TCTAP 2024 (29th)

Vulnerable Plaque Treatment 2024
26th April 2024
14:00-15:20

TCTAP 2024
What is a Vulnerable Plaque?
Insights From Non-Invasive Imaging Modalities

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Disclosure

- **The authors have no financial conflicts of interest to disclose concerning the presentation.**

ESC
European Society of Cardiology
European Heart Journal (2020) **0**, 1–10
doi:10.1093/eurheartj/ehaa227
CURRENT OPINION
Coronary artery disease

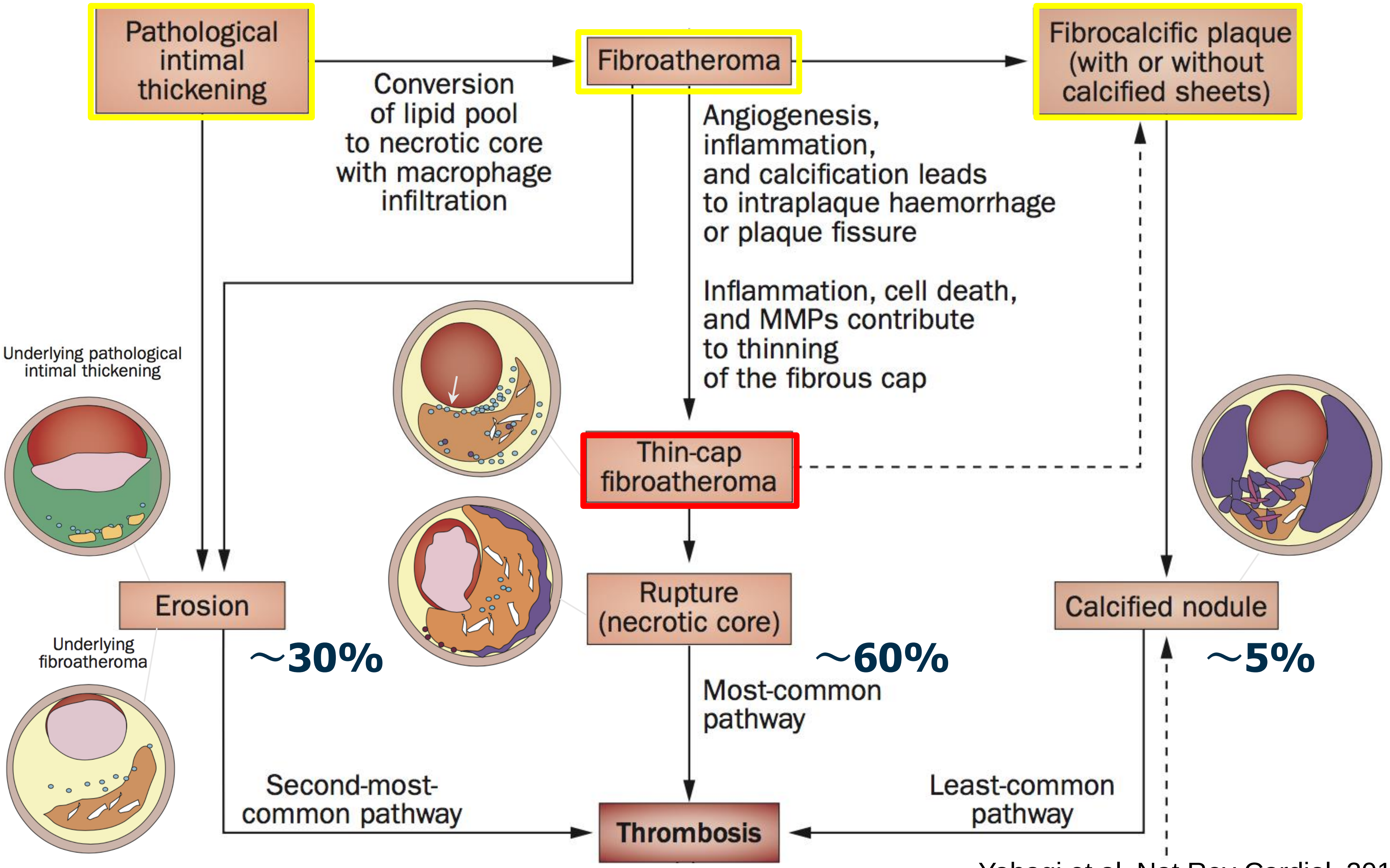
Vulnerable plaques and patients: state-of-the-art

- In the 1980s, Muller et al. studied coronary events triggered by morning awakening, anger, heavy exertion, and other stressors. The observation that a potential stressful trigger could be harmless on one day, yet lead to a cardiac event sometime later led to the concept of the **'vulnerable plaque'**, initially defined in 1989 as **a plaque at increased risk of thrombosis**

- The search for the precursors of culprit plaque underlying acute cardiac events has been the subject of multiple investigations using different invasive and non-invasive imaging modalities.

Tomaniak et al. European Heart Journal (2020) 0, 1–10

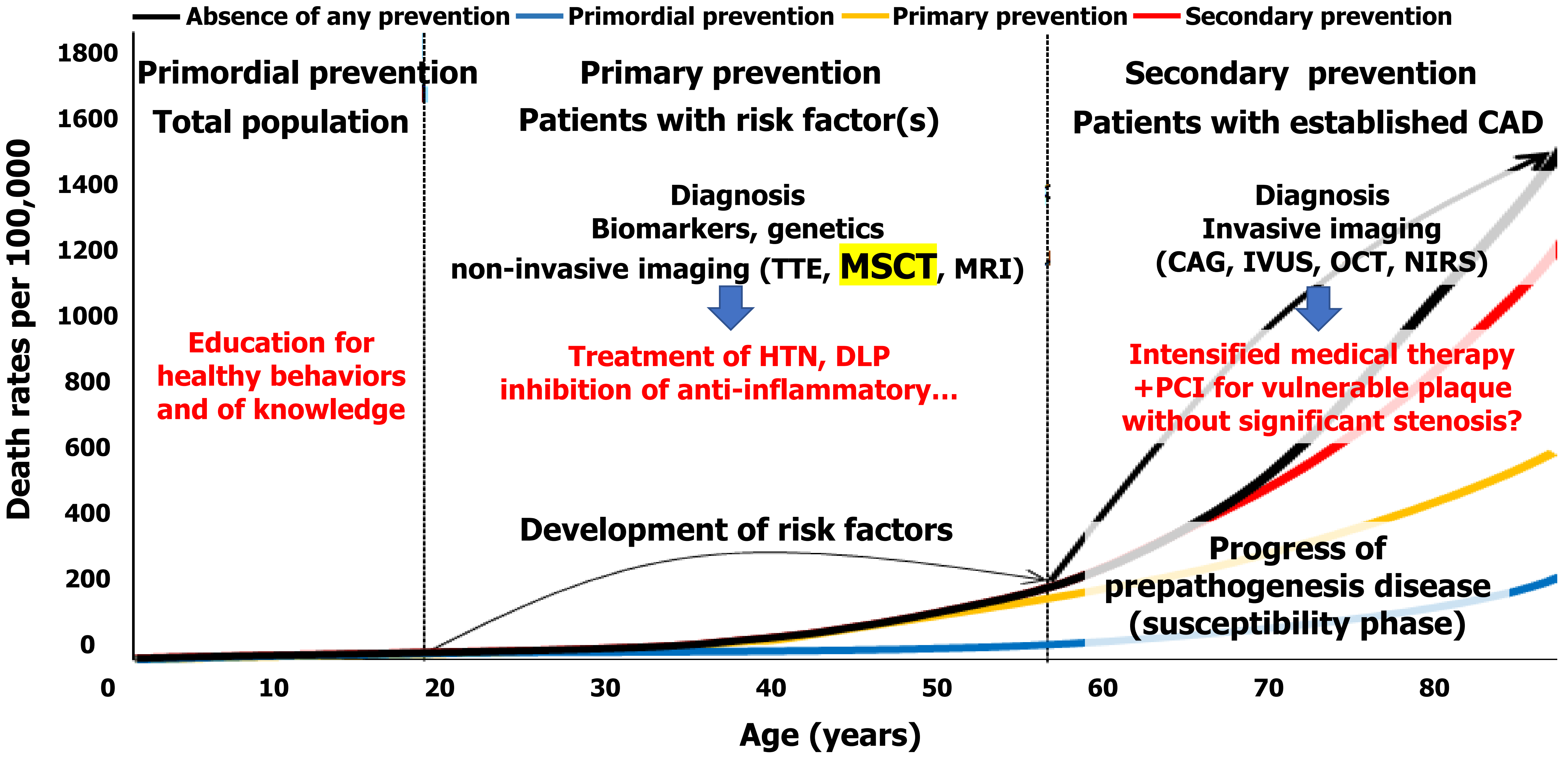
Pathways causing thrombosis in coronary artery disease



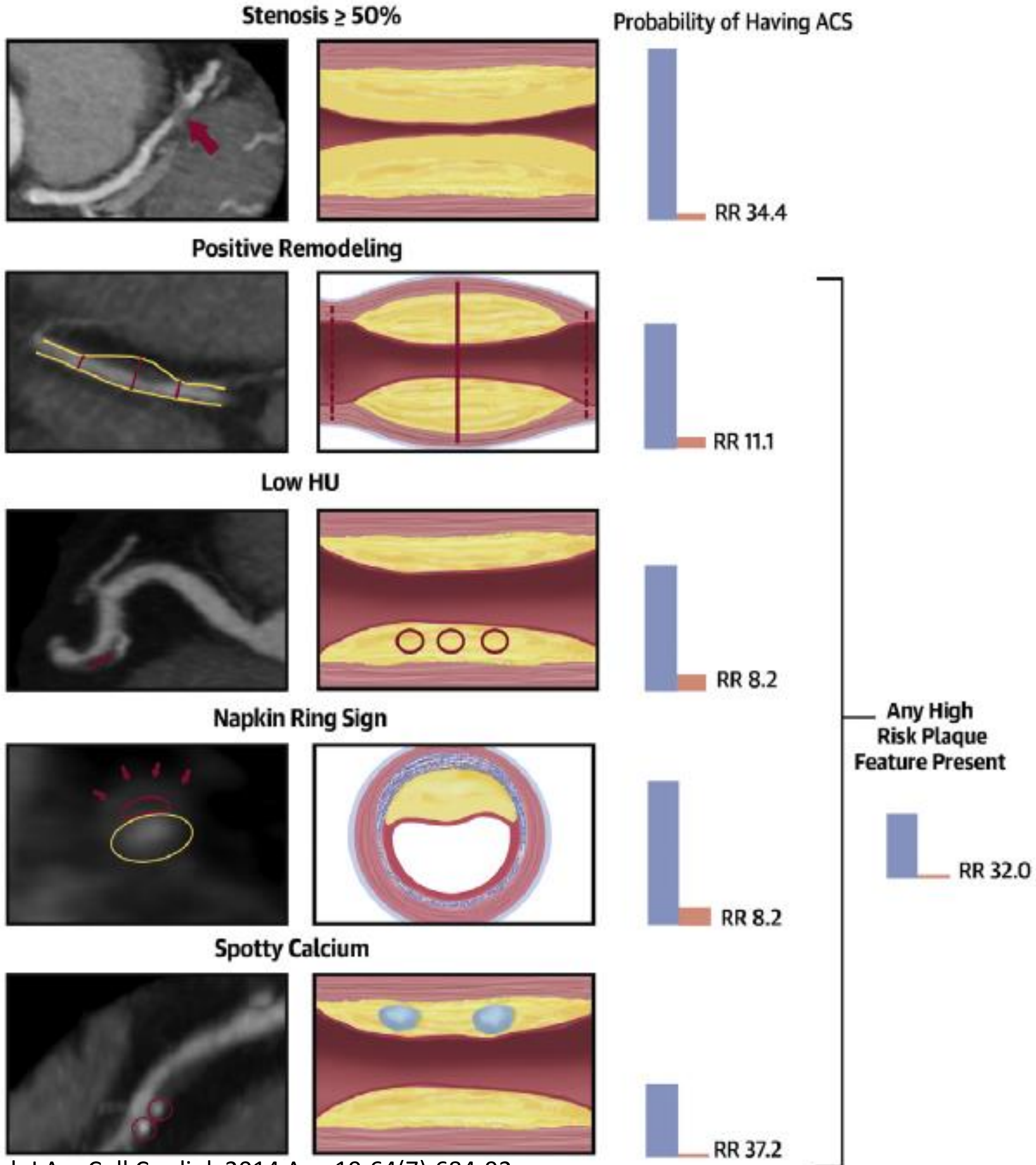
Yahagi et al. Nat Rev Cardiol. 2016;13:79-98.
Yahagi et al. Atherosclerosis 2015;239:260–267

CT is the imaging modality for primary prevention to detect vulnerable plaque in people who don't have previous cardiovascular events

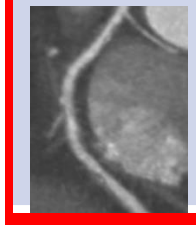
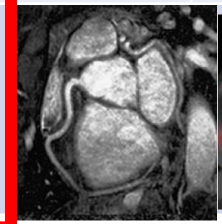
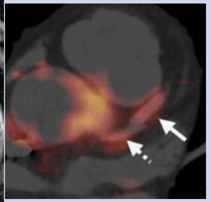
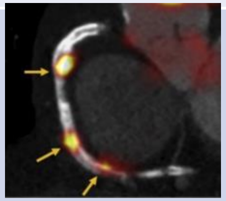
Tomaniak et al. European Heart Journal (2020) 0, 1–10



Invasive and non-invasive imaging modalities for coronary plaque



Stefan B. Puchner et al. J Am Coll Cardiol. 2014 Aug 19;64(7):684-92.

	CTCA	CMR	^{18}F-FDG PET	^{18}F-NaF PET
Technical features				
Spatial resolution	0.4 mm	0.5-1 mm	4-5 mm	4-5 mm
Tissue penetration, mm				
Detection of vulnerable plaque				
Lipid-rich core	++	+++	–	–
Fibrous cap thickness	–	–	–	–
Calcifications	+++	++	–	+++
Positive remodeling (PR)	+++	+	–	–
Inflammation	+	+	+++	–
Neovascularization	–	++	–	–
Intraplaque hemorrhage	–	–	–	–
Features of vulnerable plaque	**Low attenuation Plaque, Positive Remodeling , Spotty calc, Napkin ring, FFR CT, Perivascular inflammation**	LRP, PR, Inflammation, Angiogenesis	Inflammation (uptake by macrophage)	Microcalcification High risk plaque (PR, necrotic core)
Image				

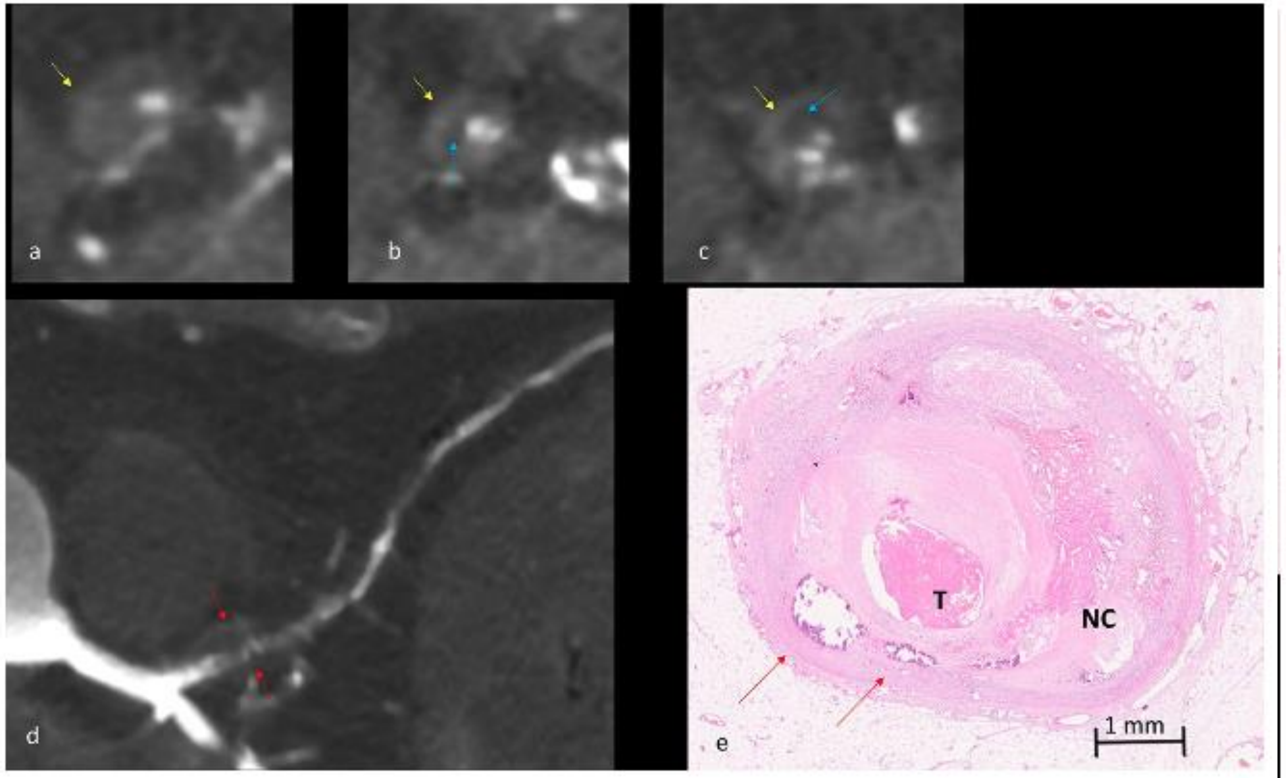
van Veelen A, et al. J Clin Med. 2022;11(5):1361

High-risk coronary plaque of sudden cardiac death victims: postmortem CT angiographic features and histopathologic findings

Katarzyna Michaud[1] · David C Rotzinger[2] · Mohamed Faouzi[1,3] · Silke Grabherr[1] · Salah D Qanadli[4,5] · Allard C van der Wal[6,7] · Virginie Magnin[1]

Michaud et al. International Journal of Legal Medicine. 2024 Apr.

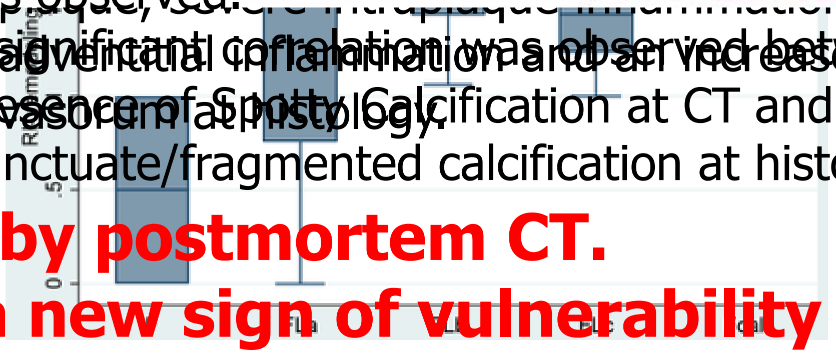
- Postmortem CT and histology were invetigated in 40 sudden cardiac cases due to ACS.
- Postmortem CT showed a positive remodeling index (RI≧1.1) in 75% of cases.
- Napkin-ring sign, Low attenuation plaque and spotty calcifications were observed in 40%, 46.3% and 48.7% of cases, respectively.
- **In 58.3% of cases, plaque enhancement was observed**.



Correlation between enh... plaque at CT and plaq... inflammation and the fib... composition at histolog... was observed.

...plaque, severe intraplaque inflammation, severe adventitial inflammation and an increased vasa vasorum at histology.

A significant correlation was observed between the presence of Spotty Calcification at CT and the presence of punctuate/fragmented calcification at histology.

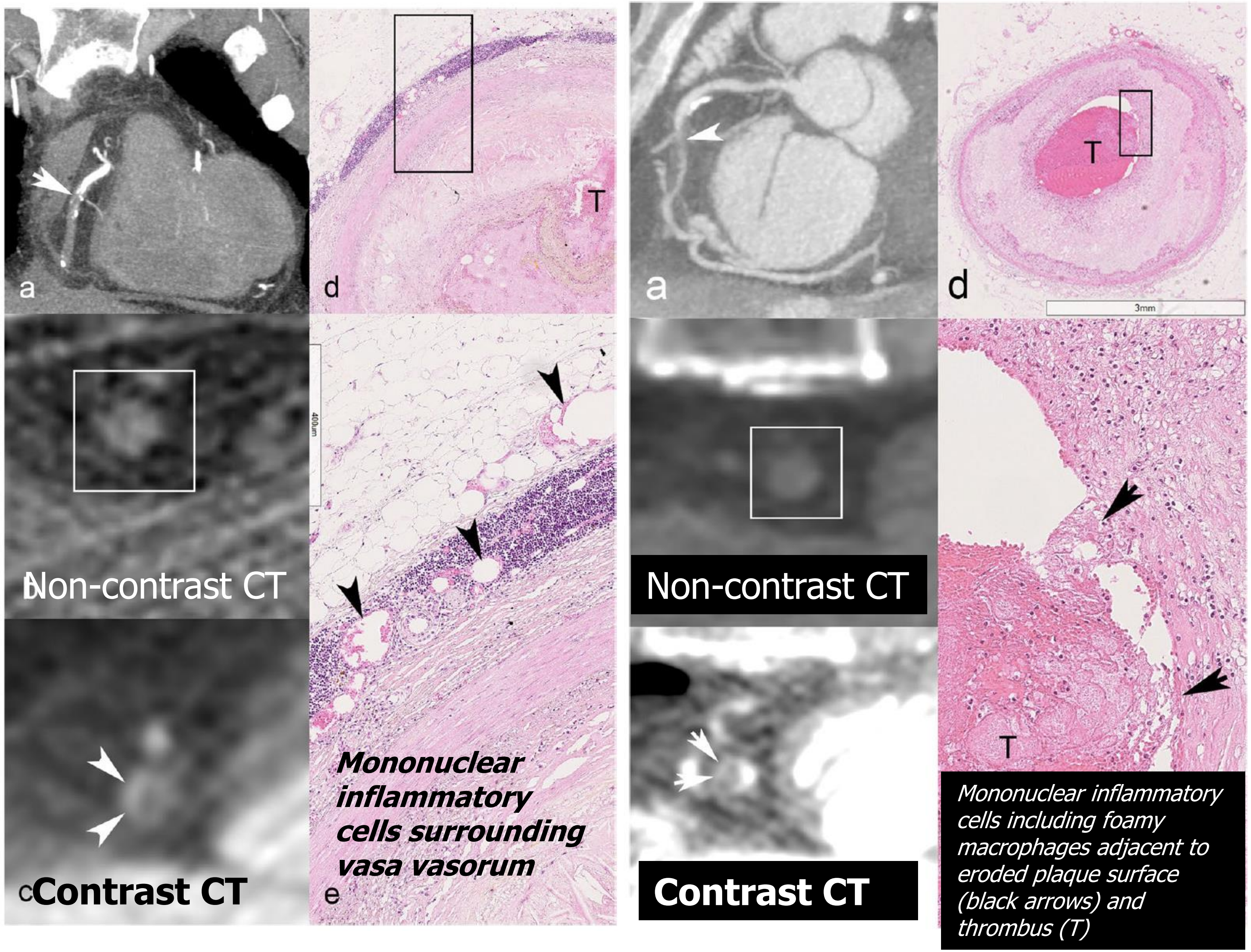


Various HRP signs can be detected by postmortem CT.
Plaque enhancement appeared as a new sign of vulnerability

RI values were lower in cases with fibrotic plaques.

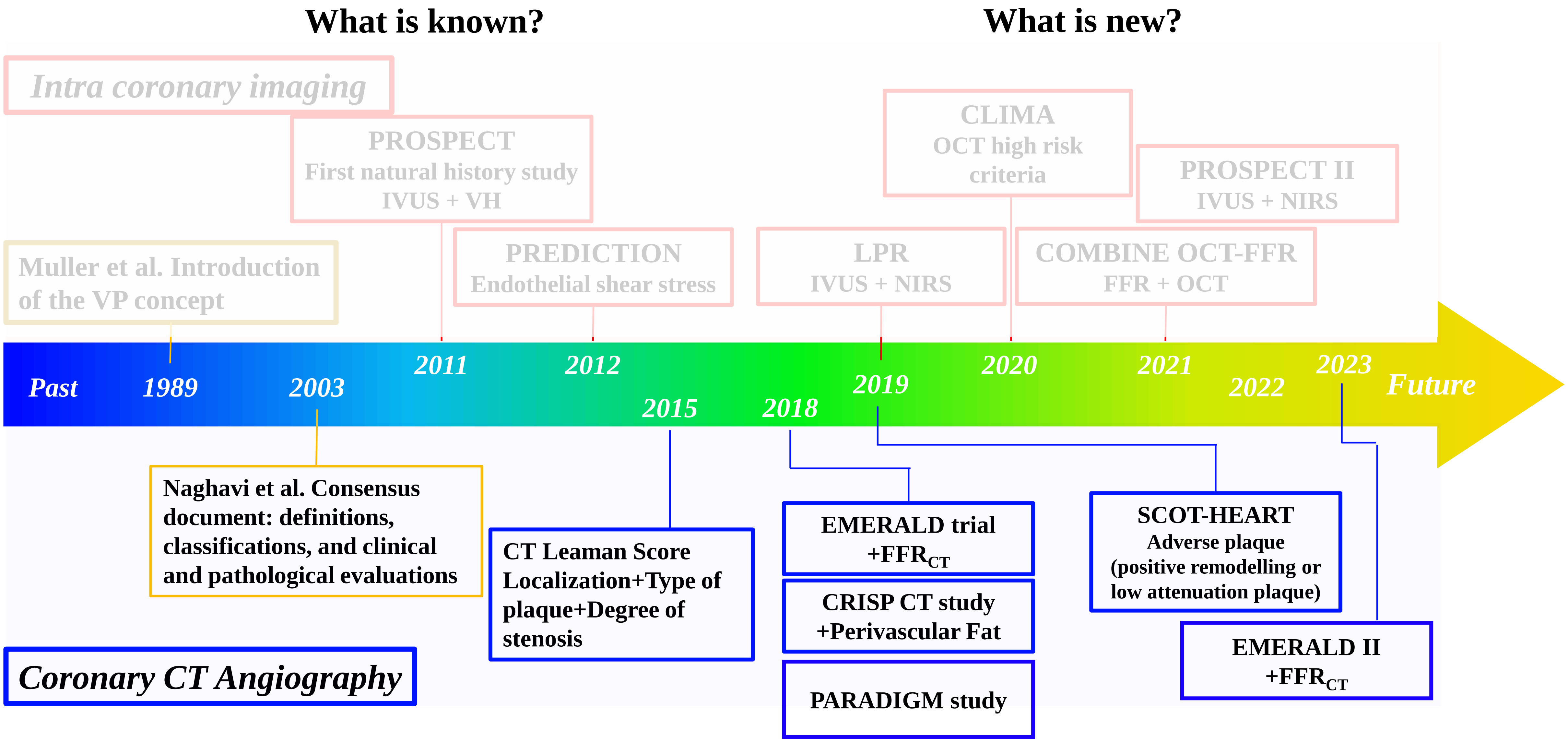
Coronary CT angiography for the assessment of atherosclerotic plaque inflammation: postmortem proof of concept with histological validation

- 35 cases (12 women, 34%; median [IQR] age, 52 [11] years), with autopsy-proven coronary thrombosis, histological examination, and **multiphase** post-mortem CT Angiography.
- Plaque enhancement at multiphase PMCTA was reported in 21 (60%)
- Furthermore, plaque enhancement correlated with histopathological plaque inflammation and increased vasa vasorum density.
- **Plaque enhancement on multiphase CT angiography** could potentially serve **as a noninvasive marker of inflammation** in high-risk populations.



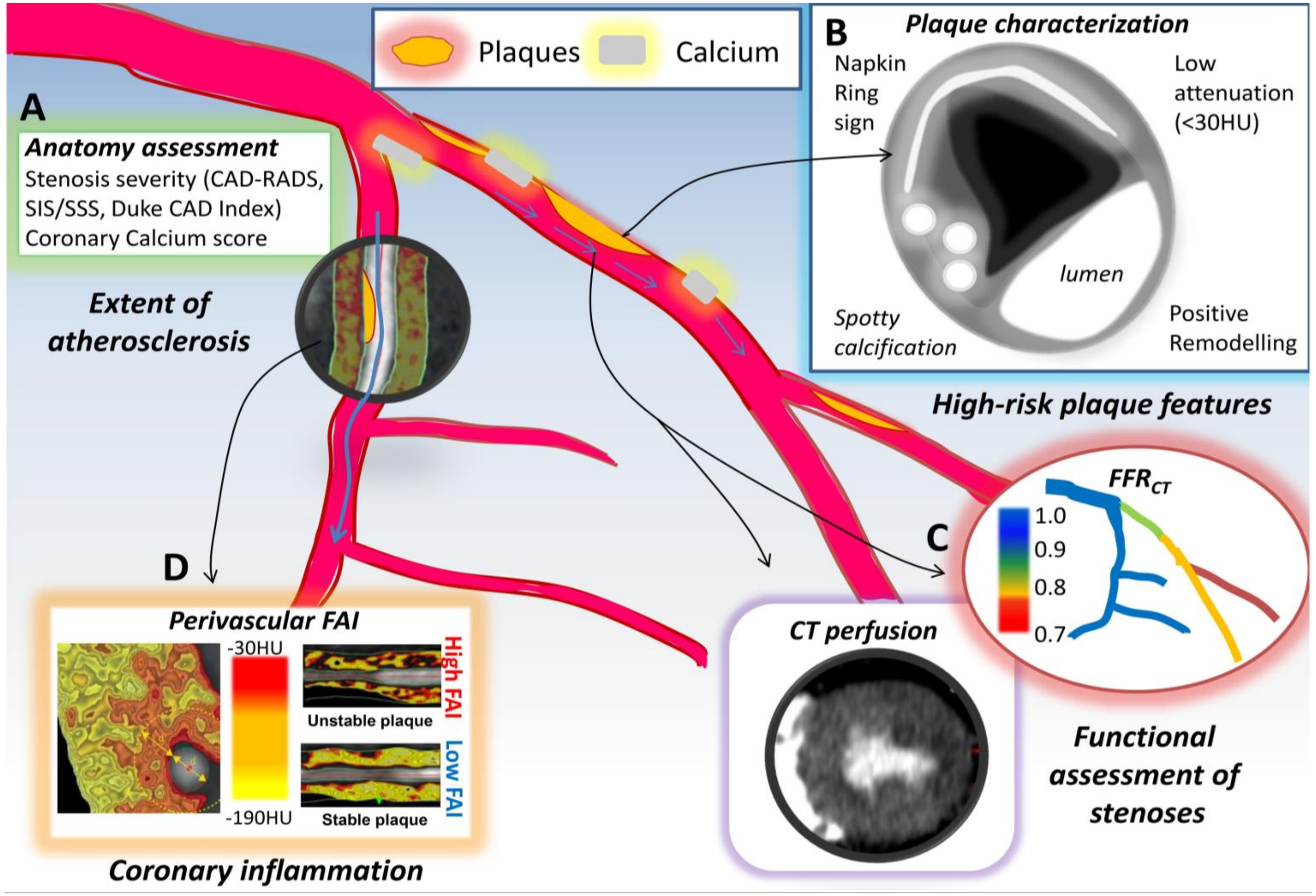
Eur Radiol. 2024 Mar;34(3):1755-1763.

Timeline of development and future directions for clinical trials in coronary vulnerable plaque (VP)



ESC European Society of Cardiology
European Journal of Preventive Cardiology
doi:10.1093/eurjpc/zwab067
REVIEW

Cardiovascular risk stratification by coronary computed tomography angiography imaging: current state-of-the-art



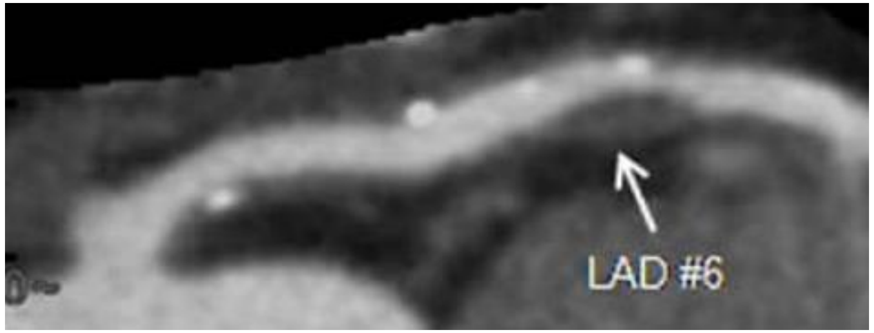
- Cardiovascular risk assessment by clinical risk score system or biomarkers is good but not satisfactory.
- CT technology allows the anatomical assessment (plaque burden, stenosis), plaque characterization (identification of high-risk plaques), functional assessment and quantification of coronary inflammation.

CT angiography offers an elegant way to risk stratification of patients.

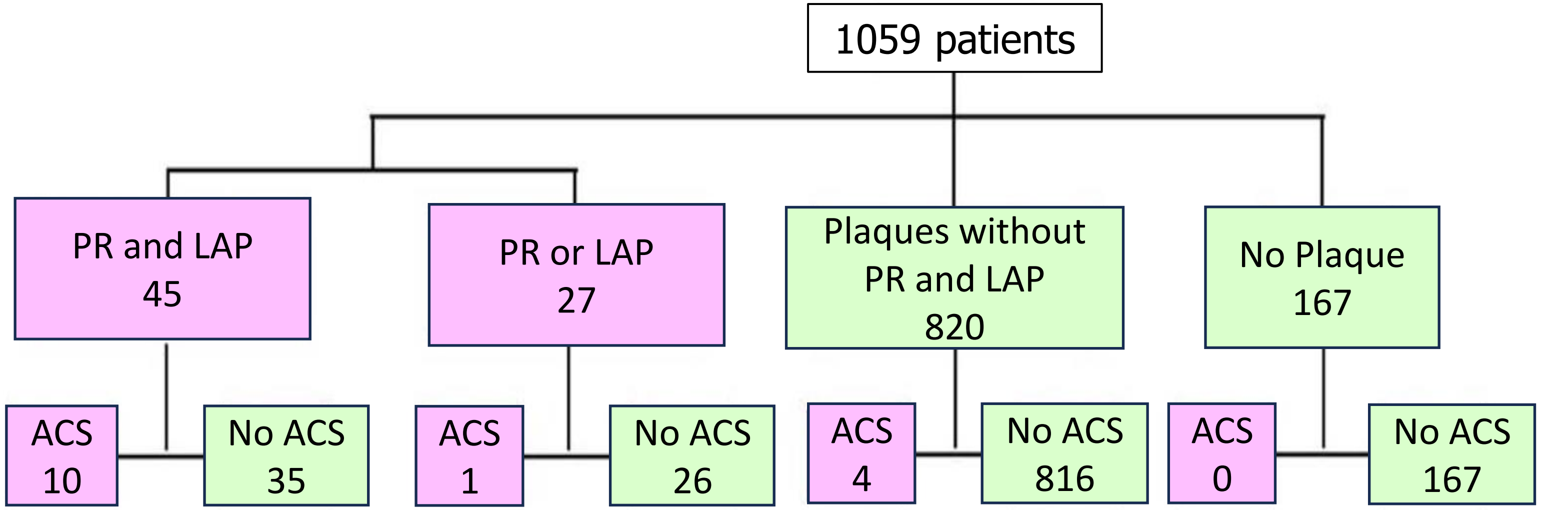
Antonopoulos AS, et al. Eur J Prev Cardiol 2022;29(4):608-624

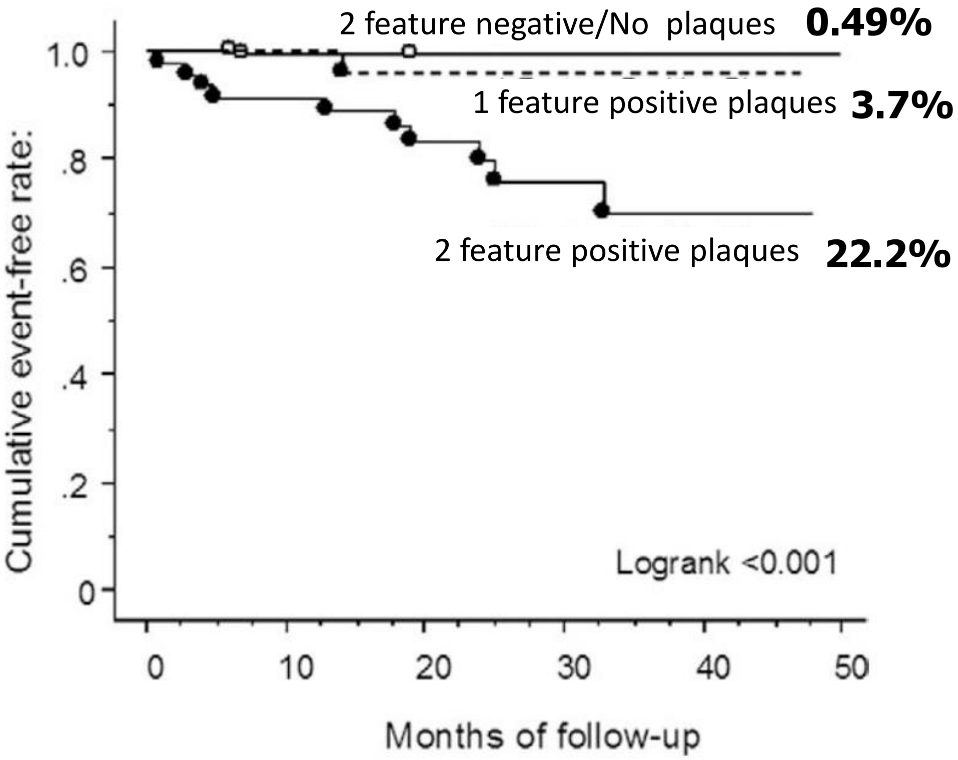
Computed Tomographic Angiography Characteristics of Atherosclerotic Plaques Subsequently Resulting in Acute Coronary Syndrome

- 1059 patients (10,037 segments) undergoing CTA
- Follow-up period of 12-50 months
- Endpoint: ACS (ischemic discomfort with elevated troponin and ischemic discomfort of CCS 3/4 without elevated troponin)



Positive remodeling (PR)
and
low-attenuation plaque (LAP)





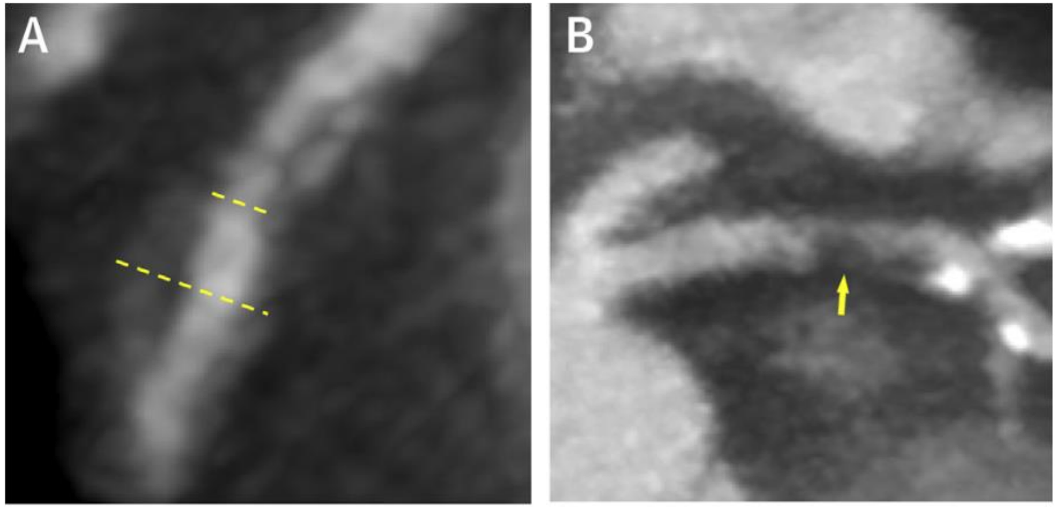
Positive remodeling with low-attenuation plaques on CTA predict future ACS.

Motoyama S, et al. *J Am Coll Cardiol.* 2009;54(1):49-57.

Coronary Artery Plaque Characteristics Associated With Adverse Outcomes in the SCOT-HEART Study

Williams, M.C et al. JACC 2019;73:291-301.

SCOT-HEART
-The Scottish Computed Tomography of the HEART-

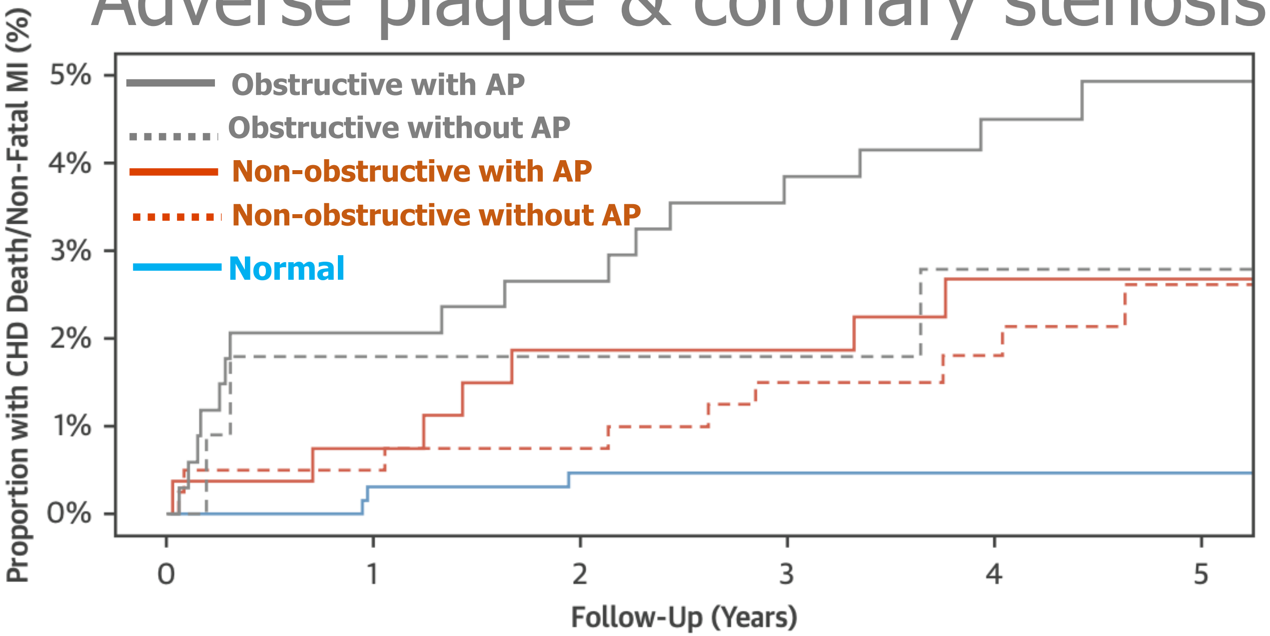


Positive remodeling (PR) Low-attenuation plaque (LAP)

Adverse plaque (AP)

- 1,769 patients with stable chest pain undergoing CTA
- Average FU: 4.7 years
- Adverse plaque (AP): PR and/or LAP
- Obstructive plaque: cross-sectional area stenosis≧70%
  Non-obstructive plaque: <70%
- Endpoint: coronary heart disease death or MI

Adverse plaque & coronary stenosis



- **3 times** more frequent event in patients with AP.
- **Twice** more frequent event in patients with obstructive plaque than those with non-obstructive disease.
- **10 times** more frequent event in patients with both AP and obstructive plaque than those with normal.

Circulation

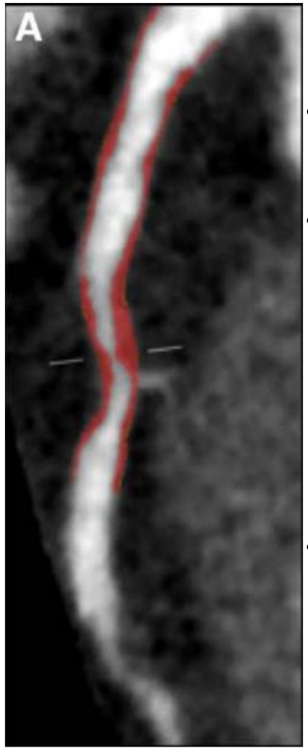
ORIGINAL RESEARCH ARTICLE

SCOT-HEART

Low-Attenuation Noncalcified Plaque on Coronary Computed Tomography Angiography Predicts Myocardial Infarction

Results From the Multicenter SCOT-HEART Trial (Scottish Computed Tomography of the HEART)

Williams, M.C et al.Circulation.2020;141:1452–1462.

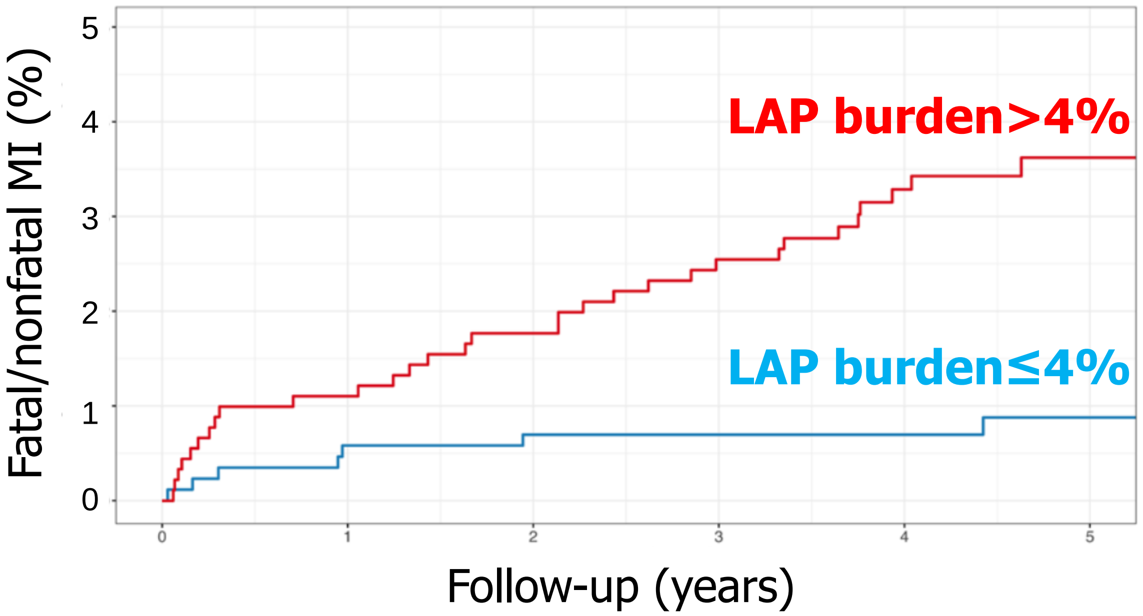


- Plaque burden=plaque volume/vessel volume
- Each burden of total, calcified, noncalcified and low-attenuation plaque were assessed.

  e.g. low attenuation plaque (LAP) burden = LAP volume/vessel volume
- LAP was defined as <30 HU.

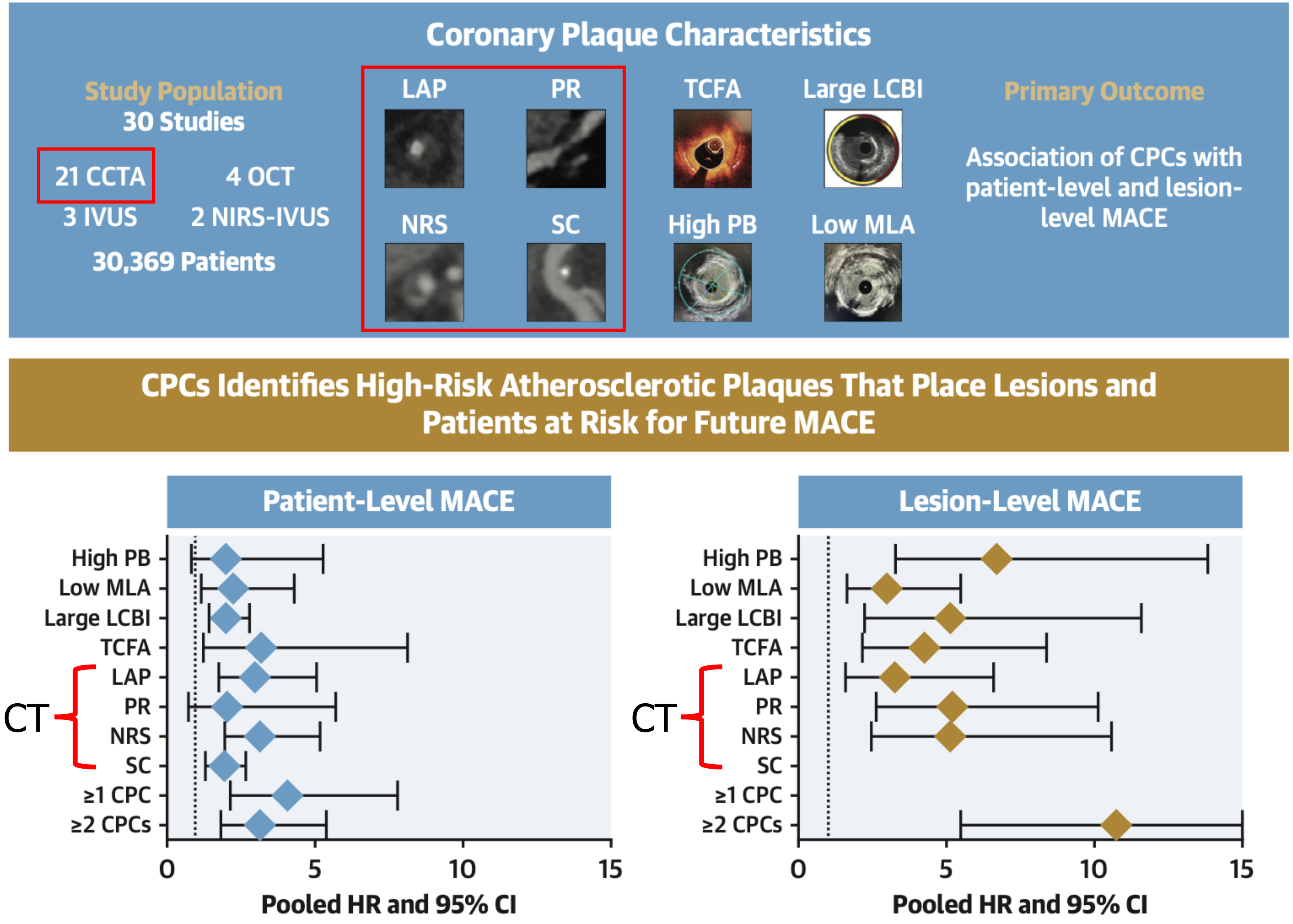
- 1769 patients with stable chest pain undergoing CTA
- Median Follow-up : 4.7 years
- Endpoint: fatal and nonfatal MI

Low attenuation plaque burden



- **All types of plaque are related with higher risk of MI.**
- **LAP is the strongest predictor of MI.**
- **Patients with LAP burden >4% are 5 times more likely to suffer MI.**

Coronary plaque characteristics associated with cardiovascular events



Gallone et al. J Am Coll Cardiol Img 2023;16:1584–1604

Oikonomou EK, et al.Lancet.2018;392(10151):929-939.

Non-invasive detection of coronary inflammation using computed tomography and prediction of residual cardiovascular risk (the CRISP CT study): a post-hoc analysis of prospective outcome data

Evangelos K Oikonomou*, Mohamed Marwan*, Milind Y Desai*, Jennifer Mancio, Alaa Alashi, Erika Hutt Centeno, Sheena Thomas, Laura Herdman, Christos P Kotanidis, Katharine E Thomas, Brian P Griffin, Scott D Flamm, Alexios S Antonopoulos, Cheerag Shirodaria, Nikant Sabharwal, John Deanfield, Stefan Neubauer, Jemma C Hopewell, Keith M Channon, Stephan Achenbach, Charalambos Antoniades

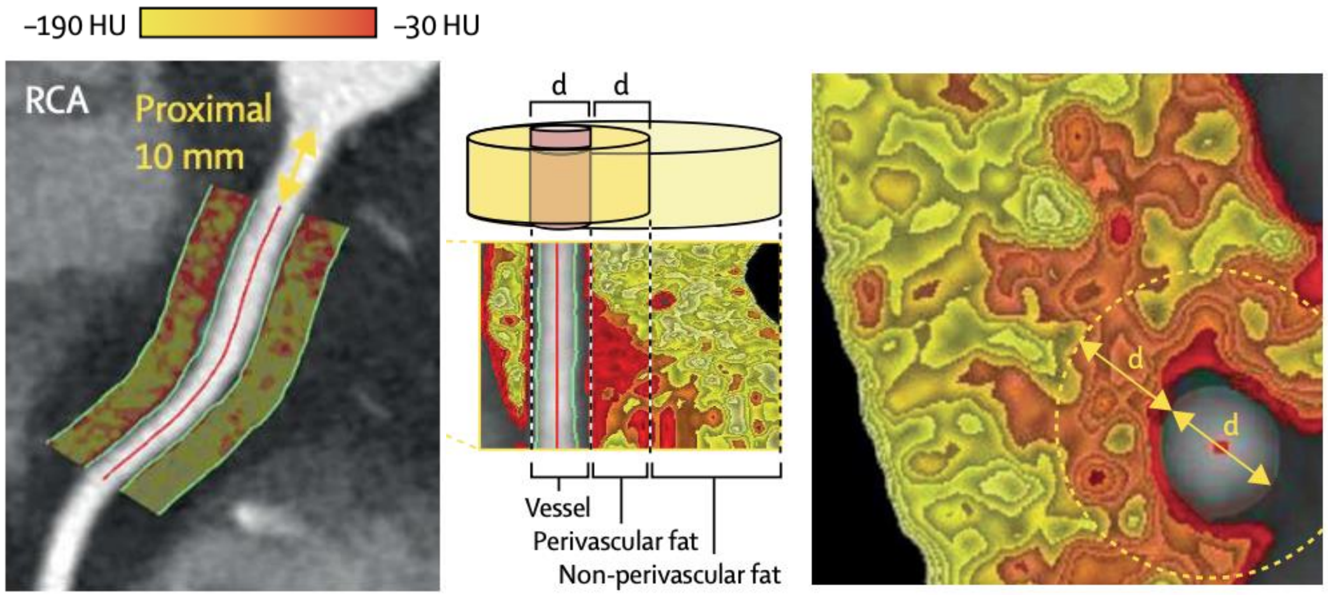
CRISP-CT study

Derivation cohort: 1872 patients / Validation cohort: 2040 patients

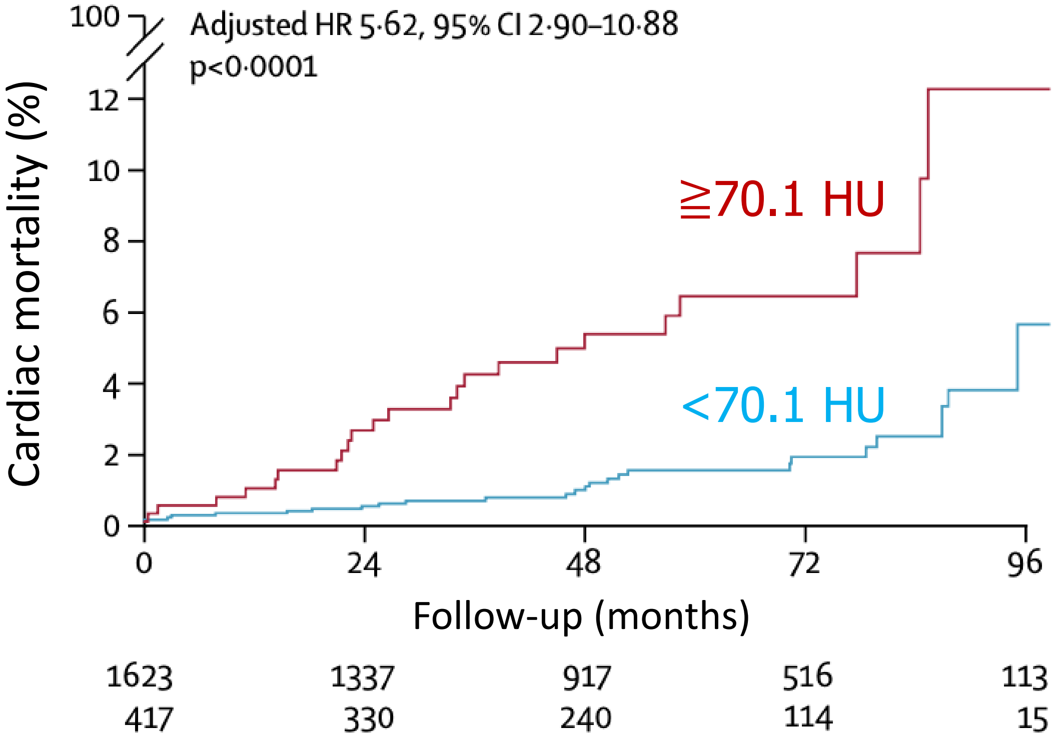
Median FU: 72 months / Median FU: 54 months

FAI of 70.1 HU is an optimal cutoff value for prediction of all-cause or cardiac death.

Perivascular fat attenuation index (FAI) captures the inflammatory changes in perivascular fat.



Derivation cohort / Validation cohort



High perivascular fat attenuation index (≧70.1 HU) is an indicator of increased all-cause and cardiac mortality.

ORIGINAL RESEARCH

EMERALD

Identification of High-Risk Plaques Destined to Cause Acute Coronary Syndrome Using Coronary Computed Tomographic Angiography and Computational Fluid Dynamics

Patient with ACS

Patients who underwent CTA before ACS event (1 month – 2 year before the event)

Enrollment (Patient N=72, Lesion N=216)

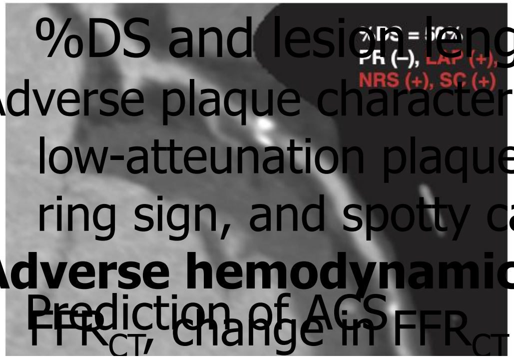
CASE	CONTROL
Culprit lesion (n=66)	Non-culprit lesion (n=150)

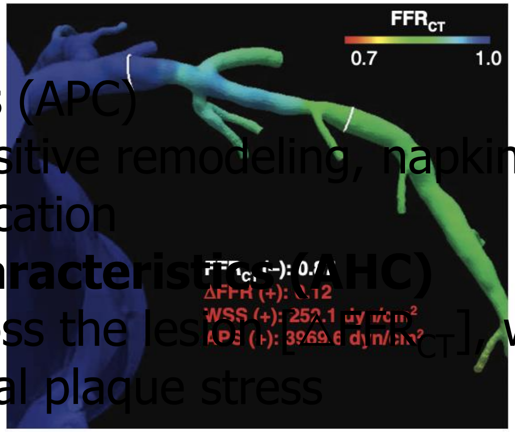
CTA analysis
Plaque characteristics & **Hemodynamics**

CT analysis

Plaque analysis | Hemodynamic analysis

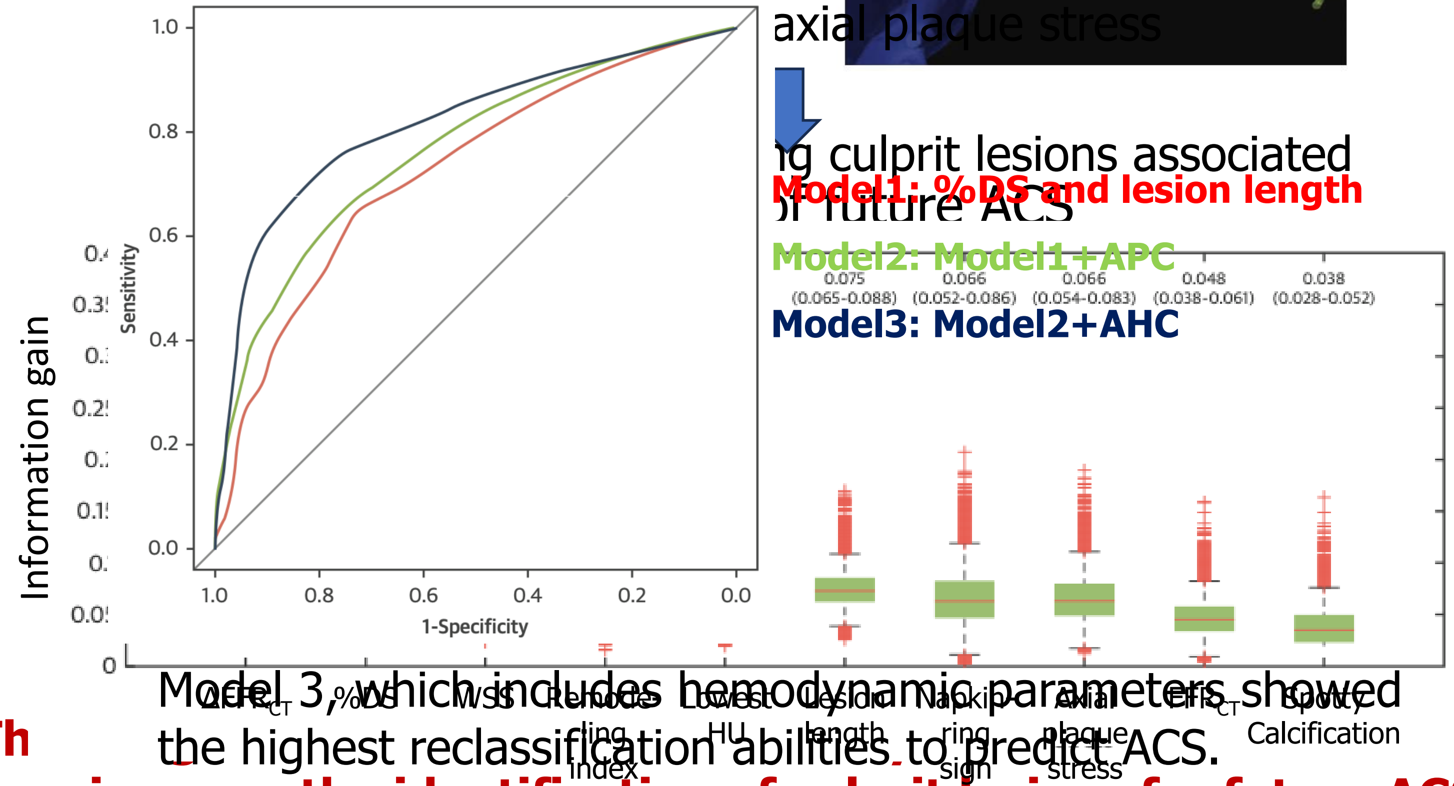
- Anatomical assessment
  - %DS and lesion length
- **Adverse plaque characteristics (APC)**
  - low-atteunation plaque, positive remodeling, napkin-ring sign, and spotty calcification
- **Adverse hemodynamic characteristics (AHC)**
  - FFR_{CT}, change in FFR_{CT} across the lesion [ΔFFR_{CT}], wall shear stress, axial plaque stress





Prediction of ACS

…g culprit lesions associated …r future ACS



Model 3, which includes hemodynamic parameters showed the highest reclassification abilities to predict ACS.

Th

may improve the identification of culprit lesions for future ACS.

Lee JM, et al.JACC Cardiovasc Imaging 2019;12(6);1032-1043.

EMERALD II

Artificial Intelligence-Enabled Quantitative Plaque and Hemodynamic Analysis for Predicting Acute Coronary Syndrome Risk and Prevention Strategy

The EMERALD II Study

Patient with ACS

↓

Patients who underwent CTA before ACS event
(1 month – 3 year before the event)

↓

351 ACS patients

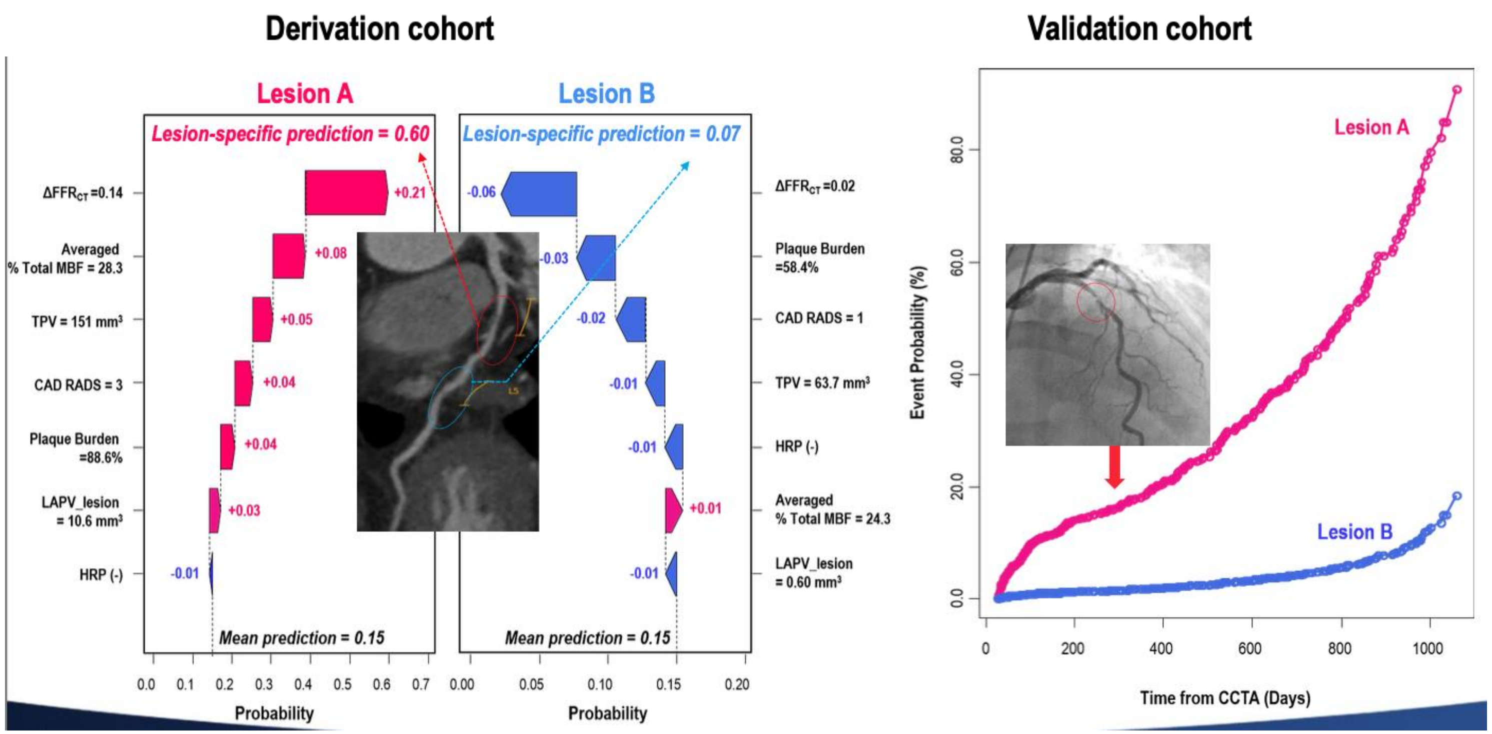
↓

Derivation cohort (243 patients: 248 culprit vs 1247 non-culprit)	Validation cohort (108 patients: 115 culprit vs 841 non-culprit)

New prediction model
(Standard analysis + AI-QCPHA features)

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

Prediction of ACS Time-dependent event probability

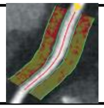
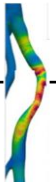


The best AI-QCPHA features provided the incremental value for ACS culprit lesions over conventional CCTA analysis.

The model also provides the time-dependent ACS event probability.

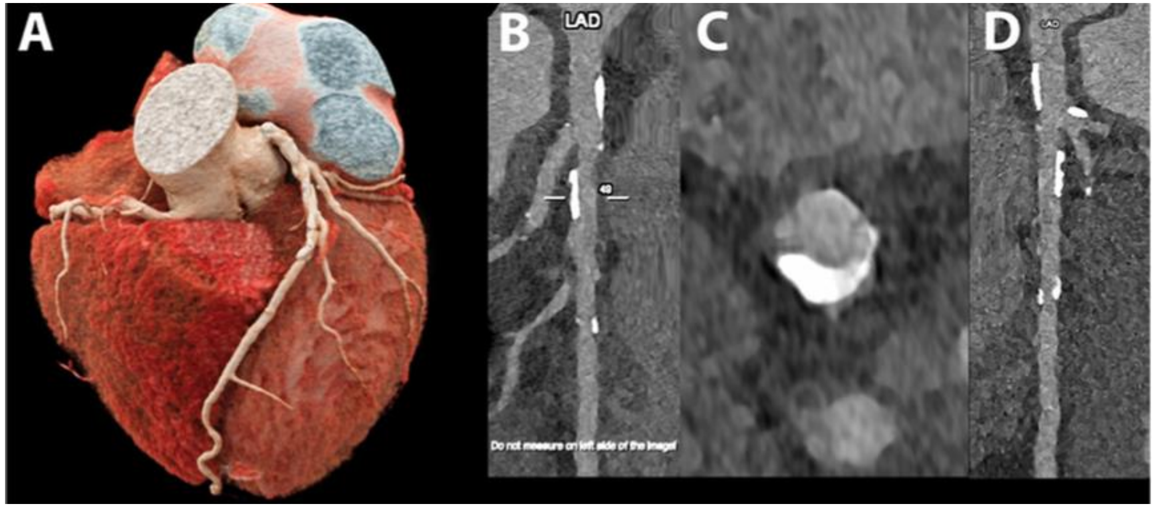
Bon-Kwon Koo, et al. TCT 2023

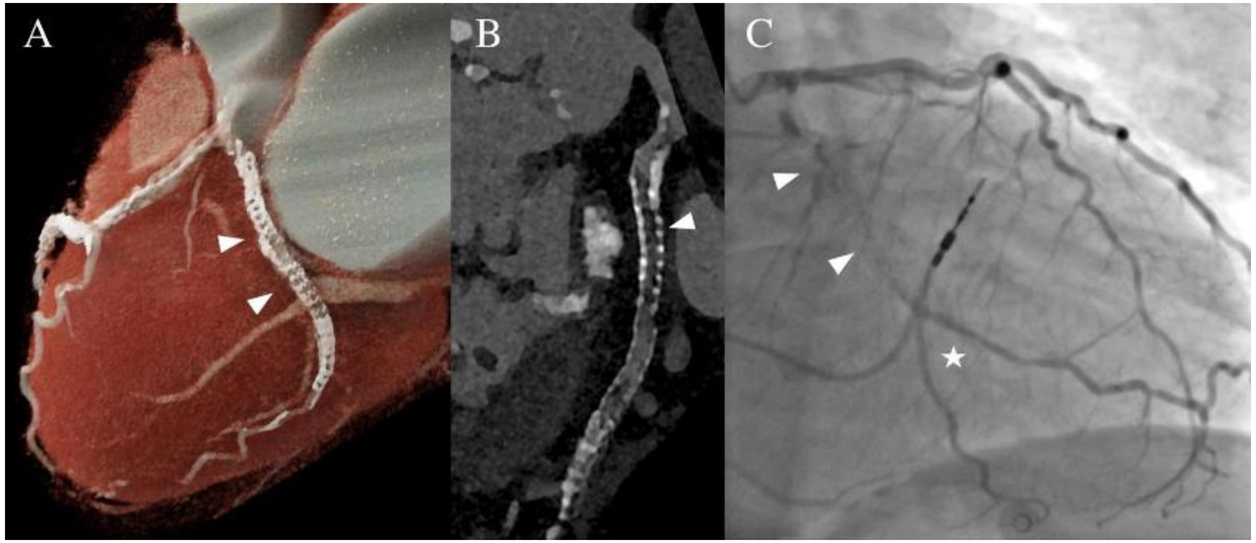
Summary of previous studies of CTA for prediction of future events

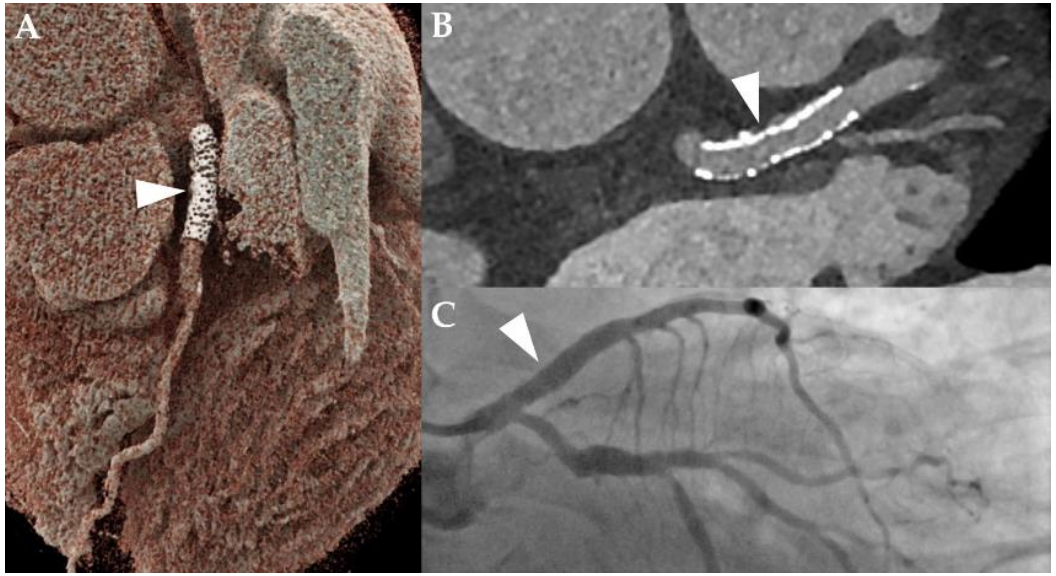
Study	Population	Identified parameters	Endpoint	Duration	PPV	NPV
Motoyama S	n=1,059 Pts undergoing CTA	Positive remodeling (PR) and Low-attenuation plaque (LAP)	ACS	27 M	22.2%	99.5%
Motoyama S	n=3,158 Pts undergoing CTA	HRP (PR and/or LAP)	ACS	3.9 Y	16.3%	98.6%
		HRP + ≧70% stenosis			18.8%	97.8%
SCOT-HEART	n=1,769 Pts with chest pain undergoing CTA	PR and/or LAP	Coronary heart disease death or MI	4.7 Y	4.1%	98.6%
		LAP>4%	MI	4.7 Y	NA	NA
		Agatston calcium score	MACE	4.8 Y	NA	NA
PARADIGM	n=1297 Pts with NOCA	Total percent atheroma volume, %DS	Progression to obstructive lesions	3.8 Y	NA	NA
CRISP-CT 	n=1,872 Pts undergoing CTA	Perivascular fat attenuation index ≧70.1 HU	All-cause or cardiac death	72 M	5.9%	99.5%
van Diemen PA	n=539 Pts with suspected CAD	RCA pericoronary adipose tissue attenuation	MI	5.0 Y	11.4%	95.9%
EMERALD 	n=72 Pts ACS who underwent CTA before ACS	Plaque and hemodynamic characteristics	ACS	338 D	NA	NA
EMERALD II	n=351 Pts ACS who underwent CTA before ACS	AI-QCPHA (AI-based plaque and hemodynamic characteristics)	ACS	NA (1M-3Y)	NA	NA
DISCOVER-FLOW	n=93 Pts with suspected or known stable CAD	Hemodynamic characteristics	TVF, TLF	10.1 Y	NA	NA

Photon Counting Detector is a Quantum Leap in the MSCT technology

ECG–synchronized ultra-high-resolution photon counting CT:
maximum resolution of 0.11 mm







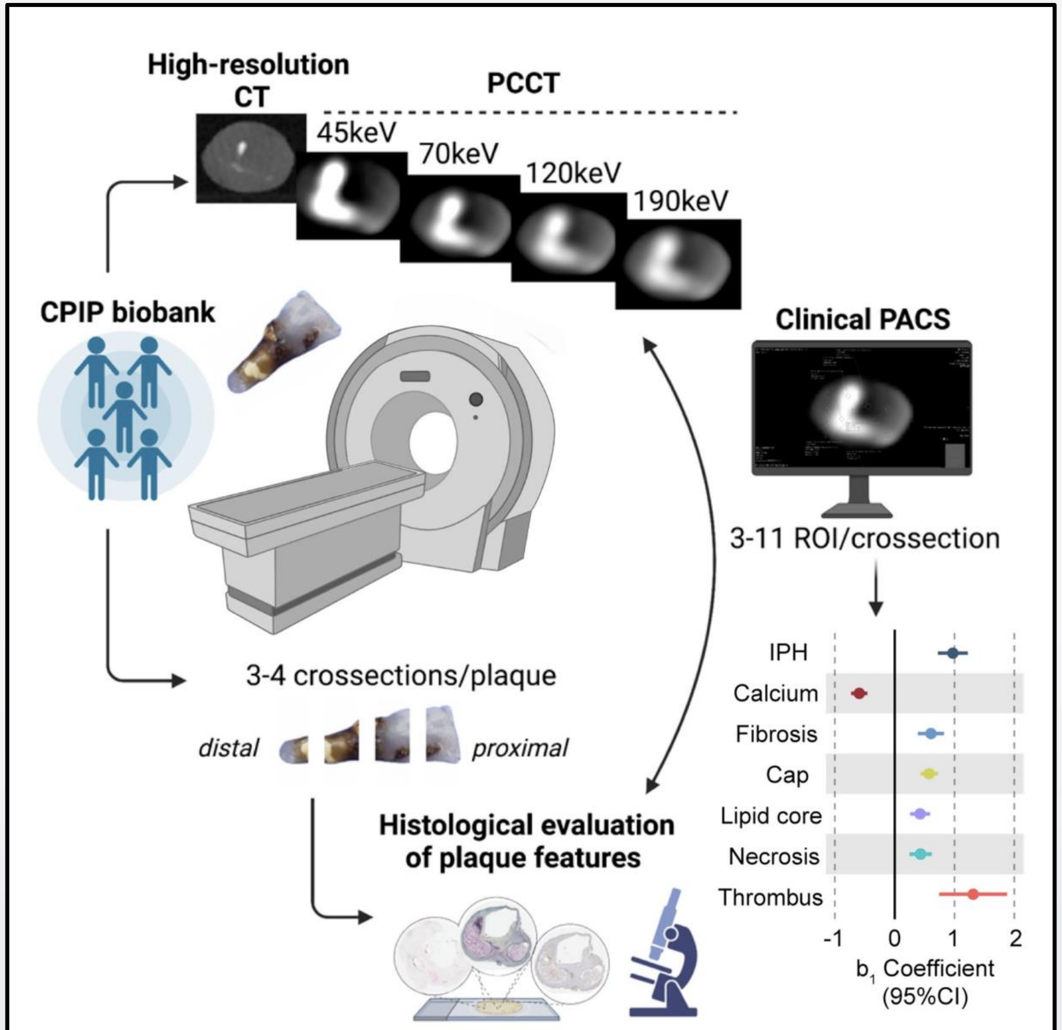
Hagar et al. European Radiology 2024

Meloni et al. J Cardiovasc Dev Dis 2023;10(9):363

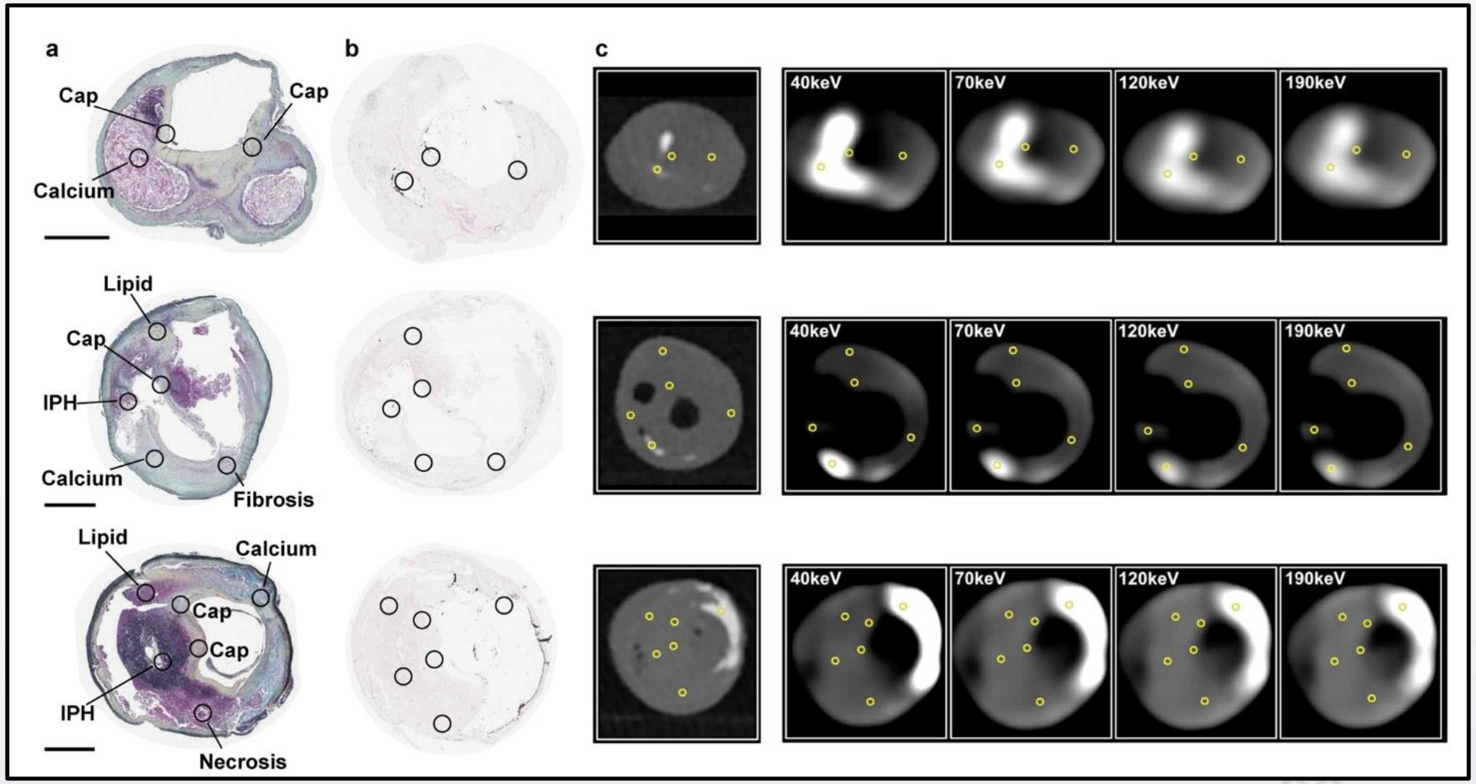
Shami et al. European Radiology Experimental (2024) 8:14
https://doi.org/10.1186/s41747-023-00410-4
European Radiology EXPERIMENTAL

ORIGINAL ARTICLE **Open Access**

Atherosclerotic plaque features relevant to rupture-risk detected by clinical photon-counting CT *ex vivo*: a proof-of-concept study



- Human carotid artery specimens were analyzed by photon counting CT and histologically.
- HU of each plaque type were measured in the energy of 45, 70, 90 and 180 keV.
- Using the mixed effect model, the relationship between HU of plaque type and energy was evaluated as the following formula:
  $HU=b_0 + b_1*log(Energy) + (1|ROI) + Error$
- Each coefficient (b1) was compared among different plaque type.



Shami, Gonçalves et al. European Radiology Experimental (2024) 8:14

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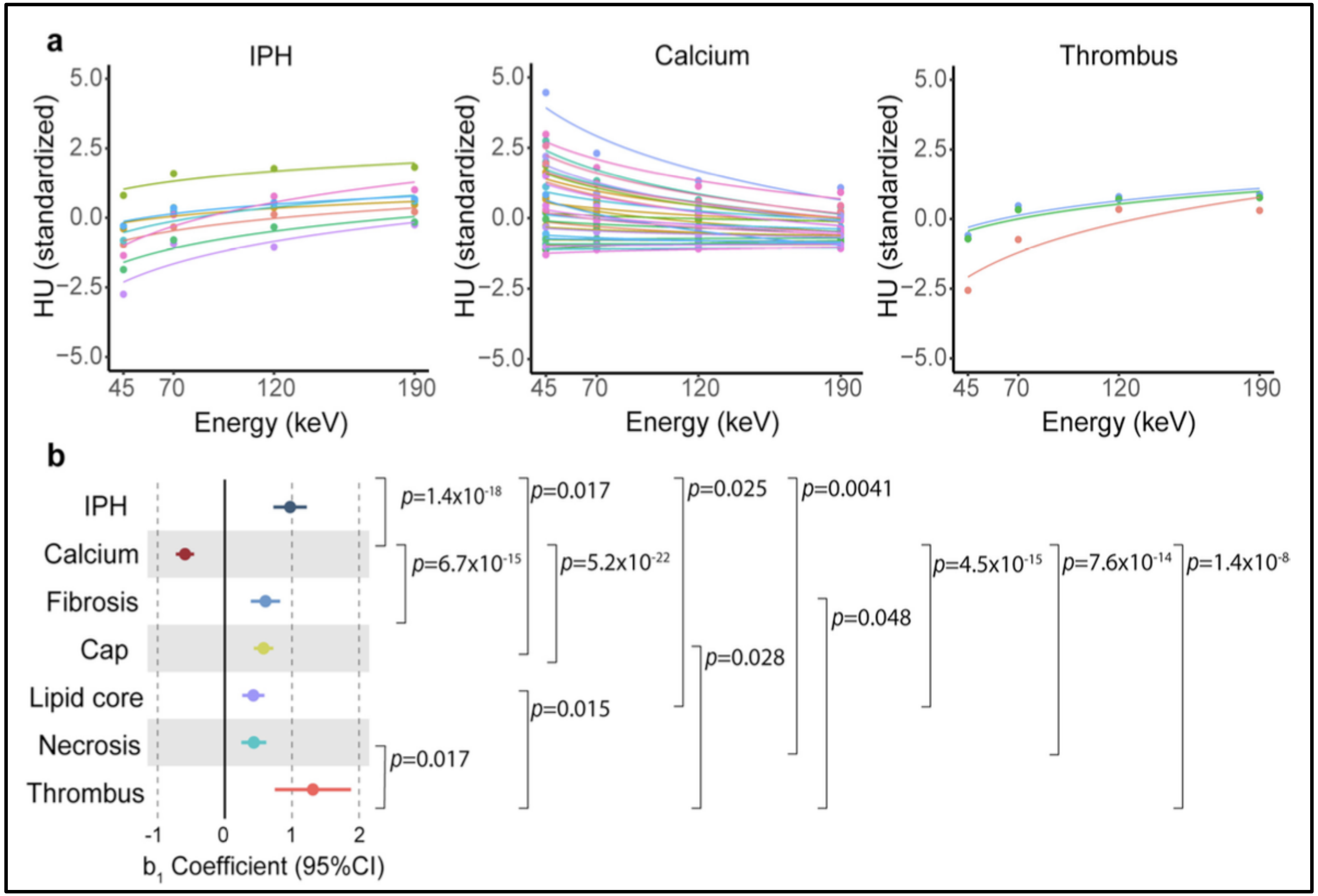
Atherosclerotic plaque features relevant to rupture-risk detected by clinical photon-counting CT *ex vivo*: a proof-of-concept study



Intraplaque hemorrhage was disccernible from fbrous cap, lipids and necrosis.
Thrombus was distingguishable from fibrosis, fibrous cap, lipids and necrosis.

Photon counting CT may enable us to distinguish plaque features such as hemorrhage and thrombus.

Shami et al. European Radiology Experimental (2024) 8:14

Conclusion

- CCTA is an emerging non-invasive imaging tool to screen patients with vulnerable plaques by providing comprehensive assessment of coronary arteries including plaque morphology, plaque burden, hemodynamic characteristics and perivascular fat inflammation.
- Autopsy studies with post-mortem CTA in patients with sudden death suggested that plaque enhancement is as a non-invasive marker of inflammation.
- High risk plaque characteristics on CTA include Low attenuation plaque (LAP), positive remodelling, napkin-ring sign and spotty calcification. LAP is a strong predictor of future MI. Perivascular fat and use of AI for quantification of plaque/ hemodynamics could further improve the risk prediction.
- A new generation of CT, – photon-counting CT-, will further improve spatial resolution and may enable to further characterise the individual feature of vulnerable plaque such as haemorrhage and thrombus.