

Pathology of Vulnerable Plaque

Angioplasty Summit 2005

TCT Asia Pacific, Seoul, April 28-30, 2005



Renu Virmani, MD

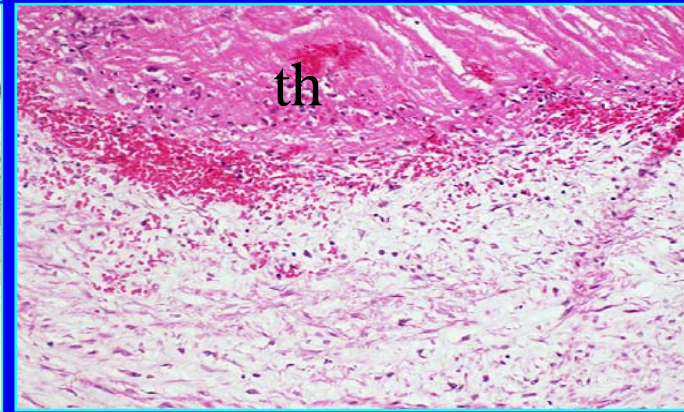
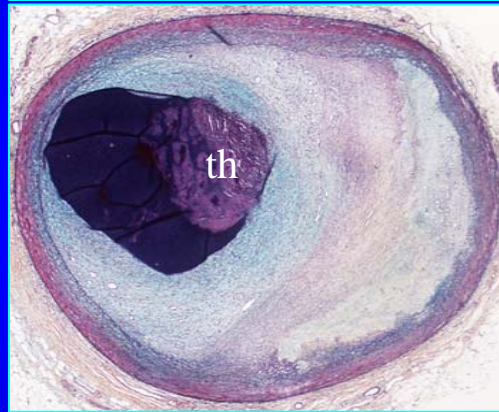
CVPath, A Research Service of the International
Registry of Pathology
Gaithersburg, MD

Plaque Morphology of Thrombi in SCD

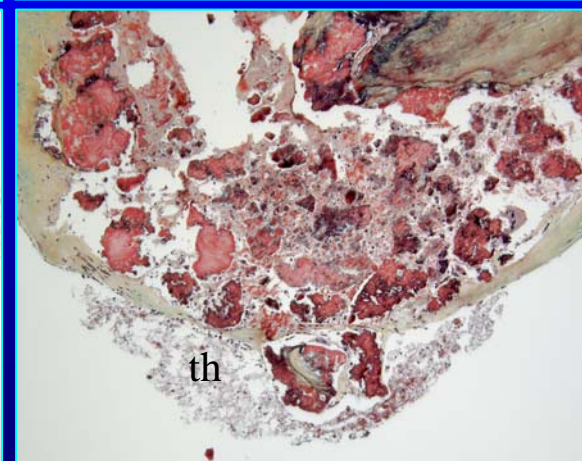
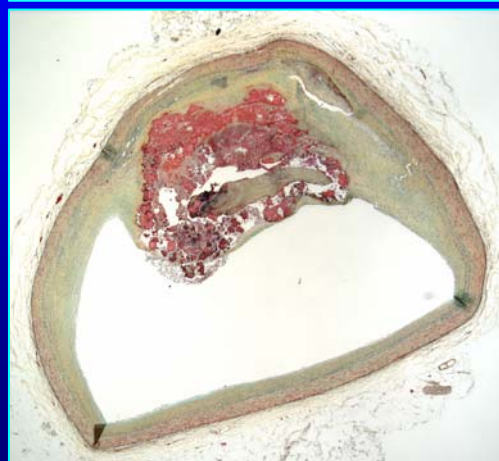
Plaque Rupture
55 - 60%



Plaque Erosion
30 - 35%

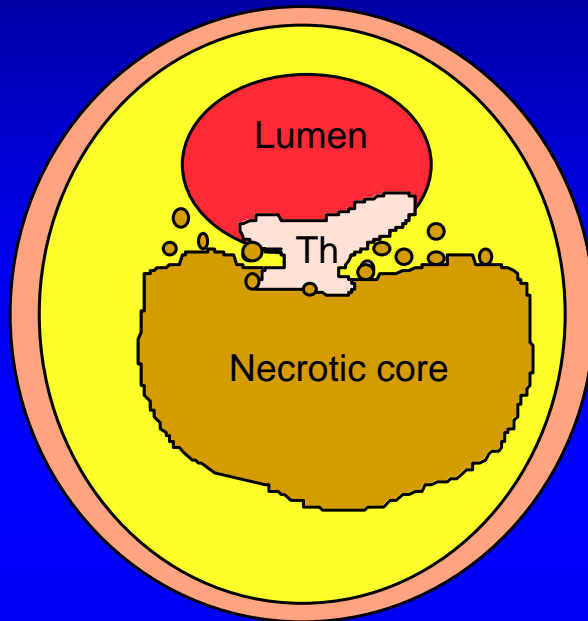


Calcified Nodule
2 - 7 %

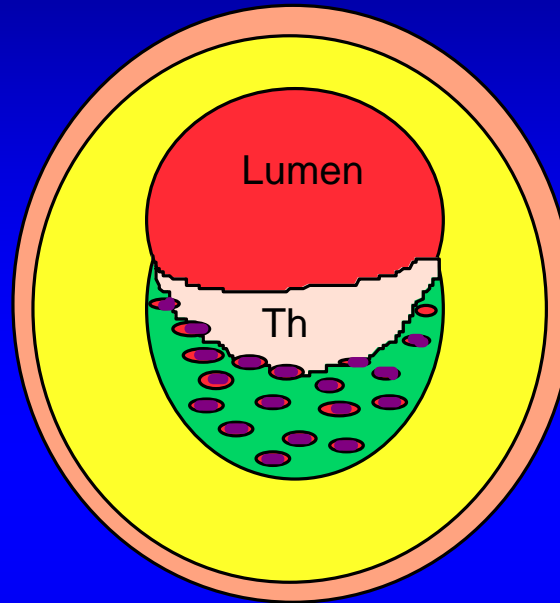


Clinical and Morphologic Difference in Plaques Associated with Luminal Thrombi

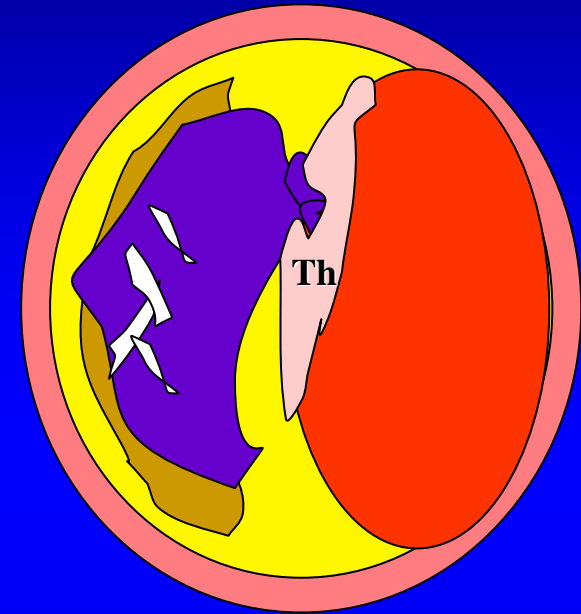
Plaque rupture



Plaque erosion



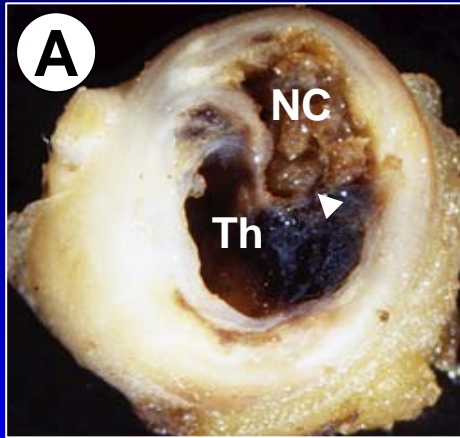
Calcified nodule



45-55% thrombi in SCD
 M>F, Older, Ca⁺⁺
 Eccentric = concentric
 Greater % stenosis
 Macs, T cells,HLADr

35-40% thrombi in SCD
 M=F, younger
 Usually eccentric
 Lesser % stenosis
 SMC rich, proteoglycans

4-7% thrombi in SCD, calcified plates
 M>F, older, mid RCA
 Usually eccentric
 Stenosis variable
 Nodules of bone



Gross and Light Microscopic Features of Plaque Rupture

60% of Thrombi in Sudden Coronary Death Are from Plaque Rupture

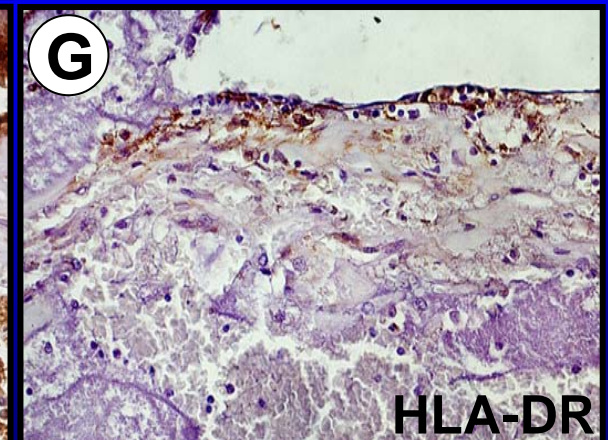
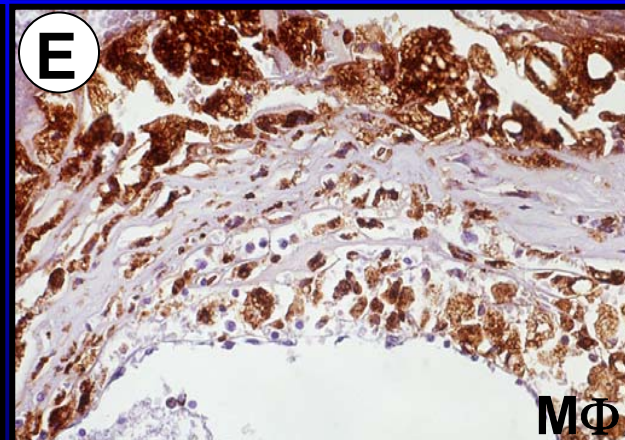
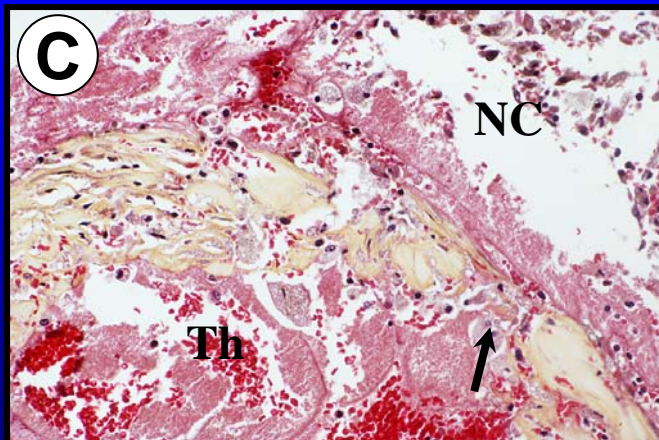
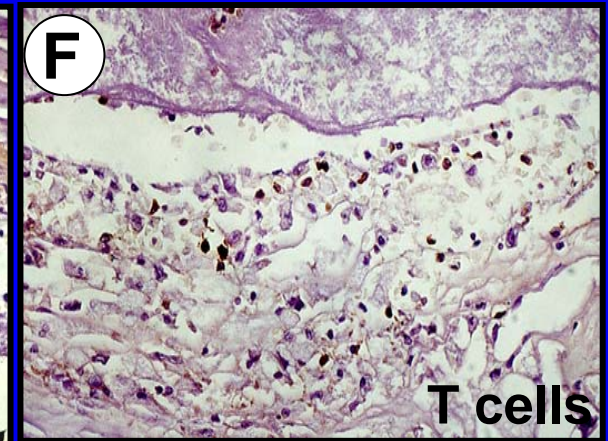
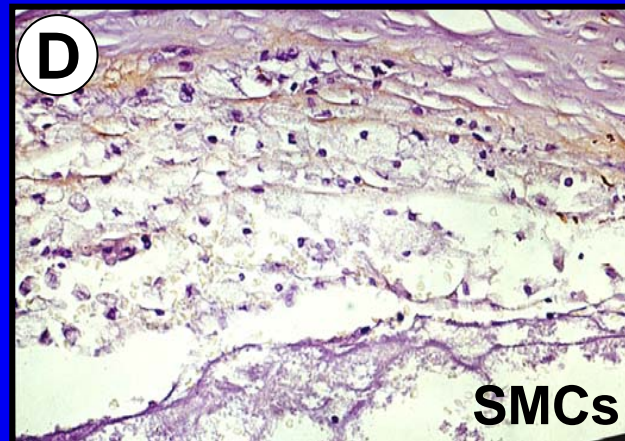
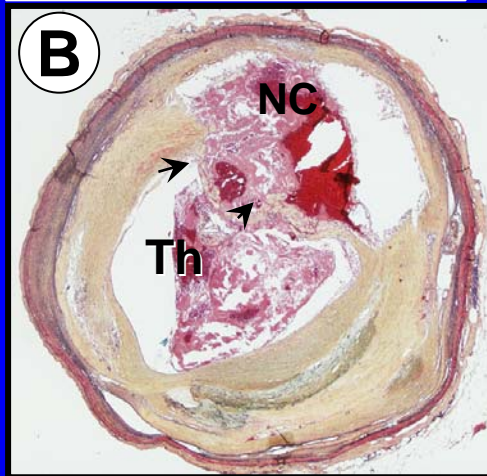
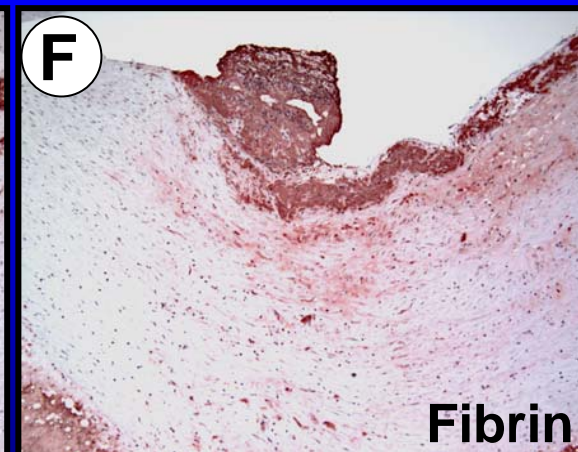
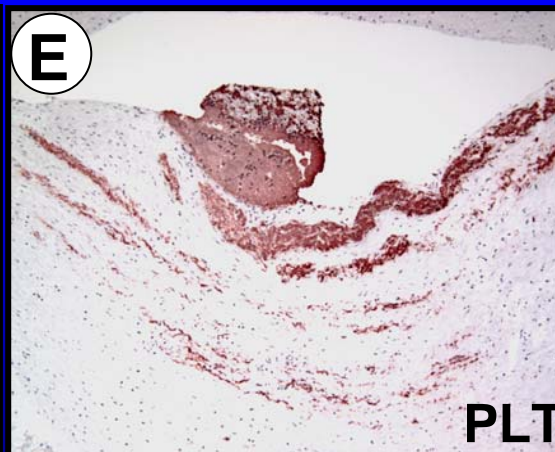
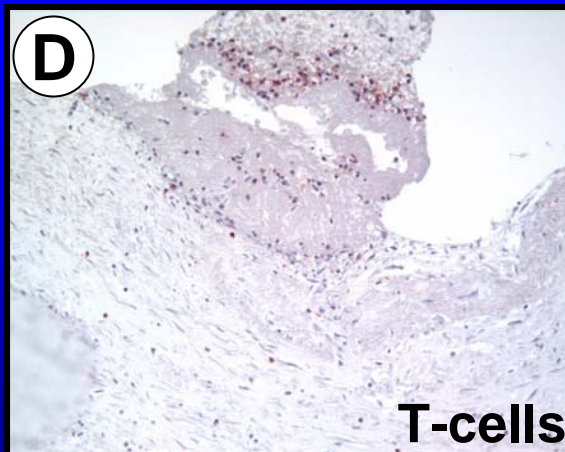
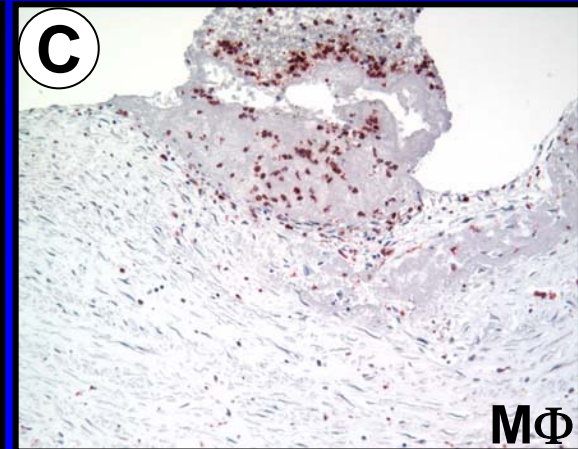
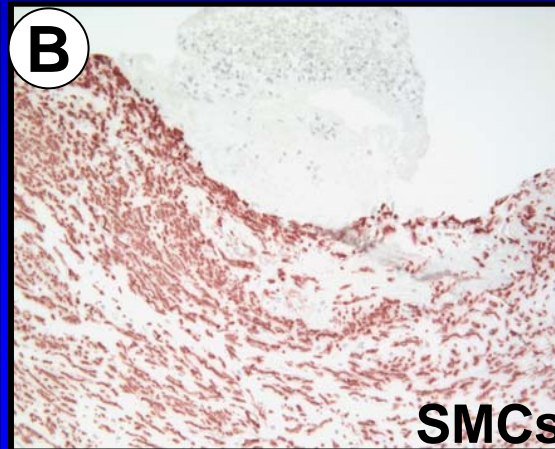
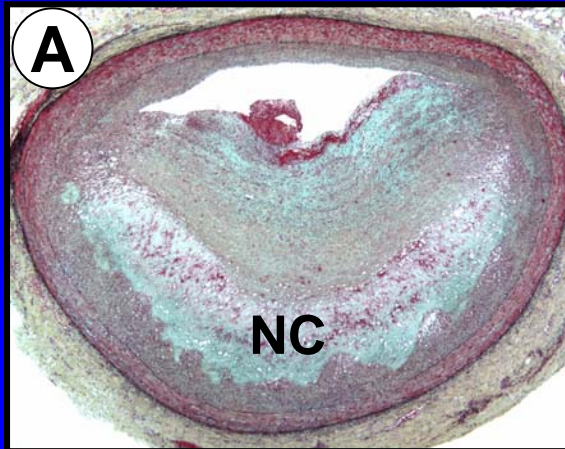


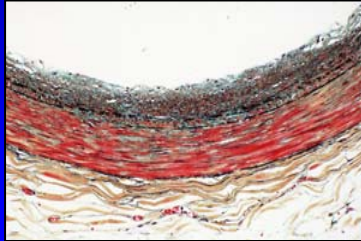
Fig 3-1

Plaque erosion in a 33 year-old female complaining of chest pain for two-weeks and discharged from the emergency room with a diagnoses of anxiety.

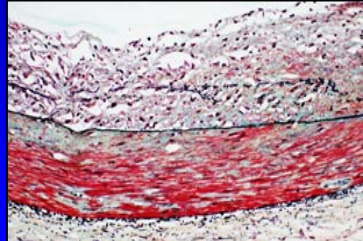


Development of Human Coronary Atherosclerosis

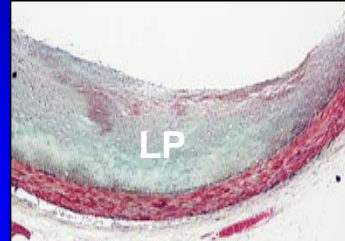
Intimal thickening



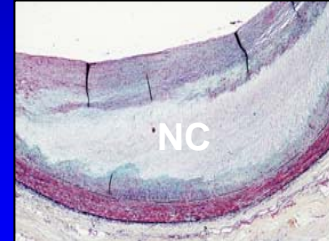
Intimal xanthoma



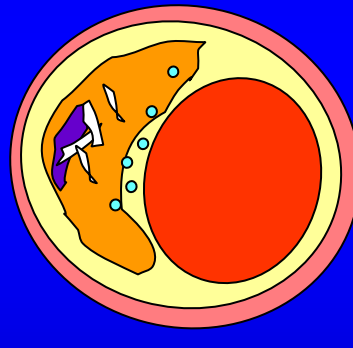
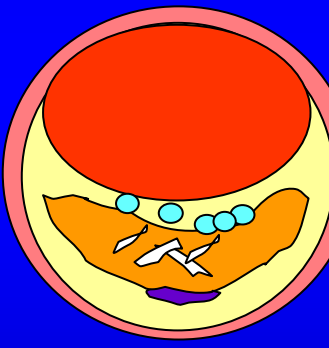
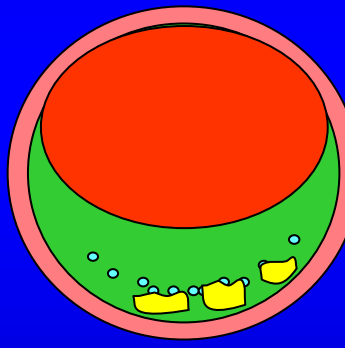
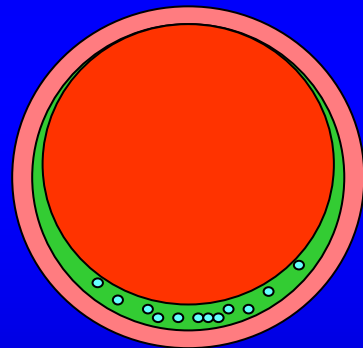
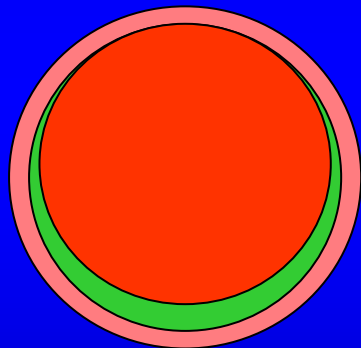
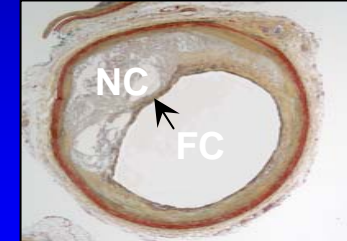
Pathologic intimal thickening



Fibrous cap atheroma



Thin-cap Fibroatheroma



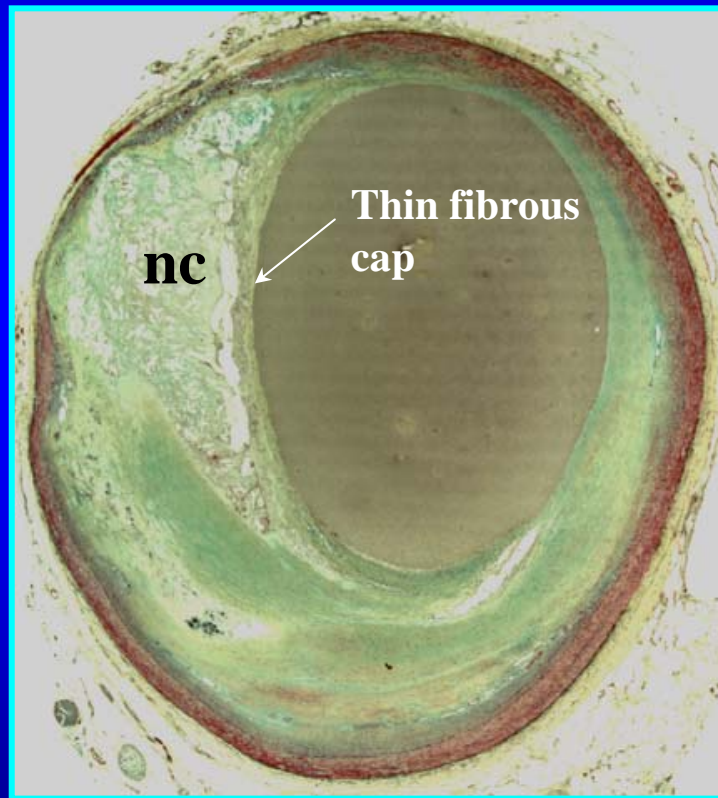
- Smooth muscle cells
- Macrophage foam cells
- Extracellular lipid
- Cholesterol clefts
- Necrotic core
- Calcified plaque
- Hemorrhage
- Thrombus
- Healed thrombus
- Collagen

What is a Vulnerable Plaque?

- Plaque morphology underlying luminal thrombi represents a vulnerable plaque
 - Thin-cap Fibroatheroma – **Plaque rupture**
 - Pathologic intimal thickening
 - Fibroatheroma
 - Calcified plates with bone formation –
 - **Calcified nodule** - surface thrombus
- Plaque Erosion**

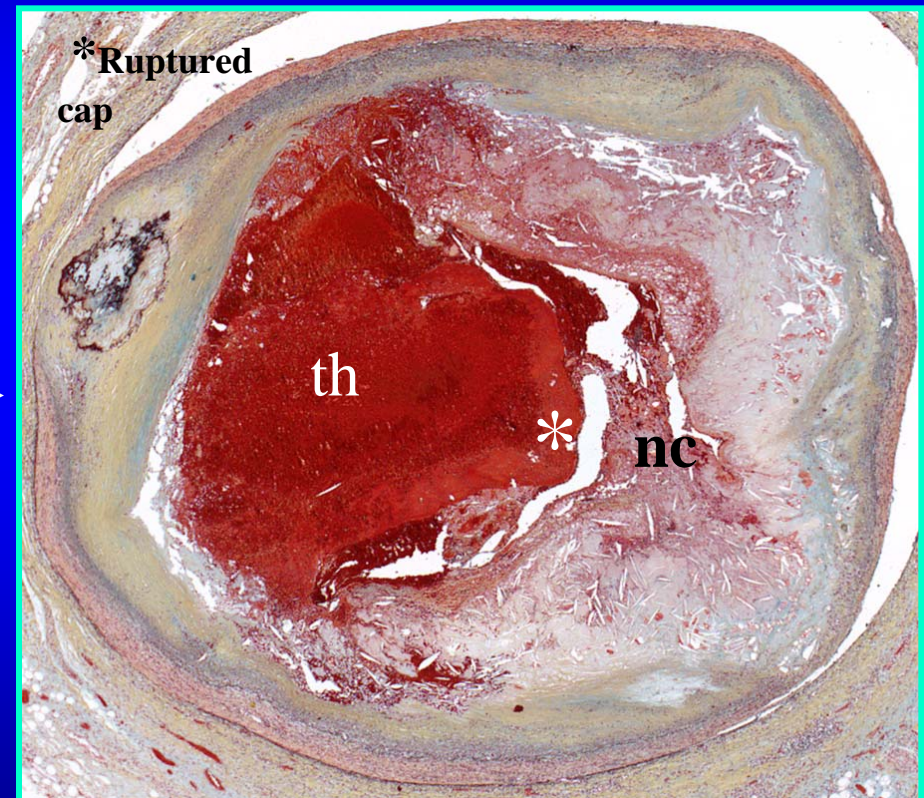
Thin cap Fibroatheroma is a Precursor lesions of Plaque Rupture

TCFA



?

Plaque Rupture



Thin-Cap Atheroma (Vulnerable Plaque) Components

- Necrotic core
- Thin fibrous cap ($< 65 \mu\text{m}$)
- Cap infiltrated by macrophages and lymphocytes
- Cap composition – type 1 collagen and few smooth muscle cells

A Non-Hemodynamically Limiting Thin-cap Fibroatheroma

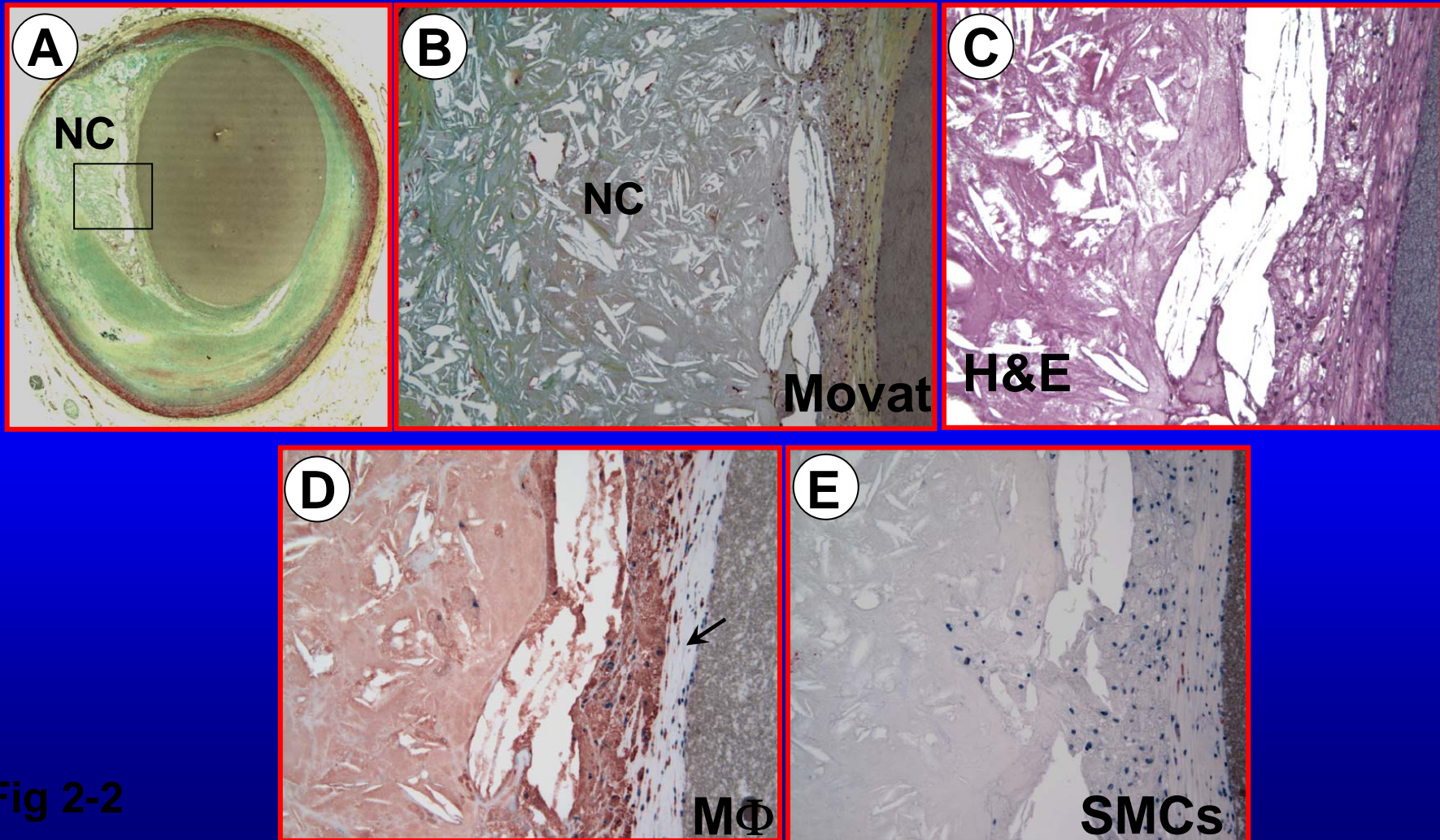


Fig 2-2

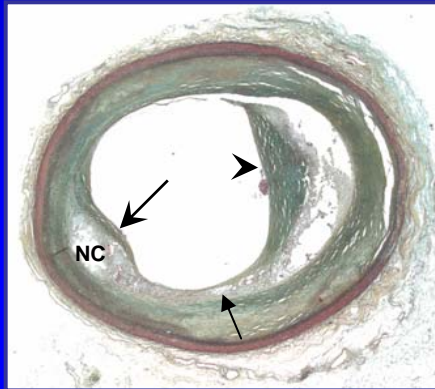
Morphologic Characteristics of Plaque Rupture and Thin-cap Fibroatheromas

Plaque type	Necrotic Core (%)	Fibrous cap Thickness (μm)	M Φ s (%)	SMCs (%)	T-lymph	Calcification Score
Rupture	34 \pm 17	23 \pm 19	26 \pm 20	0.002 \pm 0.004	4.9 \pm 4.3	1.53 \pm 1.03
Thin-cap Fibroatheroma	23 \pm 17	<65 μm	14 \pm 10	6.6 \pm 10.4	6.6 \pm 10.4	0.97 \pm 1.1
P value	0.01		0.005	ns	ns	0.014

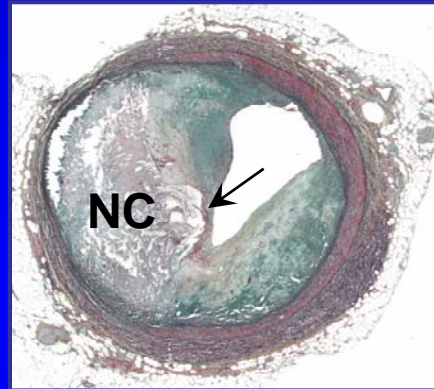
Mean values are represented \pm standard deviation. Abbreviations: M Φ s= macrophages, SMCs= smooth muscle cells, T-lymph= T-lymphocytes

Morphological Variants of the Thin-Cap Fibroatheroma

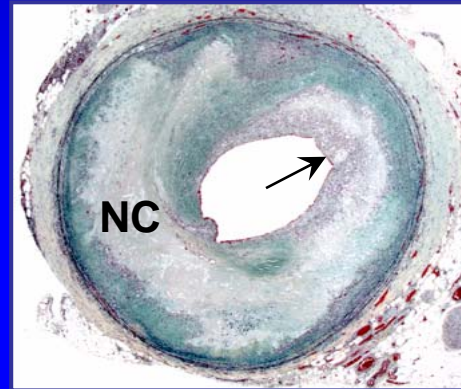
Insignificant
Plaque burden



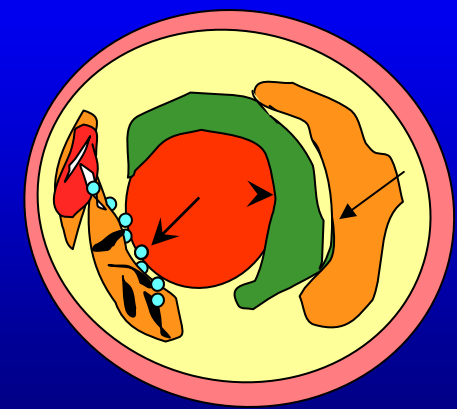
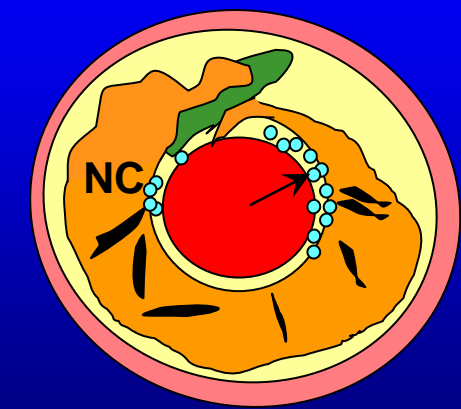
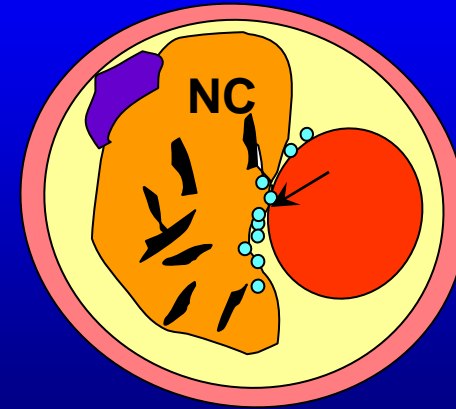
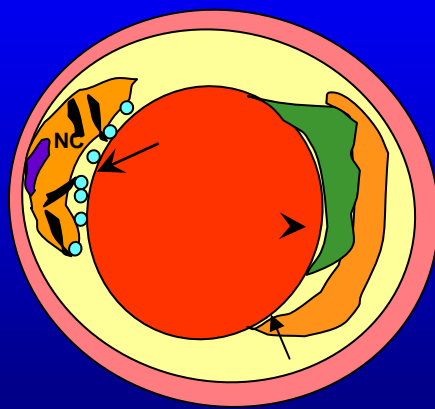
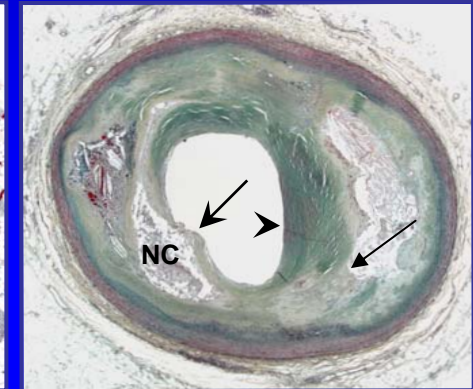
Large eccentric
necrotic core



Large concentric
necrotic core

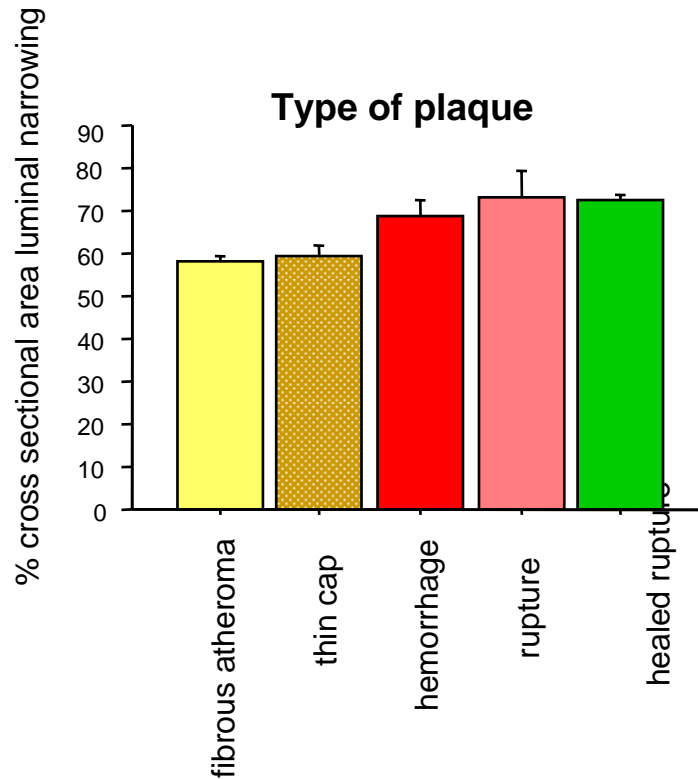


Healed
Rupture(s)



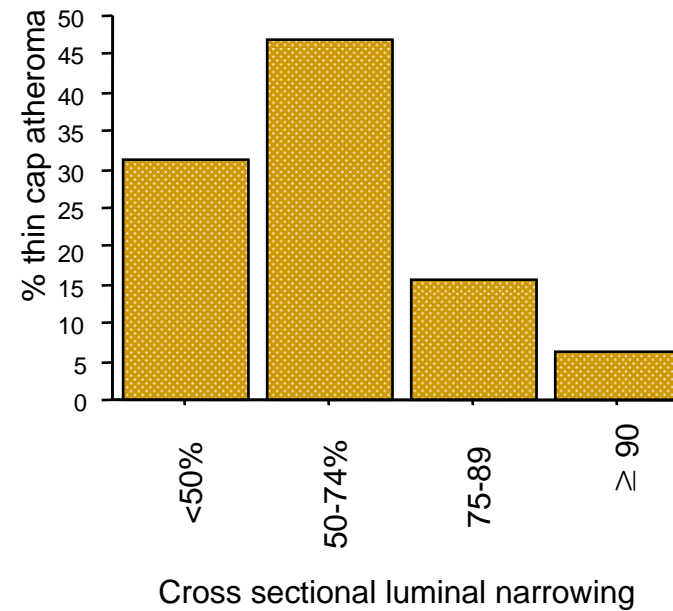
Vulnerable Plaque Characteristics

A



**Mean % x-sectional area
For TCFA is 60%**

B



**80% of thin cap atheromas occur in arteries
with < 75% x-sectional area luminal
narrowing (<50% diameter reduction)**

Distribution of Ruptures and Thin-Cap Atheromas by Plaque Area or Lipid Core Size

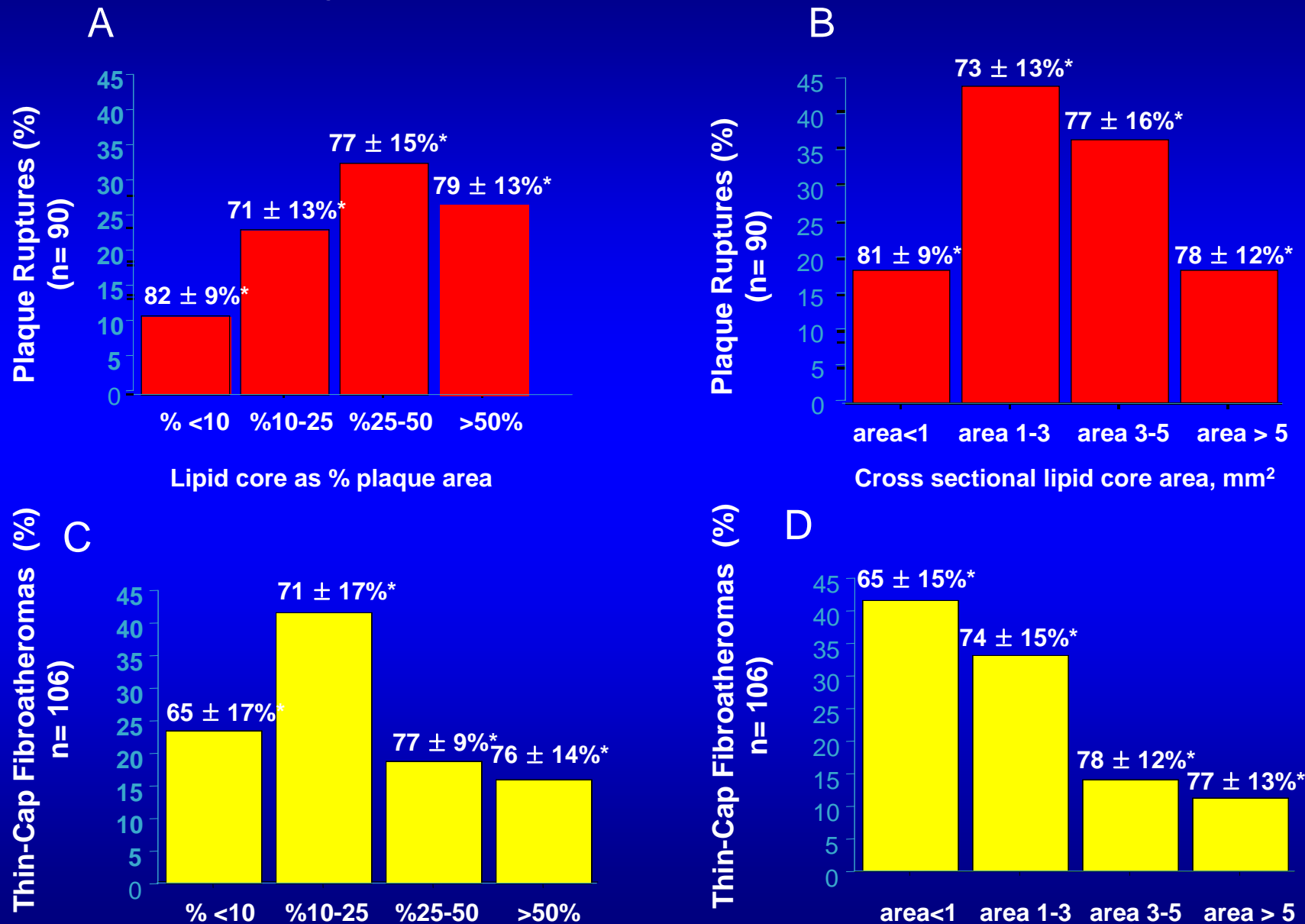
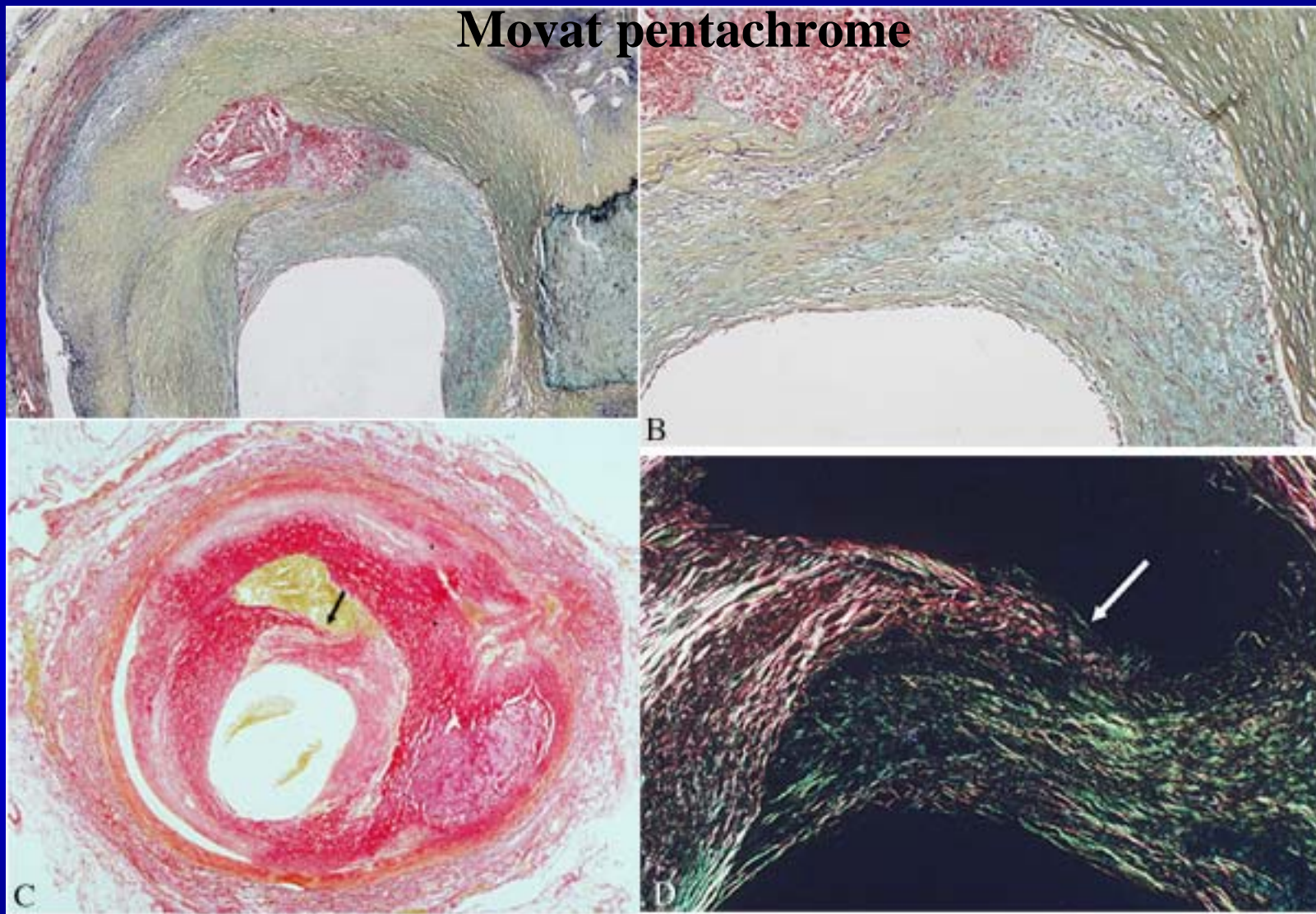


Fig 2-8

* = mean cross sectional area luminal narrowing

Do TCFAs lead to plaque progression ?



Movat pentachrome

B

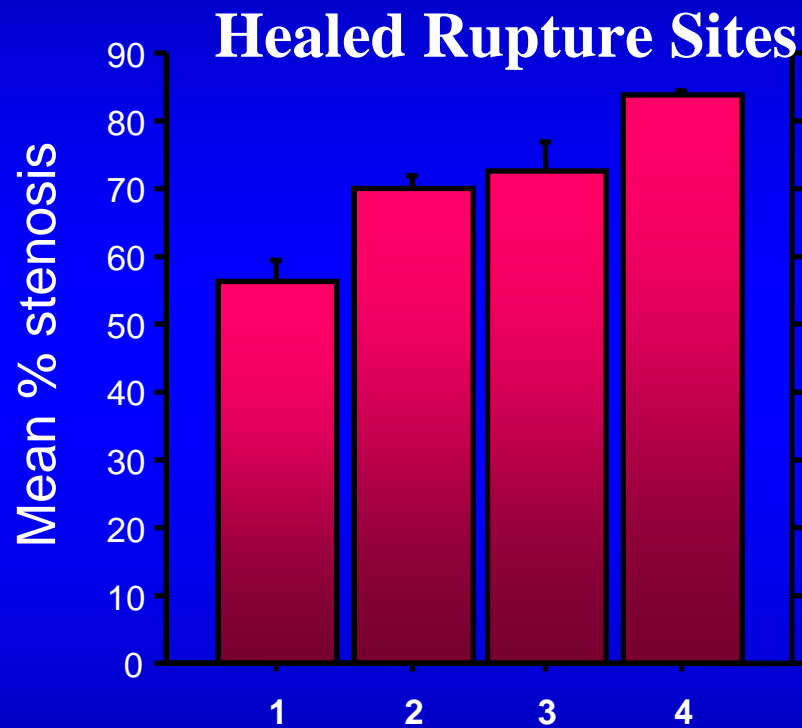
C

D

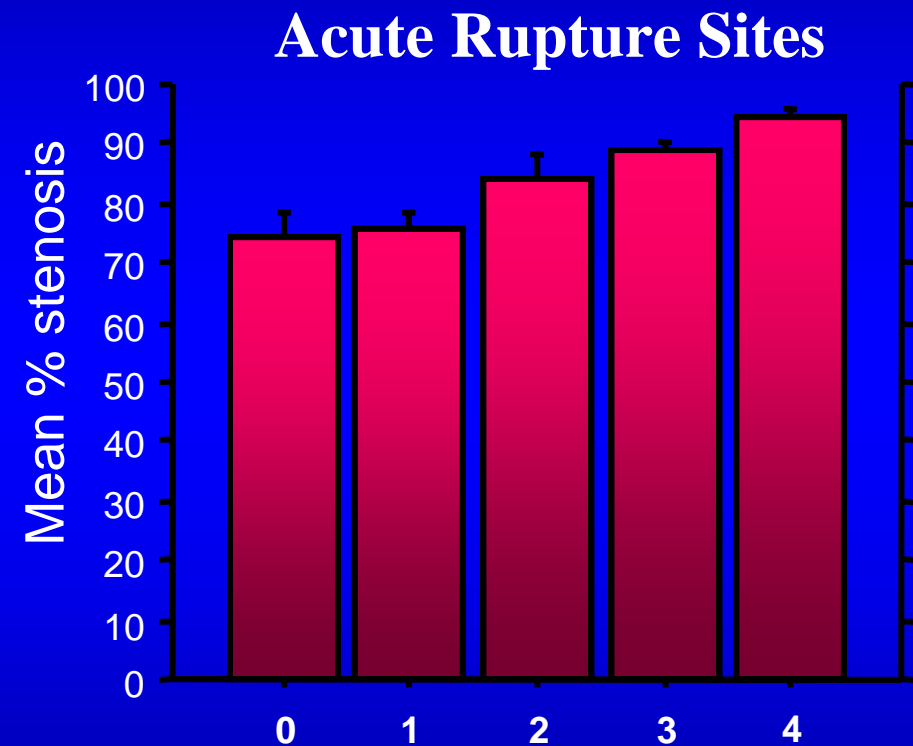
Sirius red

Sirius red with polarized light

Mean % Stenosis Increases with Number of Prior Rupture Sites but the Increase with Each New Rupture is Small (<20%)



A
Number of prior ruptures,
healed rupture sites



B
Number of prior ruptures,
acute rupture sites

Percentage of Cross-Sectional-Area Narrowing by Plaque Morphology

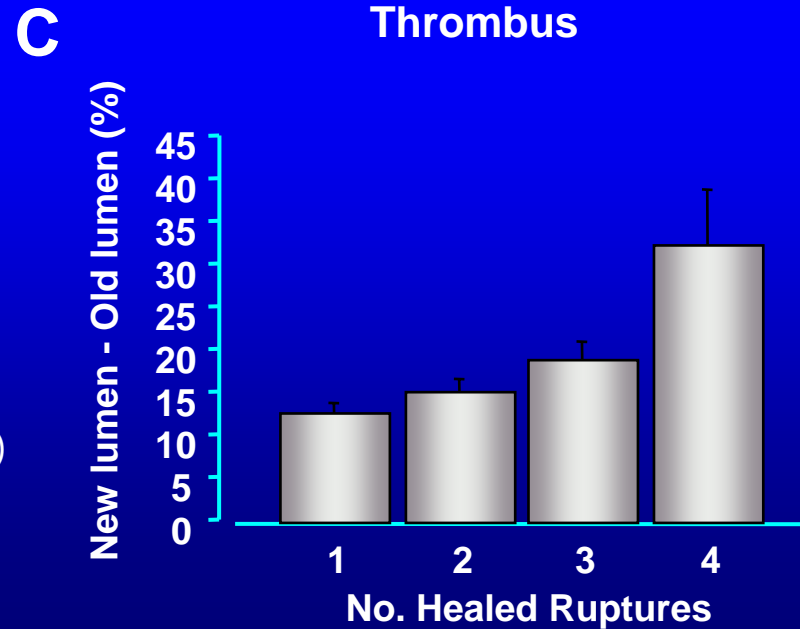
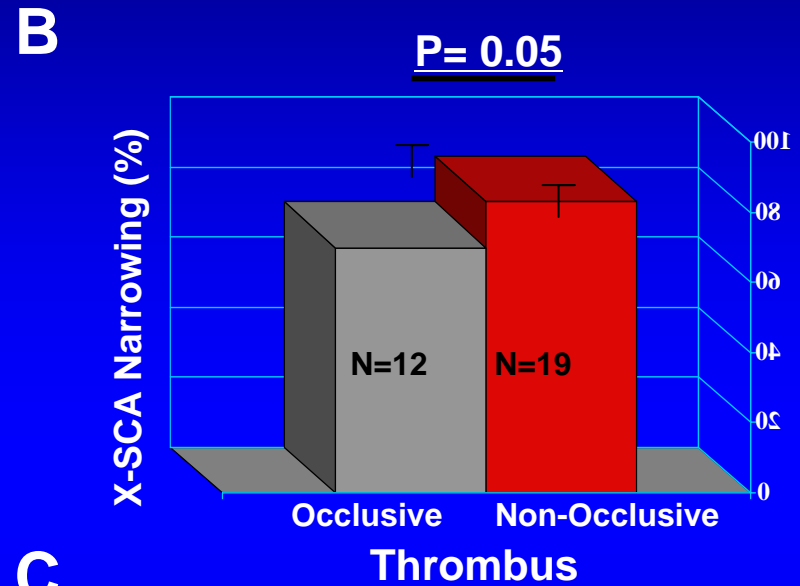
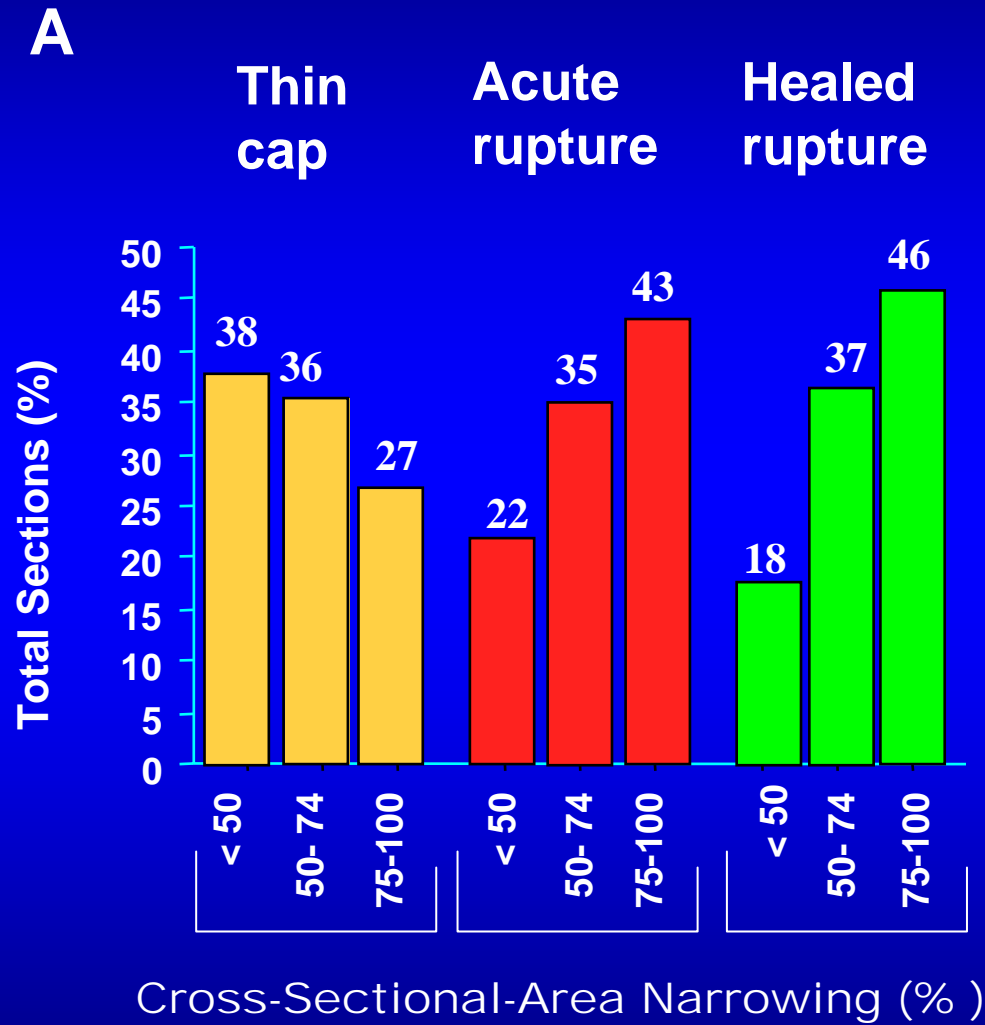
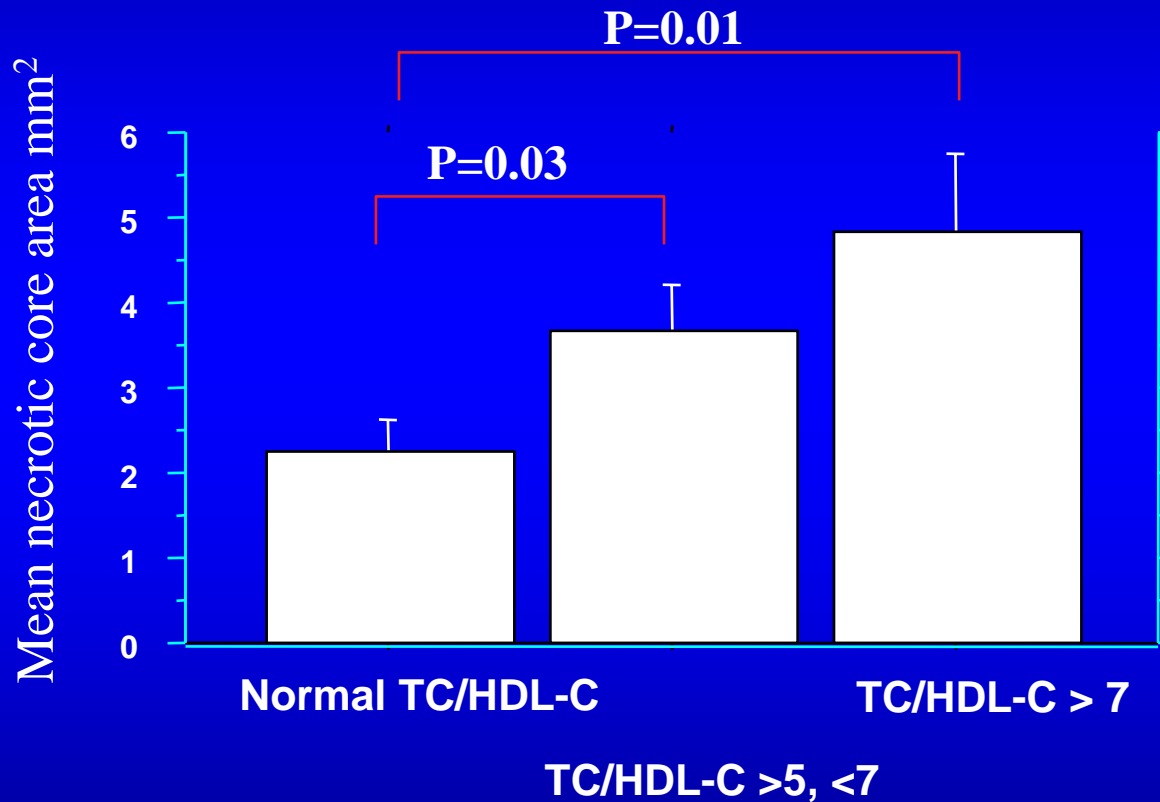
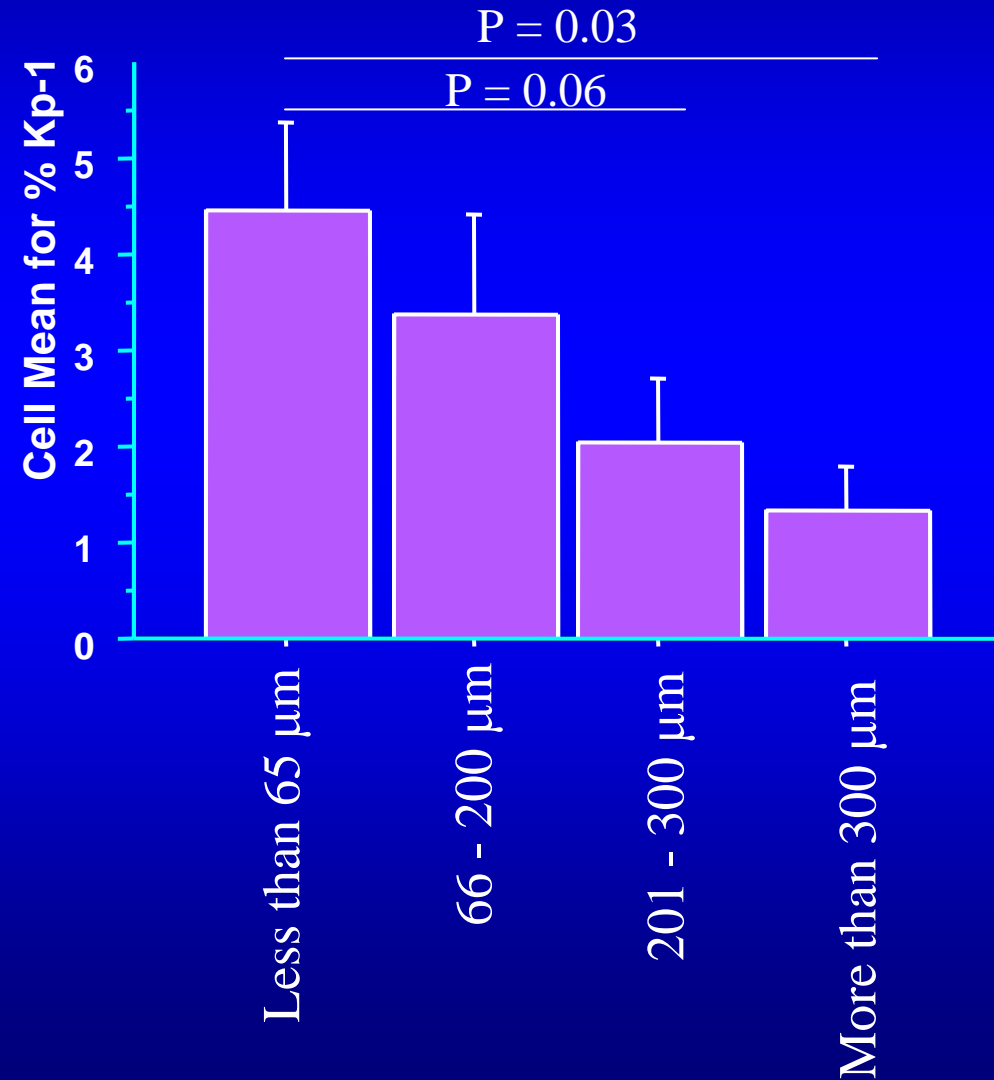


Fig 2-6

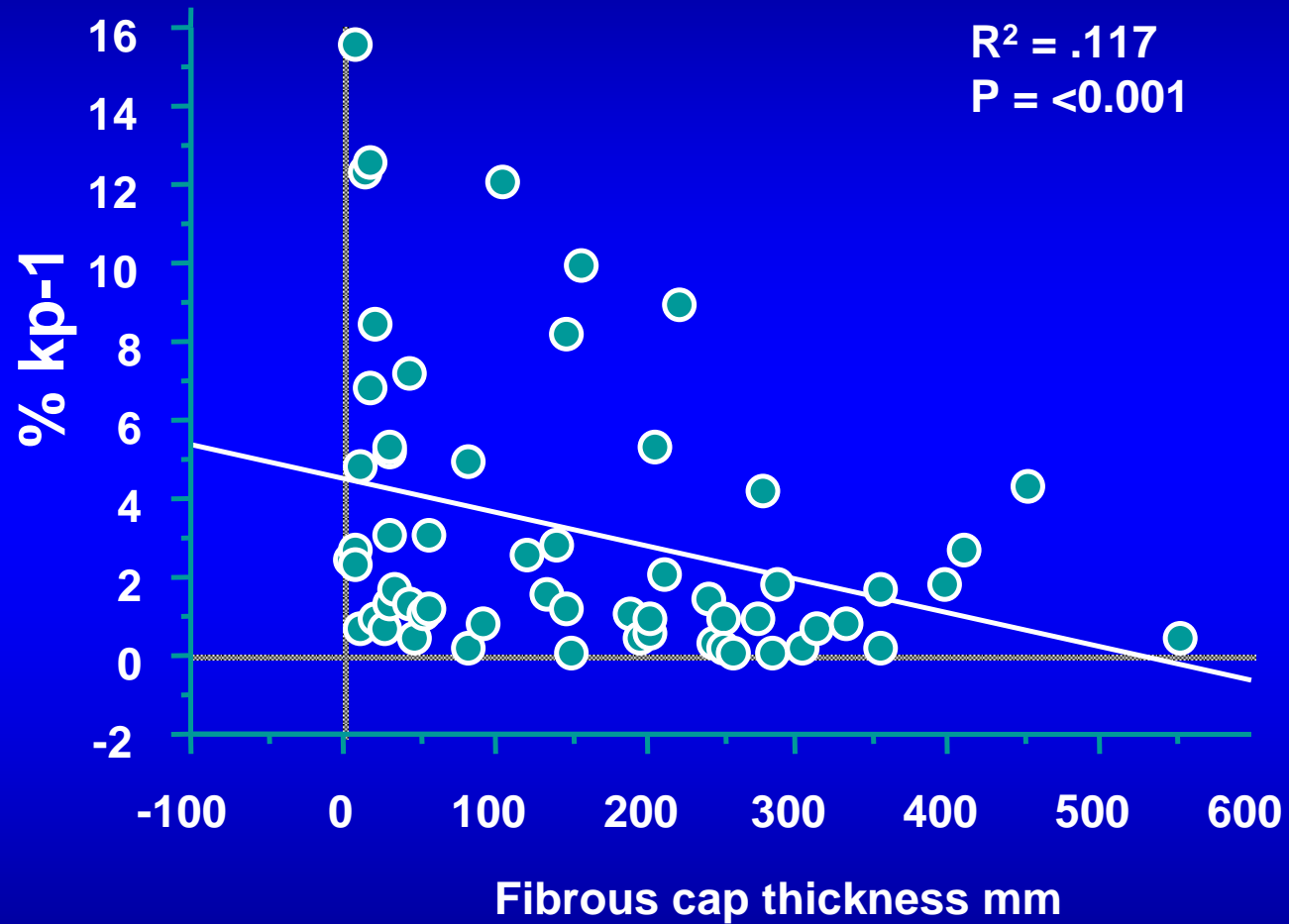
Necrotic core size, sum mm², independent of plaque area, morphometrically determined, at maximal luminal narrowing of 3 major epicardial arteries



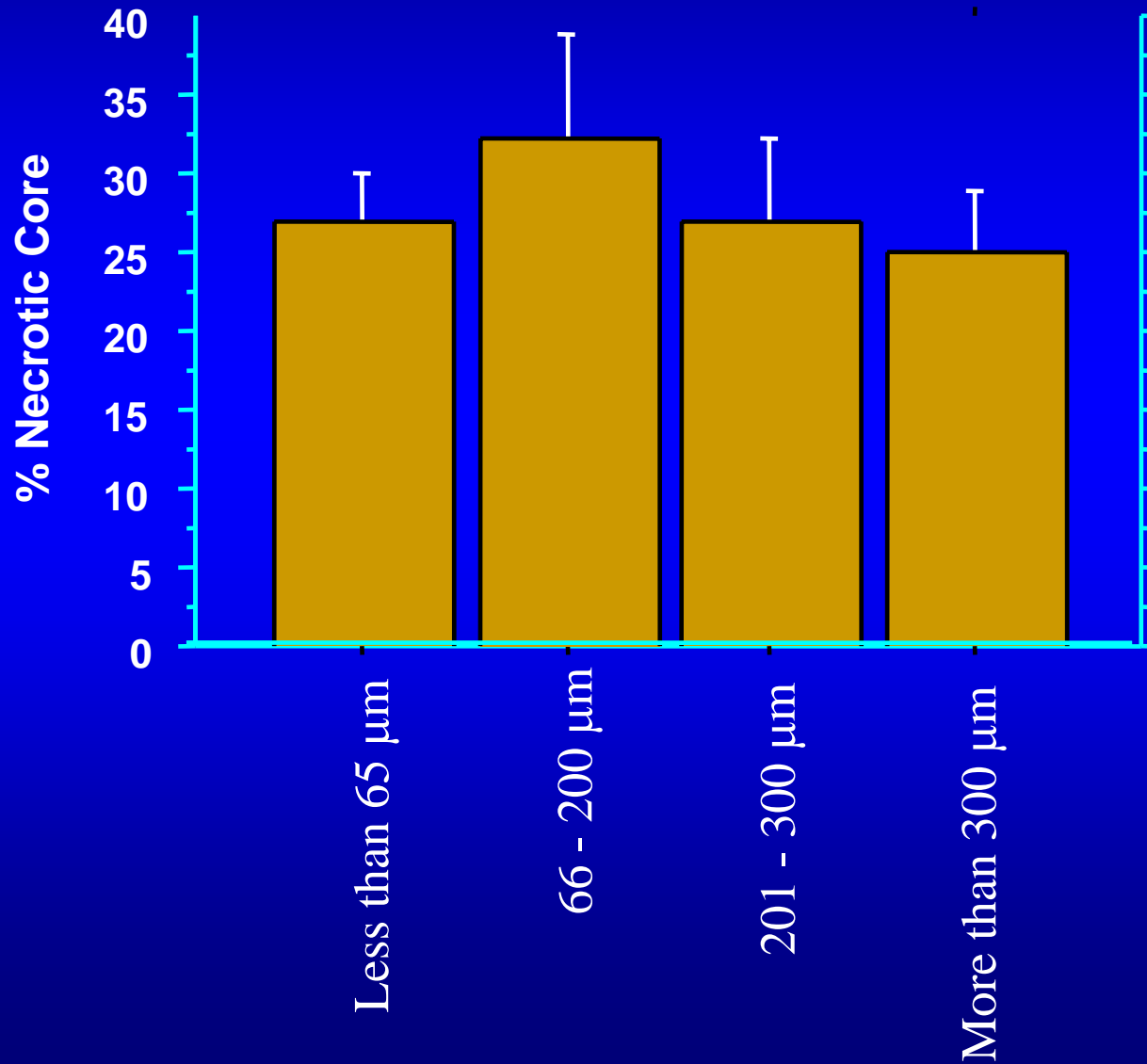
Relationship of Fibrous Cap Thickness to Macrophage Infiltration



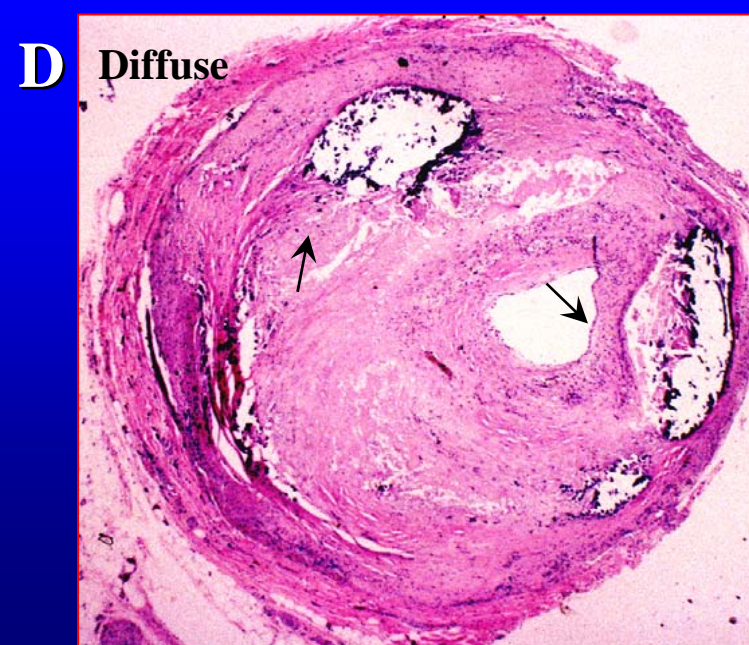
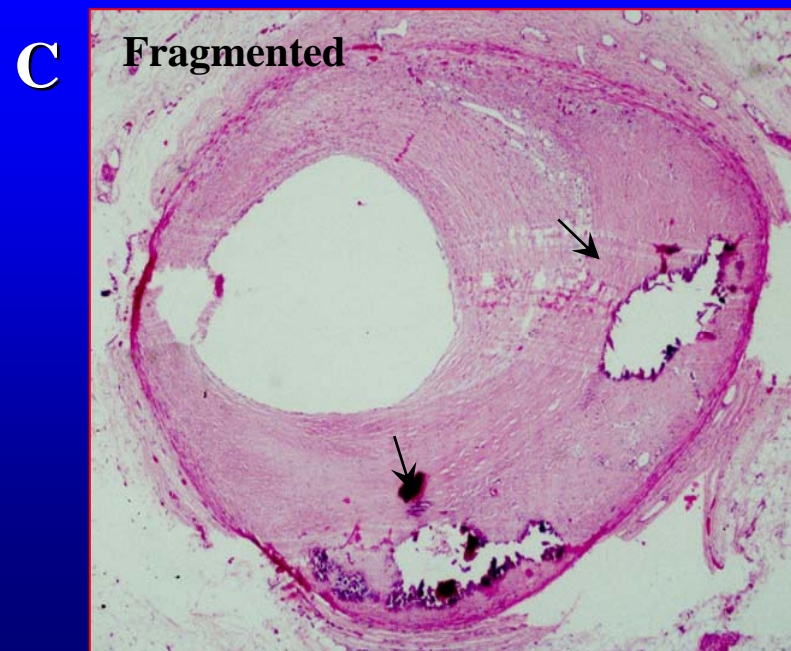
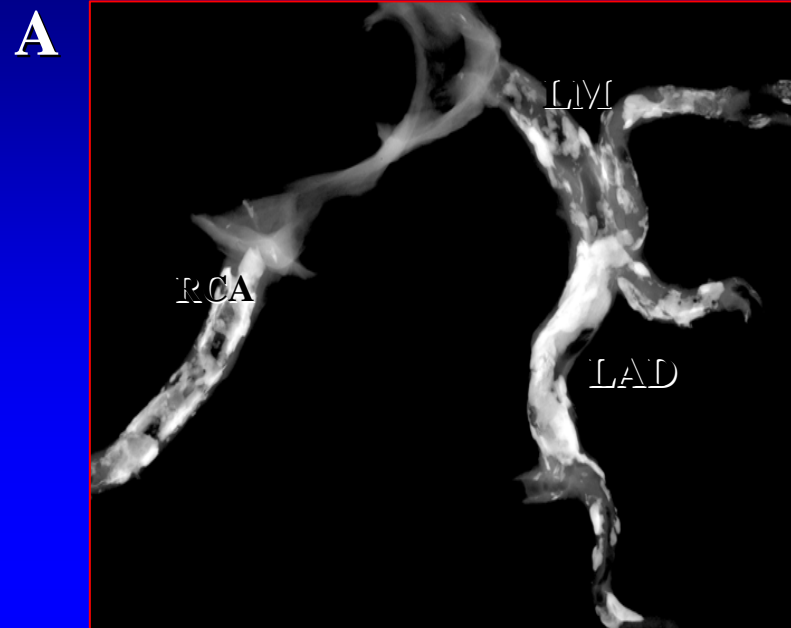
Correlation of Fibrous Cap Thickness and Macrophage Infiltration



Relationship of Fibrous Cap Thickness to Underlying Percent Necrotic Core

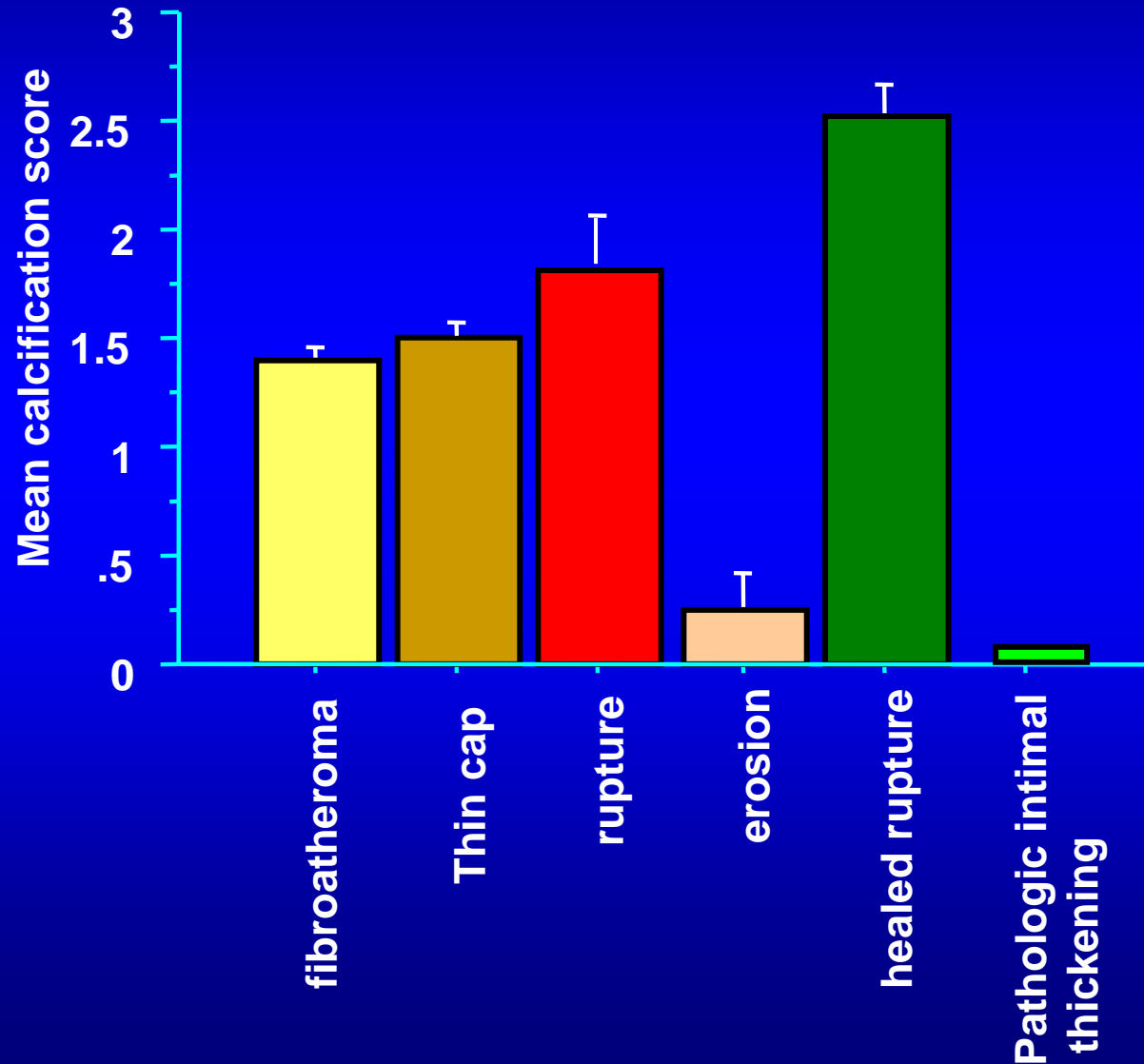


Correlation of X-Ray Calcification with Plaque type

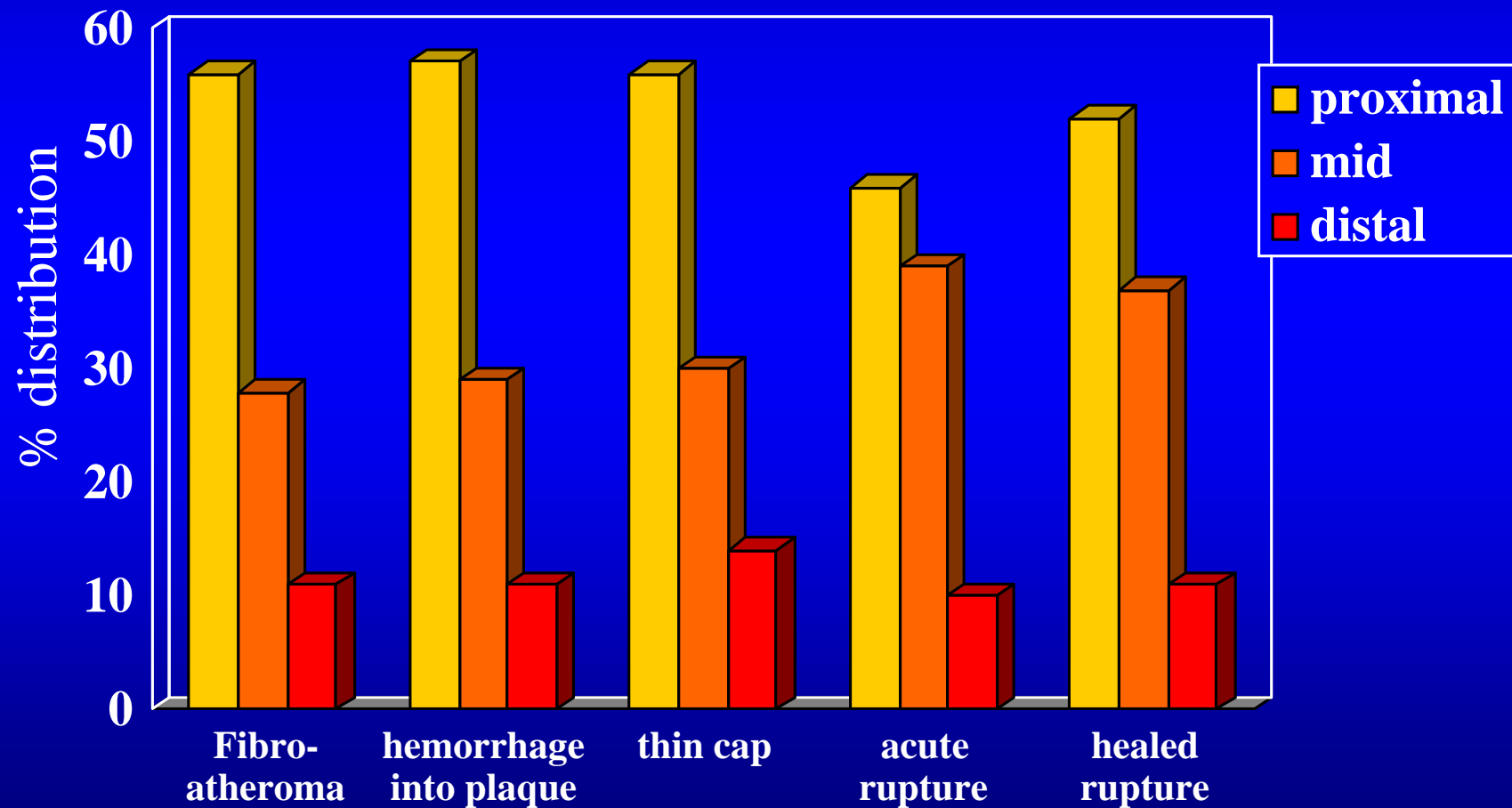


Calcified Matrix Determined Histologically

Severe Coronary Artery Disease, n=36, 64_±14 yrs
Coronary Arteries Serially Sectioned

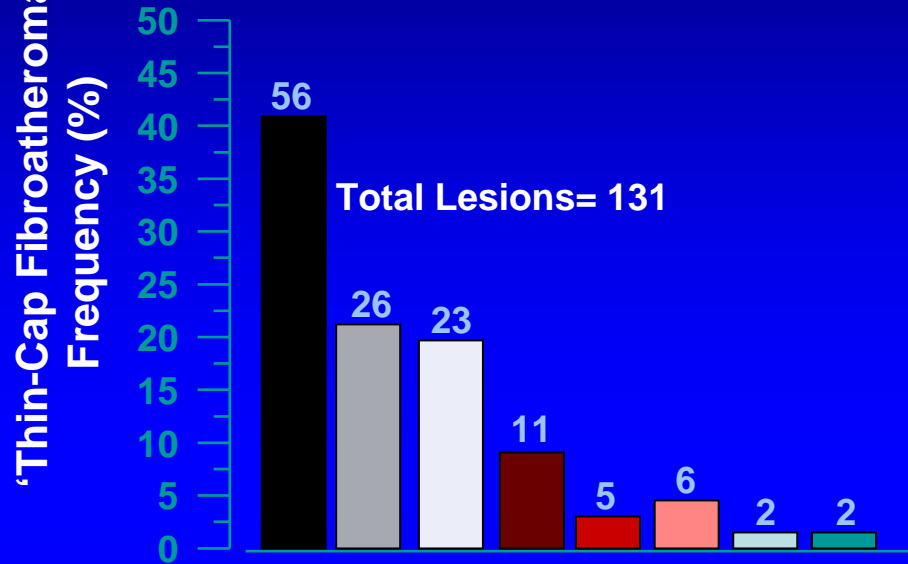


Proportion and types of “unstable” plaques, by approximate distance from ostium

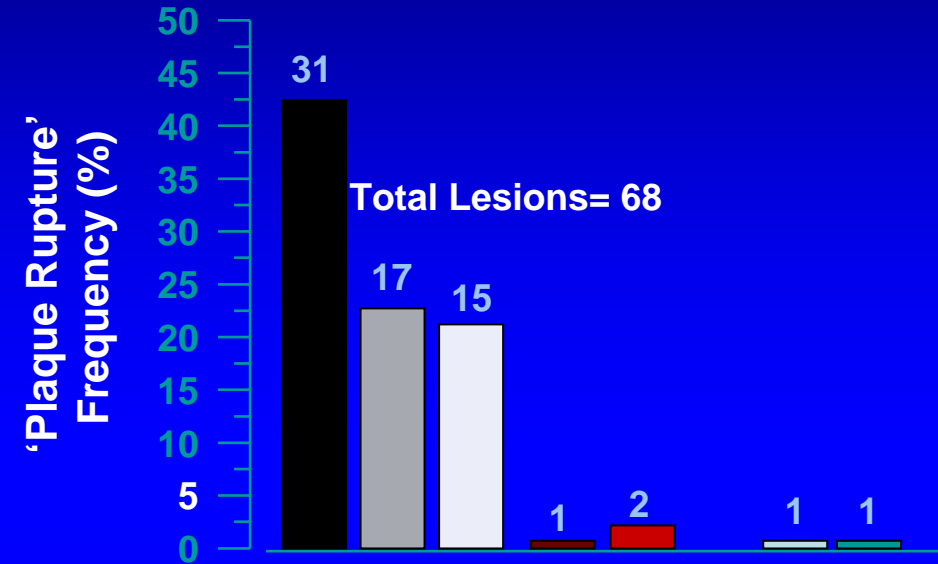


Frequency and Location of Unstable Lesions: Thin-cap Atheromas, Acute and Healed Ruptures in the Coronary Circulation

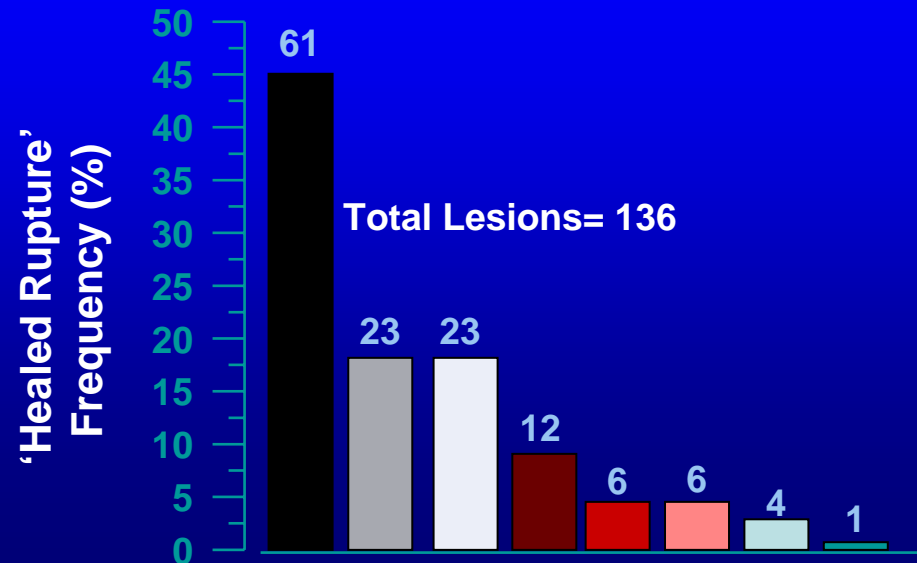
Thin-cap Fibroatheroma



Acute Plaque Rupture

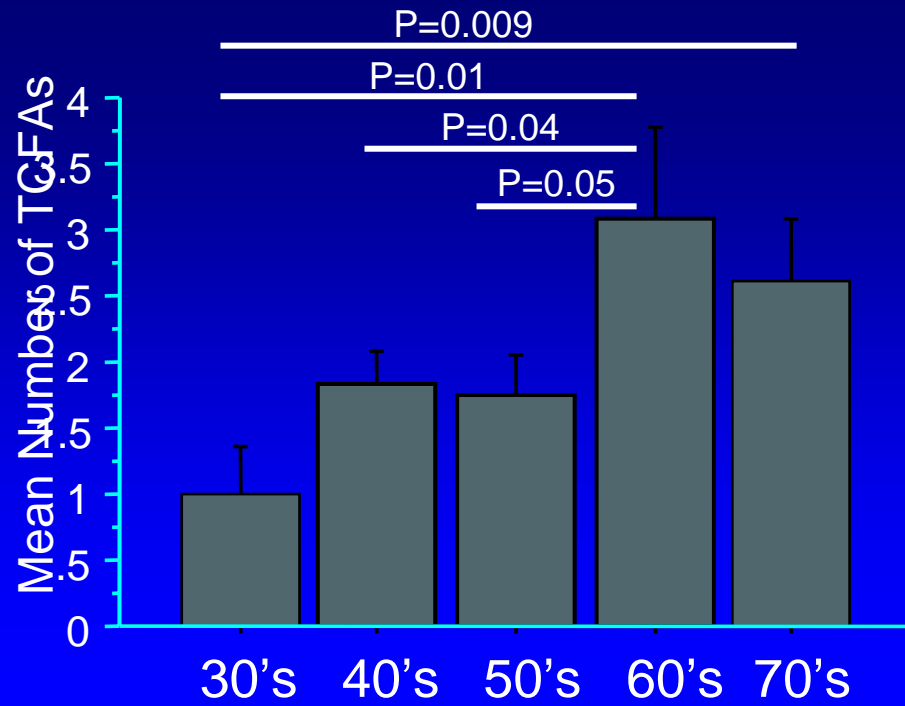


Healed Plaque Rupture



- pLAD
- pRC
- pLCx
- LM
- LOM
- dRC
- dLAD
- dLCx

A.



Frequency of Thin-Cap Fibroatheromas by Decades

B.

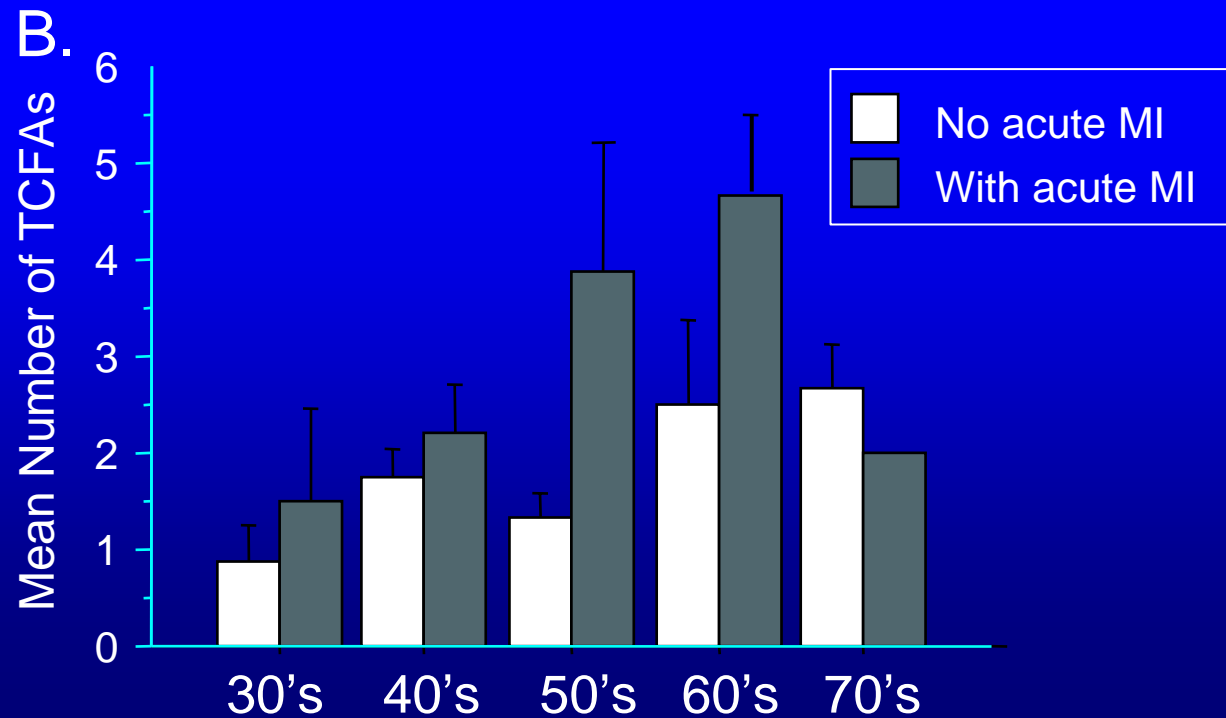


Fig 2-7

Number of Thin-Cap Atheromas in Various Coronary Syndromes in Males and Females

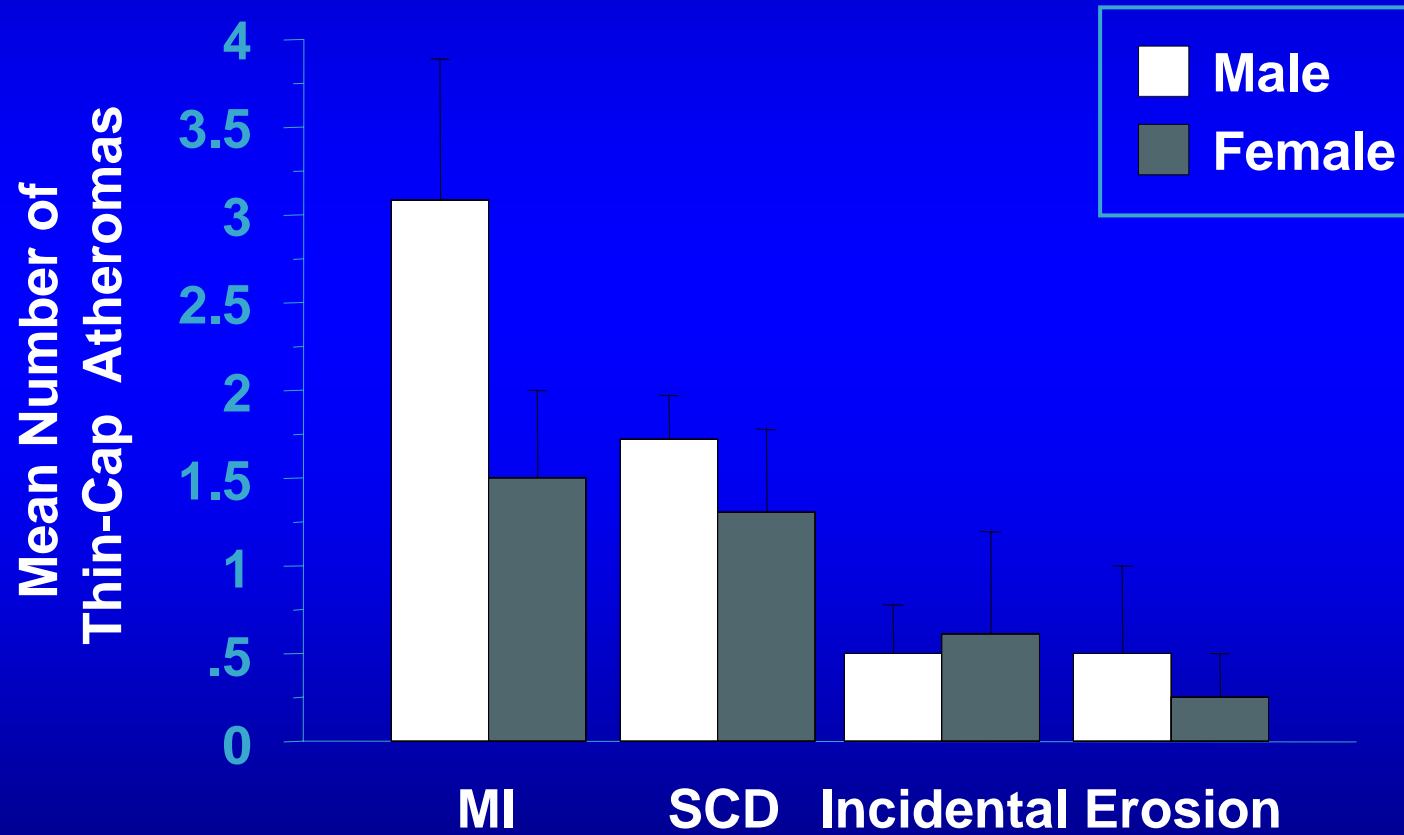
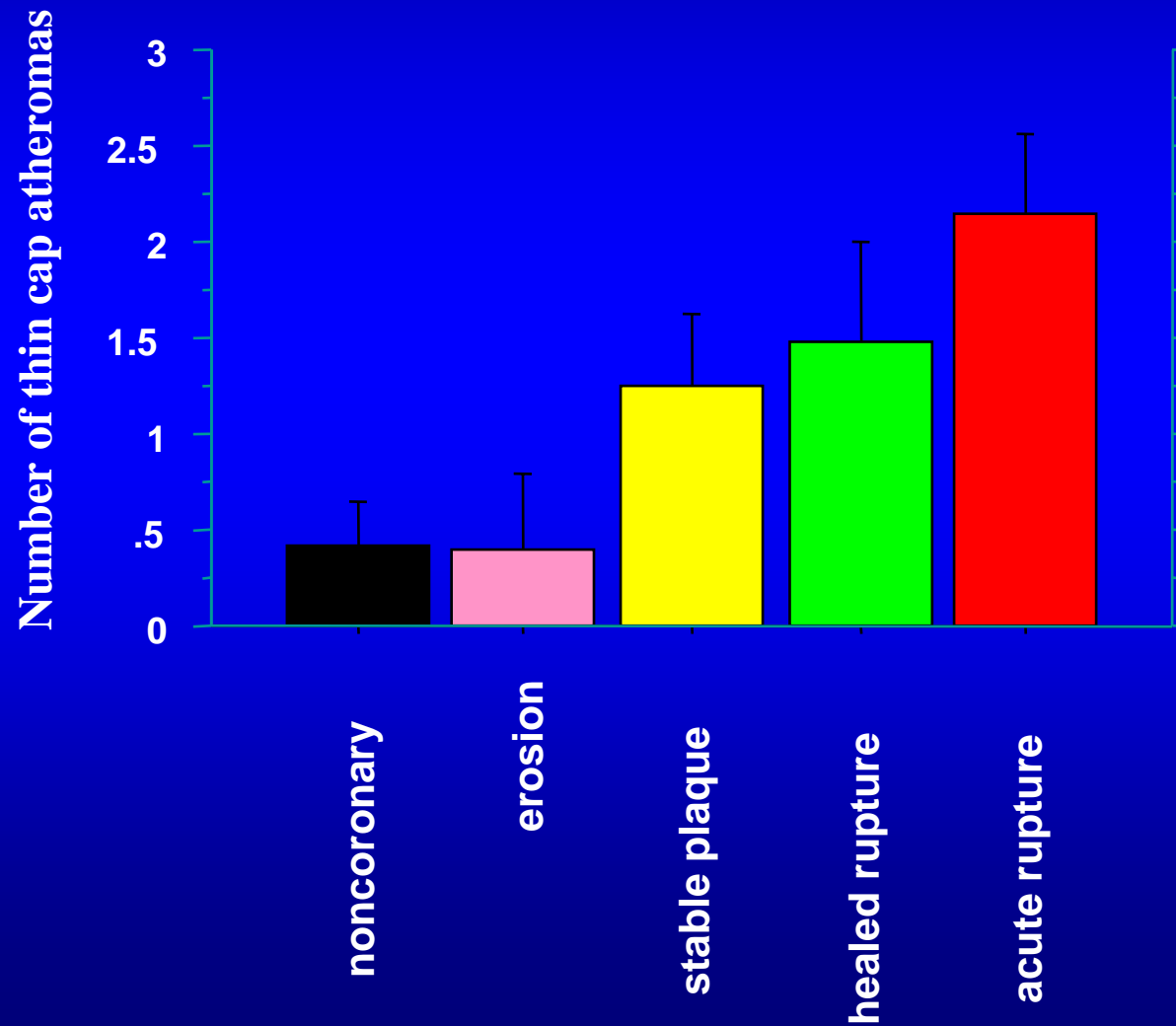
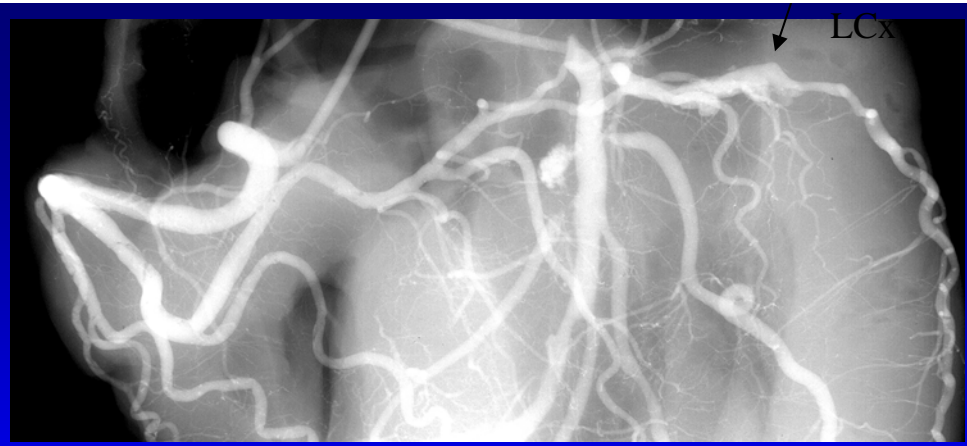


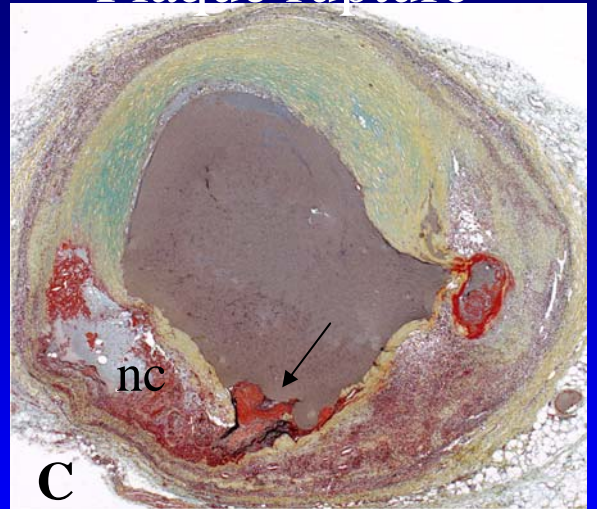
Fig 2-11

Frequency of thin cap atheroma, by mechanism of death





Plaque rupture

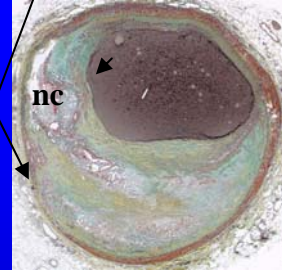
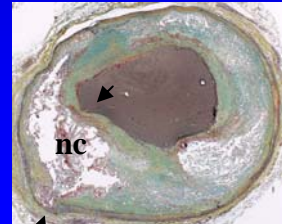


C

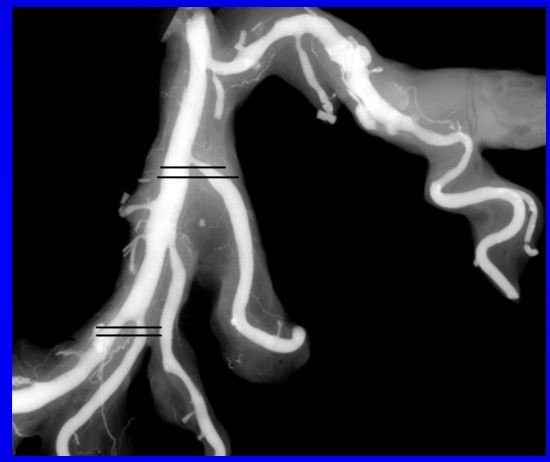
RCA



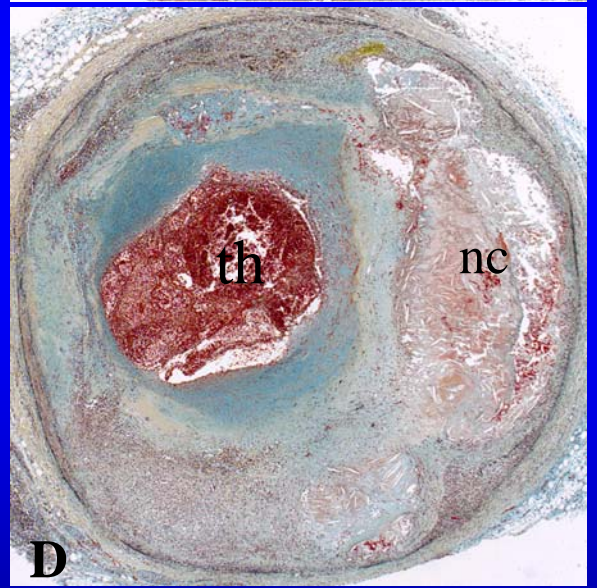
G



Thin cap
Fibro-
atheroma

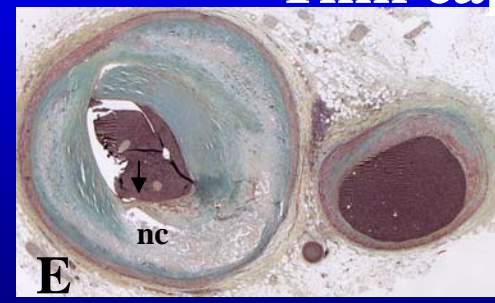


Thin cap fibroatheroma

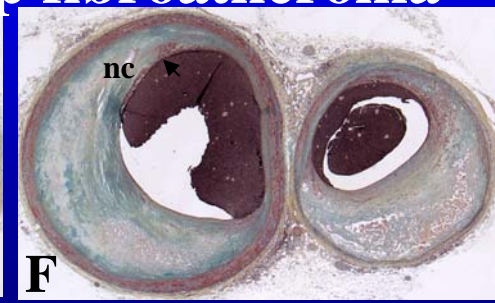


D

LAD



E



F

43-year old WM collapsed at work and could not be resuscitated.

Fig. 11

Comparison of the Length, Necrotic Core Area and % Necrotic core/plaque Area

Dimensions	Fibroatheroma	Thin-cap Atheroma	Plaque Rupture
Length, mm, mean/Range	6 mm (range 1-18 mm)	8 mm (range 2-16 mm)	9 mm (range 2.5-22 mm)
Necrotic core area mm²	1.2 ± 2.2	1.7 ± 1.1	3.8 ± 5.5
% necrotic core/plaque area	15 ± 20 %	23 ± 17 %	34 ± 17 %

Serial Sections of a Thin-Cap Fibroatheroma Cut 250 μ m apart

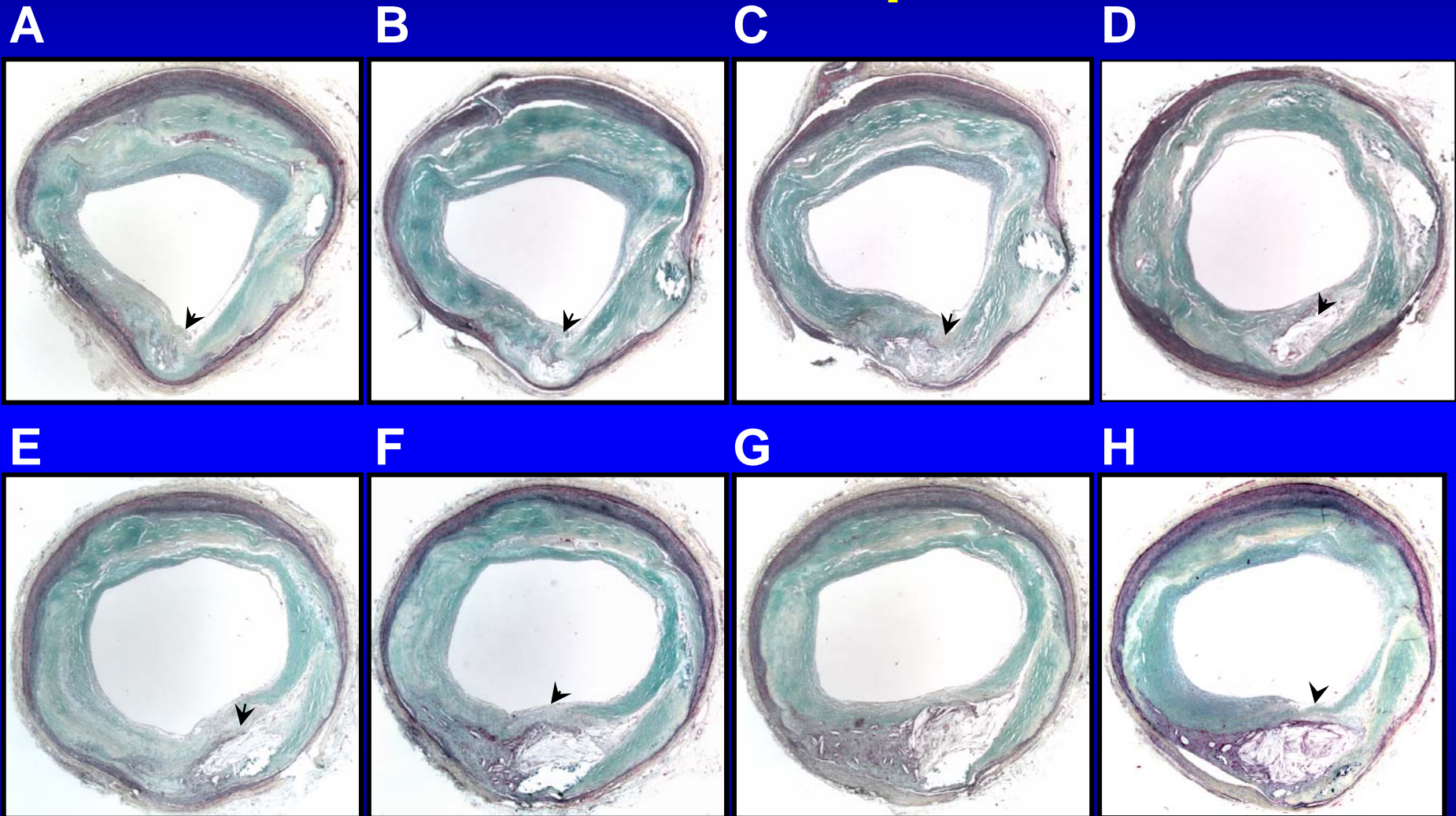
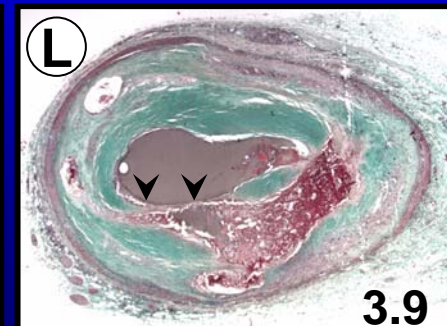
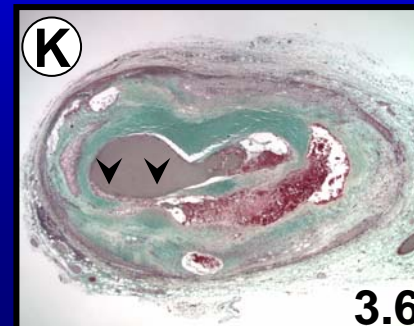
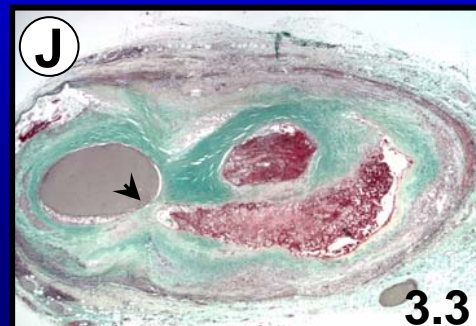
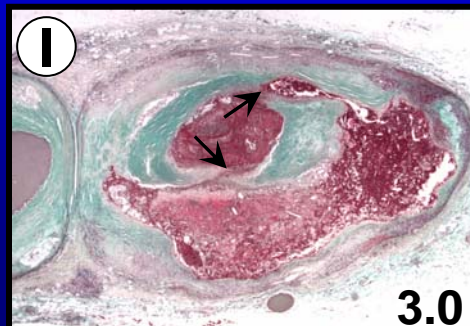
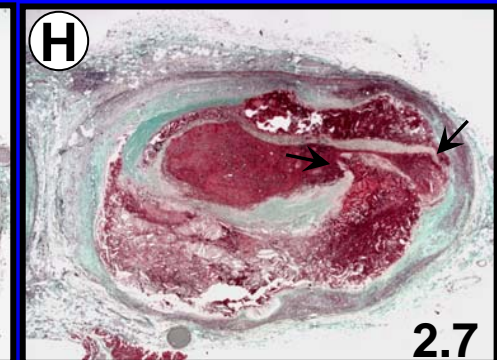
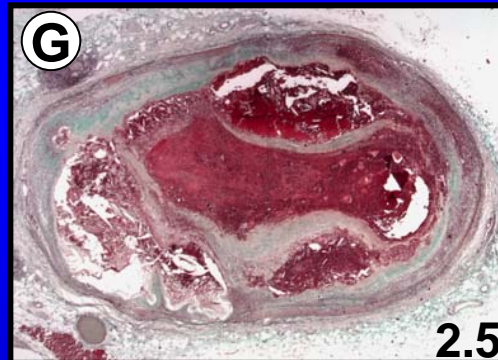
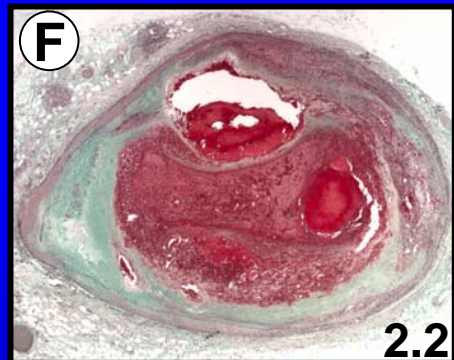
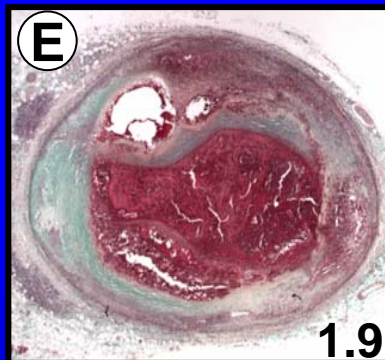
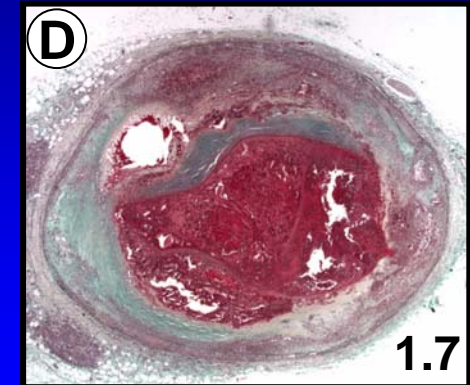
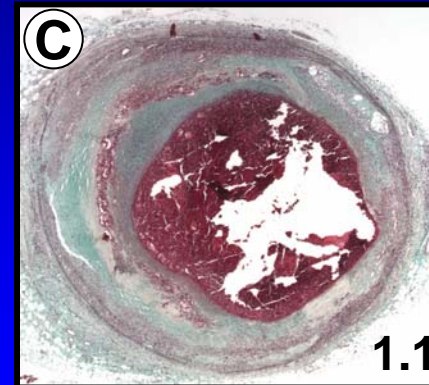
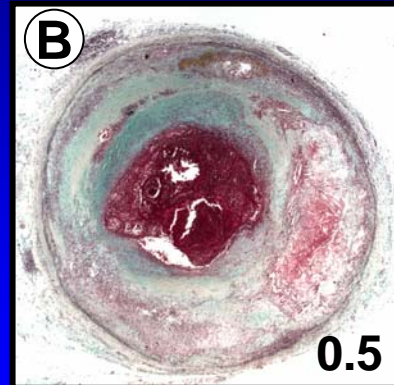
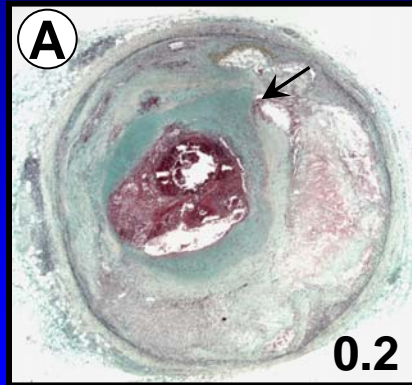


Fig 2-16

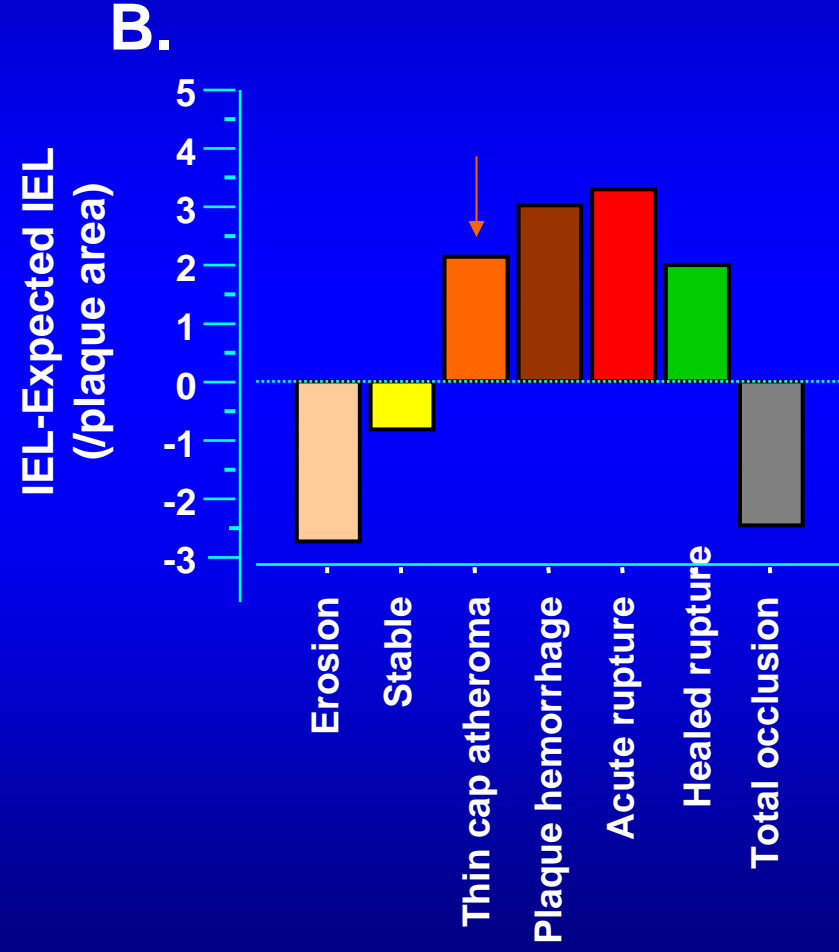
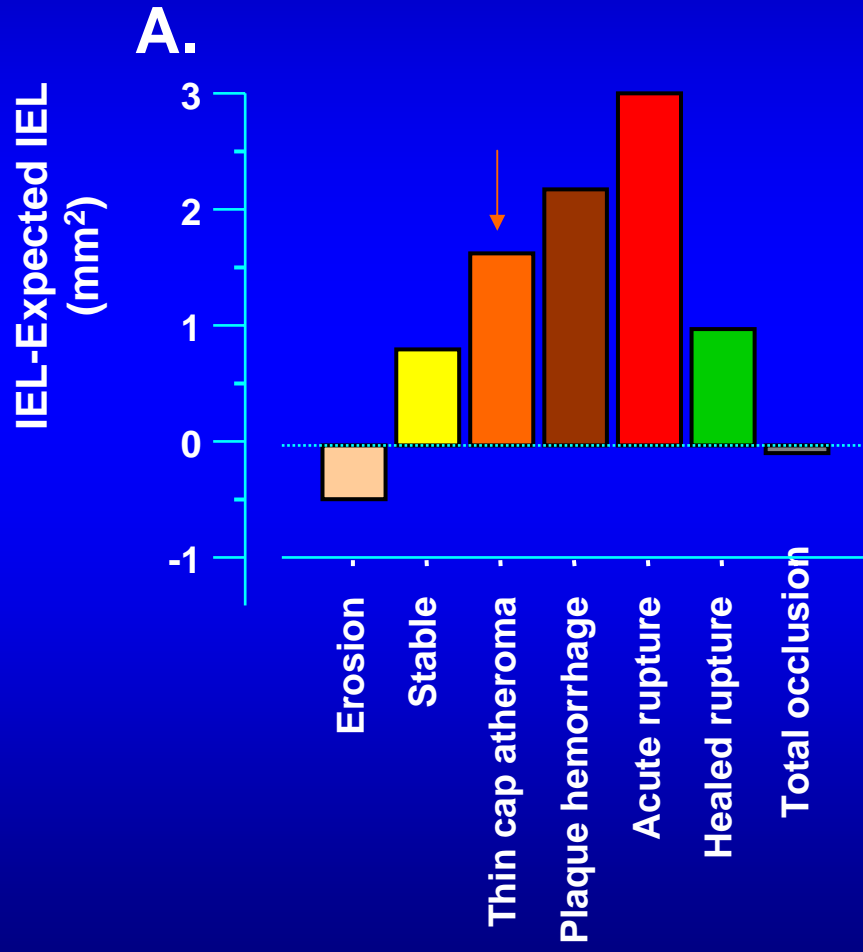
Serial Coronary Sections (mm) Demonstrating Multiple Vulnerable Plaques and Rupture Sites

→ Proximal LCx



→ Distal

Remodeling in Varying Coronary Lesion Morphologies



Mean Number of Thin Cap Fibroatheromas and Serum Cholesterol in Men

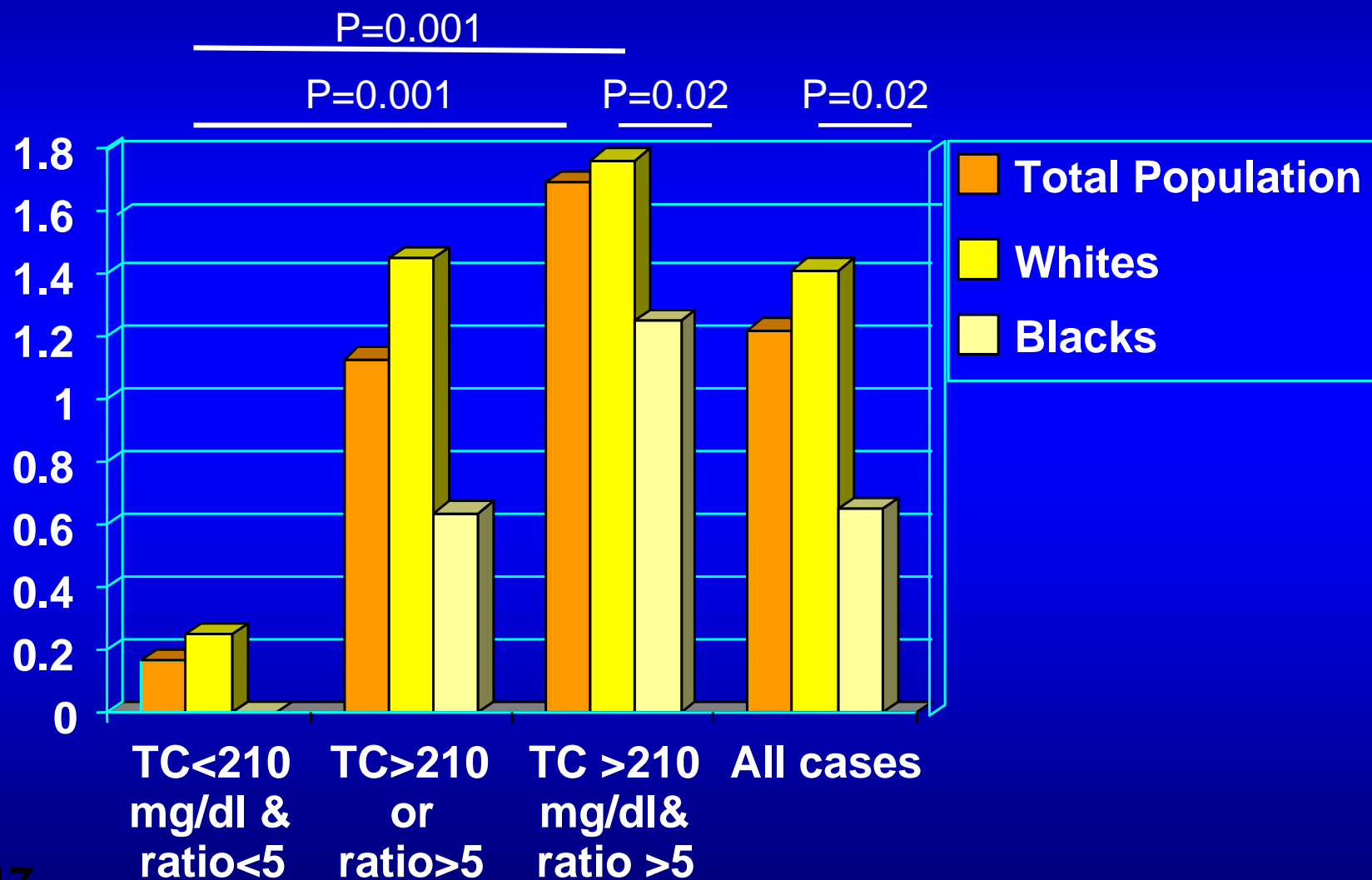
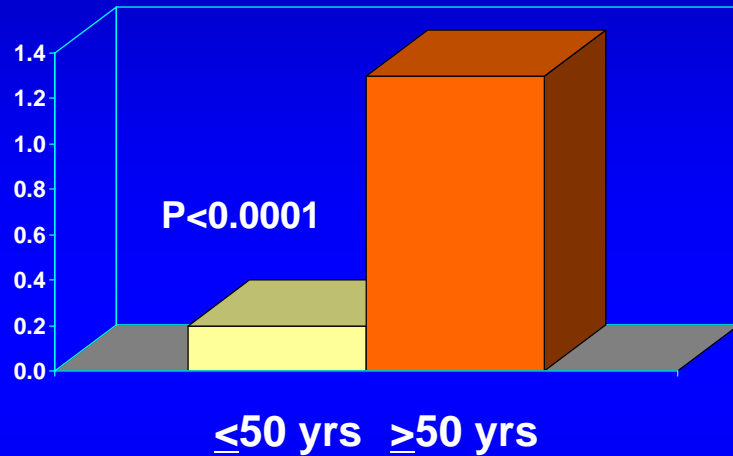


Fig 2-17

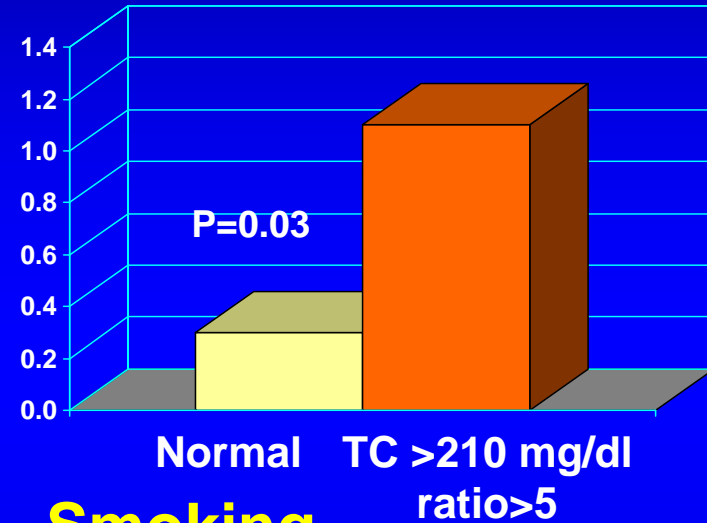
Mean Number of Thin-Cap Fibroatheromas in 51 Women with SCD and Severe Coronary Disease

A Comparison of Risk Factors

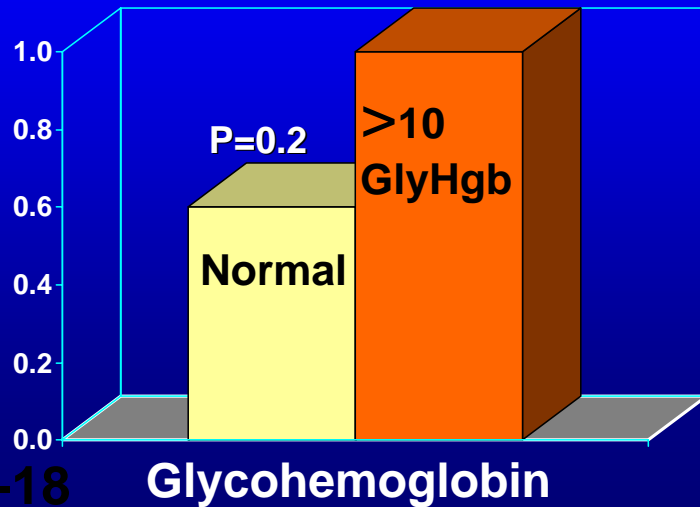
Age



Cholesterol



Diabetes



Smoking

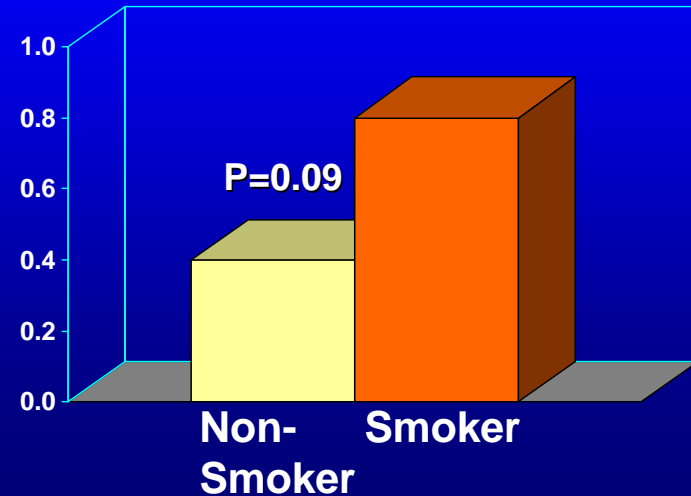


Fig 2-18

Serum hs-CRP correlated with Immunohistochemical staining intensity of Plaques and with TCFA

CRP	CRP staining intensity of plaques*	Mean number of thin cap atheroma
Low CRP group (<1.0µg/mL)	2.9 ±0.5	0.95 ±0.22
High hs-CRP group (>3.2µg/mL)	6.2±0.6	3.0 ±0.3

*Grading of staining intensity was assessed on macrophages and Lipid core. A quantitative score of 0 to 4 was applied to each. A sum of the 2 scores resulted in overall grading system of 0 to 8

Thin Cap Fibroatheroma- A plaque vulnerable to rupture ?

- ✓ **Definition**
- ✓ **Frequency is higher in AMI than SCD, >males than females**
- ✓ **Higher prevalence in the presence of high TC, low HDL-C, high TC/HDL-C ration, high hs CRP (>3.2 mg/dl)**
- ✓ **Location in SCD, proximal and mid LAD, RCA, and LCX**
- ✓ **Length 2-22 mm (mean 8 mm)**
- ✓ **% luminal narrowing (80% of TCFAs occur in lesions <50% diameter stenosis)**
- ✓ **% necrotic core is <25% of plaque area in 70% of TCFAs**
- ✓ **Calcification is not a marker of TCFA**