FFR,
Ischemia and Clinical Outcome

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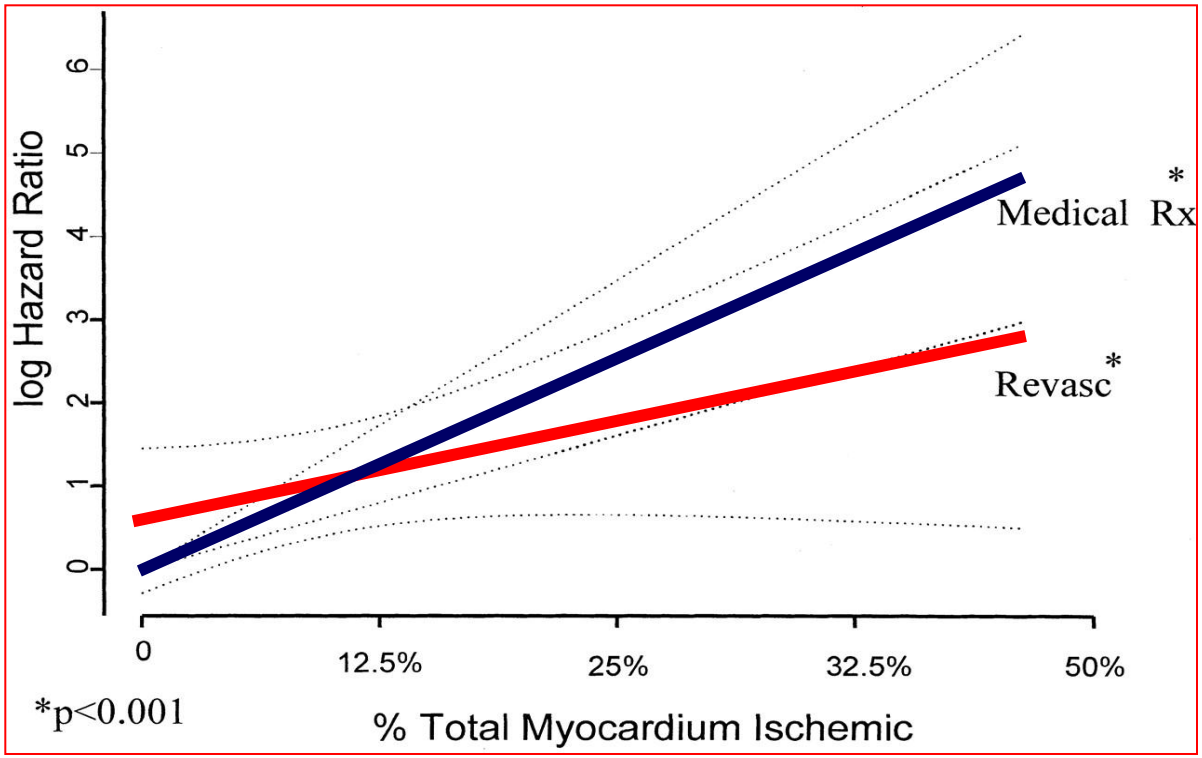
Is it important to detect ischemia ?

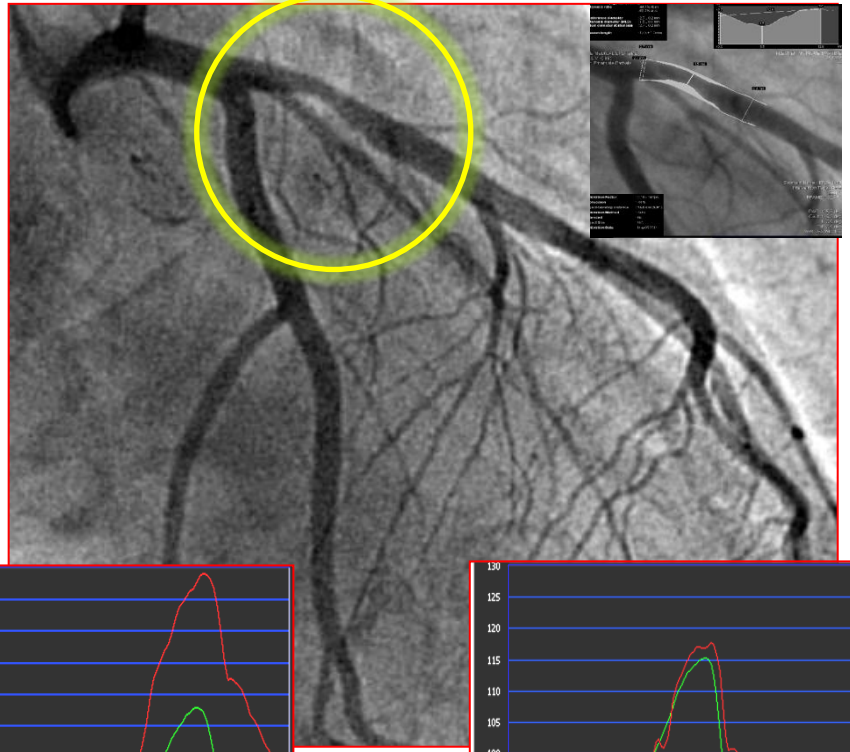
Log hazard ratio for revascularization (Revasc) vs medical therapy (Medical Rx) as a function of % myocardium ischemic based on final Cox proportional hazards model

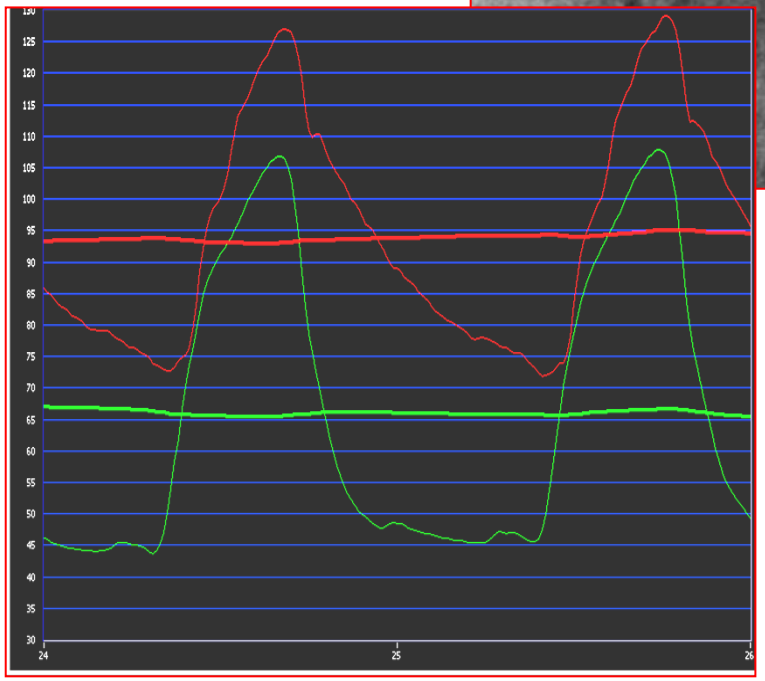


Above 10% ischemic myocardium, the survival benefit from revascularisation increases with the extent of ischemia

Hachamovitch, R. et al. Circulation 2003

FFR and Clinical Outcome





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Factors that Contribute to Abrupt Coronary Occlusion

1. Blood/Platelets/… (Biochemistery/Cytology)

2. Histopathology of the wall (Histology)

3. Hemodynamic factors (Physics)

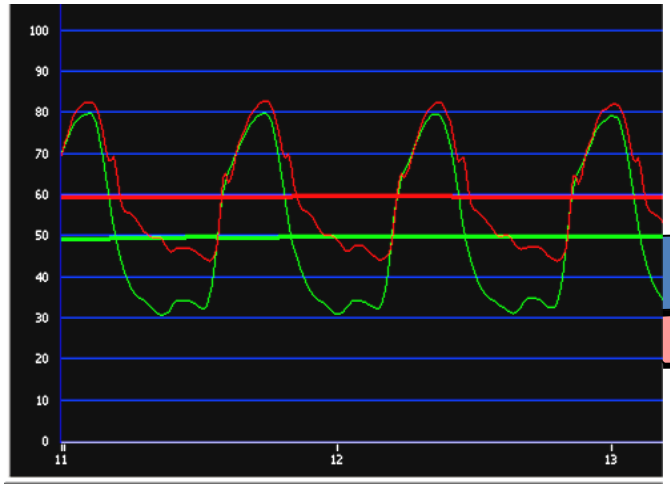
- *Plaque stress*
- *Venturi effect*
- *Vasa vasorum*
- *Shear stress*
- *Cholesterol crystal*
- *Exercise...*

Mechanical constraints on coronary stenoses

- **Plaque stress**

Mechanical constraints on coronary stenoses

40.000.000 / year



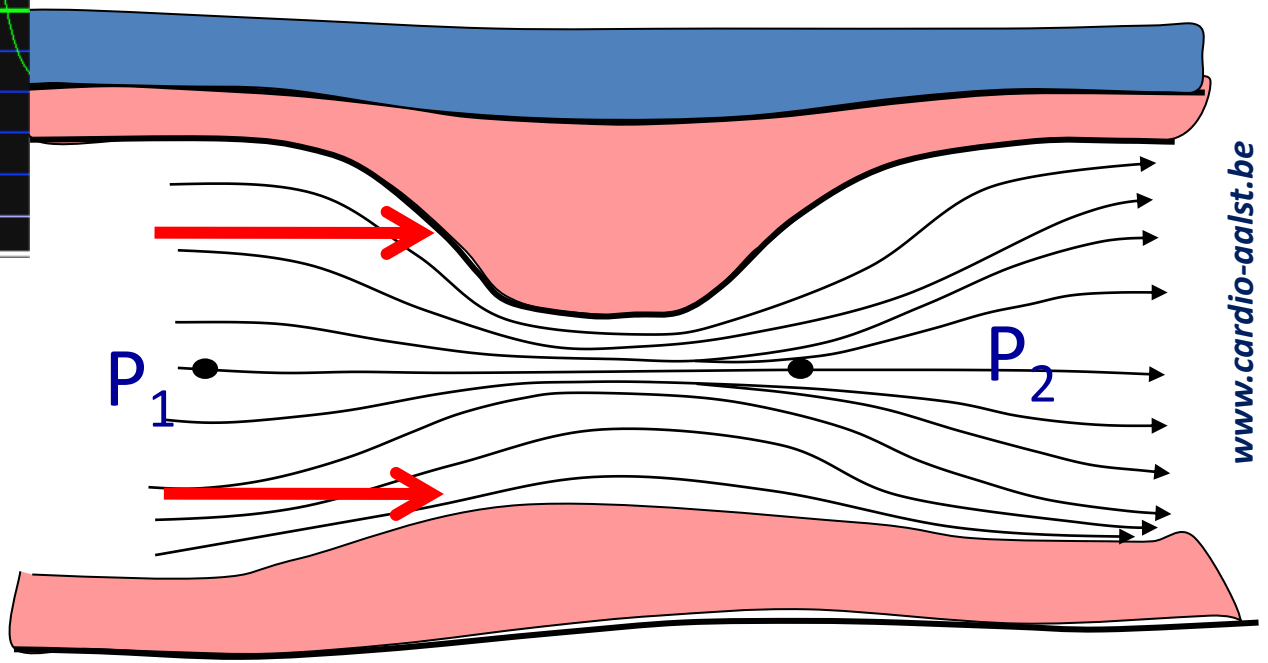
Pressure wave

↓

Slicing forces

↓

Plaque fatigue



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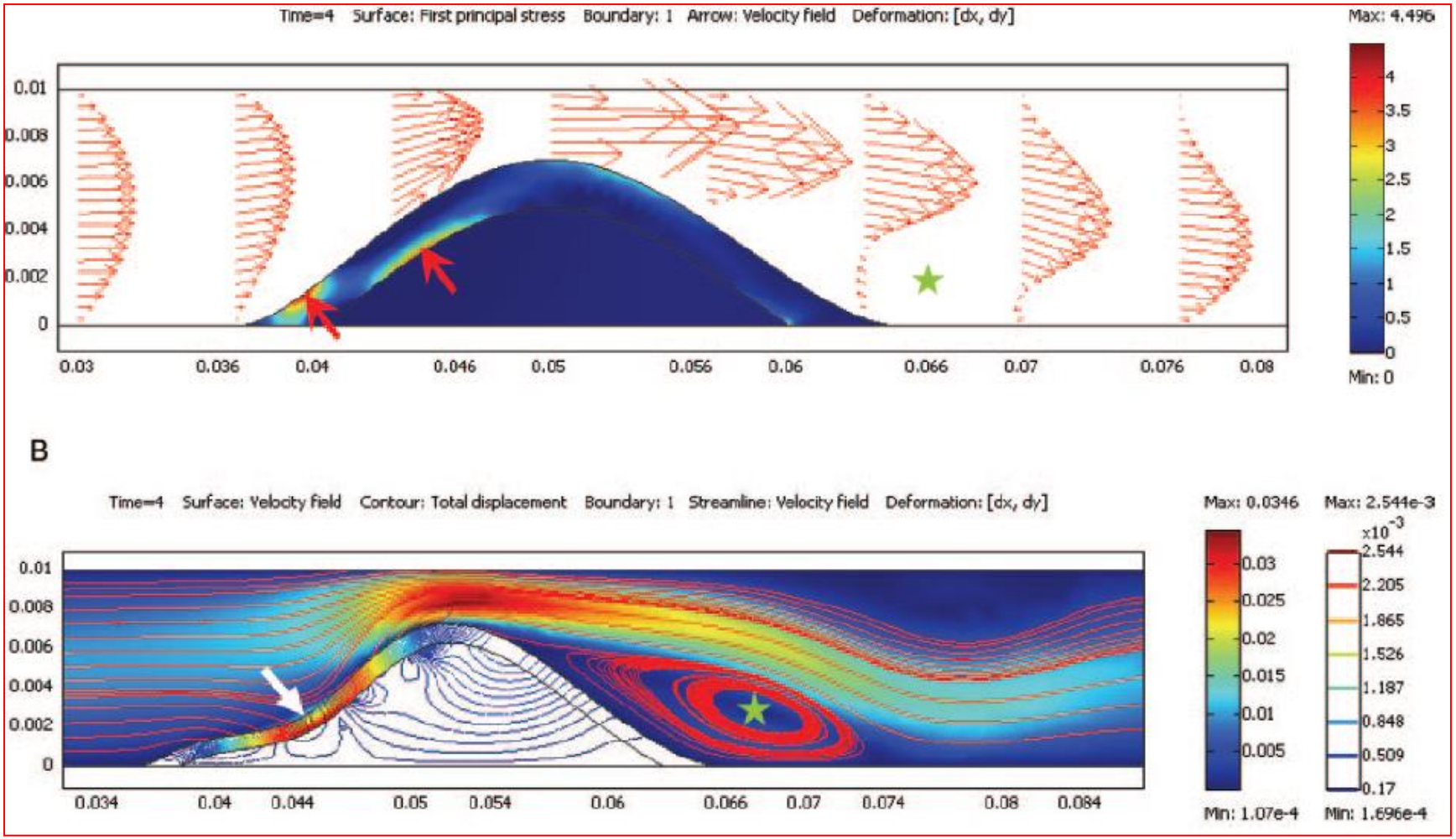
Computational Flow Dynamics
Plaque Stress and Strain Distribution



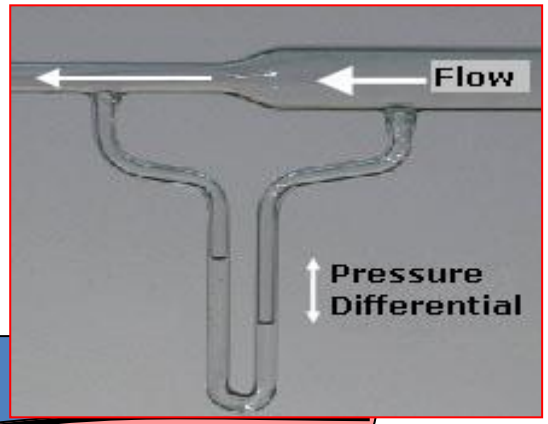
Li Y.Z. et al Stroke 2006

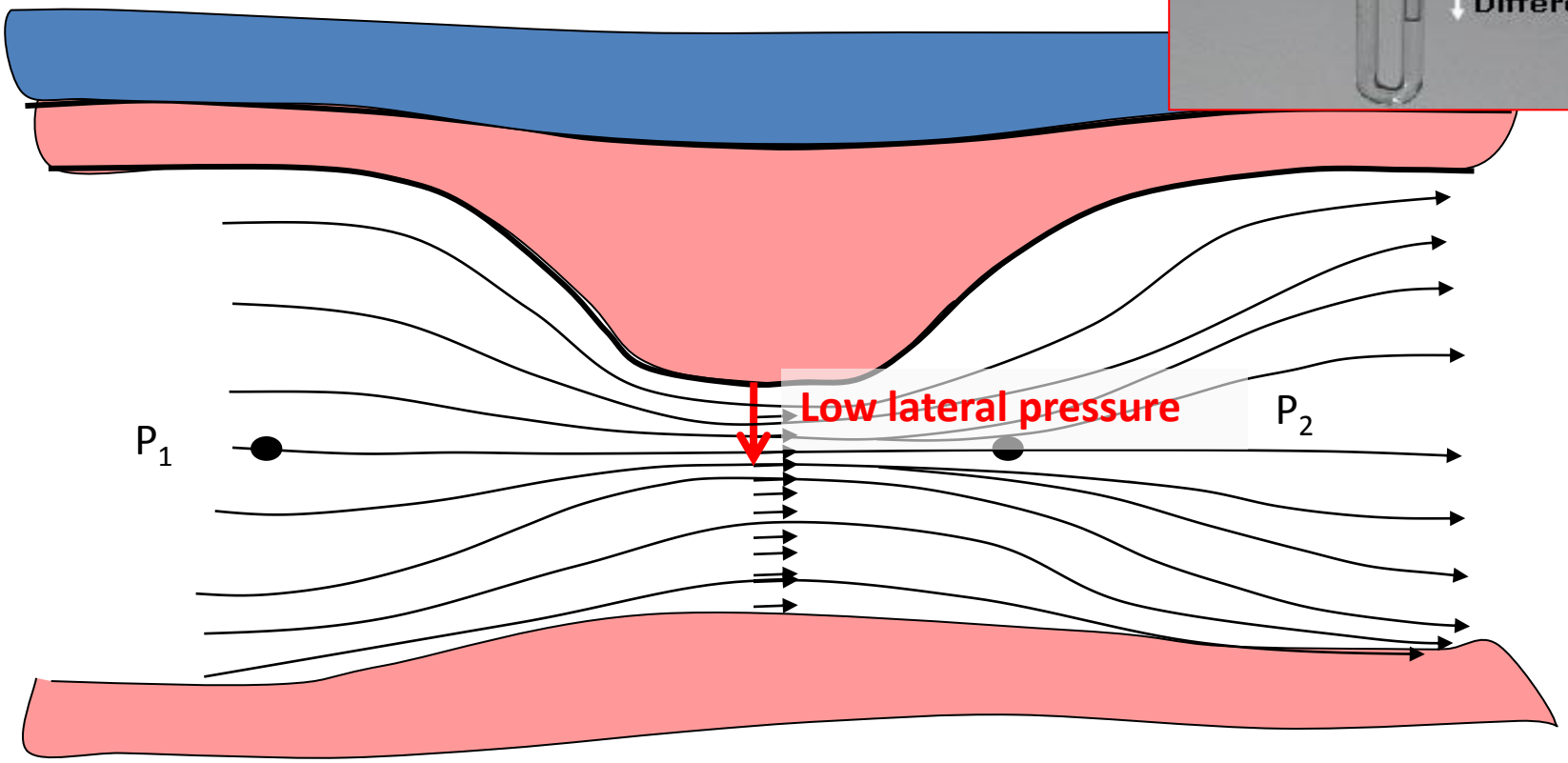
Mechanical constraints on coronary stenoses

- Plaque stress
- **Venturi Effect**

Mechanical constraints on coronary stenoses

Decreased lateral pressure (Venturi Effect)

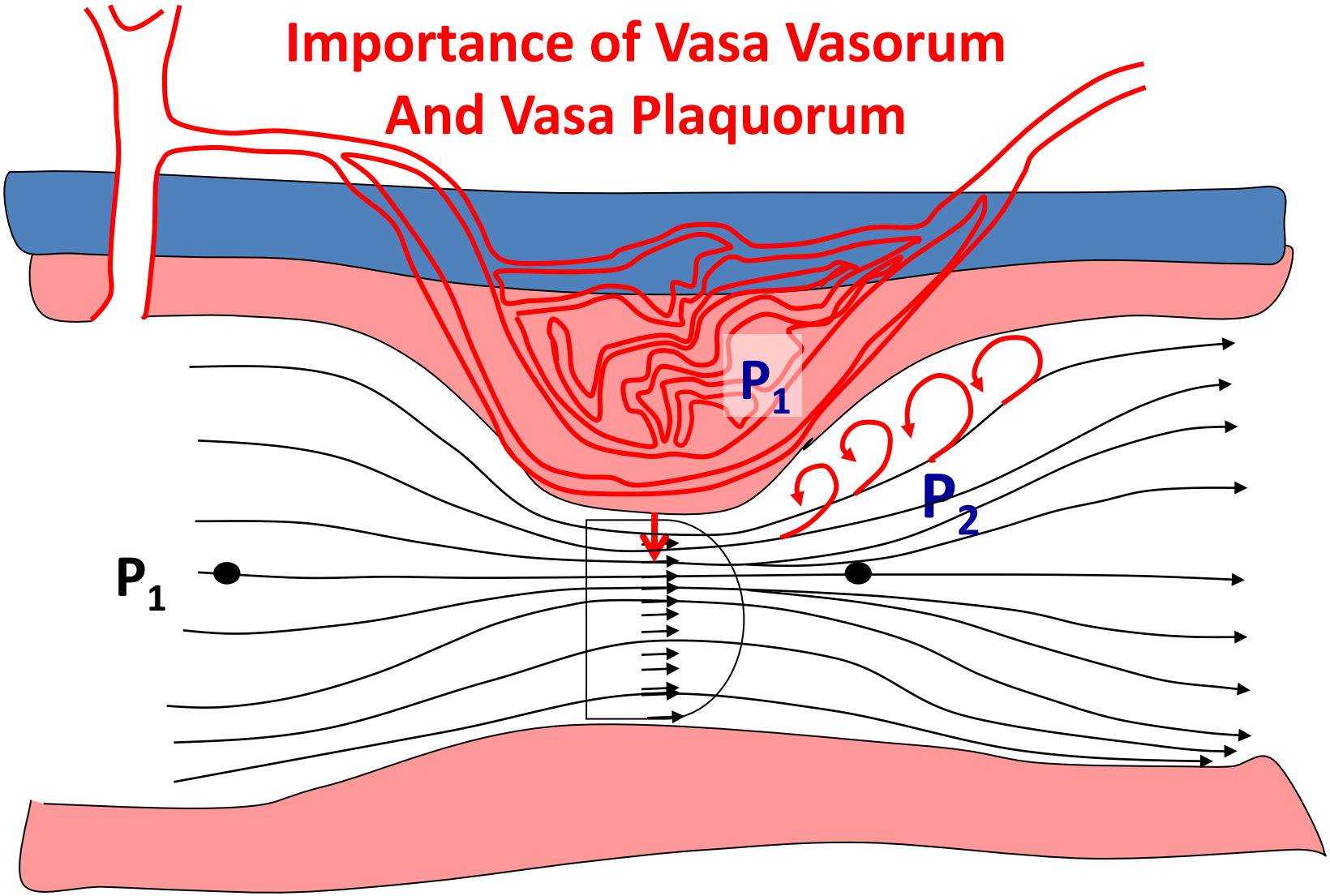




Mechanical constraints on coronary stenoses

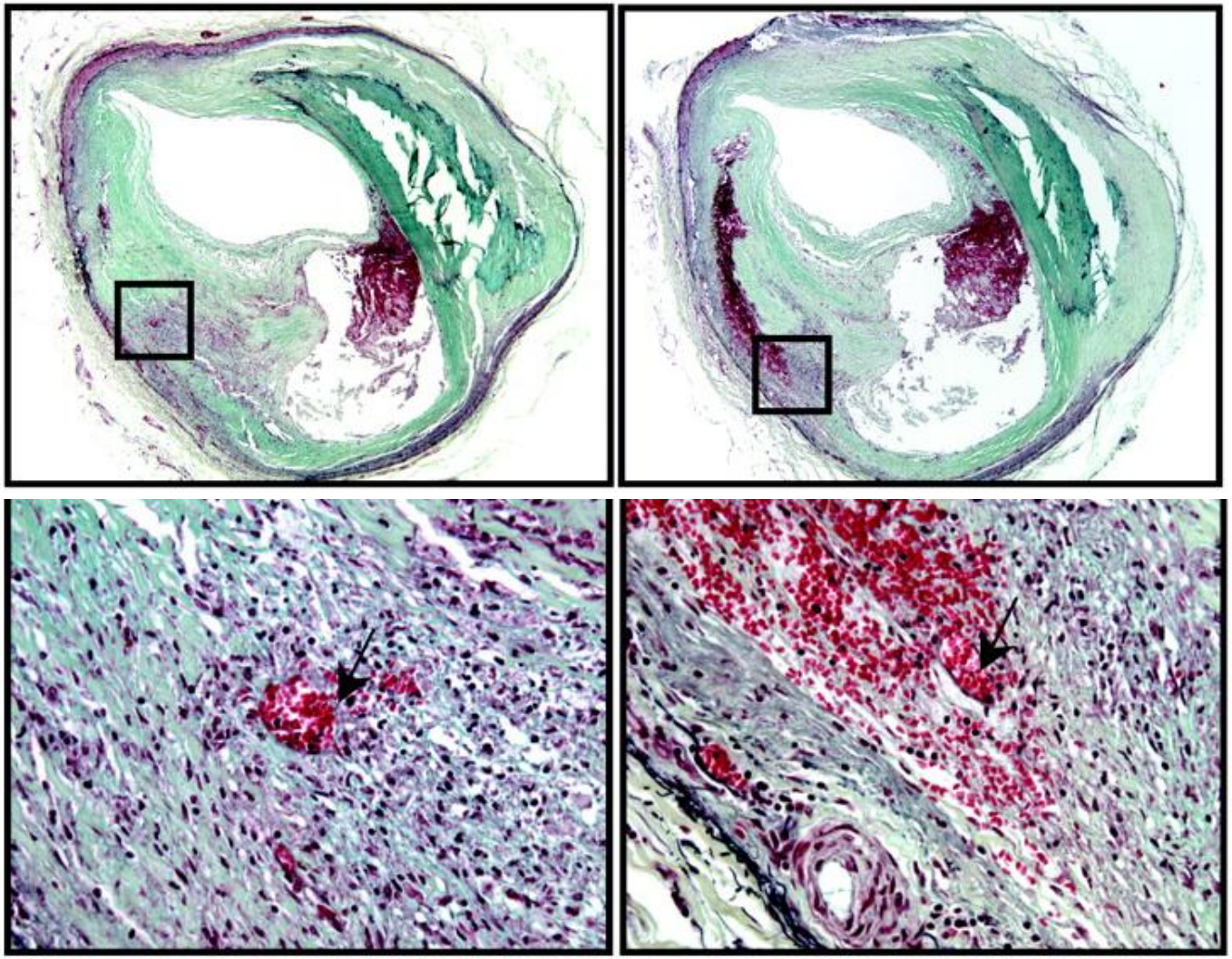
- Plaque stress
- Venturi Effect
- **Vasa Vasorum**

Mechanical constraints on coronary stenoses



Paterson JC , J Occupational Medicine 1961

Recent intraplaque hemorrhage in a thin-cap fibroatheroma



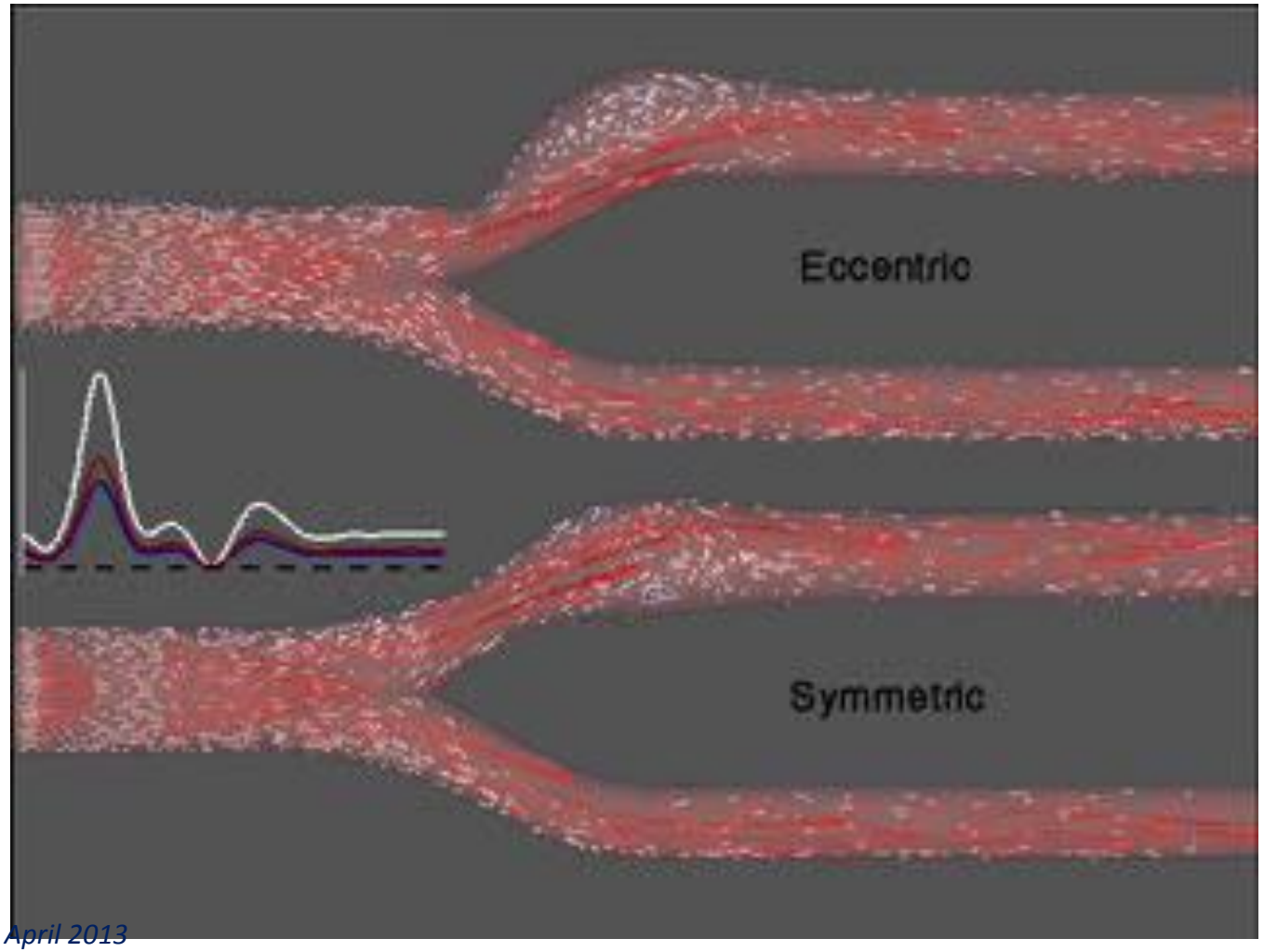
Virmani, R. et al. Arterioscler Thromb Vasc Biol 2005

Mechanical constraints on coronary stenoses

- Plaque stress
- Venturi Effect
- Vasa Vasora
- **Shear stress**

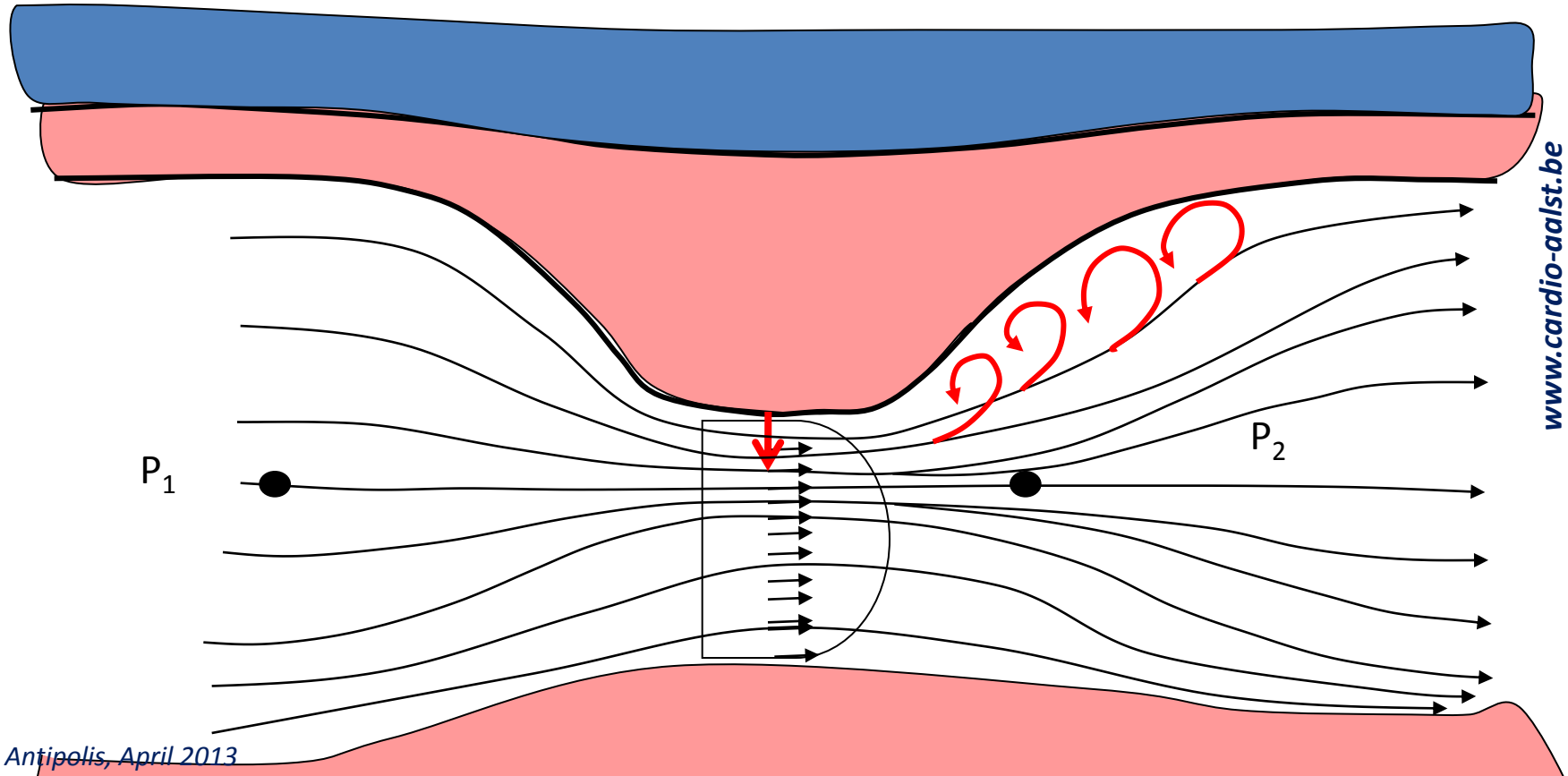
Mechanical constraints on coronary stenoses

Turbulences = unfavorable rheologic conditions



Mechanical constraints on coronary stenoses

Turbulences = unfavorable rheologic conditions



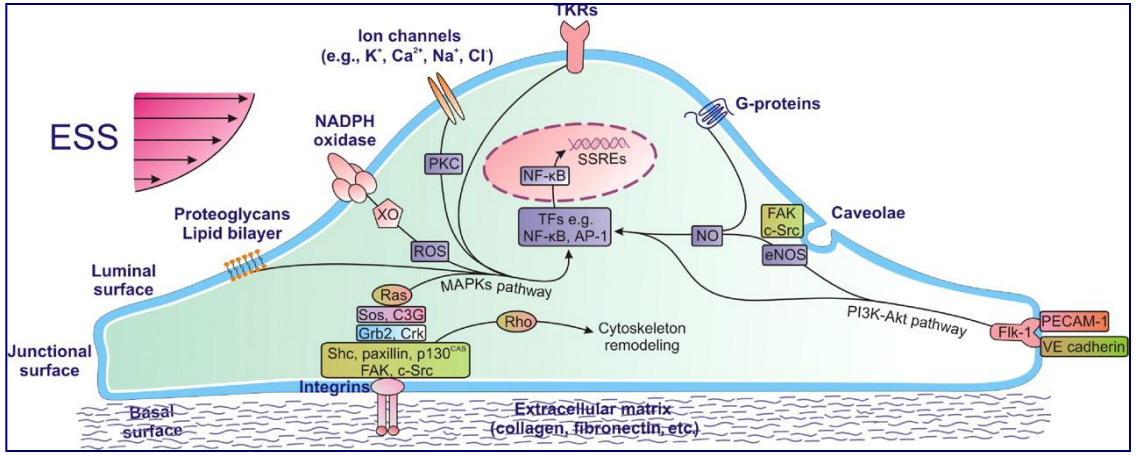
Cross-talks between rheology and biology

Influence of Endothelial Shear Stress on Plaque Progression

Normal

High Endothelial Shear Stress

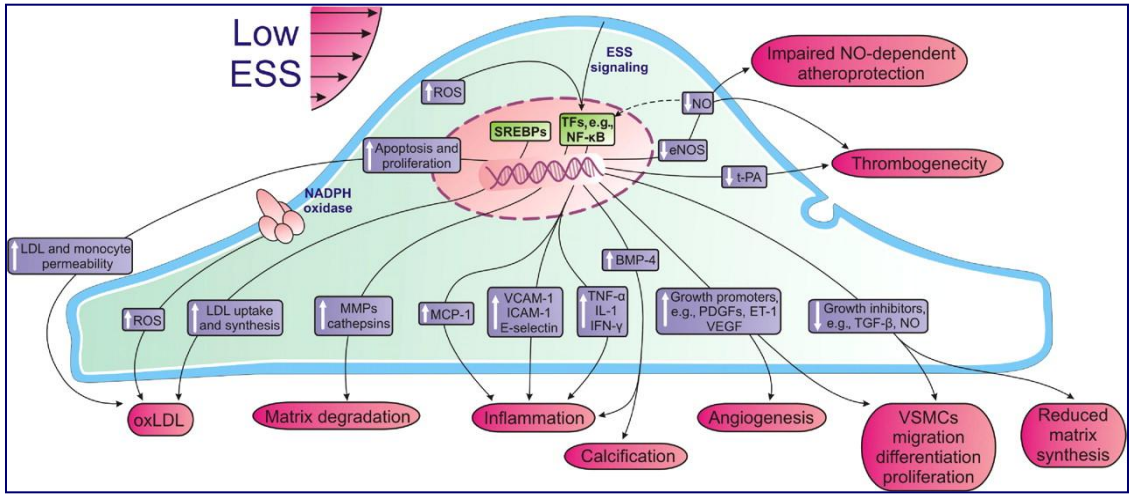
- Vasodilation
- ↓ platelet aggregation



Stenosis

Low Endothelial Shear Stress

- Vasoconstriction
- ↑ platelet aggregation
- matrix degradation
- inflammation
- SMC proliferation



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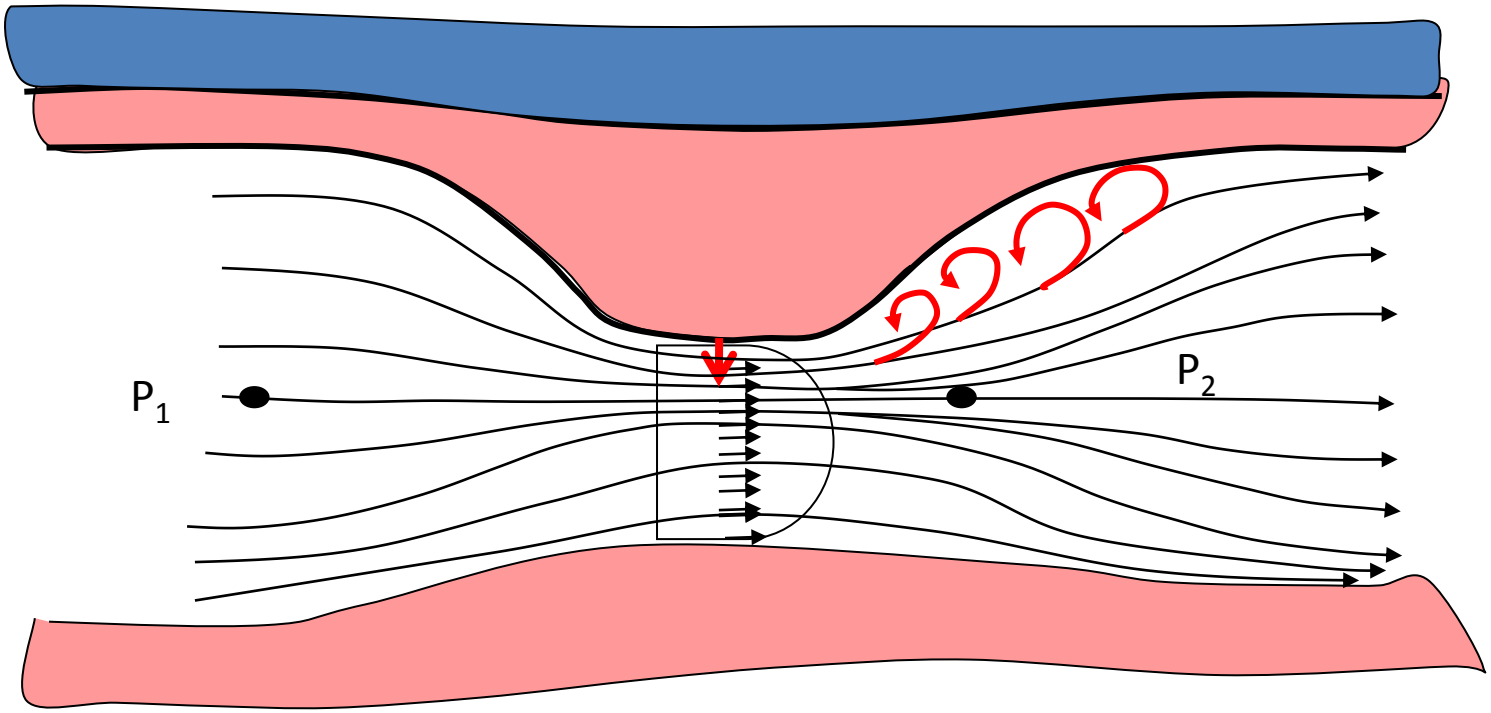
Chatzizisis et al JACC 2007;49:2379

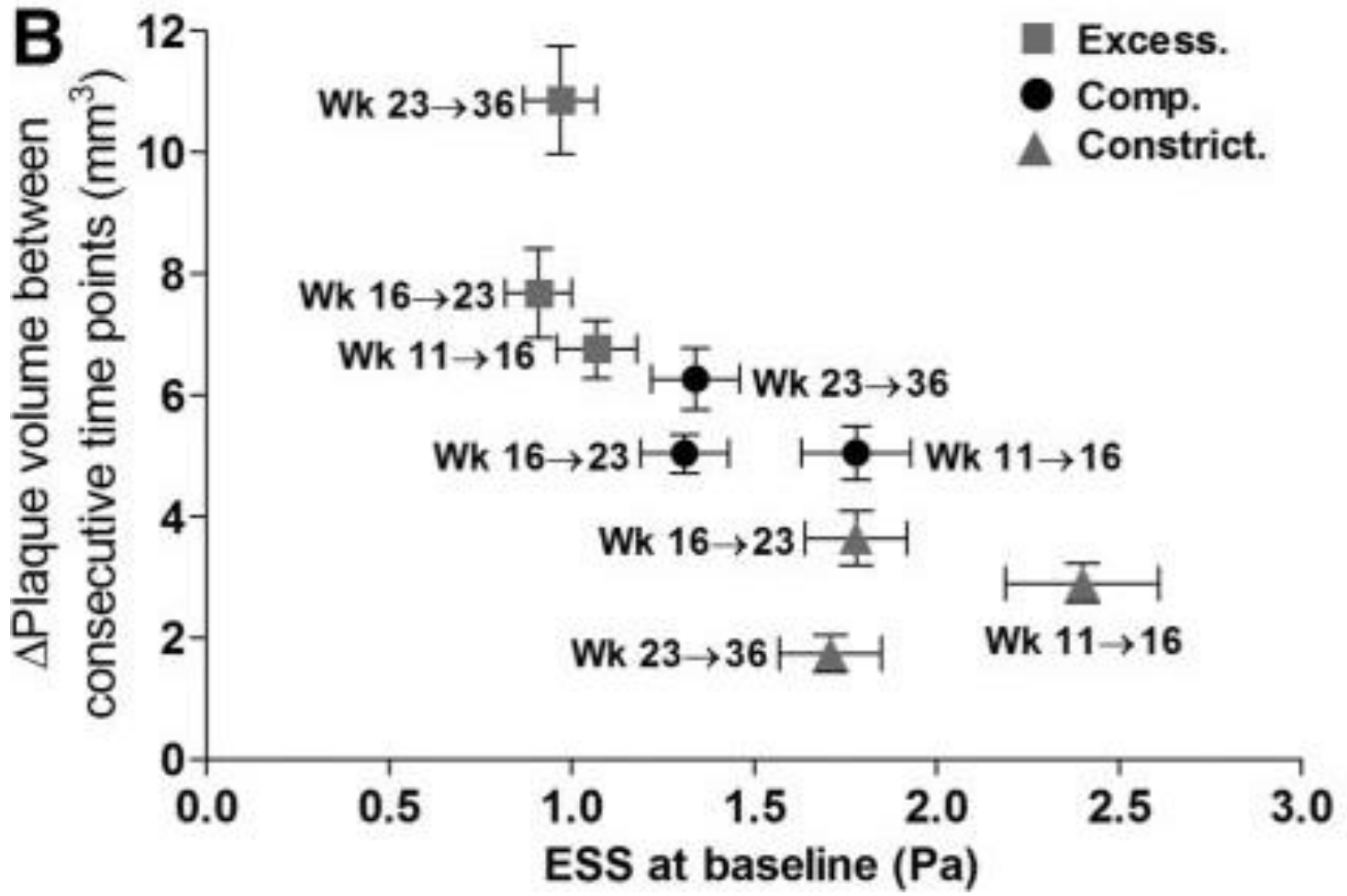
Mechanical constraints on coronary stenoses

Acceleration/deceleration/turbulences = unfavorable rheologic conditions



- Low endothelial shear stress ➔ Pro-atherogenic
- High blood shear stress ➔ Pro-thrombogenic

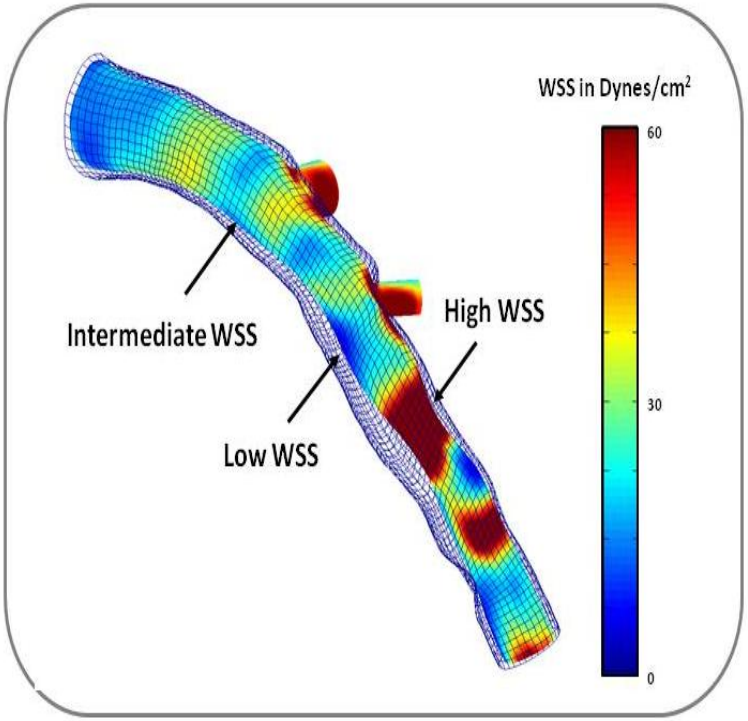
Cross-talks between rheology and biology

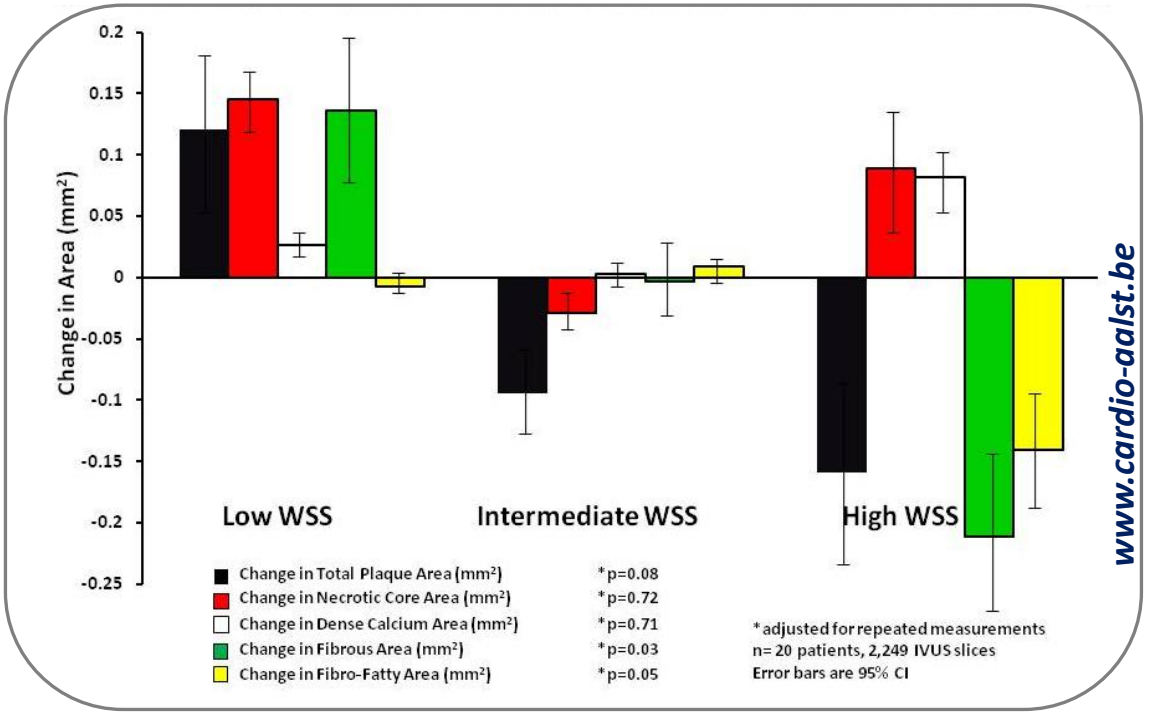


Koskinas KC et al Circulation May 2010

Low Coronary Wall Shear Stress is Associated with Plaque Progression and High Wall Shear Stress with Plaque Transformation in Patients with CAD

N= 20 pts, with CAD with baseline and 6 month follow up evaluation

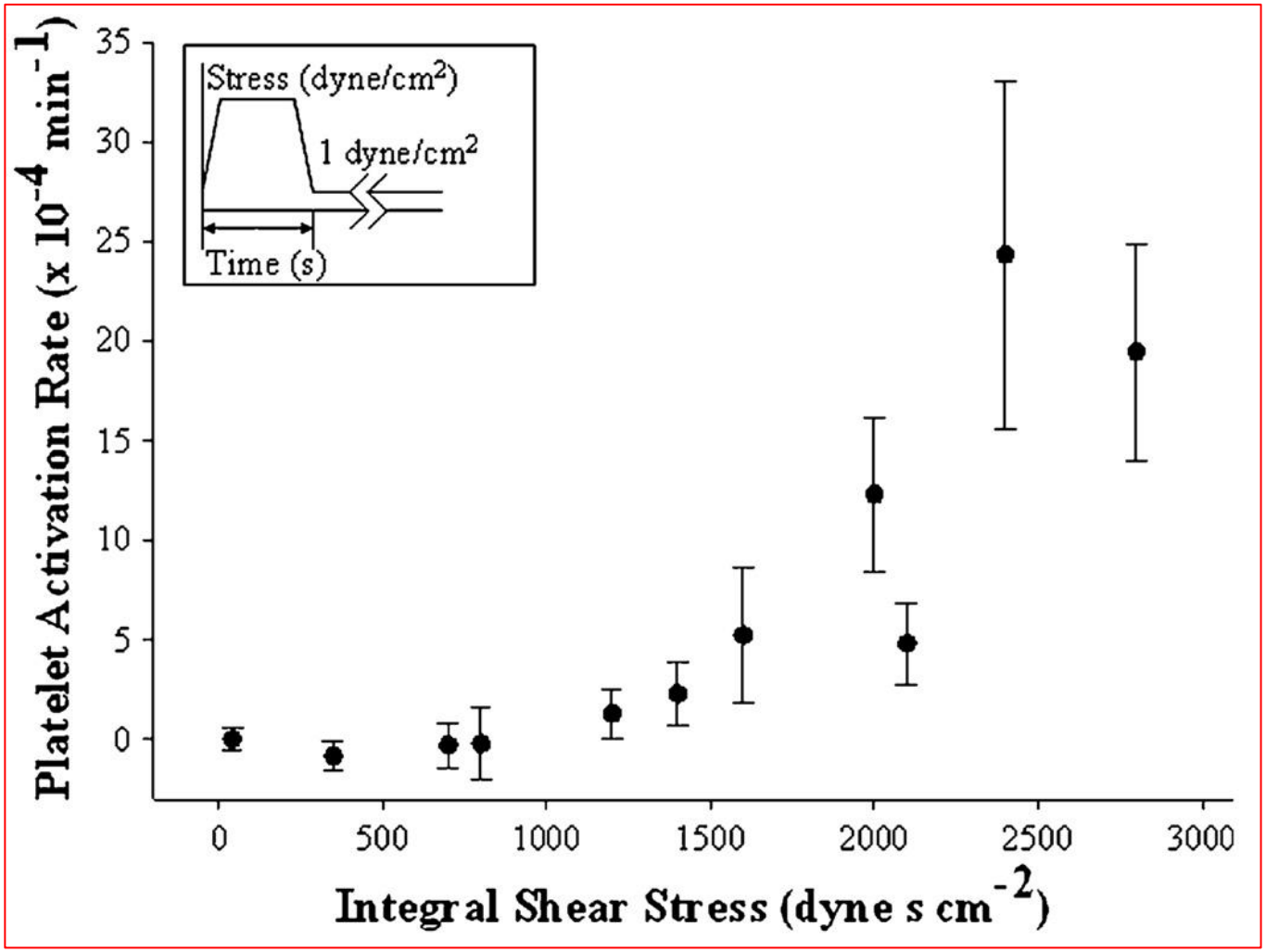




Samady H et al Circulation 2011

Cross-talks between rheology and biology

Influence of Shear Stress on Platelet Activations

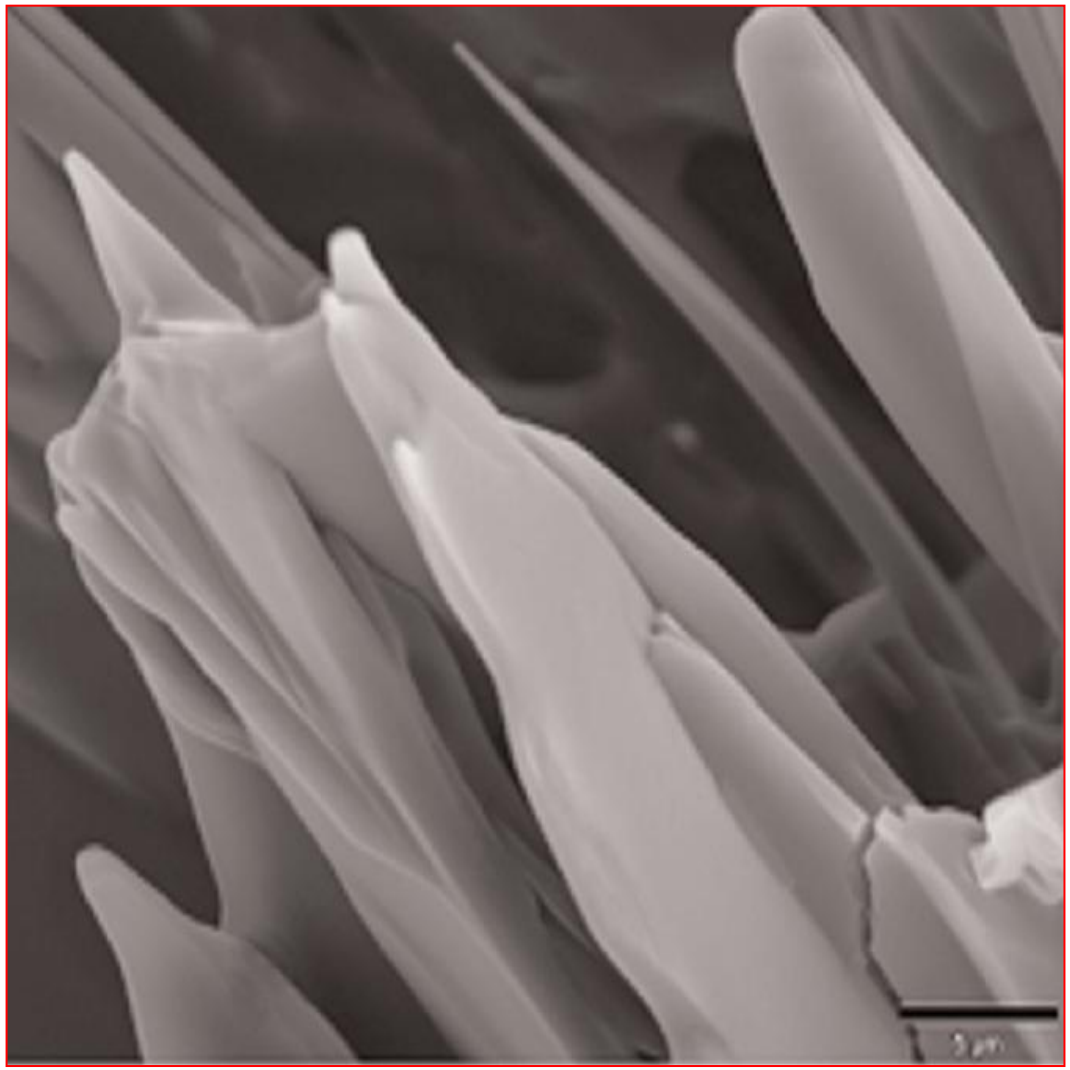


Sheriff J et al Ann Biomed Eng. 2010;38(4):1442-50

Mechanical constraints on coronary stenoses

- Plaque stress
- Venturi Effect
- Vasa Vasora
- Shear stress
- **Cholesterol Crystals**

Physical Factors Trigger Crystallization and Volume Expansion of Intraplaque Cholesterol



Crystallization and Volume increase with

- ↘ Temperature
- ↗ pH
- ↗ Hydration
- ↗ Pressure (“very likely”)

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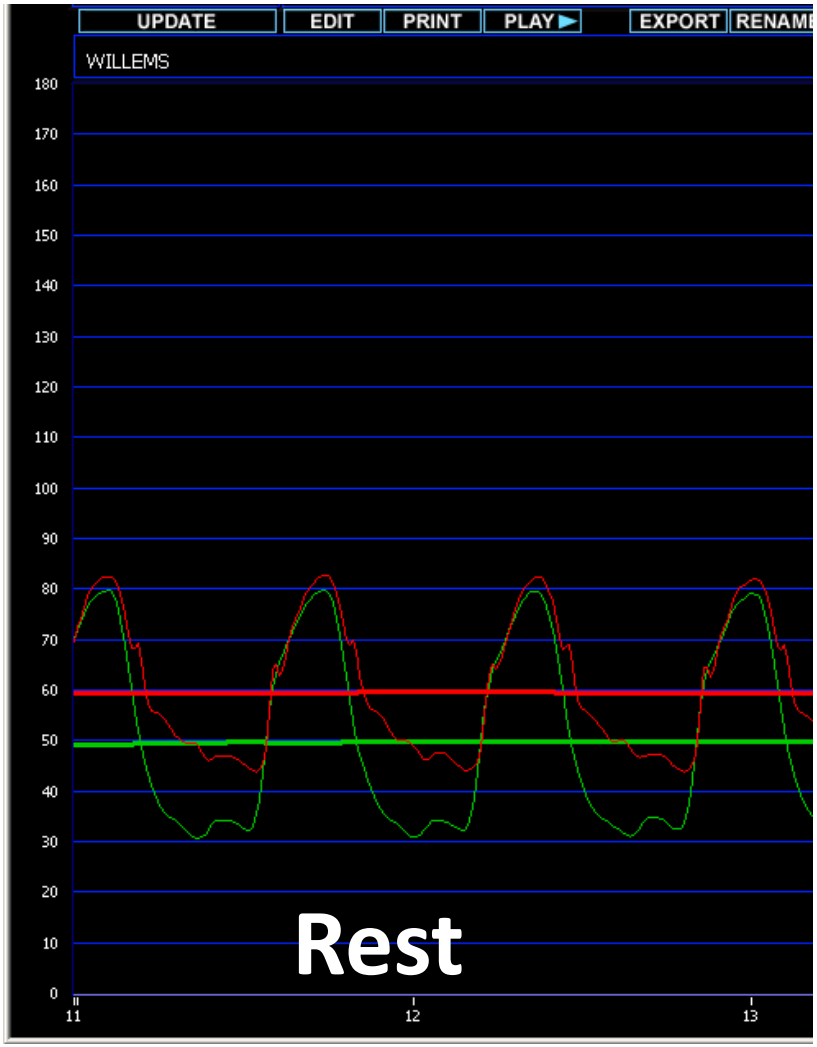
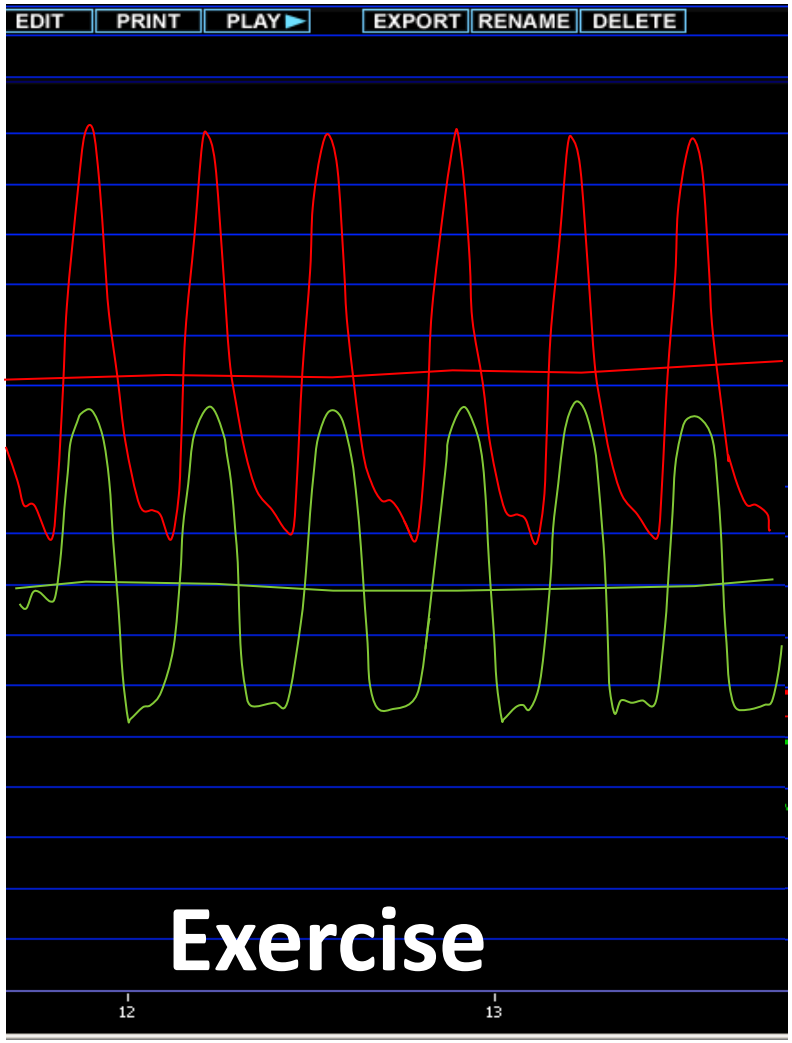
Abela GS et al Am J Cardiol 2011;107:1710

Mechanical constraints on coronary stenoses

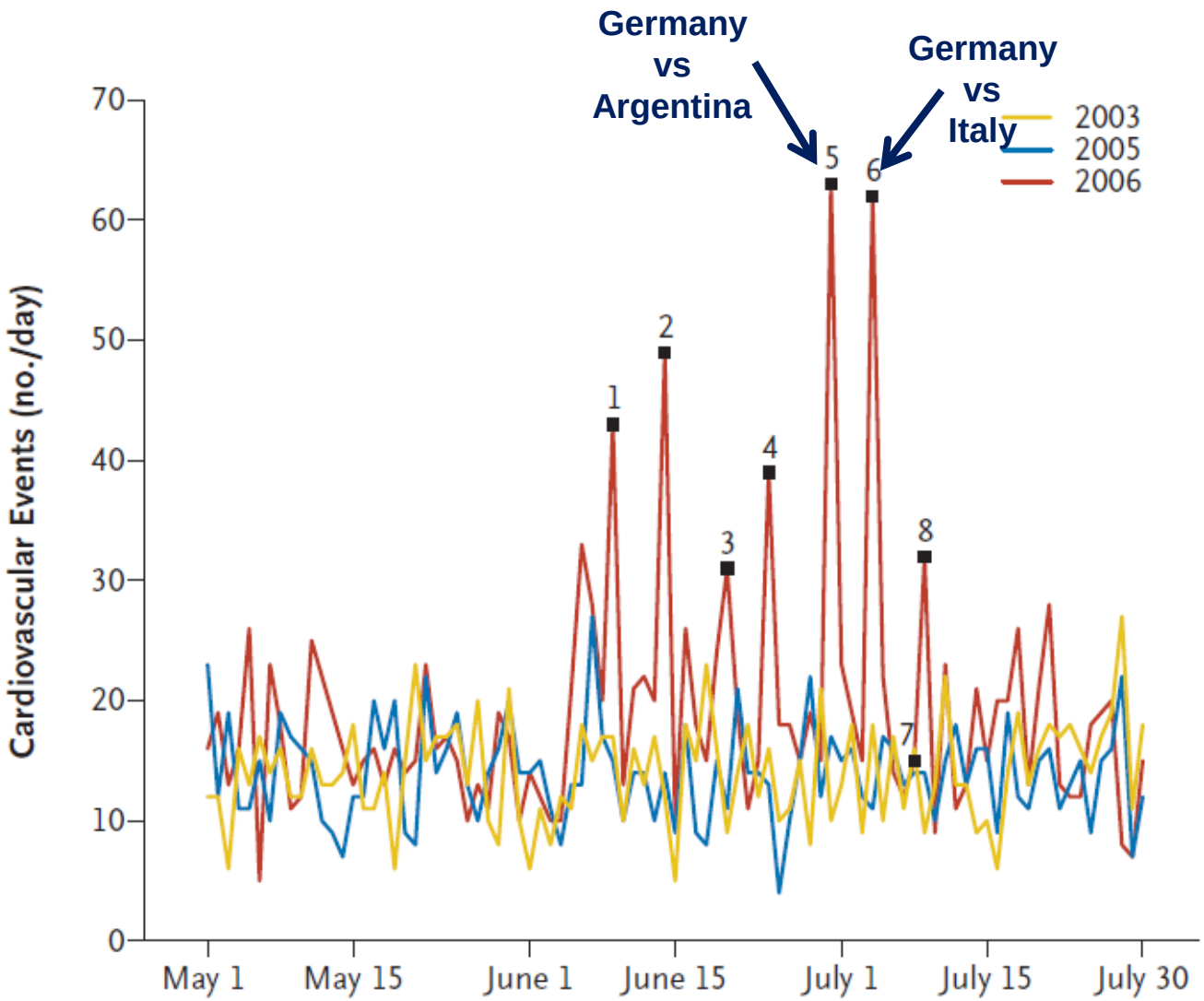
- Plaque stress
- Venturi Effect
- Vasa Vasora
- Shear stress
- Cholesterol Crystals
- **Physical exercise**

Mechanical constraints on coronary stenoses
Effect of Physical Exercise





Mechanical constraints on coronary stenoses
Effect of WATCHING Football Matches



Wilbert-Lampen U, N Engl J Med 2008

Mechanical constraints on coronary stenoses

~~Pressure gradient~~

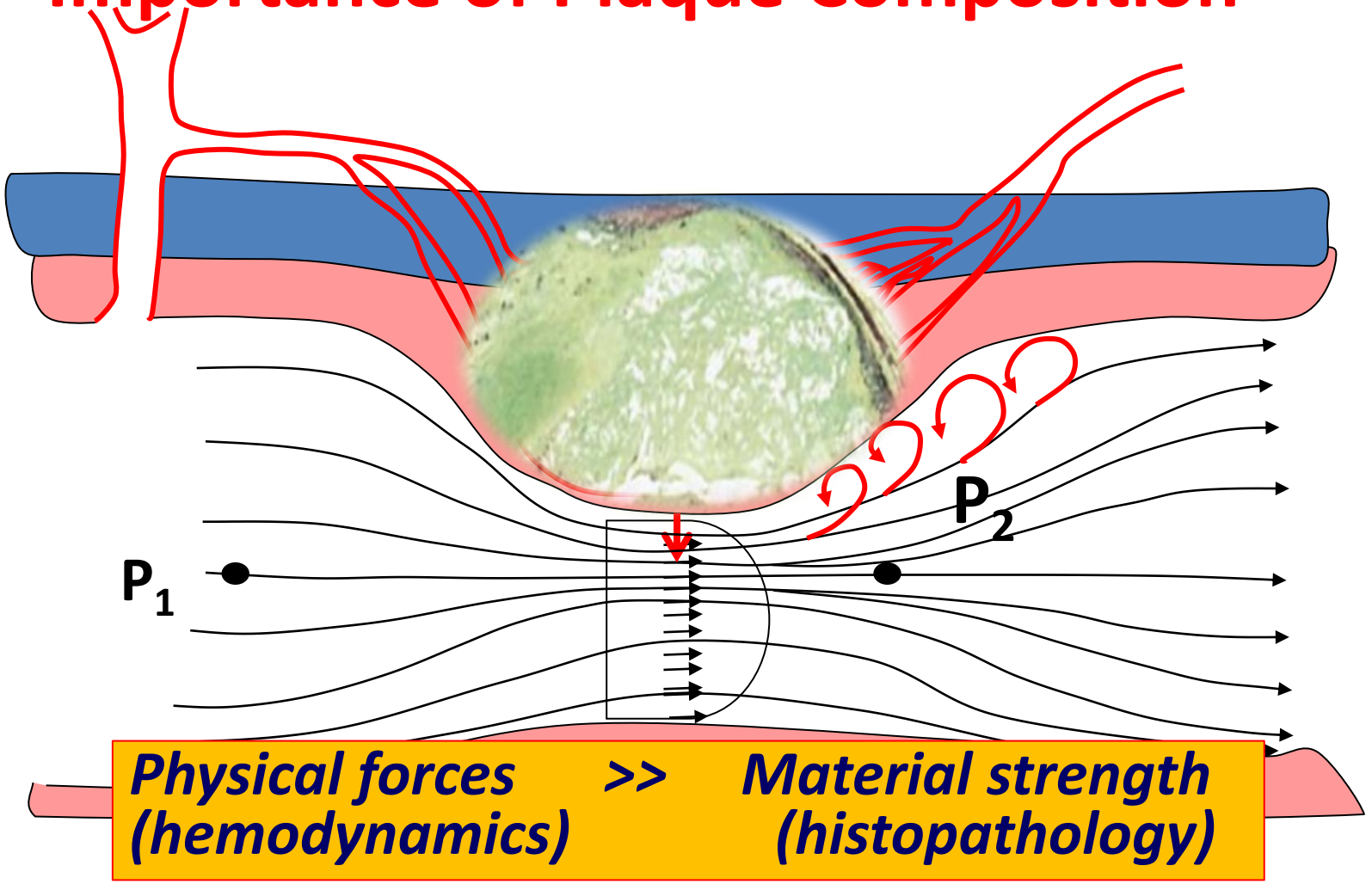
- ~~Slicing forces → plaque fatigue~~
- ~~High flow velocities → Venturi Effect~~
- ~~Turbulences → low shear stress~~
- ~~Vasa Vasorum → gradient in/out~~

~~Plaque Rupture~~
~~(Especially when Thin Cap Fibro Atheroma)~~

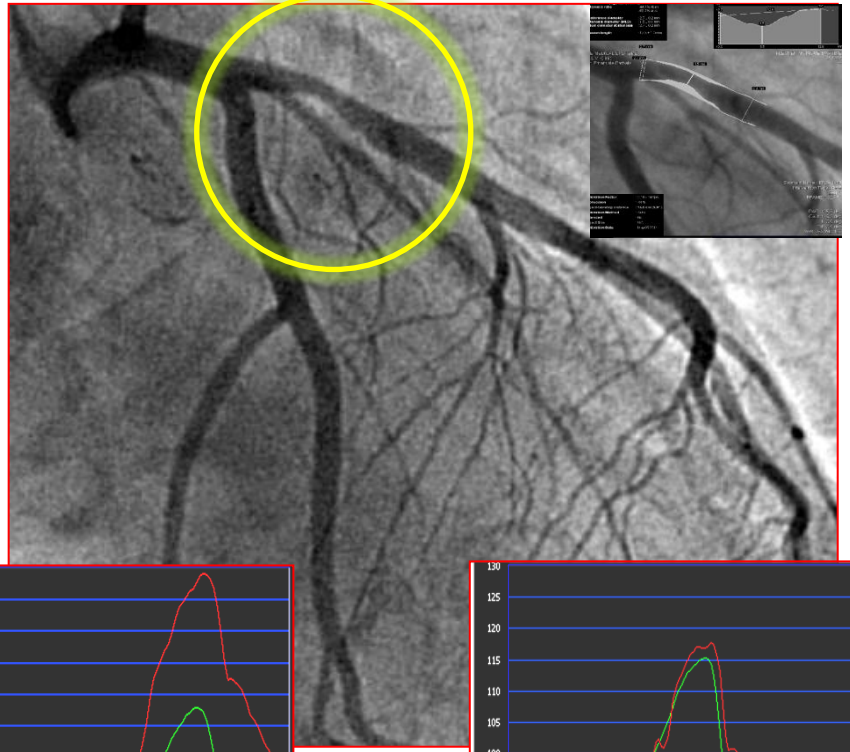
Mechanical constraints on coronary stenoses

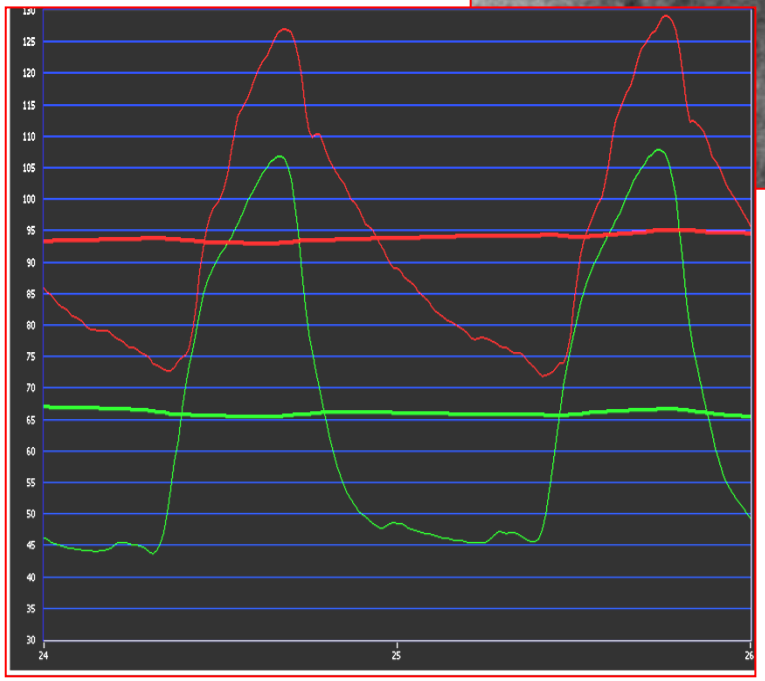
Plaque Rupture

Importance of Plaque Composition



FFR and Clinical Outcome





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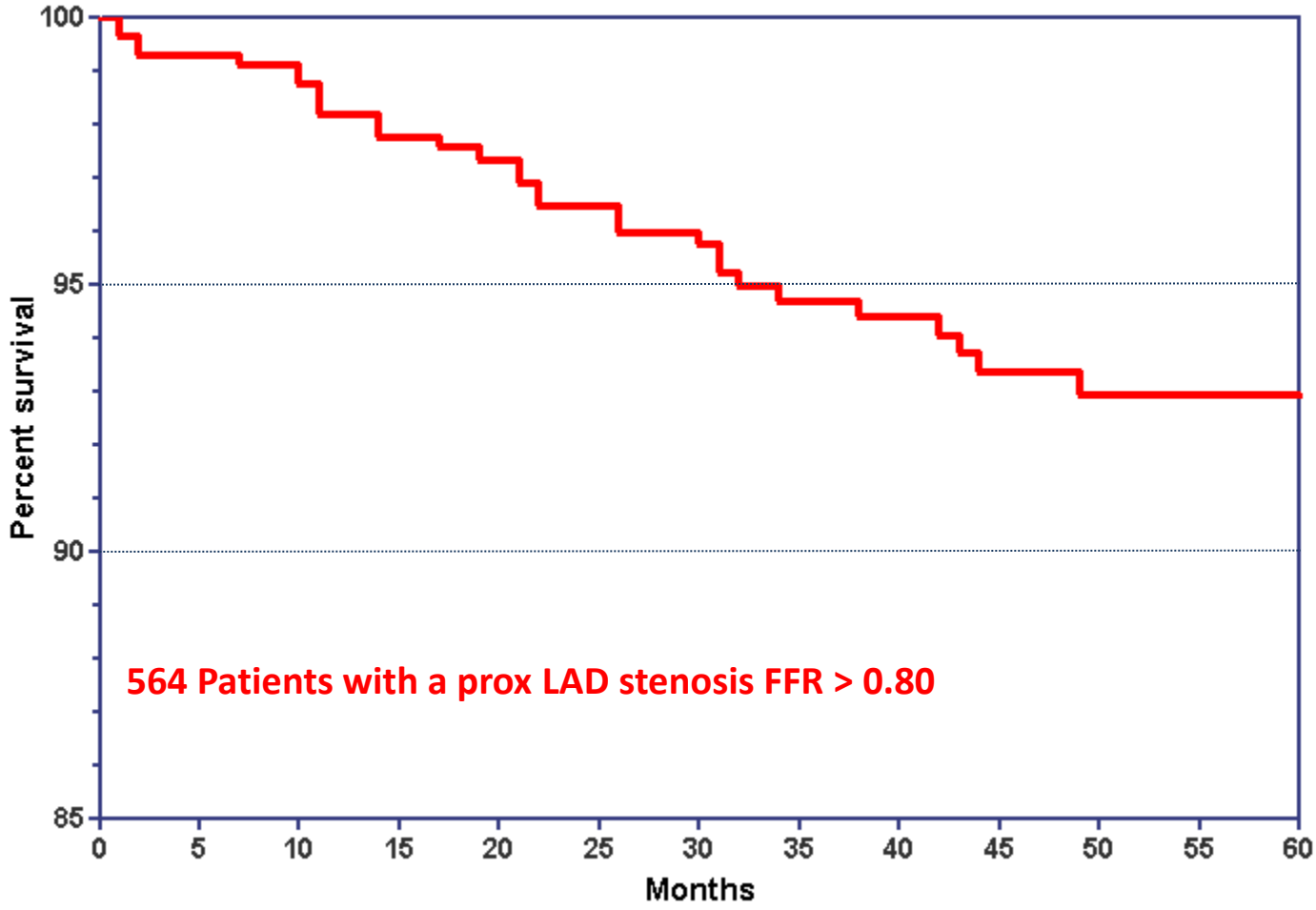
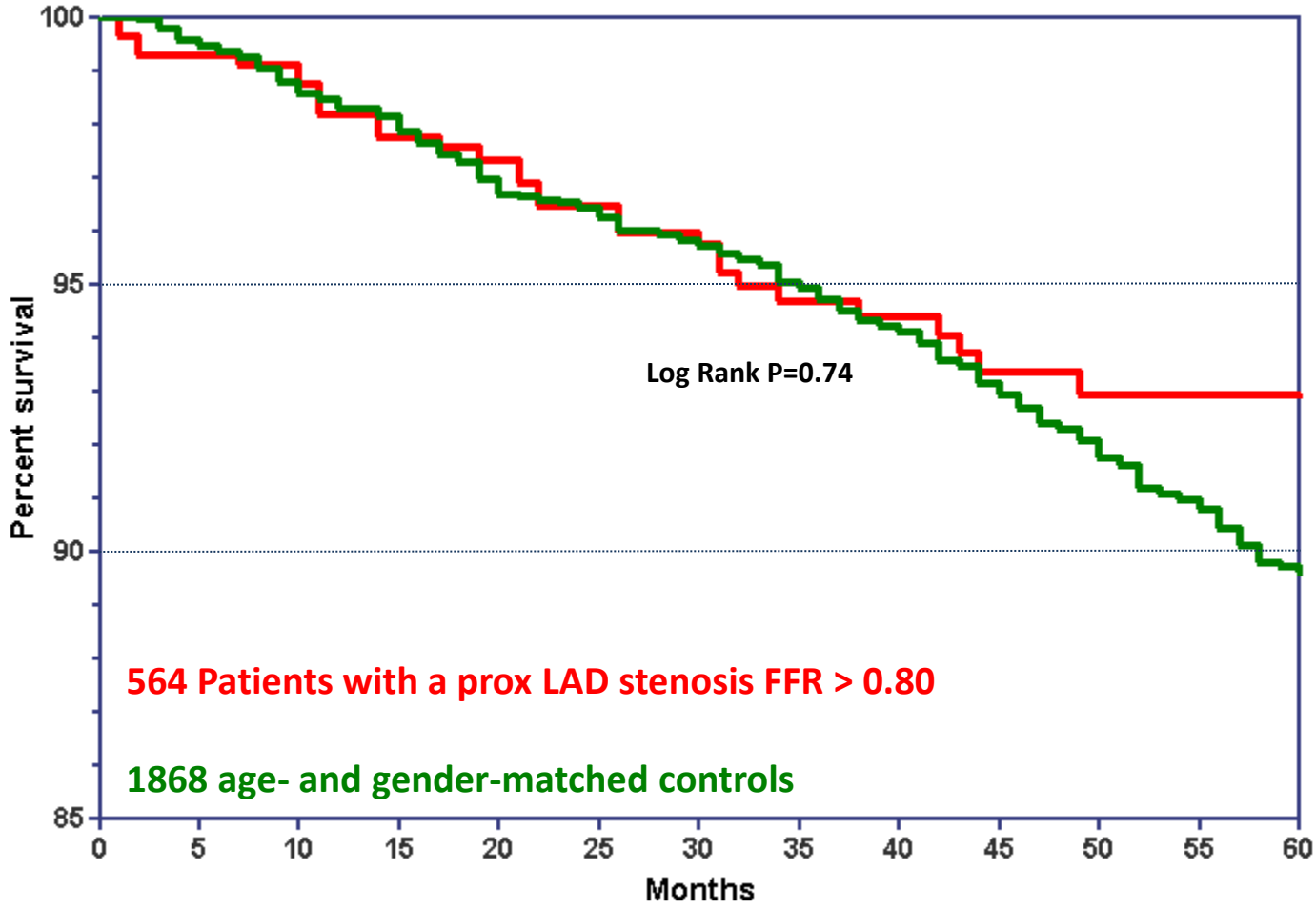
What is the Fate of Mild Stenoses ?

Proximal LAD Stenoses



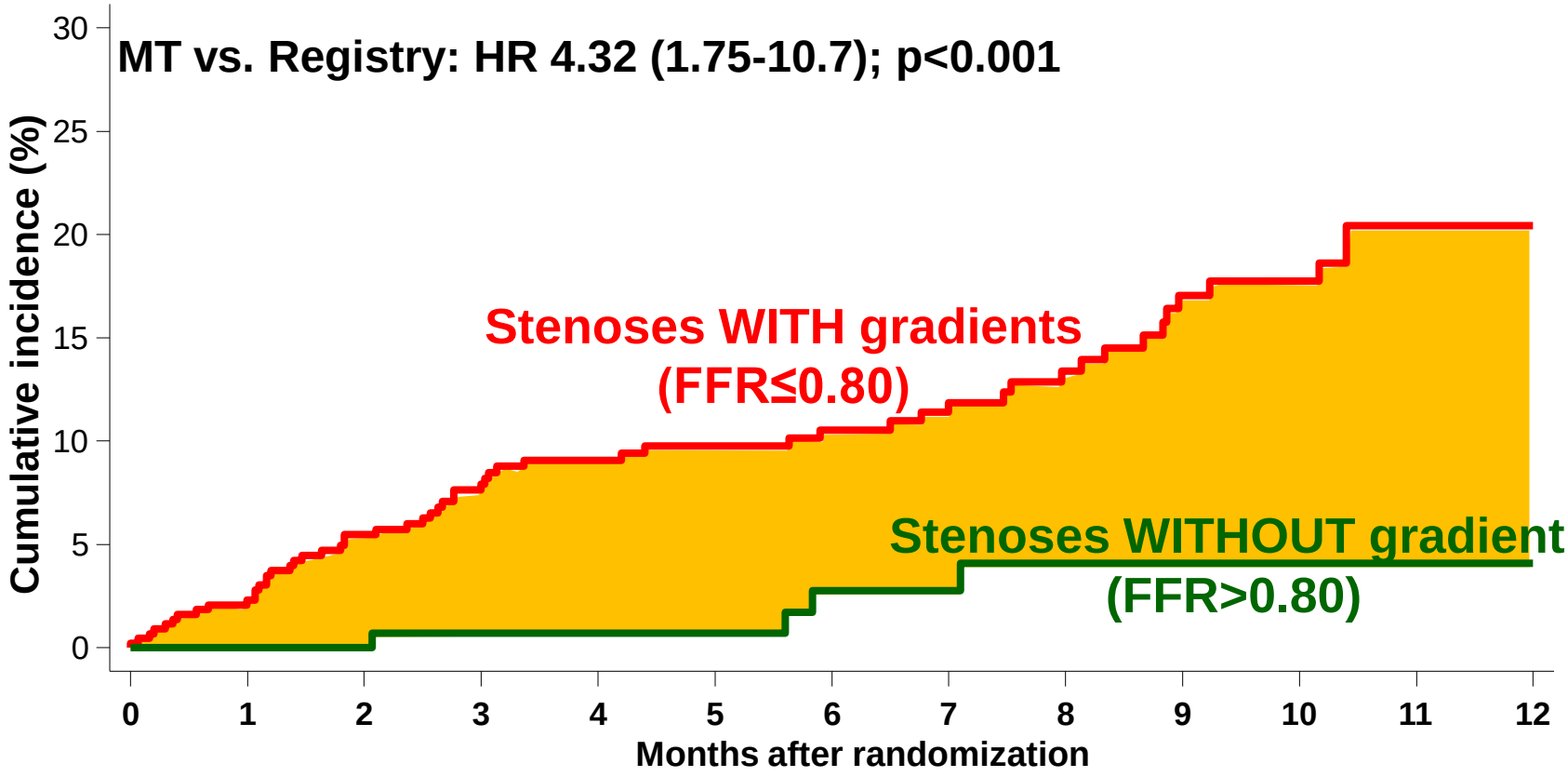
Muller O. et al. JACC Interv 2011

Proximal LAD Stenoses



Muller O. et al. JACC Interv 2011

FAME 2 Trial
Primary Outcomes



No. at risk

MT	441	414	370	322	283	253	220	192	162	127	100	70	37
PCI+MT	447	414	388	351	308	277	243	212	175	155	117	92	53
Registry	166	156	145	133	117	106	93	74	64	52	41	25	13

Conclusive Remarks

1. The physical forces are a major player of the "vulnerability" of stenosis ('Conditio sine qua non' for plaque rupture)

2. Ischemia is a marker of abnormal physical forces that take place at the level of the epicardial vessels

Conclusive Remarks

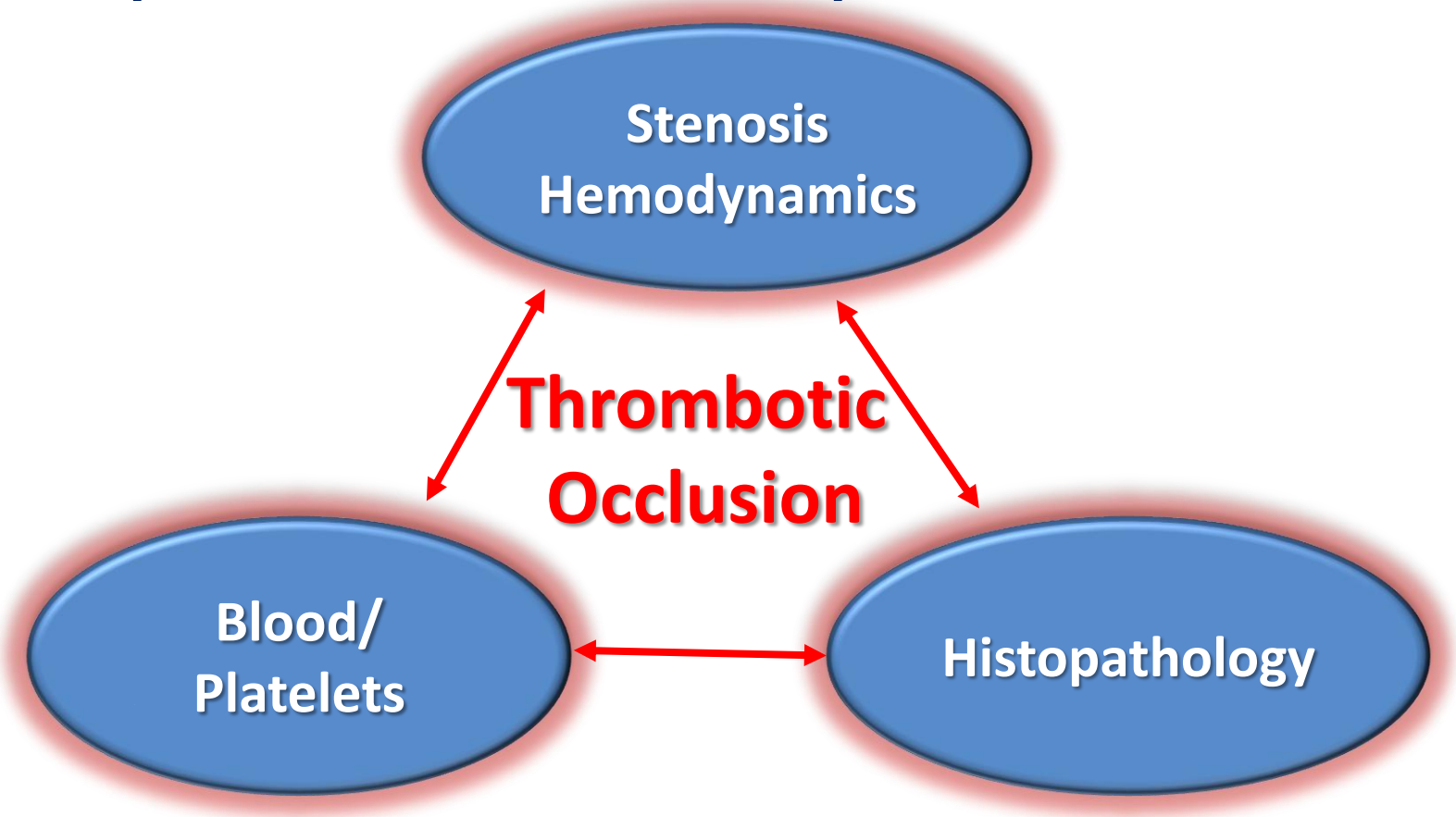
1. The physical forces are a major player of the “vulnerability” of stenosis. (‘Conditio sine qua non’ for plaque rupture)

2. Ischemia is a marker (an annoying epiphenomenon) of abnormal physical forces that take place at the level of the epicardial vessels

3. Pressure gradients (and FFR) are “all-in” metrics of these physical forces and are, therefore, specific biomarkers of CAD

Conclusive Remarks

Ischemia is a marker of the abnormal physical forces that take place at the level of the epicardial vessels



Virchow's Triad Revisited