

Evolving Pathologic Perspective on the Etiology of AMI

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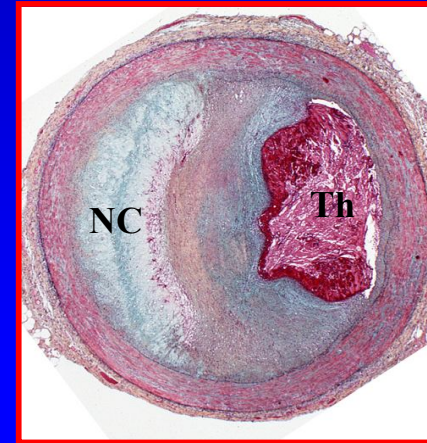
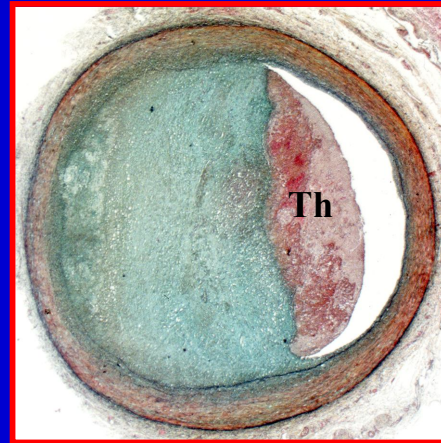
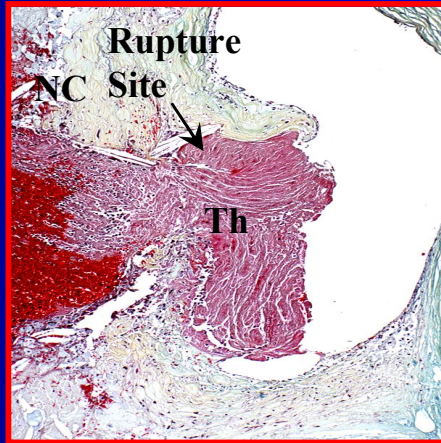
Acute Myocardial Infarction

- More than 95% of AMIs occur from underlying coronary atherosclerosis
- Atherosclerosis affects all populations but usually manifests in the sixth and seventh decade
- The major cause of epicardial coronary artery occlusion is from plaque rupture or erosion
- Mortality and morbidity from AMI has been reduced secondary to the understanding that reperfusion reduces infarct size

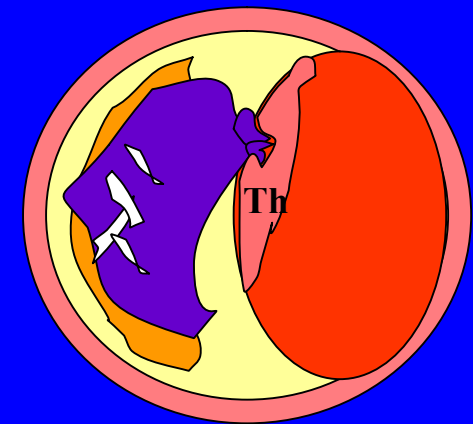
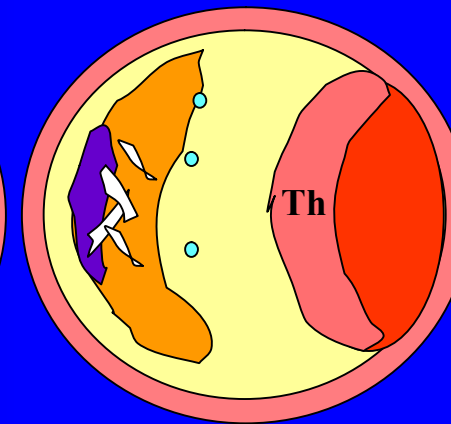
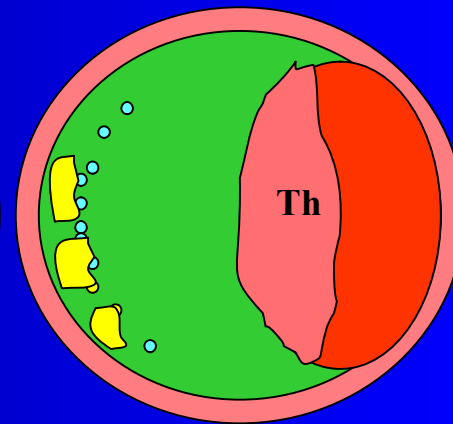
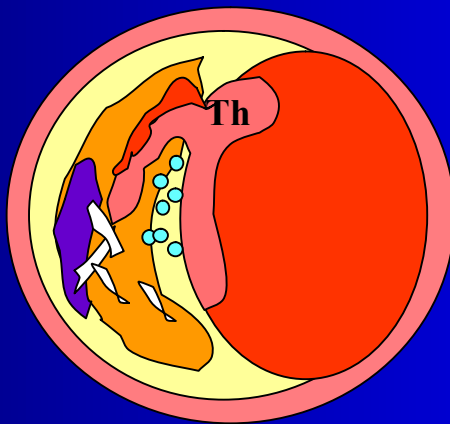
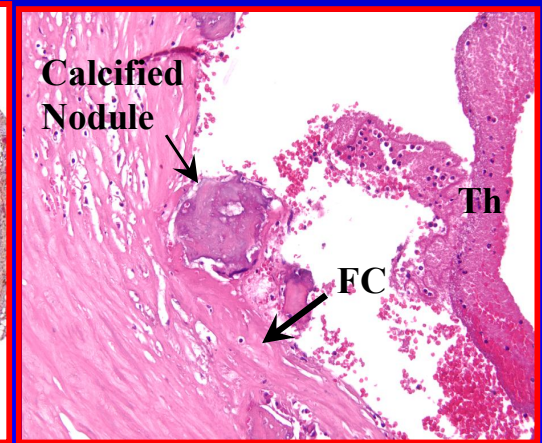
Causes of Coronary Thrombosis

Erosion

Rupture



Calcified nodule



Plaque Erosion and Rupture in Patient Dying from AMI:

	Plaque Erosion (n=74)	Plaque Rupture (n=217)	P value
Male/Female	34/40	150/67	0.0004
Age, years (mean ± SD)	70 ± 9	68 ± 11	NS
AMI site			
Anterolateral	49 (66.2%)	119 (54.8%)	NS
Lateral	3 (4.1%)	22 (10.1%)	NS
Posterior	22 (29.7%)	76 (35.1%)	NS
Heart Rupture	17 (22.9%)	27 (12.4%)	NS
Non-Q wave AMI (thrombi 11/15)	1 (1.3%)	10 (4.6%)	NS
Scars	21 (28.4%)	74 (34.1%)	NS
Multiple thrombi	11 (14.9%)	18 (8.3%)	NS

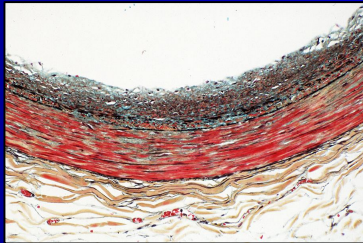
Myocardial Scarring and Heart Rupture Frequency in the AMI population at Autopsy

	Men	Women	P value
Myocardial scars	71/189 (37.5%)	24/109 (22%)	0.01
Heart Rupture	20/189 (10.5%)	24 /109 (22%)	0.01

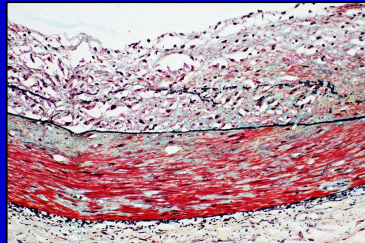
Arbustini E, et al. Heart 1999;82:269-272

Development of Human Coronary Atherosclerosis

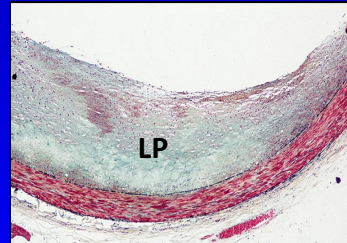
Intimal thickening



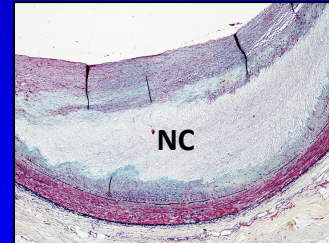
Intimal xanthoma



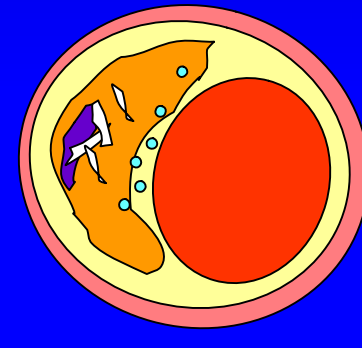
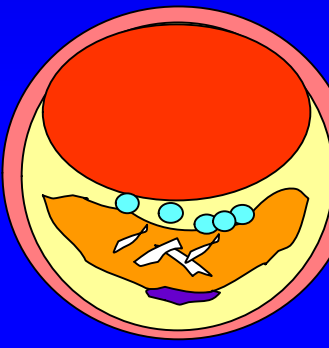
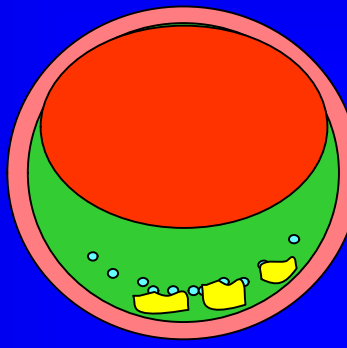
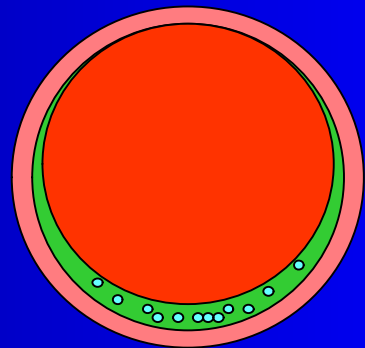
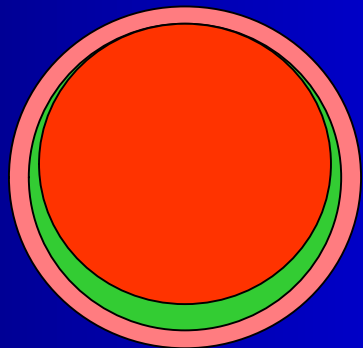
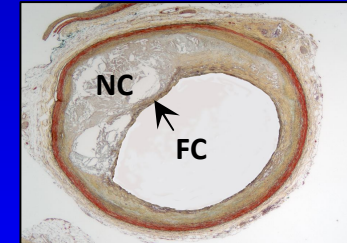
Pathologic intimal thickening



Fibrous cap atheroma



Thin-cap Fibroatheroma



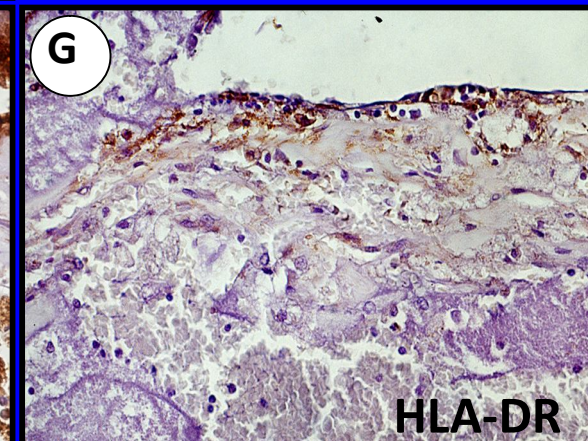
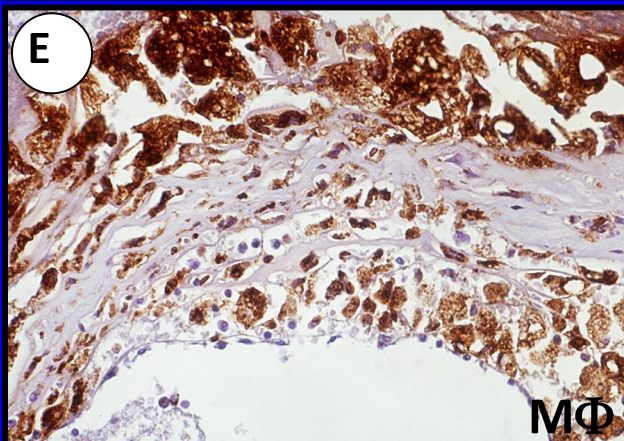
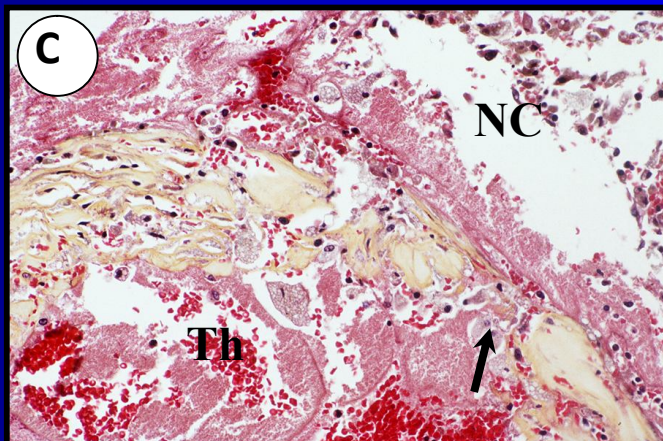
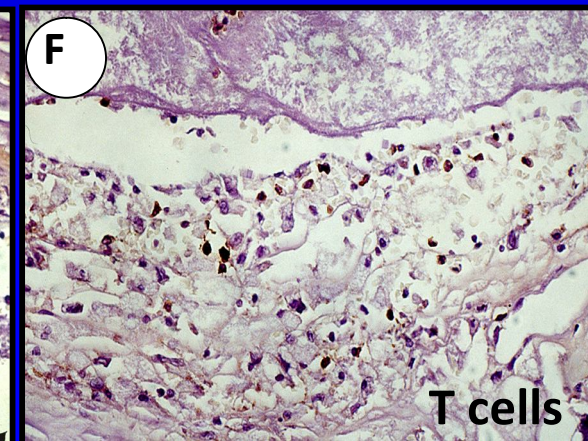
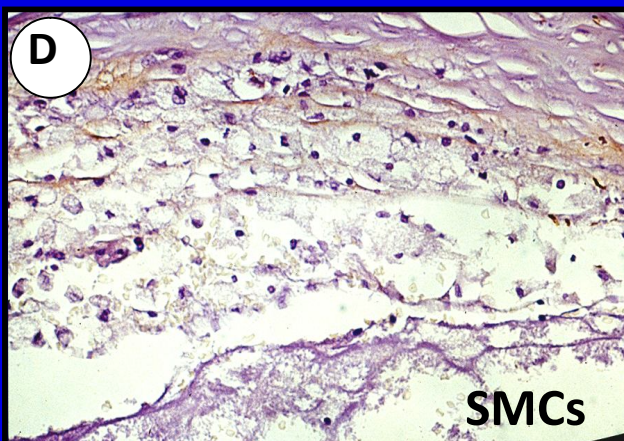
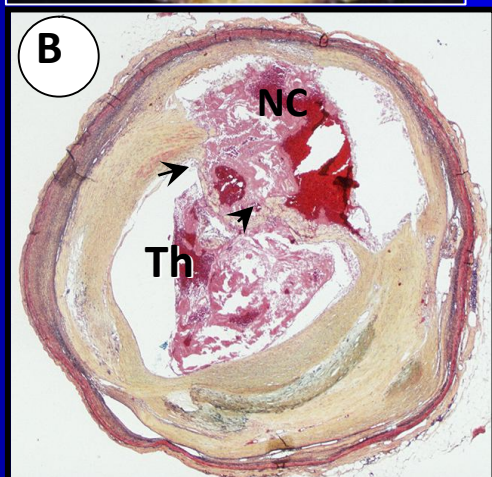
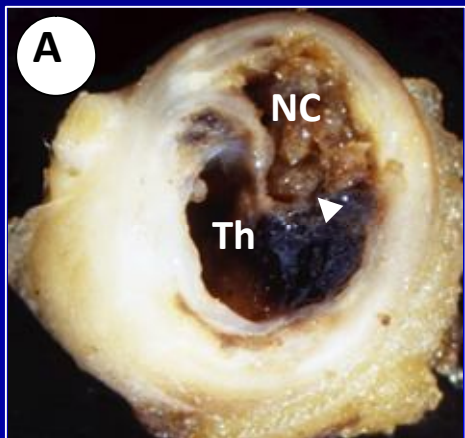
- Smooth muscle cells
- Macrophage foam cells
- Extracellular lipid
- Cholesterol clefts
- Necrotic core

- Calcified plaque
- Collagen

FC = fibrous cap
 LP = lipid pool
 NC = necrotic core

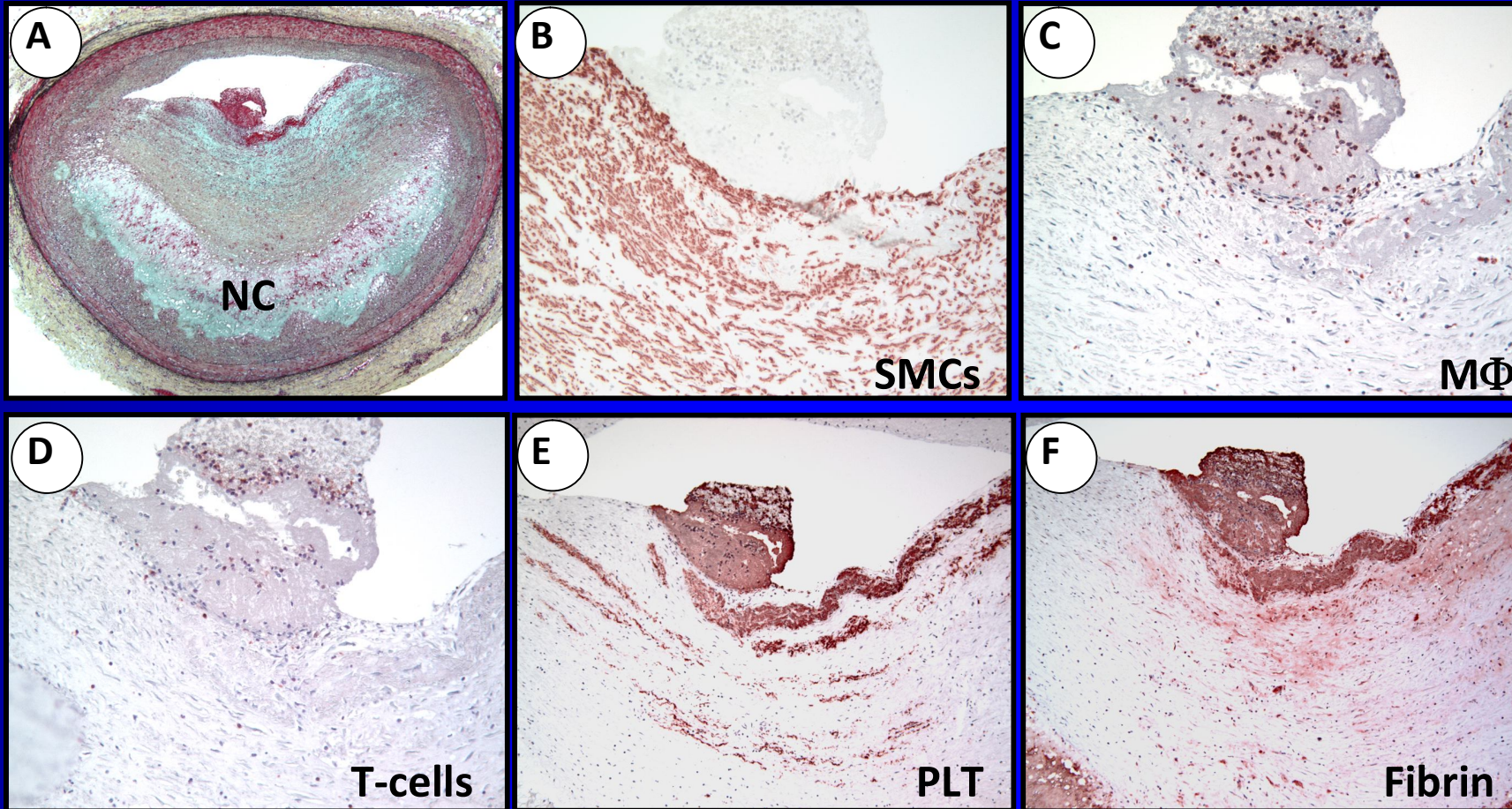
Gross and Light Microscopic Features of Plaque Rupture

70% of Thrombi in Acute Myocardial Infarction occur form Plaque Rupture



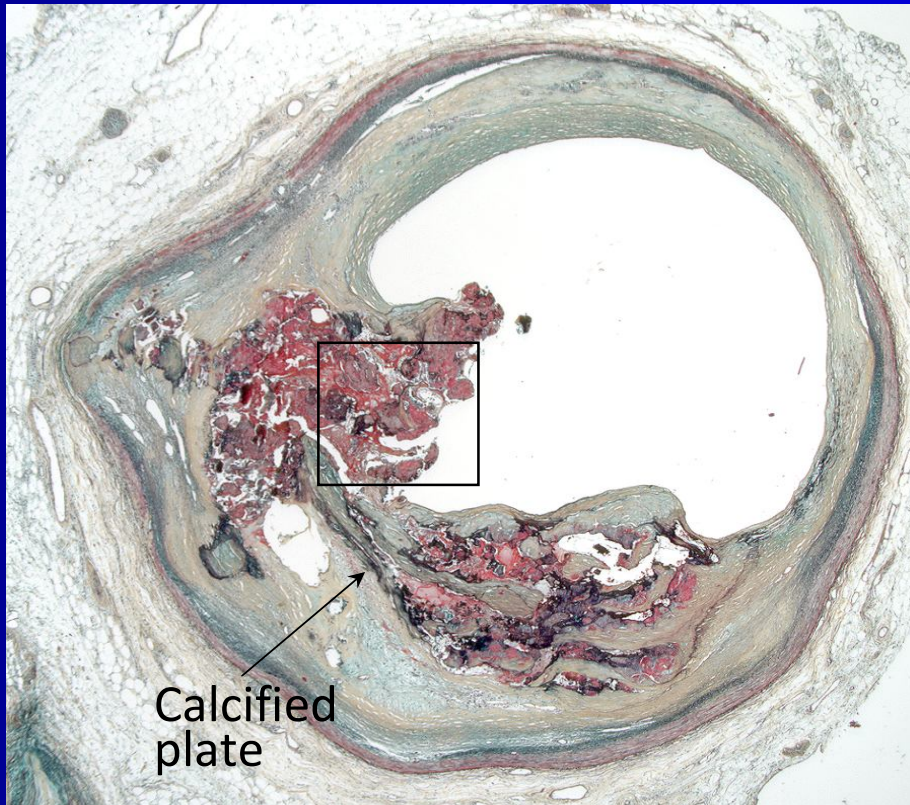
Plaque Erosion: 28% of thrombi in AMI

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.

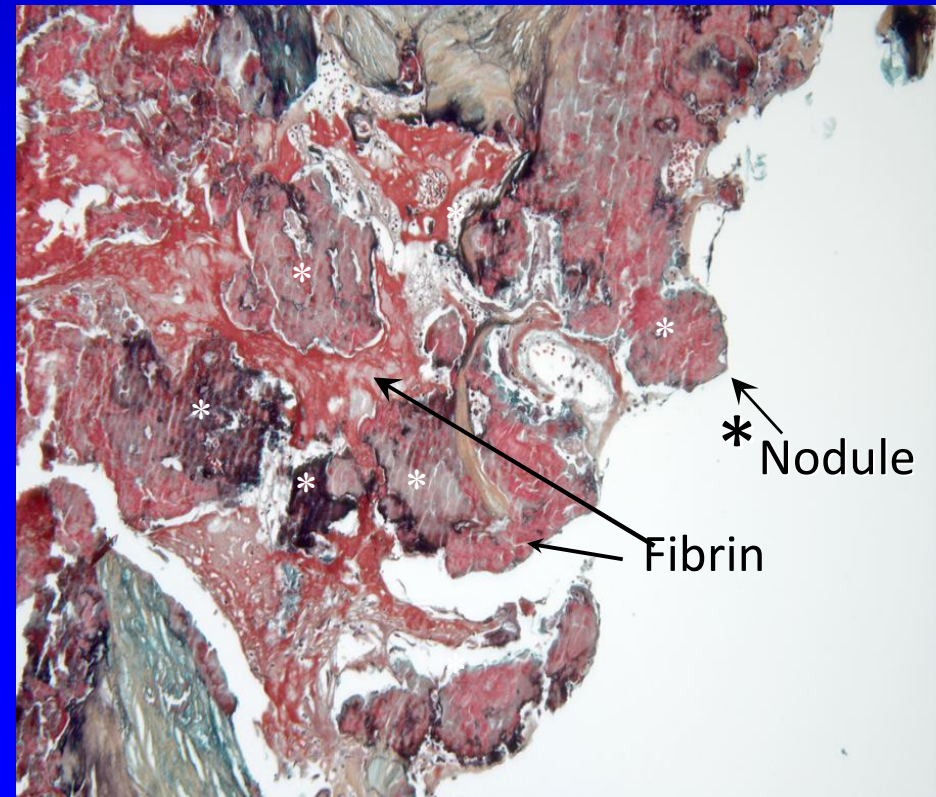


Calcified Nodule

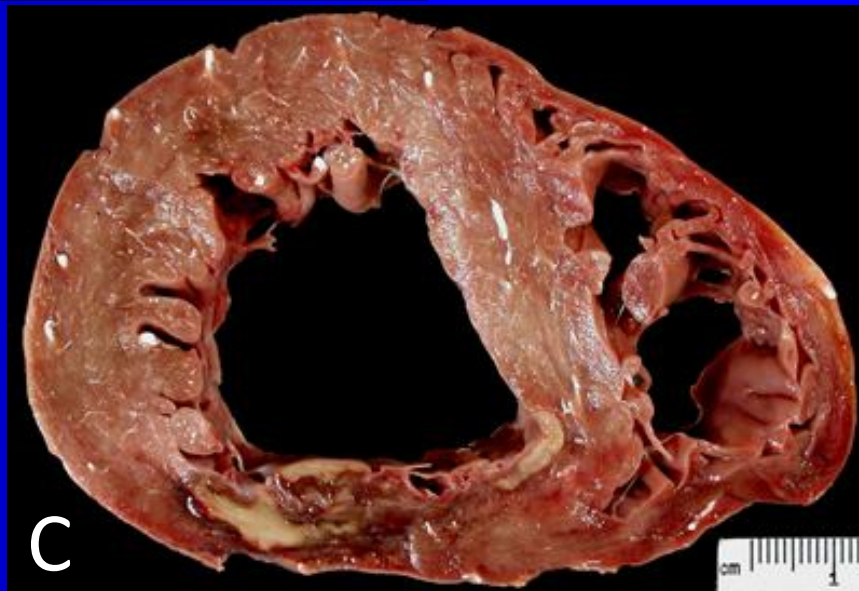
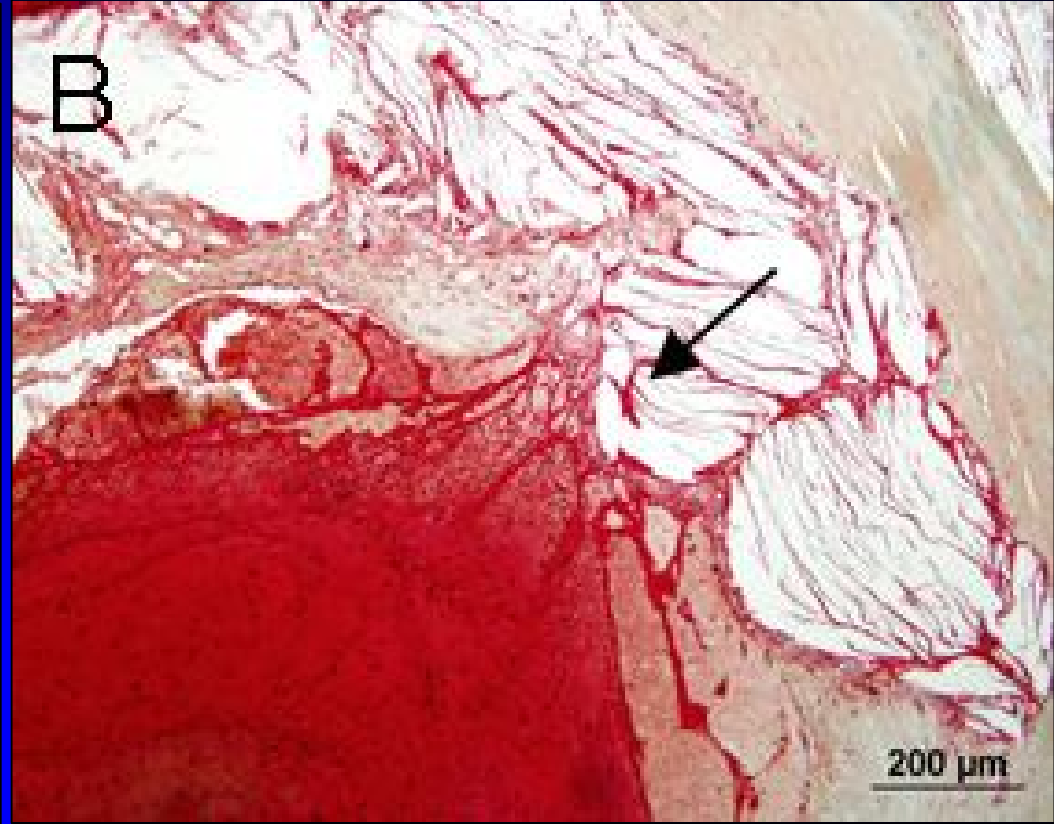
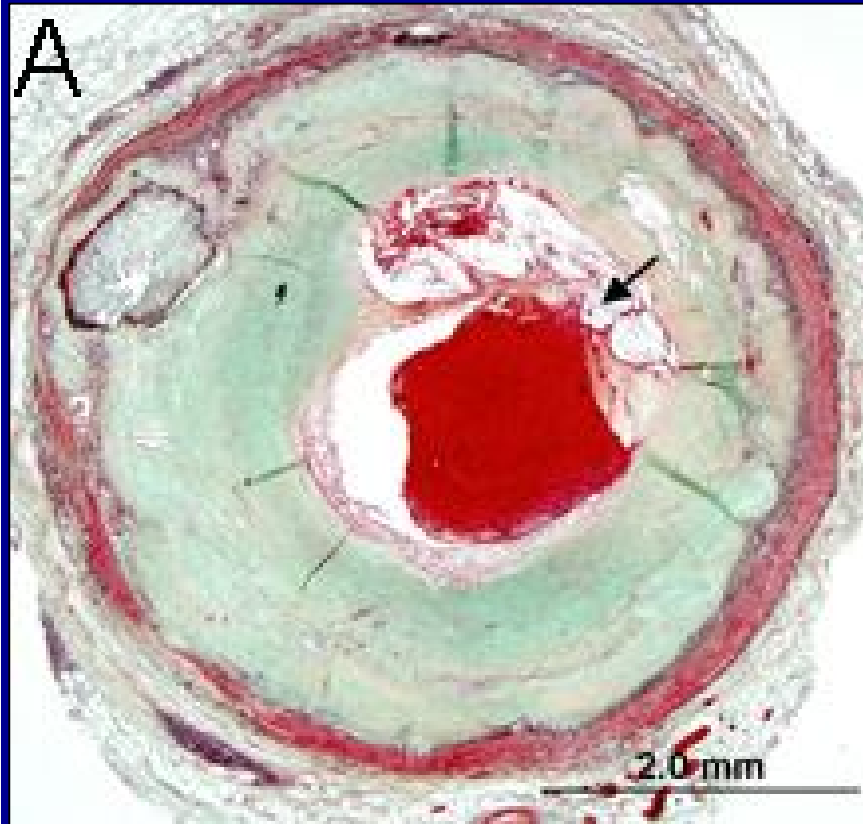
A



B



Frequency 2-7% of SCD, Older individuals, usually Men, equally common in tortuous right and left coronary arteries



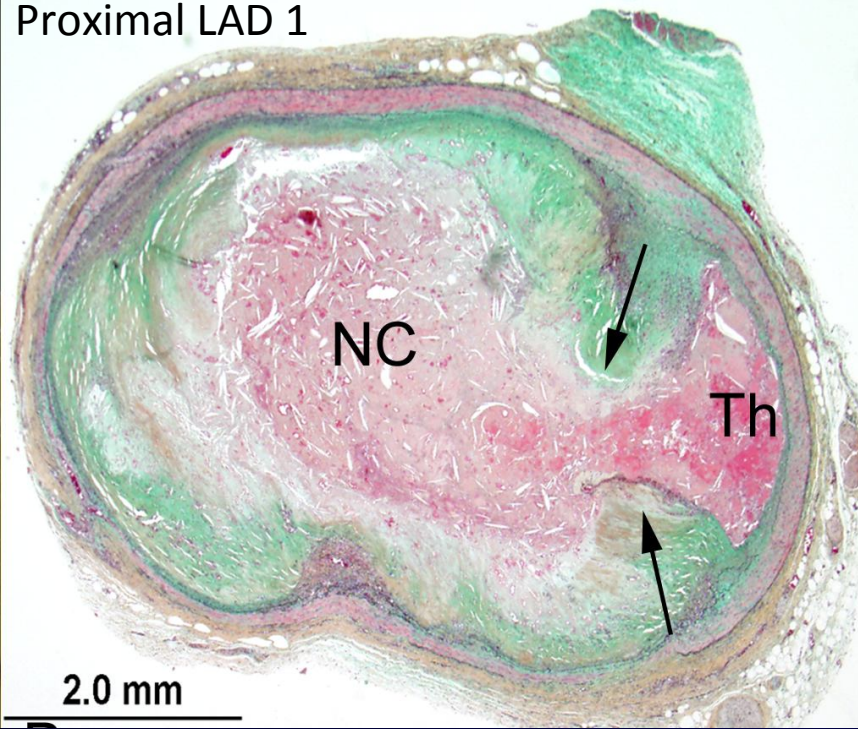
Acute myocardial infarction and coronary thrombosis secondary to plaque rupture in a 51-year-old male with H/O smoking

Acute Myocardial Infarction at Autopsy: Epicardial culprit lesions in 68 cases

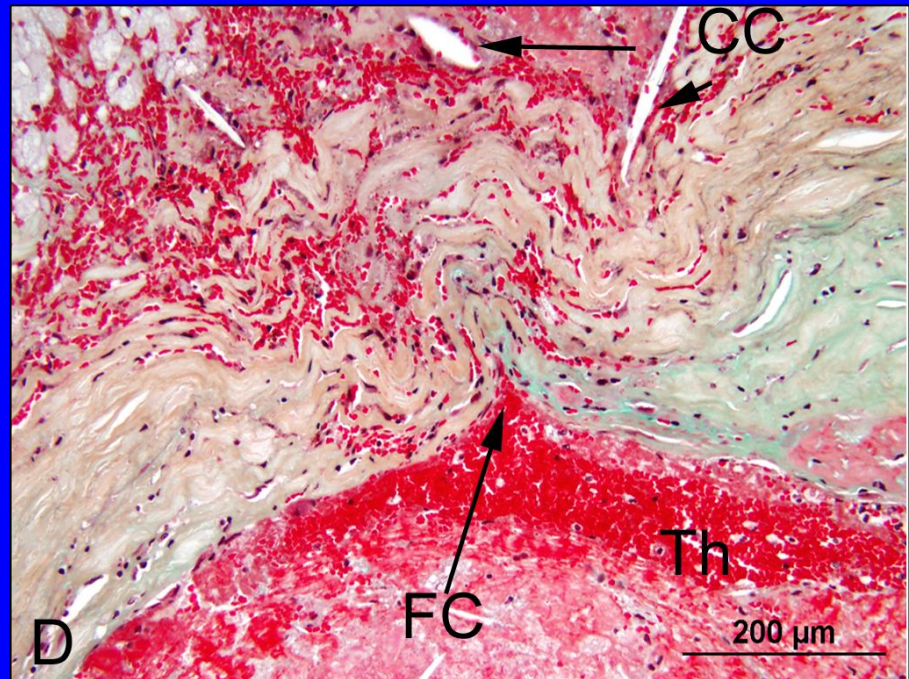
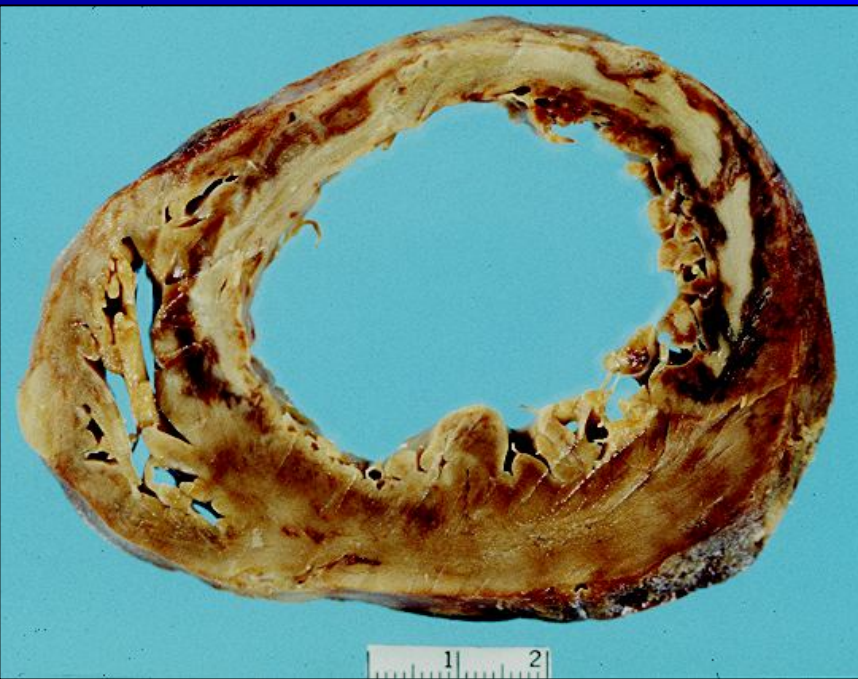
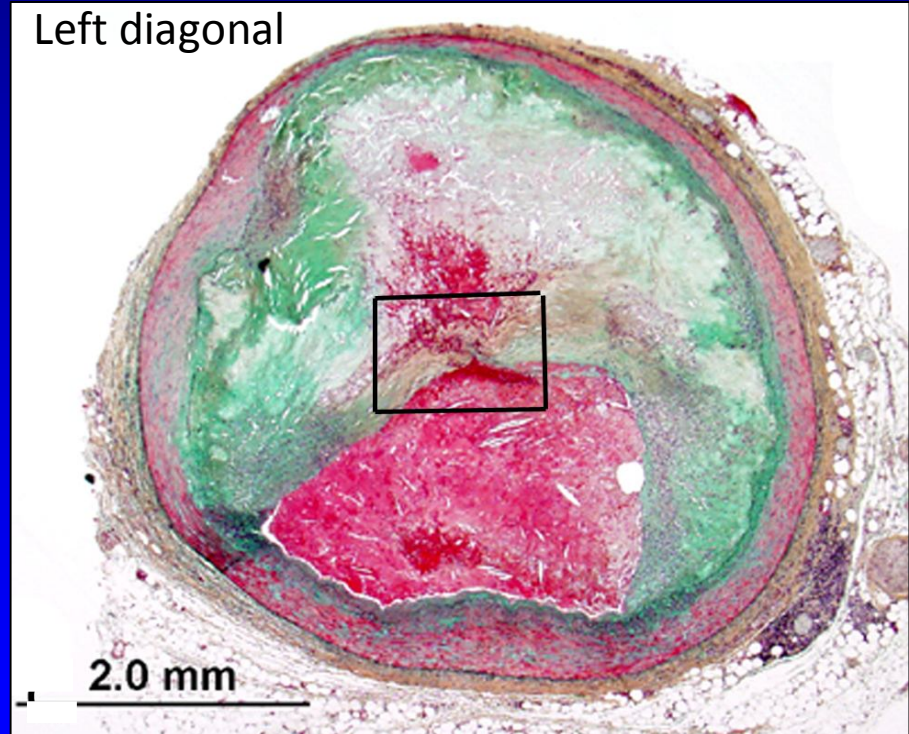
Culprit lesion	% Total	Mean age (years \pm SD)	% Women	% Occlusive	% TM AMI (occlusive thrombi)	% TM AMI (non-occlusive thrombi)
Erosion	28%	44 \pm 11**	37%	11 (58%)	10 (91%)	0%
Rupture (46)	68%	52 \pm 11	11%	25 (55%)	22 (88%)	2 (10%)***
Severe stenosis without thrombi* (3)	4%	53 \pm 6	33%	-	-	-
Total (68)	100%	50 \pm 9	27%	56%	89%	7%

• 1 patient with healed rupture and 90% stenosis, 1 thin-cap fibroatheroma with 80% stenosis, 1 fibroatheroma with 90% stenosis; all 3 patients had subendocardial infarct only; SD = Standard deviation. ** p = 0.04, vs acute rupture; *** p < 0.0001, occlusive vs. non-occlusive

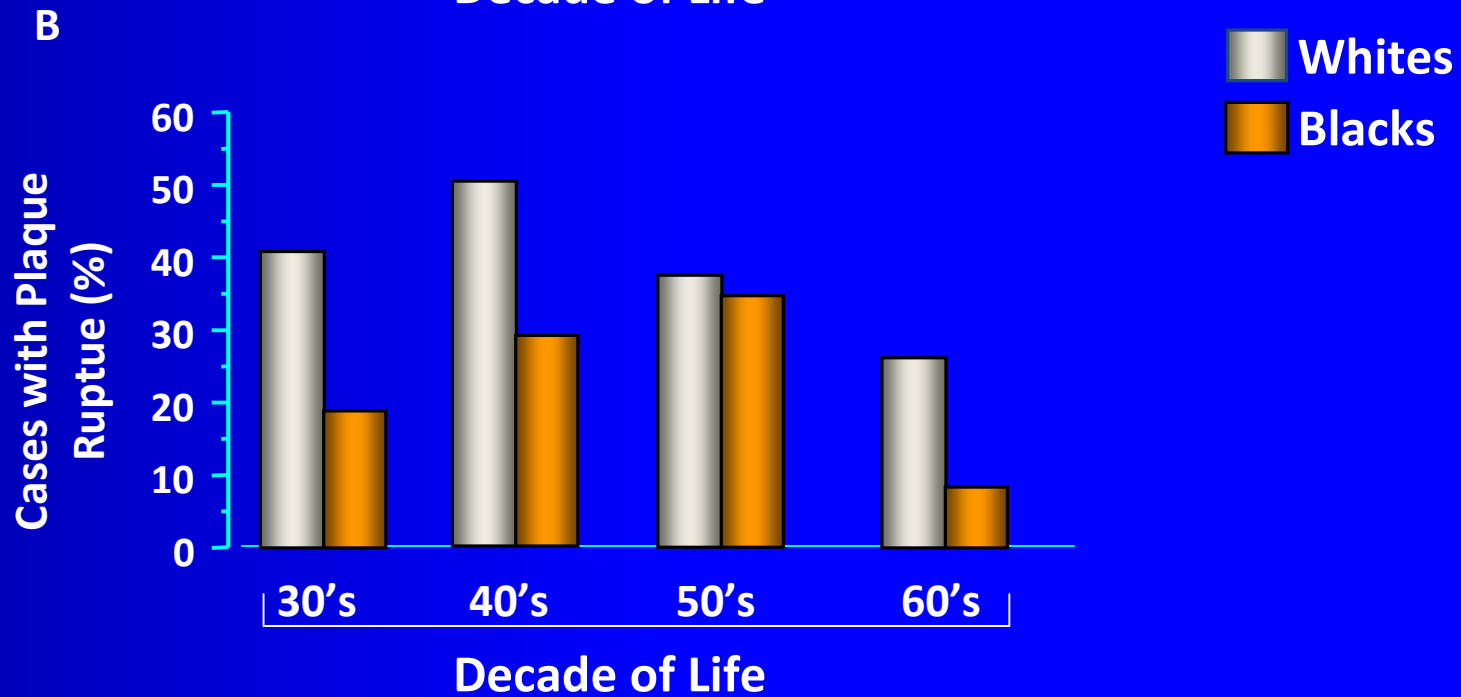
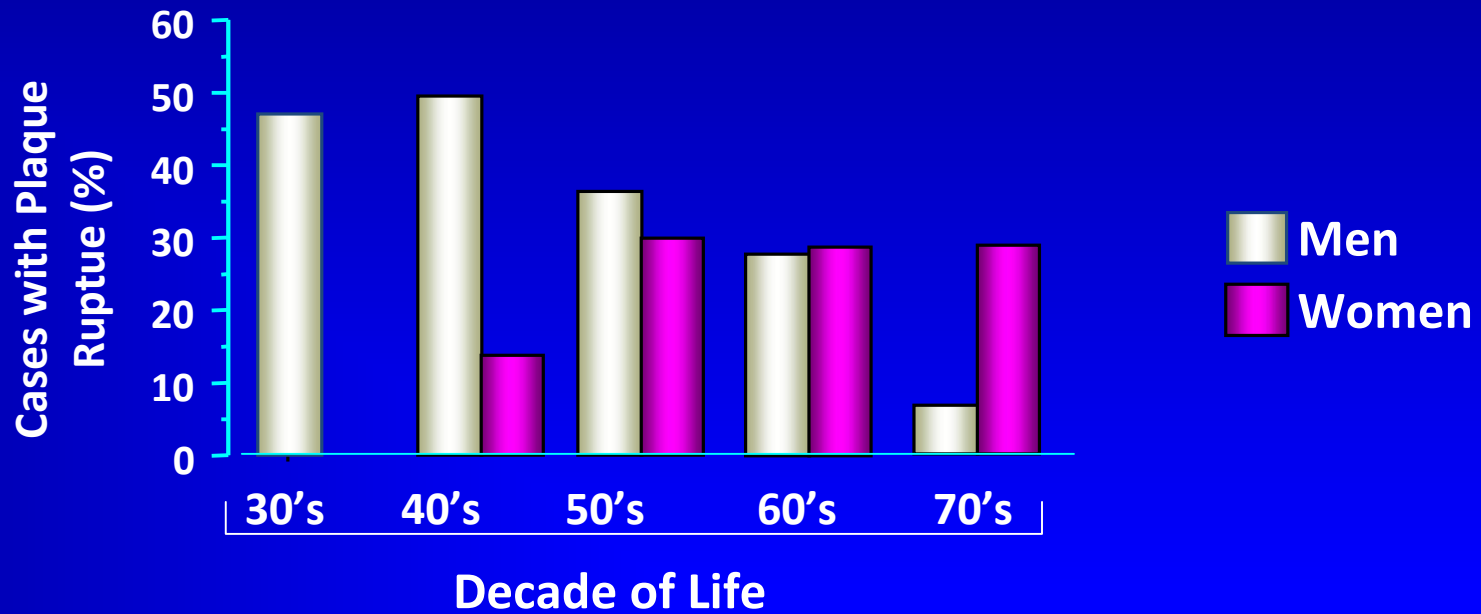
Proximal LAD 1



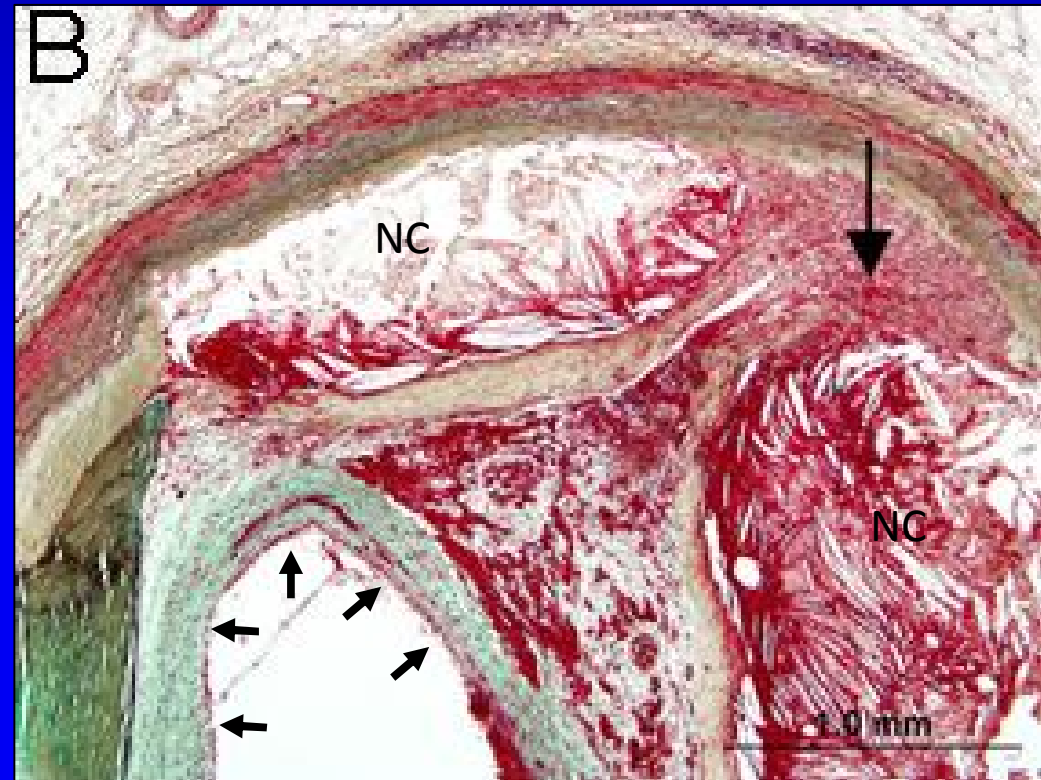
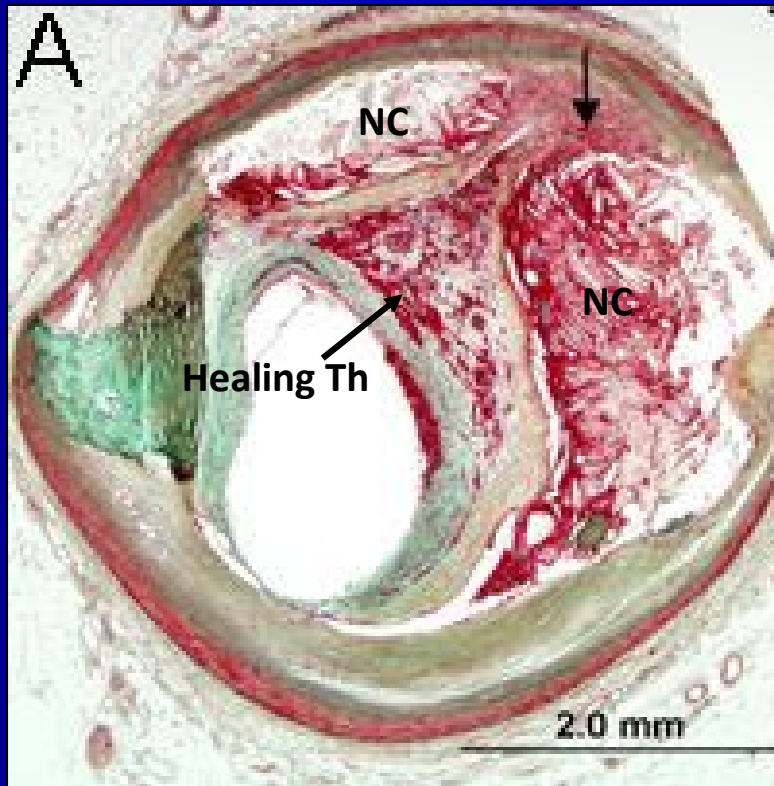
Left diagonal



A Plaque Rupture, Age, Sex and Race



Healing Plaque Rupture



nc = necrotic core, Th = thrombus, ↓ = rupture site

Location of epicardial coronary artery thrombi in 65 autopsy patients with AMI

Arterial distribution	No. of cases (% of total thrombi)	Erosion no. (% of thrombi in vessel site)	Site of infarct (n)	Segment of vessel with thrombosis	No. (% of total thrombosis)
LM	2 (3%)	2 (100%)	AS (1) Posterior (1)*		
LAD or LD	30 (46%)	9 (30%)	AS (17) Septal (5) Posterior LV (4) Lateral LV (2) Multifocal (2)	PLAD MLAD LD	18 (28%) 11 (17%) 1 (2%)
LCx/LOM	7 (11%)	1 (14%)	Lateral LV (5) Posterior LV (2)	PLCx MLCx LOM	1 (2%) 3 (5%) 3 (5%)
RCA	26 (40%)	7 (27%)	Posterior LV (24) Apical (1) Septal (1)	PRC MRC DRC	12 (19%) 9 (14%) 5 (8%)

LM = left main artery, * with wrap-around LAD, AS = anteroseptal, PLAD = proximal left anterior descending, MLAD = mid-LAD, LD = left diagonal, PLCx = proximal left circumflex artery, MLCx = mid-left circumflex artery, LOM = left obtuse marginal, PRC = proximal RCA, MRC = mid-RCA

Histomorphometric data, epicardial thrombi in patients with Acute Myocardial Infarction and Sudden Death

Epicardial culprit lesion	Occlusive vs. non-occlusive	Thrombus Length, mm \pm SD	% Underlying stenosis \pm SD	IEL area, mm ²	Necrotic core, mm ²	% calcified area, mm ²
Erosion	Occlusive: 11 Nonocclusive: 8 Total (n = 19)	10.8 \pm 2.2 5.0 \pm 1.5 8.3 \pm 11.8	73 \pm 15% 80 \pm 14% 76 \pm 3%	8.2 \pm 2.2 9.1 \pm 2.2 8.6 \pm 1.5	0.3 \pm 1.7 0 0.18 \pm .13	0.3 \pm 1.3 0.5 \pm 1.5 0.4 \pm 0.3 (range 0-4%)
Rupture	Occlusive: 25 Nonocclusive: 21 Total (n=46)	11.6 \pm 1.6 10.3 \pm 1.2 # 11.1 \pm 1.0	77 \pm 4% 80 \pm 4% 79 \pm 3%	14.1 \pm 1.6 ⁺⁺ 12.6 \pm 1.7 13.5 \pm 11.2*	4.6 \pm 1.3 ⁺⁺ 2.7 \pm 0.5* 3.8 \pm 0.9*	2.3 \pm 1.0 2.9 \pm 1.2 2.5 \pm 0.9 (range 0-14%) ⁺⁺

IEL = internal elastic lamina, SD = standard deviation,

• P = 0.01 vs. erosion

p = 0.006 vs. erosion

++ p = 0.03 vs. erosion

Characteristics of Other Findings in the Coronary tree of Patients dying with AMI

Epicardial culprit lesion	Mean number of CAs* $\geq 75\%$ x-sectional are narrowing	Number of fibro-atheromas	Number of TCFA	Number of Healed Plaque Rupture
Rupture	2.1 ± 0.6	6.8 ± 0.7	3.1 ± 0.6	6.2 ± 1.2
Erosion	1.6 ± 0.6	1.7 ± 0.7	0.3 ± 1.4	0.07 ± 2.9
P-value	0.01	0.03	0.04	0.04

•Laft main, left anterior descending and diagonal , left circumflex and marginal, right coronary artery, 1-4 possible .

Frequency distribution of percent cross-sectional area stenosis by plaque in coronary thrombosis attributed to rupture of erosion

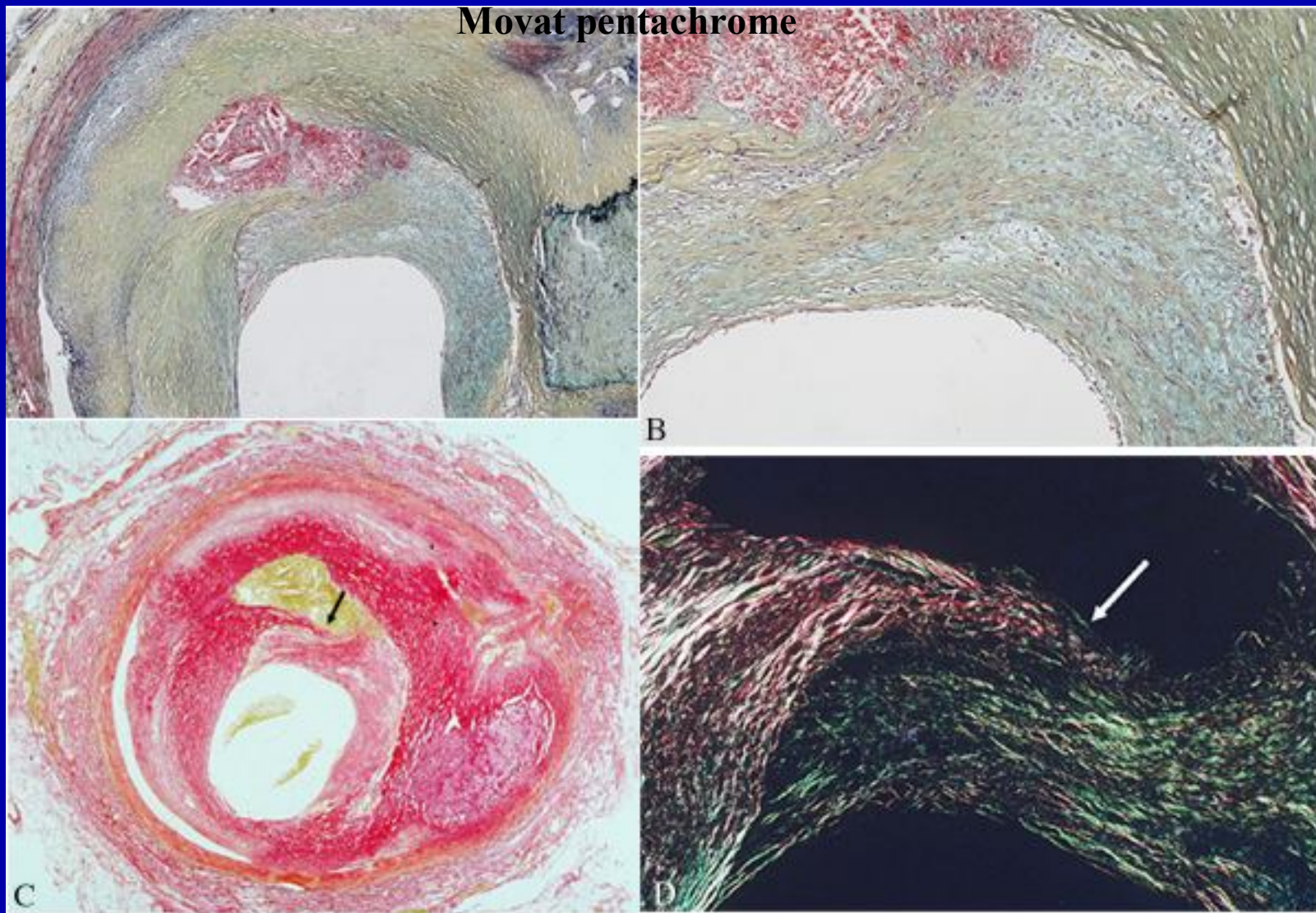
Stenosis (%)	Mean Age	Erosion [No. (%)]	Rupture [No. (%)]	Cases [No. (%)]
50-59	42 ± 5	3 (14%)	1 (4%)	4 (8%)
60-69	46 ± 7	5 (23%)	4 (14%)	9 (18%)
70-79	49 ± 10	10 (45%)	11 (39%)	21 (42%)
80-89	50 ± 5	3 (14%)	5 (18%)	8 (16%)
90-99	52 ± 16	1 (5%)	7 (25%)	8 (16%)
Total	49 ± 10	22 (100%)	28 (100%)	50 (100%)

}

68%

Farb A, et al. Circulation 1994

Do plaque ruptures lead to plaque progression ?



Movat pentachrome

B

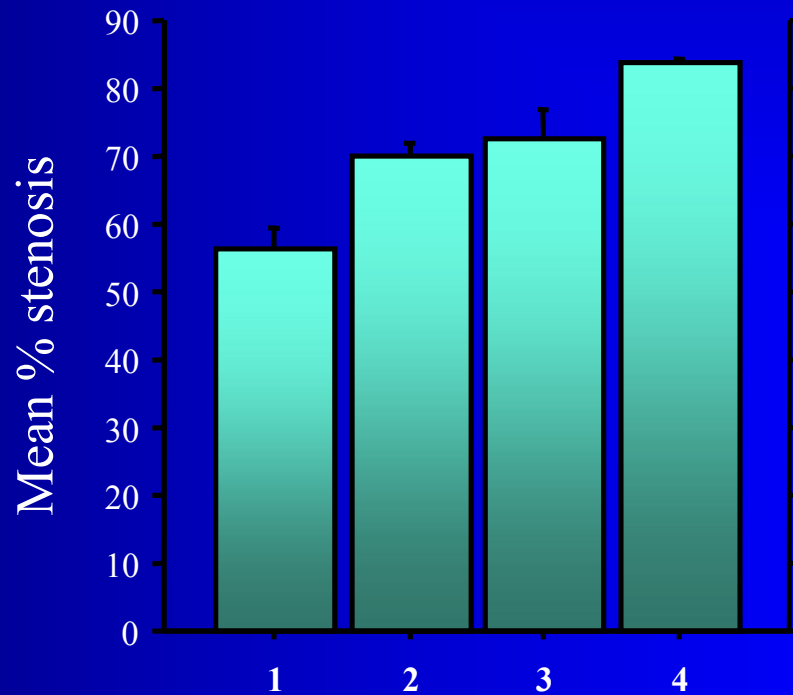
C

D

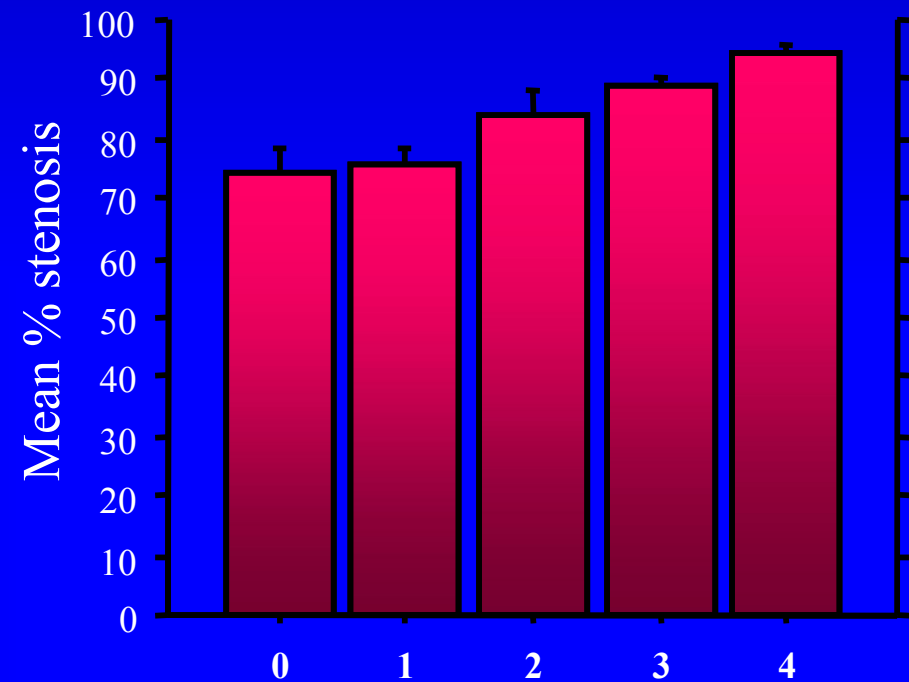
Sirius red

Sirius red with polarized light

Mean % stenosis increases with number of prior rupture sites

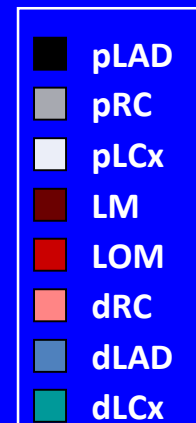
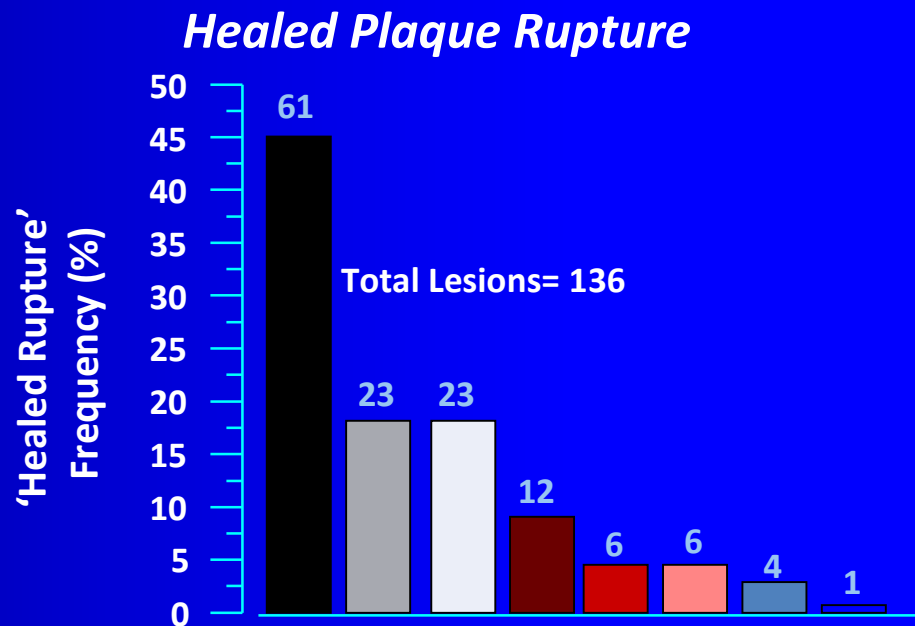
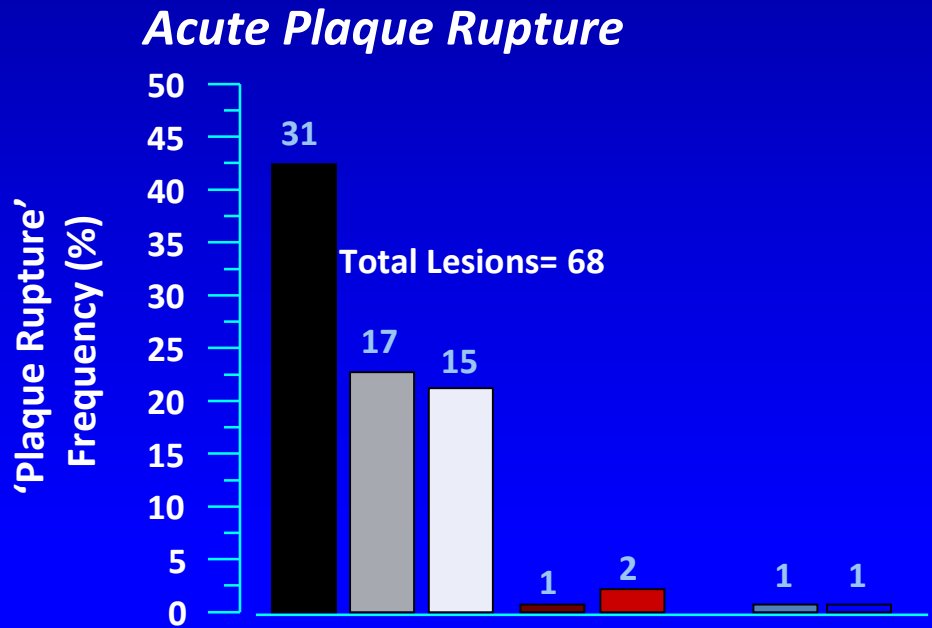
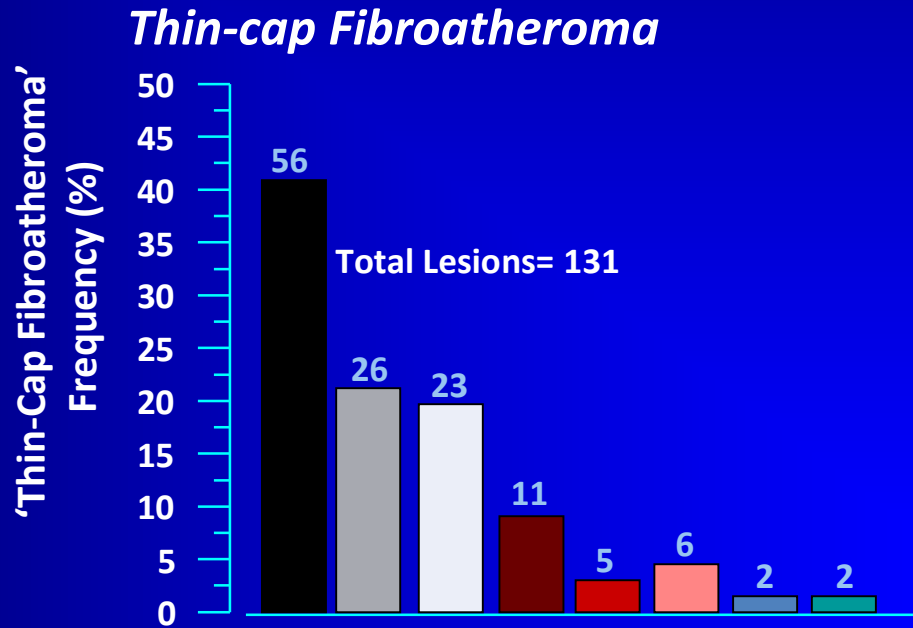


A
Number of prior ruptures,
healed rupture sites



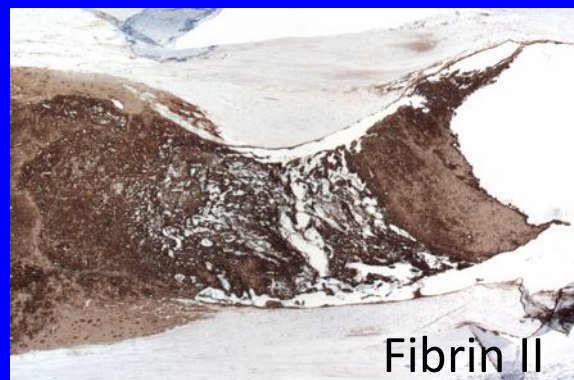
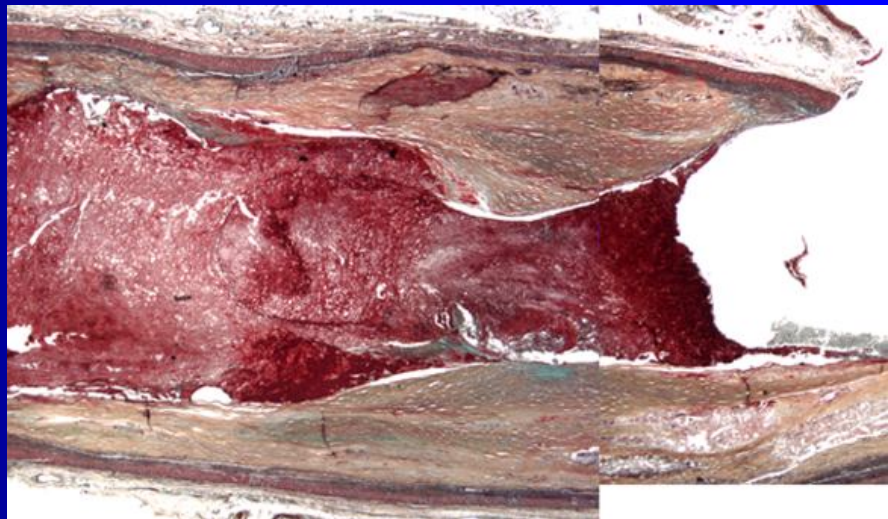
B
Number of prior ruptures,
acute rupture sites

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

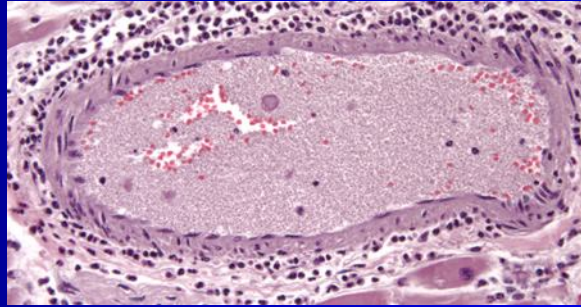


Ruptures versus Erosion: Intramyocardial emboli

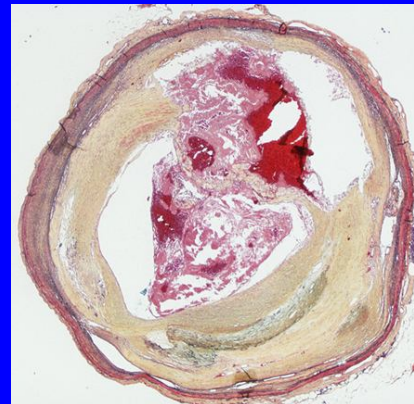
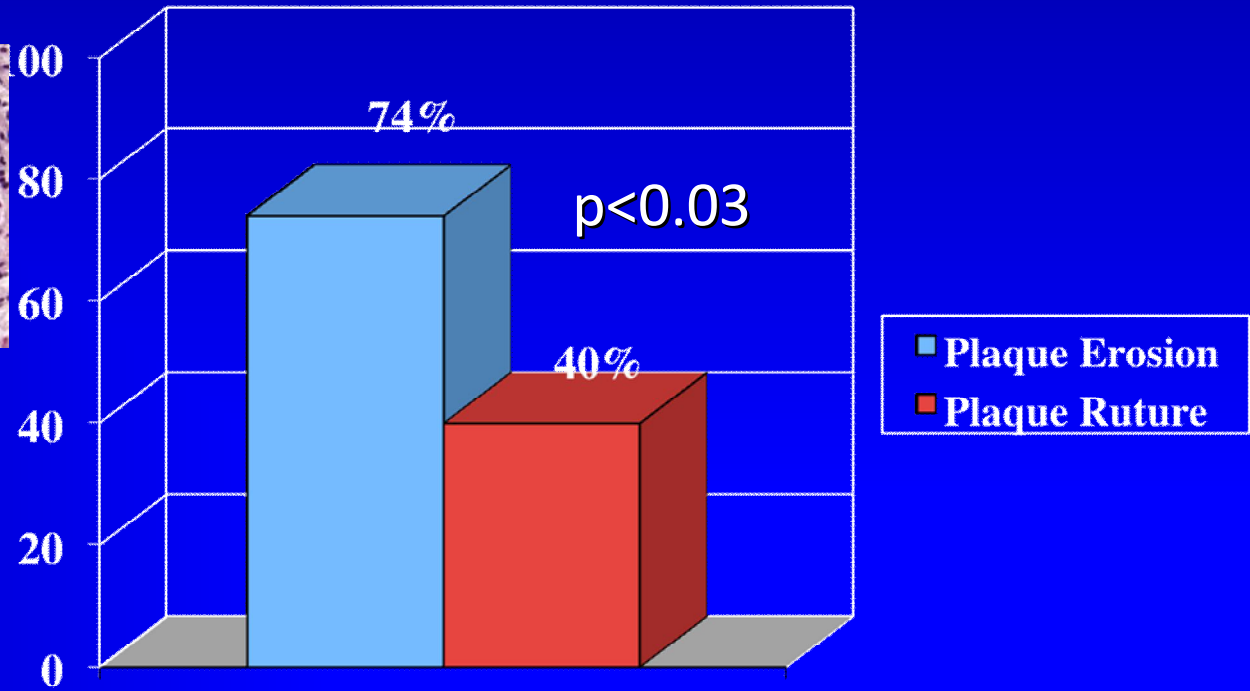
- 44 cases of sudden death due to coronary thrombosis
- 38 men, 6 women; Age: 51 ± 15 years
- 26 Plaque Ruptures (25 hearts, 1 heart with 2 ruptures)
- 21 Plaque Erosions (19 hearts, 2 hearts with 2 erosions)
- Positive staining for fibrin and platelets in all epicardial thrombi



Intramyocardial Emboli more Common in Plaque Erosion vs. Plaque Rupture



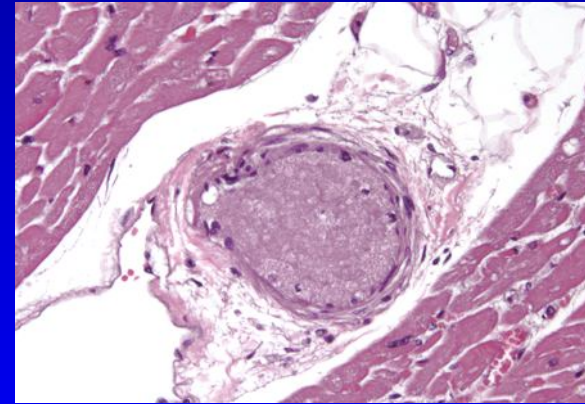
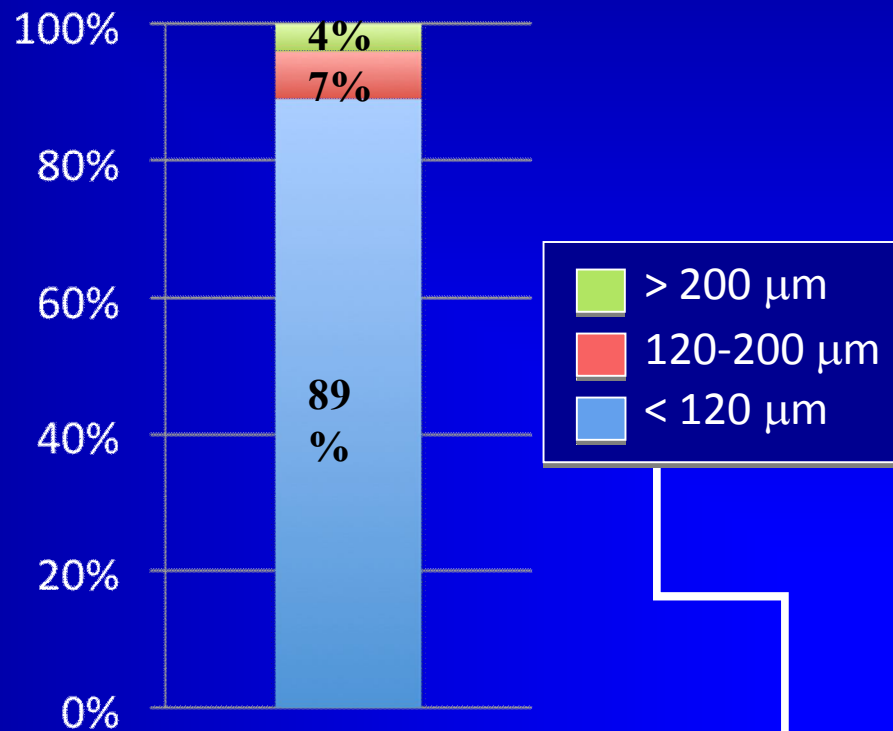
%Hearts with
Intramyocardial
Emboli



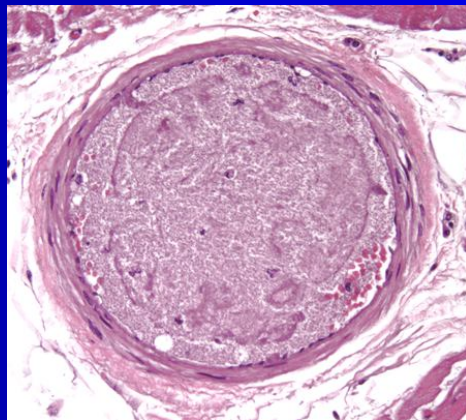
Relationship among Culprit Plaque Morphology, Embolization, Occlusive thrombus, Myocardial Necrosis, and Gender

Variable	Plaque Morphology	Frequency	P value
Embolization Rate	Erosion	70% (15/21)	0.01
	Rupture	44% (11/26)	
	Total	55%(26/47)	
Percent of heart with ≥ 5 emboli	Erosion	43% (9/21)	0.05
	Rupture	12% (3/26)	
	Total	26%(12/47)	
Totally Occlusive thrombus	Erosion	61% (14/21)	ns
	Rupture	48% (12/26)	
	Total	55%(26/47)	
Myocardial Necrosis	Erosion	86% (18/21)	0.001
	Rupture	19% (5/26)	
	Total	49%(23/47)	
Women	Erosion	71% (15/21)	0.001
	Rupture	38% (10/26)	
	Total	53%(25/47)	

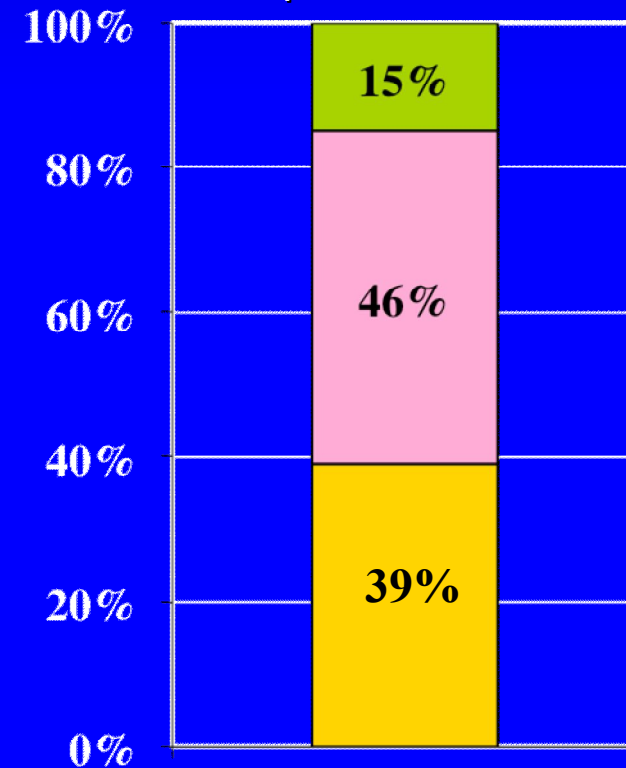
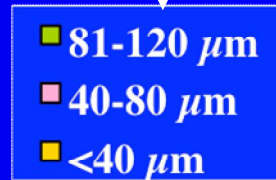
Diameter of Vessels Containing Intramyocardial Emboli



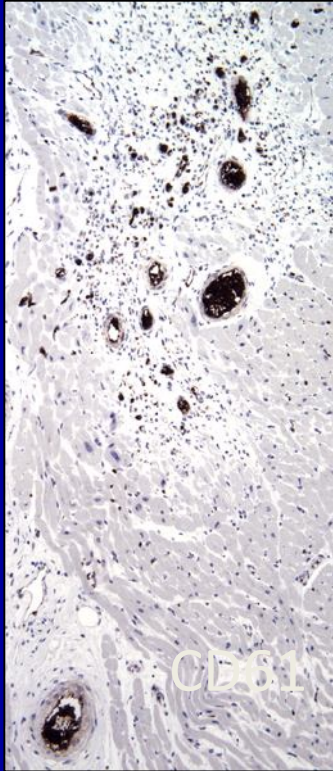
80 μm diameter



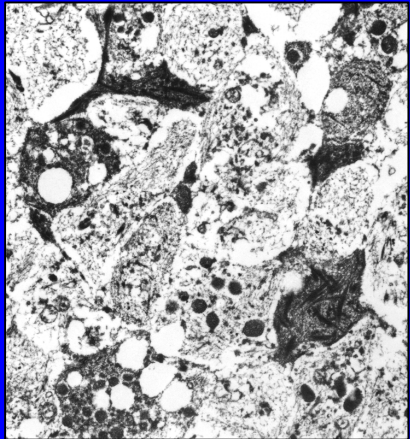
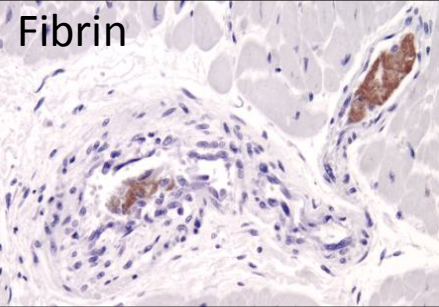
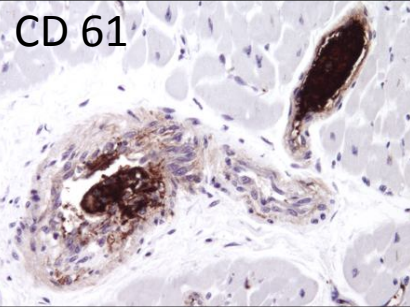
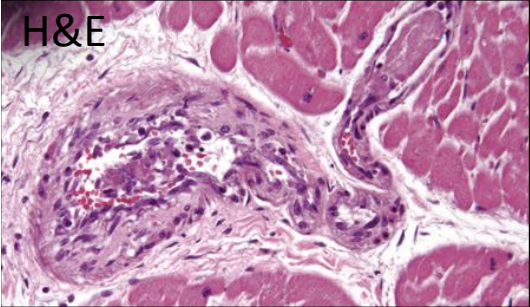
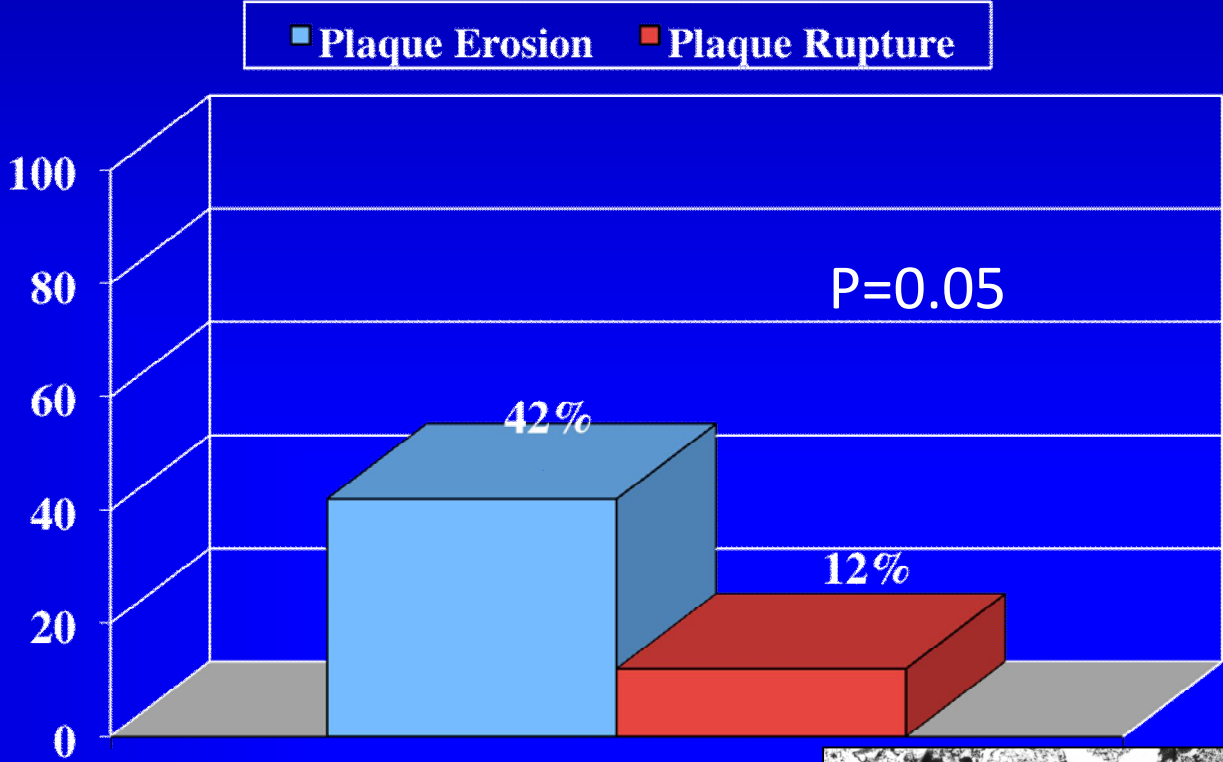
130 μm diameter



Multiple Intramyocardial Emboli more Common in Plaque Erosion vs. Plaque Rupture



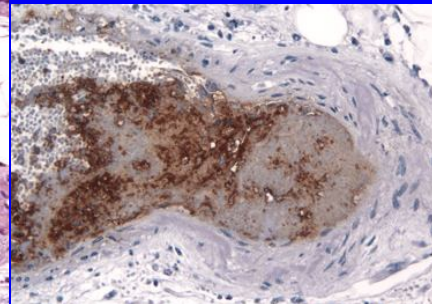
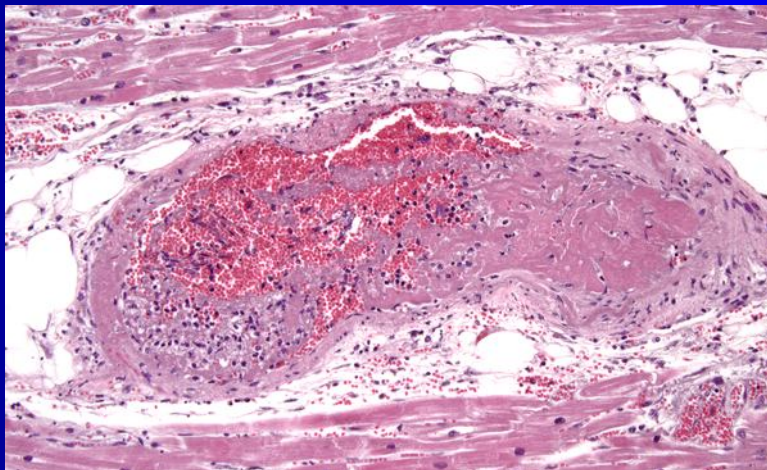
%Hearts with ≥ 5 Emboli



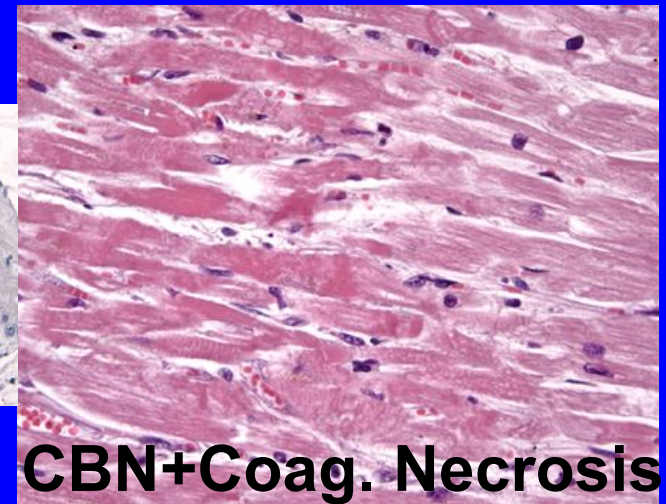
Intramyocardial Emboli and Myocardial Necrosis

In hearts with intramyocardial emboli:

- 57% associated with focal myocardial necrosis
 - Of these, 83% with multiple emboli (86% in vessels <120 μm in diameter)
- 24% associated with acute MI, 5% with myocardial scars (healed MI), 14% with normal myocardium



CD61



CBN+Coag. Necrosis

Summary

- ✓ More than 95% of AMIs occur from underlying coronary atherosclerosis
- ✓ Plaque rupture is the most frequent cause of coronary thrombosis (PR=70%, PE=30%). Positive remodeling of the vessel is seen in rupture but a negative remodeling in erosion
- ✓ In women < 50 years plaque erosion is more frequent than plaque rupture
- ✓ Occlusive thrombi occur in over 50% of cases and are associated with transmural myocardial infarcts in nearly 90% of cases
- ✓ TCFA (vulnerable plaques) are seen at least at 3 different locations within the coronary tree in patients dying with acute myocardial infarction
- ✓ Intramyocardial emboli are observed in 57% of hearts in the presence of epicardial coronary thrombosis; more frequently in erosion than rupture (74% vs. 40%)
 - In hearts with intramyocardial emboli
 - 57% are associated with focal myocardial necrosis
 - Of these, 83% with multiple emboli (86% in vessels <120 μm in diameter) and again are more frequent in erosion than rupture