AI-Enabled Coronary CT Angiogram in Clinical Practice

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Learning objectives

1. Learn why imaging can add value to and save lives.
2. Explain the pros and cons of coronary artery calcium scoring to patients.
3. Learn why CCTA with AI driven quantitative analysis is better than traditional CAC and CCTA.
4. Understand what fractional flow reserve (FFR) is.
5. Learn how to implement noninvasive coronary CT angiography in your clinical practice.
6. Know how to read a report and explain it to a patient. Cases.

Heart disease Stats

- Heart disease is the **leading cause of death** for men, women, and people of most racial and ethnic groups.
- One person dies **every 33 seconds** from cardiovascular disease.
- In 2022, **702,880 people died from heart disease**. That's the equivalent of **1 in every 5 deaths**.
- Heart disease cost about **$252.2 billion in the USA** from 2019 to 2020.This includes the cost of health care services, medicines, and lost productivity due to death.

CHD and CAD Stats

- Coronary heart disease is the most common type of heart disease. It killed 371,506 people in 2022.
- In 2022, about 1 out of every 5 deaths from cardiovascular diseases was among adults younger than 65 years old!
- In the United States, someone has a heart attack every 40 seconds.
- Every year, about **805,000 people** in the United States have a heart attack. Of these, 605,000 are a first heart attack, and 200,000 happen to be people who have already had a heart attack.
- About 1 in 5 heart attacks are silent—the damage is done, but the person is not aware of it.

Standard Risk Assessment and Algorithms Fall Short

- As many as 50 percent of all cardiac deaths occur in individuals with ***no prior history or symptoms. The first symptom might be death.***
- Standard risk factors fail to explain up to 50 percent of cardiovascular events esp in older adults. This is where you come in!
- 80 of heart attacks happen with a less than 70 stenosis
- *American Heart Journal* analyzed data from 136,905 patients hospitalized for heart attacks for 6 years: **75% had LLDL levels below 130 mg/dL. Why?**

Heart attacks are preventable.

How Do We Determine Individualized Risk?

- Serum biomarkers
- Imaging (the point of today's talk!)
- Diet, lifestyle and exercise screening
- Blood pressure
- Genetic testing and family HX (ApoE, 9P21 etc)
- Existing conditions such as sleep apnea, autoimmune disease, COVID, DM, chronic infections etc.

Serum Biomarkers

- LDL particle size, LDL and HDL particle number, lipoprotein a, apolipoprotein B, HDL particle size. Functional HDL.
- PLA2, OXLDL, Il-6, MPO, high-sensitivity CRP, uric acid, homocysteine, TMAO, Vit D, and other novel inflammation assays
- Galectin 3, proBNP, high-sensitivity troponin (T,I)
- Microalbumin, cystatin c
- Micronutrients, oxidative stress

Other testing

- Pulse-wave velocity, arterial elasticity, plethysmography
- Vasodilation testing (FMD, endopat)
- Ankle-brachial index
- Hip waist ratio
- Body composition testing
- Earlobe crease
  - Frank's sign was observed more frequently in patients with obstructive CAD than in those without it (73% vs 68% for unilateral and 55% vs 47% for bilateral. *European Heart Journal*, Volume 44, Issue Supplement_2, November 2023.

Imaging: why guess when you can know?

- Coronary artery calcium scoring
- Carotid artery ultrasound and carotid intima media thickness
- Coronary CT angiogram with or without fractional flow reserve
- Traditional angiography with or without FFR
- Coronary CT angiogram with AI driven analysis

Coronary Artery Calcium Scoring Benefits

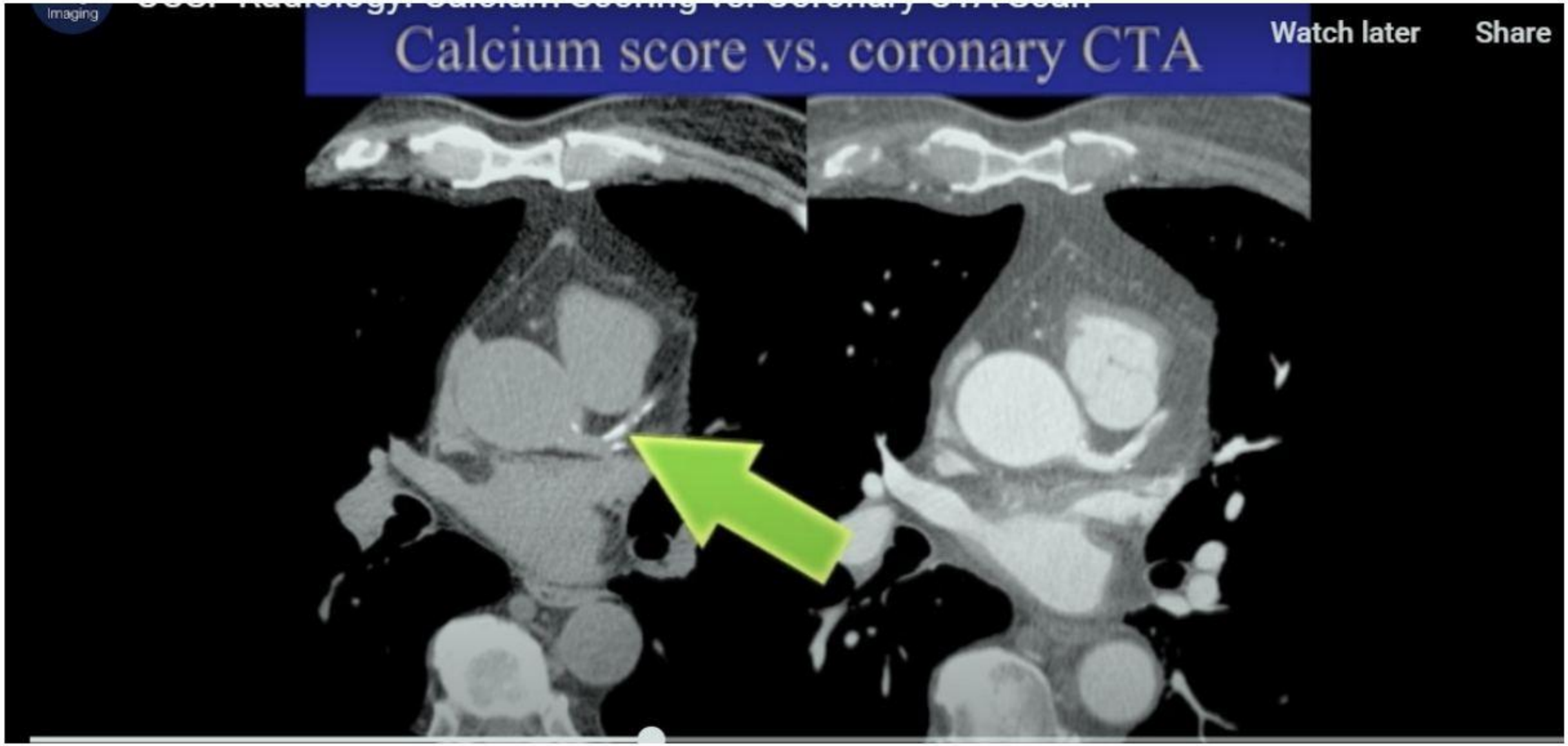
Can diagnose CAD in asymptomatic patients

- **Predicts cardiovascular events**: CAC scores are associated with coronary events, myocardial infarction, and all-cause mortality.
- **Predicts long-term risk, and stratifies risk**: CAC scores predict long-term risk because calcium buildup in the arteries is a slow process.
- **Predicts risk in different groups**: CAC scores are accurate in predicting risk for people of different ages, sexes, and clinical risk factors.
- **Has a high negative predictive value**: A CAC score of zero (no calcium buildup) is a strong indicator that there is no obstructive coronary disease.

Inexpensive $99-200

Coronary Artery Calcium Scoring Limitations

- Only measures calcium.
- Does not measure stenosis.
- The calcium score is a calcium volume score not a plaque volume score.
- May underestimate risk in patients with uncalcified unstable lesions.
- Makes tracking plaque difficult because treatment with statins (esp high dose) MAY increase arterial calcification.
- This may confuse the provider and the patient into thinking treatments are not working e.g statins MAY increase calcification.


Imaging
Calcium score vs. coronary CTA
Watch later
Share

Comparing traditional angiography to CCTA

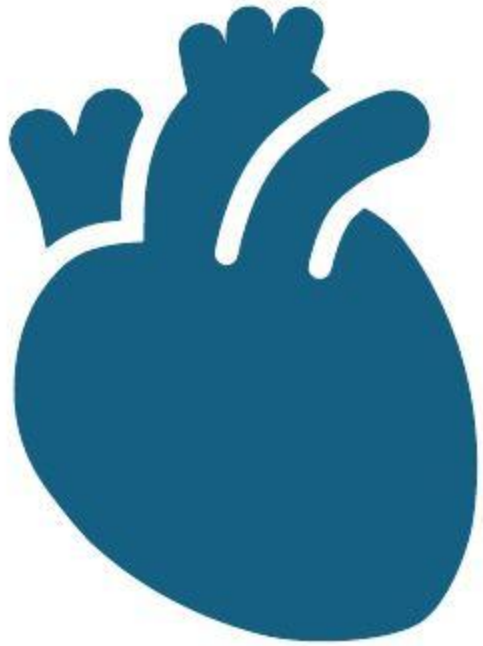
Both a coronary CT angiogram (CCTA) and a traditional angiogram (invasive coronary angiography, ICA) are valuable tools for assessing coronary artery disease (CAD) and blood flow restrictions, but their accuracy and utility depend on the context.

Traditional Angiogram (Invasive Coronary Angiography)

- **Invasive**: Involves catheter insertion and direct injection of contrast dye into coronary arteries (complications under 2%).
- **Accuracy**:
  - Considered the "gold standard" for visualizing coronary anatomy and detecting blockages.
  - High spatial resolution and fewer artifacts compared to CCTA.
  - Allows for direct assessment of lesions and their severity.
- **Functional information**: Does not always measure fractional flow reserve (FFR) or other techniques during the procedure. This must be added.

Coronary CT Angiogram (CCTA)

- **Non-invasive**: Uses advanced CT imaging and contrast dye to visualize coronary arteries.
- **Accuracy**:
  - **High negative predictive value**: Excellent for ruling out significant coronary artery disease in low-to-intermediate risk patients.
  - Sensitivity for detecting significant stenosis (narrowing) is high, but specificity may be lower due to false positives caused by artifacts (high calcium)
- **Functional information**: Does not directly assess blood flow or ischemia unless CT-derived fractional flow reserve (FFR-CT), is done. What is that?



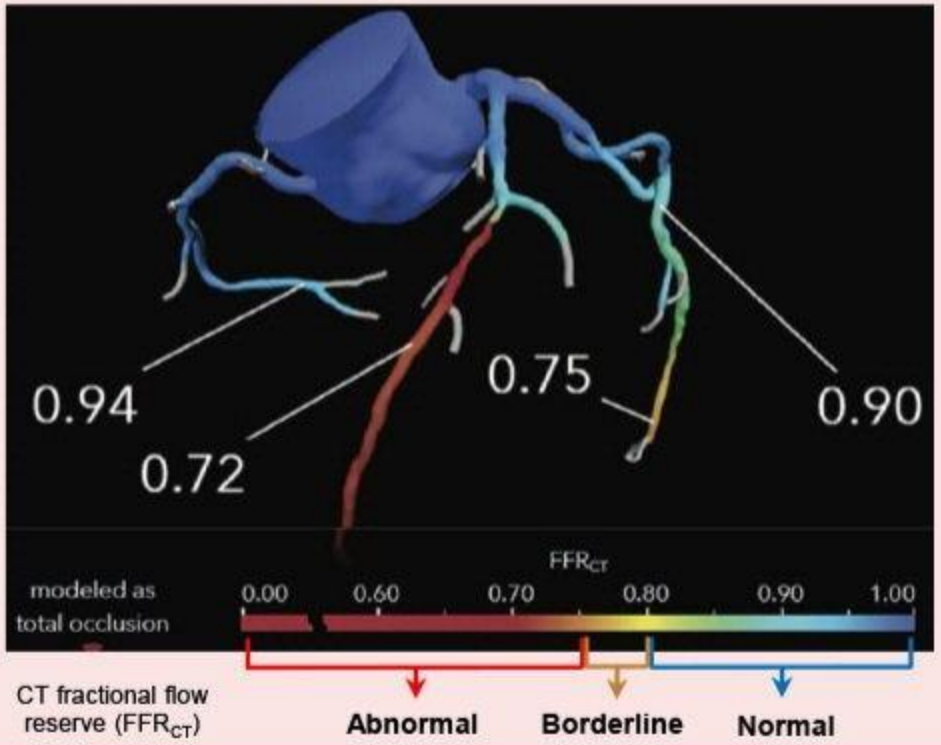
What is fractional flow reserve?

- FFR is the fraction of blood flow that goes through a stenotic artery.
- Cardiologists use a pressure sensitive wire and as they pass it through the lesion it picks up the pressure proximal to the blockage and the pressure distal and a compassion is made.
- > 0.8-1 is normal. An FFR lower than 0.75-0.80 is generally considered to be associated with myocardial ischemia.

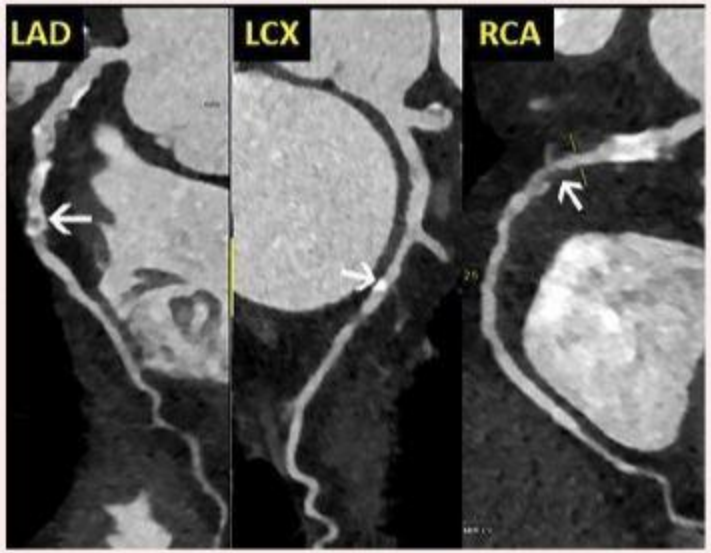
CT Fractional Flow Reserve: A Practical Guide to Application, Interpretation, and Problem Solving

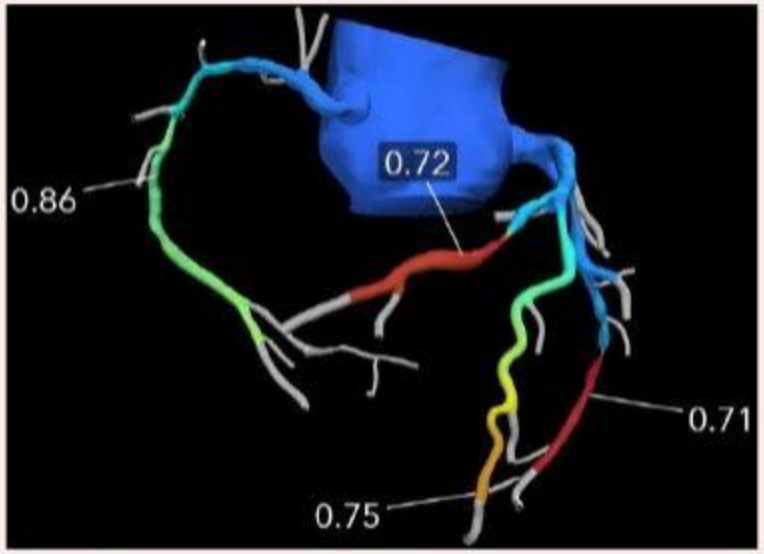
Basics

Physiologic simulation technique utilizing routine CTA data to mathematically model coronary flow, pressure, resistance



Utility in preprocedural planning





CTA FFR$_{CT}$	Left anterior descending artery	Left circumflex artery	Right coronary artery
	Severe stenosis	Severe stenosis	Moderate stenosis
	0.72	0.71	0.86

Patient underwent revascularization of the LAD and LCX

Rajiah P et al. Published online: February 4, 2022
https://doi.org/10.1148/rg.210097

Which arteries have abnormal FFR?

RadioGraphics

Which is more accurate for blood flow restrictions?

- **CCTA** is excellent for anatomical assessment and ruling out disease but may overestimate the severity of stenosis. **BUT with machine learning software it is more accurate.** Fractional flow reserve (FFR) using AI can also now be done and is accurate.
- **Traditional angiography with FFR** is more accurate for assessing **functional significance** of severe stenoses and their impact on blood flow, making it better suited for determining the necessity of interventions like stenting or bypass surgery.



AI-Guided Quantitative Plaque Staging Predicts Long-Term Cardiovascular Outcomes in Patients at Risk for Atherosclerotic CVD

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ABSTRACT

BACKGROUND The recent development of artificial intelligence-guided quantitative coronary computed tomography angiography (CCTA) analysis (AI-QCT) has enabled rapid analysis of atherosclerotic plaque burden and characteristics.

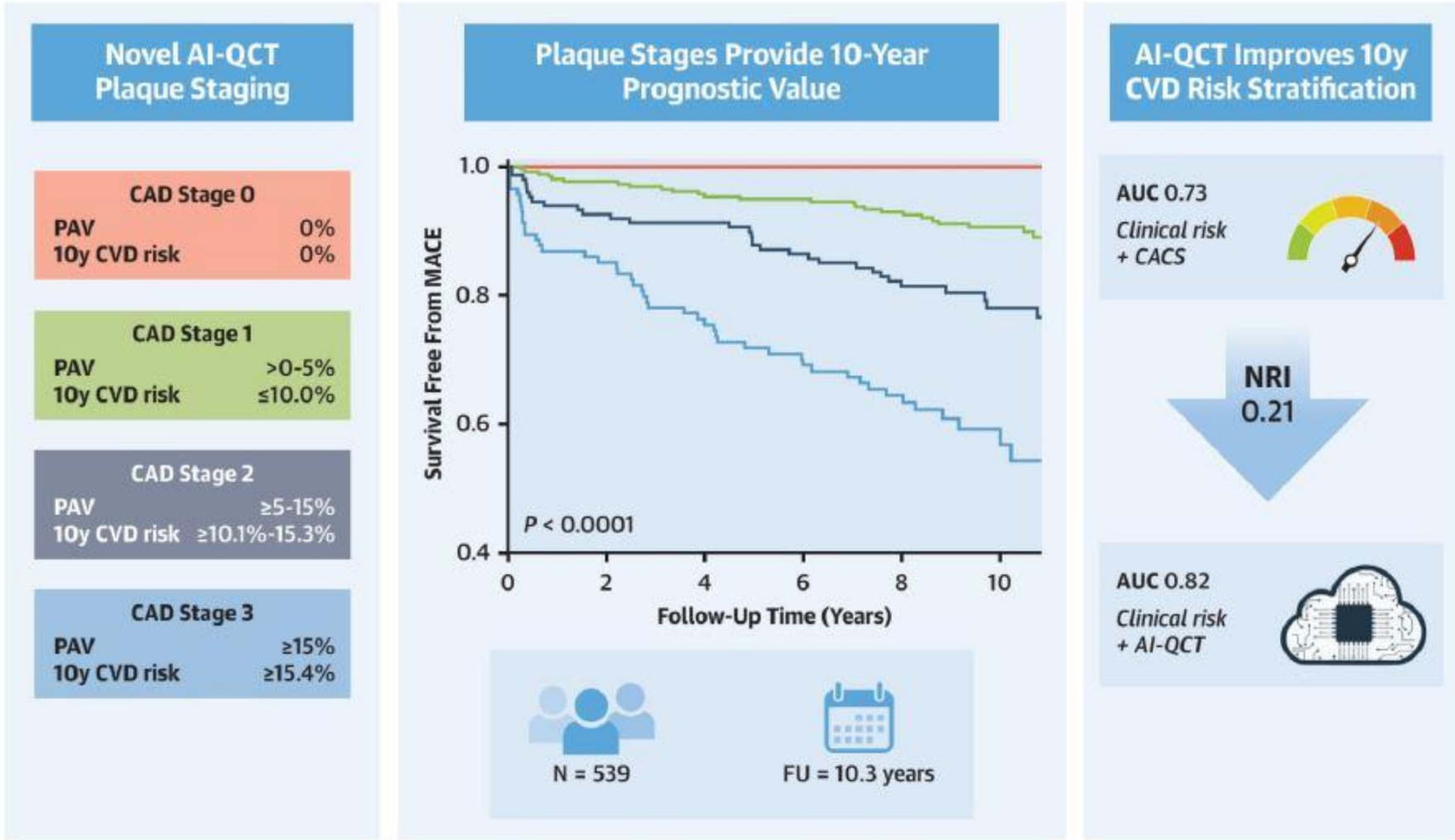
OBJECTIVES This study set out to investigate the 10-year prognostic value of atherosclerotic burden derived from AI-QCT and to compare the spectrum of plaque to manually assessed CCTA, coronary artery calcium scoring (CACS), and clinical risk characteristics.

METHODS This was a long-term follow-up study of 536 patients referred for suspected coronary artery disease. CCTA scans were analyzed with AI-QCT and plaque burden was classified with a plaque staging system (stage 0: 0% percentage atheroma volume [PAV]; stage 1: >0%-5% PAV; stage 2: >5%-15% PAV; stage 3: >15% PAV). The primary major adverse cardiac event (MACE) outcome was a composite of nonfatal myocardial infarction, nonfatal stroke, coronary revascularization, and all-cause mortality.

RESULTS The mean age at baseline was 58.6 years and 297 patients (55%) were male. During a median follow-up of 10.3 (IQR: 8.6-11.5) years, 114 patients (21%) experienced the primary outcome. Compared to stages 0 and 1, patients with stage 3 PAV and percentage of noncalcified plaque volume of >7.5% had a more than 3-fold (adjusted HR: 3.57; 95% CI 2.12-6.00; $P < 0.001$) and 4-fold (adjusted HR: 4.37; 95% CI: 2.51-7.62; $P < 0.001$) increased risk of MACE, respectively. Addition of AI-QCT improved a model with clinical risk factors and CACS at different time points during follow-up (10-year AUC: 0.82 [95% CI: 0.78-0.87] vs 0.73 [95% CI: 0.68-0.79]; $P < 0.001$; net reclassification improvement: 0.21 [95% CI: 0.09-0.38]). Furthermore, AI-QCT achieved an improved area under the curve compared to Coronary Artery Disease Reporting and Data System 2.0 (10-year AUC: 0.78; 95% CI: 0.73-0.83; $P = 0.023$) and manual QCT (10-year AUC: 0.78; 95% CI: 0.73-0.83; $P = 0.040$), although net reclassification improvement was modest (0.09 [95% CI: −0.02 to 0.29] and 0.04 [95% CI: −0.05 to 0.27], respectively).

CONCLUSIONS Through 10-year follow-up, AI-QCT plaque staging showed important prognostic value for MACE and showed additional discriminatory value over clinical risk factors, CACS, and manual guideline-recommended CCTA assessment. (J Am Coll Cardiol Img 2023;■:■-■) © 2023 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

CENTRAL ILLUSTRATION **AI-QCT Plaque Staging Improves Long-Term CVD Risk Stratification**



Nurmohamed NS, et al. J Am Coll Cardiol Img. 2023;■(■):■-■.

Through 10-year follow-up, artificial intelligence guided coronary computed tomography angiography (AI-QCT)-guided plaque staging based on percentage atheroma volume (PAV) **(left)** showed important prognostic value for atherosclerotic cardiovascular disease (CVD) **(middle)** and provided important reclassification benefit compared to clinical risk characteristics and coronary artery calcium scoring (CACS) **(right)**. AUC = area under the curve; CAD = coronary artery disease; FU = follow-up; MACE = major adverse cardiac events; NRI = net reclassification improvement.

Recommendation



Regular CCTA (without AI-quantification) is typically used for:

Low-to-intermediate risk patients for screening and baseline plaque analysis.

Asymptomatic patients.

Situations where a non-invasive test is preferred.

For tracking treatment efficacy.

Not granular enough though really.

Expensive



Traditional invasive angiography is used for:

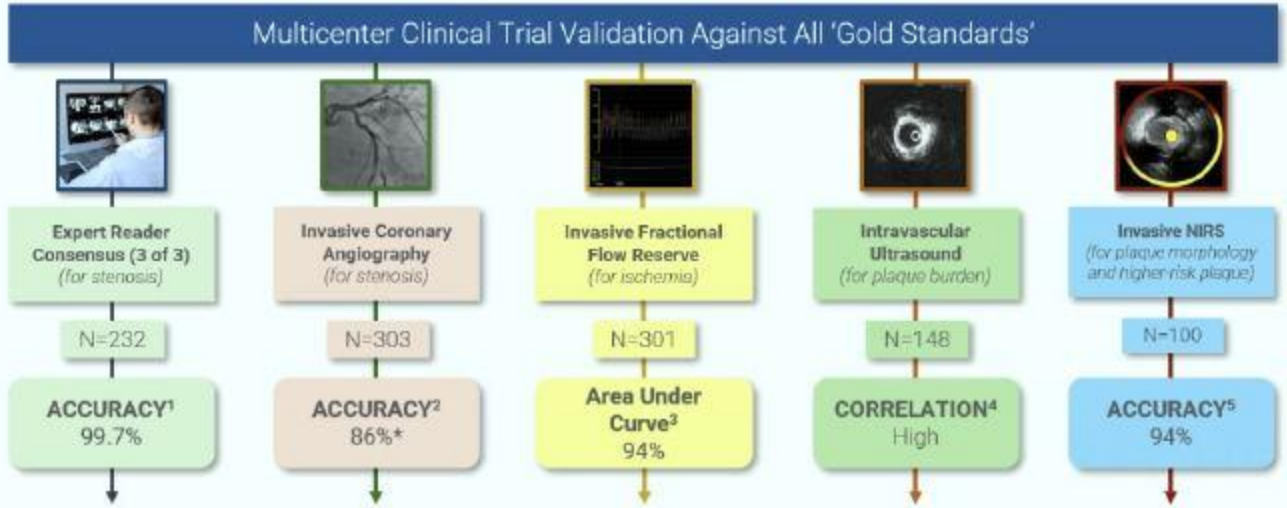
High-risk patients or when revascularization (e.g., stent placement) is being considered.

Cases where precise functional assessment of blood flow is needed.

Symptomatic patients

Ah but what if a CCTA could be even more accurate?

- Measure each stenosis, even small ones.
- Add FFR only if needed after imaging has been completed.
- Provide accurate baseline for follow up testing.
- Indicate three types on plaque morphology.
- Engage the patient. Nice graphics.
- ~ $1,500 for everything out of pocket. Conventional CCTA average cost **without** AI QCT $1,000 to $2,500 and this is NOT easy to get from providers.



CLARIFY1 - Cleerly vs 3 expert level 3 readers

- Mult-center clinical trial of 232 consecutive patients undergoing CCTA with a parameter of stenosis severity
- We had correlation to the level 3 readers consensus, and were superior to each individual reader
- High risk plaques were detected 57% more often than level 3 readers
- CAD-RADS score agreement 98%

Stenosis	Accuracy	Sensitivity	Specificity	PPV	NPV
>70%	99.7%	90.9%	99.8%	93.3%	99.9%

CLARIFY2 - Cleerly vs Invasive Coronary Angiography (ICA)

- 303 consecutive patients undergoing CCTA, ICA and Cleerly, with a blinded core lab performing invasive quantitative coronary angiography for stenosis severity
- Low discordance rate of 7%; for discordances, Cleerly demonstrated higher agreement with invasive FFR than QCA

Stenosis	Accuracy	Sensitivity	Specificity	PPV	NPV
>70%	86%	94%	82%	69%	97%

Cleerly vs IVUS

- This was an initial study vs IVUS - Cleerly's AI-QCT demonstrates high agreement with IVUS for absolute measures of coronary plaque and lumen size
- Last year we were involved with an IVUS study at Yale University and writing is 50% complete, which should be published in the next month or so

Ischemia Validation Study

- A total of 4 studies were performed, utilizing CREDENCE, PACIFIC and two smaller studies of 40-50 patients in S. California.
- Here are the Cleerly results from the two larger data sets - CREDENCE and PACIFIC



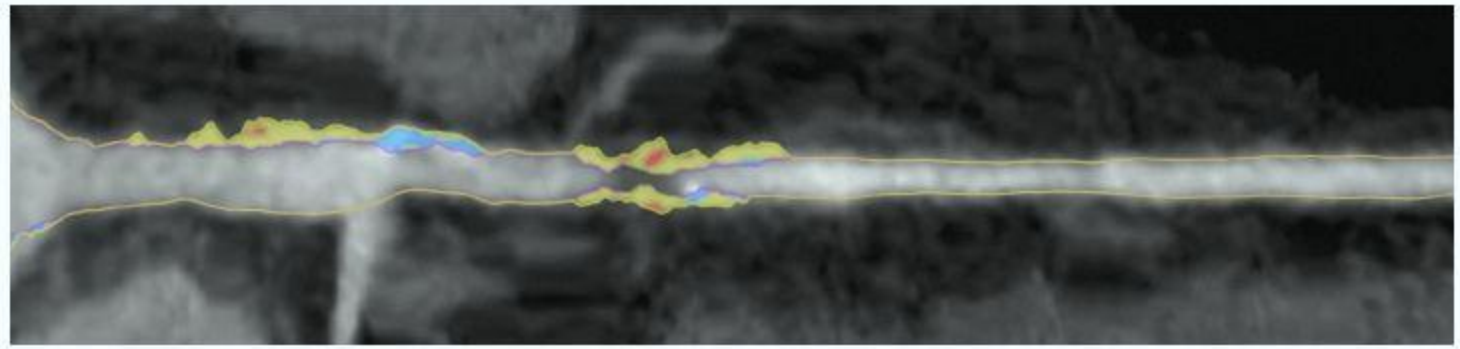
Better



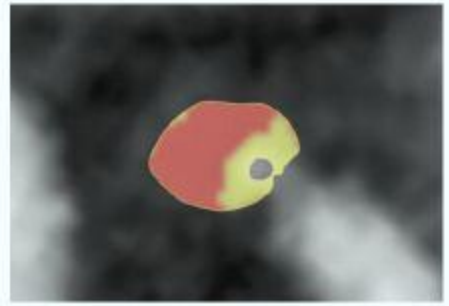


How To Interpret AI Driven CCTA-QCT

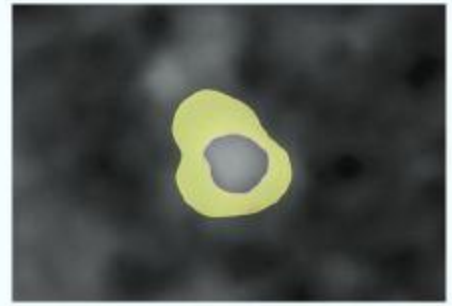
Straightened Vessel



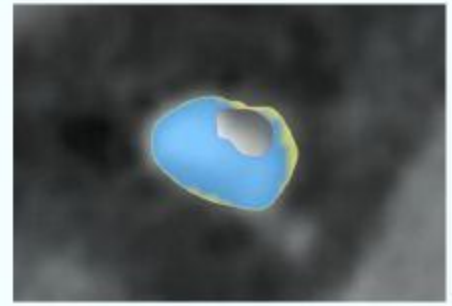
Low-density Non-calcified Plaque



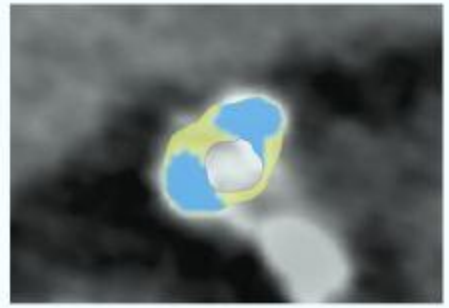
Non-calcified Plaque



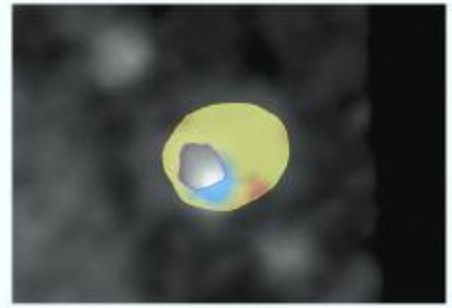
Calcified Plaque



Calcfied + Non-calcified Plaque



All Plaque Types



Endurance athletes/ CAC

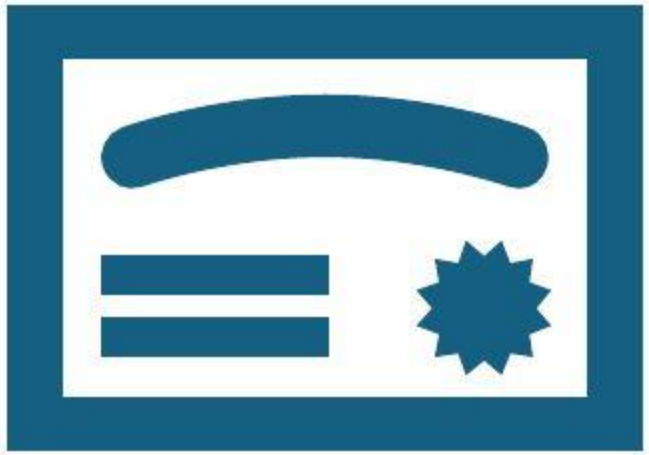
Observational Studies: Aengevaeren et al., 2017 :Compared lifelong endurance athletes to sedentary controls and found that male endurance athletes had a significantly higher prevalence of CAC and more coronary plaques, including calcified plaques. These plaques were more often calcified and stable, not mixed or soft/vulnerable plaques.

Möhlenkamp et al., 2008 found that Male marathon runners had higher CAC scores than matched controls.The presence of CAC correlated with years and intensity of endurance training. Merghani et al., 2017: In a cohort of veteran male athletes, CAC and plaque burden were higher than in controls, but plaques were more calcified and less likely to be mixed/vulnerable.

Coronary Plaque Morphology and Stability Studies: While endurance athletes may have a higher total CAC score, they tend to have more calcified (stable) plaques and fewer mixed or non-calcified (vulnerable) plaques.This distinction may reduce the associated cardiovascular risk despite higher CAC scores.

Prognostic Implications: The prognostic value of CAC in endurance athletes is unclear. Some researchers argue that increased CAC in this group may not carry the same risk as in sedentary individuals because the plaques are more stable and athletes tend to have better overall cardiovascular profiles.

Ah, ok but why some ex-pro athletes have a 0 score then?



How do follow up testing

- Minimal Mild plaque (1-24% stenosis): follow up with CCTA in 3-5 years.
- Mild (24-49%): 1-2 years.
- Moderate to severe (>50%) Can also use Carotid US with plaque morphology with IMT every 6 mo to monitor treatment effect (if you can find it).
- Hot plaque/ mainly uncalcified plaque 1-2 years/ your choice
- 60% stenosis or greater with symptoms refer.
- Can also add FFR before referring.

Treatment basics

- Plant centered Mediterranean/whole foods diet (not keto or carnivore). If vegan/WFPB they need your nutritional advice and need to screen for deficiencies. Paleo is ok but must low sat fat and contain fruits, nuts and veg. Pasture raised, organic. No dairy or refined carbohydrate.
- Minimum 200 minutes of aerobic based on your exercise prescription. Strength always good too. Walking is rarely enough.
- Treat lipids 60/60/60 goal.
- Do all the testing. What is this?
- Then, treat everything.
- We don’t always no the reasons why.

Summary:

Traditional screening and risk assessment often falls short.

Preventive cardiology is a perfect match for inquisitive integrative and holistic minded providers.

Consider specializing. The public is underserved in this area, low competition and you will be busy.

Naturopathic doctors have all the basics and just need to learn cardiology.

Detection, prevention and treatment!!!

Through individualized risk assessment and treatment plaque may regress and stabilize.