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Coronary Microvascular Dysfunction :

Small vessels, Big world

- Pathophysiology
Assessment

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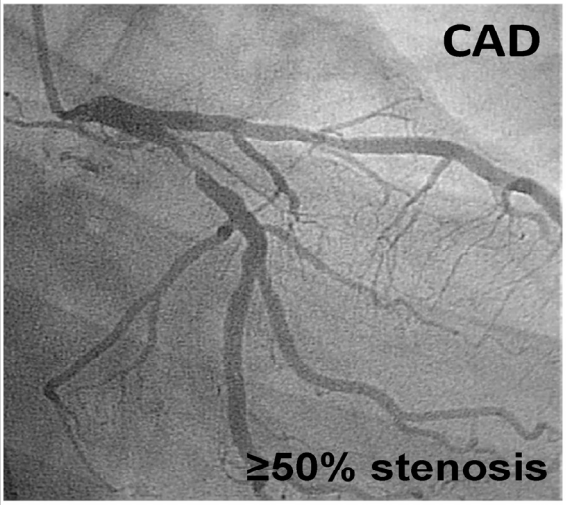
Inje University College of Medicine

A black box beyond epicardial lesion

'Microcirculation'



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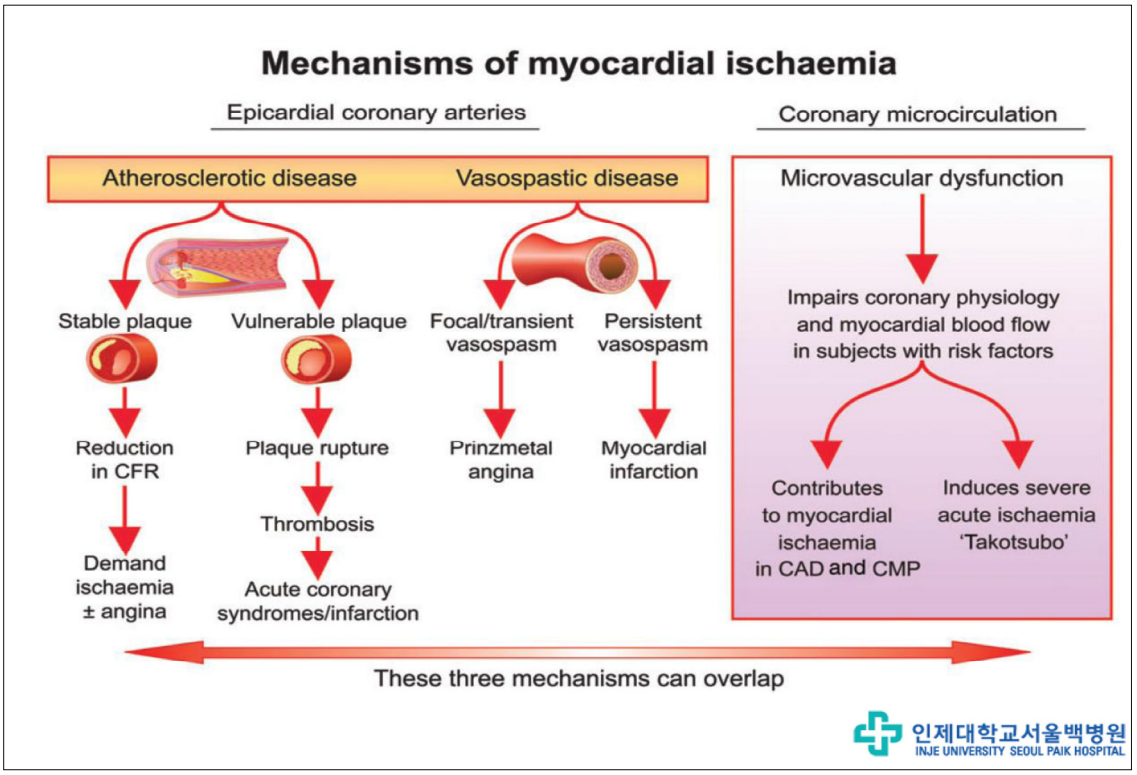
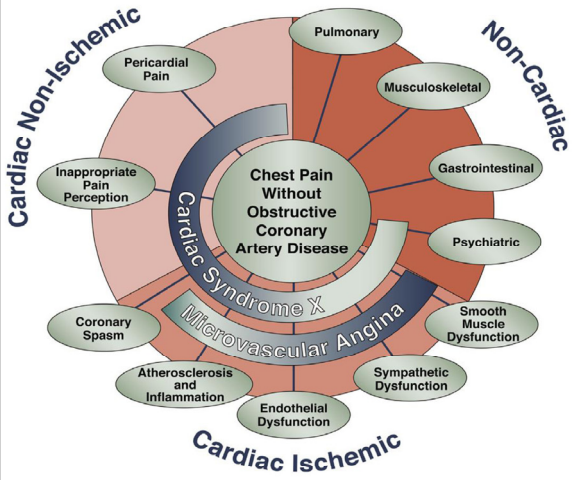


Microvascular angina



- Patients with angina
  - 30-40% No significant CAD
  - 50-65% of these patients microvascular dysfunction
- Also known as microvascular angina
  - more commonly seen in women
  - Risk factors included obesity, diabetes, hypercholesterolemia, hypertension, and smoking

Mark A. et al. *JACC* 2015 vol.8 210-20

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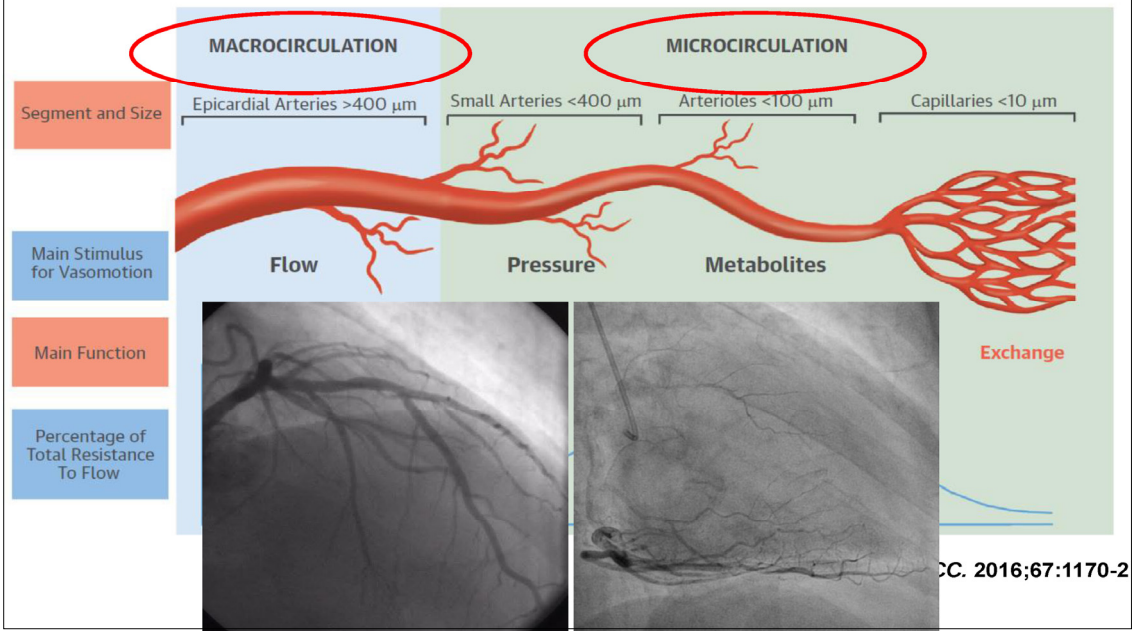
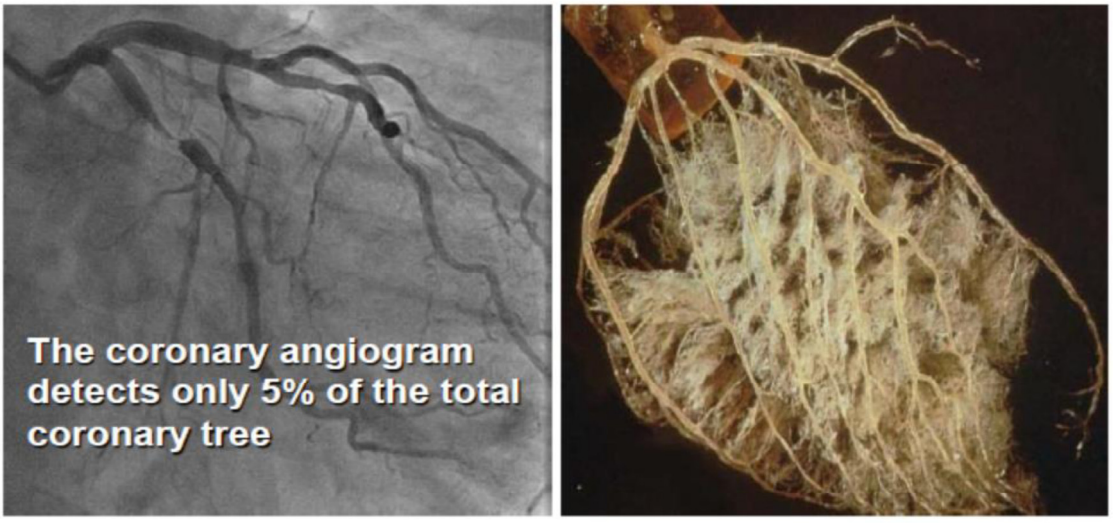
Two Compartment Model



CC. 2016;67:1170-2

What is the microcirculation?



- Lined up end-to-end, vessels stretch 100,000km
- Earth circumference is 40,000km

- Capillaries make up ~80% of the vascular bed
- 90% of the blood volume is in the microcirculation
- 80% of LV mass is the vessel
- All important action takes place in the mircocirculation

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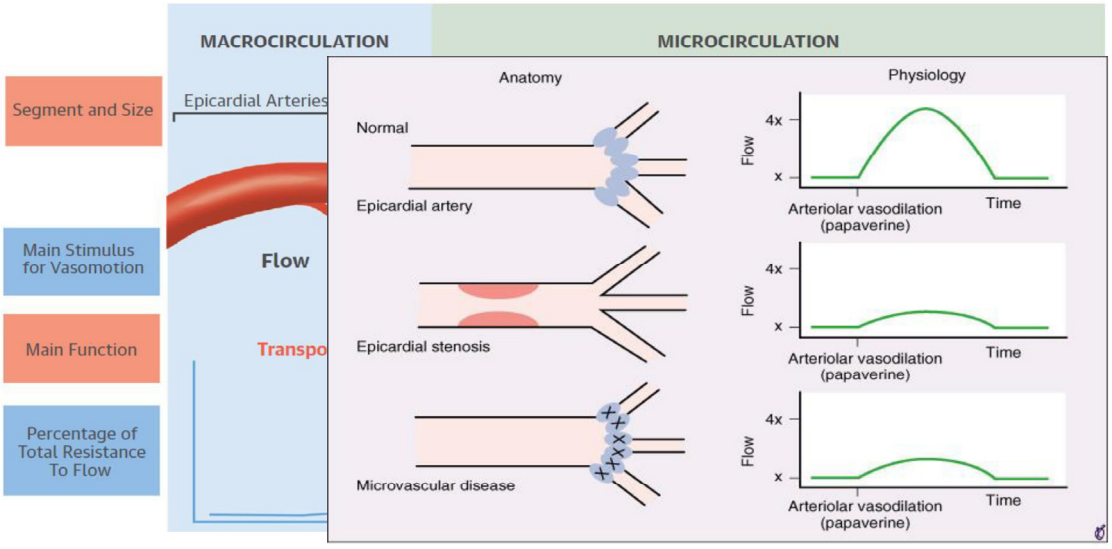
Regulation of coronary blood flow
: Coronary Artery Resistance



Assessment of the microvasculature

- Extremely challenging diagnosis
  - Heterogenous patient population
  - Variety of pathogenic mechanisms
  - Poor anatomic resolution
  - Potentially patchy nature of the disease
- Therefore, assessment of the microcirculation is primarily functional and physiological, not anatomic

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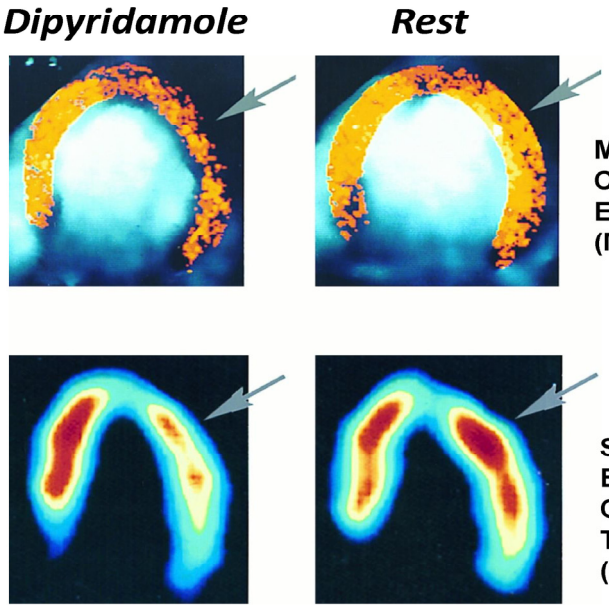


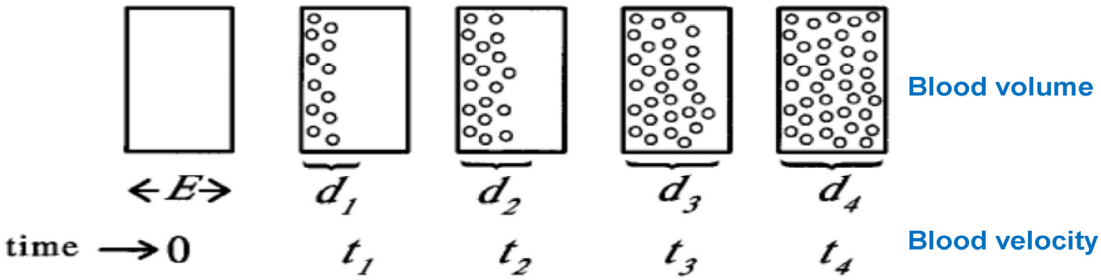
Myocardial Contrast Echocardiography (MCE)

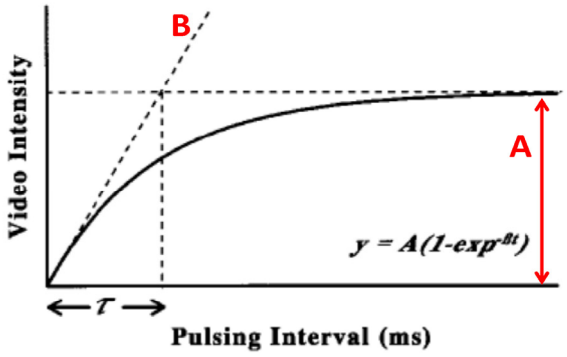
Single Photon Emission Computed Tomography (SPECT)

Circulation. 1997;96:785-792

Myocardial Contrast Echocardiography (MCE)
- blood flow quantification

- Microbubble contrast
  - rheology, or behaviour or microbubbles in the microcirculation, is nearly identical to that of red blood cells (RBCs)
  - ability to destroy microbubbles with ultrasound at high transmitted acoustic powers



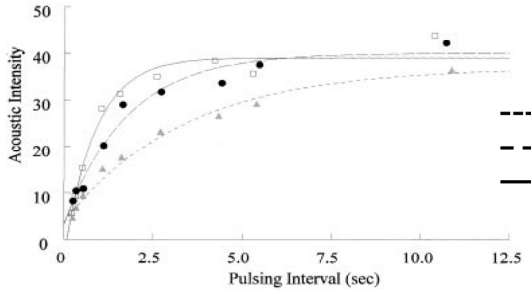


A = Plateau VI (MBV)
B = rate of rise of VI (mean mircobubble velocity)

A·B = MCE derived MBF

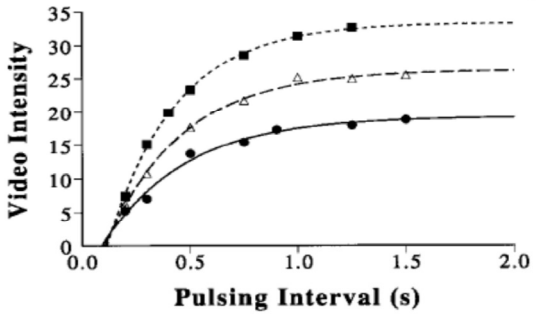
Wei et al. *Circulation*. 1998;97:473-483

Intracoronary Adenosine



	MBF	MBV
------	1.0	1.0
- - - -	3.0	1.0
———	5.0	1.0

Intracoronary Adenosine + stenosis



MBF	MBV
5.0	1.0
3.0	0.8
2.0	0.6

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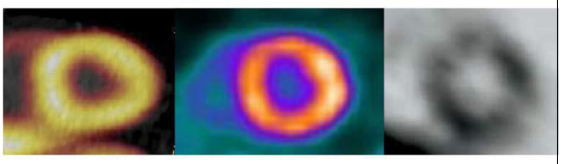
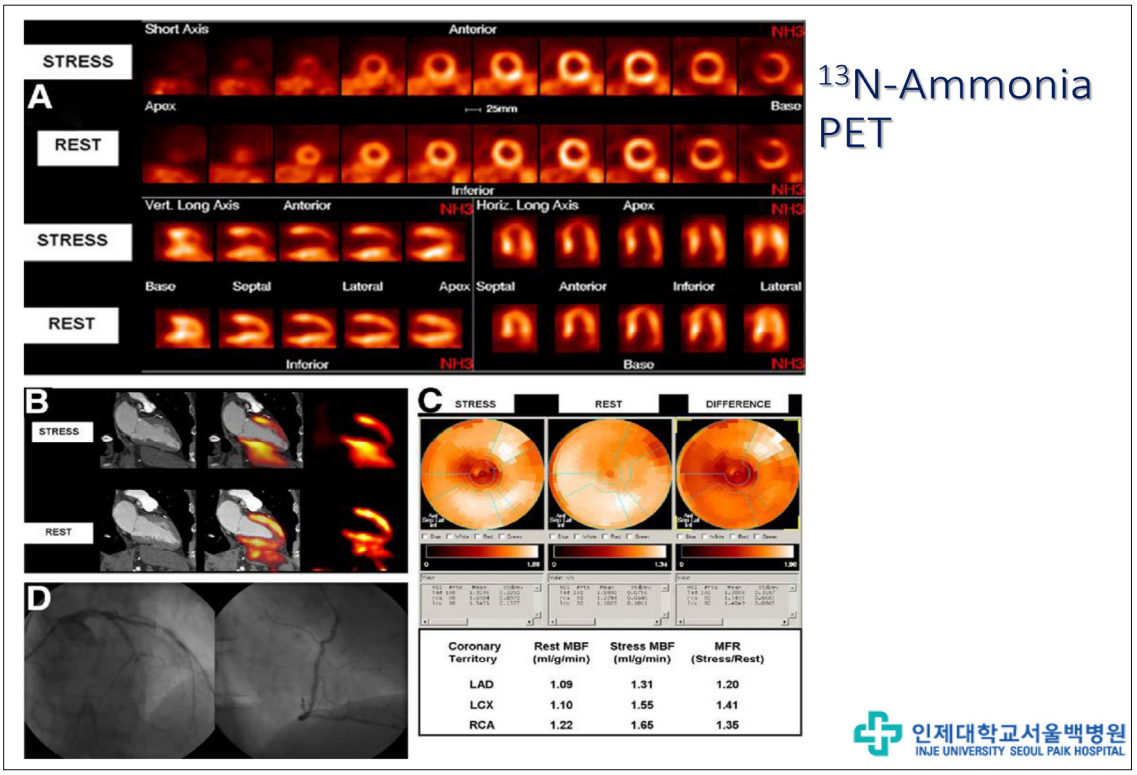
Positron emission tomography (PET)

- current gold standard
  - quantification of myocardial blood flow in absolute terms (ml/g/min)
- IV injection of a perfusion ratdiotracer
  - ^{13}N-ammonia
  - ^{15}O-water
  - ^{82}Rubidium
- Dynamic acquisition of images of the radiotracer
  - First-pass extraction fraction
  - Positron range
  - Half-life

PET Perfusion Imaging



N-13 Ammonia Rubidium-82 O-15 Water


STRESS
A
REST
Short Axis
Anterior
NH3
Apex
25mm
Base
Inferior
Vert. Long Axis
Horiz. Long Axis
Septal
Lateral
B
C
D
DIFFERENCE
Coronary Territory
Rest MBF (ml/g/min)
Stress MBF (ml/g/min)
MFR (Stress/Rest)
LAD 1.09 1.31 1.20
LCX 1.10 1.55 1.41
RCA 1.22 1.65 1.35
^{13}N-Ammonia PET
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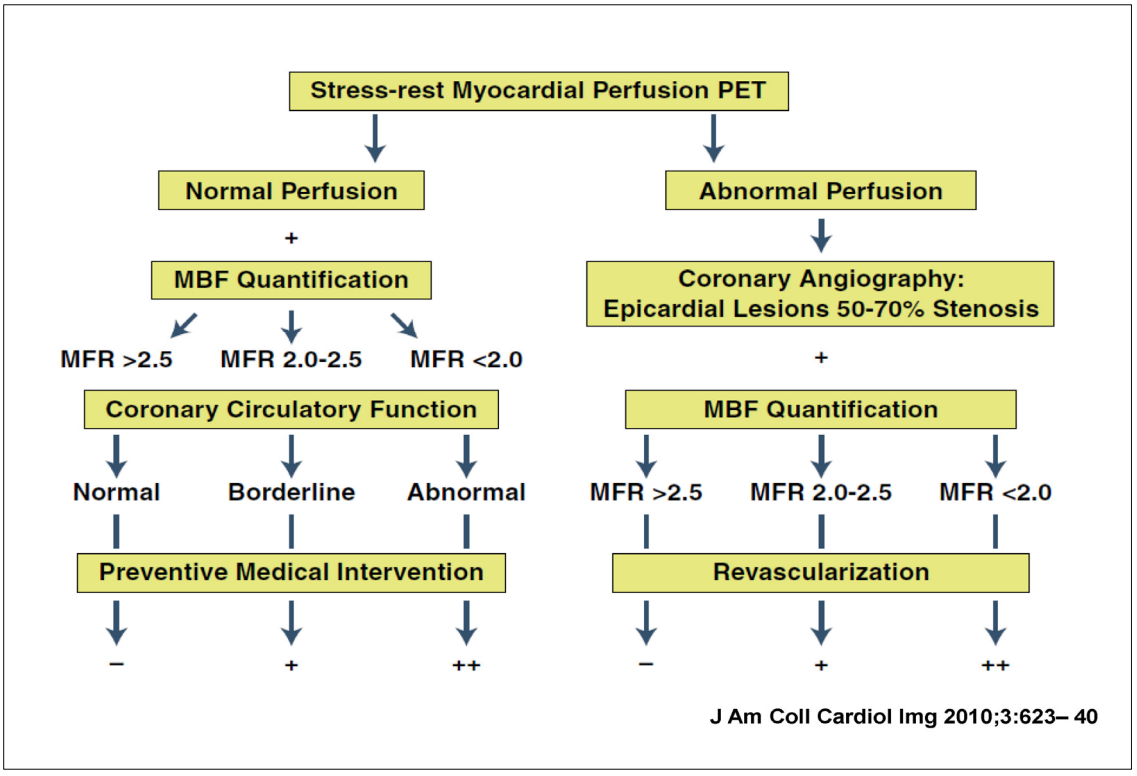
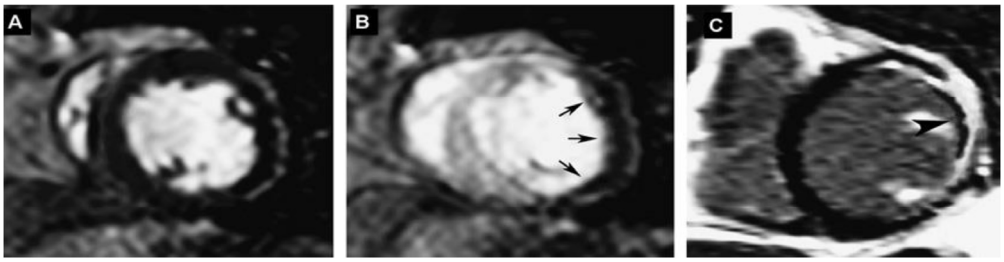
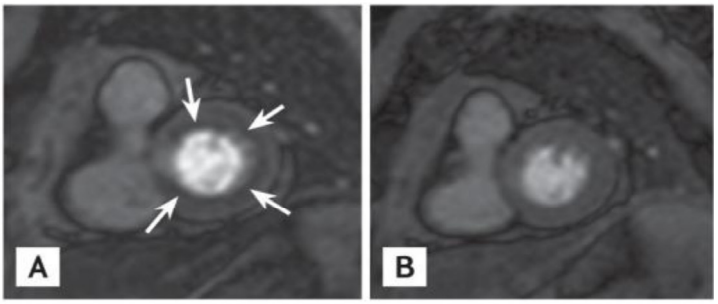

Stress-rest Myocardial Perfusion PET
Normal Perfusion
+
MBF Quantification
MFR >2.5
MFR 2.0-2.5
MFR <2.0
Coronary Circulatory Function
Normal
Borderline
Abnormal
Preventive Medical Intervention
–
+
++
Abnormal Perfusion
Coronary Angiography: Epicardial Lesions 50-70% Stenosis
+
MBF Quantification
MFR >2.5
MFR 2.0-2.5
MFR <2.0
Revascularization
–
+
++
J Am Coll Cardiol Img 2010;3:623– 40

First pass Magnetic Resonance myocardial perfusion imaging

- assessment of myocardial blood flow for detection of myocardial ischaemia
- Myocardial perfusion defects detected may be due either to epicardial coronary disease or microvascular dysfunction or disruption



Cardiac MRI in microvascular angina

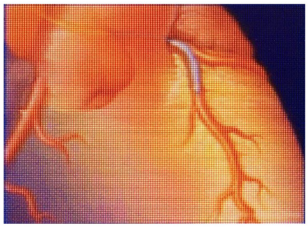


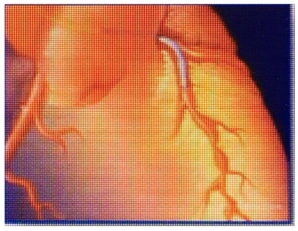
Stress perfusion image Resting image

- Superior temoral and spatial resolution
- Lack of ionizing radiation
- Wider scanner availability

Coronary Endothelial Functional Protocol

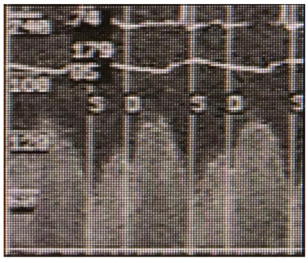
Diagnostic angiography

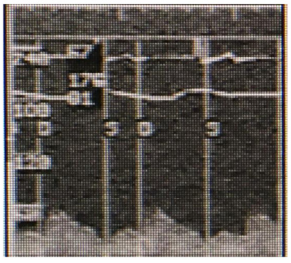




Acetylcholine (endothelial dependent Vasodilator)

Epicardial





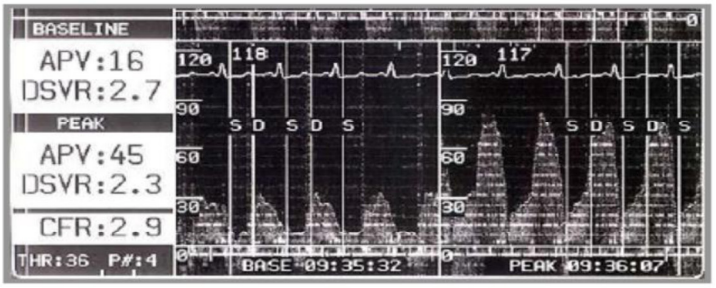
Microcirculation

Doppler Wire Coronary Flow Reserve (CFR)

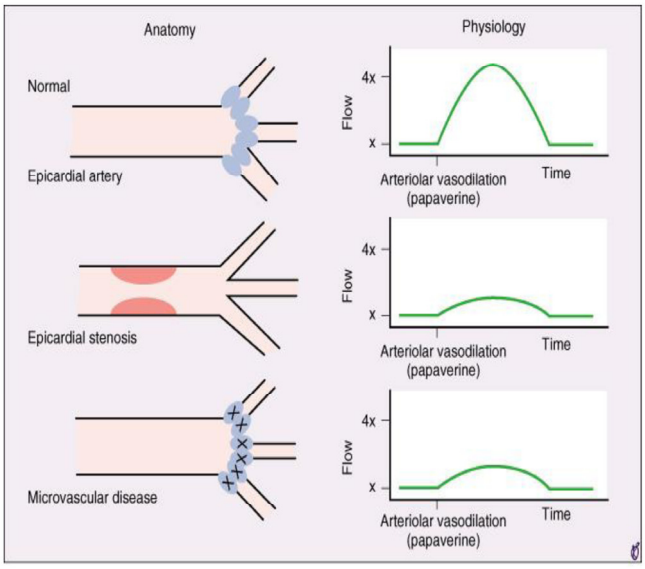
Temperature and pressure sensor tipped wire

Intracoronary Adenosine

$$CFR = \frac{\text{Hyperemic Flow}}{\text{Resting Flow}} = \frac{\text{Mean transit time}_{Basal}}{\text{Mean transit time}_{Hyperemia}}$$



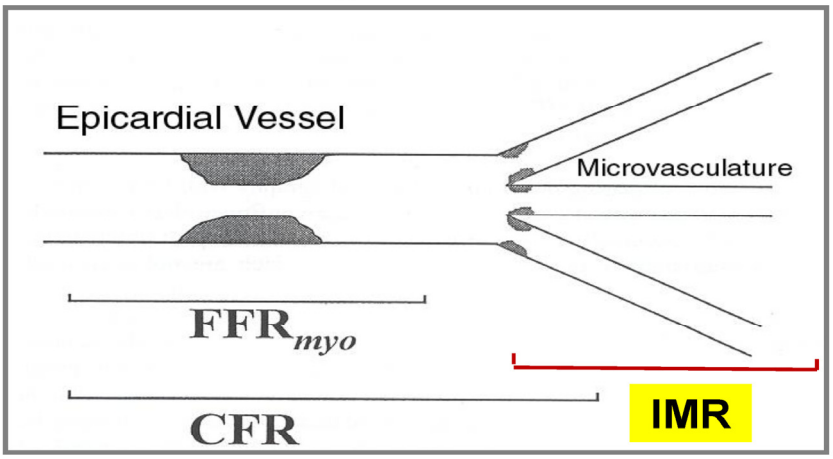
Doppler Wire Coronary Flow Reserve (CFR)



- **Not microvascular specific**
- **No clearly defined normal value**
- **High variabilty in test-retest value**
- **Affected by resting hemodynamics (baseline flow velocity)**
  - **Heart rate**
  - **contractility**

Index of Microcirculatory Resistance (IMR)

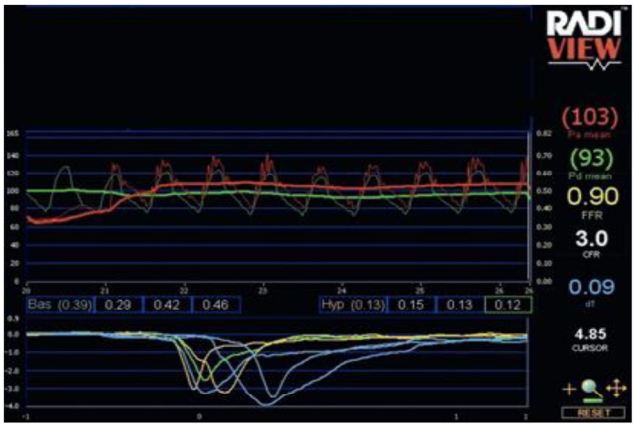
$$IMR = \frac{P_d}{Q_{hyperemia}} = P_d * \text{Mean transit time}$$



Circulation 2003;107:3129-3132

Index of Microcirculatory Resistance (IMR)

In a patient with normal coronary microvascular function



At maximal hyperemia with IV adenosine

- Mean proximal pressure 103mmHg
- Mean distal pressure 93mmHg
- FFR : 93/103 = 0.9

Intracoronary thermodilution curves

- The mean transit time
  - Basal state 0.39
  - Hyperemia 0.13
- CFR : 0.39/0.13 = 3

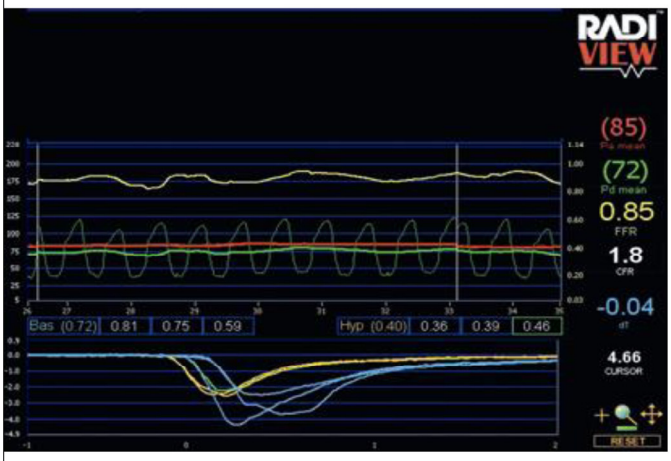
IMR = distal pressure x transit time at maximal hyperemia

: 93 x 0.13 = 12.09

Normal microvascular function

Index of Microcirculatory Resistance (IMR)

In a patient with coronary microvascular function



- **FFR = 0.85**
- **CFR = 1.8**
- **IMR = 72 x 0.4 = 28.8**

Slightly impaired microvascular function

Index of Microcirculatory Resistance (IMR)

- Much lower variability
- Not significantly affected by changes in hemodynamic conditions
- Can be assessed in the presence of epicardial CAD

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Summary (1)

- The coronary microvasculature is an often ignored entity.
- MVD is associated with worse outcomes.
- Diagnosing coronary MVD has been a challenge for doctors
  - Non-invasive indices : needs high index of suspicion, cost…
  - Invasive indices : needs sophisticated equipments and expertise, potential complications such as coronary artery dissection

Summary (2)

- At present, definite diagnosis of MVD
  - normal epicardial coronaries
  - absence of spasm of epicardial coronaries on acetylcholine provocation
  - coronary flow reserve less than 2.5 on adenosine induced hyperemia
- Assessment recommendation
  - patients with refractory symptoms with unconfirmed diagnosis
  - requiring repeated hospitalization and evaluation with failure of empirical therapy