

Comparison of Biomarkers for Coronary Plaque Rupture in Patients with Acute Coronary Syndrome

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Background

- **Biomarkers** have become increasingly important in ACS to supplement electrocardiographic findings and patient history because one or both can be misleading
 - “Cardiac troponin I and T”
- Some of new markers appear to improve risk stratification in ACS and might be able to supplement the information provided by cardiac troponin

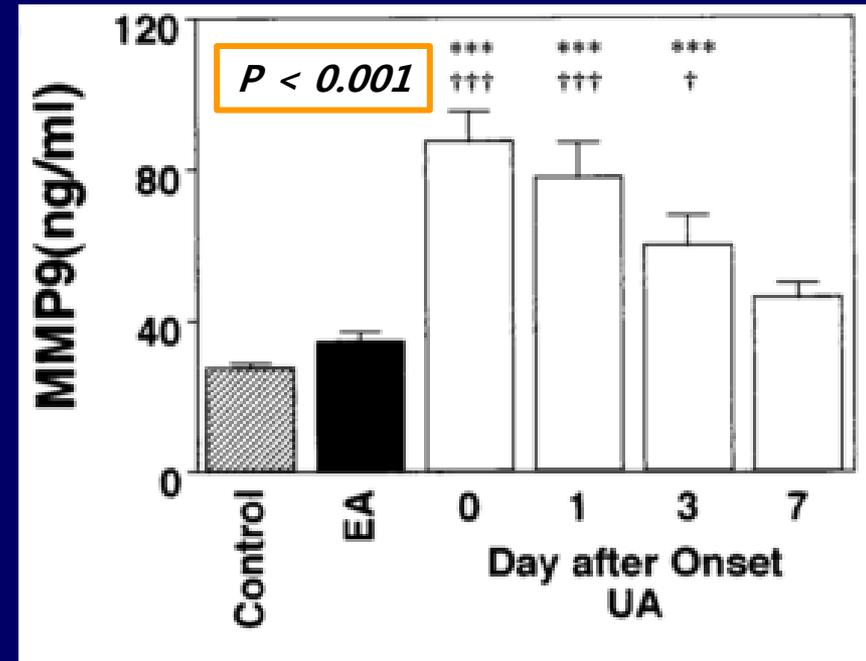
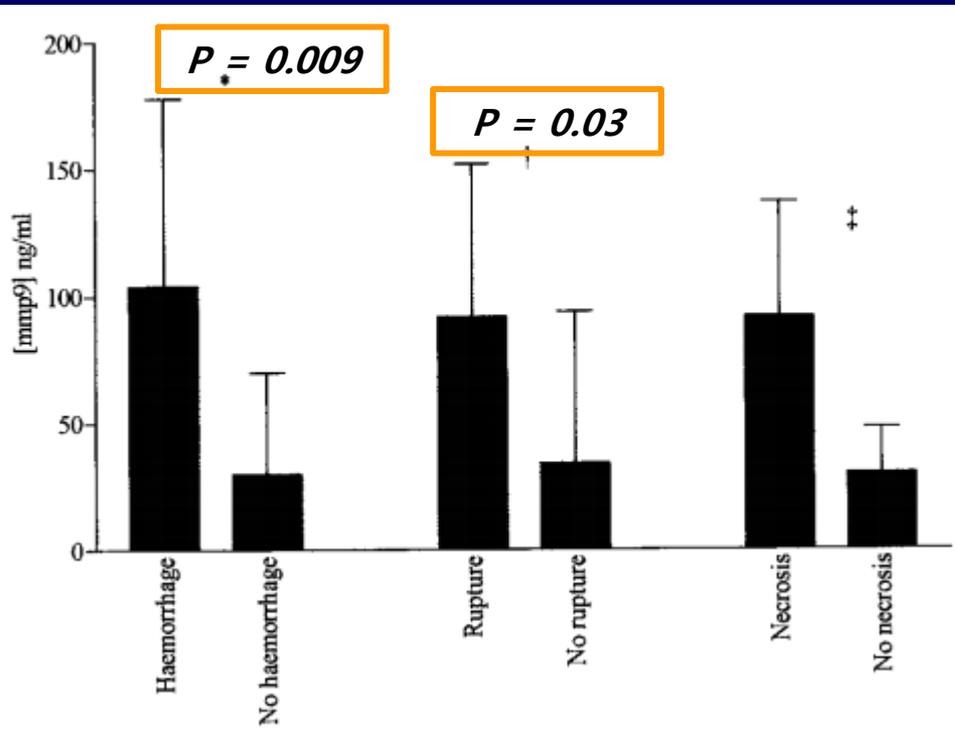
Hochholzer et al. Am Heart J 2010;160:583-94



Biomarker : MMP-9

Kai H et al. *J Am Coll Cardiol* 1998;32:368–72

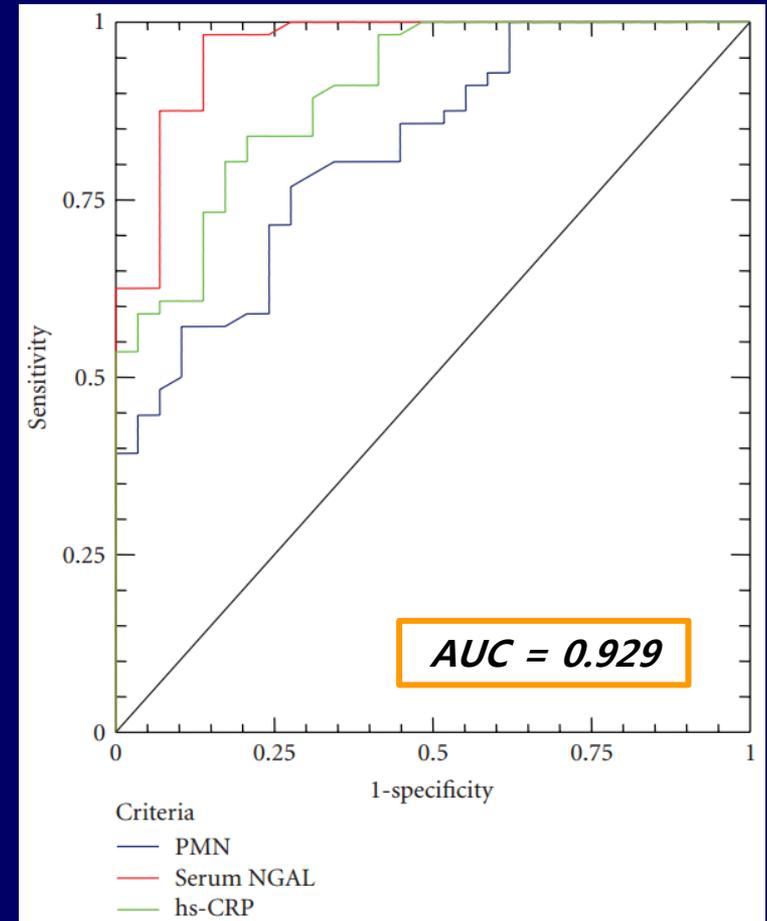
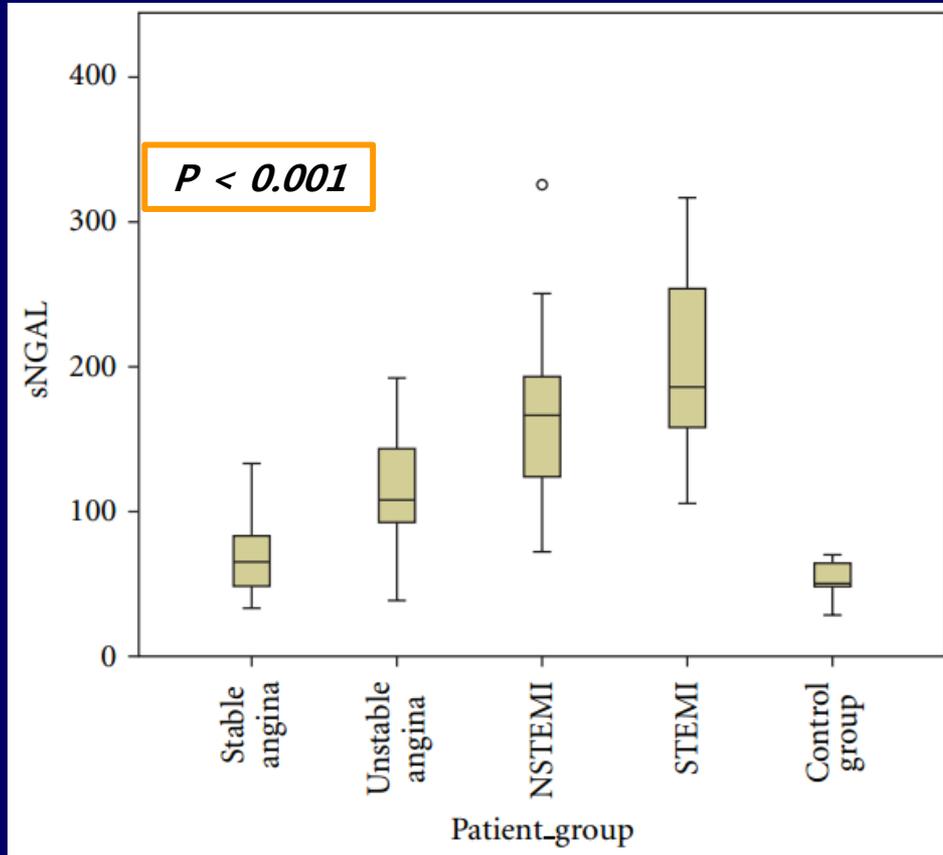
Loftus IM et al. *Stroke*. 2000;31:40-47



- MMP-9 concentration was significantly higher with histological evidence of **plaque instability** in carotid artery.
- Transient elevation of MMP-9 levels in patients with UA may be associated with the increased expression of MMP-9, probably in activated macrophages or VSMCs in the **plaque prone to rupture**.

Biomarker : NGAL

Kafkas N et al. *Int J Inflamm.* 2012;2012:189797



- Diagnostic value for serum-NGAL in discriminating ACS patients from patients with SA is high.

Background

- The 3 most common underlying mechanisms contributing to acute coronary syndrome (ACS) are believed to be plaque rupture (PR), plaque erosion, and calcified nodule (CN)

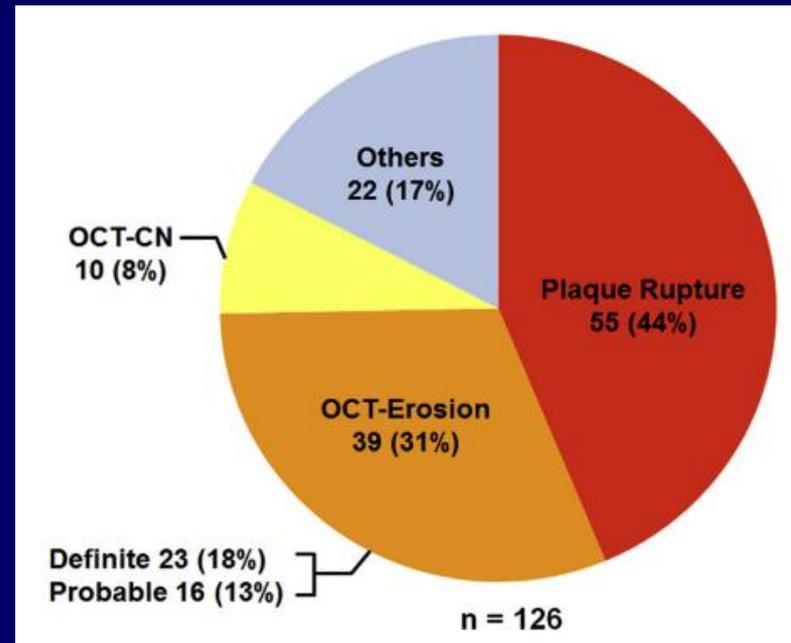
Virmani R et al. *Arterioscler Thromb Vasc Biol* 2000;20:1262–75.
Naghavi M et al. *Circulation* 2003;108:1664–72.

- The frequency of erosion and CN might be underestimated in patients with ACS due to the lack of diagnostic modalities



Background

- Optical coherence tomography (OCT) is an emerging intravascular imaging modality with a high resolution which can visualize microstructures of atherosclerotic plaque
- Recent studies are focusing on characterizing the morphological, pathophysiological features of plaque erosion and CN in patients with ACS by OCT

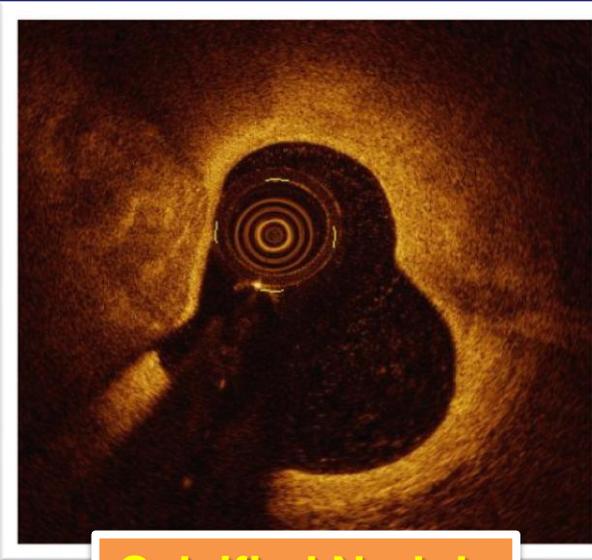


Intravascular OCT Imaging

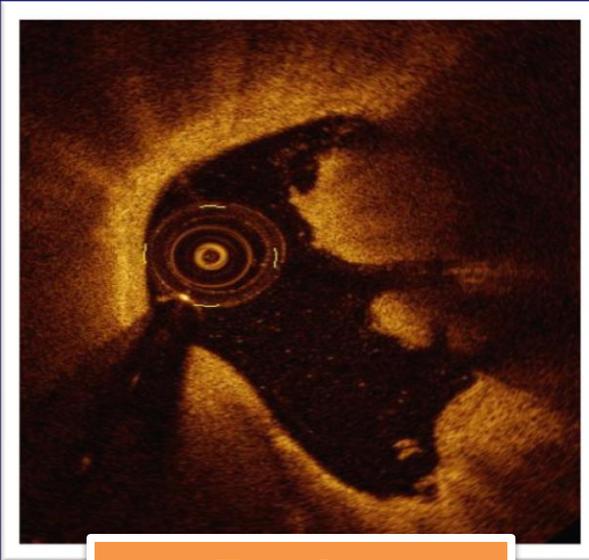
Plaque Classification



Rupture



Calcified Nodule



Erosion

Underlying plaque :
Lipid

Underlying plaque :
Calcium

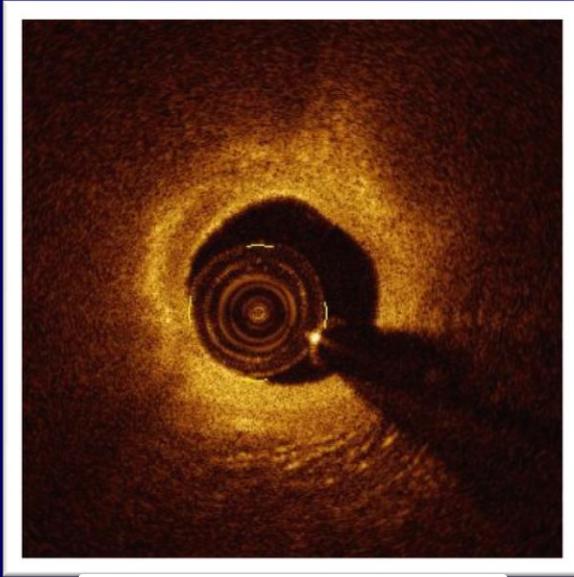
Disrupted Fibrous Cap

1. Thrombus with intact underlying plaque visualized
2. No thrombus with irregular surface
3. Thrombus with underlying plaque not visualized

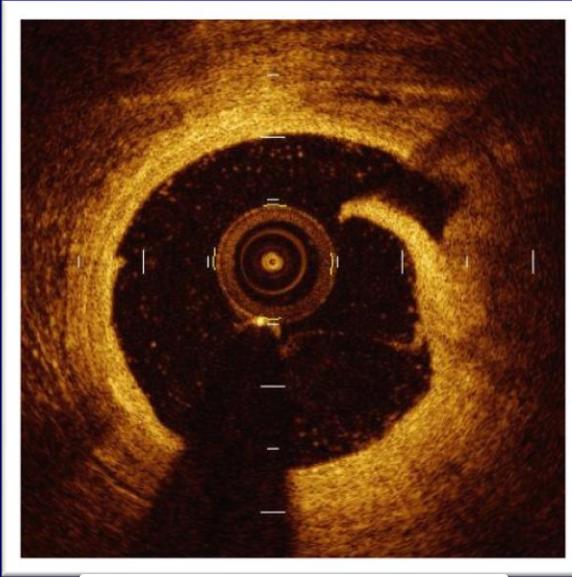
Intact Fibrous Cap

Intravascular OCT Imaging

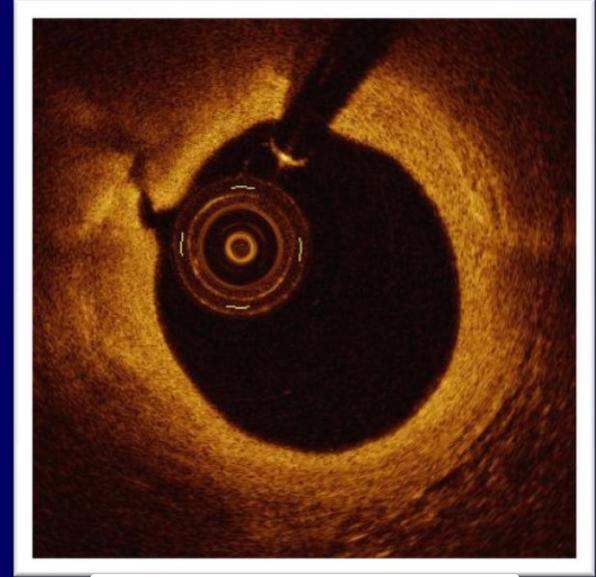
Other Features



Tight stenosis



Dissection



Fissure

Objective

- To characterize culprit lesions in patients with ACS by OCT and compare the several new biomarkers according to the morphological features of the culprit lesions



Methods

- Retrospective data from Korea University Anam Hospital OCT registry
- A total of 123 patients with ACS [unstable angina (UA, n=85), non-ST elevation myocardial infarction (NSTEMI, n=14), ST elevation myocardial infarction (STEMI, n=24)] who had undergone pre-intervention OCT imaging were included and analyzed
- Demographic, clinical, lesional and procedural data were also analyzed



OCT Analysis

- Optical coherence tomography (OCT) (C7XR Fourier-Domain System, LightLab Imaging, Westford, Mass) was performed (LightLab Imaging, Ilumien Offline review workstation, Ver D.O 2, MA, USA).
- Analysis encompassed the culprit lesion of the vessel on the basis of coronary angiogram and OCT.



Laboratory Analysis

- MMP-9 was quantified using Luminex's xMAP Technology with the Milliplex kits (Millipore, Billerica, MA), which is similar to the sandwich ELISA procedure, according to the manufacturer's instructions.
- Plasma NGAL was determined using an in-house time resolved immunofluorometric (TRIFMA) assay based on NGAL antibodies and recombinant NGAL from R&D Systems (Abingdon, UK)



Results:

Baseline Patient Characteristics (1)

Variable	STEMI (n= 24)	NSTEMI (n= 14)	UA (n= 85)	p-value
Age (year)	54.70±9.87	65.67±11.16	68.24±13.01	0.022
Male sex (%)	24 (100.0%)	10 (72.7%)	55(63.2%)	0.113
BMI (kg/m ²)	25.59±1.86	23.73±2.67	22.80±1.90	0.018
Comorbidity				
Hypertension, n (%)	19 (75.0%)	6 (45.5%)	46 (52.6%)	0.419
Diabetes mellitus, n (%)	9 (37.5%)	8 (54.5%)	27 (31.6%)	0.460
Smoking, n (%)	11 (44.4%)	10 (72.7%)	14 (15.8%)	0.008
Dyslipidemia, n (%)	3 (12.5%)	5 (36.4%)	27 (31.6%)	0.494
CAD family history, n (%)	9 (37.5%)	5 (36.4%)	26 (22.2%)	0.622

Results:

Baseline Patient Characteristics (2)

Variable	STEMI (n= 24)	NSTEMI (n= 14)	UA (n= 85)	p- value
Laboratory data				
Creatinine (mg/dl)	2.59±4.56	0.94±0.25	0.94±0.22	0.148
Glucose (mg/dl)	153.11±73.95	140.64±40.26	140.56±55.49	0.846
Total cholesterol (mg/dl)	166.89±28.03	181.73±50.61	186.22±48.14	0.577
Triglyceride (mg/dl)	105.00±60.83	103.10±56.220	147.42±78.10	0.169
HDL-cholesterol (mg/dl)	37.89±7.64	44.30±8.06	43.58±10.75	0.267
LDL-cholesterol (mg/dl)	115.33±27.79	126.40±43.27	130.57±36.48	0.599
Biomarkers (n=39)				
NGAL (ng/mL)	4.52±4.27	2.67±1.93	1.78±0.70	0.036
MMP-9 (ng/mL)	3.72±3.94	3.69±2.84	2.12±1.73	0.397
hs-CRP (ng/mL)	21.83±21.71	18.59±17.55	17.05±17.74	0.830



Results:

Angiographic and procedural data (1)

Variable		STEMI (n= 24)	NSTEMI (n= 14)	UA (n= 85)	p- value
TIMI flow grade, n (%)	TIMI 0	3 (11.1%)	2 (18.2%)	0	0.122
	TIMI 1	3 (11.1%)	4 (27.3%)	5 (5.3%)	
	TIMI 2	8 (33.3%)	0	18 (21.1%)	
	TIMI 3	10 (44.4%)	8 (54.5%)	63 (73.7%)	
Culprit vessel, n (%)	LAD	19 (77.8%)	9 (63.6%)	63 (73.7%)	0.580
	LCx	0	1 (9.1%)	13 (15.8%)	
	RCA	5 (22.2%)	4 (27.3%)	9 (10.5%)	
Segment of culprit vessel, n (%)	Prox	8 (33.3%)	9 (63.6%)	45 (52.6%)	0.275
	Mid	16 (67.6%)	4 (27.3%)	40 (47.4%)	
	Distal	0	1 (9.1%)	0	
Multivessel disease, n (%)		16 (67.6%)	9 (63.6%)	40 (47.4%)	0.728
Thrombus burden, n (%)	Grade 0	10 (44.4%)	9 (63.6%)	49 (57.9%)	0.298
	Grade 1	3 (11.1%)	2 (18.2%)	13 (15.8%)	
	Grade 2	3 (11.1%)	0	9 (10.5%)	
	Grade 3	0	2 (18.2%)	9 (10.5%)	
	Grade 4	8 (33.3%)	0	5 (5.3%)	

Results:

Angiographic and procedural data (2)

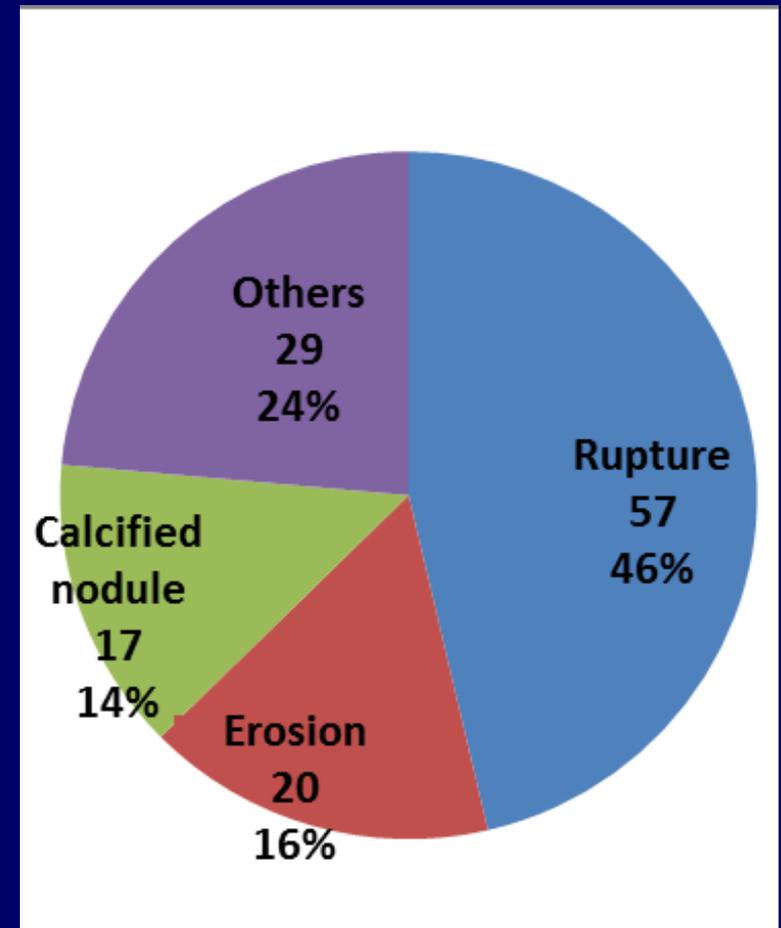
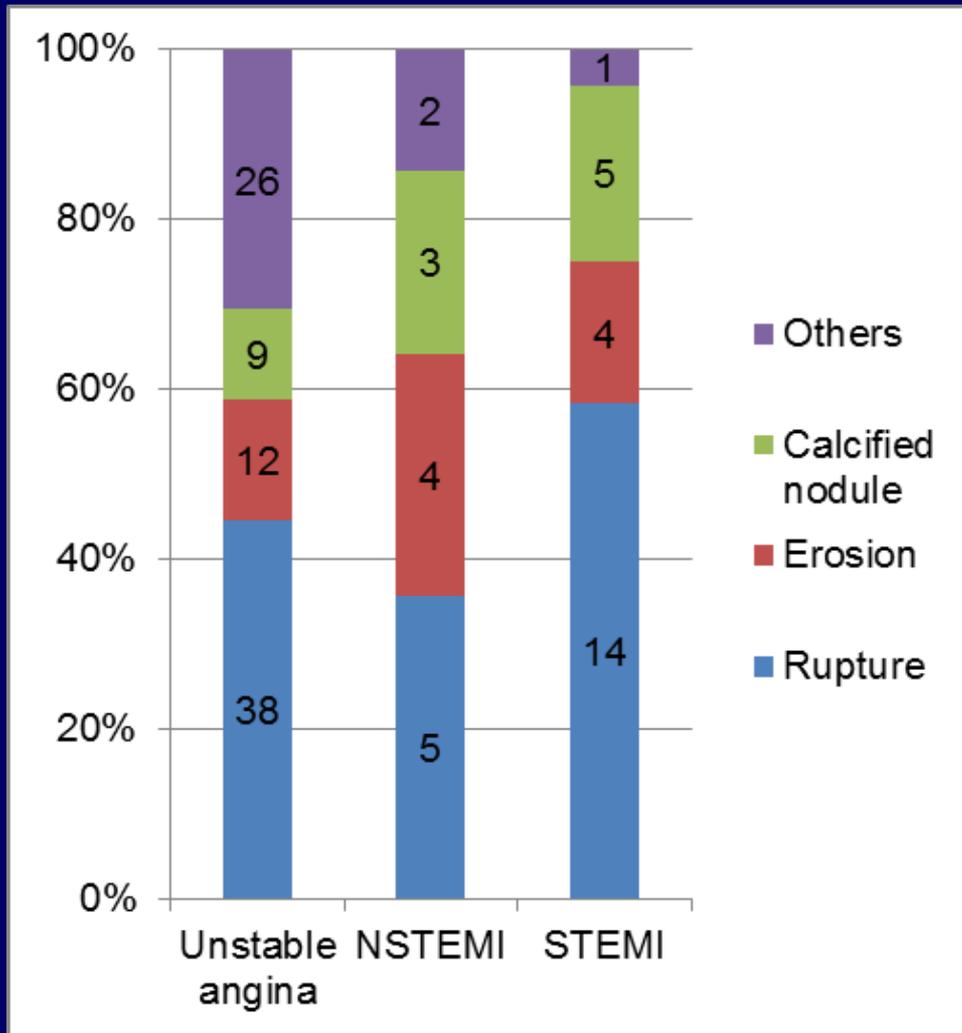
Variable	STEMI (n= 24)	NSTEMI (n= 14)	UA (n= 85)	p-value
Quantitative Coronary Angiography				
Reference diameter (mm)	3.09±0.27	3.07±0.40	2.95±0.23	0.364
Mean lumen diameter (mm)	0.50±0.40	0.68±0.58	1.05±0.53	0.031
Stenosis area (%)	92.00±9.94	91.36±8.27	89.17±7.64	0.663
Lesion length (mm)	11.62±4.81	13.27±5.29	16.73±6.75	0.101
Gensini score	73.62±14.52	62.17±15.63	57.00±12.89	0.050

Comparison of OCT Images

Variable	STEMI (n= 24)	NSTEMI (n= 14)	UA (n= 85)	p-value
Rupture	14 (58.3)	5 (35.7)	38 (44.7)	0.347
Erosion	4 (16.7)	4 (28.6)	12 (14.1)	0.373
Calcified nodule	5 (20.8)	3 (21.4)	9 (10.6)	0.279
Others	1 (4.2)	2 (14.3)	26 (30.6)	0.013



Plaque rupture (PR) was the most frequent finding in patients with ACS !!



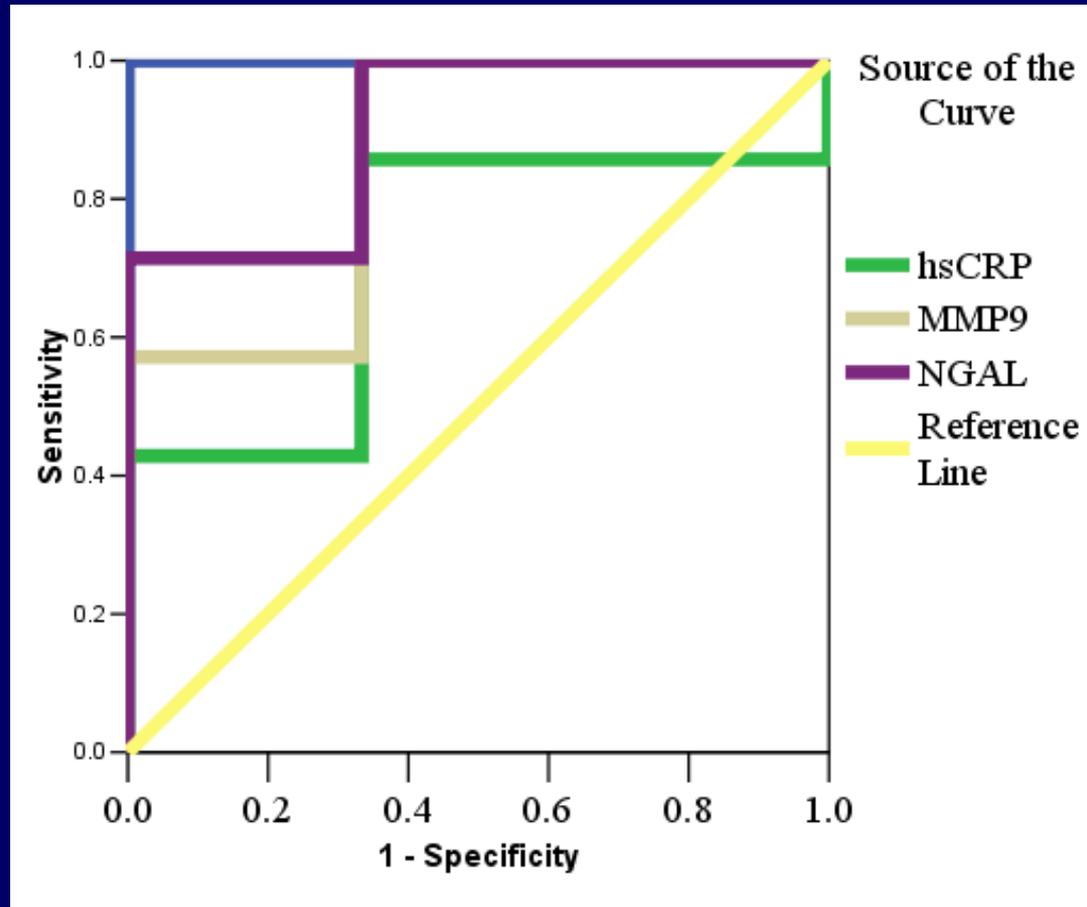
Serum level of MMP-9, hs-CRP, NGAL

OCT findings	MMP-9 (ng/mL)	p	hs-CRP (ng/mL)	p	NGAL (ng/mL)	p
Plaque rupture (n=24)	3.75±1.88	0.028	20.52±18.07	0.011	2.77±1.39	0.045
Non-ruptured plaque (n=15)	1.72±1.18		7.82±6.63		1.73±0.44	



NGAL was the most meaningful biomarker to detect plaque rupture determined by OCT

ROC curves



Area under the curve (AUC) were hs-CRP 0.714 ($p=0.305$), MMP-9 0.857 ($p=0.087$), **NGAL 0.905 ($p=0.050$)**, consistently.

Conclusion

The main findings of present study were the followings:

- **OCT detected more frequently ruptured plaques in STEMI patients, and 44.7% of the UA patients had plaque rupture.**
- **Elevated concentration of NGAL, MMP-9 and hs-CRP were related to the presence of ruptured coronary plaques.**
- **The NGAL could predict the presence of plaque rupture with excellent accuracy, superior to MMP-9 and hs-CRP.**



CASE

M/49

Visit to ER for chest pain (2 month)

Medicated for HTN, T2DM, Dyslipidemia

CK-MB

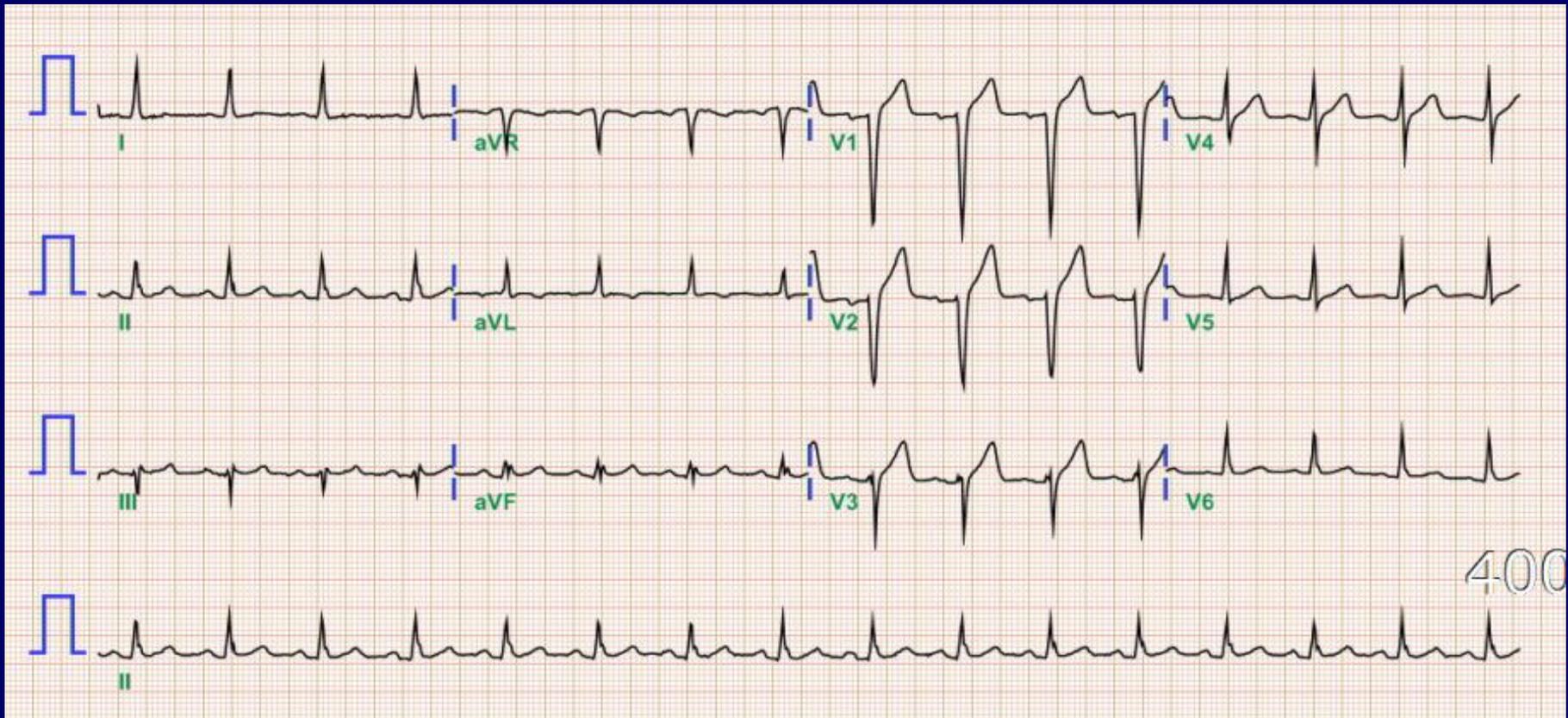
3.02 ng/ml

Troponin I

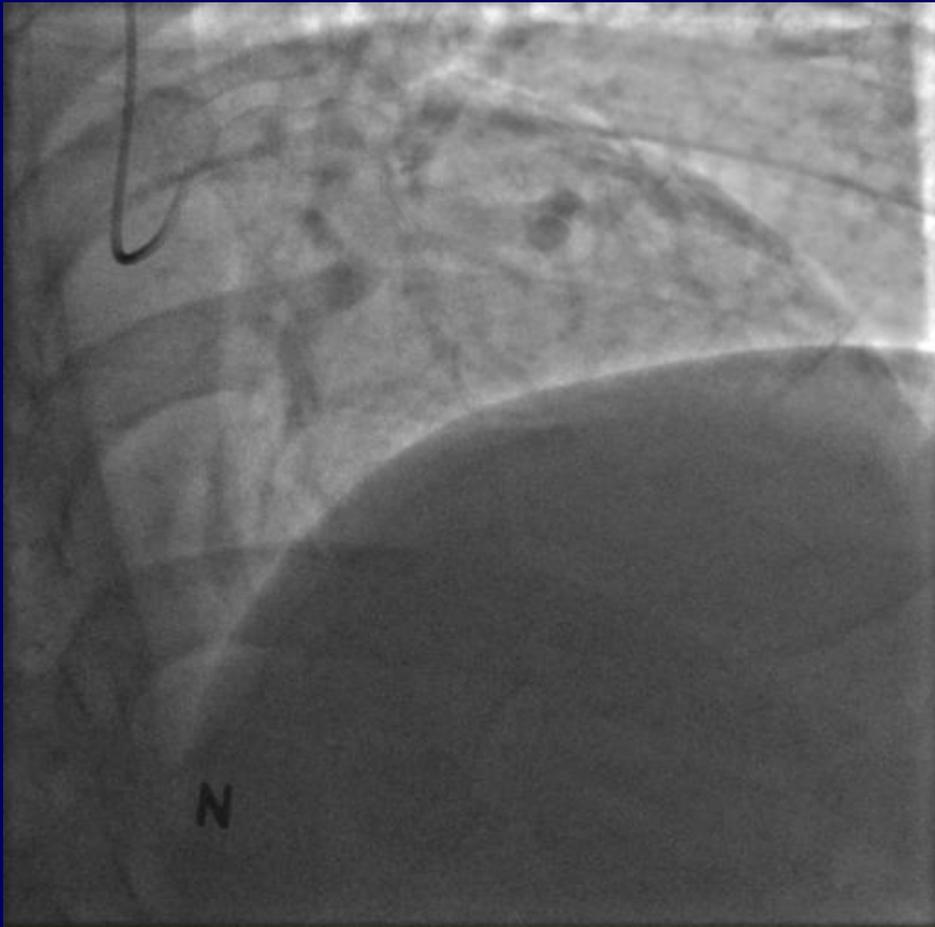
< 0.01 ng/ml

NGAL

6.43 ng/ml

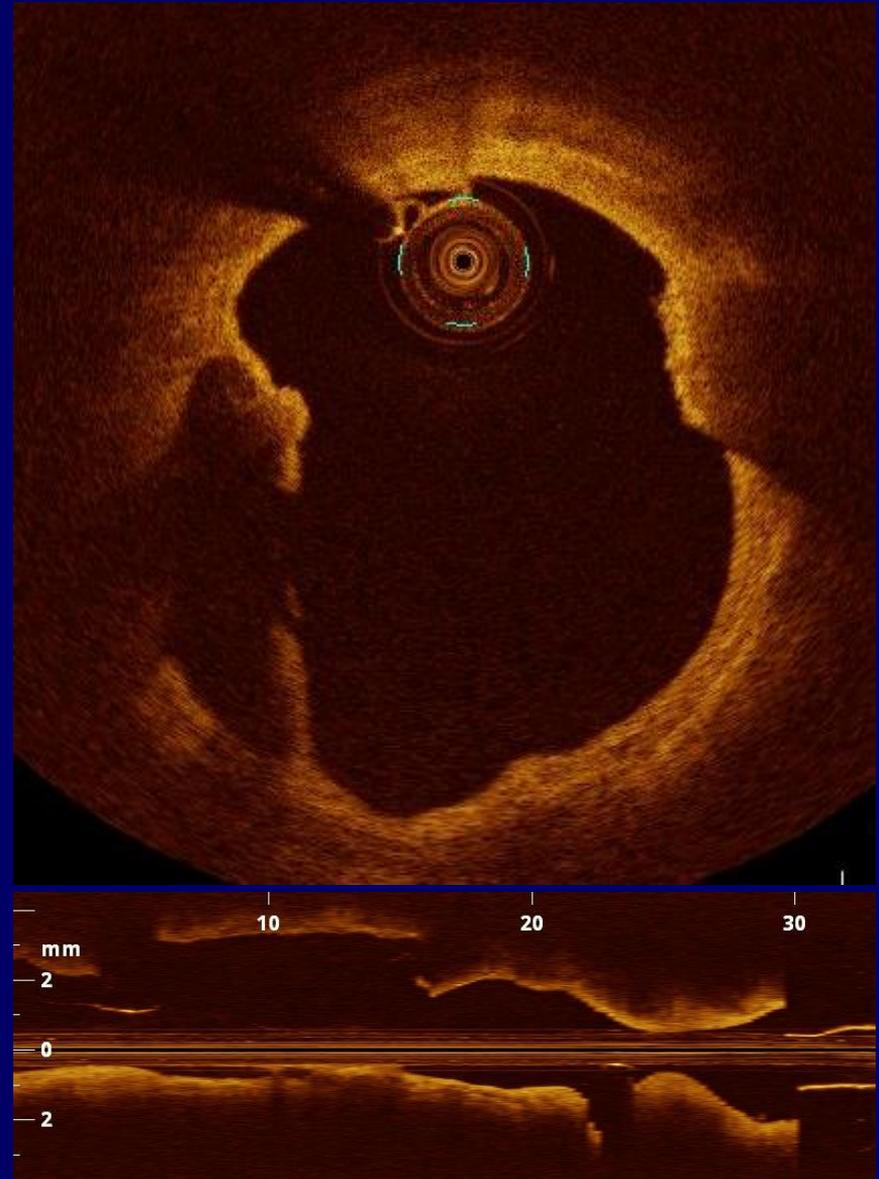
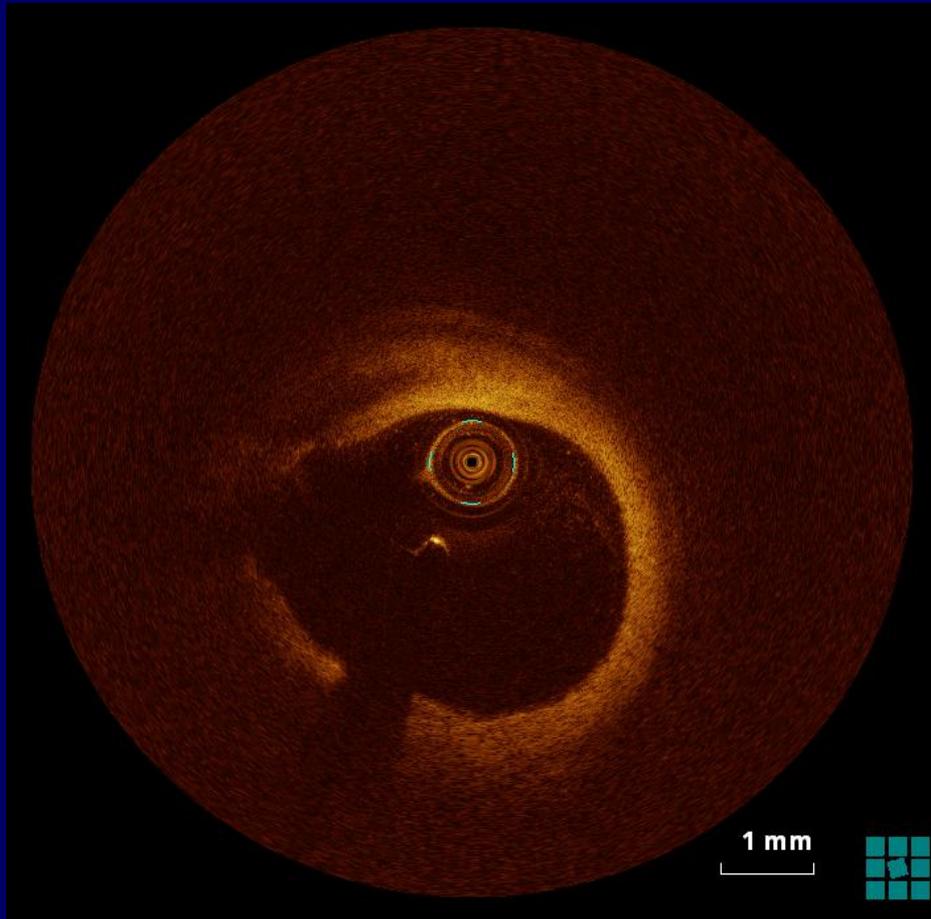


Coronary angiography



Optical coherence tomography

Right coronary artery



Thank you for your attention!

