AI-Enabled Vulnerable Plaque Characterization

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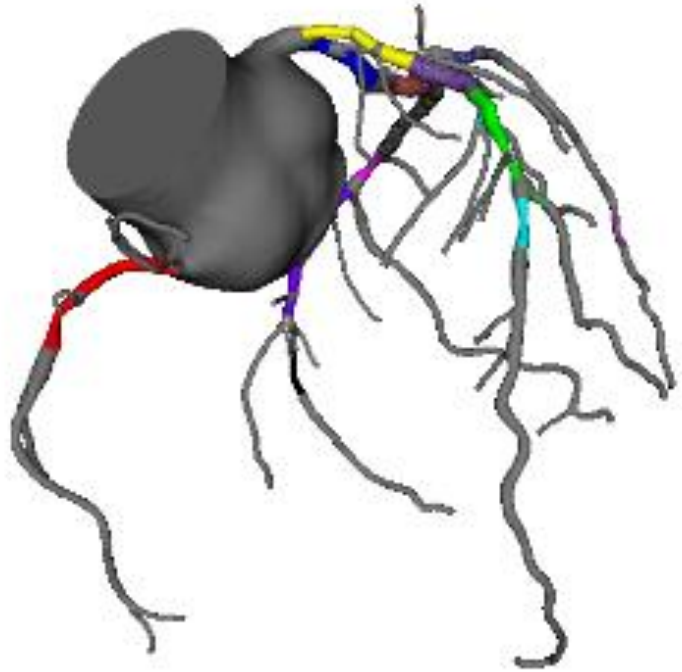
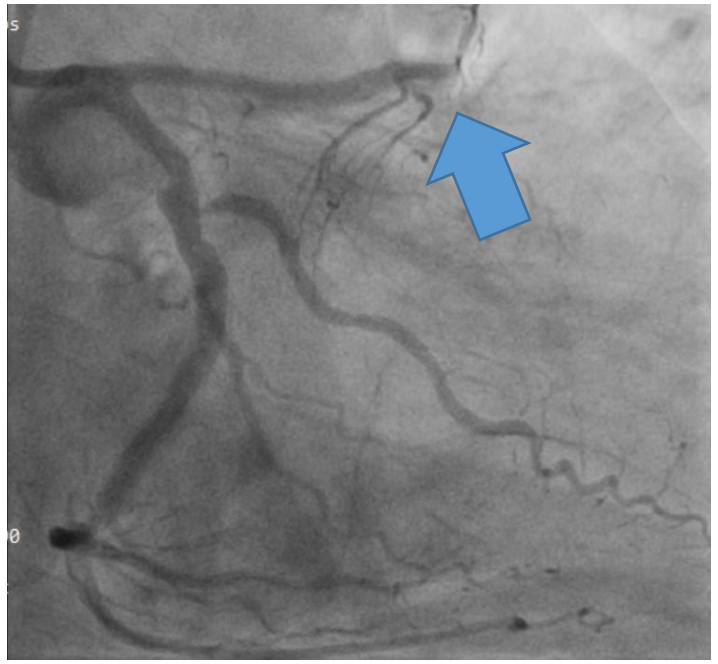
ACS prevention is Necessary, but Difficult!

- Three-fourths of myocardial infarction and two-thirds of sudden death present as new coronary artery events. Accordingly, upfront risk evaluation is required.

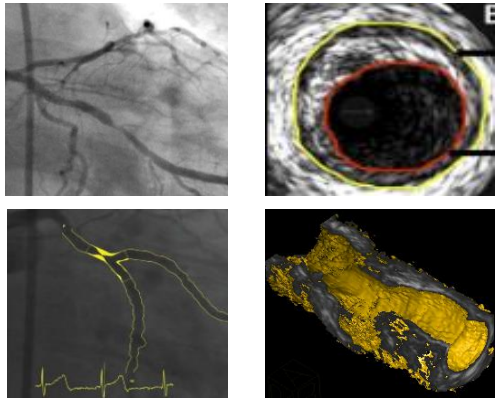




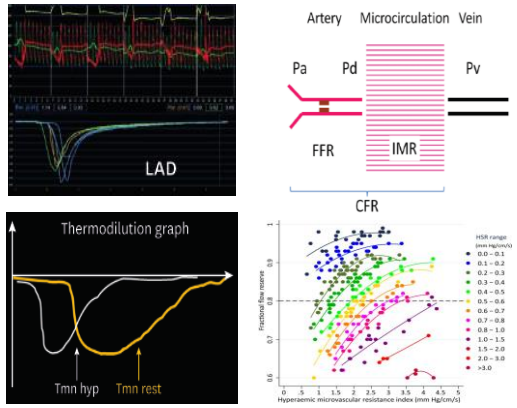
How can we define the future culprit for ACS among these 15 lesions?

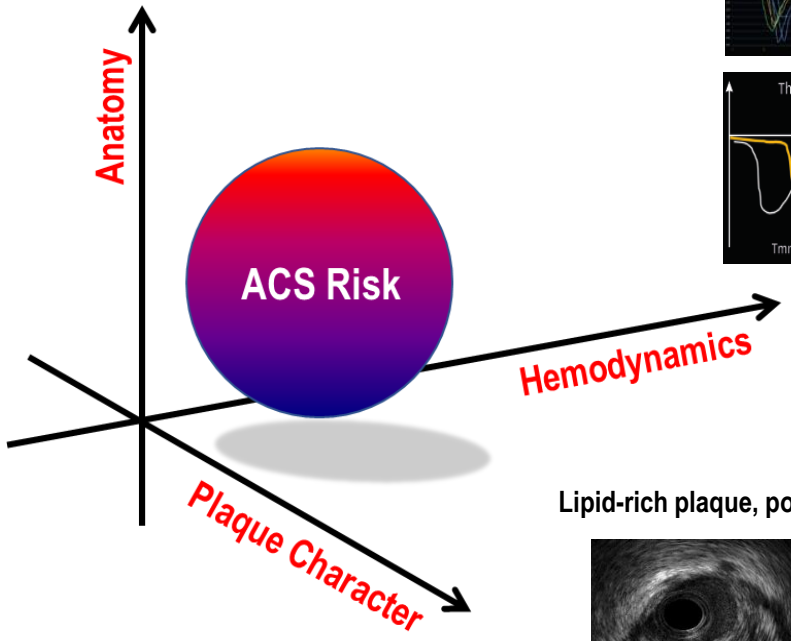
ACS risk assessment, Which one?

% Diameter stenosis, MLA, plaque burden…

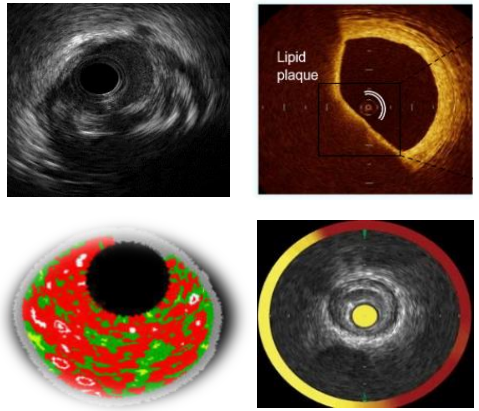


FFR, CFR, IMR, NHPR…





Lipid-rich plaque, positive remodeling, TFCA...



Choi G & Lee JM, et al. JACC Cardiovasc Imaging 2015;8:1156-66
Lee JM, et al. JACC Cardiovasc Imaging 2016
Lee JM, et al. Korean Circ J. 2018 Mar;48:179-190
Kaul S, Narula J, et al. J Am Coll Cardiol. 2014 Dec 16;64:2519-24

Vulnerability Assessment using CCTA

High-Risk Attributes

Hemodynamics
Flow disturbance
Ischemia

+

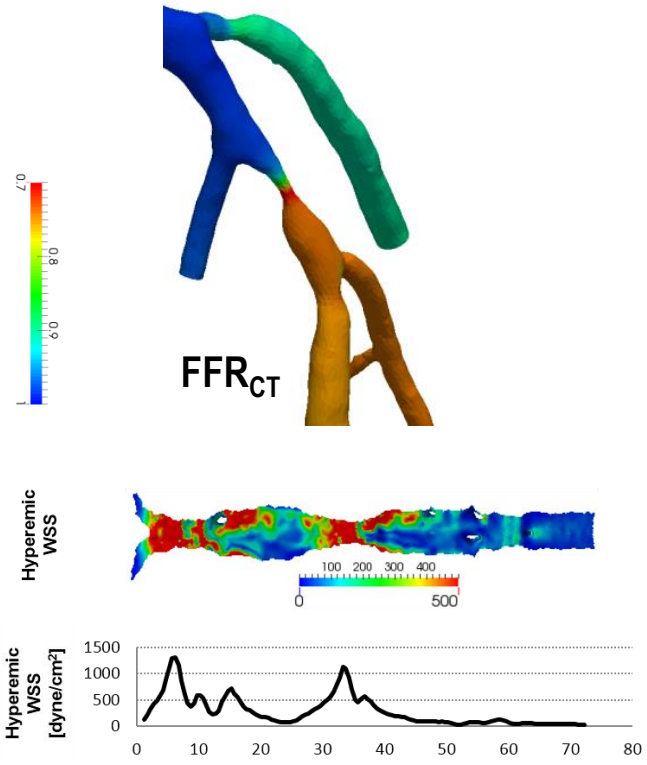
Global
Disease Burden

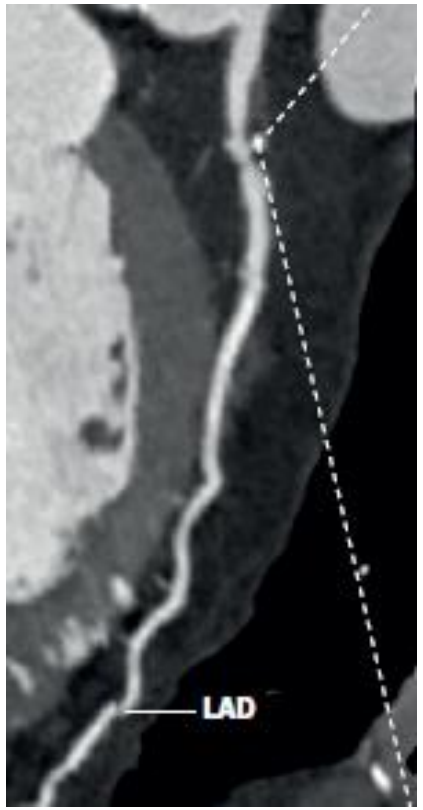
+

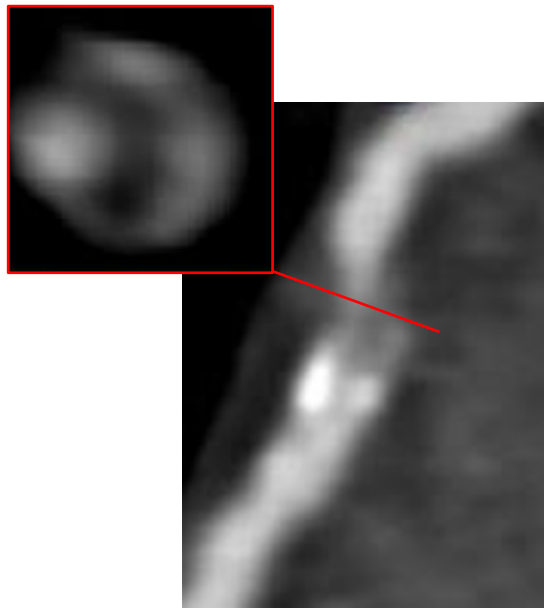
Plaque Characteristics

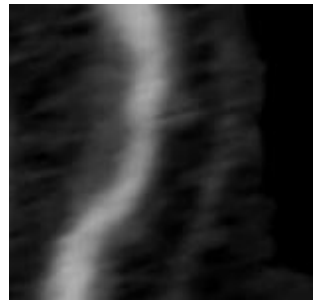
+

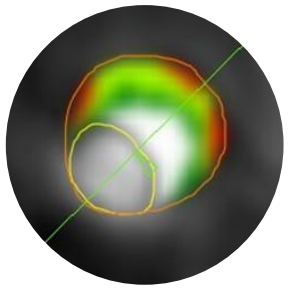
Local
Disease Burden







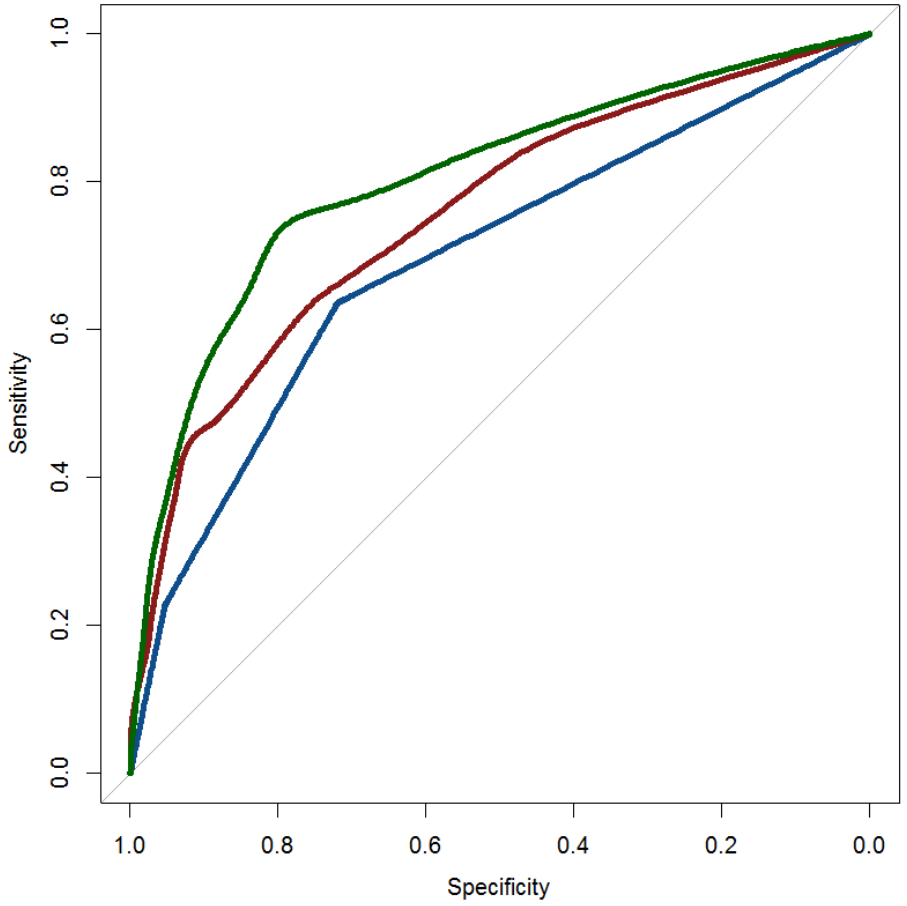




Prediction of acute coronary syndrome using CCTA

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



Model 1: % diameter stenosis (%DS)+Lesion length(LL)
Model 2: %DS/LL + adverse plaque characteristics (APC)
Model 3: %DS/LL + APC + Adverse Hemodynamic Characteristics (AHC)

Prediction Model	C-index	Difference with Prev. Model	P value	NRI	P value	IDI	P value
Model 1	0.709						
Model 2	0.747	0.038	0.006	0.355	0.001	0.671	<0.001
Model 3	0.789	0.025	0.014	0.287	0.047	0.368	<0.001

Lee JM & Choi GW, Koo BK..... JACC imaging 2019

The EMERALD II Trial

Artificial Intelligence-Enabled Quantitative Plaque and Hemodynamic Analysis (AI-QCPHA) for Predicting ACS Risk and Prevention Strategy

Objectives

The current study aims to

1. Identify the coronary CT angiography (CCTA) features that can define the high risk lesion for future ACS using **AI-based quantitative analysis (AI-QCPHA)**
2. Investigate the additive value of AI-QCPHA to the conventional CCTA assessment
3. Explore the potential implication of AI-QCPHA for selecting ACS prevention strategies

Study Population

- **The EMERALD II (Exploring the Mechanism of Plaque Rupture in Acute Coronary Syndrome using Coronary CT Angiography and Computational Fluid Dynamics II) study** (NCT03591328)
  - From 9 countries (United States, Canada, Denmark, Italy, Hungary, Belgium, Australia, Japan, and South Korea).
  - ACS patients who underwent CCTA 1 month to 3 years prior to the ACS event
- **Exclusion criteria**
  - No clear evidence of culprit lesion
  - Previous stent implantation in two or more coronary arteries prior to CCTA
  - Revascularization between CCTA and the ACS event
  - ACS culprit lesion in a previously stented segment, secondary ACS, or history of coronary artery bypass graft surgery
  - Poor quality CCTA not suitable for quantitative plaque and hemodynamic analysis

Primary Hypothesis and Sample Size Calculation

- **Working hypothesis**
  - AI-enabled quantitative plaque and hemodynamic analysis could enhance the discrimination ability for identification of ACS culprit lesions.
- **Sample size calculation**

Derivation cohort:

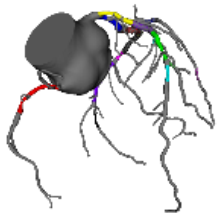
- EMERALD I study - Addition of $\triangle FFR_{CT}$, WSS, and % NCPV to conventional CCTA analysis (% diameter stenosis and APC) improved predictability for culprit lesions: area under the curve 0.76 → 0.80
- 241 patients for the increment in the discrimination index of the new prediction model with 80% of power at a type I error rate of 5%.

Validation cohort:

- Required sample size with the assumption of ICC of 0.01 was at least 102 patients to secure a certain level of precision.

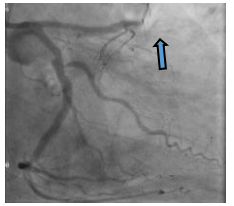
Total population: 429 patients needed to be enrolled considering a potential drop-out rate of 20%.

Study Flow



449 ACS patients who underwent coronary CT angiography (CCTA) from 1 month to 3 years prior to the event

47 Poor CCTA quality
51 no identifiable culprit lesions



351 ACS patients with definite culprit lesions

CCTA

Invasive coronary angiography

Core Laboratory for AI-enabled CCTA analysis (HeartFlow Inc., USA)

Core Laboratory for the standard CCTA analysis (University of British Columbia, Canada)

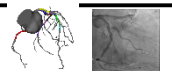
Core Laboratory for Invasive Coronary Angiography (Samsung Medical Center)

Artificial Intelligence-Enabled Quantified Coronary Plaque and Hemodynamic Analysis (AI-QCPHA) (Blinded to ICA findings)

CAD-RADS, Adverse plaque characteristics (Blinded to ICA findings)

Defining Culprit lesion (Blinded to CCTA findings)

Matching culprit and non-culprit lesion data between ICA and CCTA findings



Culprit lesions were defined as cases, and non-culprit lesions as internal controls.

Derivation Cohort (243 Patients: 248 culprit vs. 1247 non-culprit)

Validation Cohort (108 patients: 115 culprit vs. 841 non-culprit)

Defining the best AI-QCPHA features

New Prediction Model
(Reference model + AI-QCPHA features)

Reference Model
(CAD-RADS and APC ≥2)

Compare the model performance between the new prediction model and the reference model

Koo BK, Yang SH, et al. JACC imaging 2024

Standard CCTA analysis vs. AI-QCPHA

Standard CCTA analysis

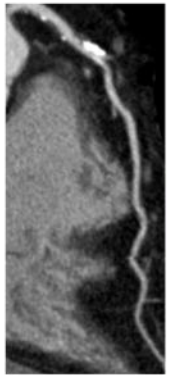
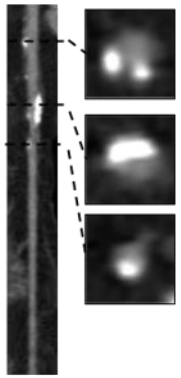


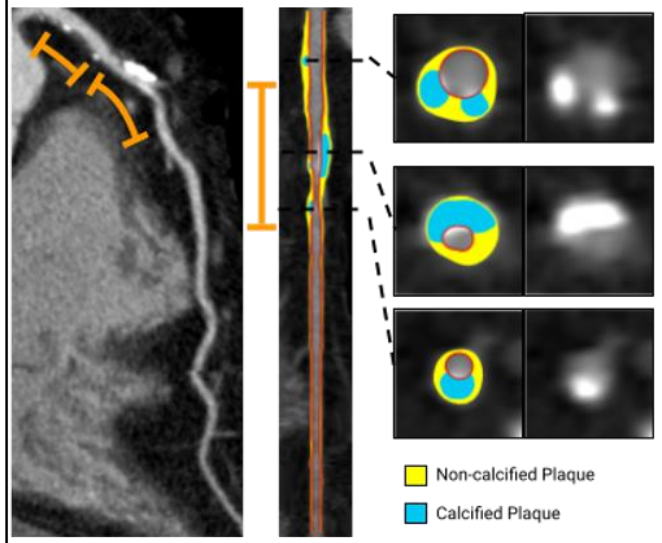
TABLE 4 CAD-RADS Reporting and Data System

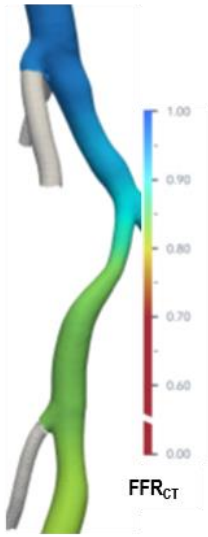
Category	Degree of Maximal Coronary Stenosis
CAD-RADS 0	0% (No plaque or stenosis)
CAD-RADS 1	1–24% (Minimal stenosis or plaque with no stenosis[b])
CAD-RADS 2	25–49% (Mild stenosis)
CAD-RADS 3	50–69% (Moderate stenosis)
CAD-RADS 4	**A** - 70–99% stenosis or **B** - Left main ≥50% or 3-vessel obstructive (≥70%) disease
CAD-RADS 5	100% (total occlusion)

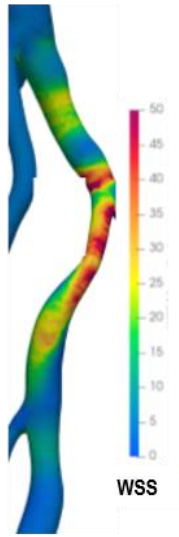


CAD-RADS + HRP Feature	Value
CAD-RADS Score	1
Positive Remodeling	0
Spotty Calcification	0
Napkin Ring Sign	0
Low Attenuation Plaque	0

Artificial Intelligence-enabled Quantitative Coronary Plaque and Hemodynamic Analysis (AI-QCPHA)







Features from AI-QCPHA

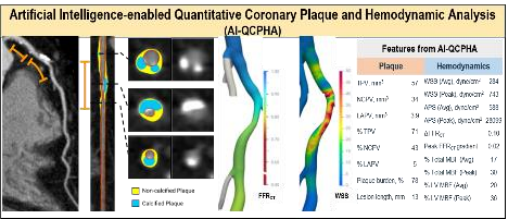
Plaque		Hemodynamics	
TPV, mm^3	57	WSS (Avg), dyne/cm^2	284
NCPV, mm^3	34	WSS (Peak), dyne/cm^2	743
LAPV, mm^3	3.9	APS (Avg), dyne/cm^2	588
% TPV	71	APS (Peak), dyne/cm^2	28099
% NCPV	43	ΔFFR_{CT}	0.10
% LAPV	5	Peak FFR$_{CT}$ gradient	0.02
Plaque burden, %	78	% Total MBF (Avg)	17
Lesion length, mm	13	% Total MBF (Peak)	30
		% LV MBF (Avg)	20
		% LV MBF (Peak)	36

Baseline Patient Characteristics

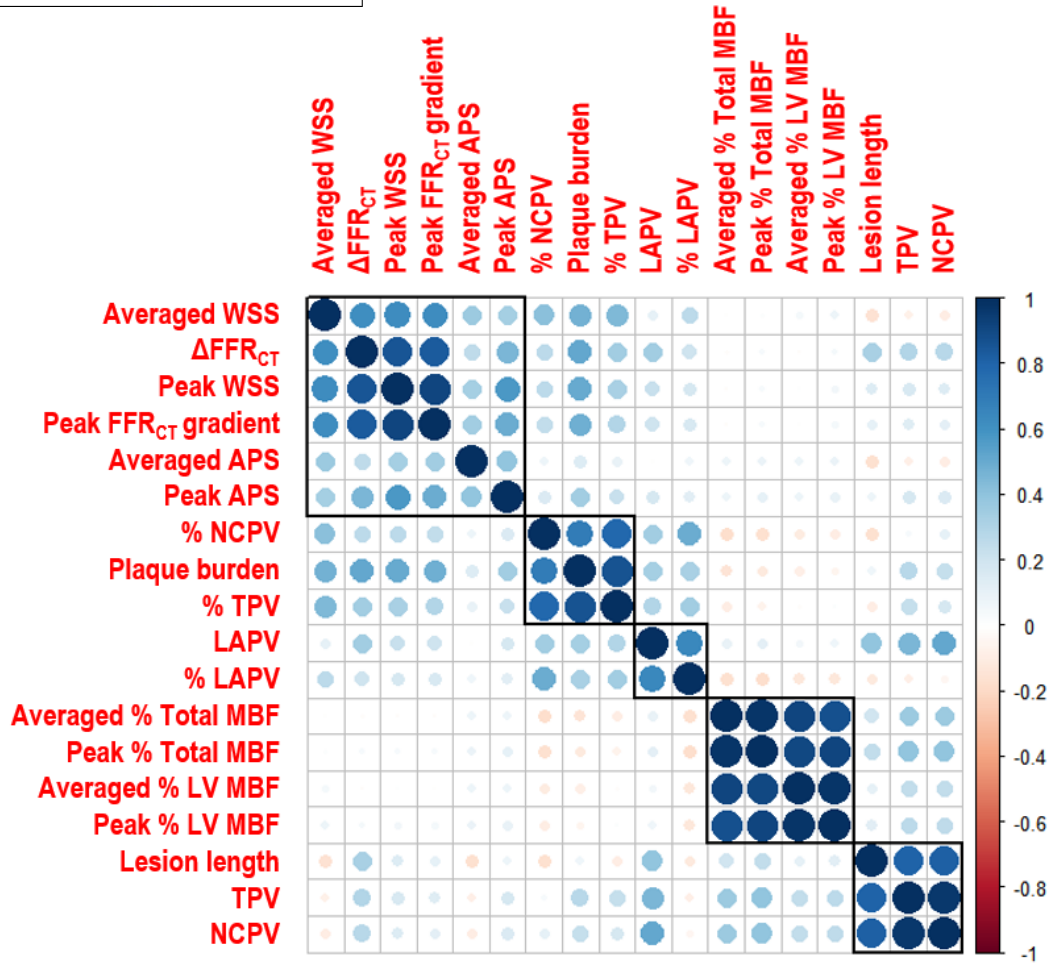
	Total patients (n=351)
Age	65.9±11.7
Male	261 (74.4)
Diagnosis	
Myocardial infarction	223 (63.5)
NSTEMI	128 (36.5)
STEMI	95 (27.1)
Unstable angina	128 (36.5)
Diabetes	116 (33.0)
Hypertension	258 (73.5)
Hyperlipidemia	218 (62.1)
Current smoker	84 (23.9)
Time from CCTA to ACS event (days)	375.0 [95.0; 644.5]
Medications at the time of CCTA	
Aspirin or P2Y12 inhibitor	155 (44.3)
ACEi/ARB	127 (36.3)
Beta-blocker	82 (23.4)
Calcium channel blocker	89 (25.4)
Statin	134 (38.3)

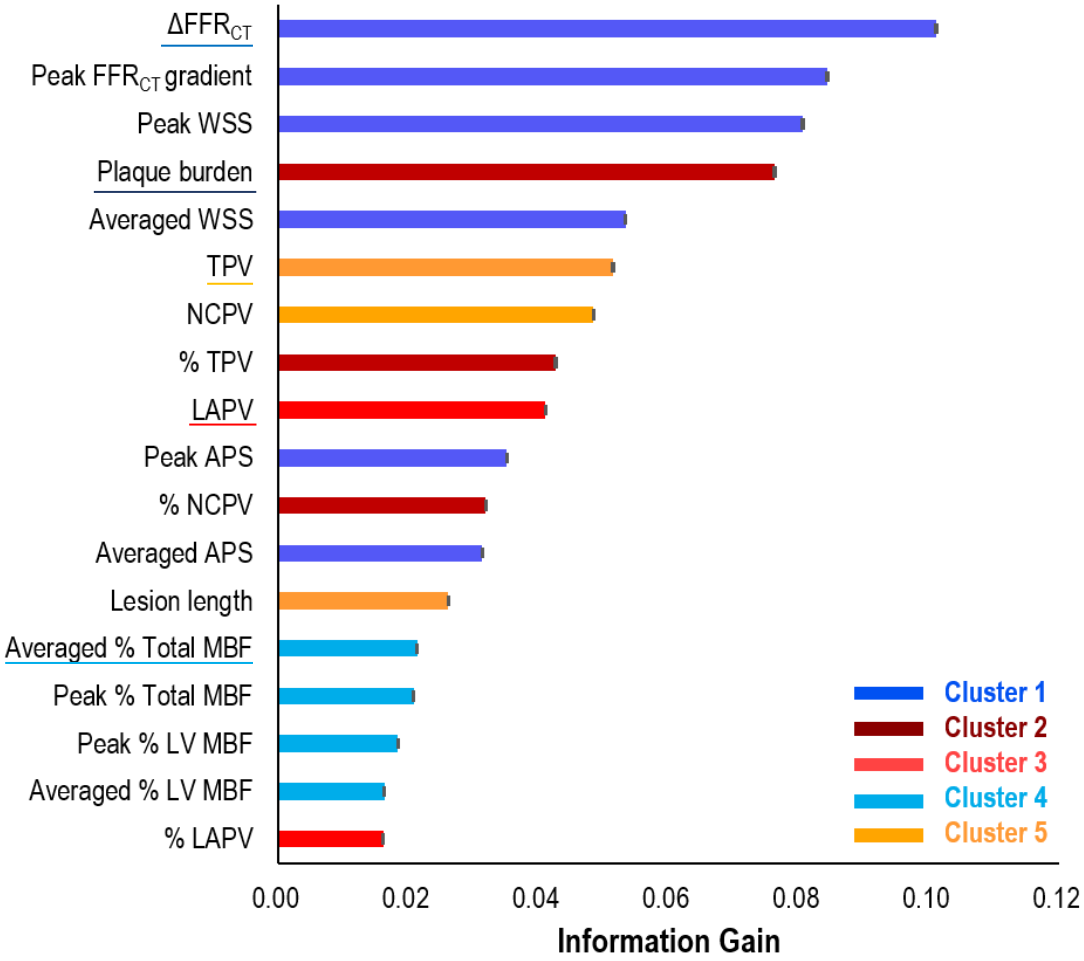
AI-QCPHA: Culprit vs. Non-culprit in CCTA before ACS

	Derivation cohort		
	Non-culprit lesion (n=1,247)	**Culprit lesion** (n=248)	**P-value**
Quantitative plaque analysis			
Plaque burden, %	73.1±15.0	85.2±10.2	<0.001
Total Plaque Volume (TPV), mm^3	79.9±72.3	132.8±96.9	<0.001
Non-calcified plaque volume (NCPV), mm^3	70.1±60.1	114.9±82.4	<0.001
Low attenuation plaque volume (LAPV), mm^3	2.2±2.9	4.5±5.1	<0.001
% TPV	60.1±14.5	69.3±10.8	<0.001
% NCPV	54.2±13.1	61.5±12.0	<0.001
% LAPV	2.0±2.3	2.8±3.0	<0.001
Quantitative hemodynamic analysis			
ΔFFR_{CT}	0.05±0.08	0.16±0.14	<0.001
Peak FFR_{CT} gradient	0.02±0.05	0.08±0.09	<0.001
Averaged WSS, $dyne/cm^2$	151.2±103.0	229.8±133.7	<0.001
Peak WSS, $dyne/cm^2$	598.2±861.4	1550.1±1509.6	<0.001
Averaged axial plaque stress (APS), $dyne/cm^2$	1084.1±1970.8	1671.6±1845.1	<0.001
Peak APS, $dyne/cm^2$	30572.7±15631.5	39968.8±17575.6	<0.001
Averaged % total myocardial blood flow (MBF)	22.6±12.2	25.0±9.6	0.001
Peak % total MBP	23.6±13.1	27.2±11.7	<0.001
Averaged % left ventricular MBF	23.8±13.7	26.9±11.4	<0.001
Peak % left ventricular MBF	24.7±14.8	29.3±14.3	<0.001



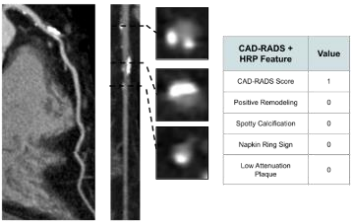
Selection of best AI-QCPHA features





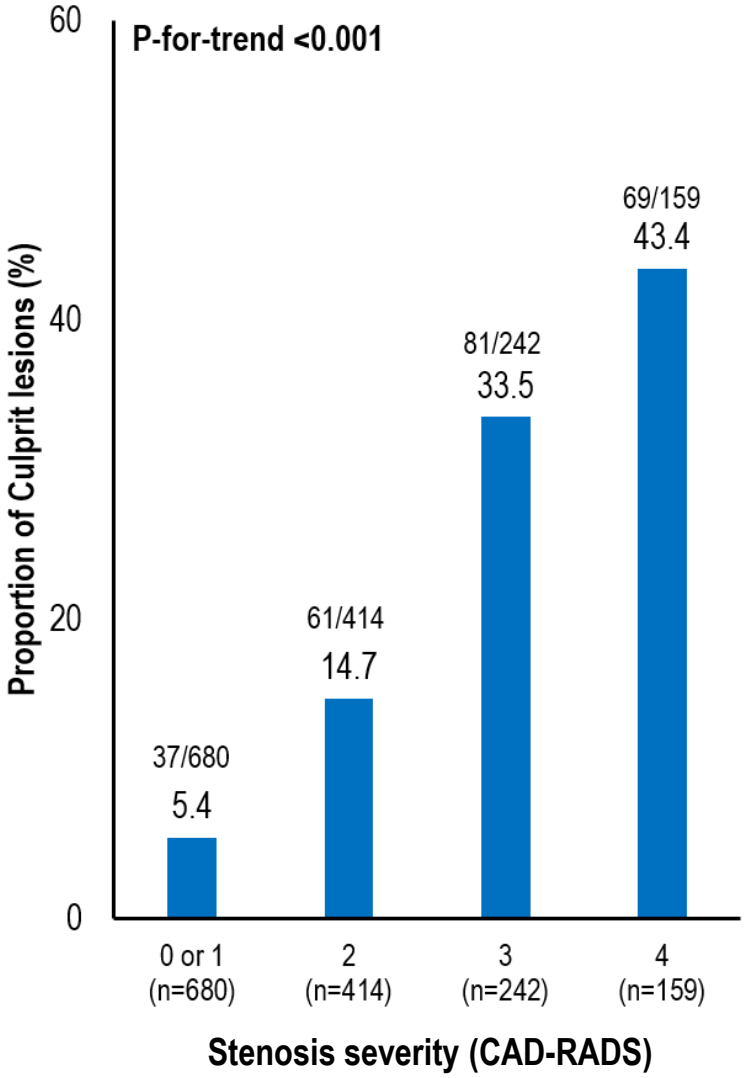
Best AI-QCPHA features: **ΔFFR_{CT}, plaque burden, total plaque volume, low attenuation plaque volume, and % total myocardial blood flow (myocardial mass at risk)**

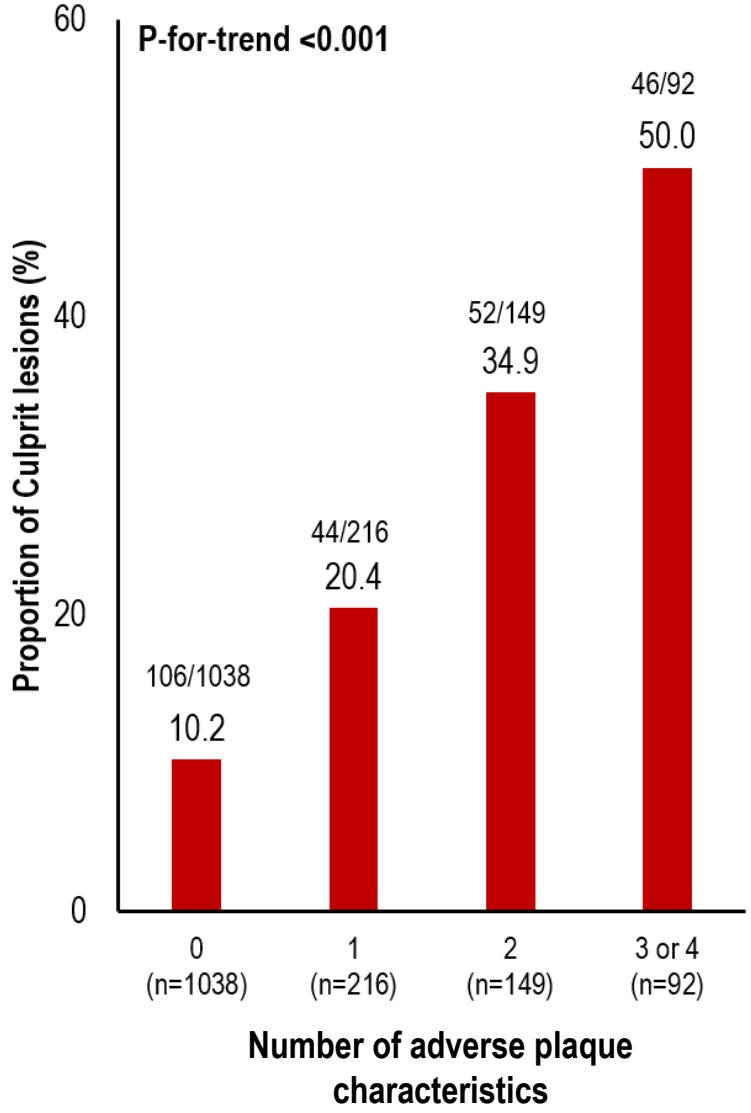
Standard CCTA analysis



CAD-RADS + HRP Feature	Value
CAD-RADS Score	1
Positive Remodeling	0
Spotty Calcification	0
Napkin Ring Sign	0
Low Attenuation Plaque	0

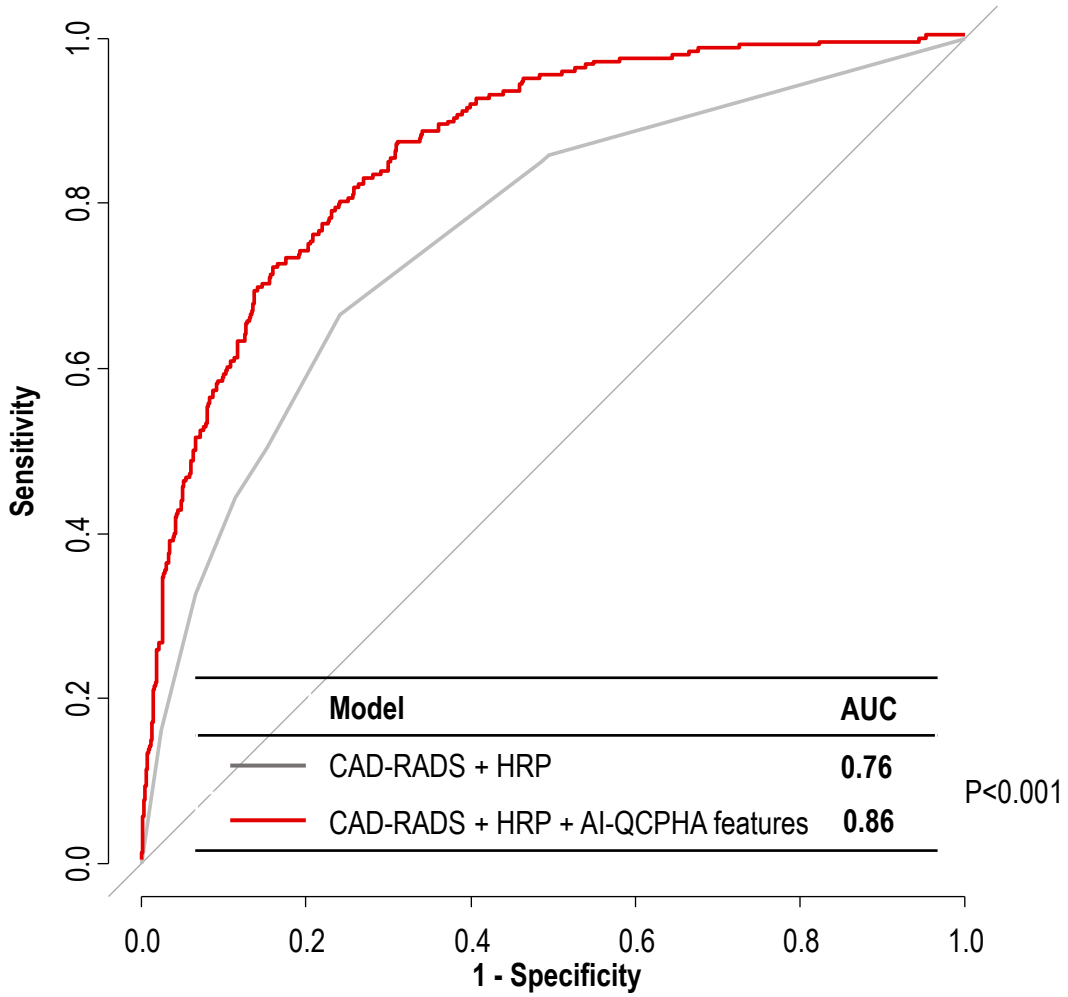
ACS risk according to stenosis and plaque character



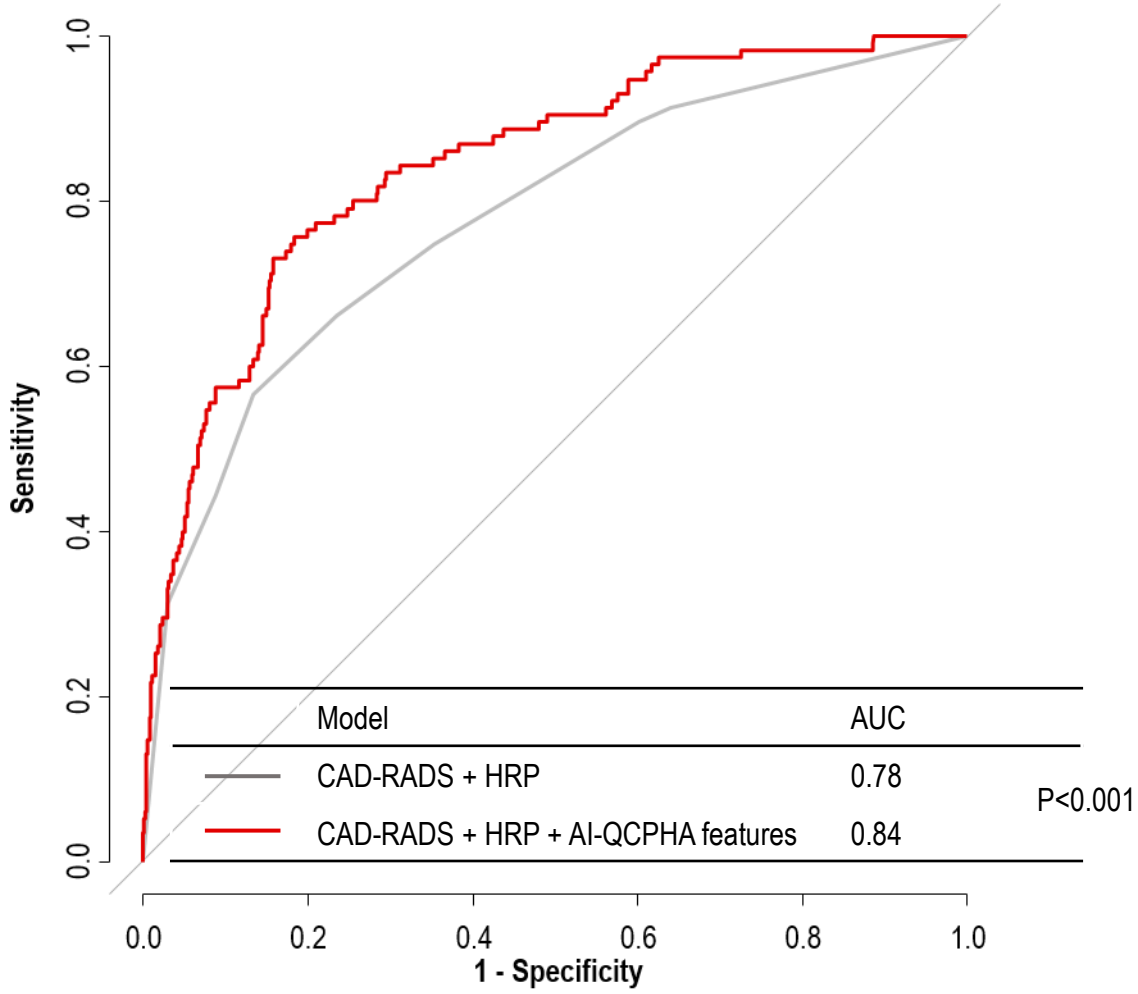


Incremental value of AI-QCPHA features over conventional assessment

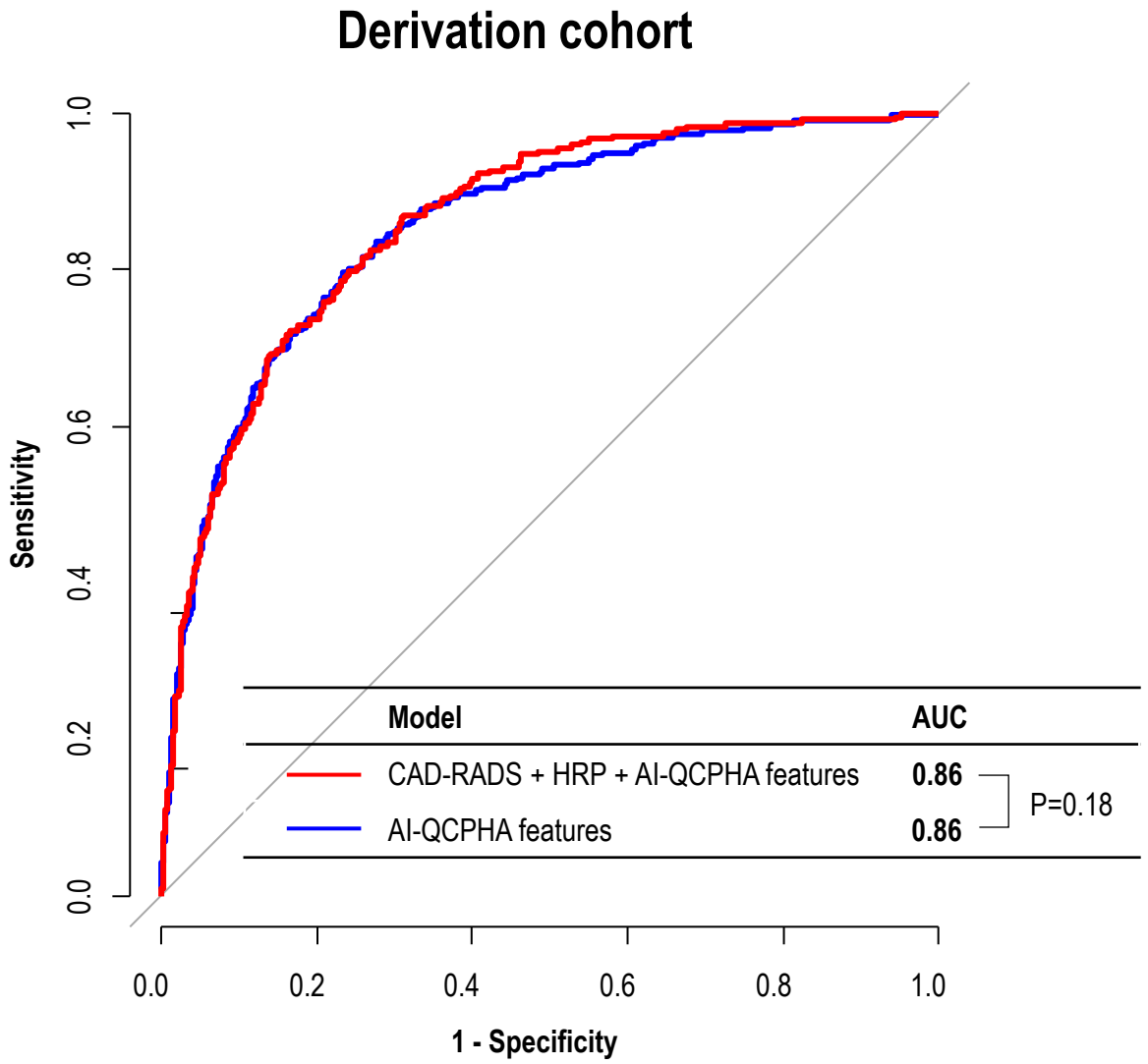
Derivation cohort

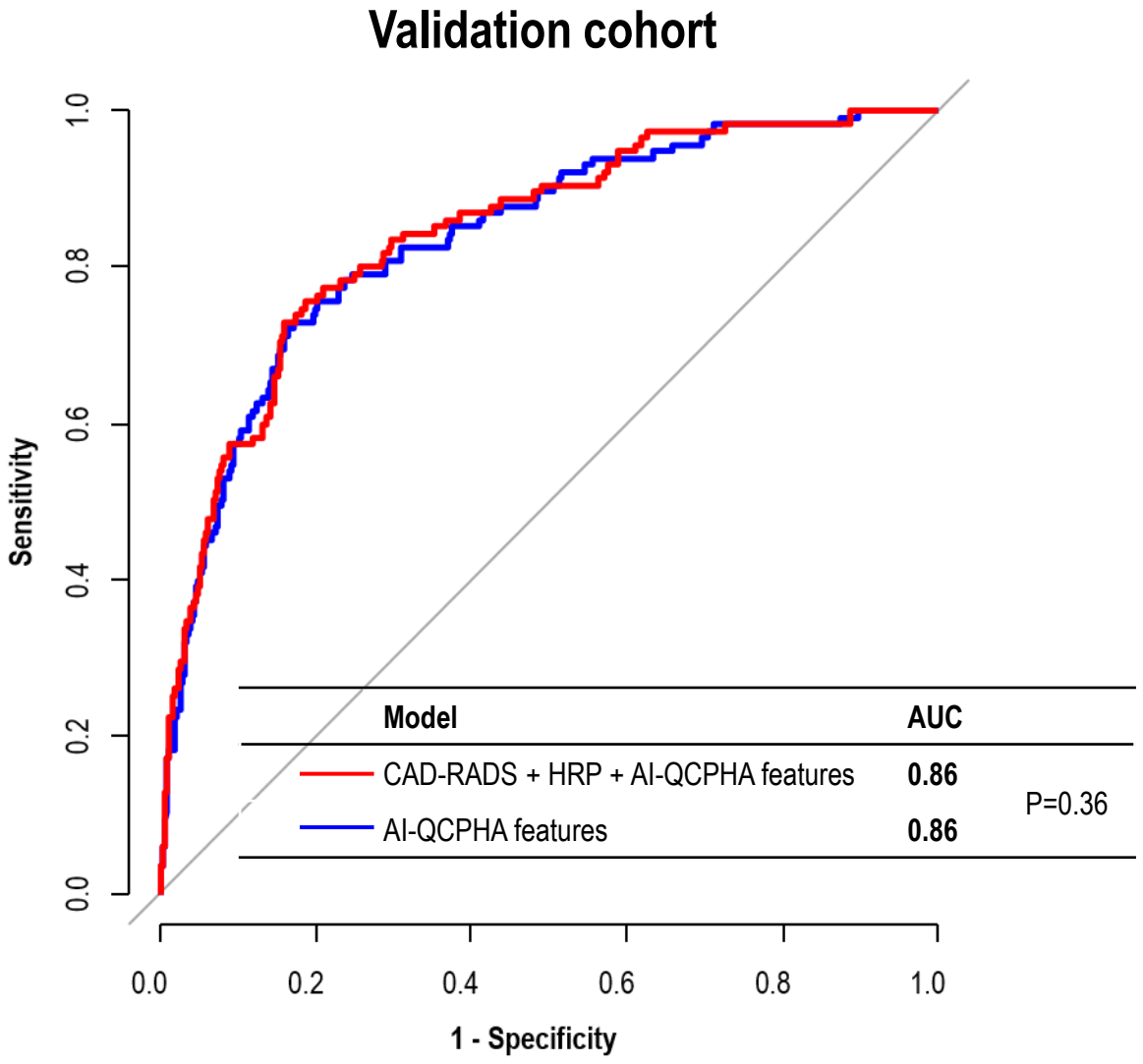


Validation cohort

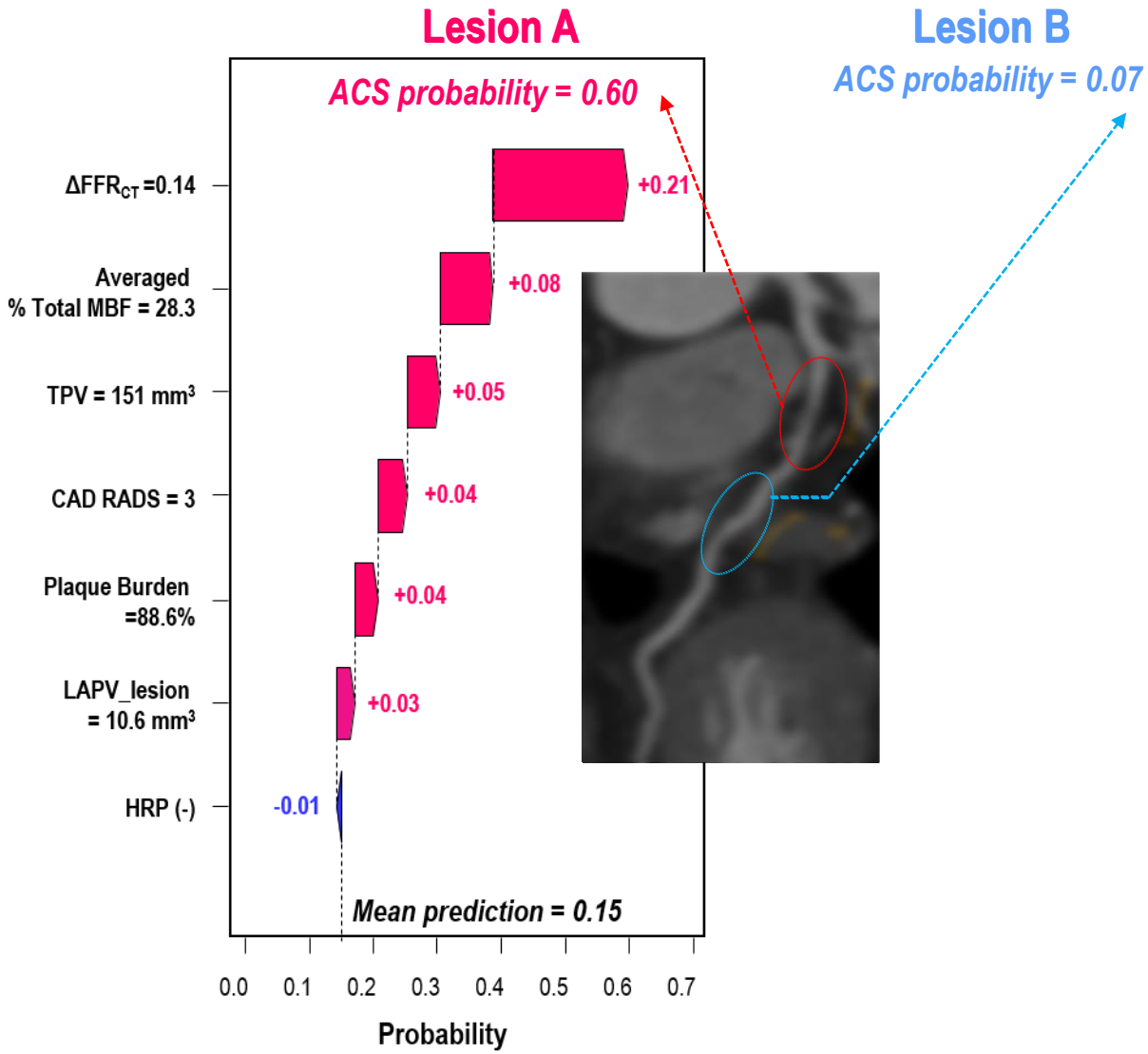


Comparison between AI-QCPHA features and the best model





Selection of Treatment Strategy: Probability is not enough!

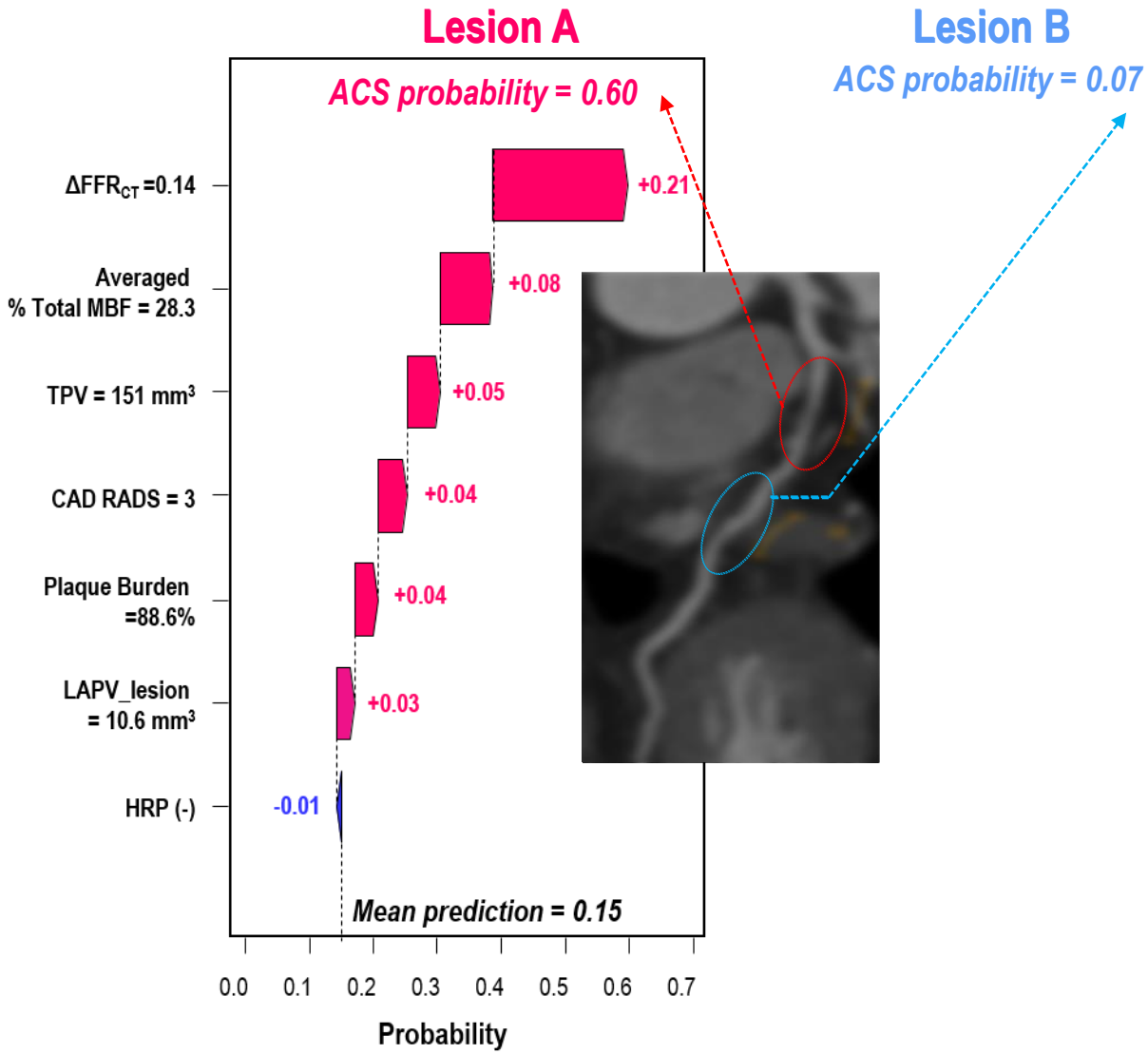


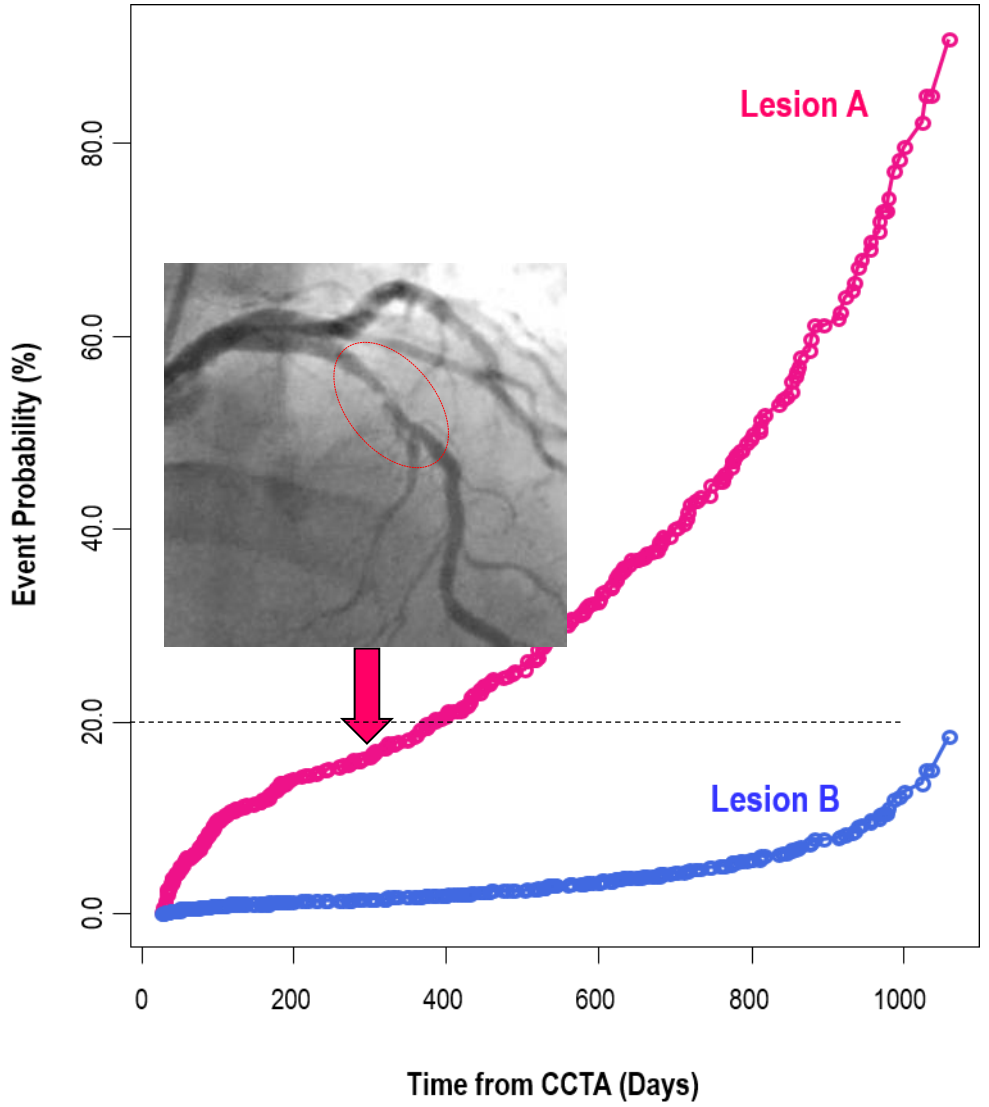
PCI vs. OMT

1. **Probability for events**
2. **Treatment target:** Plaque quantity? Plaque quality?

   Degree of luminal narrowing? Physiologic significance?
3. **Time to event:** 6months? 2 years? 5 years?

Selection of Treatment Strategy: Probability is not enough!





AI-Enabled Vulnerable Plaque Characterization

- AI-enabled non-invasive plaque and hemodynamic analysis can enhance the prediction of ACS risk and the detection of the target lesions for revascularization.

- Integration of this novel algorithm in clinical practice can prevent ACS/sudden cardiac death and optimize treatment strategy for patients with coronary artery disease.