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IMAGING NON INVASIVO NELLA STRATIFICAZIONE E RIDUZIONE DEL RISCHIO CARDIOVASCOLARE



AGENDA

- Calcio coronarico
- Valutazione luminale e di parete
- Caratterizzazione di placca e caratteristiche di vulnerabilità
- Infiammazione del tessuto adiposo perivascolare
- Prospettive future



BACKGROUND

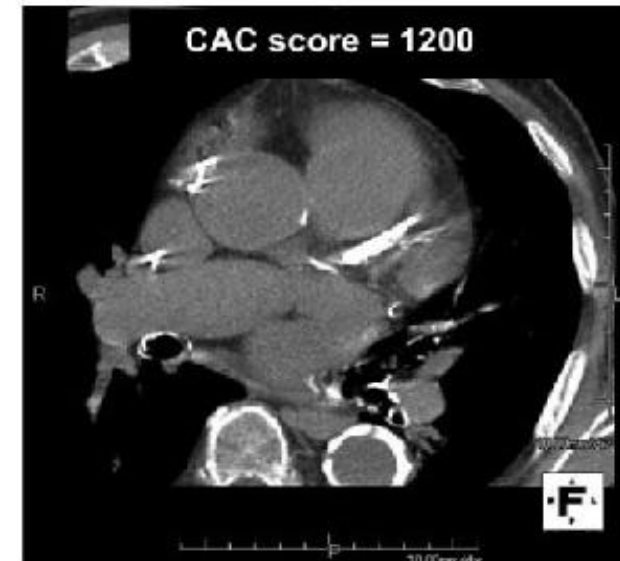
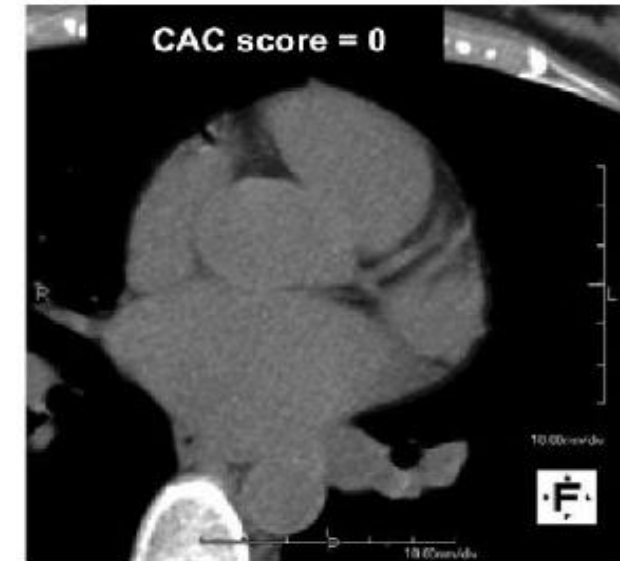


- TC ha visto un grande sviluppo tecnologico negli ultimi 10 anni
- Incremento dei detettori con progressivo miglioramento della risoluzione spaziale e temporale
- Implementazione di sistemi per la riduzione della dose (in media < 3 mSv)
- Maggiore possibilità di impiego nello studio delle coronarie

CALCIUM SCORE CORONARICO

CALCIUM SCORE CORONARICO (CACS)

- Scansioni a bassa dose di radiazioni (≤ 1 mSv), ECG-gated, ottenute senza utilizzo di mdc, a bassa risoluzione spaziale, elaborate con software che permette di calcolare **Calcium Score sec. Agatston**
- Viene espresso sia in valore assoluto sia come percentile all'interno di un gruppo omogeneo per età, sesso, razza (percentile MESA)
- Non correla con stenosi luminale



ORIGINAL ARTICLE

Coronary Calcium as a Predictor of Coronary Events in Four Racial or Ethnic Groups

Table 3. Risk of Coronary Events Associated with Increasing Coronary-Artery Calcium Score after Adjustment for Standard Risk Factors.*

Coronary-Artery Calcium Score	No./No. at Risk	Major Coronary Event†			Any Coronary Event	
		Hazard Ratio (95% CI)	P Value		Hazard Ratio (95% CI)	P Value
0	8/3409	1.00			15/3409	1.00
1–100	25/1728	3.89 (1.72–8.79)	<0.001		39/1728	3.61 (1.96–6.65)
101–300	24/752	7.08 (3.05–16.47)	<0.001		41/752	7.73 (4.13–14.47)
>300	32/833	6.84 (2.93–15.99)	<0.001		67/833	9.67 (5.20–17.98)
Log ₂ (CAC+1)‡		1.20 (1.12–1.29)	<0.001			1.26 (1.19–1.33)

* CAC denotes coronary-artery calcium score, and CI confidence interval.
† Major coronary events were myocardial infarction and death from coronary heart disease.
‡ Each unit increase in log₂(CAC+1) represents a doubling of the coronary-artery calcium score.

Aumentati valori di CACS correlano con eventi coronarici

**CUT OFF > 300
OPPURE > 75%**
identifica pazienti a maggior rischio

Coronary Artery Calcium Score Combined With Framingham Score for Risk Prediction in Asymptomatic Individuals

Figure 1. Predicted 7-Year Event Rates From COX Regression Model for CHD Death or Nonfatal Myocardial Infarction for Categories of FRS or CACS

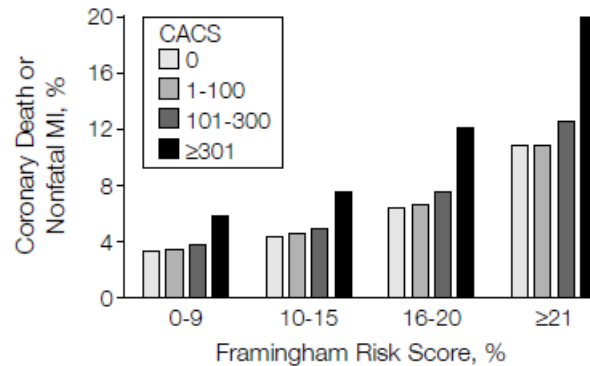
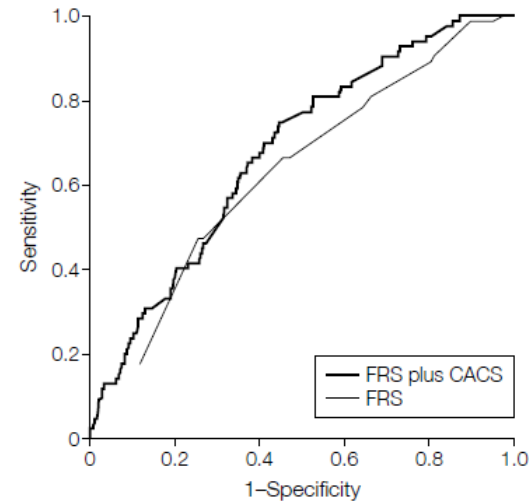


Figure 2. Predicting Coronary Death or Nonfatal Myocardial Infarction for Framingham Risk Scores (FRS)



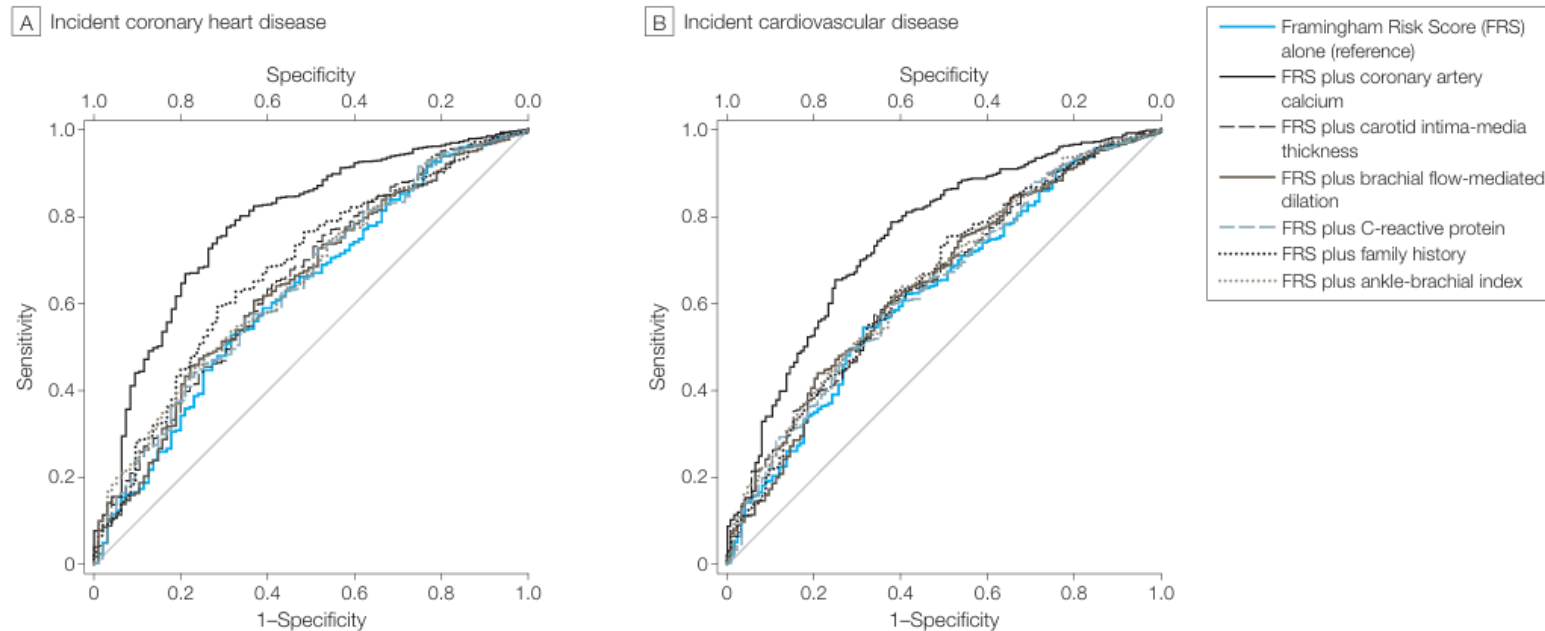
The receiver operating characteristic curves illustrate FRS alone or plus coronary artery calcium score (CACS). Areas under the curves are 0.63 for FRS alone, 0.68 for FRS plus CACS. $P < .001$ for the comparison between the 2 areas.

- CACS E' un marker di malattia aterosclerotica e correla con eventi CV
- Permette di riclassificare i pazienti rispetto ai fattori di rischio tradizionali (Framingham risk score)

Comparison of Novel Risk Markers for Improvement in Cardiovascular Risk Assessment in Intermediate-Risk Individuals

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Figure. Receiver Operator Characteristic Curves Showing Area Under the Curve for Incident Coronary Heart Disease and Incident Cardiovascular Disease in Intermediate-Risk MESA Participants



A, Receiver operator characteristic curves showing area under the curve for FRS alone, 0.623; FRS plus coronary artery calcium, 0.784 ($P<.001$); FRS plus intima-media thickness, 0.652 ($P=.01$); FRS plus flow-mediated dilation, 0.639 ($P=.06$); FRS plus high-sensitivity C-reactive protein, 0.640 ($P=.03$); FRS plus family history, 0.675 ($P=.001$); and FRS plus ankle-brachial index, 0.650 ($P=.01$). B, Receiver operator characteristic curves showing area under the curve for FRS alone, 0.623; FRS plus coronary artery calcium, 0.784 ($P<.001$); FRS plus intima-media thickness, 0.652 ($P=.01$); FRS plus flow-mediated dilation, 0.639 ($P=.06$); FRS plus high-sensitivity C-reactive protein, 0.640 ($P=.03$); FRS plus family history, 0.675 ($P=.001$); and FRS plus ankle-brachial index, 0.650 ($P=.01$). MESA indicates Multi-Ethnic Study of Atherosclerosis.

CACS migliora la classificazione dei pazienti a rischio intermedio rispetto ad altri biomarker (IMT, PCR...)

Coronary Calcium Score and Cardiovascular Risk

CENTRAL ILLUSTRATION Proposed Decision-Making Approach to Selective Use of Coronary Artery Calcium Measurement for Risk Prediction				
Using 10-year ASCVD risk estimate plus coronary artery calcium (CAC) score to guide statin therapy				
Patient's 10-year atherosclerotic cardiovascular disease (ASCVD) risk estimate:	<5%	5-7.5%	>7.5-20%	>20%
Consulting ASCVD risk estimate alone	Statin not recommended	Consider for statin	Recommend statin	Recommend statin
Consulting ASCVD risk estimate + CAC				
If CAC score =0	Statin not recommended	Statin not recommended	Statin not recommended	Recommend statin
If CAC score >0	Statin not recommended	Consider for statin	Recommend statin	Recommend statin
Does CAC score modify treatment plan?	✗ CAC not effective for this population	✓ CAC can reclassify risk up or down	✓ CAC can reclassify risk up or down	✗ CAC not effective for this population
Greenland, P. et al. J Am Coll Cardiol. 2018;72(4):434-47.				
The figure shows a modified approach to the guideline-based decision making by incorporating a consideration of coronary artery calcium (CAC) testing to reclassify a patient's risk up or down where it would make a clinically important change in the clinical decision. Adapted with permission from Nasir et al. (90).				

Risvolti pratici: proposta di riclassificazione del rischio dei pazienti che integri CACS e le conseguenti modifiche all'introduzione di terapia con statina in prevenzione primaria

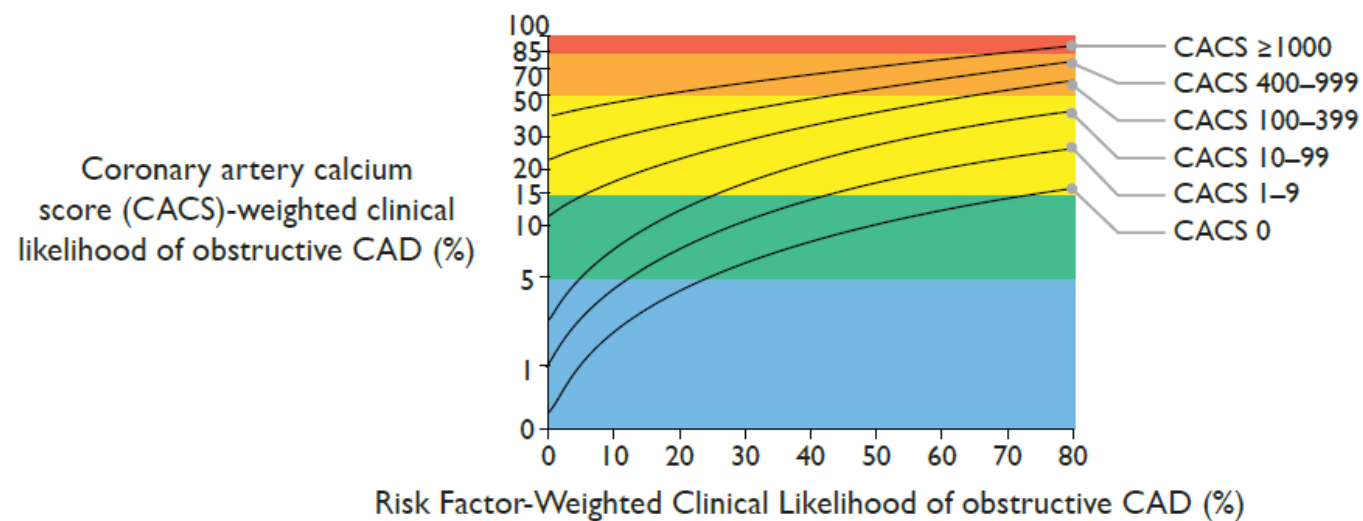
CALCIUM SCORE CORONARICO

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In individuals with a *low* (>5%–15%) pre-test likelihood of obstructive CAD, CACS should be considered to reclassify subjects and to identify more individuals with very low ($\leq 5\%$) CACS-weighted clinical likelihood.

IIa

B



CALCIUM SCORE CORONARICO

Pro:	Facilità di acquisizione, valore prognostico indipendente e riclassificazione del rischio in pazienti asintomatici <i>senza</i> nota CAD
Contro:	Non utilizzabile in pazienti con nota CAD o già in terapia con statina (aumenta componente calcifica della placca); coronaropatia a maggior rischio è prevalentemente <i>soft</i> e non calcifica

Modificato da: Cardiovascular Risk stratification by coronary computed tomography angiography imaging: current state-of-the-art.
Antonopoulos et al, Eur J of Preventive Cardiology (2022) 29, 608-624

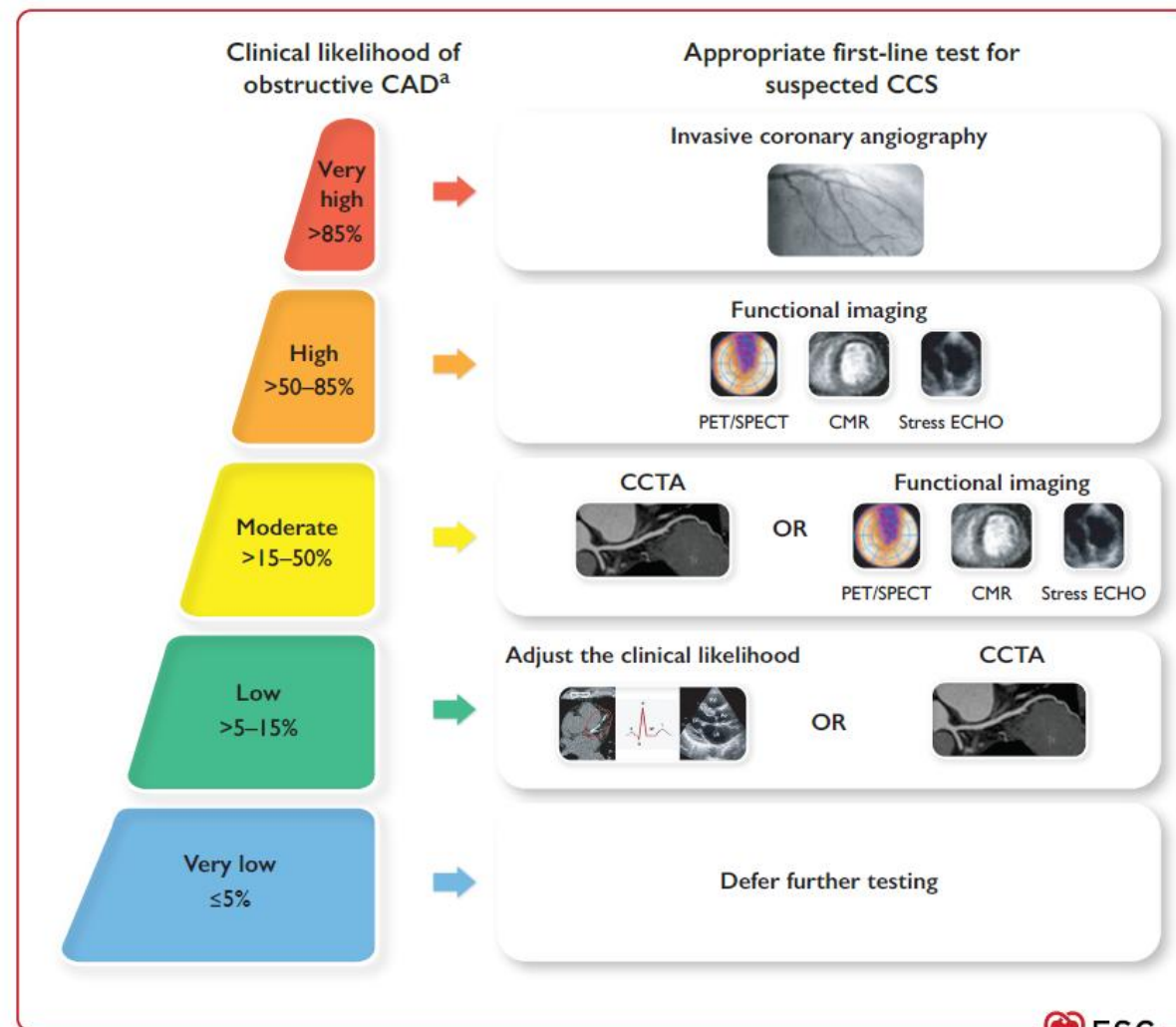
VALUTAZIONE LUMINALE E DI PARETE

VALUTAZIONE LUMINALE E DI PARETE

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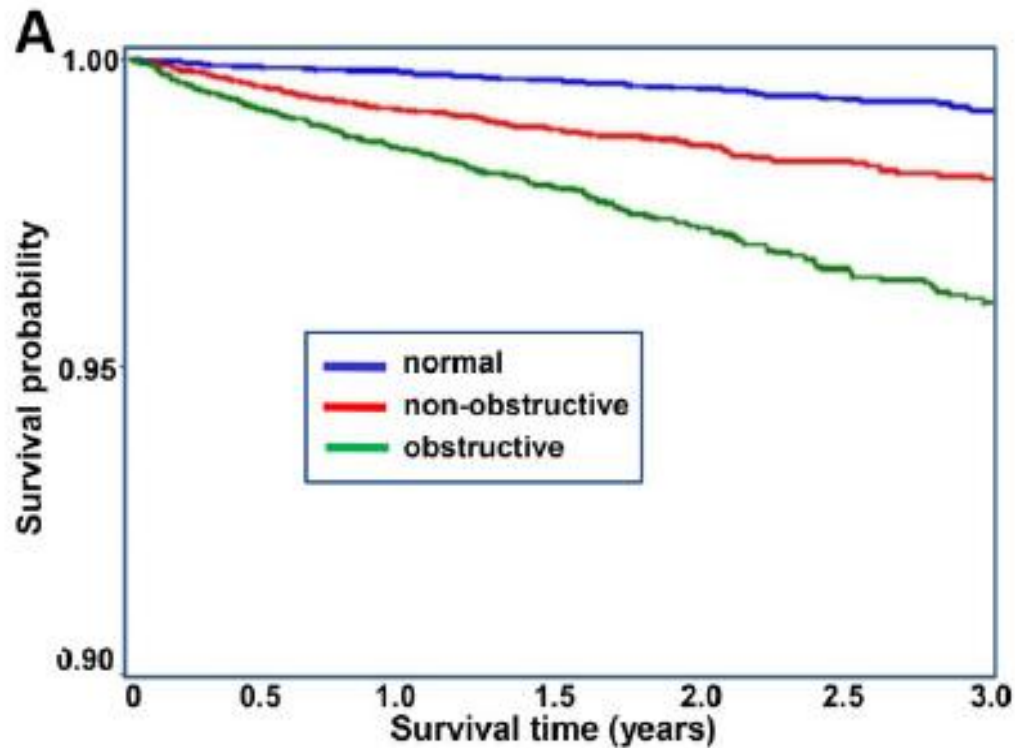
Recommendations	Class ^a	Level ^b
In individuals with suspected CCS and low or moderate (>5%–50%) pre-test likelihood of obstructive CAD, CCTA is recommended to diagnose obstructive CAD and to estimate the risk of MACE. ^{33,34,145,212,214–221}	I	A
CCTA is recommended in individuals with low or moderate (>5%–50%) pre-test likelihood of obstructive CAD to refine diagnosis if another non-invasive test is non-diagnostic. ²²²	I	B

2024 ESC Guidelines for the management of chronic coronary syndromes



Age- and Sex-Related Differences in All-Cause Mortality Risk Based on Coronary Computed Tomography Angiography Findings

Results From the International Multicenter CONFIRM (Coronary CT Angiography Evaluation for Clinical Outcomes: An International Multicenter Registry) of 23,854 Patients Without Known Coronary Artery Disease



STUDIO CONFIRM:

- Non solo la coronaropatia ostruttiva ma anche quella **non ostruttiva** diagnosticata con CCTA è associata a maggiore incidenza di eventi CV
- Lo scopo del referto TC è quello di spostare l'attenzione del clinico dalla stenosi alla **presenza o assenza** della malattia aterosclerotica
- Pazienti con coronaropatia non ostruttiva possono essere avviati a terapia medica tailorizzata (es. Statina, ASA...)

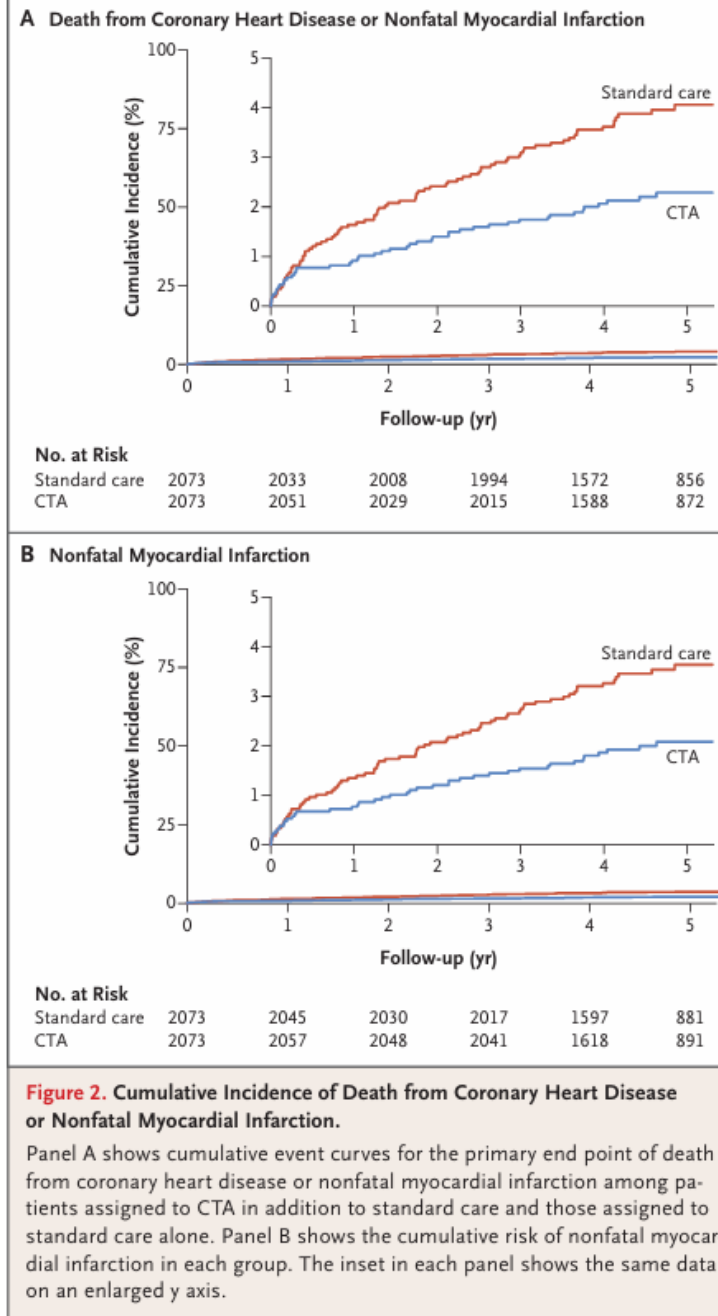
ORIGINAL ARTICLE

Coronary CT Angiography and 5-Year Risk of Myocardial Infarction

The SCOT-HEART Investigators*

I risultati dello SCOT-HEART trial A 5 anni:

- CCTA ha una migliore capacità di **stratificazione della malattia coronarica**
- **maggiore impiego delle terapie farmacologiche**
- **migliore selezione** dei pazienti da avviare a coronarografia
- **significativa riduzione di eventi cardiovascolari a 5 anni rispetto allo standard of care**



Prognostic Value of Nonobstructive and Obstructive Coronary Artery Disease Detected by Coronary Computed Tomography Angiography to Identify Cardiovascular Events

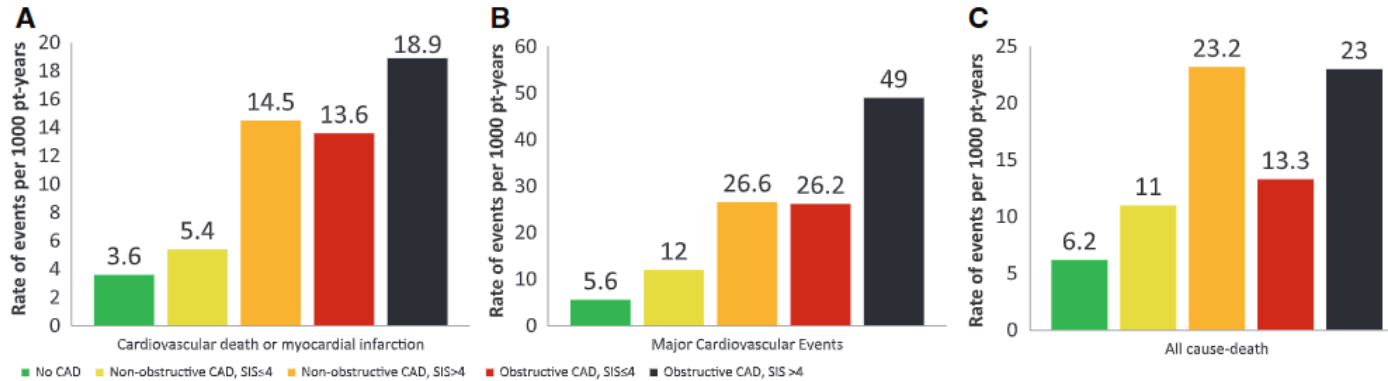


Figure 1. A, Rate of cardiovascular death or myocardial infarction according to the presence, severity, and extent of coronary artery disease (CAD). There is a significant difference ($P < 0.01$) in rates for all comparisons except nonobstructive CAD with segment involvement score (SIS) > 4 and obstructive CAD with SIS ≤ 4 . B, Rate of major cardiovascular events. C, Rate of all-cause death. Log-rank $P < 0.01$ for all graphs.

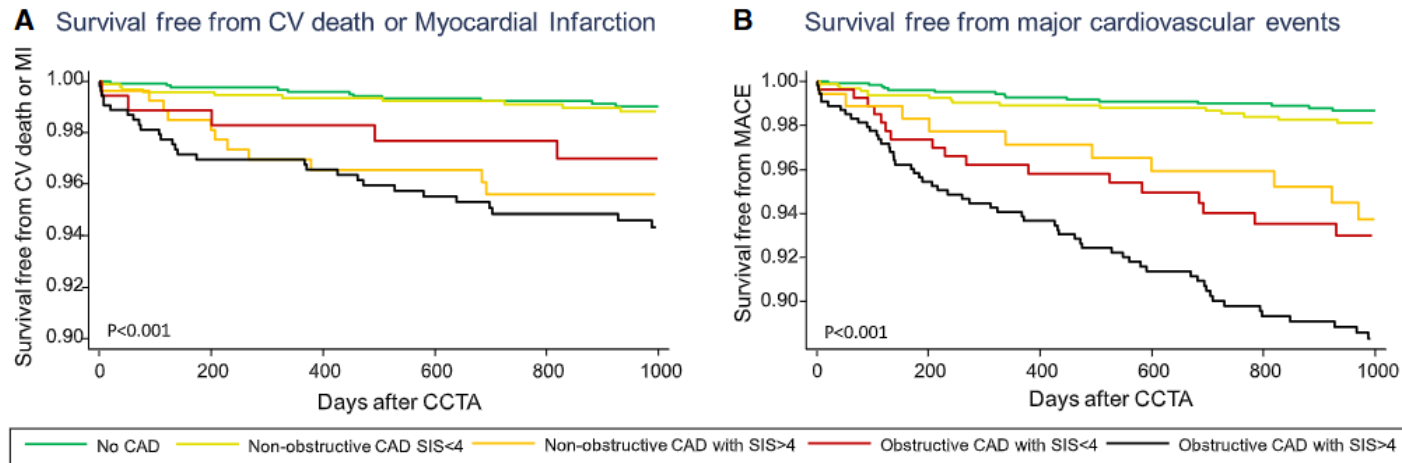


Figure 3. A, Survival free from cardiovascular (CV) death or myocardial infarction (MI) according to the presence, severity, and extent of coronary artery disease (CAD). B, Survival free from major cardiovascular events. CCTA indicates coronary computed tomography angiography; and SIS, segment involvement score.

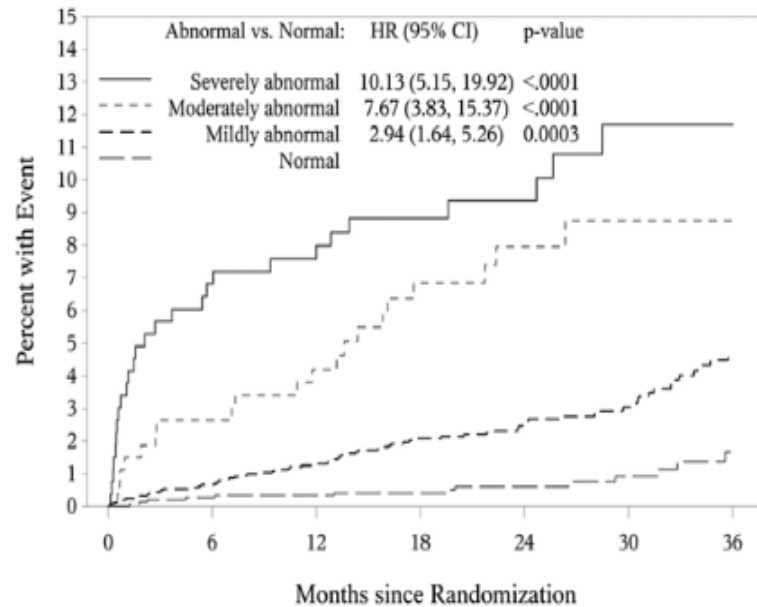
Pazienti con
coronaropatia non
ostruttiva ma **estesa**
hanno rischio
comparabile a pazienti
con coronaropatia
ostruttiva

Prognostic Value of Noninvasive Cardiovascular Testing in Patients With Stable Chest Pain

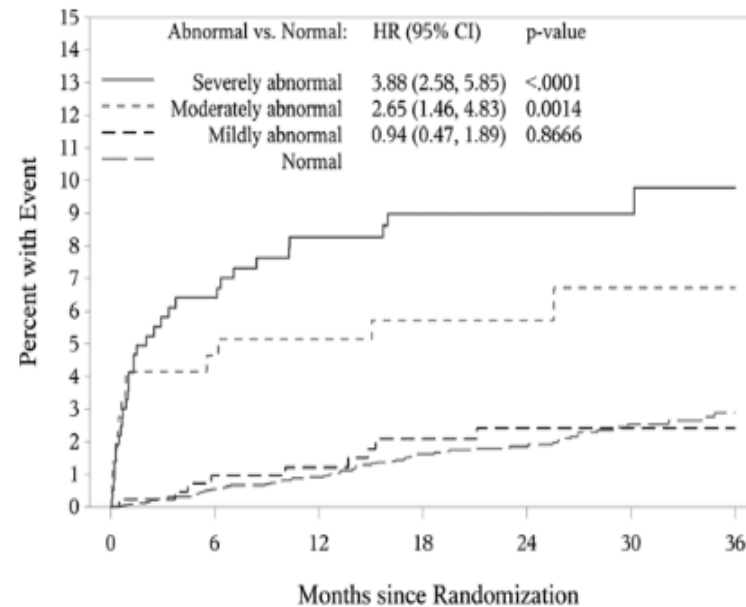
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Insights From the PROMISE Trial (Prospective Multicenter Imaging Study for Evaluation of Chest Pain)

A Anatomic Testing



B Functional Testing

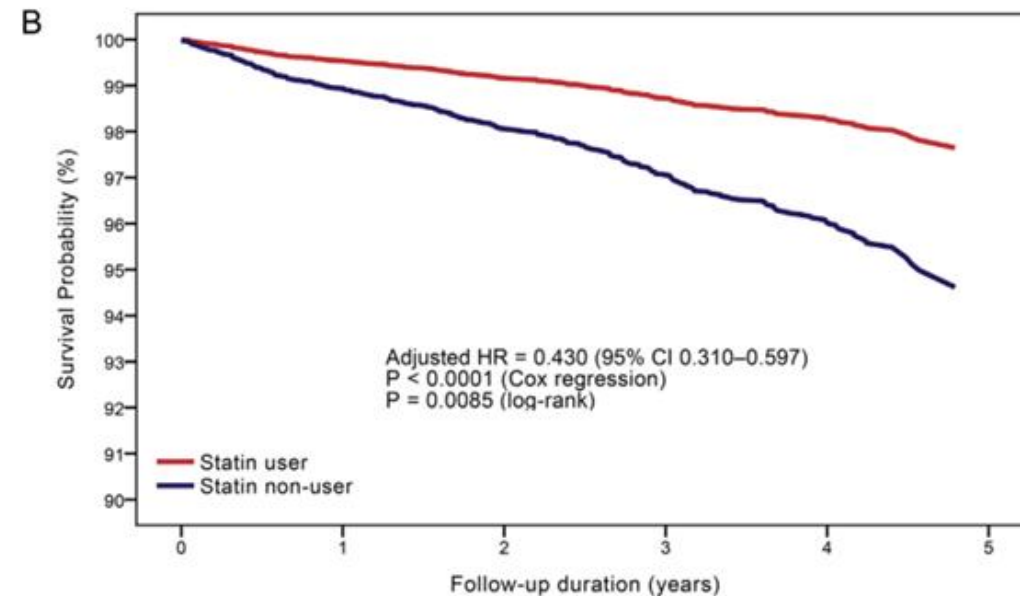
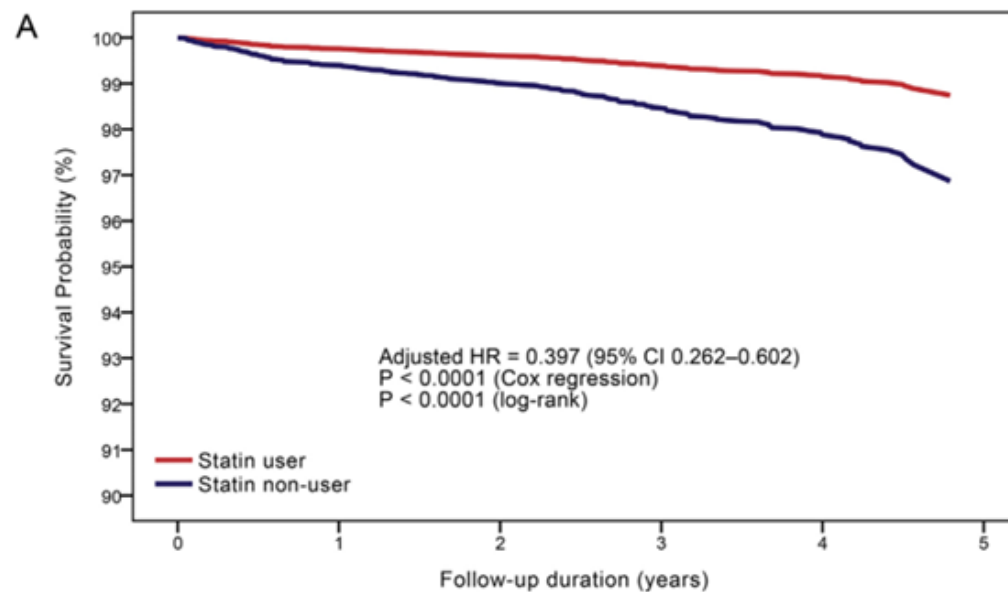


CCTA permette diagnosi di coronaropatia non ostruttiva **lieve** con migliore stratificazione del rischio rispetto a test funzionale

Hoffman U et al, Circulation 2017

Statin therapy is associated with lower all-cause mortality in patients with non-obstructive coronary artery disease

In-Chang Hwang^{a, b}, Joo-Yeong Jeon^c, Younhee Kim^d, Hyue Mee Kim^{a, b},
Yeonyee E. Yoon^{a, e}, Seung-Pyo Lee^{a, b}, Hyung-Kwan Kim^{a, b}, Dae-Won Sohn^{a, b},
Jidong Sung^{f, g, **, 1}, Yong-Jin Kim^{a, b, *, 1}

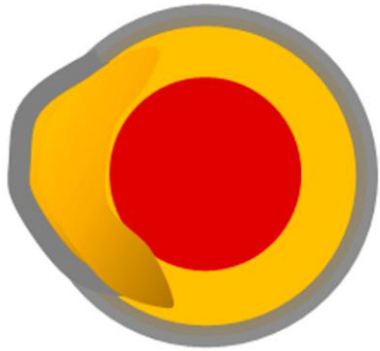


CARATTERIZZAZIONE DI PLACCA

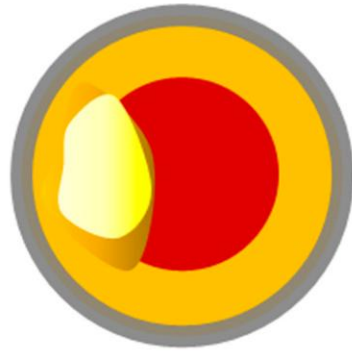
PLACCA AD ALTO RISCHIO (HRP)

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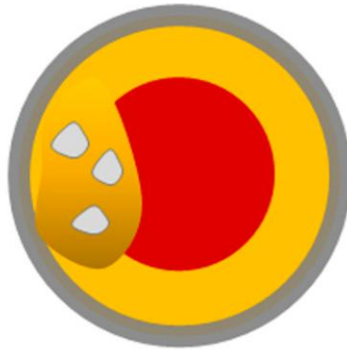
Positive remodeling



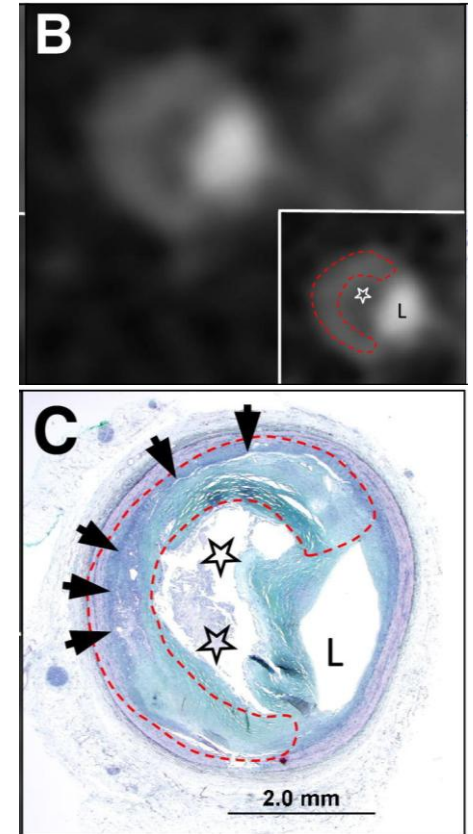
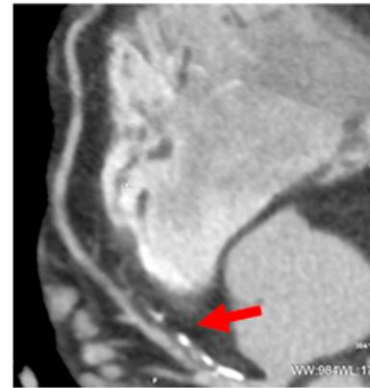
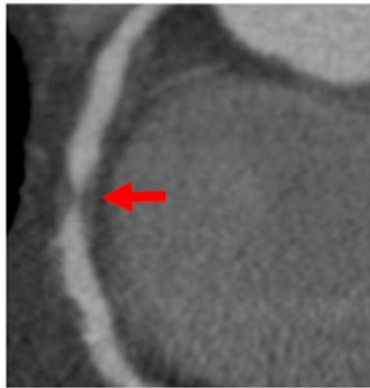
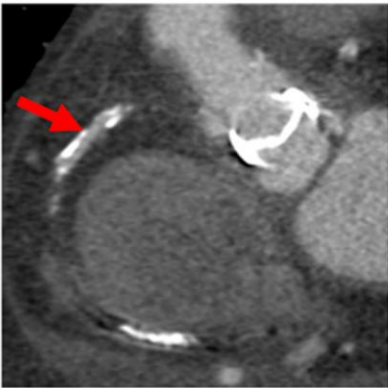
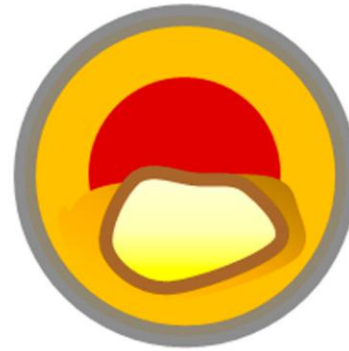
Low-attenuation plaque



Spotty calcification



Napkin-rings sign



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

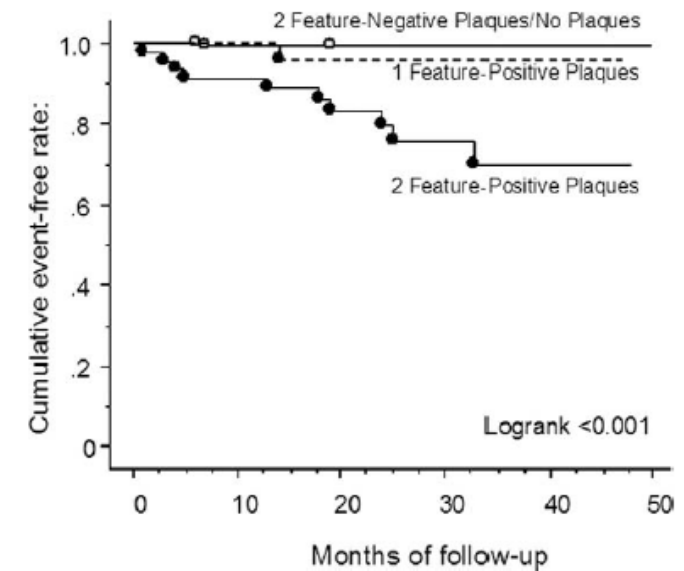
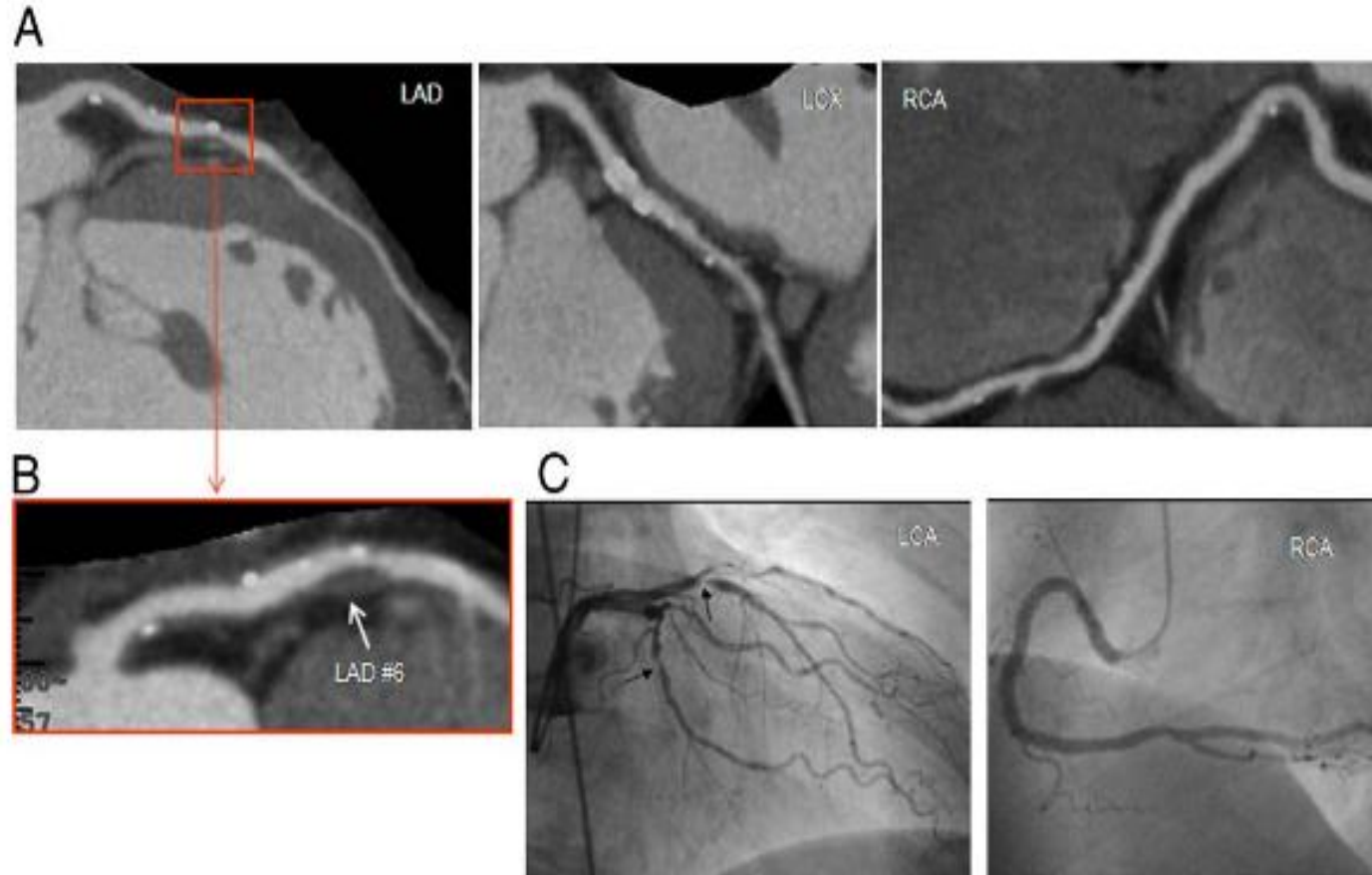


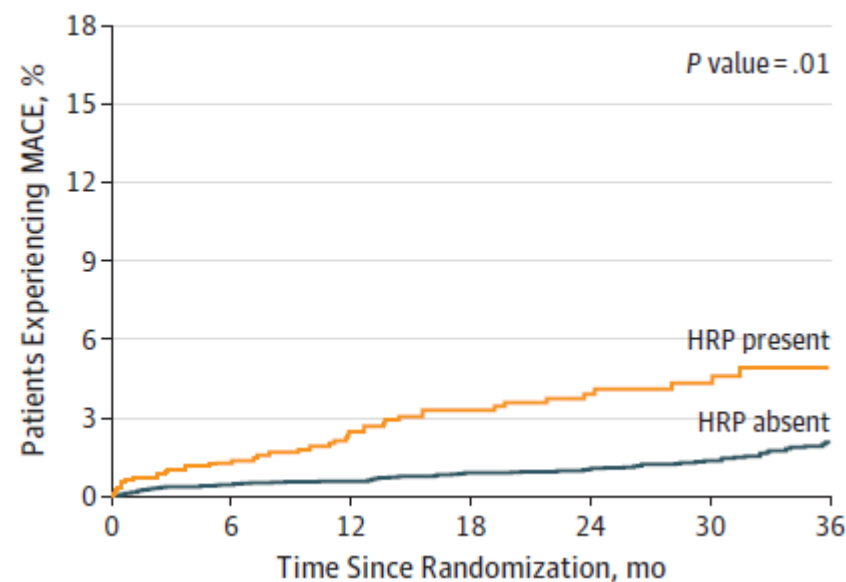
Figure 3 Kaplan-Meier Curve for Development of ACS on the Basis of Plaque Characteristics

Patient stratification according to the presence of 2- and 1-feature positive, and 2-feature negative plaques/no plaques. The y-axis represents cumulative event-free rate (log-rank test, $p < 0.001$). ACS = acute coronary syndrome.

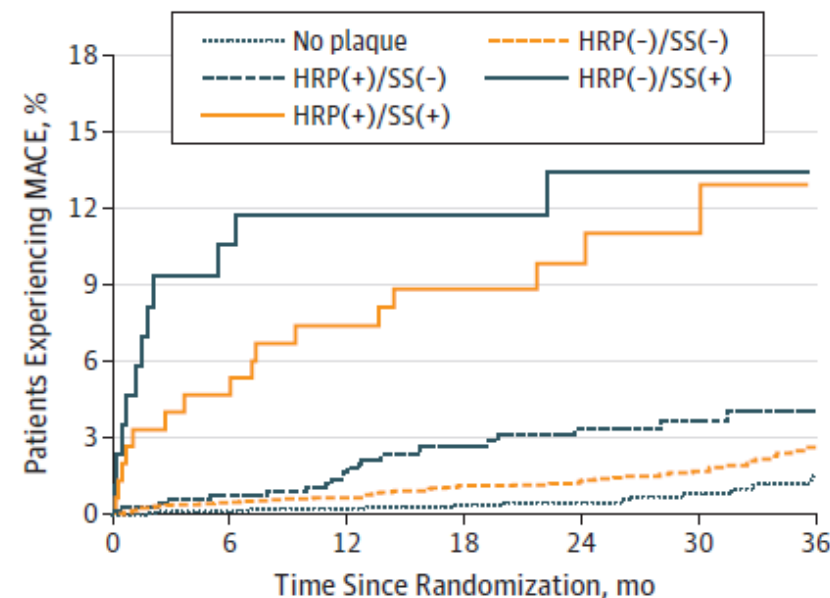
Use of High-Risk Coronary Atherosclerotic Plaque Detection for Risk Stratification of Patients With Stable Chest Pain

A Secondary Analysis of the PROMISE Randomized Clinical Trial

A Kaplan-Meier estimates stratified by HRP

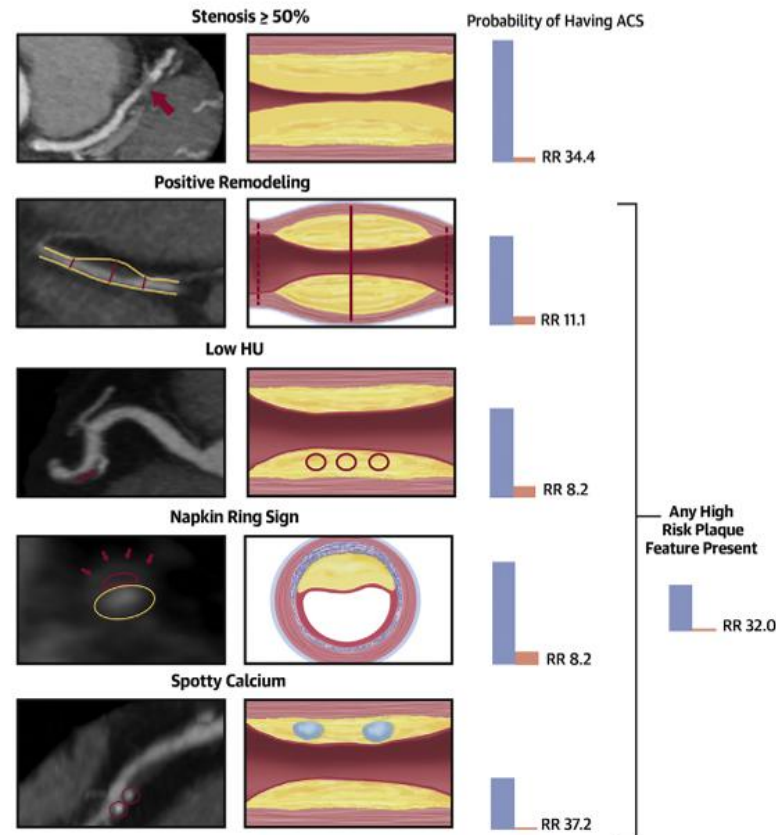
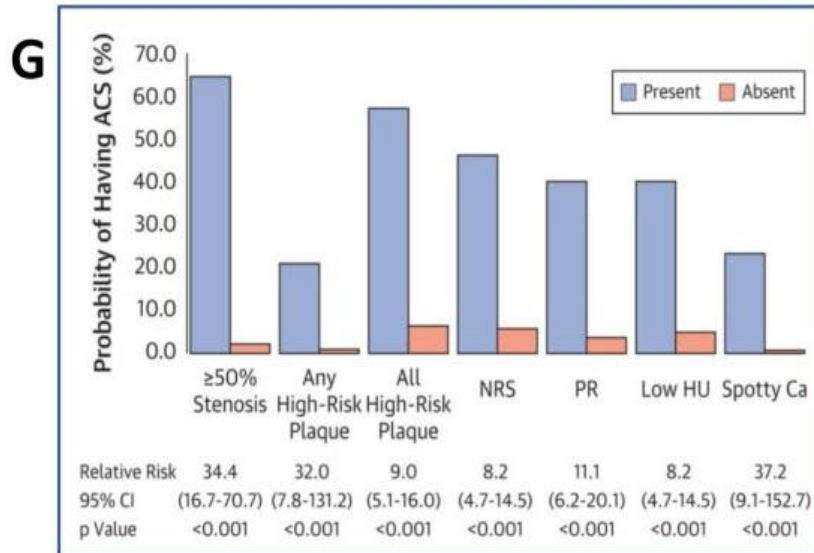
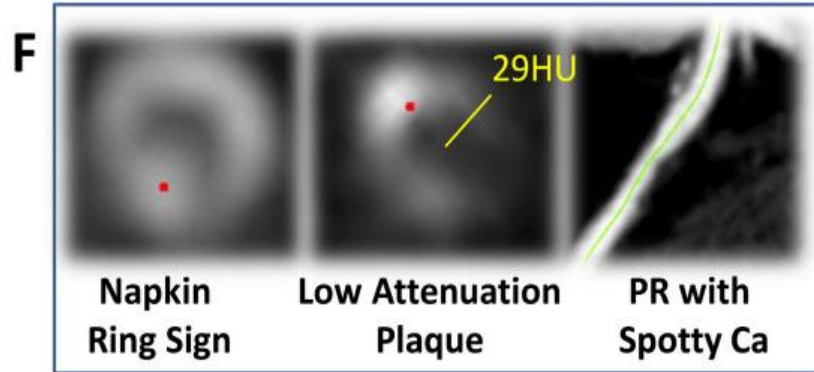


B Kaplan-Meier estimates stratified by HRP and SS



High-Risk Plaque Detected on Coronary CT Angiography Predicts Acute Coronary Syndromes Independent of Significant Stenosis in Acute Chest Pain

Results From the ROMICAT-II Trial



CENTRAL ILLUSTRATION Significant Stenosis and High-Risk Coronary Plaque Features and Their Association With the Probability of ACS During Index Hospitalization

Pazienti con dolore toracico, TnI ed ECG negativi sottoposti a CCTA:

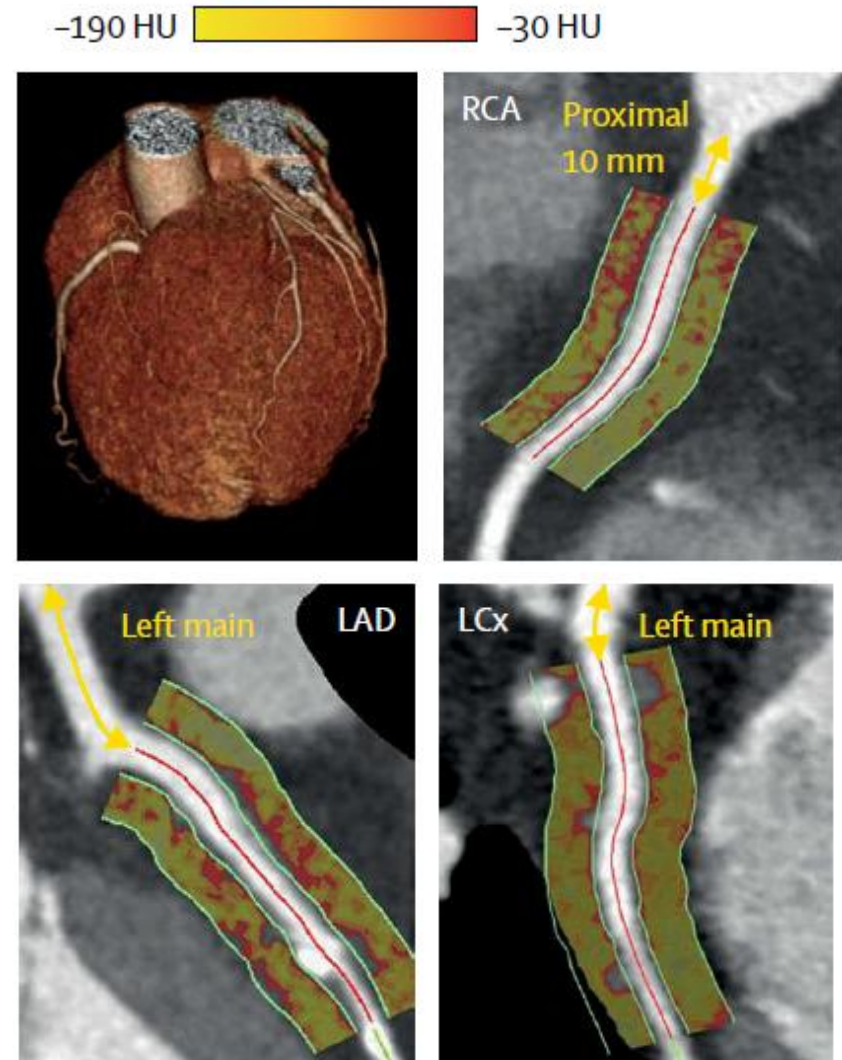
La presenza di placche ad alto rischio aumenta la probabilità di diagnosi di SCA indipendentemente dalla presenza di coronaropatia ostruttiva

INFIAMMAZIONE CORONARICA: IMAGING DEL TESSUTO ADIPOSO PERICORONARICO

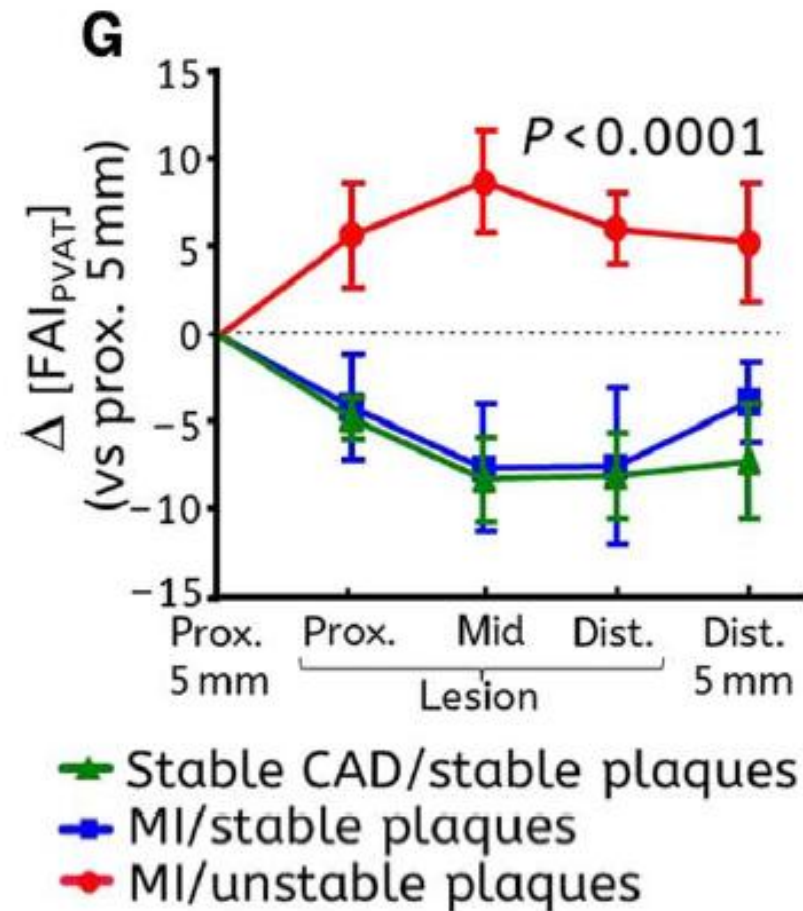
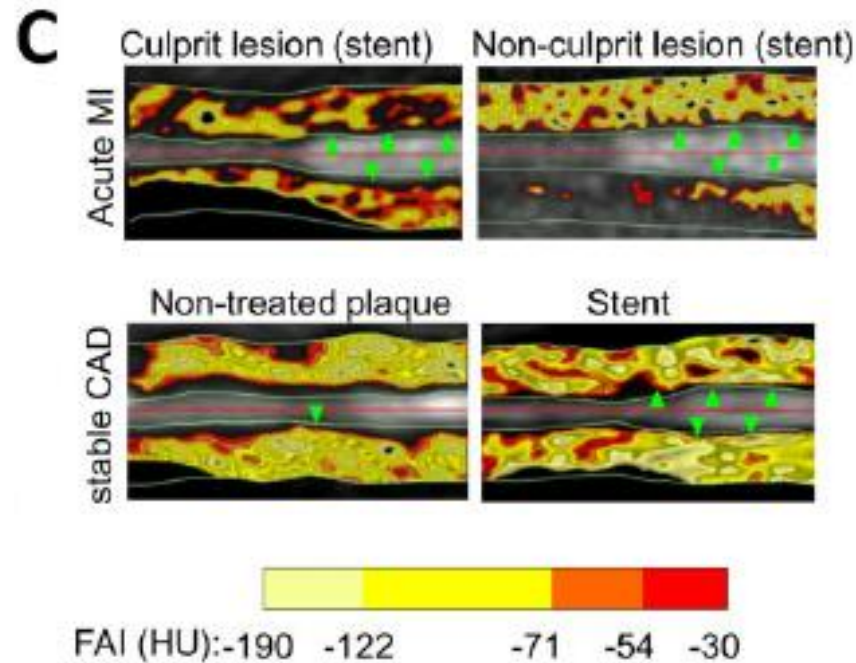
INFIAMMAZIONE PERIVASCOLARE

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- Comunicazione bidirezionale tra parete arteriosa e tessuto adiposo perivascolare (PVAT) attraverso rilascio di citochine
- PVAT costituisce un “sensore” di infiammazione vascolare e la sua composizione si modifica in base ad essa
- FAI (Fat attenuation Index) perivascolare può essere valutato con TC ed è un marker dinamico di infiammazione che individua placche instabili o ad alto rischio

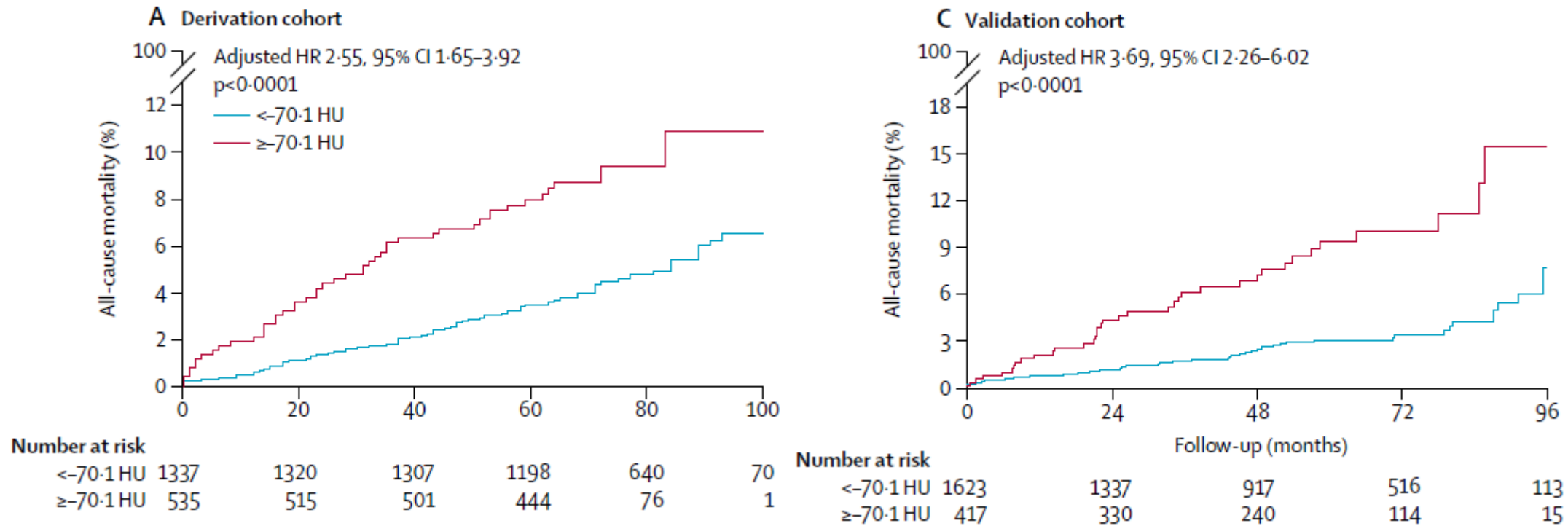


Detecting human coronary inflammation by imaging perivascular fat



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

Cut off = - 70 UH



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

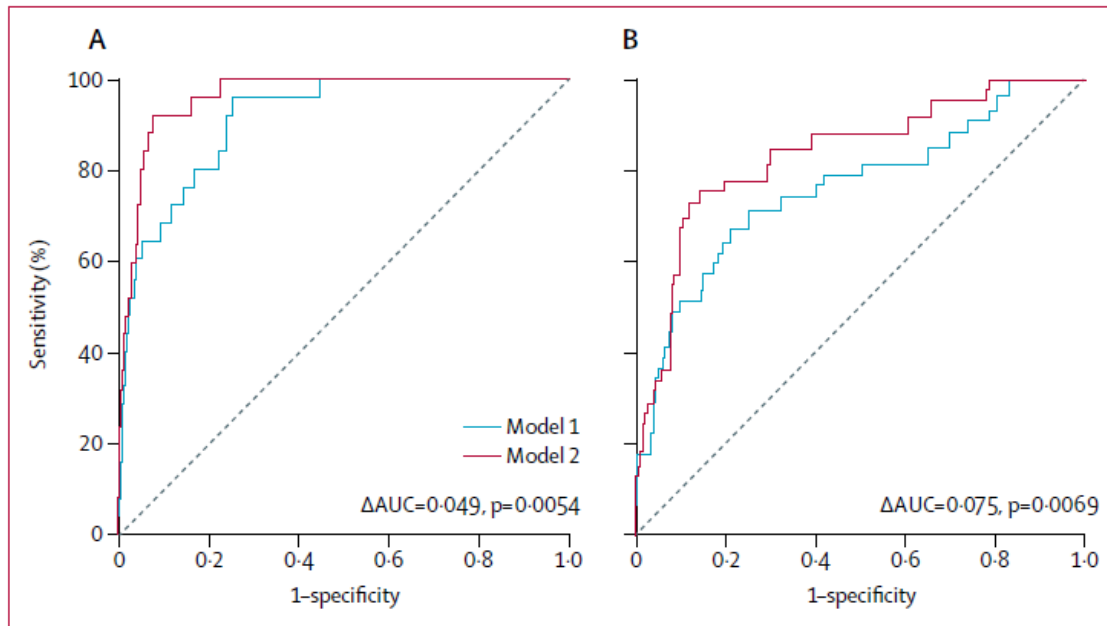


Figure 3: Incremental prognostic value of the perivascular FAI beyond current coronary CTA-based risk stratification

Comparison of time-dependent ROC curves (at 6 years) and respective AUC of two nested models for discrimination of cardiac mortality in the (A) derivation and (B) validation cohorts. Model 1 represents the current state-of-the-art in risk assessment and consisted of age, sex, risk factors (hypertension, hypercholesterolaemia, diabetes mellitus, smoker status, epicardial adipose tissue volume), modified Duke coronary artery disease index, and number of high-risk plaque features on coronary CTA. Model 2 incorporates perivascular FAI values (≥ -70.1 HU vs < -70.1 HU) into model 1. AUC=area under the curve. CTA=computed tomography angiography. FAI=fat attenuation index. HU=Hounsfield unit. ROC=receiver operating characteristic.

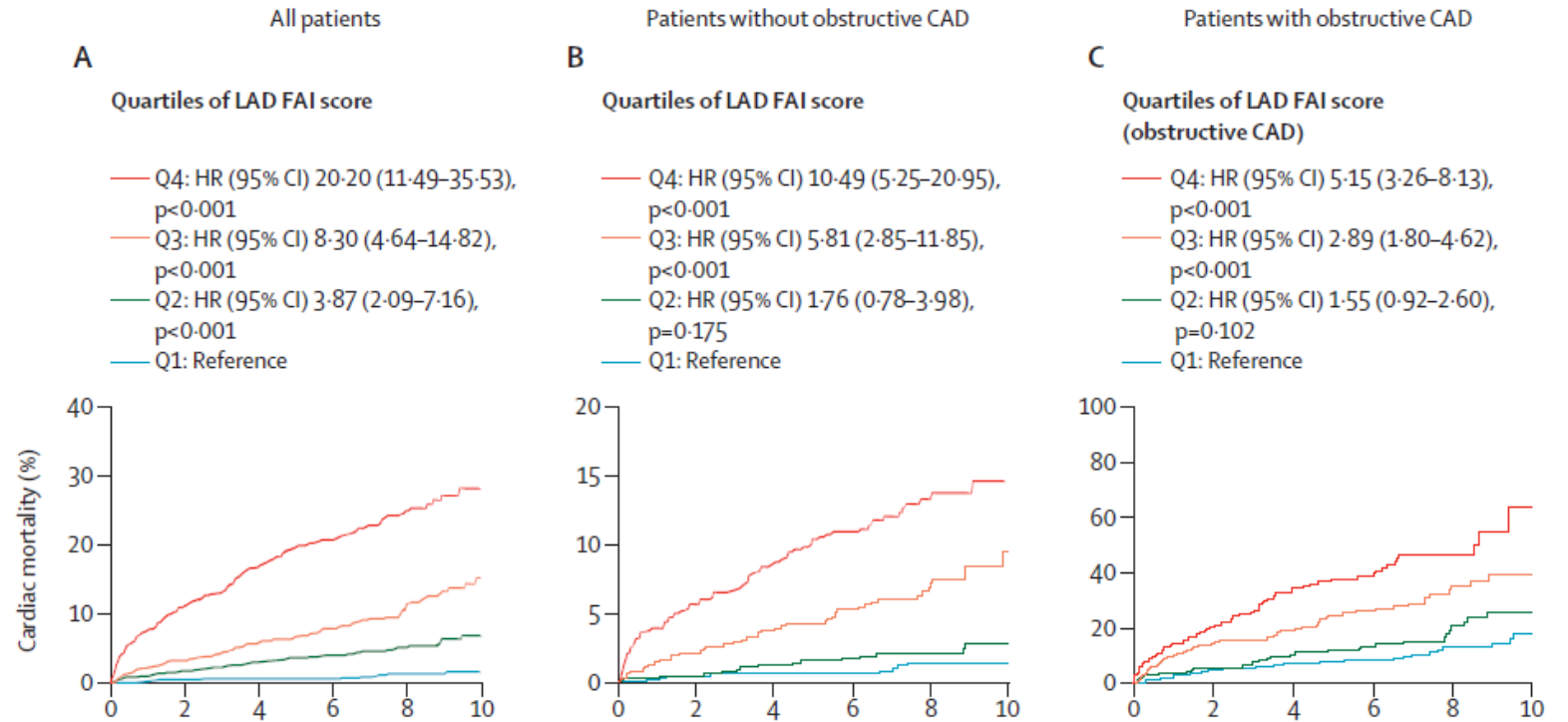
FAI migliora la stratificazione del rischio dei pazienti rispetto allo standard of care con valore prognostico indipendente rispetto a:

- FDR tradizionali
- Burden aterosclerotico
- Presenza di placche ad alto rischio

Inflammatory risk and cardiovascular events in patients without obstructive coronary artery disease: the ORFAN multicentre, longitudinal cohort study

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- 40091 pazienti arruolati
- FU medio 7,7 anni
- Valutazione FAI perivascolare
- AI risk-classification che integra FAI, burden di placca e fattori di rischio tradizionali

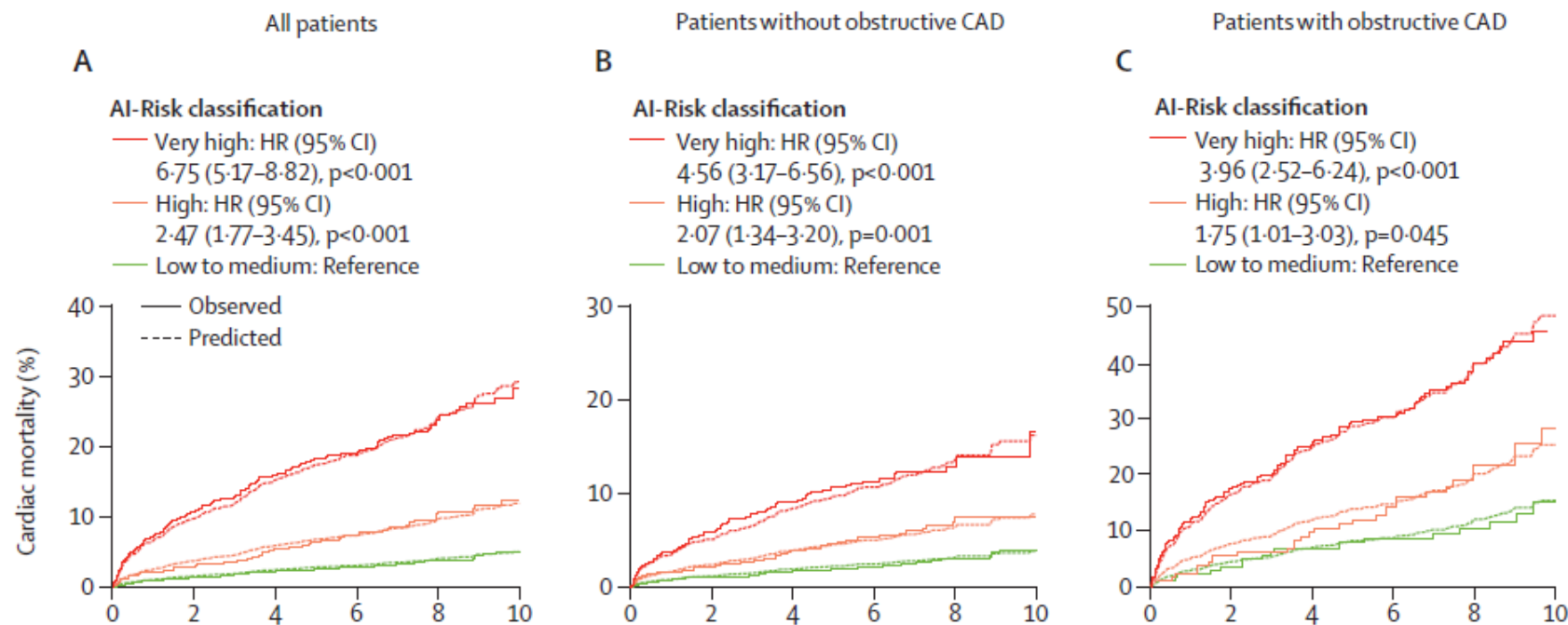


Inflammatory risk and cardiovascular events in patients without obstructive coronary artery disease: the ORFAN multicentre, longitudinal cohort study

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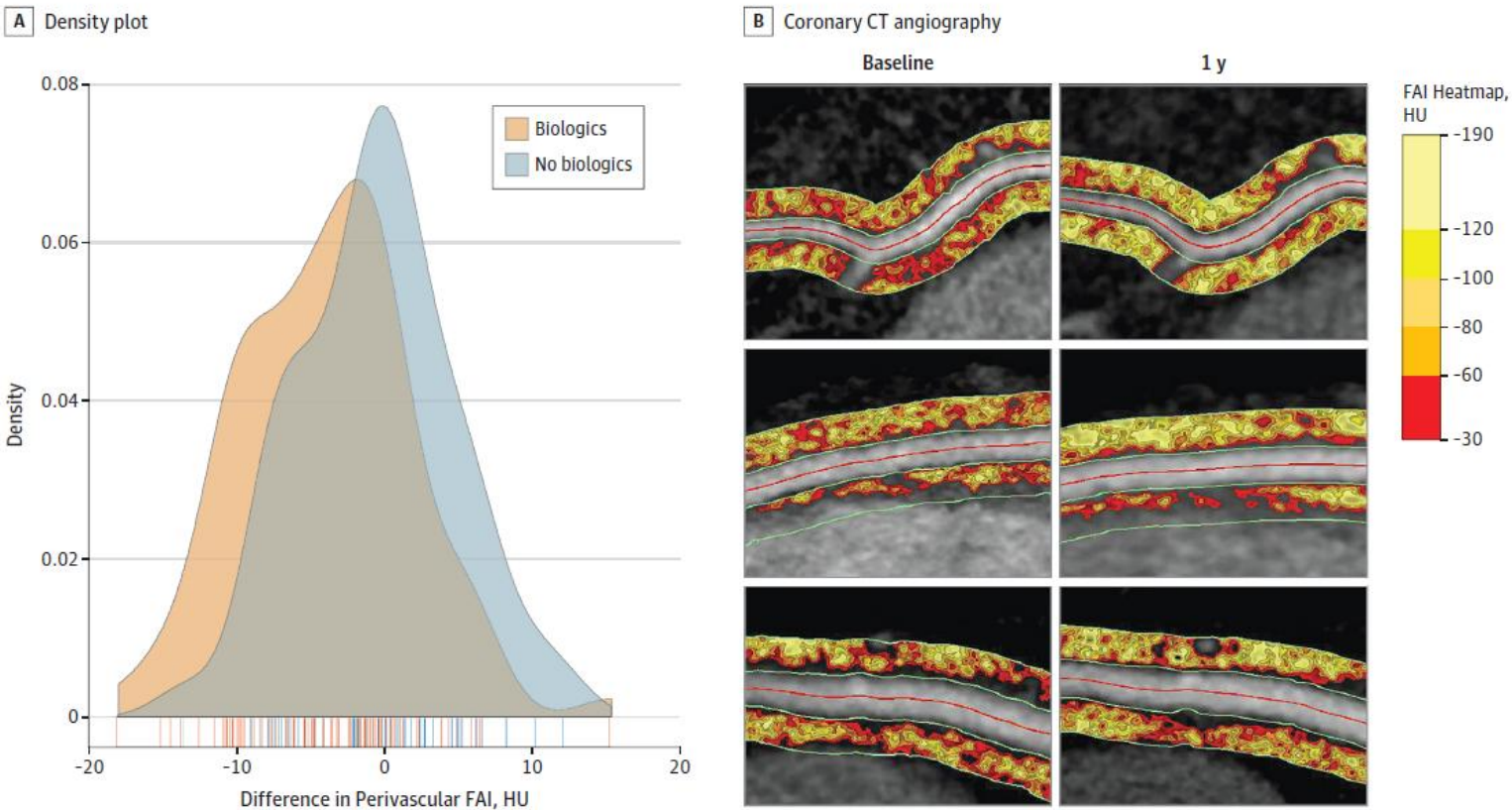
RISULTATI:

- Aumento di FAI ha potere predittivo indipendente per morte cardiaca e MACE rispetto a FDR tradizionali e presenza di CAD
- AI risk classification è predittivo di morte cardiaca



Association of Biologic Therapy With Coronary Inflammation in Patients With Psoriasis as Assessed by Perivascular Fat Attenuation Index

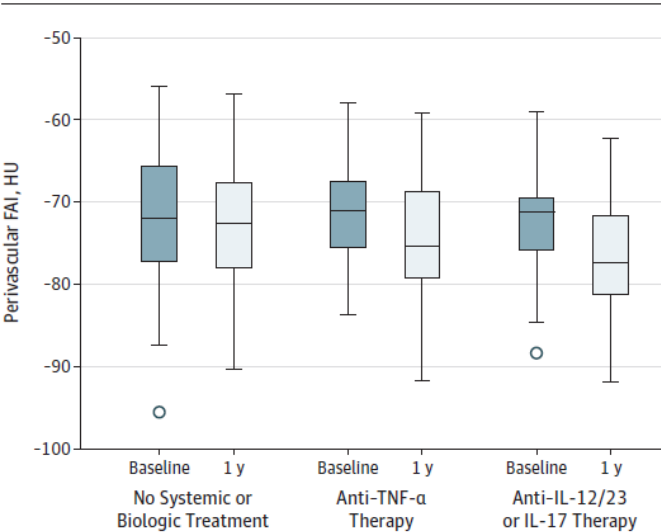
Figure 2. Response to Biologic Therapy During 1 Year in Patients With Psoriasis



A, Density plot depicting the changes in perivascular fat attenuation index (FAI) in patients with treated and untreated psoriasis during 1 year (FAI at follow-up minus FAI at baseline) ($P = .001$). B, Coronary computed tomography (CT) angiography images of the coronary arteries depicting the perivascular FAI

before and after biologic therapy at 1 year of follow-up for patients with excellent response (top), moderate response (middle), and modest response (bottom) to biologic therapy. HU indicates Hounsfield units.

Figure 1. Perivascular Fat Attenuation Index (FAI) After 1 Year of Treatment



Pazienti sottoposti a terapia biologica mostrano riduzione di infiammazione coronarica a 1 anno

A photograph of a medical examination room. In the center is a large, white CT scanner with a patient bed extended from its gantry. To the left is a mobile C-arm X-ray unit with a large circular detector and a control panel. The room has white walls with a blue decorative stripe near the ceiling and floor. A white door is visible on the right side of the frame.

PROSPETTIVE FUTURE

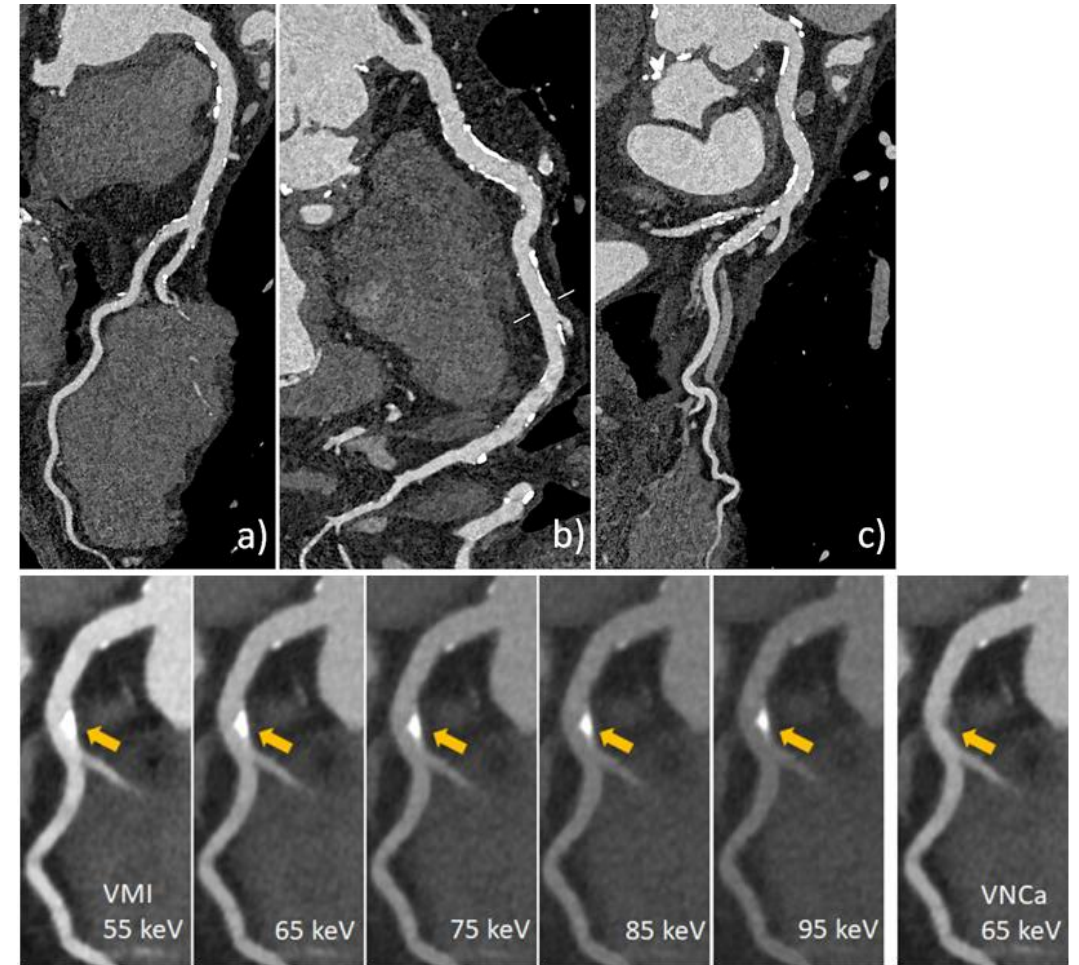
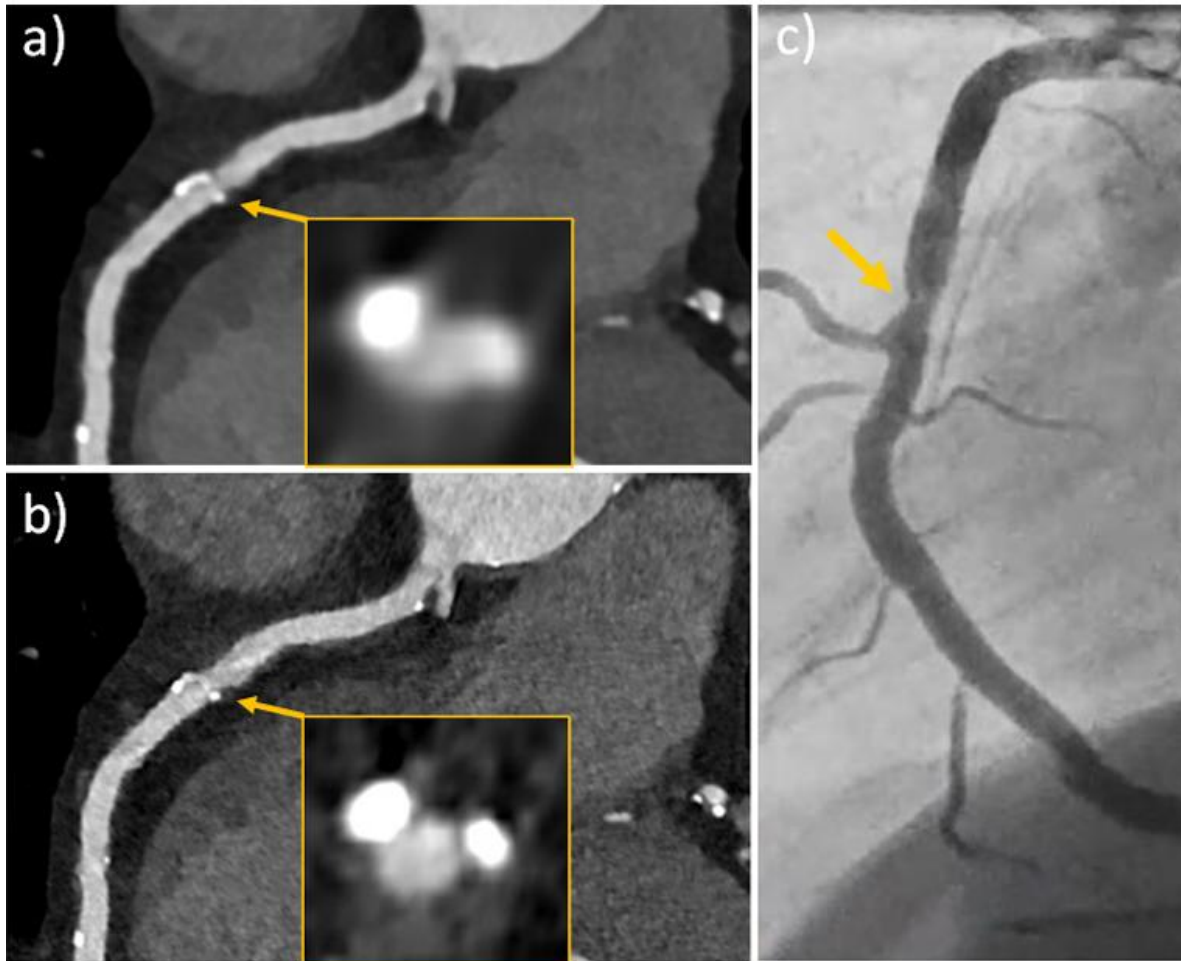
IMAGING CORONARICO CON CT PHOTON COUNTING

- Utilizza detettori di materiali semi-conduttori che convertono direttamente i fotoni prodotti dalla radiazione ionizzante in segnali elettrici
- Ogni fotone viene misurato singolarmente
- Eliminazione del «rumore» di fondo
- Maggiore risoluzione spaziale (0,2 mm vs 0,6 mm)
- Minore dose di radiazioni
- Migliore caratterizzazione tissutale



Cardiac imaging with photon counting CT

¹THOMAS FLOHR, PhD, ¹BERNHARD SCHMIDT, PhD, ¹STEFAN ULZHEIMER, PhD and ²HATEM ALKADHI, MD

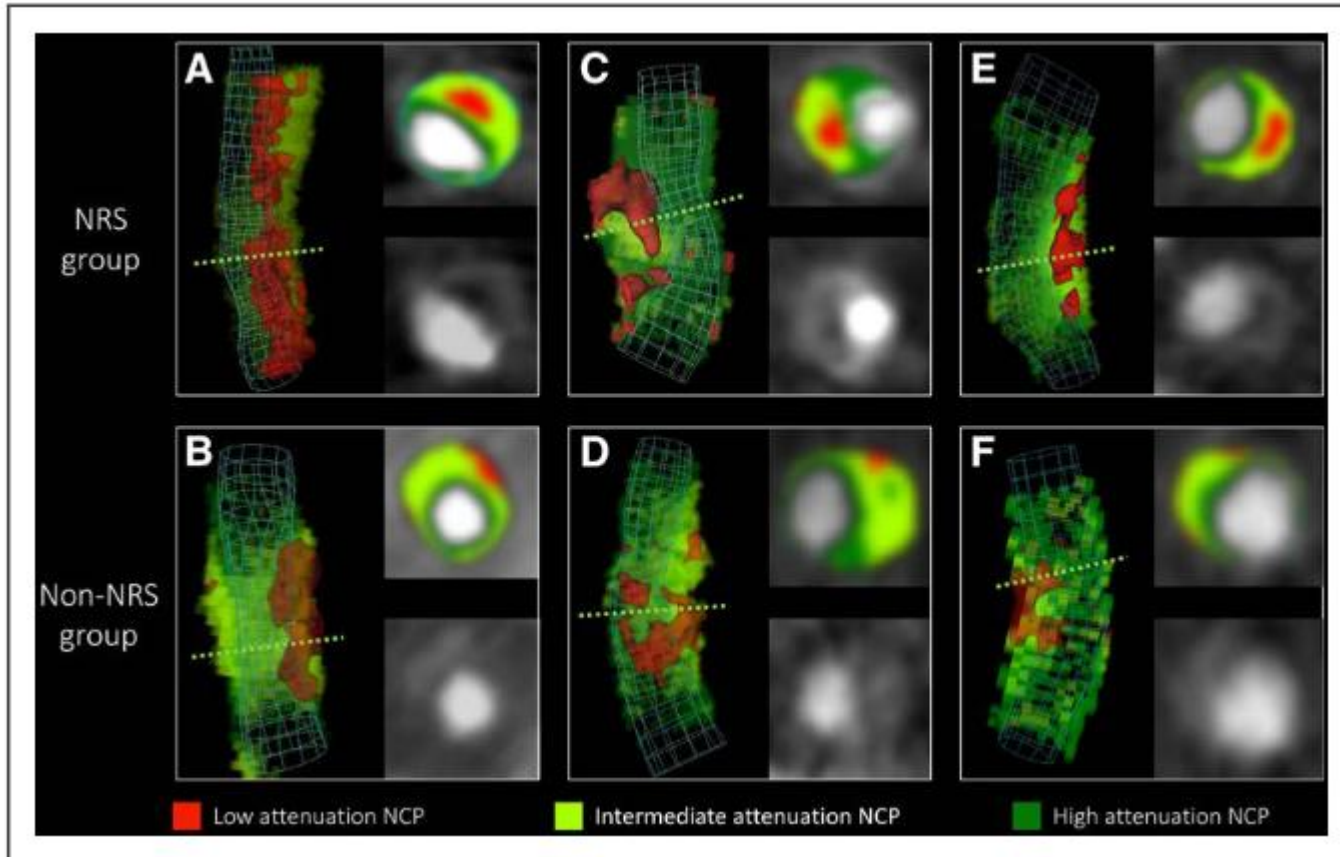


RADIOMICA E INTELLIGENZA ARTIFICIALE

- Utilizza tecnologie di machine learning per l'analisi delle immagini radiologiche
- Le immagini sono convertite in informazioni numeriche che vengono poi estrapolate tramite programmi di analisi di Big Data
- I dati di imaging vengono integrati con altre informazioni genetiche, cliniche e biologiche

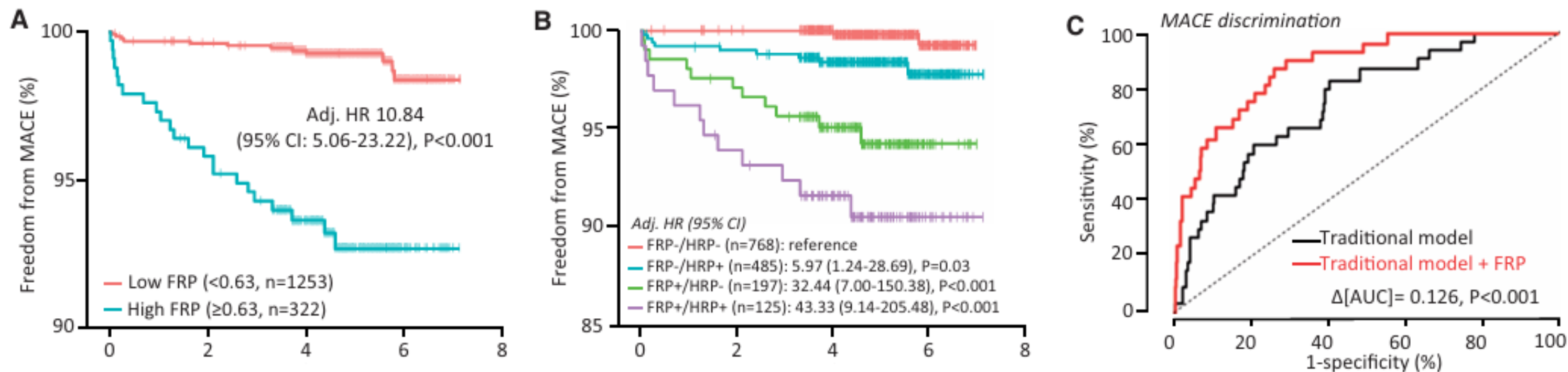


Radiomic Features Are Superior to Conventional Quantitative Computed Tomographic Metrics to Identify Coronary Plaques With Napkin-Ring Sign



Radiomica permette di distinguere placche con e senza NRS con precisione superiore rispetto a CCTA tradizionale

A novel machine learning-derived radiotranscriptomic signature of perivascular fat improves cardiac risk prediction using coronary CT angiography

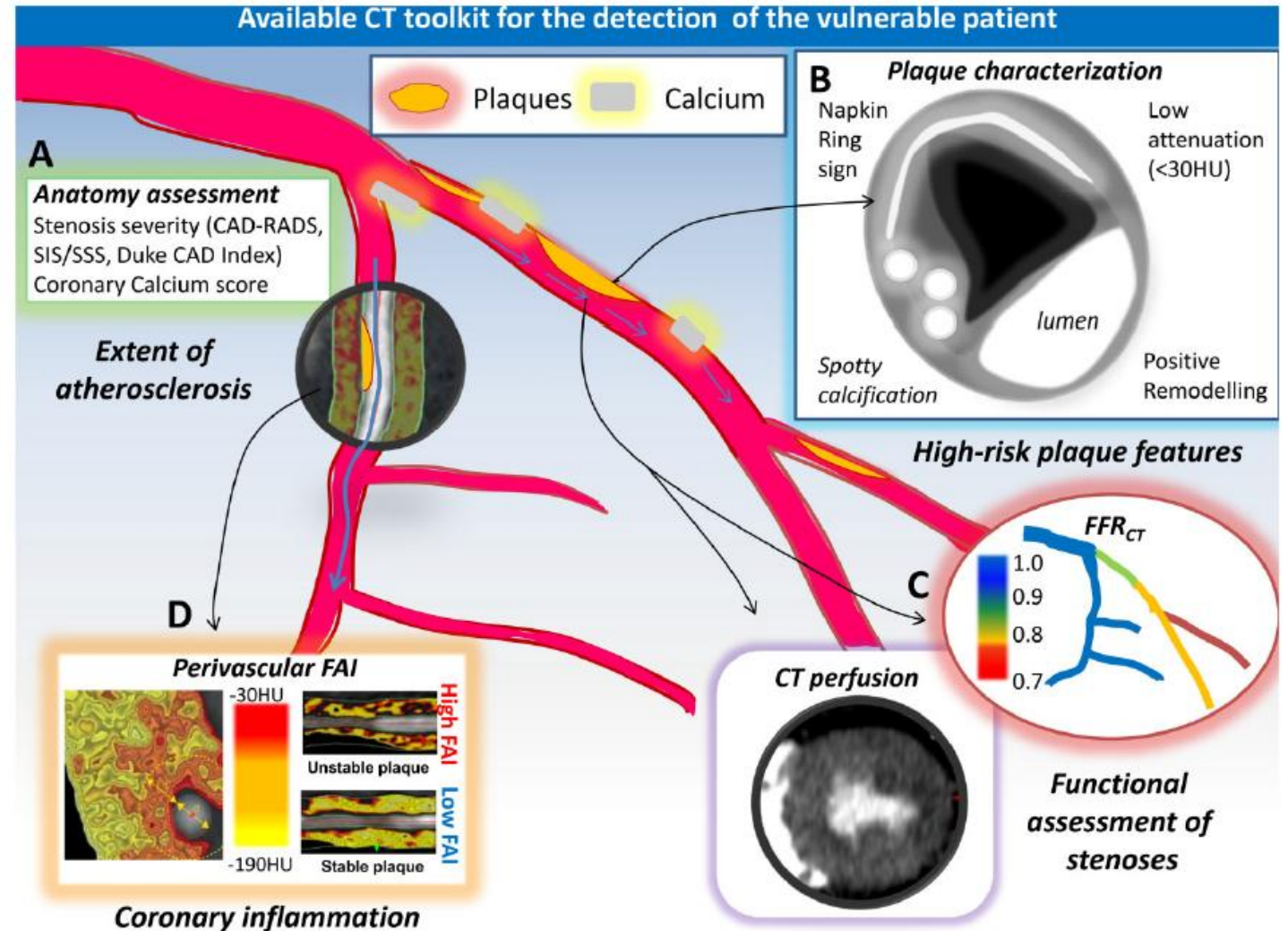


FAT radiomic profile (FRP) migliora il potere predittivo di eventi avversi rispetto a valutazione FAI/HRP

TAKE HOME MESSAGES

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- CCTA permette di diagnosticare precocemente **coronaropatia non ostruttiva**
- CCTA consente la caratterizzazione di placche ad alto rischio di **evolutività**
- La valutazione CT del FAI del tessuto adiposo coronarico costituisce un **imaging biomaker** di infiammazione coronarica che correla con rischio aumentato di eventi
- CCTA permette di identificare pazienti a **rischio aumentato** che possono beneficiare di **terapie di precoci di prevenzione primaria** o di **strategie di prevenzione secondaria avanzata**



GRAZIE