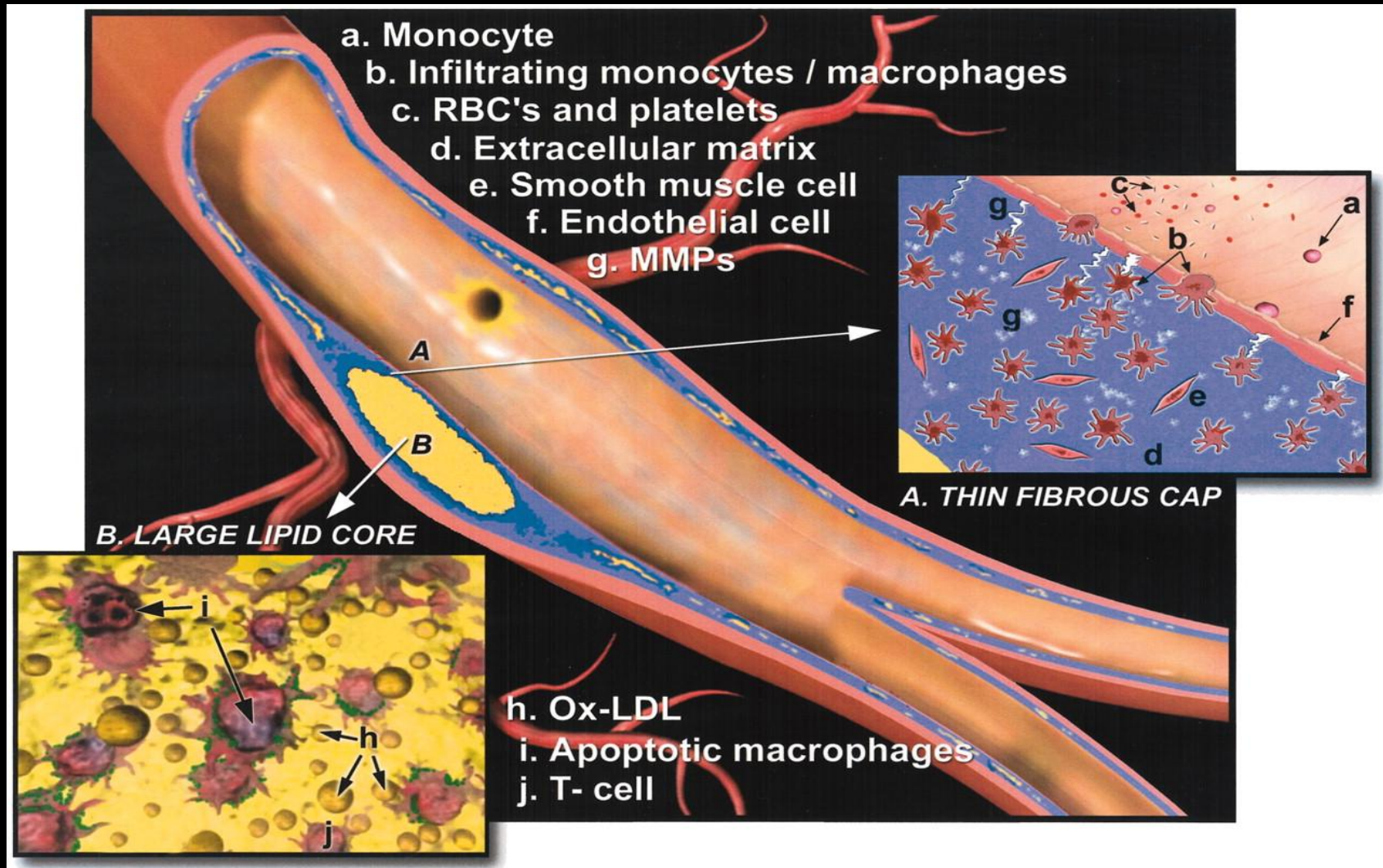


# **RCF 2014**

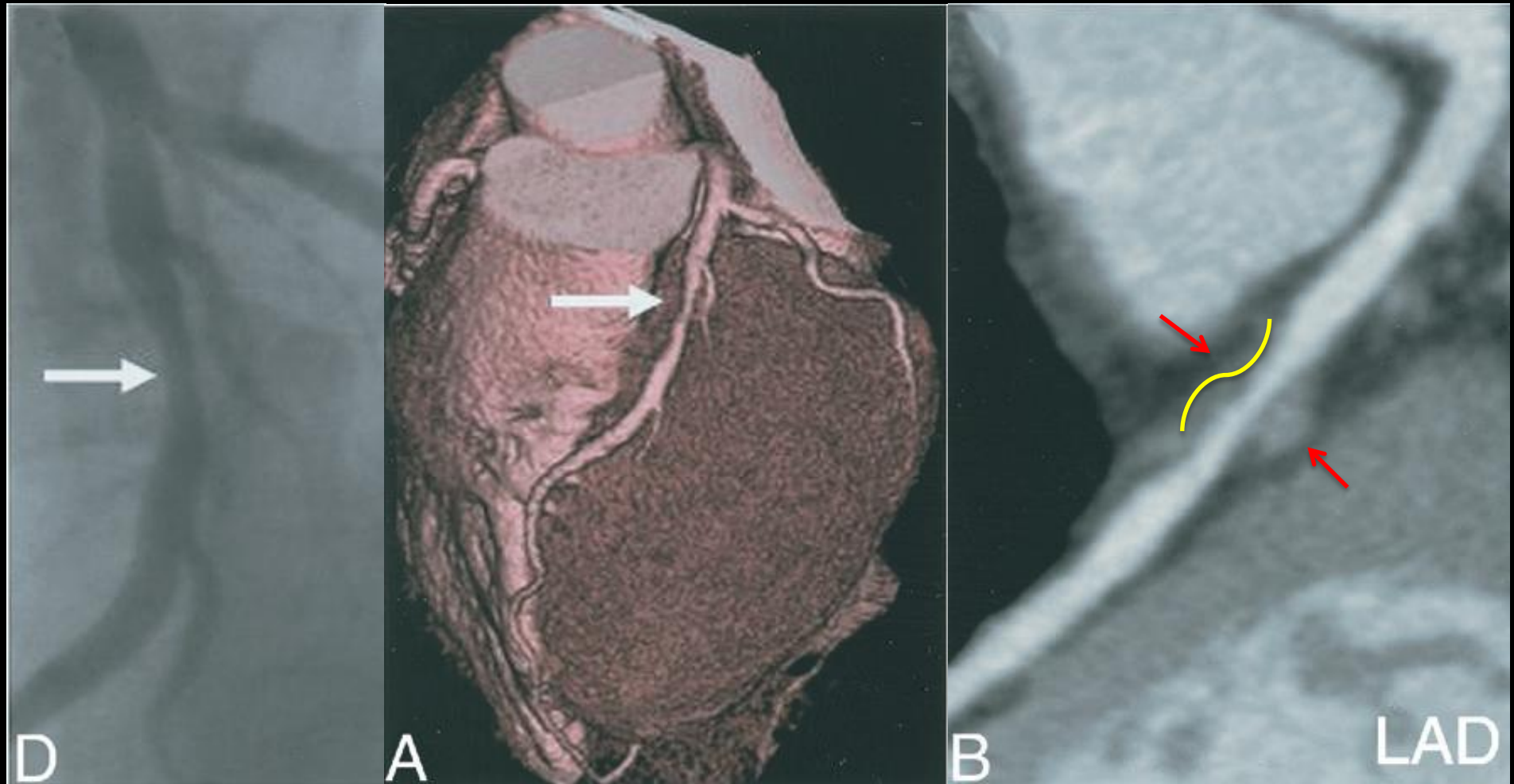
## **The vulnerable plaque in the natural history of atherosclerosis**

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

# The search for the “Holy Grail”



# The search for the “Holy Grail” by CT coronary angiography



(Motoyama et al, JACC 2007)

# The search for the “Holy Grail” by CT coronary angiography

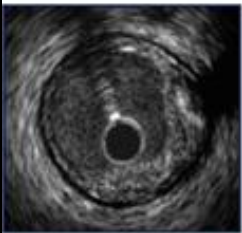
n= 1059	Cutoff Value	Sens (%)	Spec (%)	PPV (%)	NPV (%)
Remodeling Index (%)	116.5	72.7	61.9	25.0	69.0
Total Plaque Volume (mm <sup>3</sup> )	63.13	72.7	68.3	28.6	93.5
LAP Volume (mm <sup>3</sup> )	0.99	90.0	66.7	32.3	97.7

(Motoyama et al, JACC 2009)

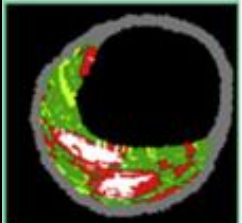


# Invasive imaging modalities

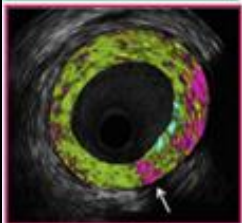
## Sound-based Imaging modalities



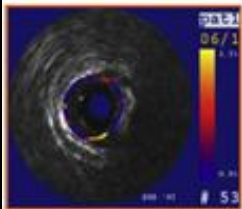
**IVUS (gray scale)**  
(plaque burden)  
(remodelling)



**Virtual Histology**  
(plaque composition - NC)



**iMap**  
(plaque composition - NC)

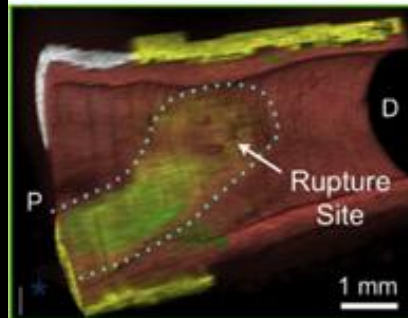


**Palpography**  
(mechanical properties)

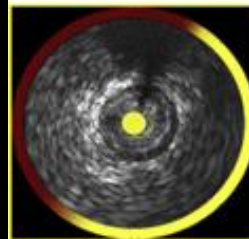
## Light-based Imaging modalities



**OCT**  
Fibrous cap thickness,  
ruptured plaques  
thrombus

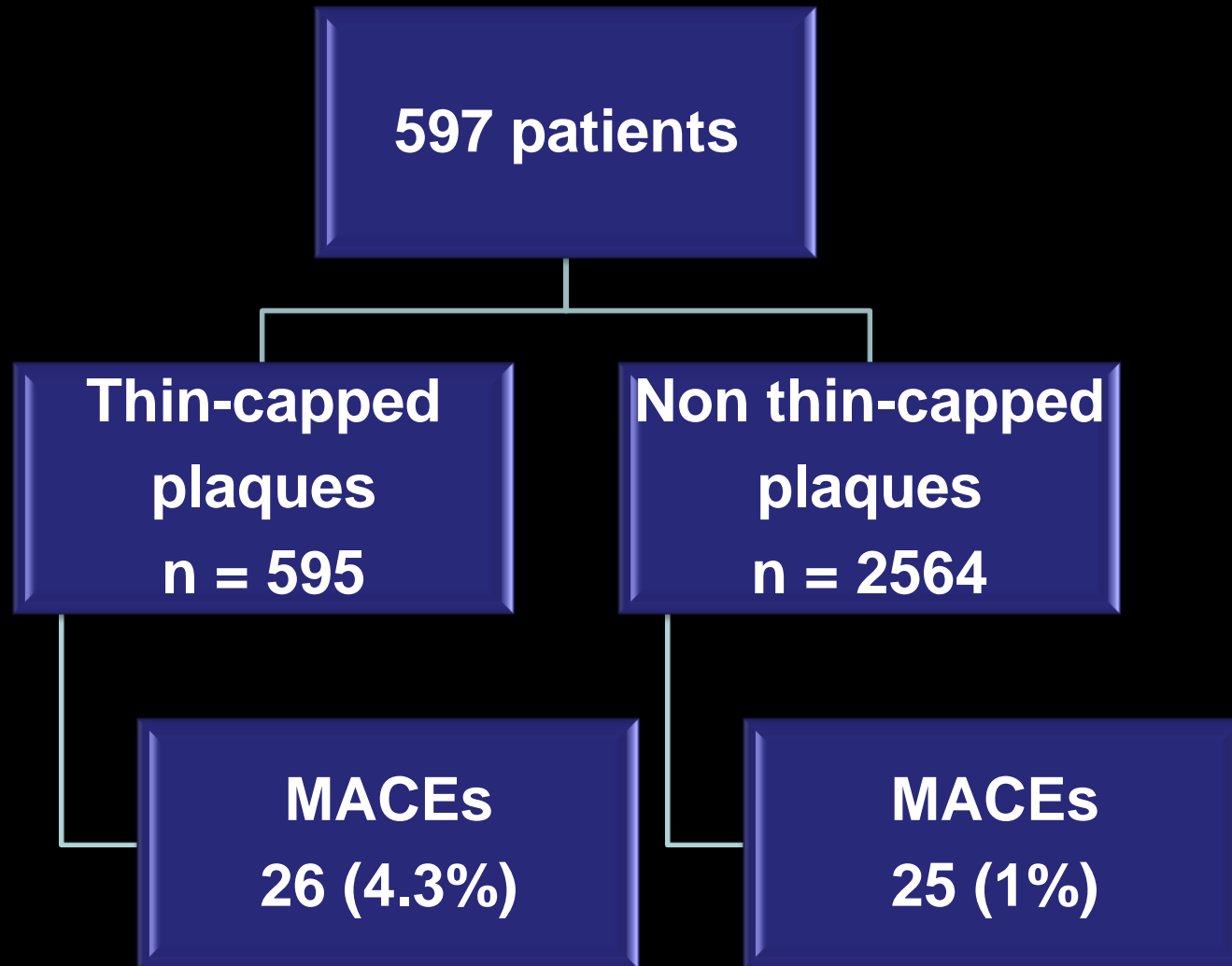


**Tissue  
characterization  
OCT**  
Macrophages,  
NC, Ca<sup>++</sup>



**NIR spectroscopy**  
(plaque burden and  
plaque composition - NC)

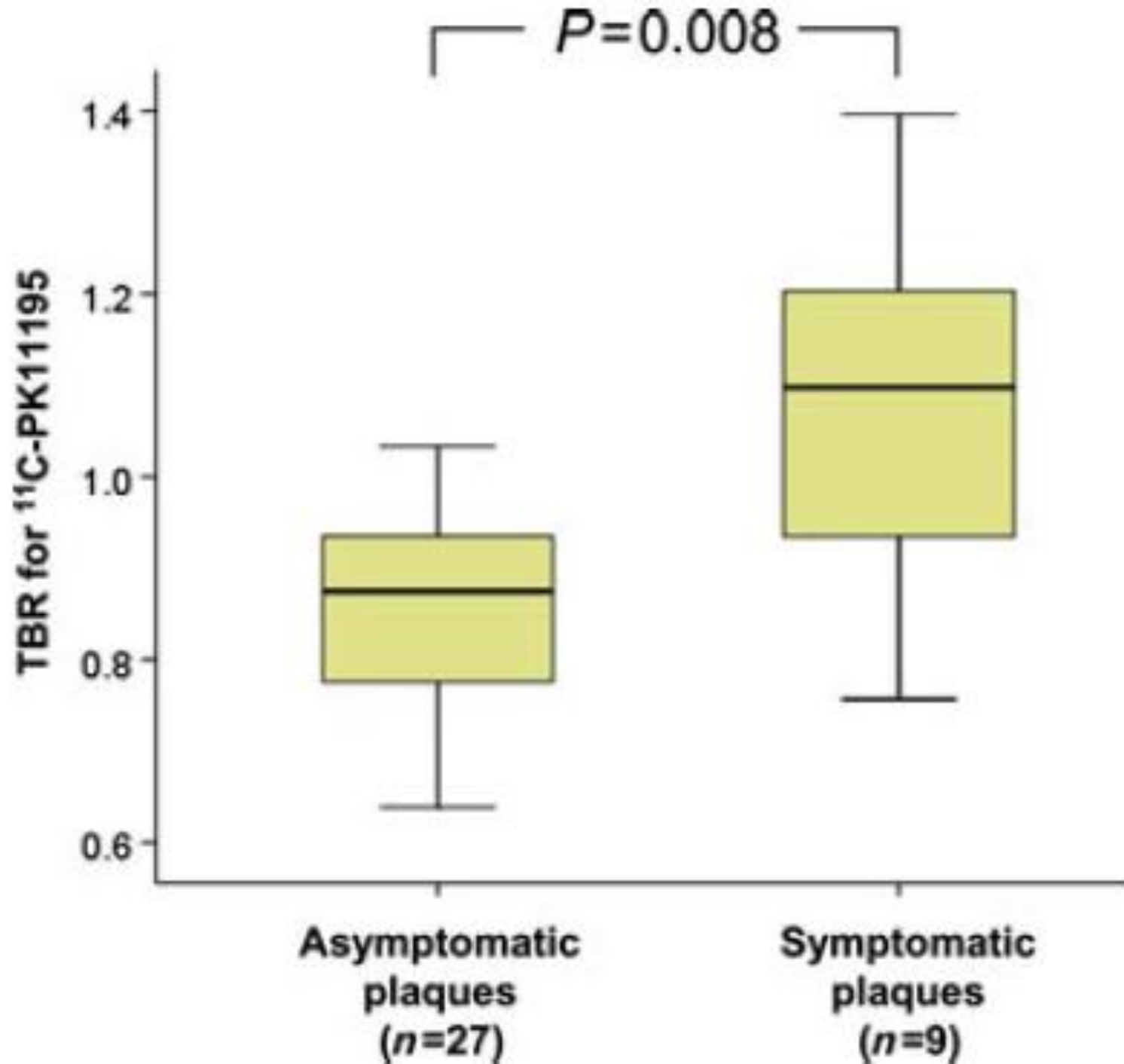
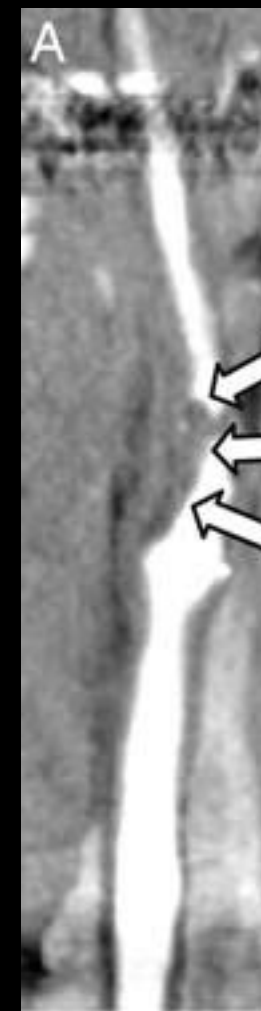
# The search for the “Holy Grail” by RF-IVUS



(Stone et al, NEJM 2011)

Ident

ques



# Mechanisms of progression in CAD: role of healed plaque disruption



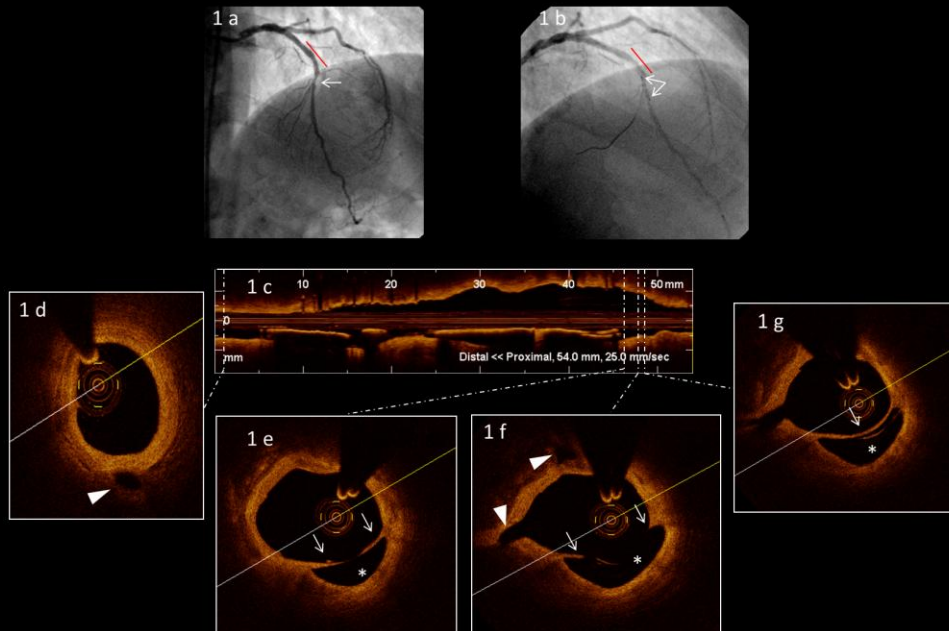
**Subclinical episodes of plaque disruption followed by healing are a frequent stimulus to plaque growth.**

**(Mann & Davies, Heart 1999)**



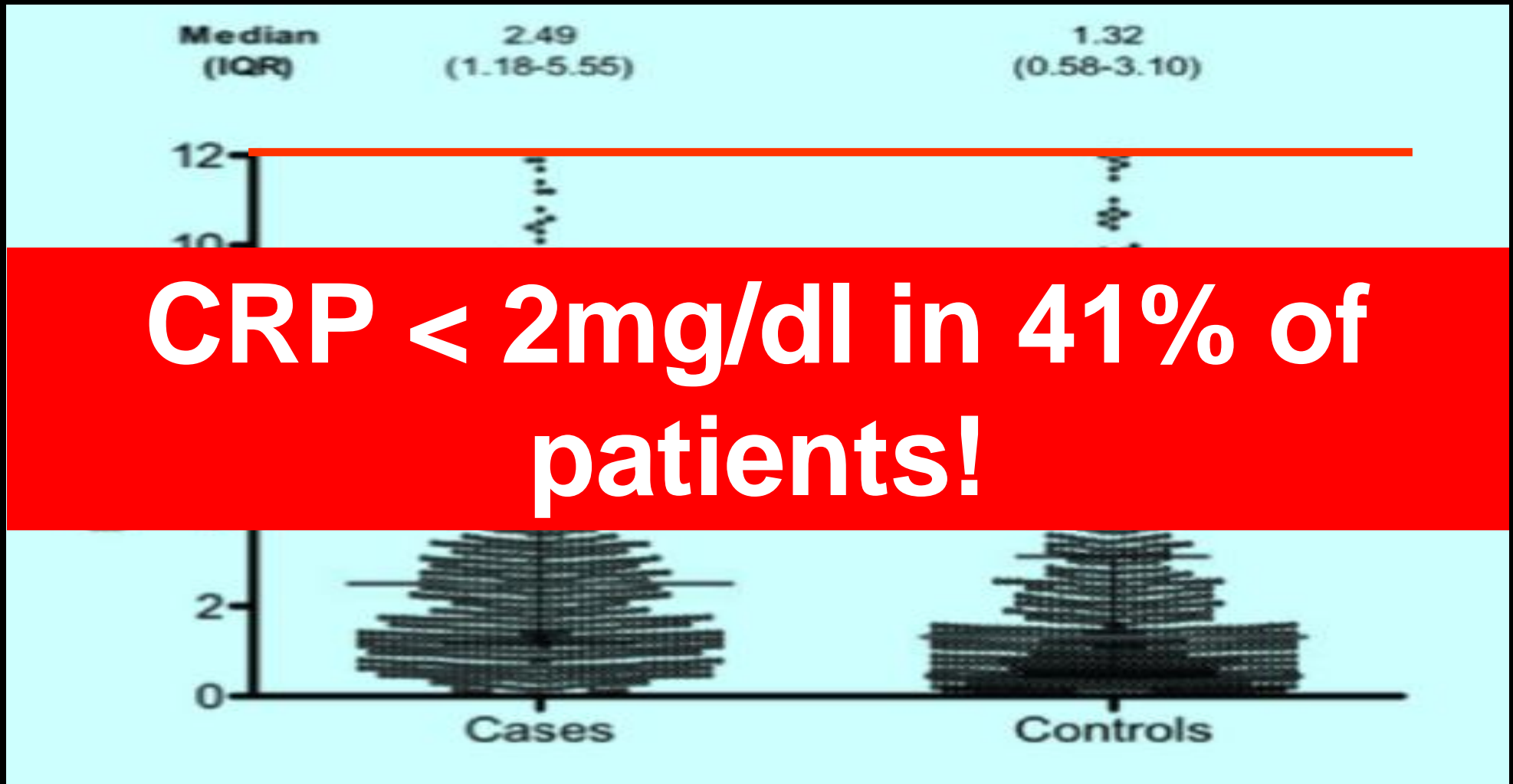
# “Stable” plaque fissure

## Baseline

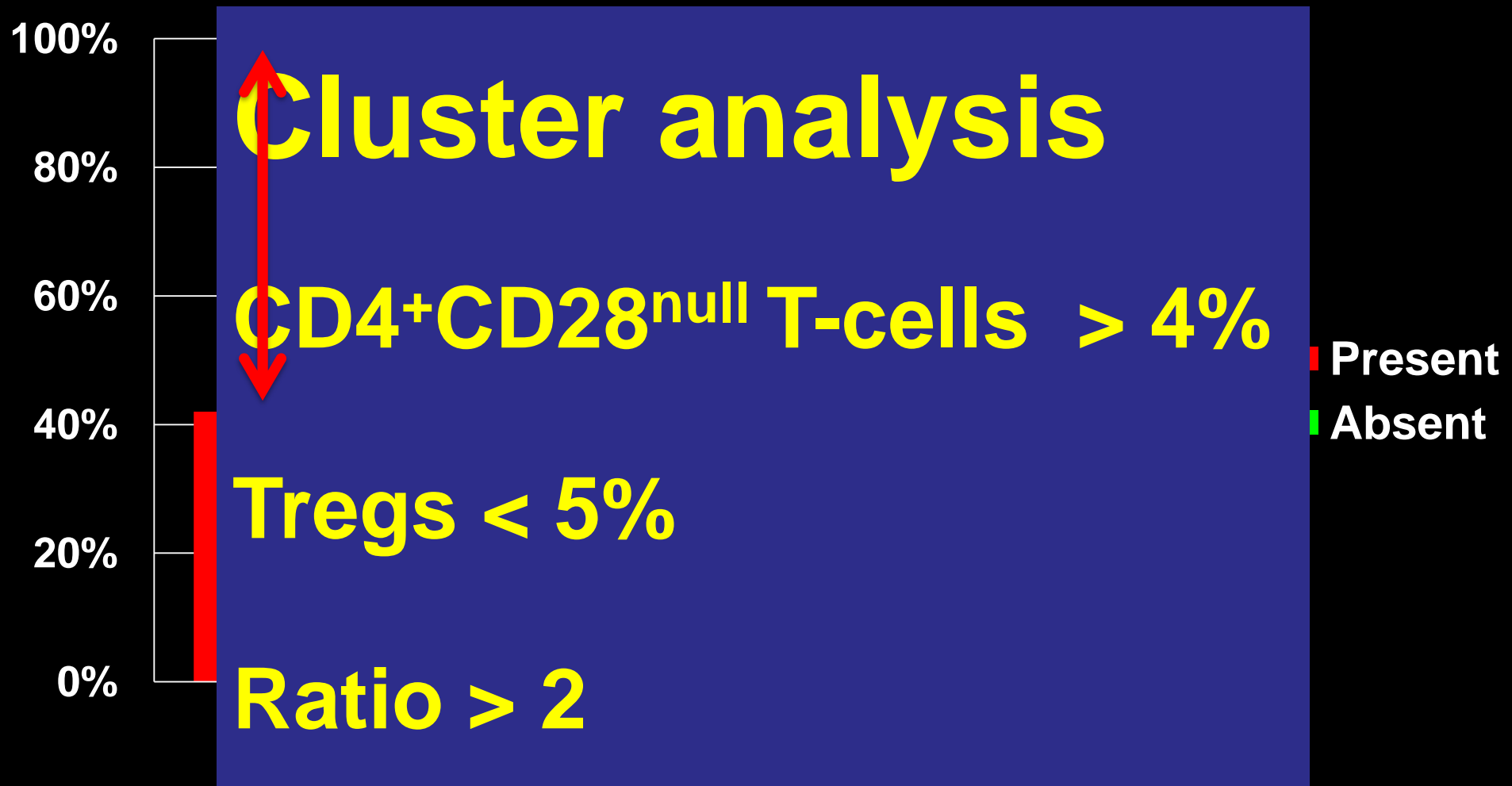


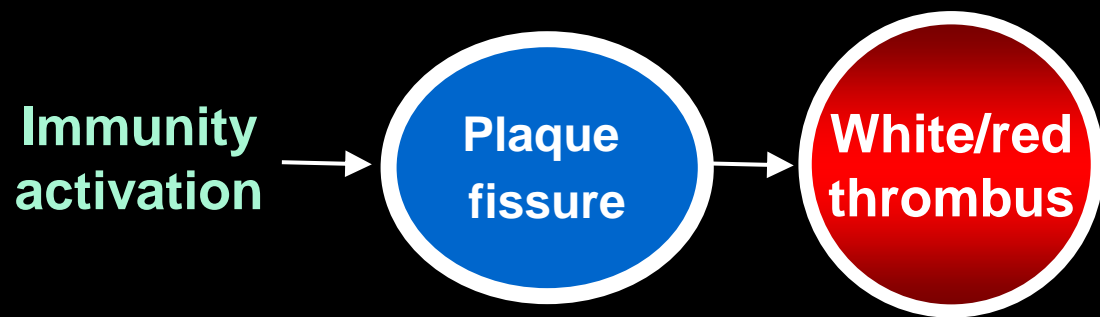
(Prati et al, JACC Cardiovasc Int. 2013)

# Association between inflammation and CV events



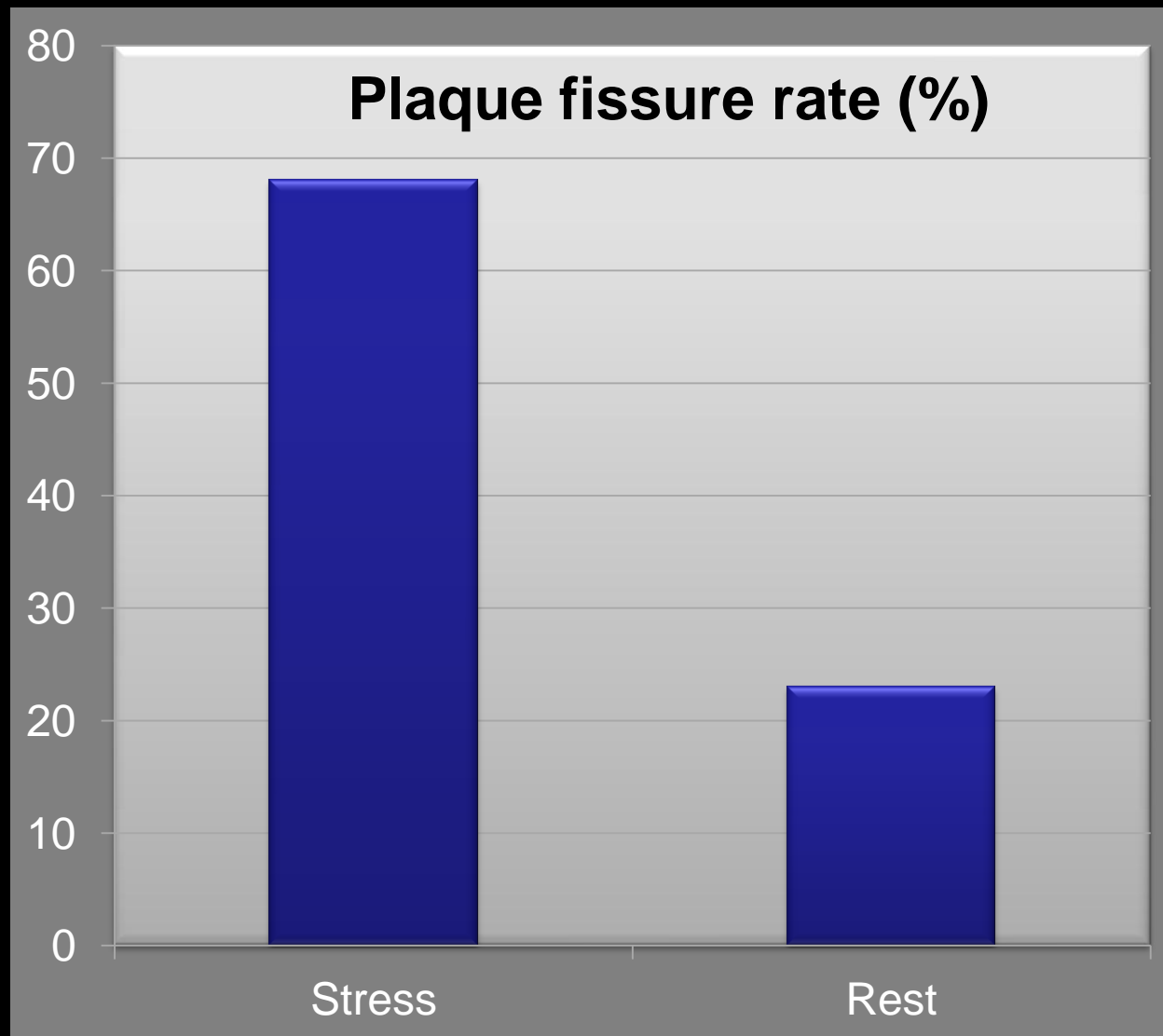
# Identification of a unique adaptive immune signature in ACS







# Mechanical triggers of plaque fissure: systemic stress

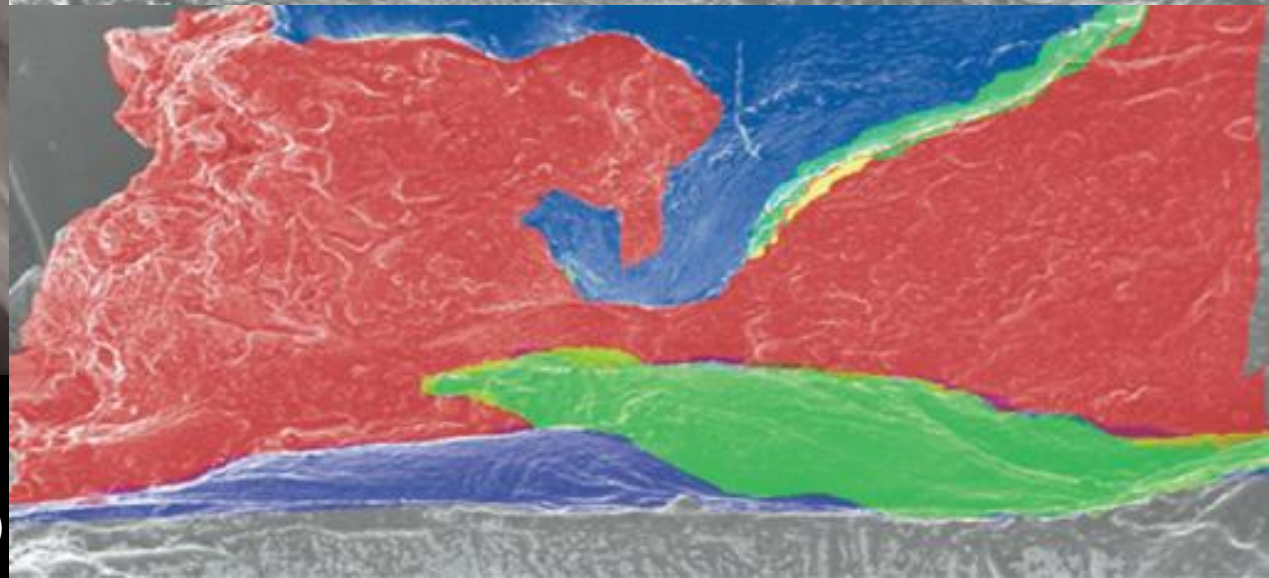
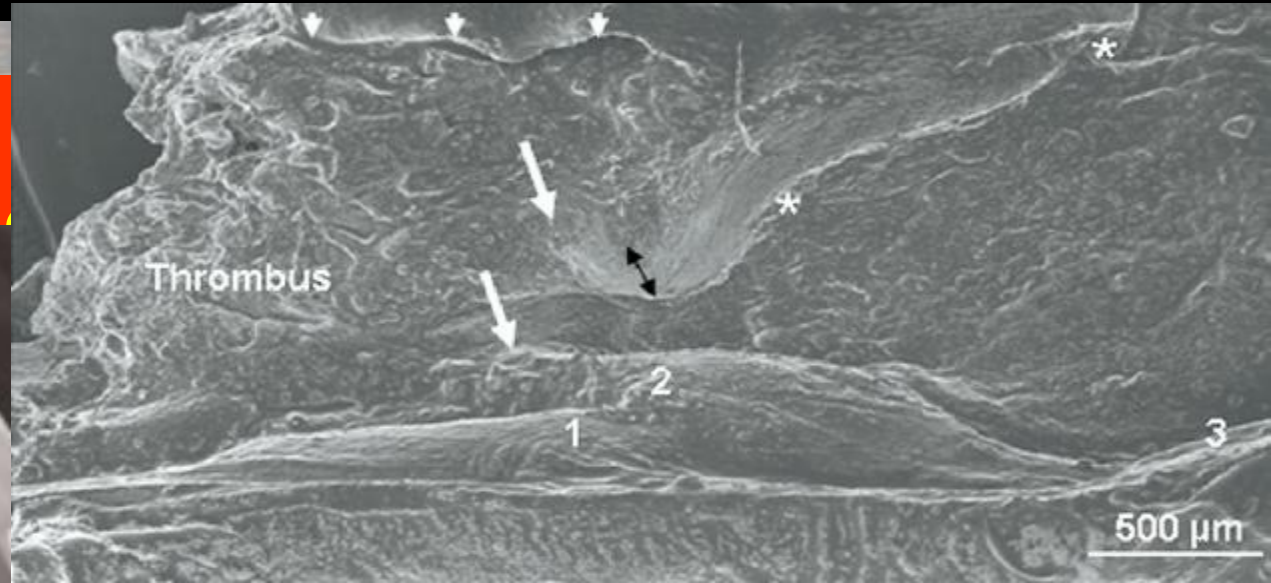


(Burke et al, JAMA 1999)

# Mechanical triggers of plaque fissure: cholesterol crystallization

## Factors affecting cholesterol crystallization

- Cholesterol saturation
- Hydration
- Temperature
- pH



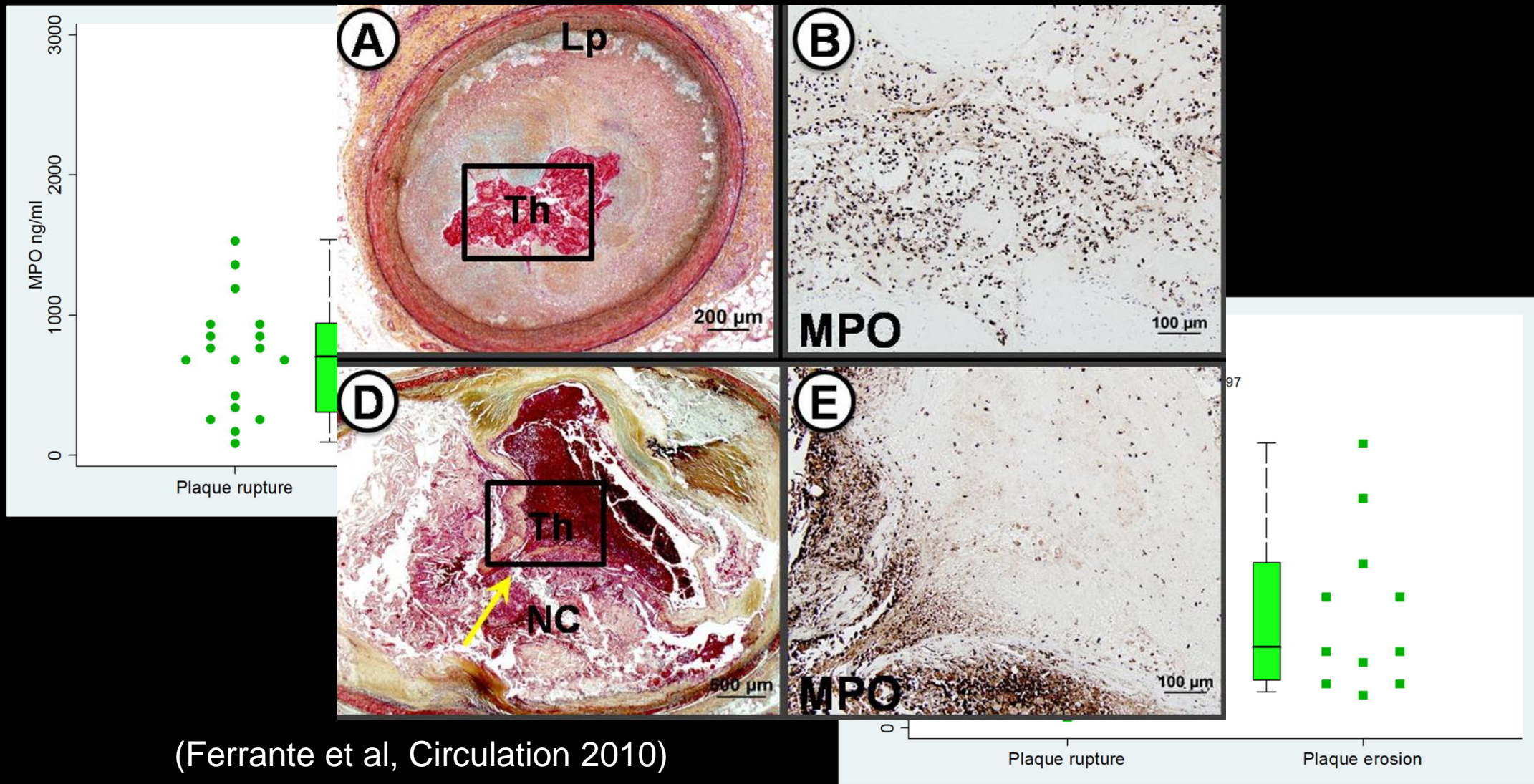


# Plaque erosion



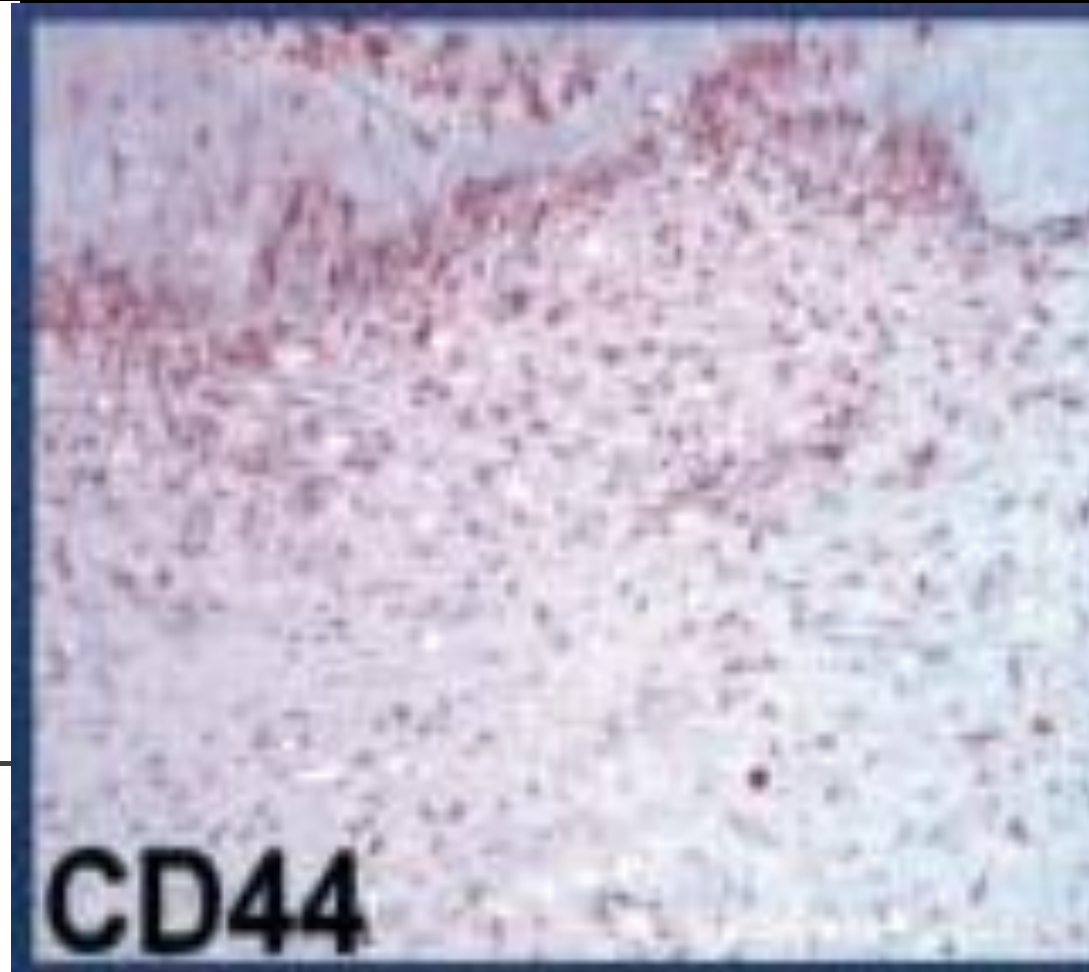
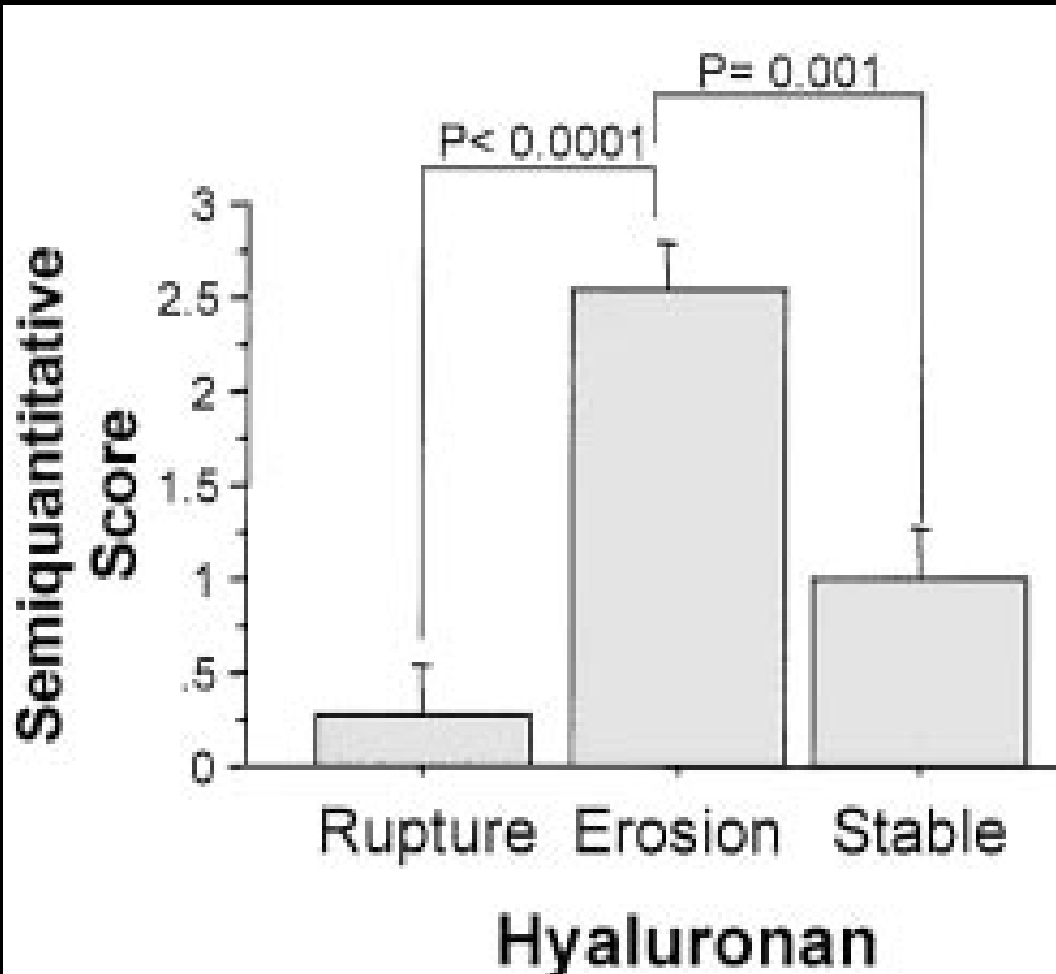


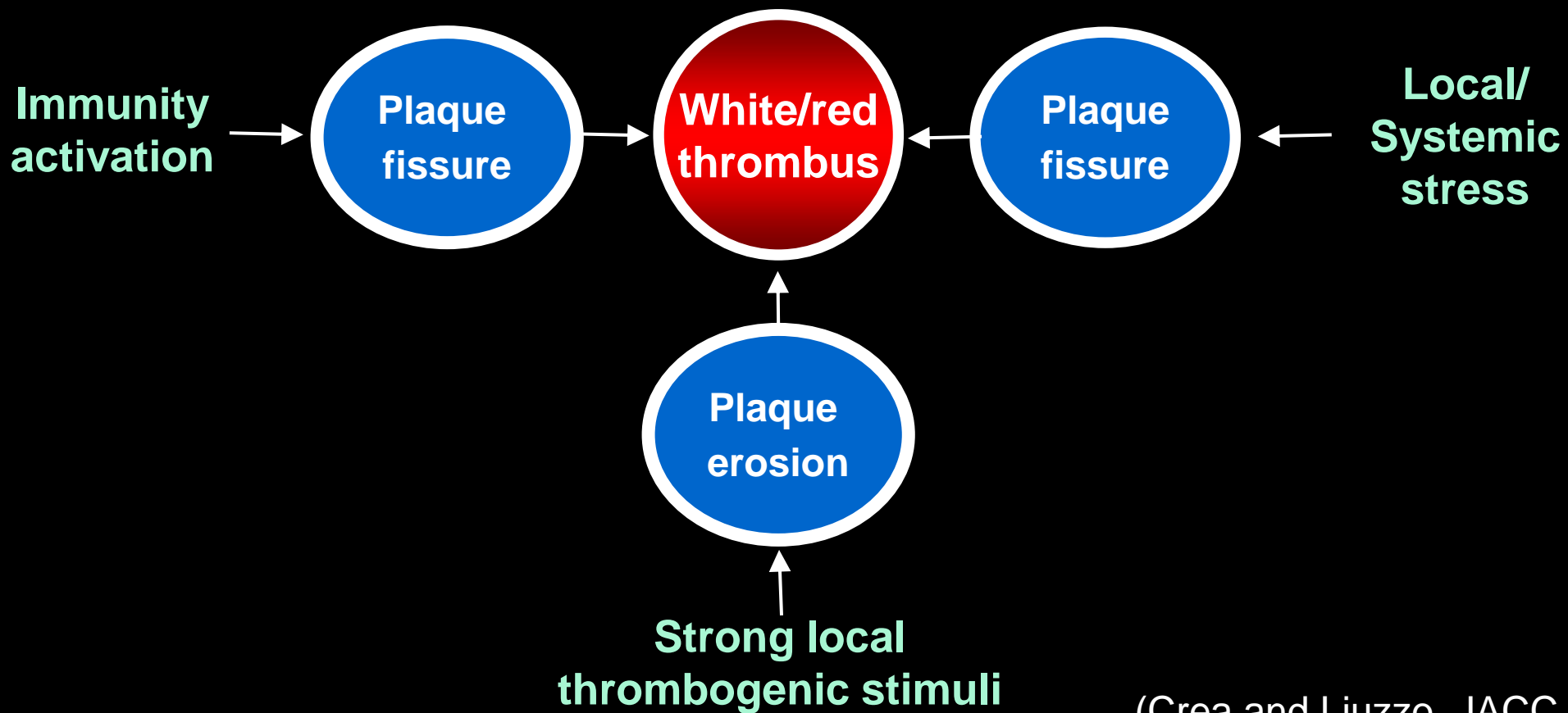
# Myeloperoxidase is associated with coronary plaque erosion



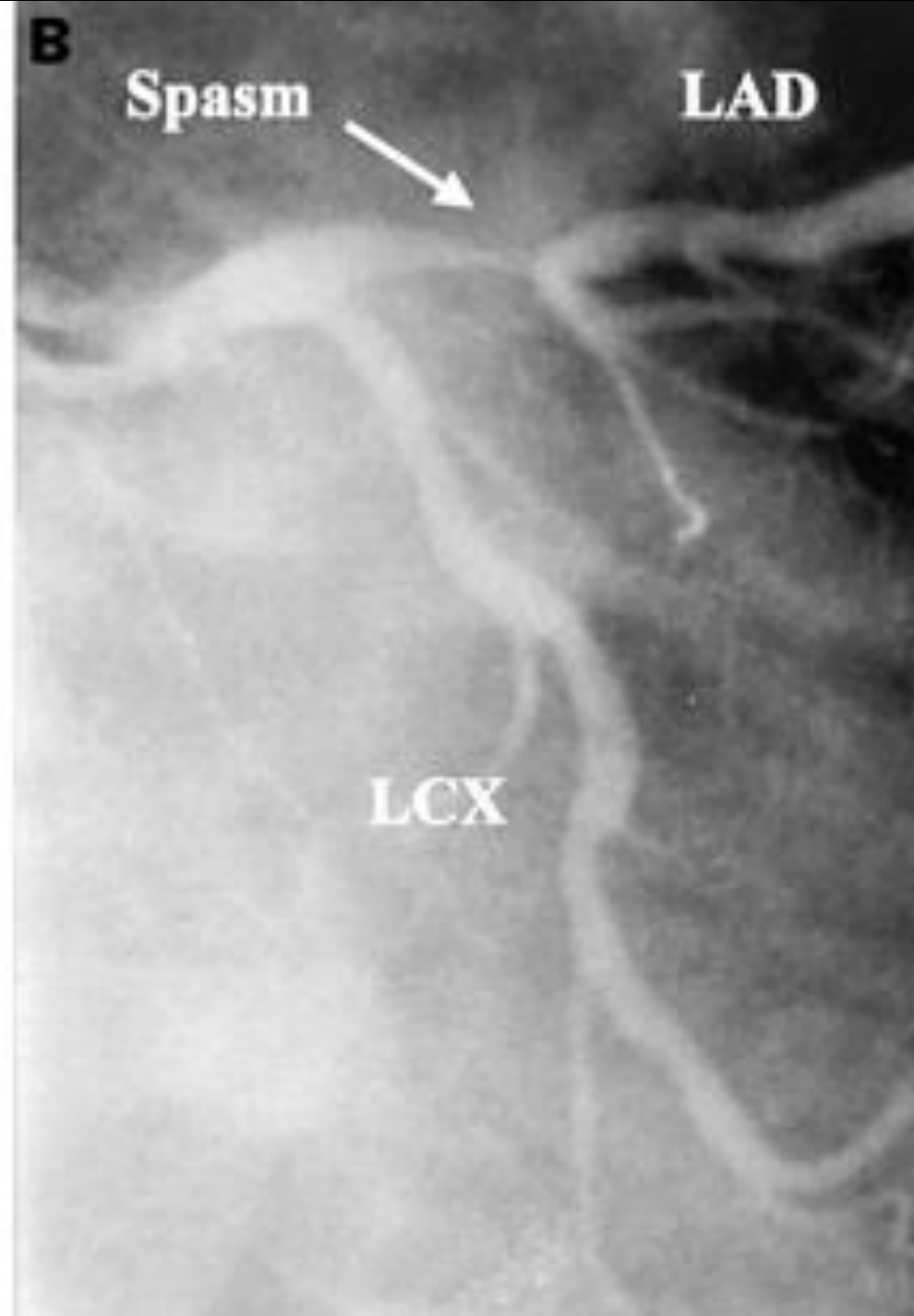
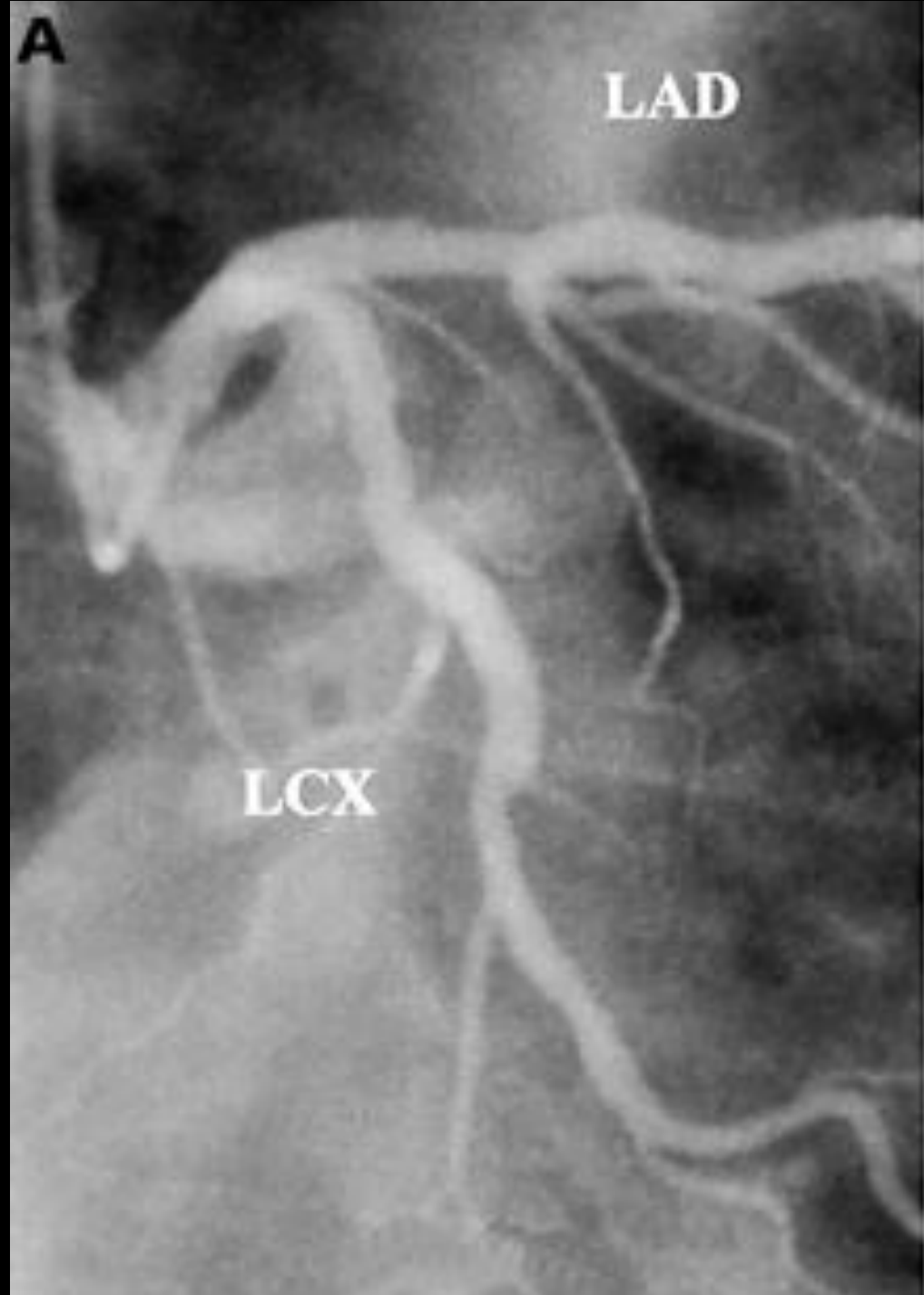
(Ferrante et al, Circulation 2010)

# Differential accumulation of hyaluronan expressing CD44 in culprit lesions



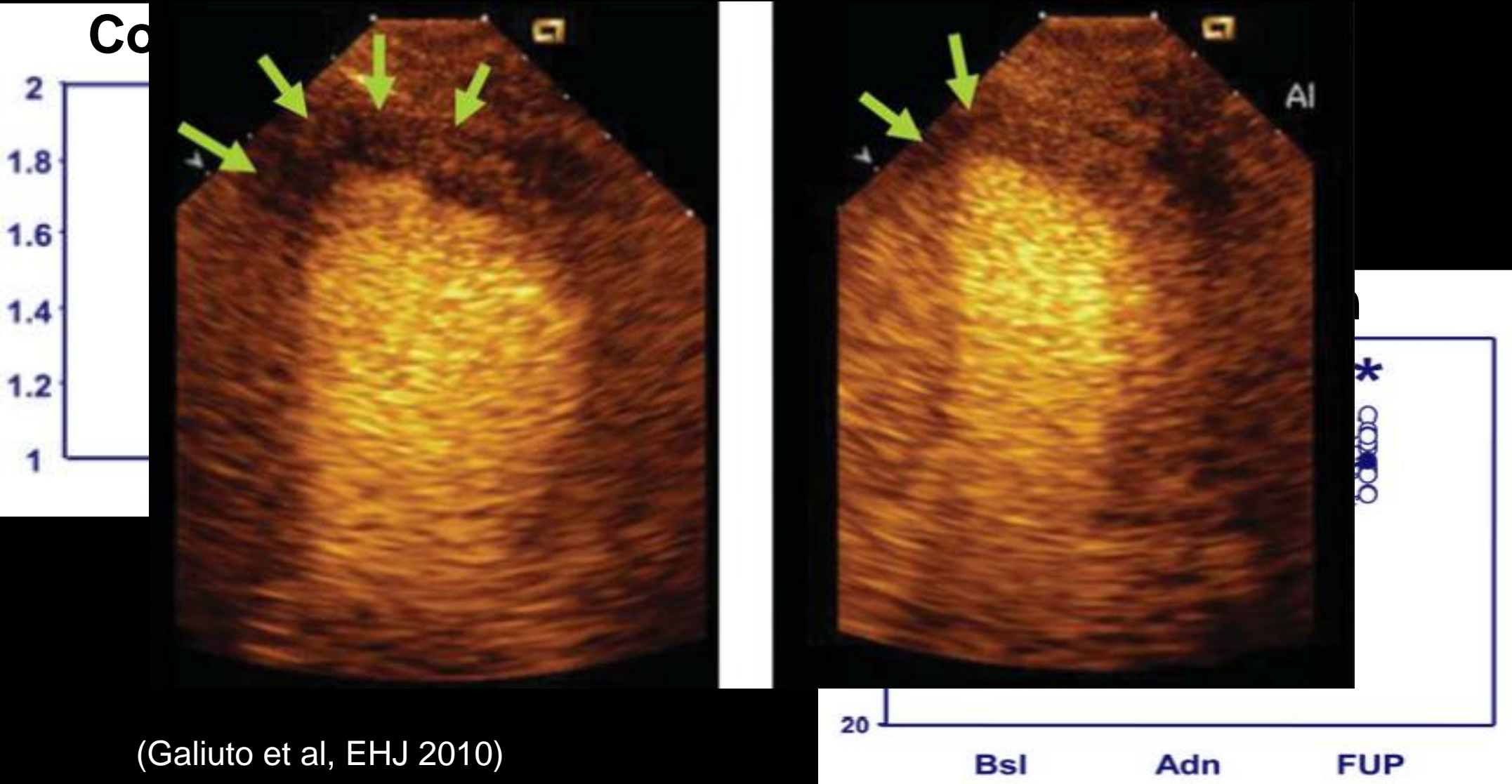


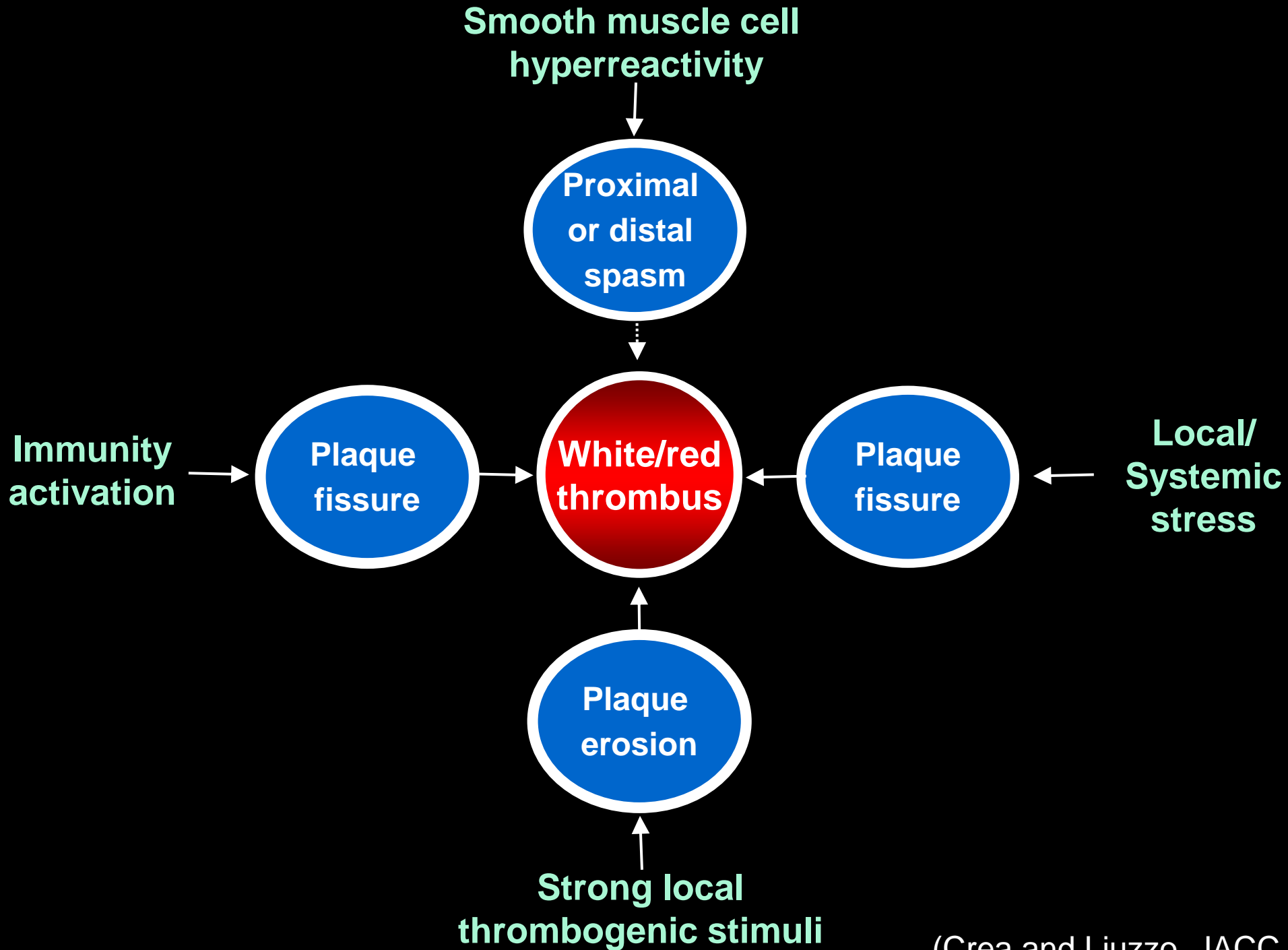
(Crea and Liuzzo, JACC 2013)





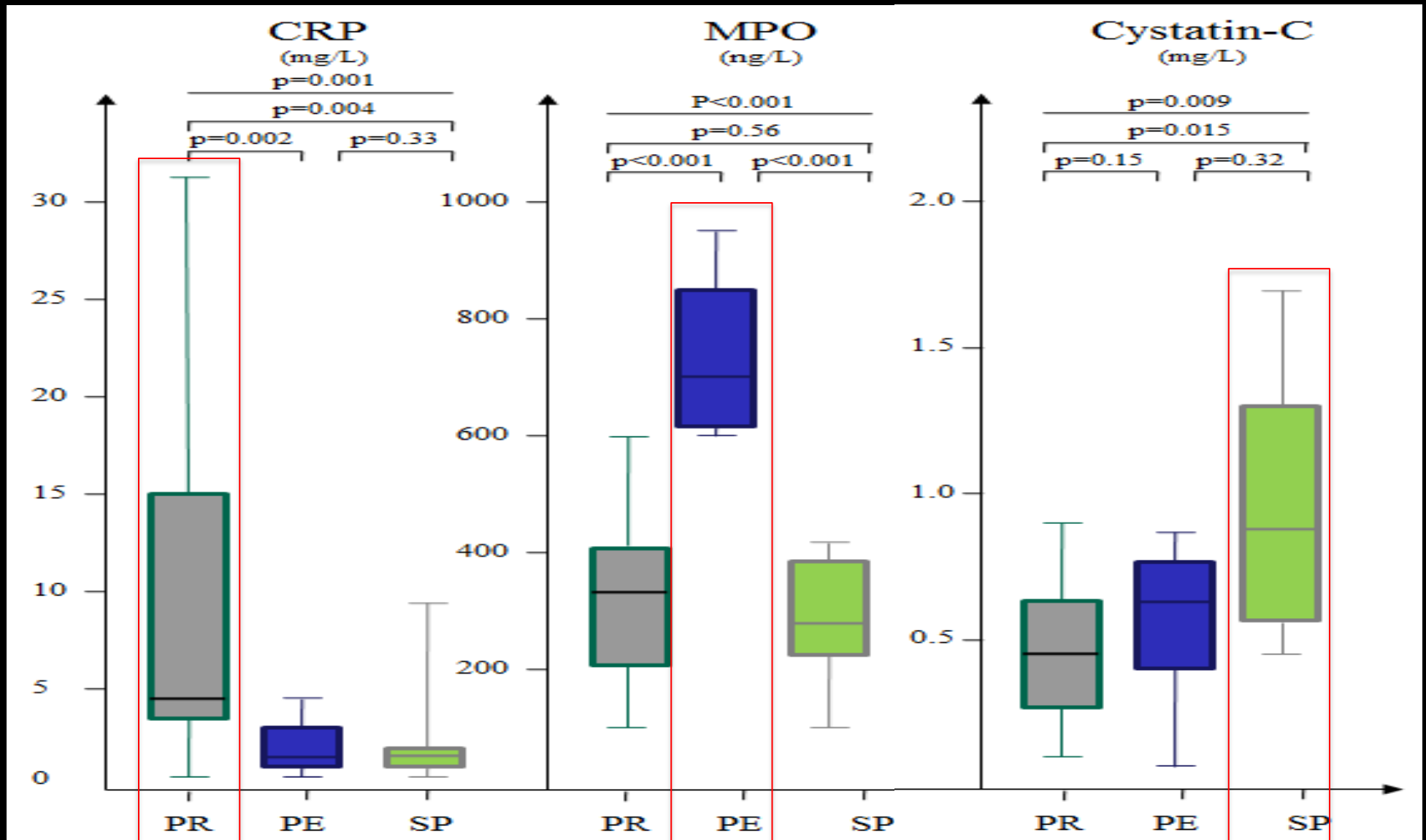
# Coronary microvascular dysfunction in Tako-tsubo syndrome

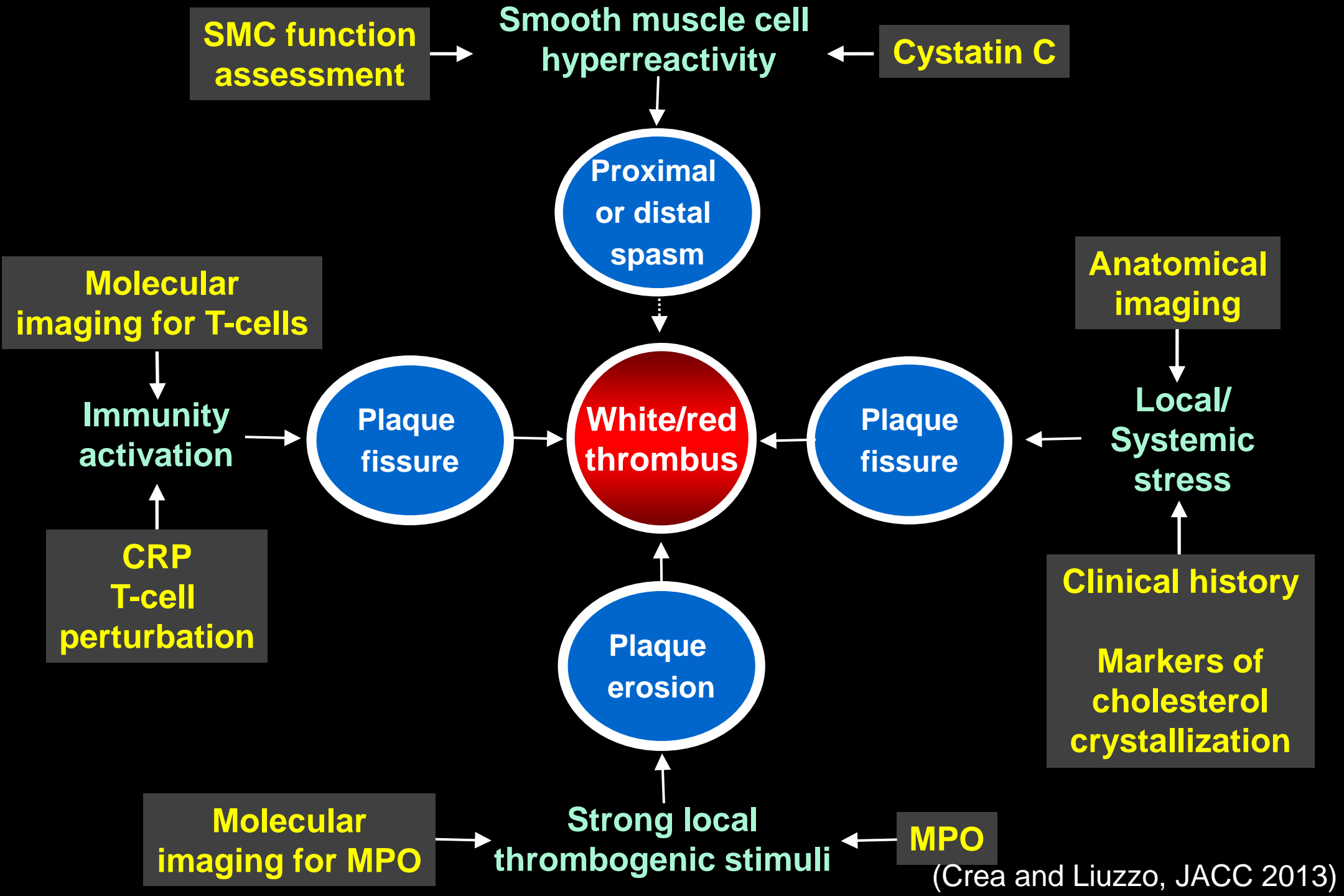




(Crea and Liuzzo, JACC 2013)

# Morpho-functional correlations in NSTE-ACS







# Targeting the mechanisms of ACS

**Plaque fissure with inflammation**

- **Methotrexate, IL-1 $\beta$  antagonists, Treg expansion, Vaccines**

**Plaque fissure without inflammation**

- **Statins**
- **Modulators of cholesterol crystallization**

**Plaque erosion**

- **Antithrombotics**

**SMC hyperreactivity**

- **Vasodilators**

**It is complex**

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