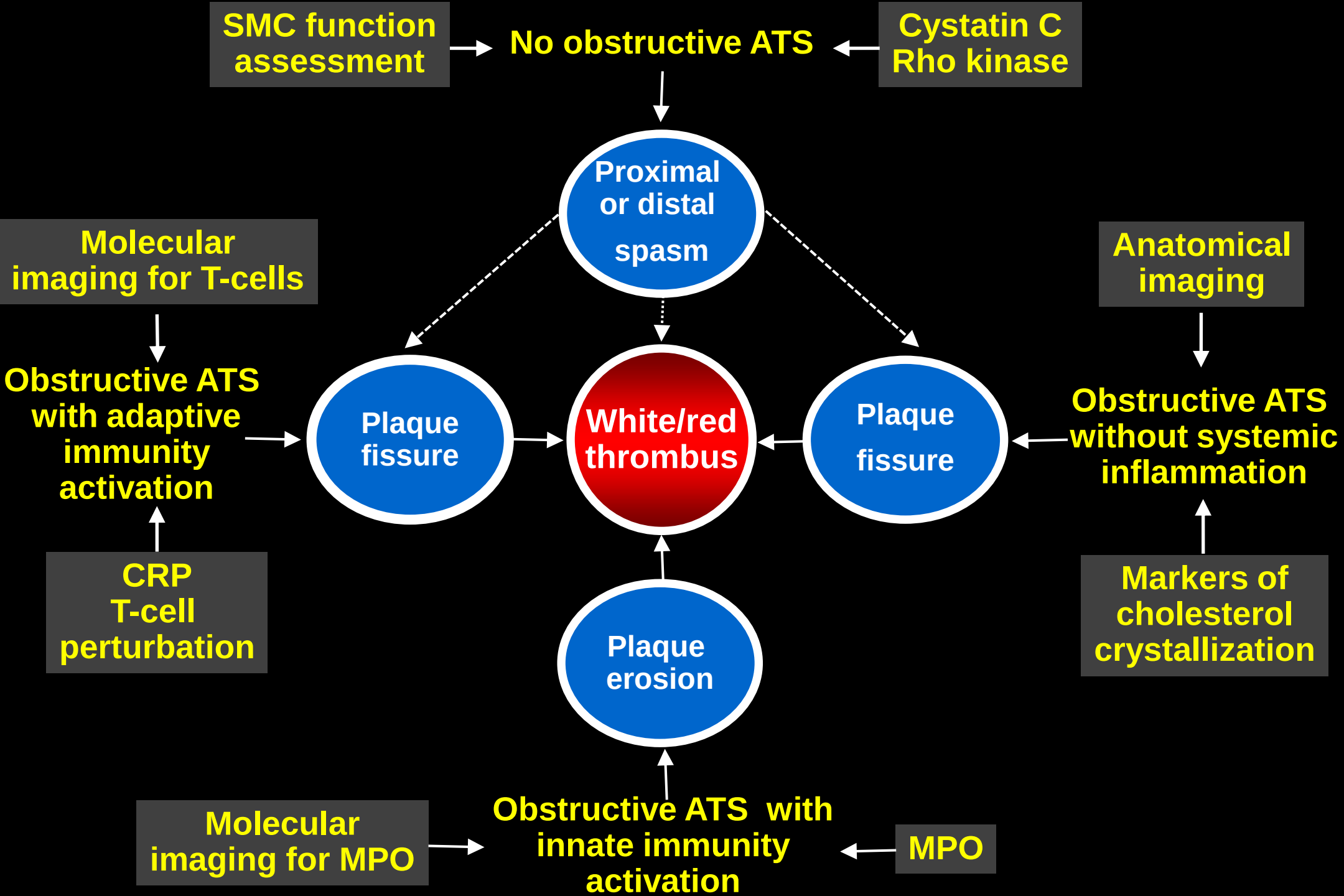
- Antithrombotics

SMC hyperreactivity

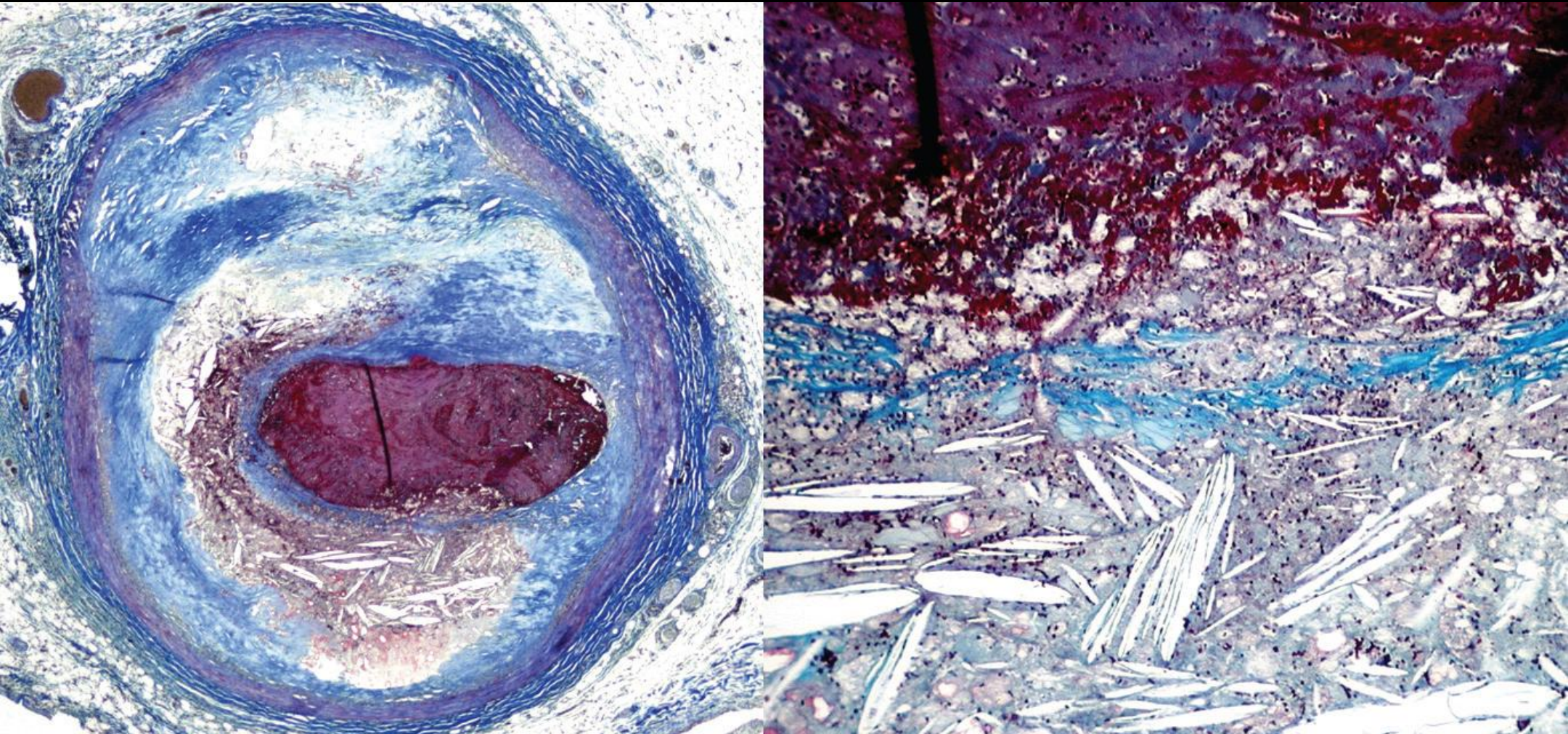
- Vasodilators

It is complex

**I am sorry,
it is not my fault!**



Cholesterol crystals and plaque fissure



(Fog Bentzon et al, Circ Res 2014)