EMERALD

(*E*xploring the *ME*chanism of plaque *R*upture in *A*cute coronary syndrome using coronary CT angiography and computationa*L* fluid *D*ynamics)

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SNUH *Seoul National University Hospital Cardiovascular Center*

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- **Martin Penicka, MD, Bernard de Bruyne, MD** (Cardiovascular Center Aalst)
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- **Jagat Narula, MD** (Icahn School of Medicine at Mount Sinai Hospital)
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- **Joon-Hyung Doh, MD** (Inje University Ilsan Paik Hospital)
- **Chang-Wook Nam, MD** (Keimyung University Dongsan Medical Center)
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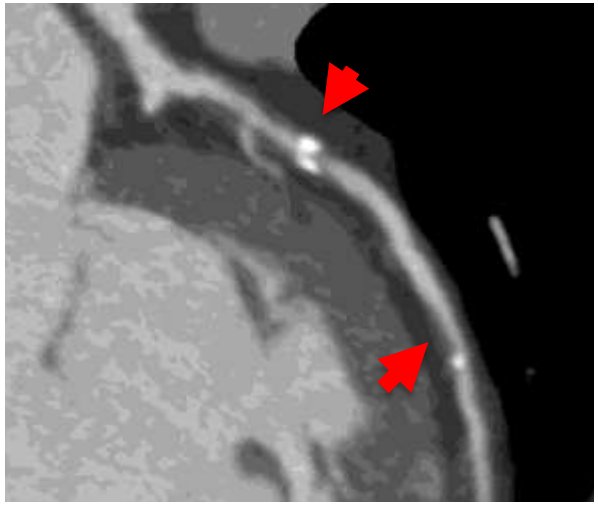
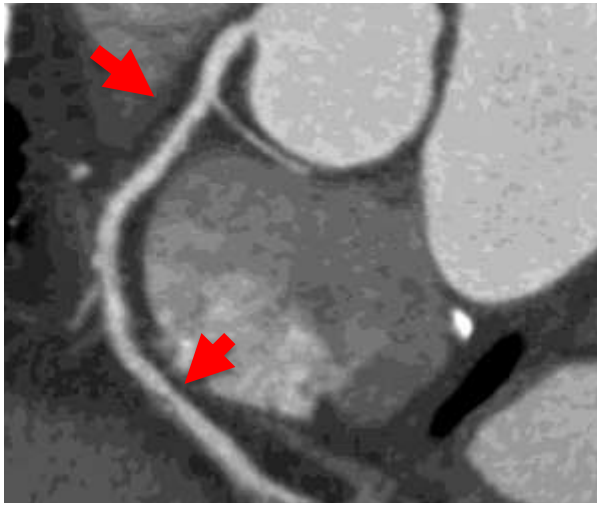
- **Gilwoo Choi, PhD, Hyun Jin Kim, PhD, Leo Grady, PhD, Charles A. Taylor, PhD** (HeartFlow)

How can we identify the culprit lesion for future ACS?

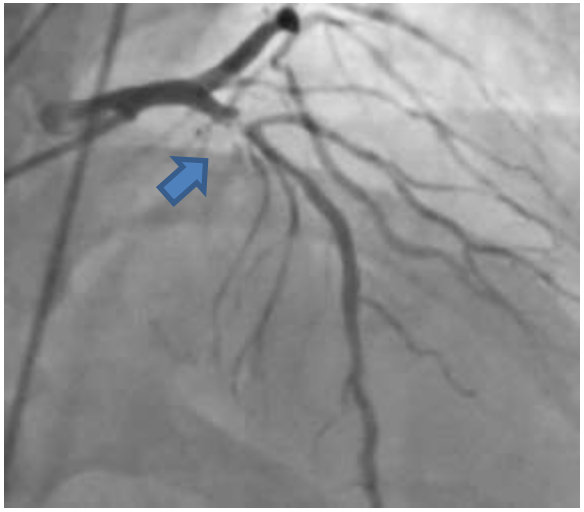
M/69, Asymptomatic

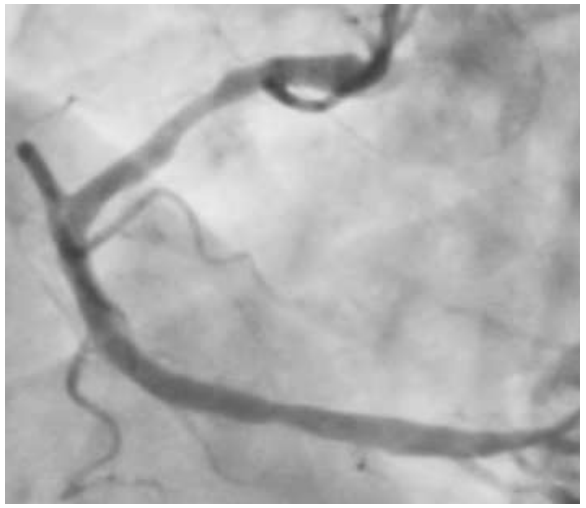




116 days later, the patient visited ER.

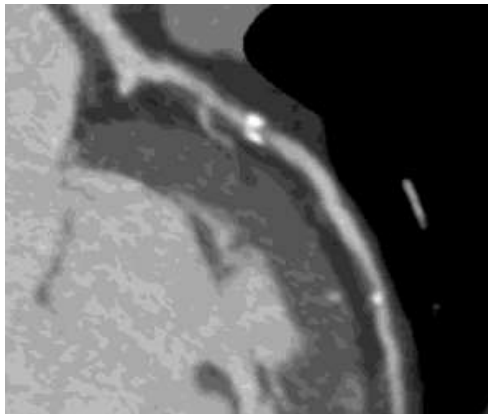
M/70, Non-ST elevation MI



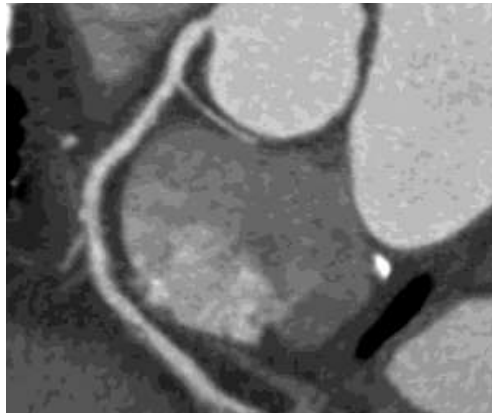


How can we identify the culprit lesion for future ACS?

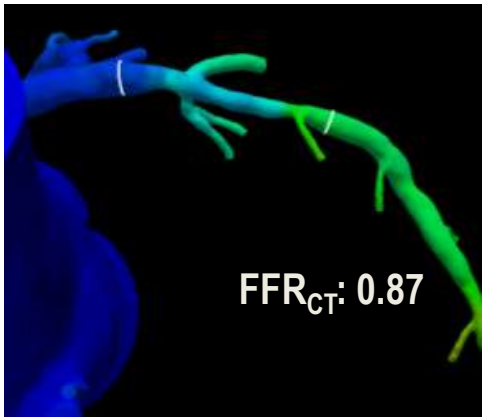
Current Paradigm



Stenosis severity
Adverse plaque characteristics



Non-invasive hemodynamic assessment

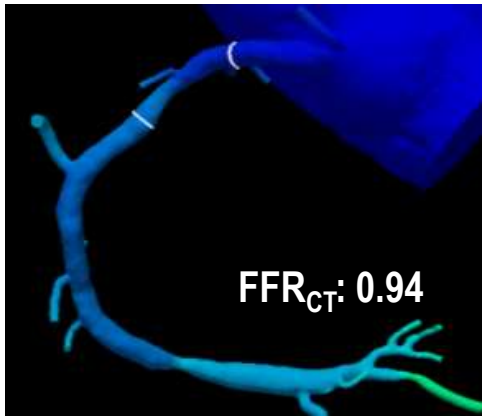


$$\triangle FFR_{CT} = \text{proximal } FFR_{CT} - \text{distal } FFR_{CT} = \frac{P_X}{P_{Aorta}} - \frac{P_Y}{P_{Aorta}} = \frac{\Delta P}{P_{Aorta}}$$

where X and Y represent the lesion start and ending points, respectively, and P represents pressure.

$$WSS_{lesion} = \frac{1}{A}\int_X^Y \left\|\overrightarrow{WSS}\right\| dA$$

where A represents the surface area of defined lesion from X and Y



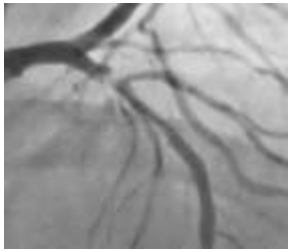
$$\left|\text{Axial Plaque Stress}_{lesion}\right| = \left|\frac{1}{A}\int_X^Y (\vec{t}\cdot\vec{c})\,dA\right|$$

where $\vec{t}\cdot\vec{c}$ represents the dot product of the traction vector ($\vec{t}$) and tangential vector of vessel centerline ($\vec{c}$).

De Bruyne B, et al. N Engl J Med 2014:371:1208-17
Samady H, et al. Circulation 2011;124:779
Park JB, et al. Heart 2016;102:1655-61
Choi G & Lee JM, et al. JACC Cardiovasc Imaging 2015;8:1156-66
Lee JM, et al. JACC Cardiovasc Imaging 2016

EMERALD study

Exploring the **ME**chanism of the Plaque **R**upture in **A**cute Coronary Syndrome using Coronary CT Angiography and Computational **L** Fluid **D**ynamics



Patients with Acute Coronary Syndrome
From 11 International Cardiovascular Centers
(Korea, Japan, Belgium, Denmark, the Netherlands)

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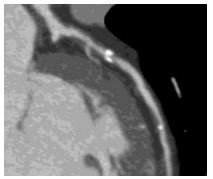
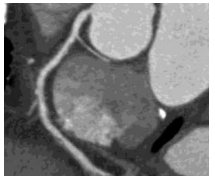
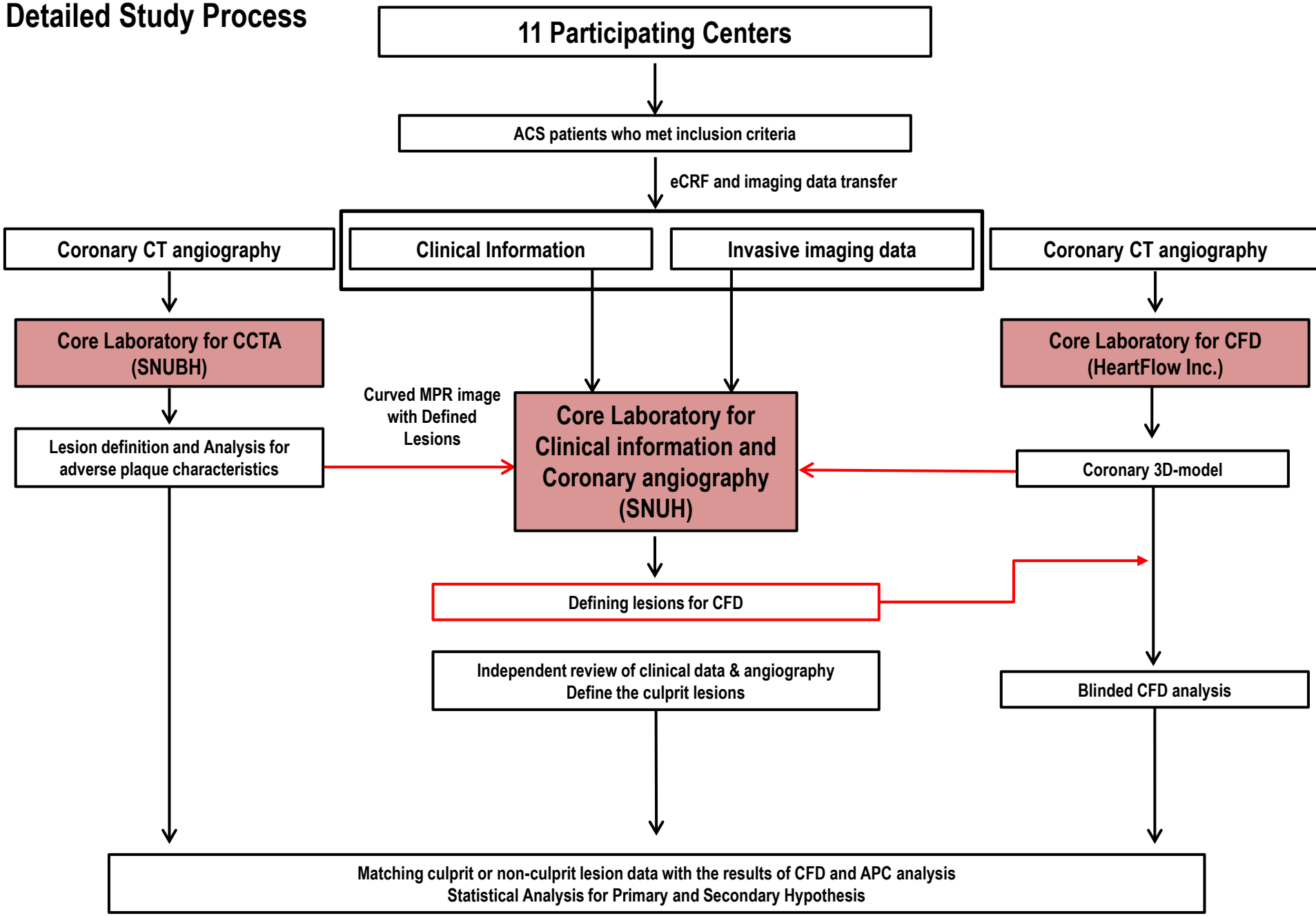
Patients who underwent Coronary CT angiography
before ACS event (1 month – 2 year before the event)
(N=120)



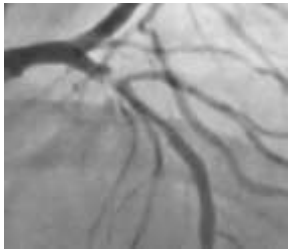


Detailed Study Process



EMERALD study

Exploring the **ME**chanism of the Plaque **R**upture in **A**cute Coronary Syndrome using Coronary CT Angiography and Computationa**L** Fluid **D**ynamics



Patients with Acute Coronary Syndrome
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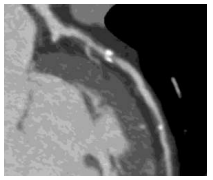
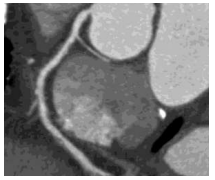




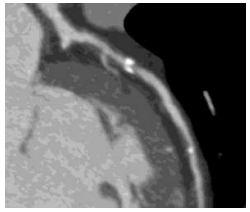
Patients who underwent Coronary CT angiography
before ACS event (1 month – 2 year before the event)
(N=120)

Validation with clinical data, cCTA and coronary angiography (3 independent core labs)

Exclusion (N=41)
- No adequate CT image: 27
- Unclear diagnosis or No definite culprit lesion on Angiography: 10
- No definite lesion on cCTA: 4

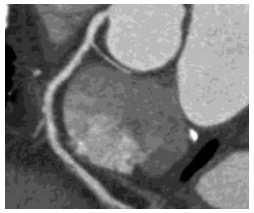
Exclusion by core laboratory due to CT image quality (N=7)

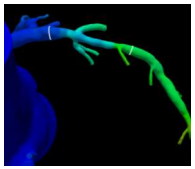
Final Enrollment for cCTA and CFD analysis
(72 patients, 216 lesions)



CASE
Culprit for subsequent ACS (N=66)

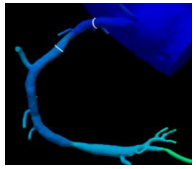
CONTROL
Non- Culprit Lesion (N=150)





cCTA analysis
adverse plaque characteristics
(Core Lab – SNU Bundang Hospital)

CFD analysis
Non-invasive hemodynamics
(Core Lab - HeartFlow Inc.)



Characteristics of the Patients and Lesions

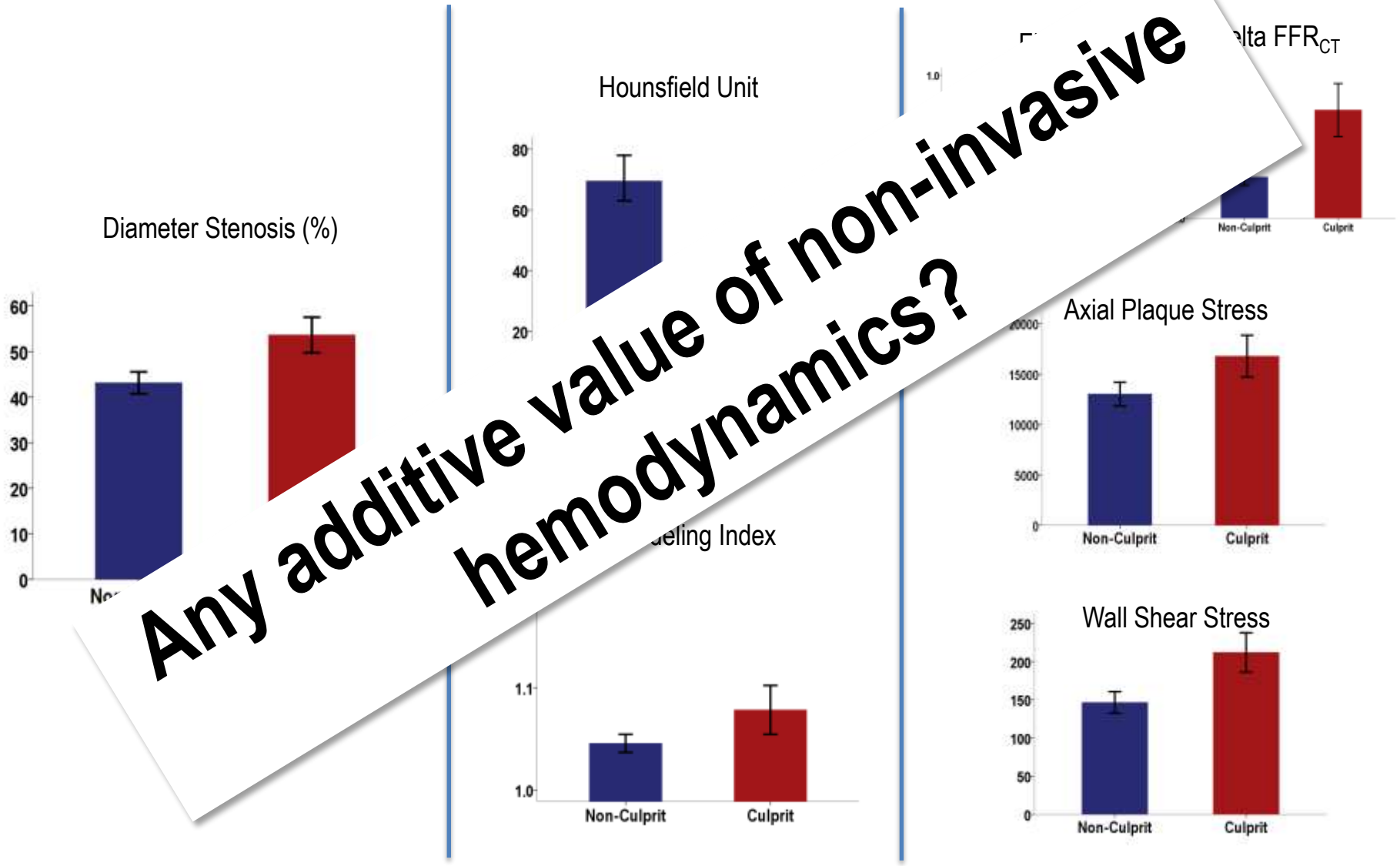
Patients (n = 72)	
Age, years	69·9 ± 12·7
Male	54 (75·0%)
Median interval between cCTA and ACS, days	338·0 (161·5-535·0)
Cardiovascular Risk Factors	
Hypertension	46 (63·9%)
Diabetes mellitus	37 (51·4%)
Hypercholesterolemia	35 (48·6%)
Clinical Presentation	
Myocardial infarction	67 (93·0%)
NSTEMI	41 (56·9%)
STEMI	26 (36·1%)
Unstable angina	5 (6·9%)

Lesion characteristics (n = 216)	
Lesion location	
Left main to LAD	87 (40·3%)
LCX / RCA	48 (22·2%) / 81 (37·5%)
Culprit vessel (n=66)	
Left main to LAD	39 (59·1%)
LCX / RCA	9 (13·6%) / 18 (27·3%)
Lesion profile	
Minimal lumen area, mm^2	2·75 ± 1·59
Diameter stenosis, %	46·9 ± 16·1
Distance from ostium to MLA, mm	47·1 ± 22·6
Lesion length, mm	17·6 ± 7·4
FFR_{CT}	0·77 ± 0·15

Culprit vs. Non-Culprit Lesions

	Non-culprit lesion (N=150)	Culprit lesion (N=66)	P value
Vessel location			0·001
LAD	48 (32·0%)	39 (59·1%)	
LCX	39 (26·0%)	9 (13·6%)	
RCA	63 (42·0%)	18 (27·3%)	
Anatomical severity			
Lesion length, mm	**16·9 ± 7·0**	**19·2 ± 8·1**	**0·038**
MLA, mm^2	**3·02 ± 1·58**	**2·11 ± 1·43**	**<0·001**
Diameter stenosis, %	**43·1 ± 15·0**	**55·5 ± 15·4**	**<0·001**
Distance from ostium, mm	47·8 ± 20·4	45·5 ± 27·2	0·489
Adverse Plaque Characteristics			
Low-plaque density	**43 (28·7%)**	**41 (62·1%)**	**<0·001**
Positive remodeling	**16 (10·7%)**	**23 (34·8%)**	**<0·001**
Napkin-ring sign	**13 (8·7%)**	**22 (33·3%)**	**<0·001**

EMERALD study: Culprit vs. Non-culprit

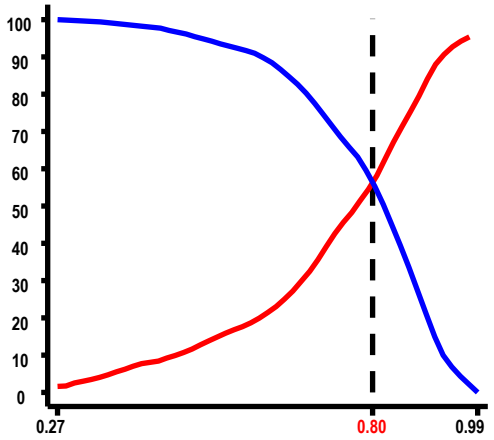


Any additive value of non-invasive hemodynamics?

All P values: significant

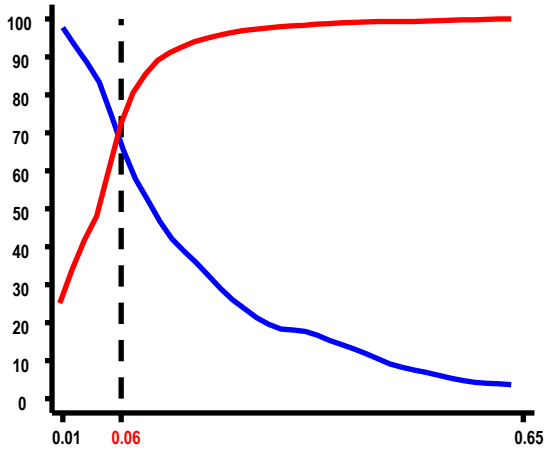
Cut-off Value for Adverse Hemodynamic Characteristics (AHC)

FFR_{CT}: 0.80



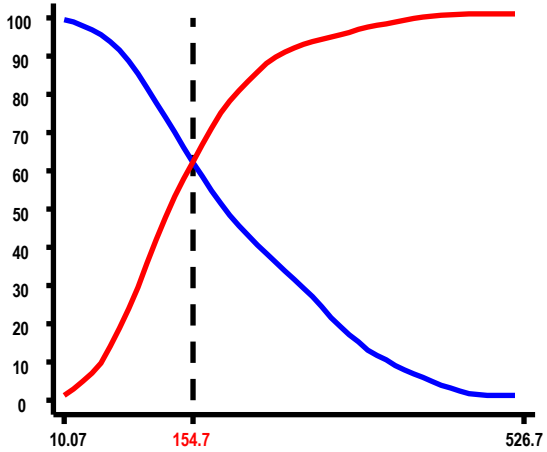
FFR_{CT}	
BCV	0.80
Sensitivity	54.6%
Specificity	58.0%
PPV	40.0%
NPV	71.3%
Accuracy	56.8%

△FFR_{CT}: 0.06



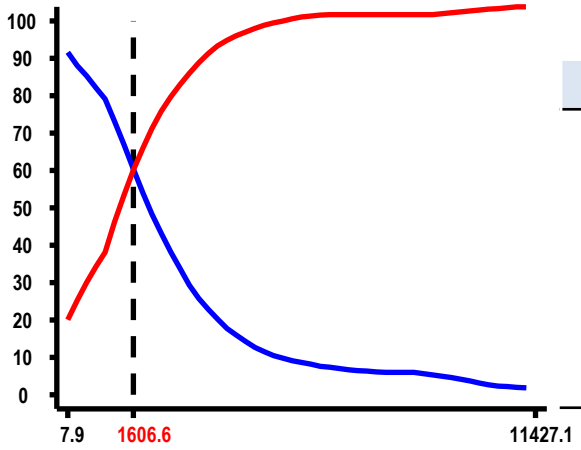
Delta FFR_{CT}	
BCV	0.06
Sensitivity	62.3%
Specificity	71.3%
PPV	52.8%
NPV	78.7%
Accuracy	68.2%

Wall Shear Stress (dyn/cm^2): 154.7



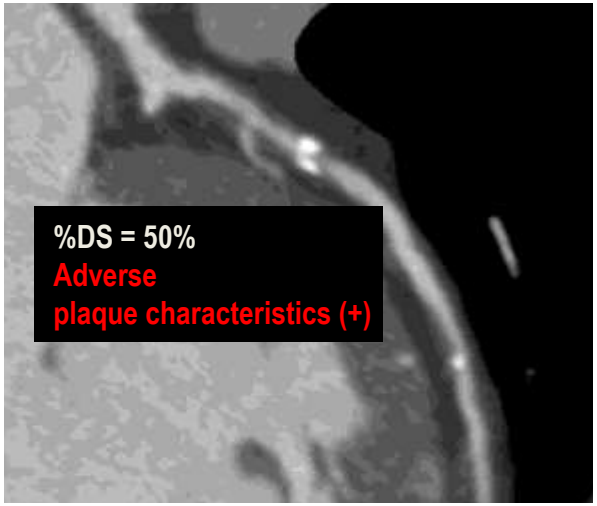
Wall Shear Stress	
BCV	154.7
Sensitivity	64.9%
Specificity	61.3%
PPV	46.3%
NPV	77.3%
Accuracy	62.6%

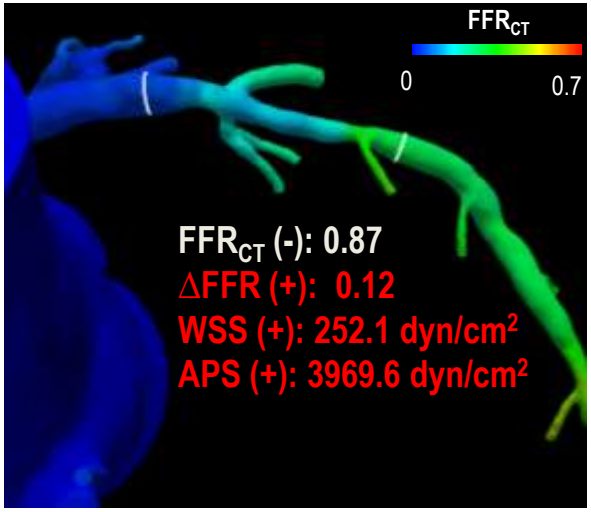
Axial Plaque Stress (dyn/cm^2): 1606.6

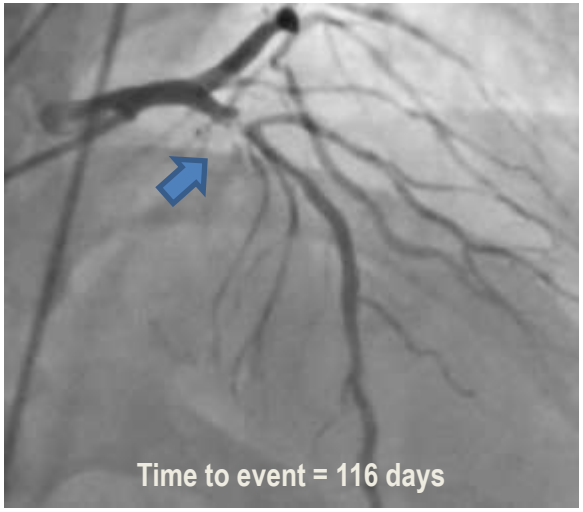


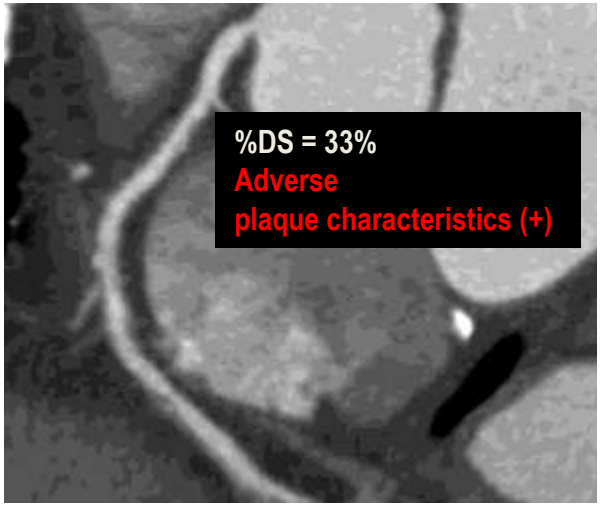
Raw APS	
BCV	1606.6
Sensitivity	59.7%
Specificity	62.0%
PPV	41.2%
NPV	77.5%
Accuracy	61.3%

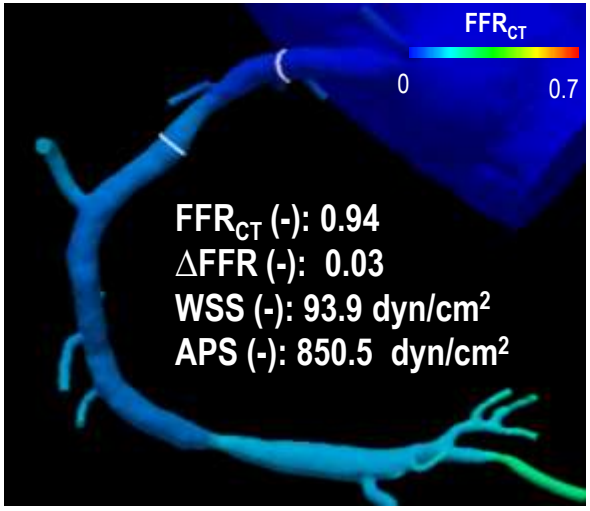
How can we identify the culprit lesion for future ACS?

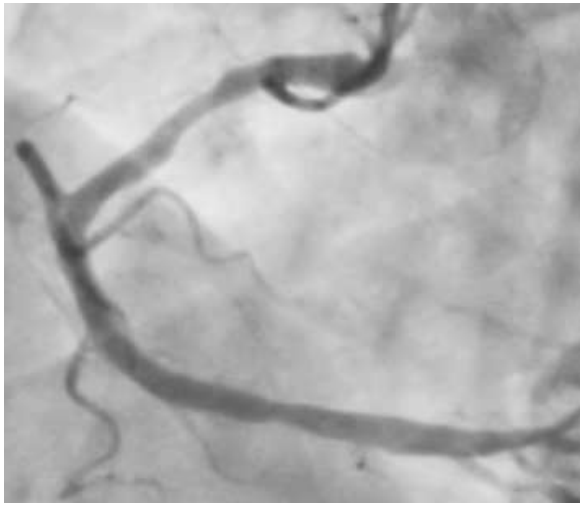






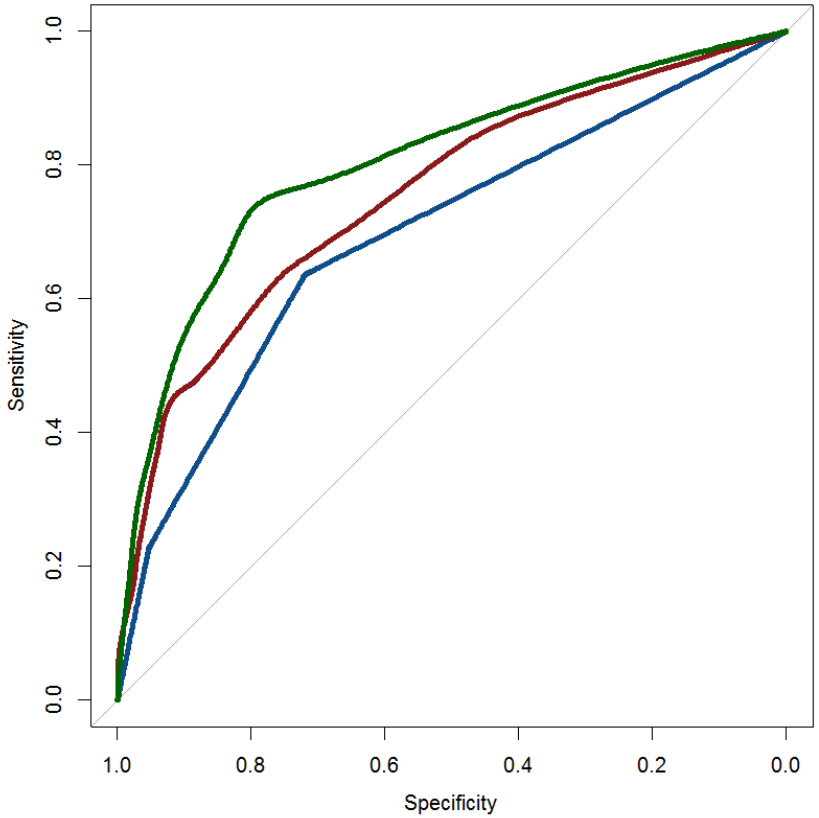






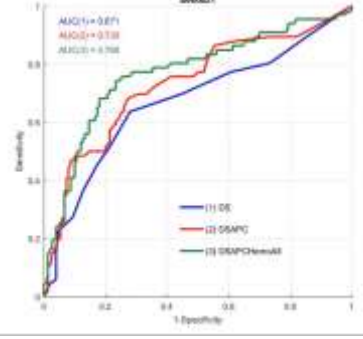
Prediction of ACS risk

Model 1: % diameter stenosis (%DS)
Model 2: %DS + adverse plaque characteristics (APC)
Model 3: %DS + APC + adverse hemodynamic characteristics (AHC)



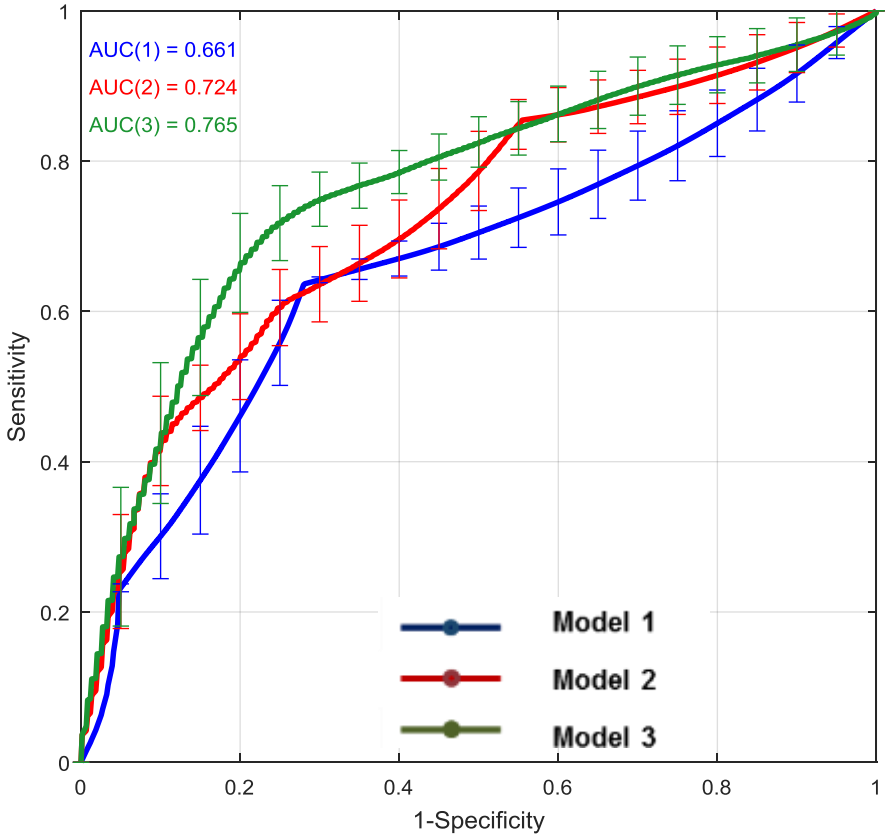
Prediction Model	C-index	Difference with Prev. Model	P value	NRI	P value	IDI	P value
Model 1	0.682						
Model 2	0.756	0.074	0.006	0.310	0.017	0.545	0.004
Model 3	0.788	0.032	0.014	0.235	0.003	0.497	<0.001

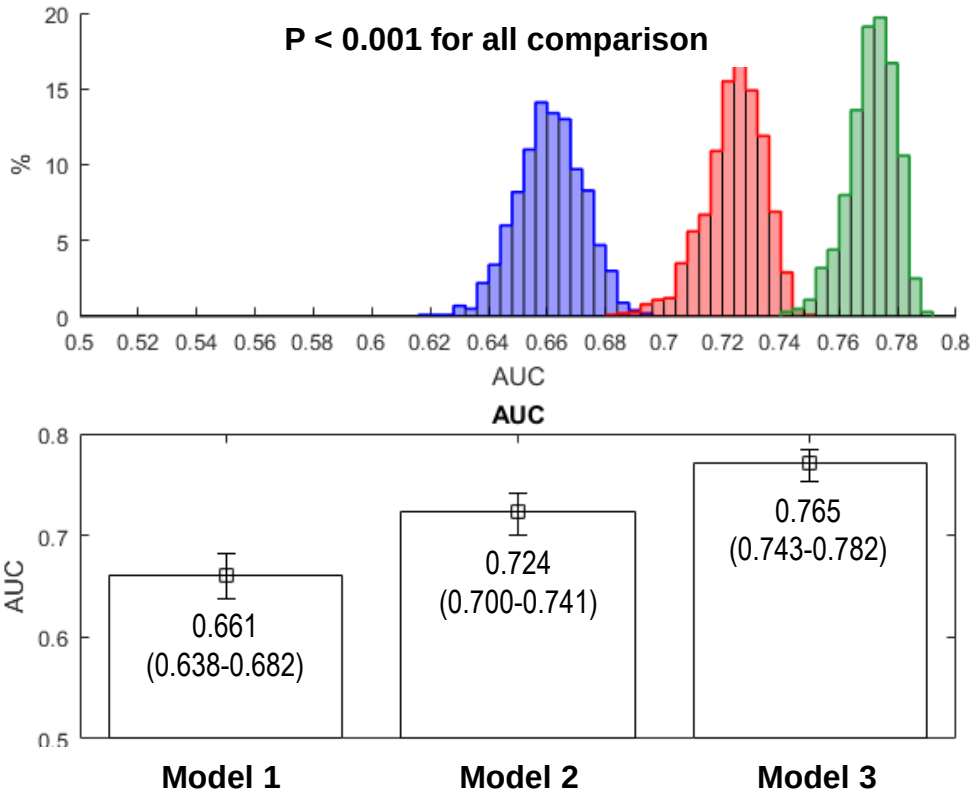
SNUH



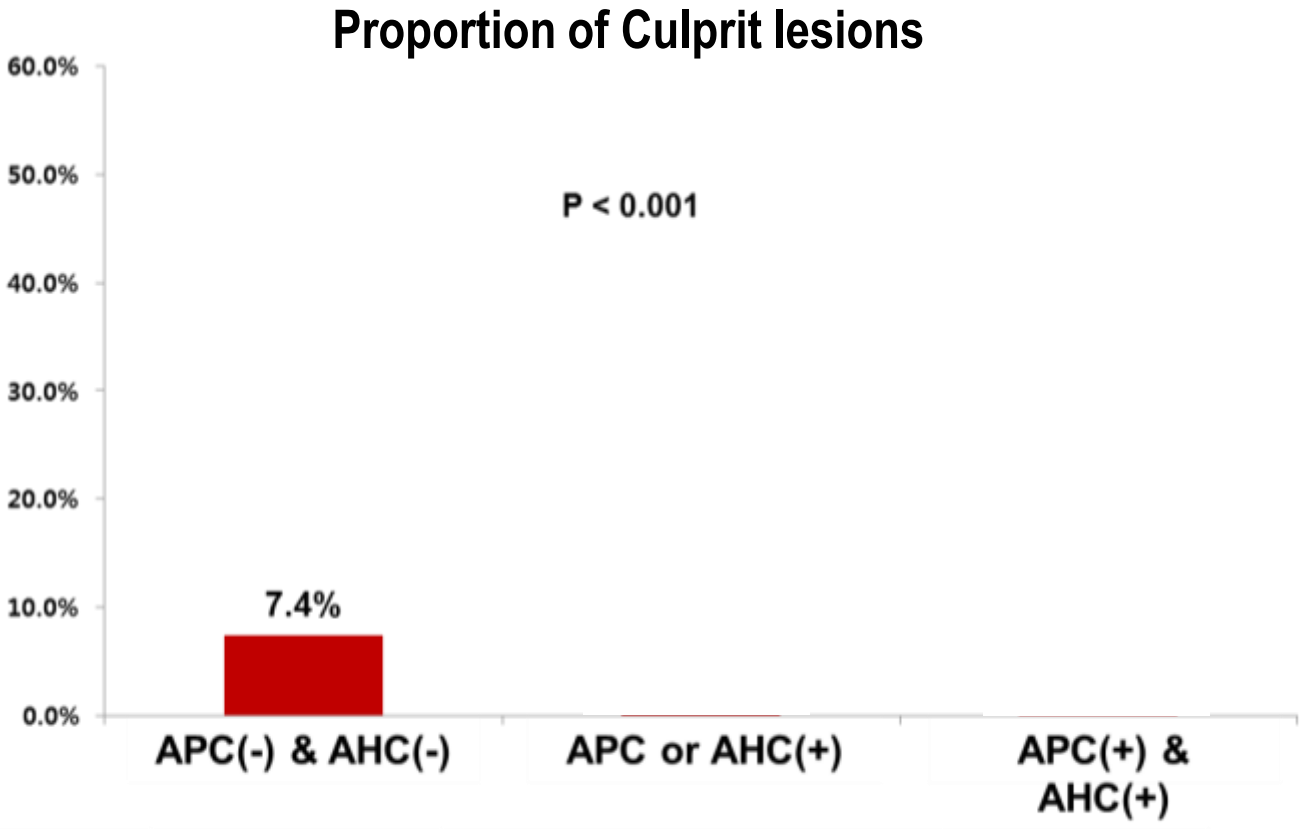
Prediction of ACS risk

5-fold cross-validation (1000 random permutations)



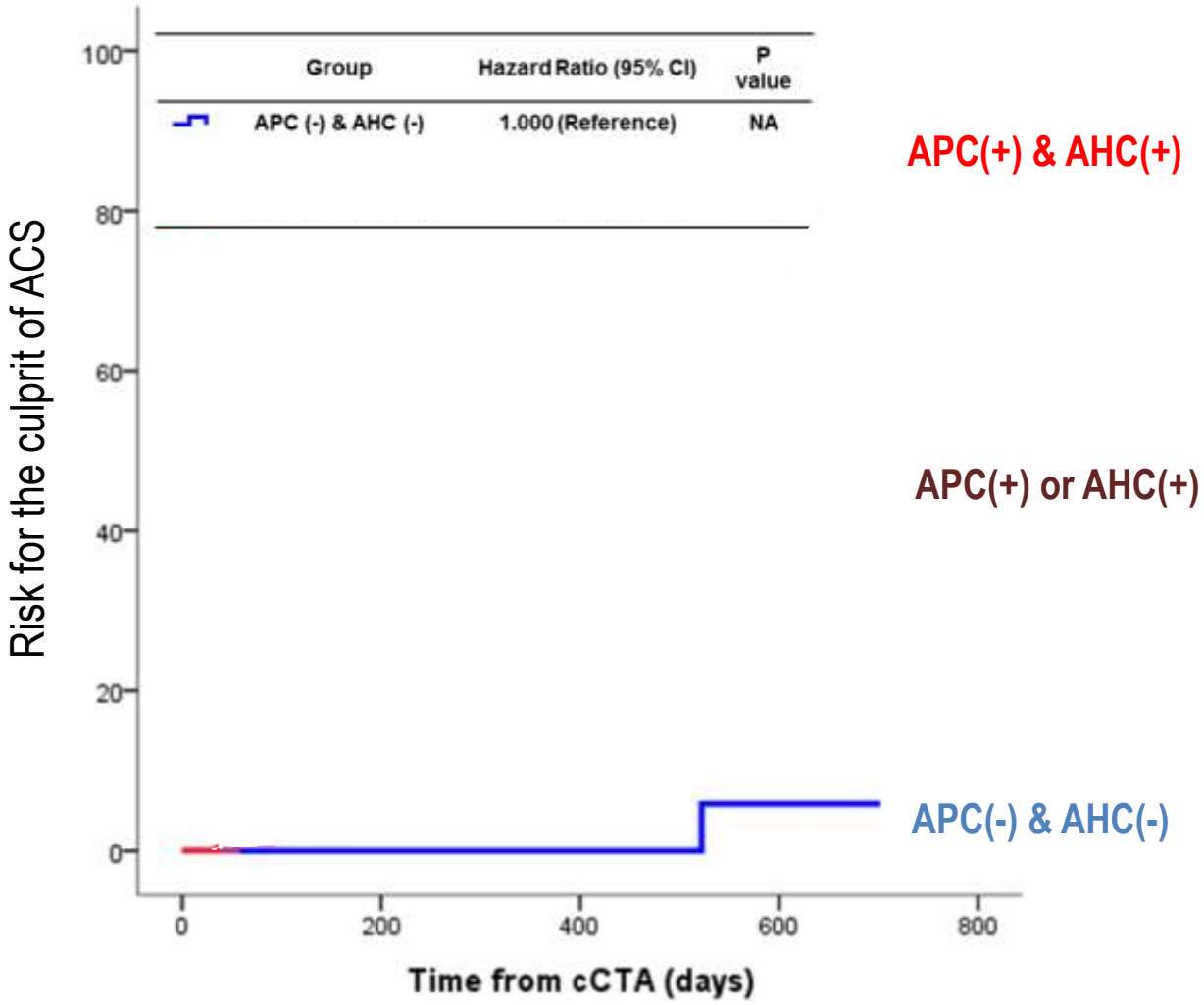


Plaque characteristics (APC), Hemodynamic characteristics (AHC) and Risk for the culprit of future ACS



Lesion No	27	99	90
Culprit No	2	18	46

Plaque characteristics (APC), Hemodynamic characteristics (AHC) and Risk for the culprit of future ACS



Summary

ACS was ascertained in all patients whose coronary lesions had been previously identified at CT angiography. This allowed us to investigate the characteristics of lesions that would eventually be responsible for an acute event.

- Culprit lesions had a more severe degree of stenosis, higher incidence of APC and worse hemodynamic parameters than non-culprit lesions.
- Comprehensive assessment of hemodynamic characteristics improved the ability for the identification of the culprit for subsequent ACS.
- Lesions with both APC and AHC showed significantly higher risk for the culprit of subsequent ACS than the other lesions.

Conclusion

- Non-invasive hemodynamic assessment enhanced the identification of high risk plaques that subsequently caused ACS.

- Integration of non-invasive hemodynamic assessment would improve the prediction of ACS risk and may help guide optimal treatment for high risk patients.