

Dr.A.M.Thirugnanam, MD, MSCIP, FSCAI, PhD  
Senior Interventional Cardiologist

[www.cardiologycourse.com](http://www.cardiologycourse.com), [www.bestmedicalschoollonline.com](http://www.bestmedicalschoollonline.com)

# MANAGEMENT OF CHRONIC STABLE ANGINA IN CURRENT PRACTICE



# Brain twisters

- What is the best and no cost diagnostic tool to diagnose stable angina?
- Do you believe that the stable angina is the reason for ACS
- Do you accept treatment should be based on symptoms not on plaque morphology
- Do you believe that atypical symptoms of angina is unbelievable

# Continuum of stable angina

Chronic stable angina



Acute coronary syndrome




CHF



ESHF



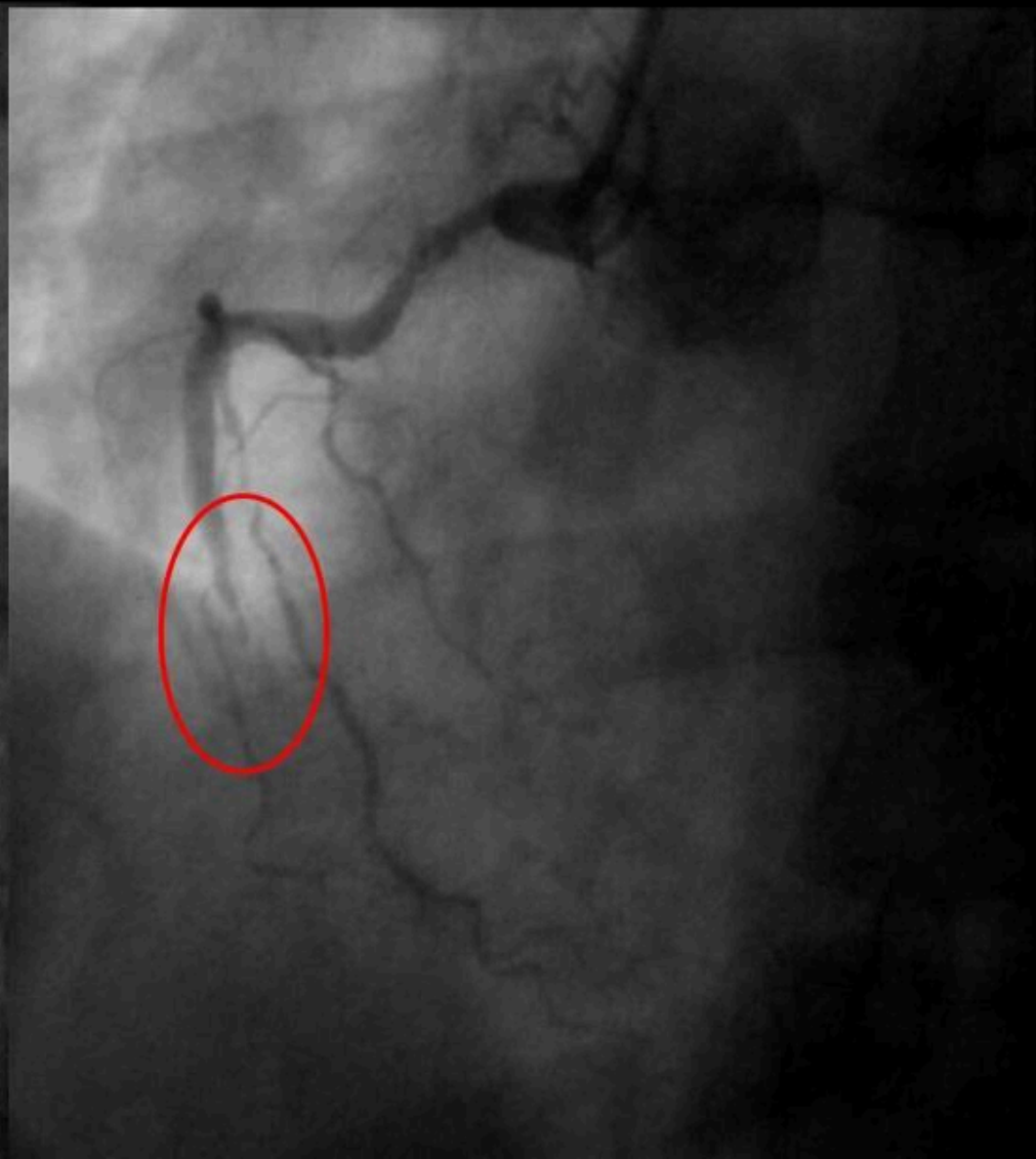
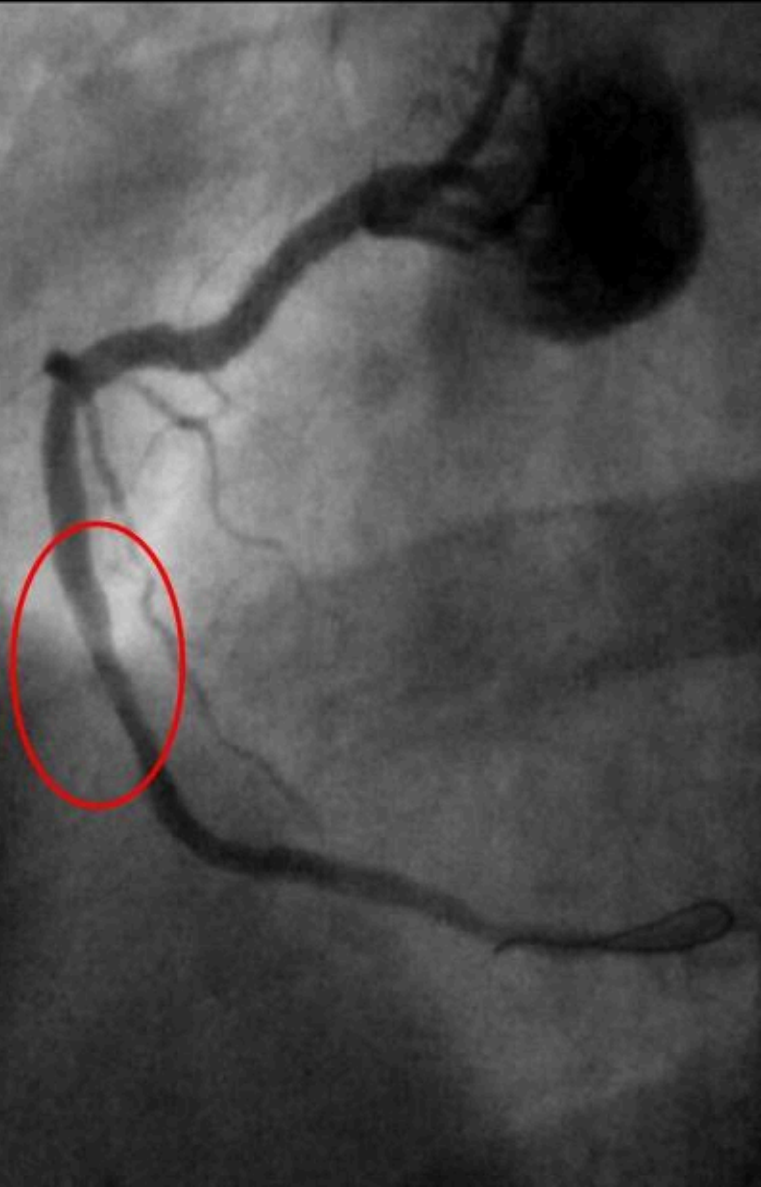
# What leads to ACS?

- Undermining risk factors
  - No appropriate biological markers to detect future event
  - Underestimating plaque biology and morphology
  - Still we are lacking proper guidelines to manage chronic stable angina
  - Not giving proper attention to patients angina equalant symptoms
- 

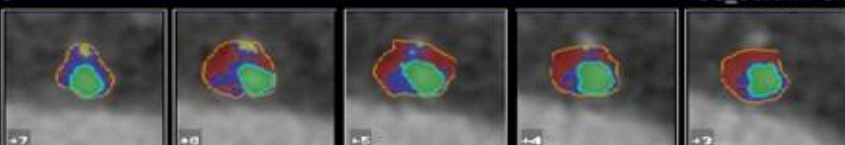
April 2001

July 2002

Acute Inferior Wall MI

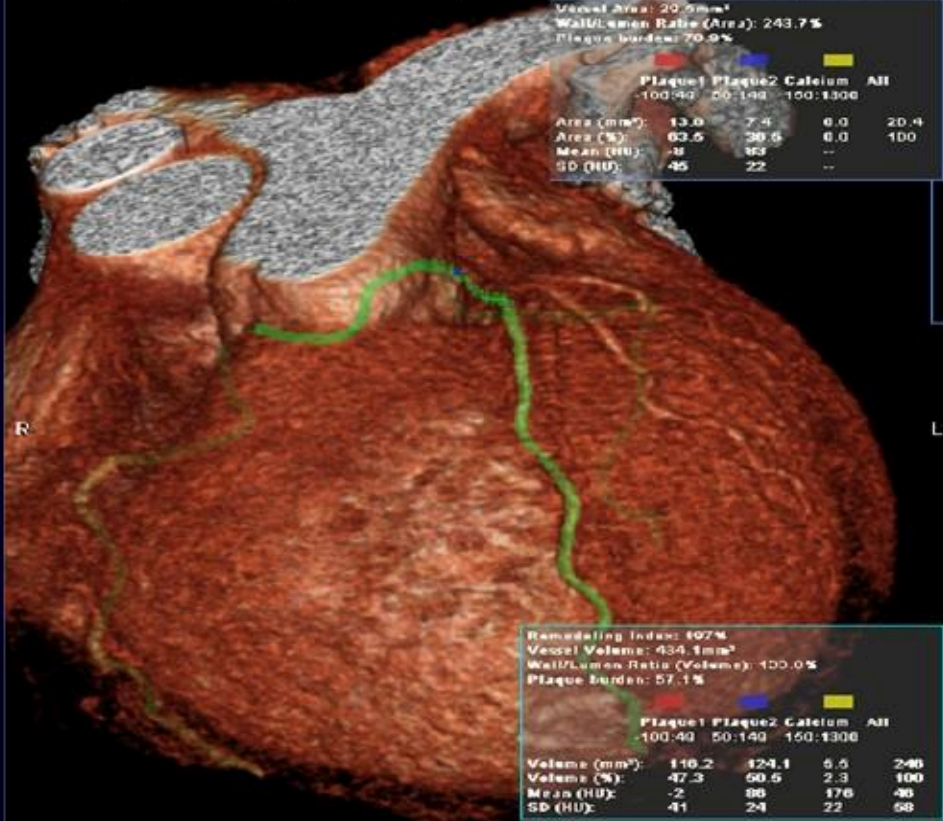
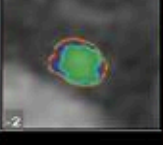
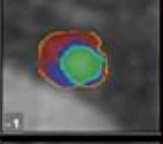
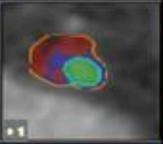
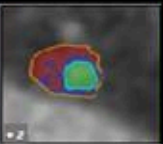


16:00:00



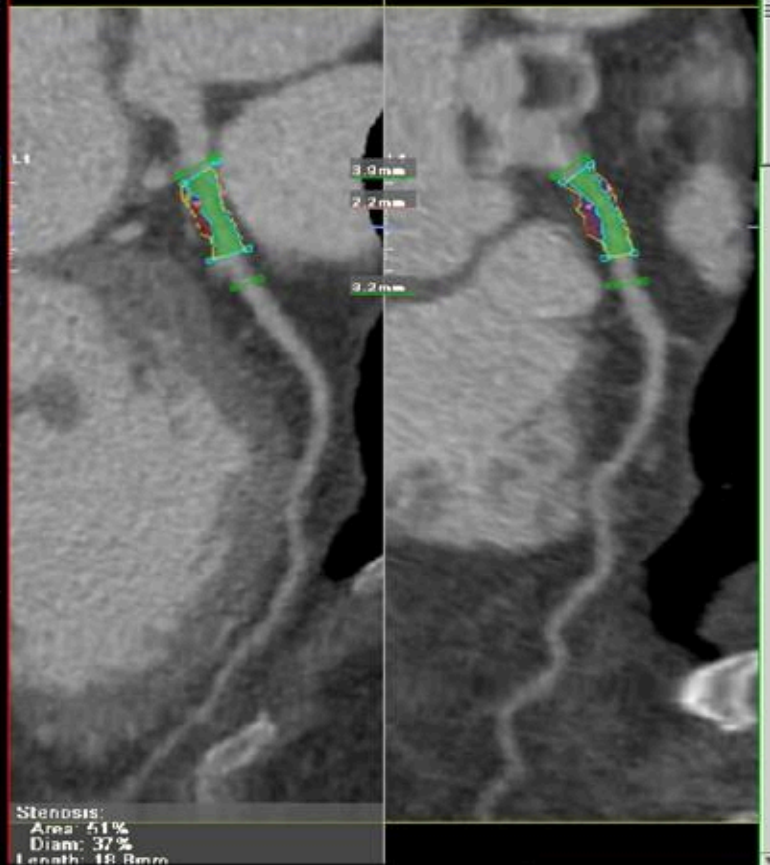
Vessel Area: 20.9mm<sup>2</sup>  
 Wall/Lumen Ratio (Area): 243.7%  
 Plaque burden: 70.0%

	Plaque1	Plaque2	Calcium	All
Area (mm <sup>2</sup> )	13.0	7.4	0.0	20.4
Area (%)	63.5	36.5	0.0	100
Mean (HU)	-8	83	--	--
SD (HU)	46	22	--	--



Remodelling Index: 107%  
 Vessel Volume: 434.1mm<sup>3</sup>  
 Wall/Lumen Ratio (Volume): 100.0%  
 Plaque burden: 57.1%

	Plaque1	Plaque2	Calcium	All
Volume (mm <sup>3</sup> )	116.2	124.1	5.5	246
Volume (%)	47.3	50.5	2.3	100
Mean (HU)	-2	86	176	46
SD (HU)	41	24	22	58



Stenosis:  
 Area: 51%  
 Diam: 37%  
 Length: 18.8mm

Phase %070

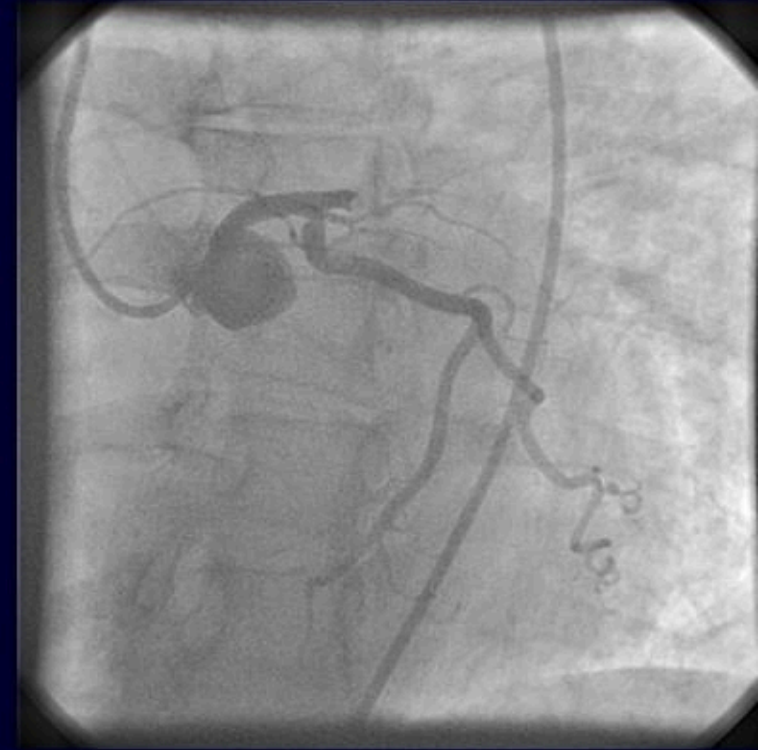
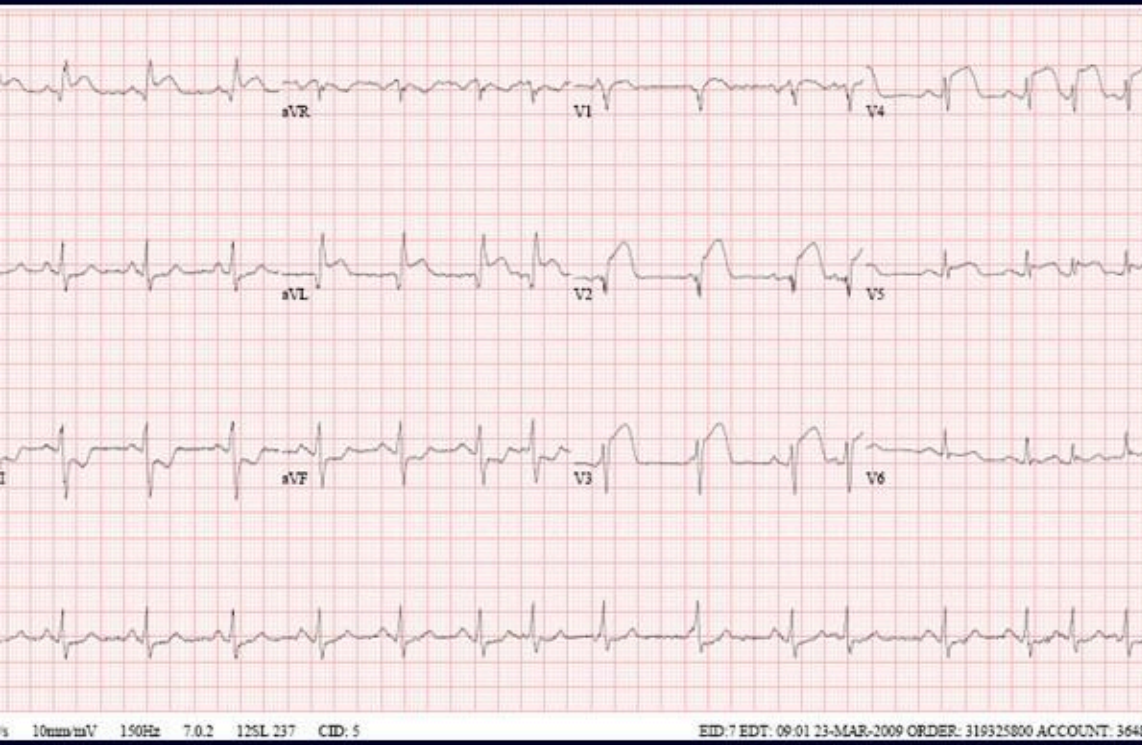
kVP: 120  
 mA: 515  
 msec: 330  
 mAs: 169  
 Thk: 0.75 mm  
 Definition  
 LAO38 CRA28

Courtesy of Drs. Madder and Goldstein, William Beaumont Hospital, 2010





# One year later



## IABP and LAD stent

Hospital course complicated by:

**Atrial fibrillation, EF 20%, LV Thrombi**

Transferred to inpatient **rehab** one week later on **coumadin**

**Embolic Stroke** while at rehab

# PET/CT for Cardiology....

Early  
Detection

Non-Invasive  
Diagnosis

Pre-Procedural  
Planning

Follow-Up

Stable Highrisk of CAD

Stable  
Angina

Unstable  
Angina

NSTEMI

STEMI

50 Million patients\*

4-6 Million patients

1.4 Million patients

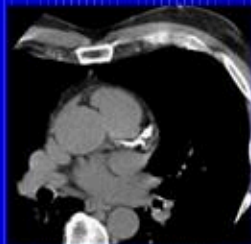
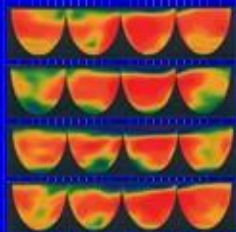
xx Million patients

73 y.o woman  
3-vessel CAD  
angio confirmed

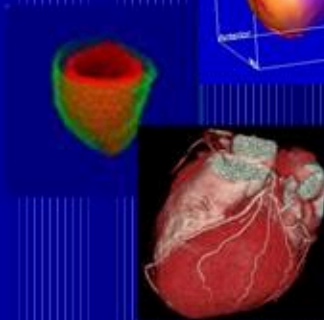
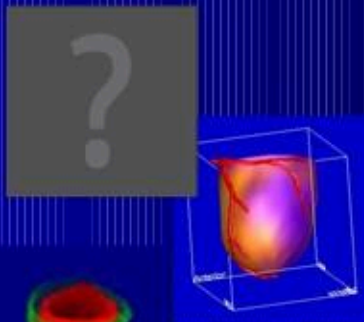
Son #1

Son #2

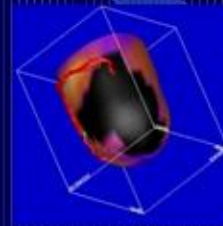
Son #3



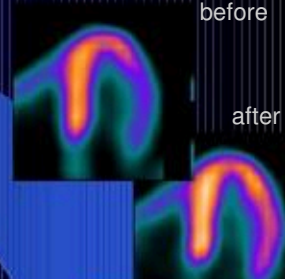
Primary Prevention



Secondary Prevention



Intervention



Monitor the Vascular  
Response

asymptomatics



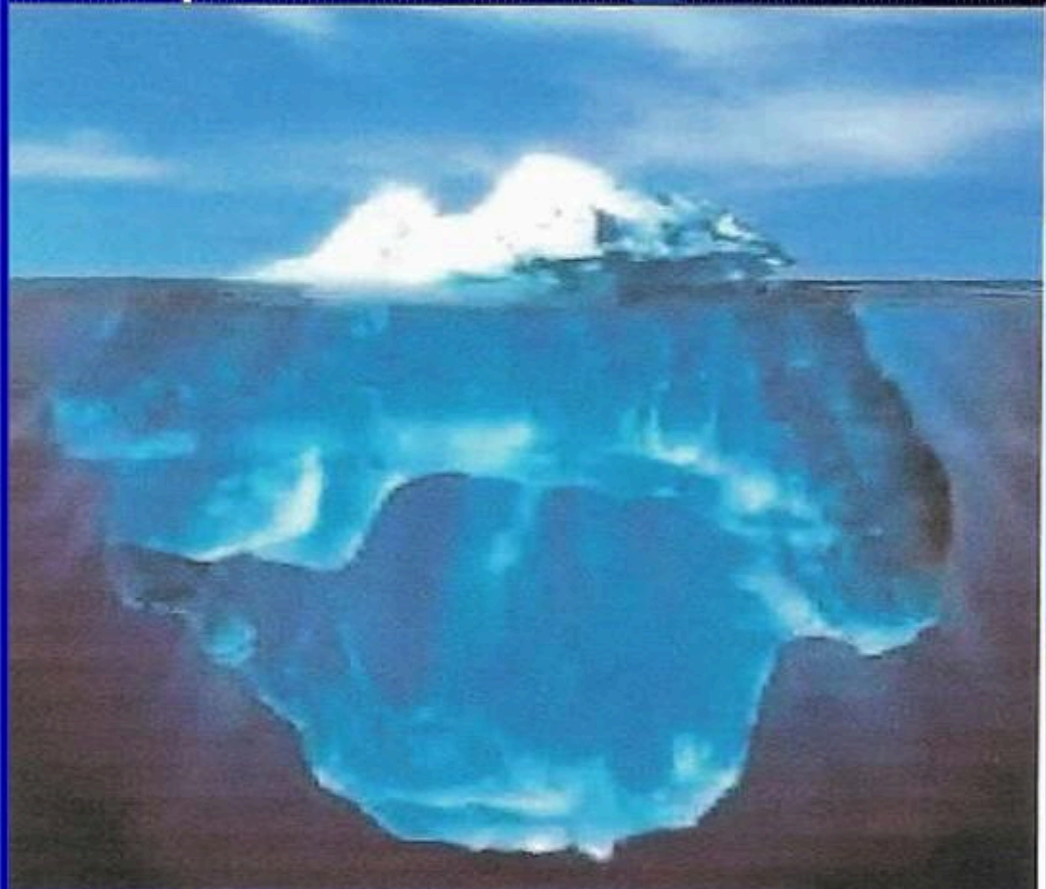
# Total Coronary Artery Plaque Burden

**20% Calcified**

**Fibrotic**

**80%**

**Lipid Rich**

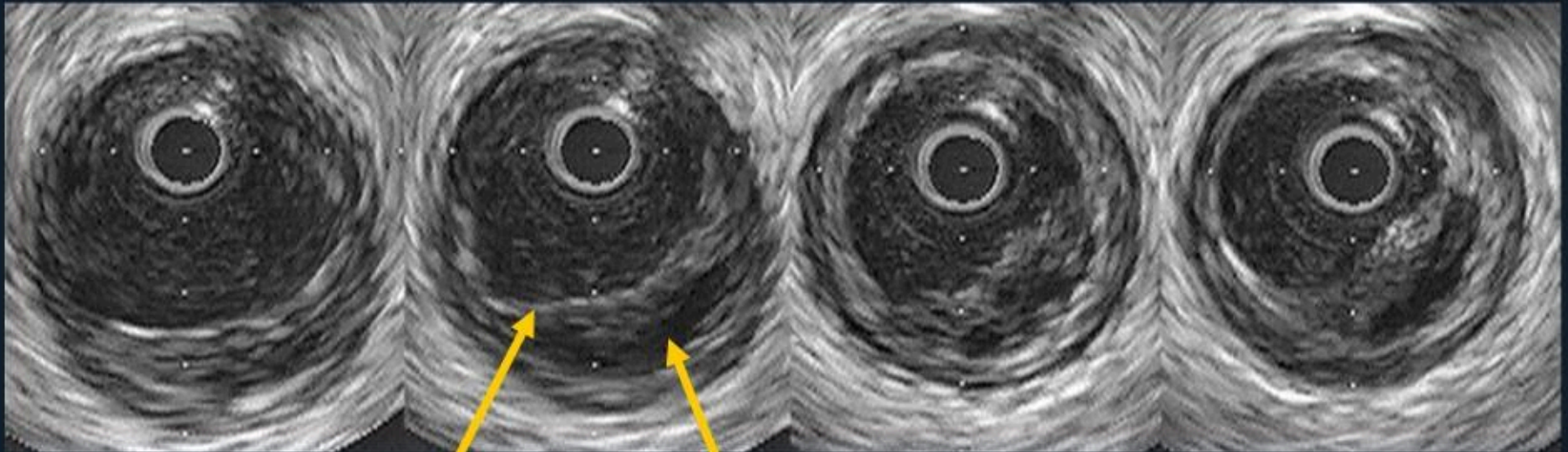




Imaging of plaque is playing vital role in treating CAD

# **IVUS, FFR, OCT NEW TECHNIQUE IN TREATING CAD**

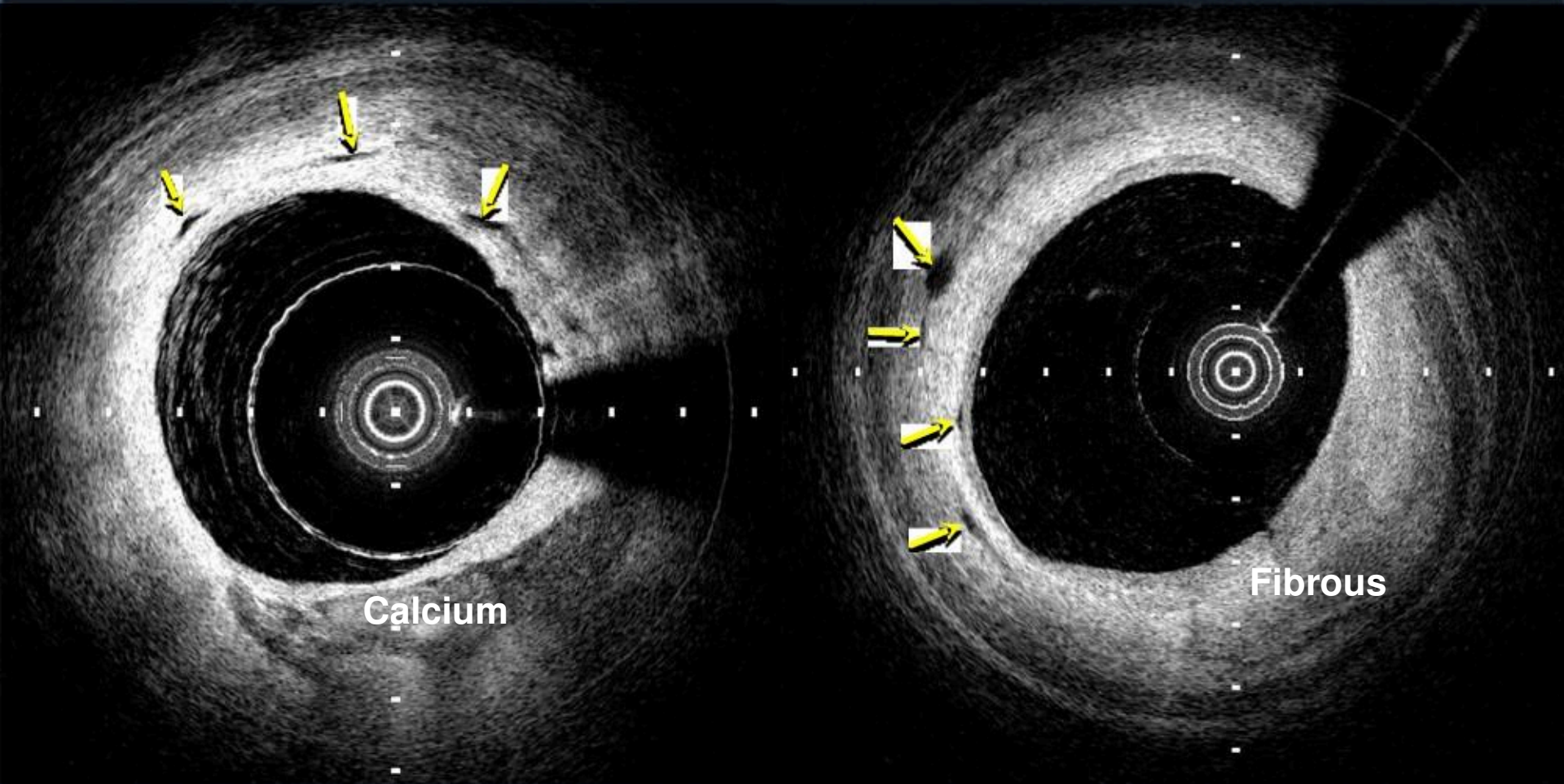
# Thin Cap Fibro-Atheroma in IVUS



**Fibrous Cap**

**Lipid Core**

# Plaque morphology imaging

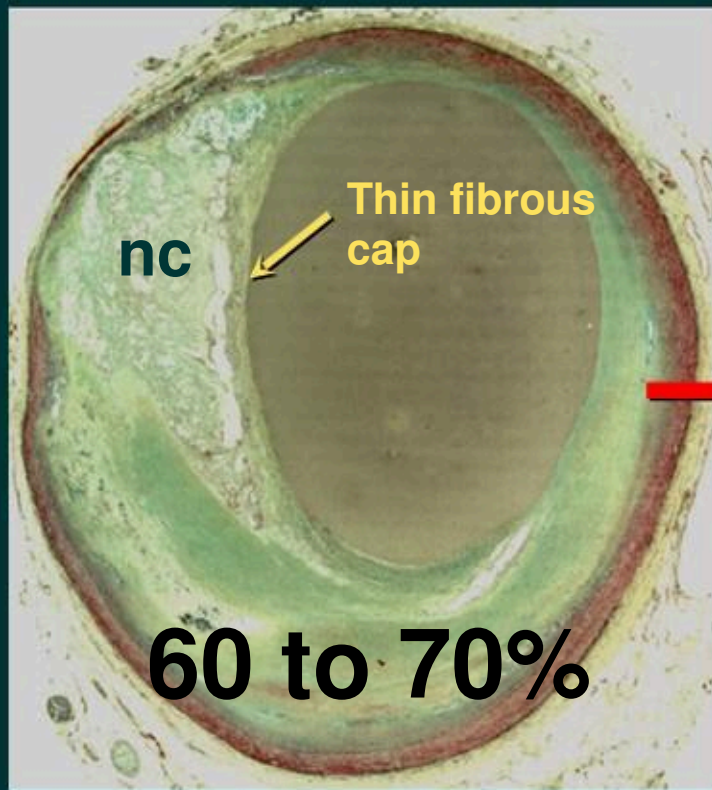


Columbia Medical Center



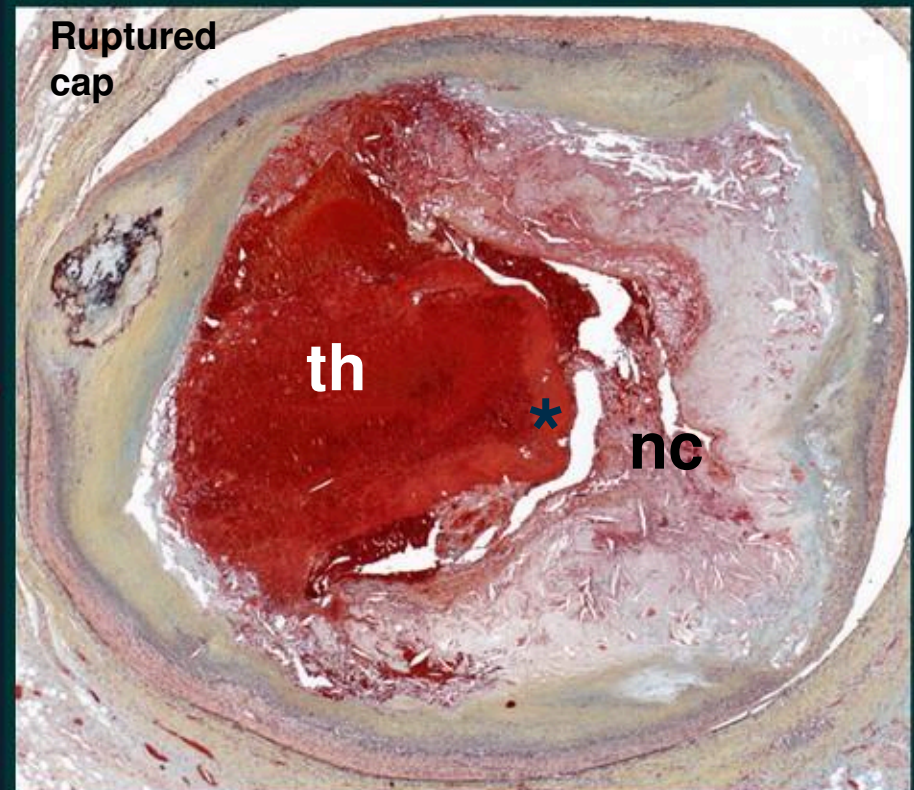
# Is the TCFA Always the Precursor Lesion of Plaque Rupture?

## TCFA



- Lipid rich necrotic core
- Thin fibrous cap (<65 um)

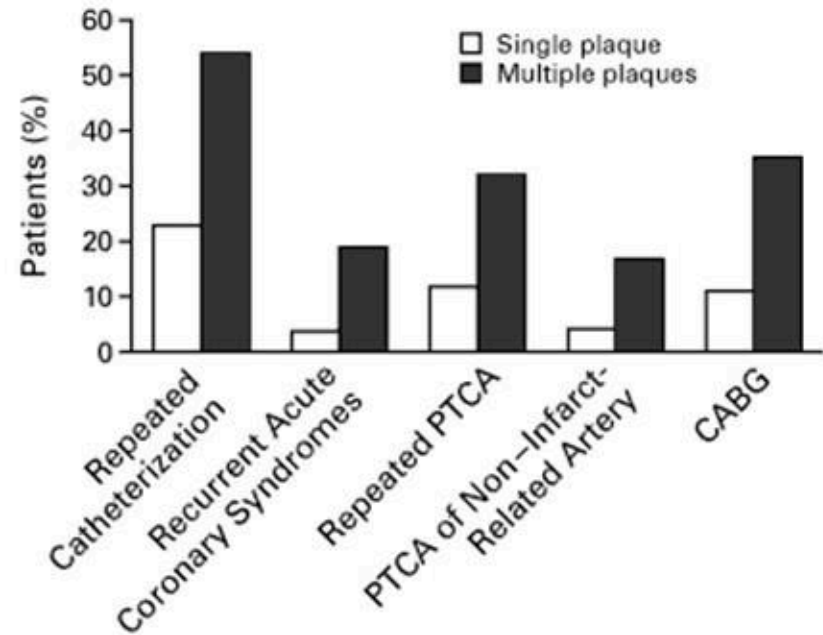
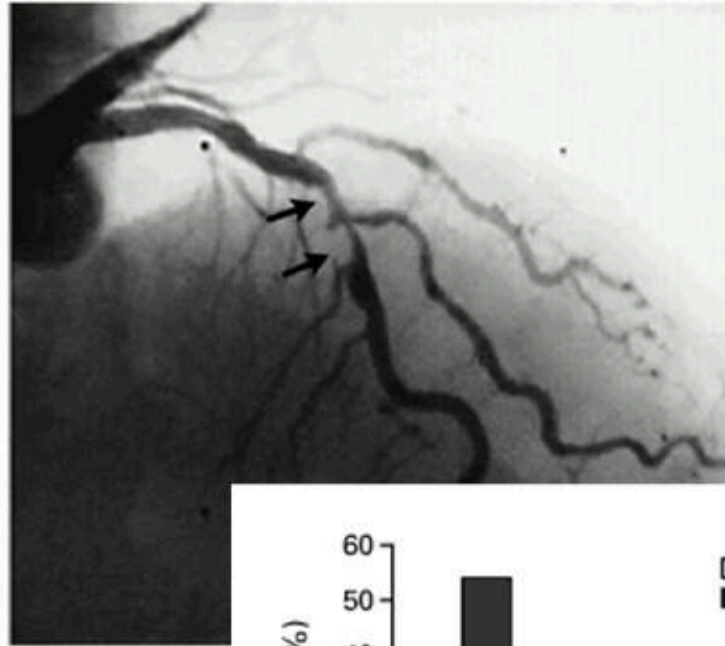
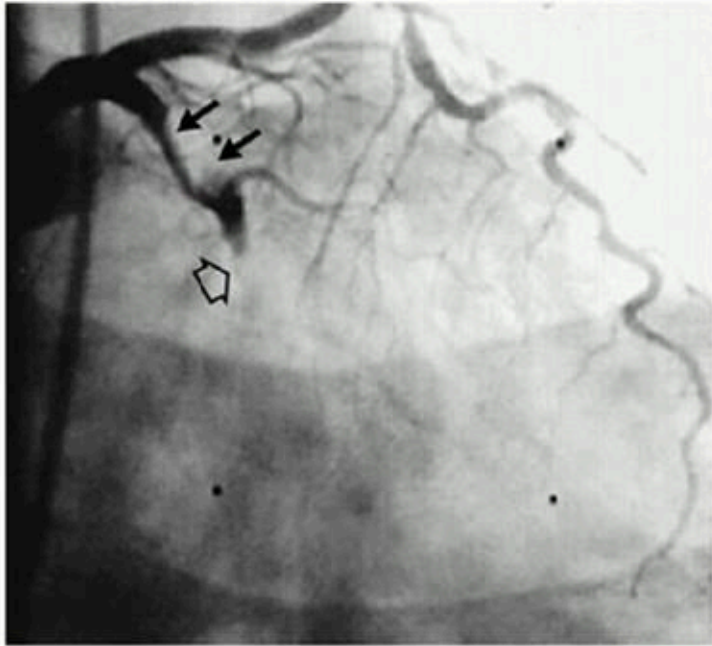
## Plaque Rupture



- Cap = Collagen type I with few SMC
- Cap infiltrated by macrophages



# Multiple vulnerable plaques

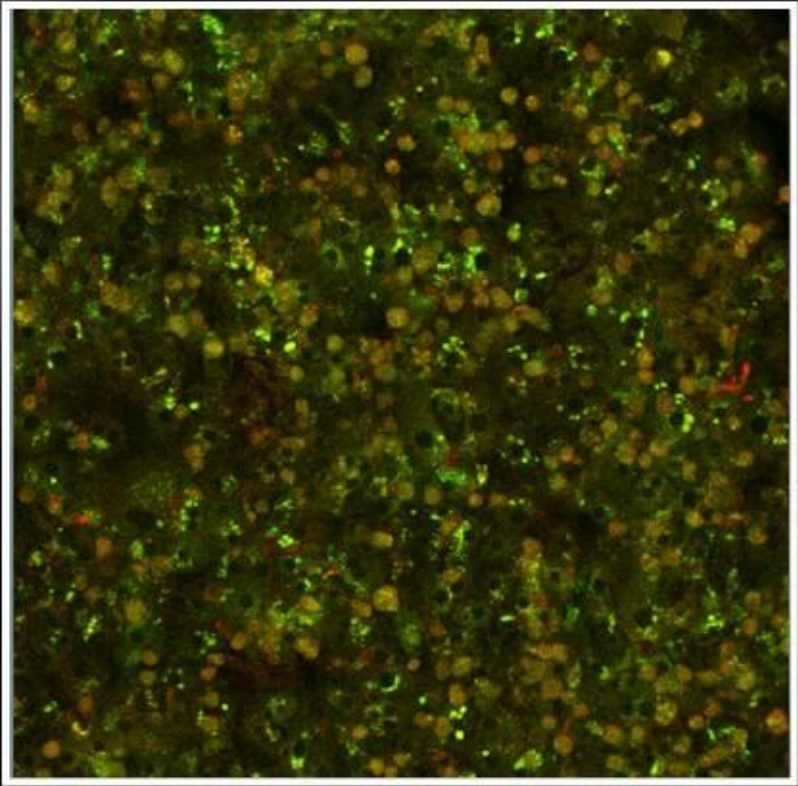


# Lipoproteins

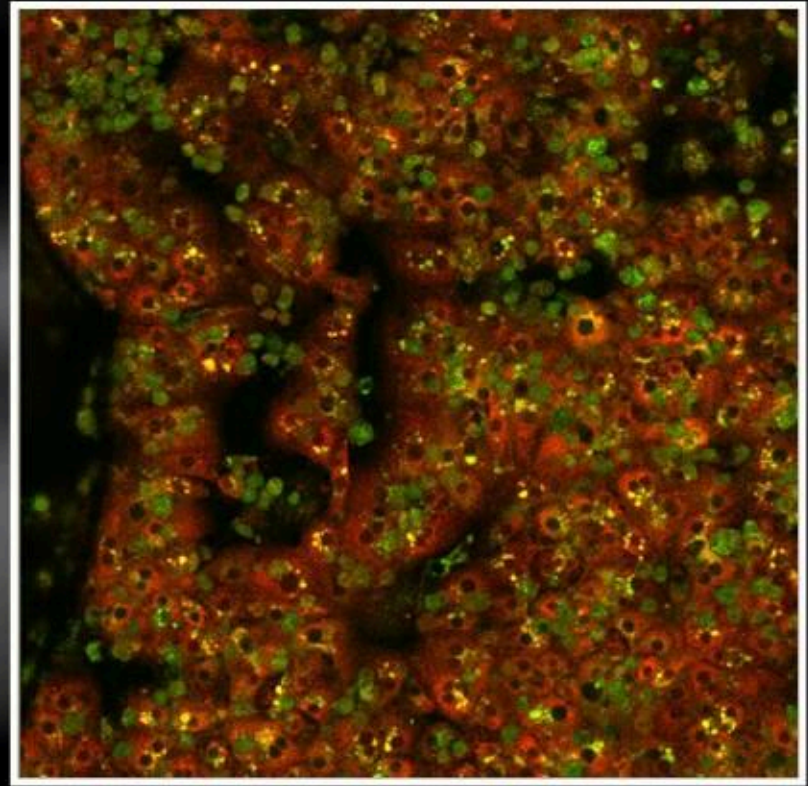
## ApoB48 and ApoB100 in Hepatocyte Culture

Fuqua Heart Center of Atlanta

**ApoB48**



**ApoB100**



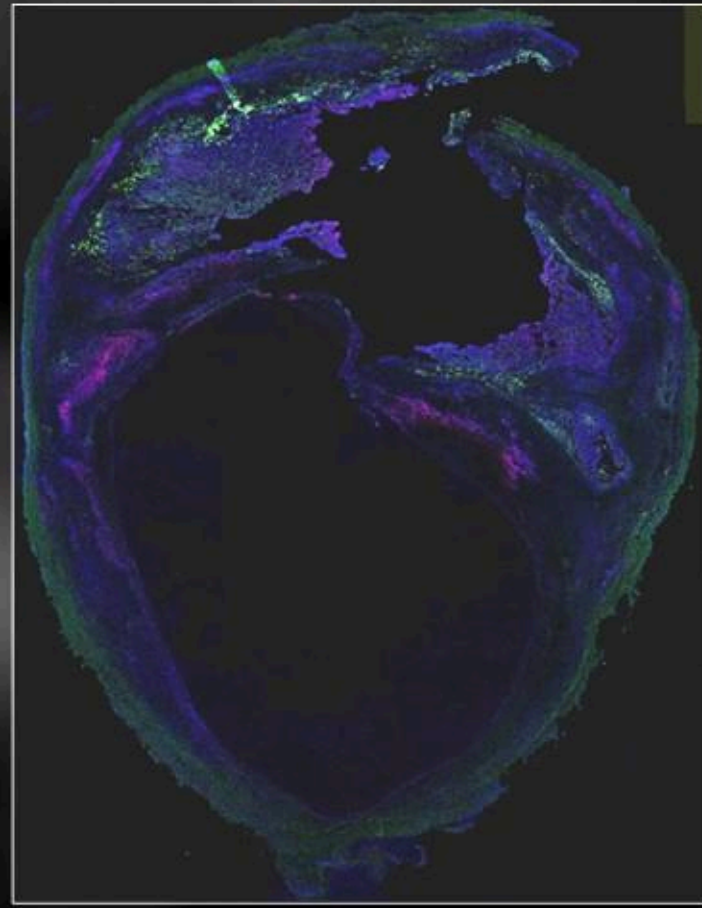


# Lipoproteins

## Hepatic and Intestinal Lipoproteins in Human Plaque

Fuqua Heart Center of Atlanta

**B100/B48  
Dual Stain**



**Red: ApoB100  
Blue: ApoB48**

# 'Do not' recommendations

Do not :

- X exclude people from treatment based on their age
- X investigate or treat symptoms differently in men and women or in different ethnic groups
- X offer vitamin or fish oil supplements
- X offer TENS, EECp or acupuncture
- X routinely offer drugs for secondary prevention of cardiovascular disease to people with suspected cardiac syndrome X.

# CCSC Angina Classification

- Class I
  - Angina only with extreme exertion
- Class II
  - Angina with walking 1 to 2 blocks
- Class III
  - Angina with walking 1 block
- Class IV
  - Angina with minimal activity




# Stable Angina Classes

- Exertional
- Variant or Prinzmetal's Angina
- Anginal Equivalent Syndrome
- Syndrome-X
- Silent Ischemia
- Decubitus angina
- Nocturnal angina




# Angina Pectoris

- Classic angina is characterized by substernal squeezing chest pain, occurring with stress and relieved with rest or nitroglycerin.
  - May radiate down the left arm
  - May be associated with nausea, vomiting, or diaphoresis.
- 



# Angina: Exertional

- Coronary artery obstructions are not sufficient to result in resting myocardial ischemia. However, when myocardial demand increases, ischemia results.
- 

# Angina: Variant Angina

- Transient impairment of coronary blood supply by vasospasm or platelet aggregation
- Majority of patients have an atherosclerotic plaque
- Generalized arterial hypersensitivity
- Long term prognosis very good



# Angina: Anginal Equivalent Syndrome

- Patient's with exertional dyspnea rather than exertional chest pain
- Caused by exercise induced left ventricular dysfunction



# Angina: Prinzmetal's Angina


- Spasm of a large coronary artery
- Transmural ischemia
- ST-Segment elevation at rest or with exercise
- Not very common

# Angina: Syndrome X

- Typical, exertional angina with positive exercise stress test
- Anatomically normal coronary arteries
- Reduced capacity of vasodilatation in microvasculature
- Long term prognosis very good
- Calcium channel blockers and beta blockers effective




# Angina: Silent Ischemia

- Very common
  - More episodes of silent than painful ischemia in the same patient
  - Difficult to diagnose
  - Holter monitor
  - Exercise testing
- 




# Investigations for CSA

- Nuclear thallium
  - Stress echo
  - Tread mill test
  - Coronary angiography is a gold standard
  - Intra vascular ultrasound
  - Fractional flow reserve
- 



# Stable Angina Guidelines for Nuclear EST

Defined CAD


- Post infarct risk stratification
  - Risk stratification to determine need for revascularization ( viability study )
- 






# Stable Angina

## Stress Echo

- Ischemia may cause wall motion abnormalities, no rise or fall in LVEF
  - Sensitivity/specificity same as nuclear testing
  - May be better in women
- 




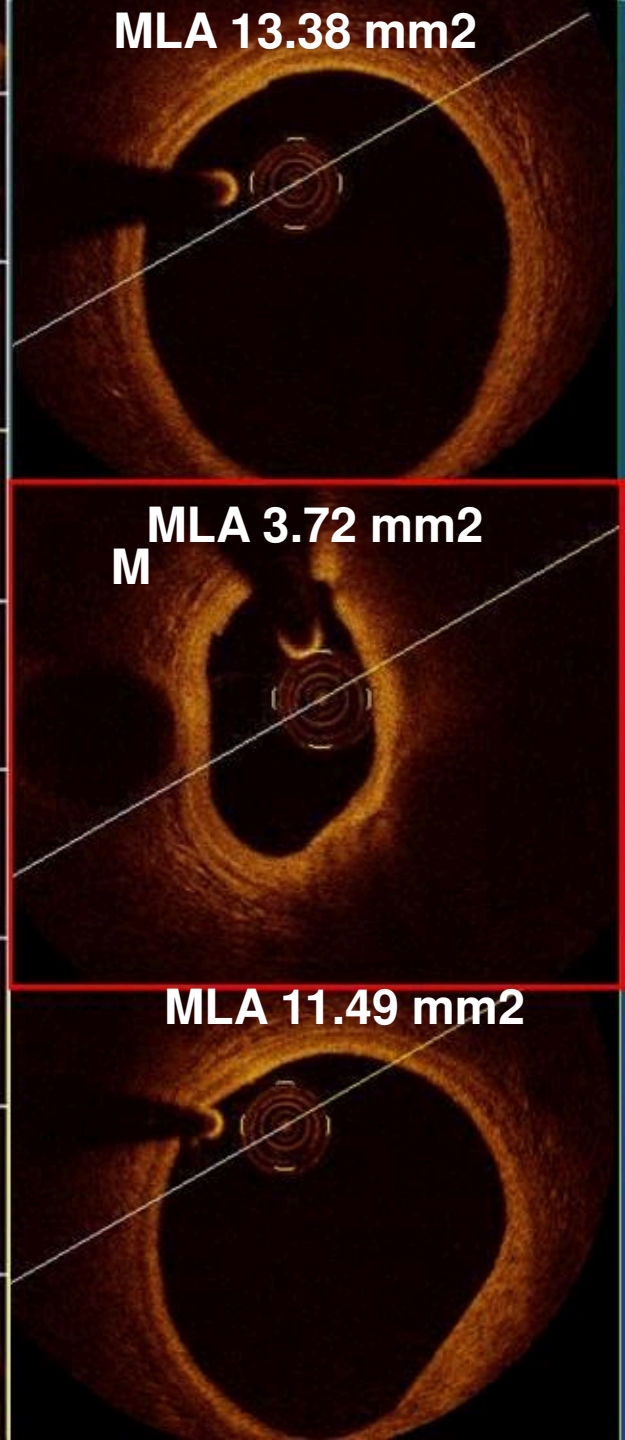
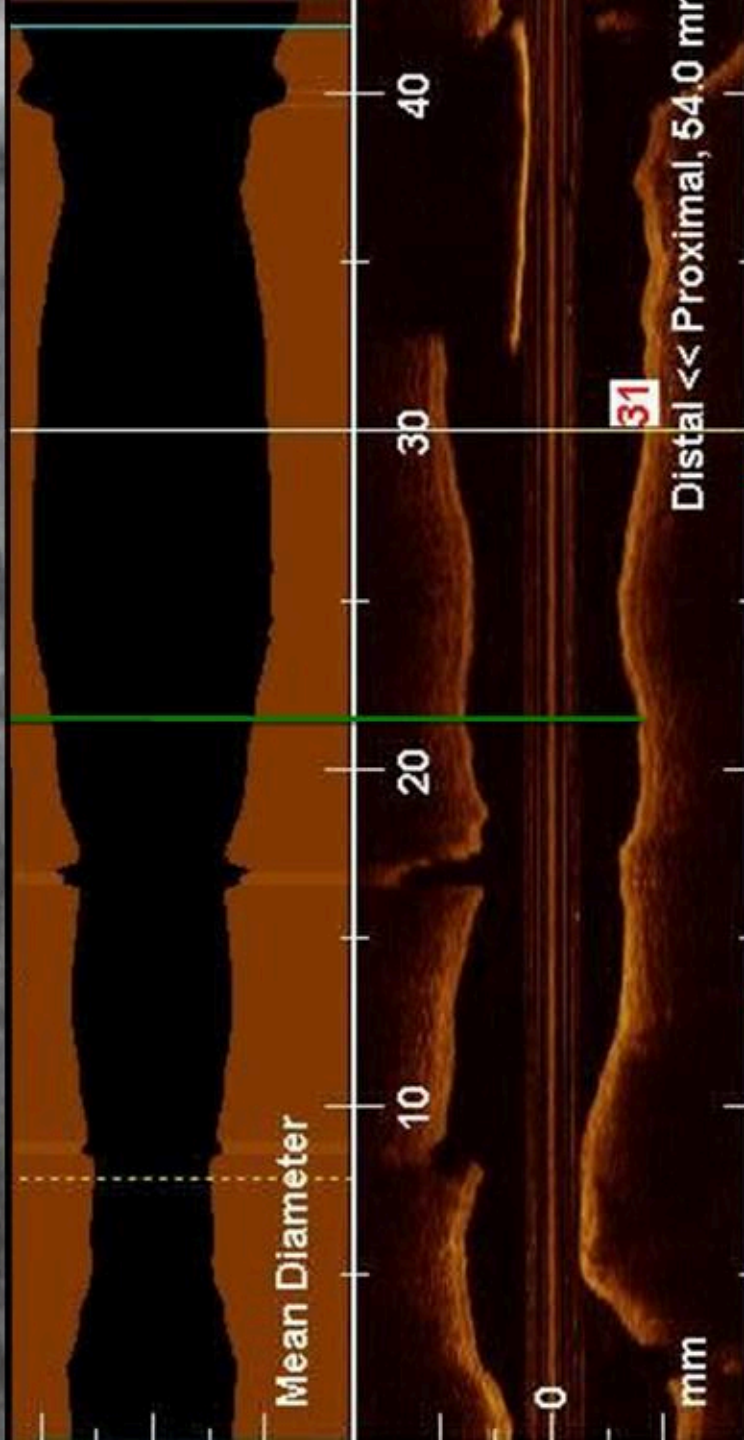
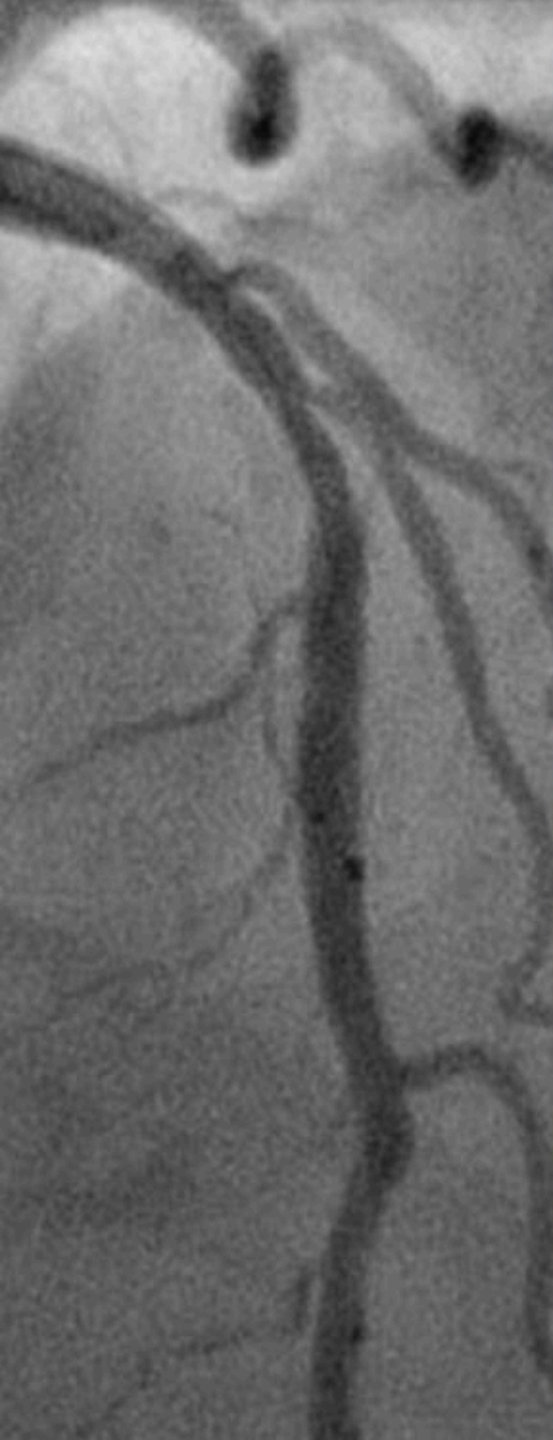
# Exercise Testing Contraindications

- MI—impending or acute
- Unstable angina
- Acute myocarditis/pericarditis
- Acute systemic illness
- Severe aortic stenosis
- Congestive heart failure
- Severe hypertension
- Uncontrolled cardiac arrhythmias



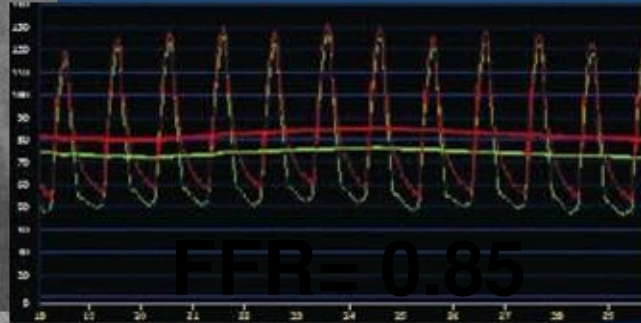
# Cardiac Catheterization Indications

- Suspicion of multi-vessel CAD
  - Determine if CABG/PTCA feasible
  - Rule out CAD in patients with persistent/disabling chest pain and equivocal/normal noninvasive testing
- 

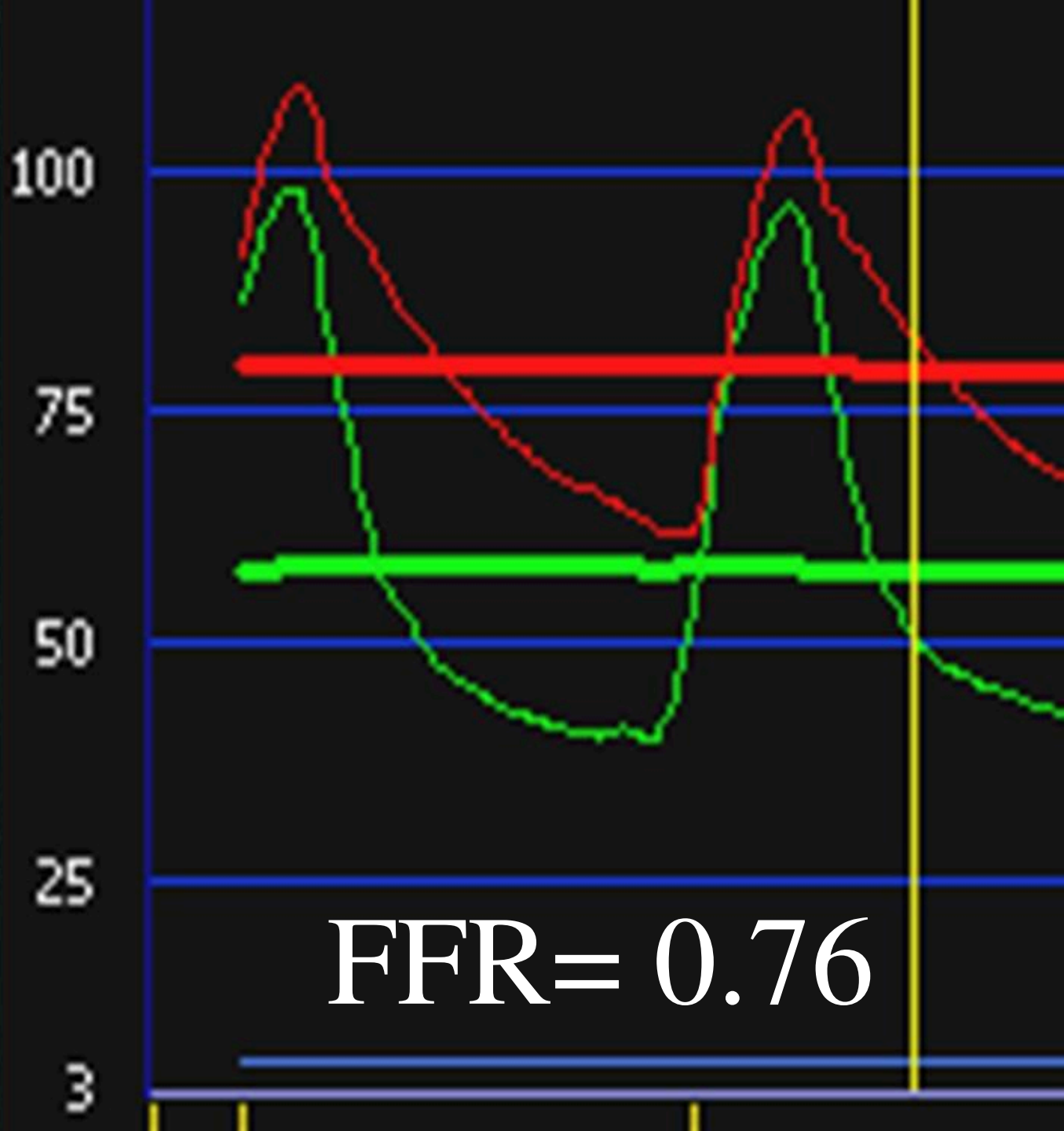
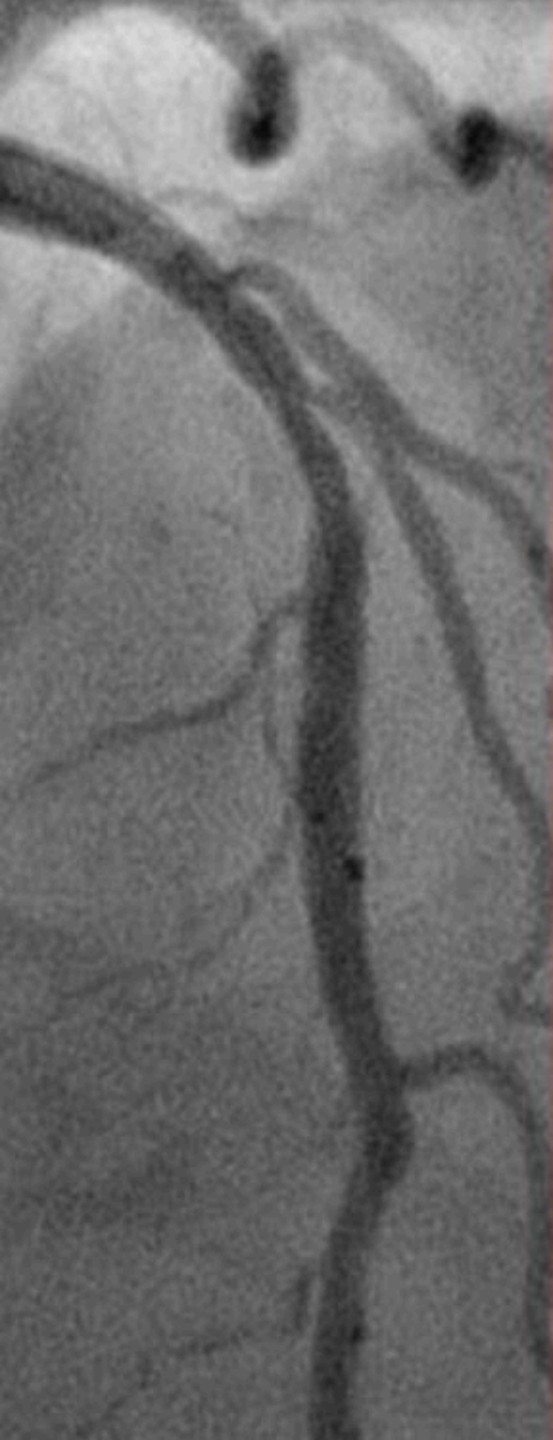


# Class CCS 2 Effort Angina

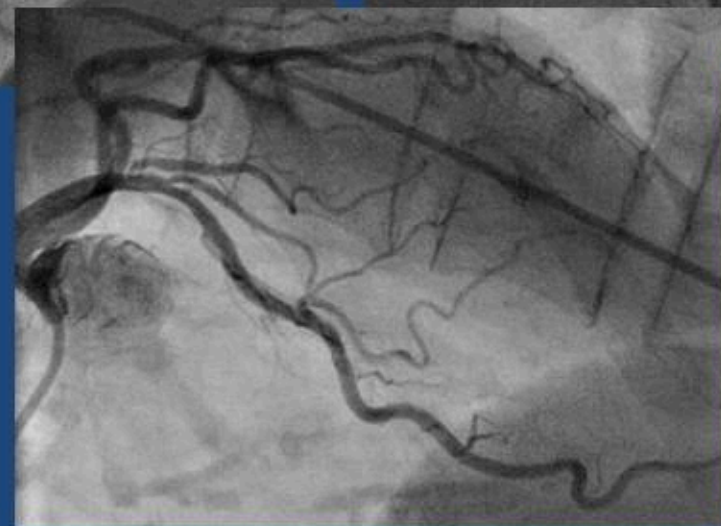
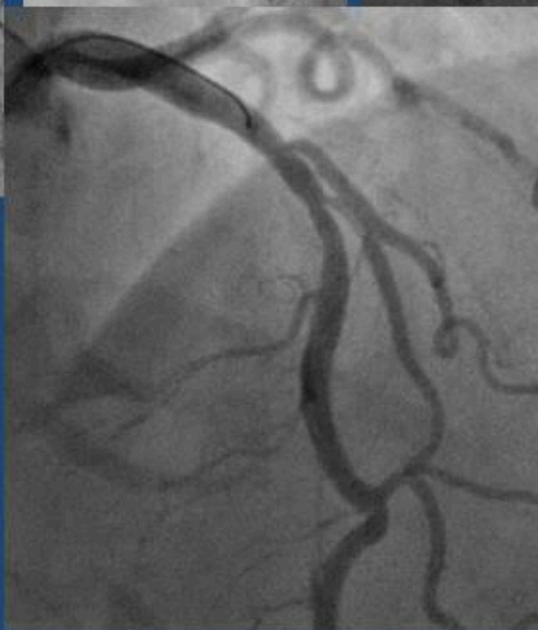
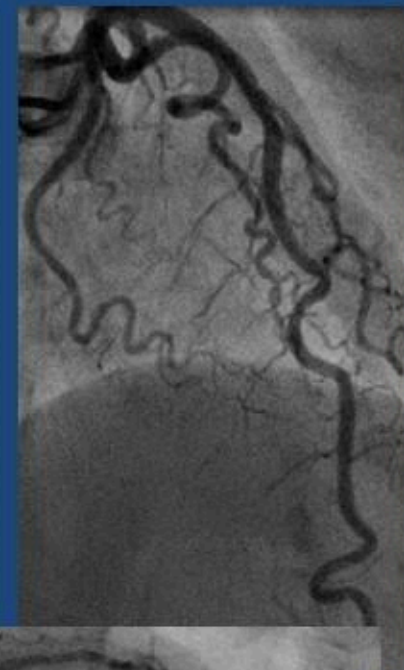
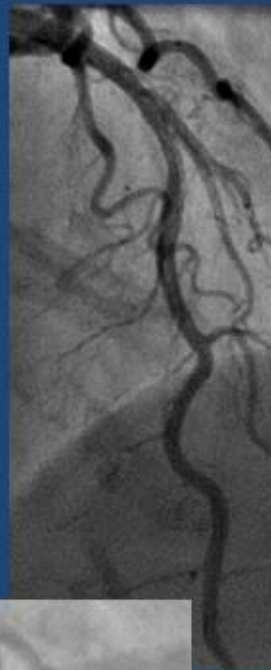
64 Yo Photographer  
Hypertension  
Hypercholesterolaemia  
Smoking







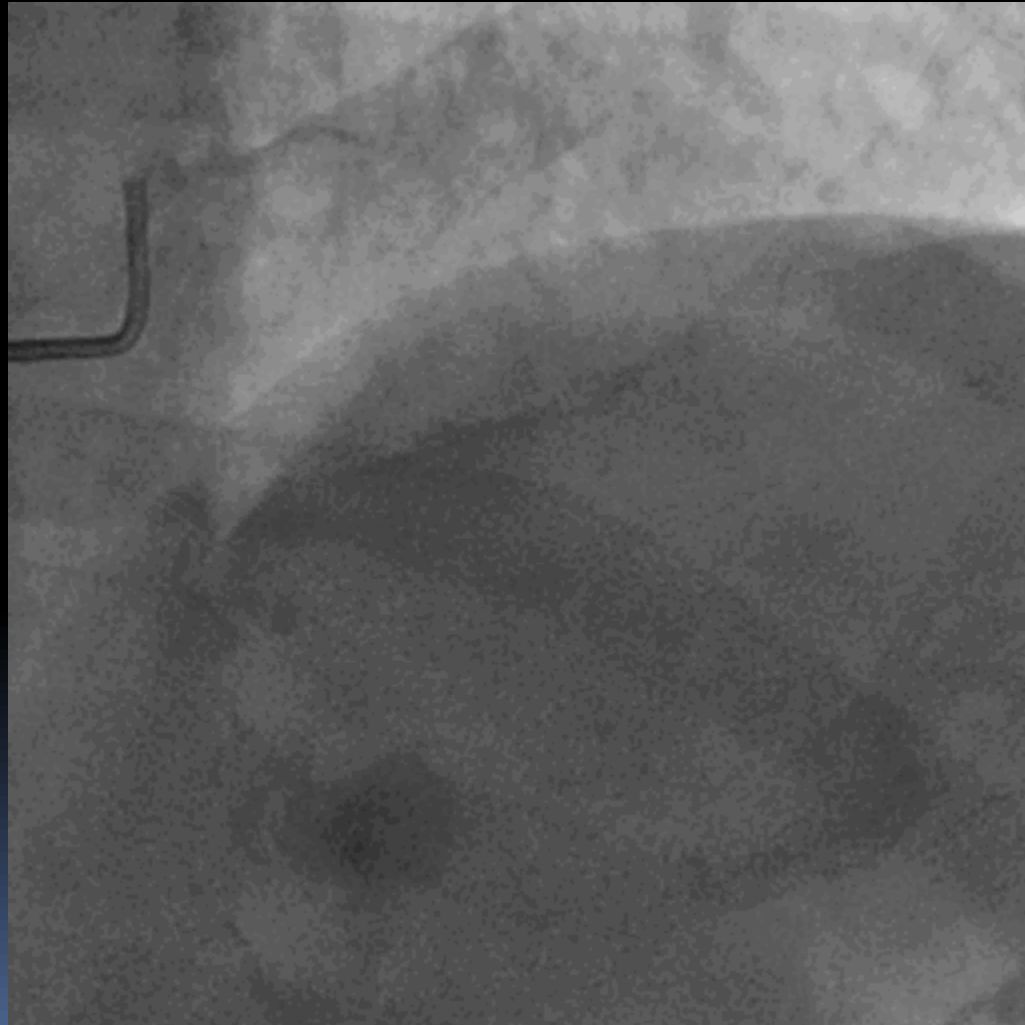
# LAD Angiography in 7 Views



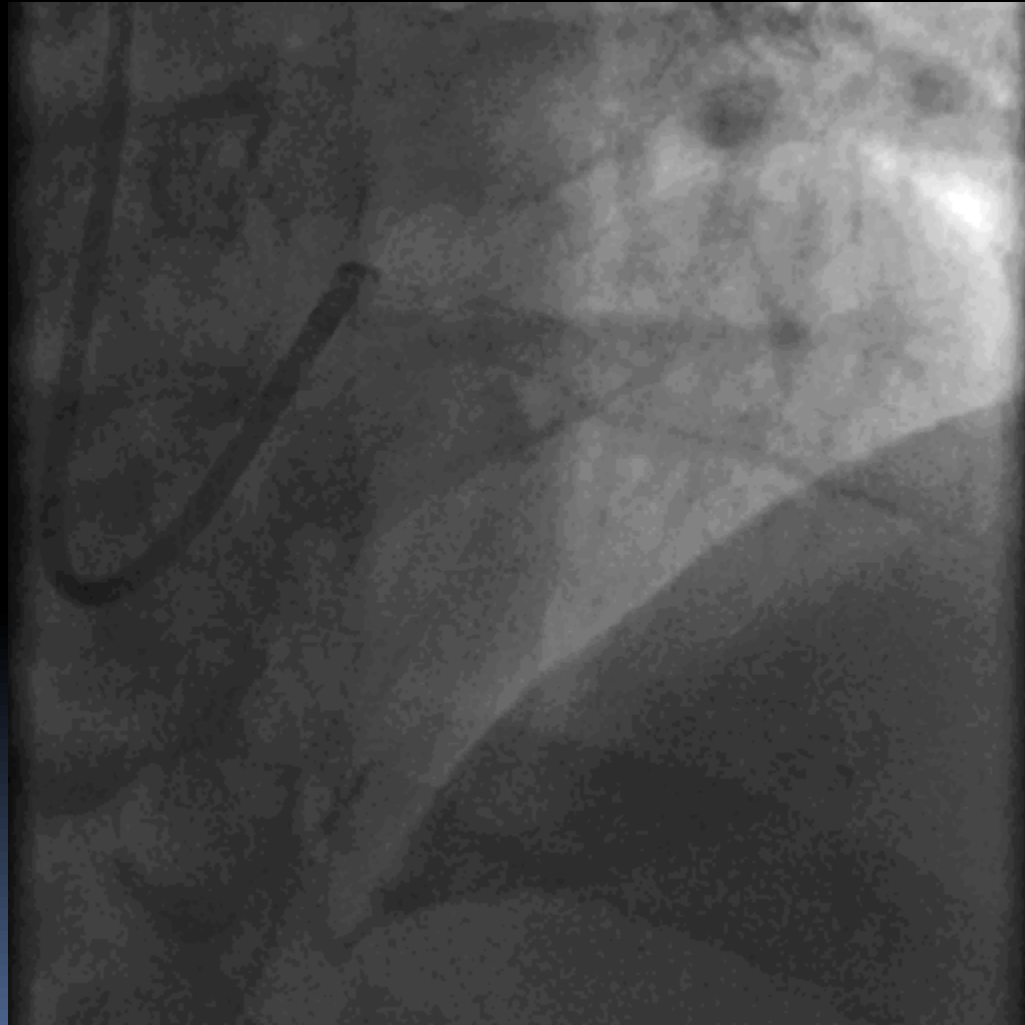
**54 Yo Woman Chest Pain for 6 months, severe hypercholesterolaemia**



76 yrs Male with DOE for 1 y



48yrs male with DOE 5yrs





45yrs male DOE & AOE class2






# Selection of drugs

- Effect on myocardium
  - Effect on cardiac conduction system
  - Effect on coronary/systemic arteries
  - Effect on venous capacitance system
  - Circadian rhythm
- 



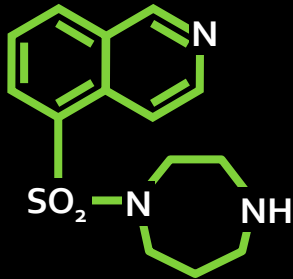
# Stable Angina

## Current Pharmacotherapy

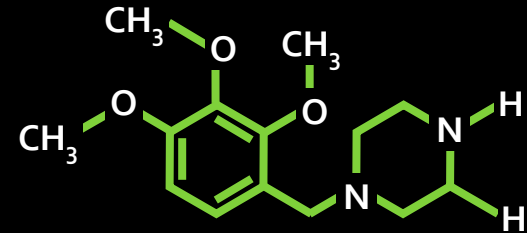
- Beta-blockers
  - Calcium channel blockers
  - Nitrates
  - Aspirin
  - Statins
  - ? ACE inhibitors
- 

# New mechanistic approaches to chronic stable angina

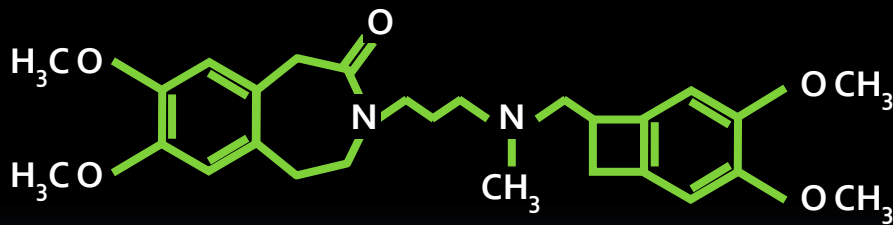
Rho kinase inhibition (fasudil)



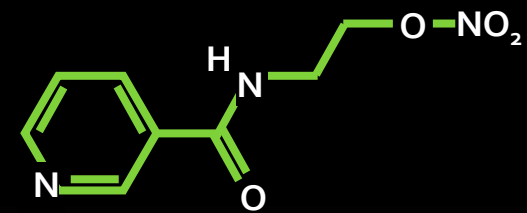
Metabolic modulation (trimetazidine)



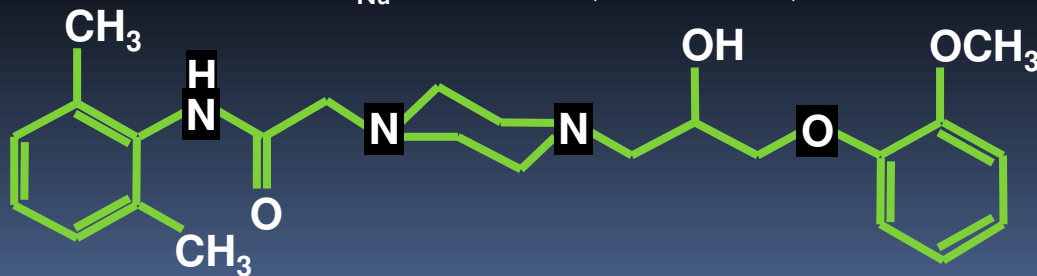
Sinus node inhibition (ivabradine)



Preconditioning (nicorandil)




Late I<sub>Na</sub> inhibition (ranolazine)

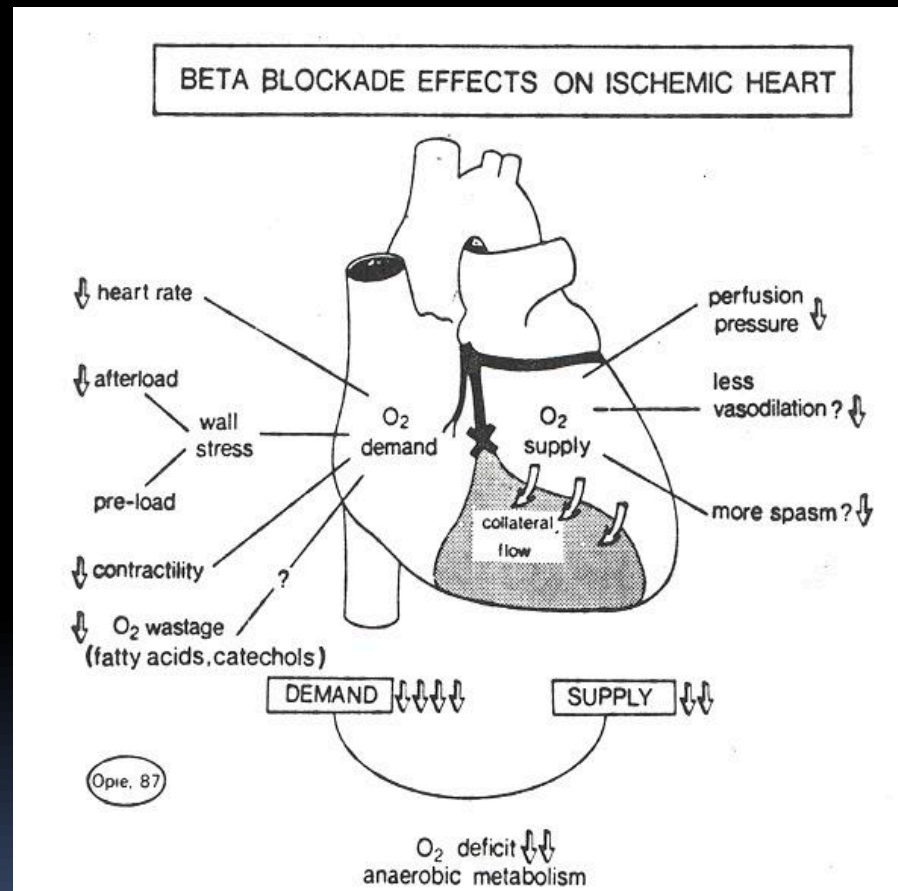




# Beta-Blockers

- Decrease myocardial oxygen consumption
  - Blunt exercise response
  - Beta-one drugs have theoretical advantage
  - Try to avoid drugs with intrinsic sympathomimetic activity
  - First line therapy in all patients with angina if possible
- 

# Beta-Blockers



**Fig. 1-2.** Effects of  $\beta$ -blockade on ischemic heart.  $\beta$ -blockade has a beneficial effect on the ischemic myocardium, unless (1) the preload rises substantially as in left heart failure or (2) there is vasospastic angina when spasm may be promoted in some patients.





# Beta Blockers


## Side Effects

- Bronchospasm
- Diminished exercise capacity
- Negative inotropy
- Sexual dysfunction
- Bradycardia
- Masking of hypoglycemia
- Increased claudication
- Hair loss



# Calcium Channel Blockers


## Mechanisms of Action

- Arterial dilation/after-load reduction
  - Coronary arterial vasodilation
  - Prevention of coronary vasoconstriction
  - Enhancement of coronary collateral flow
  - Improved subendocardial perfusion
  - Slowing of heart rate with diltiazem, verapamil
- 



# Calcium Channel Blockers


## Side Effects

- Palpitations
  - Headache
  - Ankle edema
  - Gingival hyperplasia
- 



# Nitrates


## Mechanisms of Action

- Nitric oxide has been identified as endothelium-derived relaxing factor
  - Organic nitrates are therapeutic precursors of endothelium-derived relaxing factor
- 



# Nitrates


## Mechanisms of Action

- Venous vasodilation/pre-load reduction
  - Arterial dilation/after-load reduction
  - Coronary arterial vasodilation
  - Prevention of coronary vasoconstriction
  - Enhancement of coronary collateral flow
  - Antiplatelet and antithrombotic effects
- 



# Nitrates

## Reducing Tolerance


- Smaller doses
  - Less frequent dosing
  - Avoidance of long-acting formulations unless a prolonged nitrate-free interval is provided
  - Build-in a nitrate-free interval of 8-12 hours
- 





# Nitrates

## Side Effects

- Headache
  - Flushing
  - Palpitations
  - Tolerance
- 

# Ranolazine in Ischemic Heart Disease

- Anti-anginal & anti-ischemic effects without clinically significant effect on HR or BP
- **Approved for treatment of chronic angina**
  - ↑ exercise time, ↓ angina in selected pts
- **Novel mechanism of action**
  - Inhibition of late  $I_{Na}$  → ↓  $Ca^{2+}$  overload → ↓ adverse energetic, mechanical, electrical consequences
- **Experimental evidence**
  - ↑ LV performance during ischemia
  - ↑ recovery of LV function, ↓ infarct size

# Ranolazine in Ischemic Heart Disease

- Ranolazine associated with an  $\uparrow$  in QTc (average ~5 msec)
- However, experimental data suggest suppression of pro-arrhythmic markers
- *Indication in chronic angina:* “Because ranolazine prolongs the QT interval, it should be reserved for patients who have not achieved an adequate response with other anti-anginal drugs.”

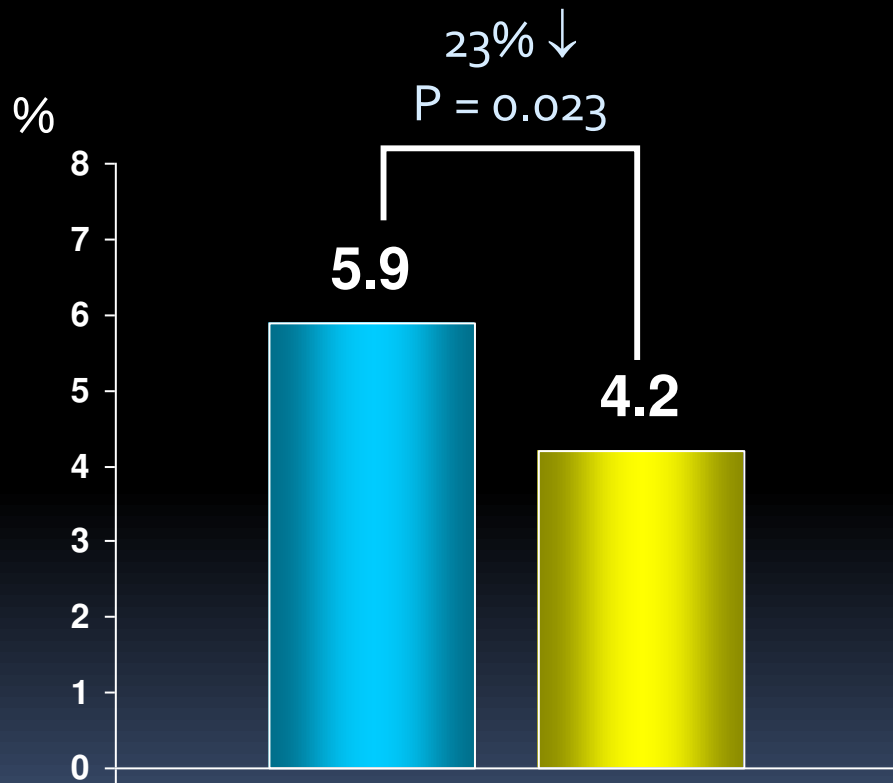
Need for additional safety information



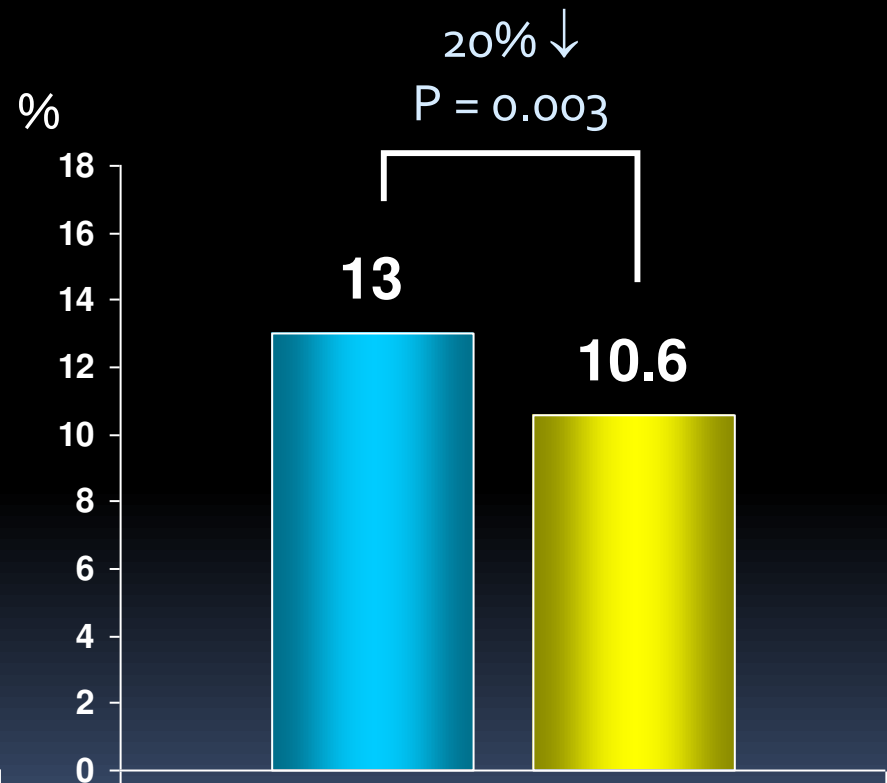
# Assessment of Anti-anginal Effects

PLACEBO  
(N=3,281)

RANOLAZINE  
(N=3,279)




Worsening Angina (%)\*




Antianginal Increase (%)\*

# Shift Study: ivabradine in heart failure and angina


- Ivabradine
  - An I(f) blocker
  - Slows the sinus node rate without other effects of beta blockers
  - Only effective if in sinus rhythm
- Contraindicated with diltiazem, verapamil, antifungal, microlides, grape juice and etc




Q-1 which drug is  
contraindicated in AF?


- A) nicorandil
  - B) Mononitrate
  - C) Ivabradine
  - D) Trimetazidine
- 





## Q-2, What is best symptom to diagnose CSA?

- A) Angina on exertion
  - B) Diaphoresis
  - C) Palpitation
  - D)Dyspnea on exertion
- 




Q-3, which type of lipoprotein is found in the plaque of CSA?

- A) ApoB<sub>100</sub> and ApoB<sub>26</sub>
- B) ApoB<sub>100</sub> and ApoB<sub>28</sub>
- C) ApoB<sub>100</sub> and Apo A
- D) ApoB<sub>100</sub> and Lpa




Q-4, how does ranolazine work on cardiac pathway?

- A) ,Inhibiting Ca channel
  - B), Inhibiting K ATP channel
  - C), Inhibiting Late Na channel
  - D), inhibiting late K channel
- 




# Q-5, contraindication with ivabradine?

- A), amiodarone
  - B), Beta blockers
  - C), ACEIs
  - D), Fluconazole
- 



# How to avoid CSA to ACS?

- Using appropriate tool to diagnose CAD
  - Assessing plaque morphology
  - Molecular based treatment
  - Periodical assessment
- 

Thank you for your attention

