

Disclosures

Past-President



Blavatnik Family Foundation

Helen Gurley Brown Foundation

Gilinksi Family

NIH-NHLBI

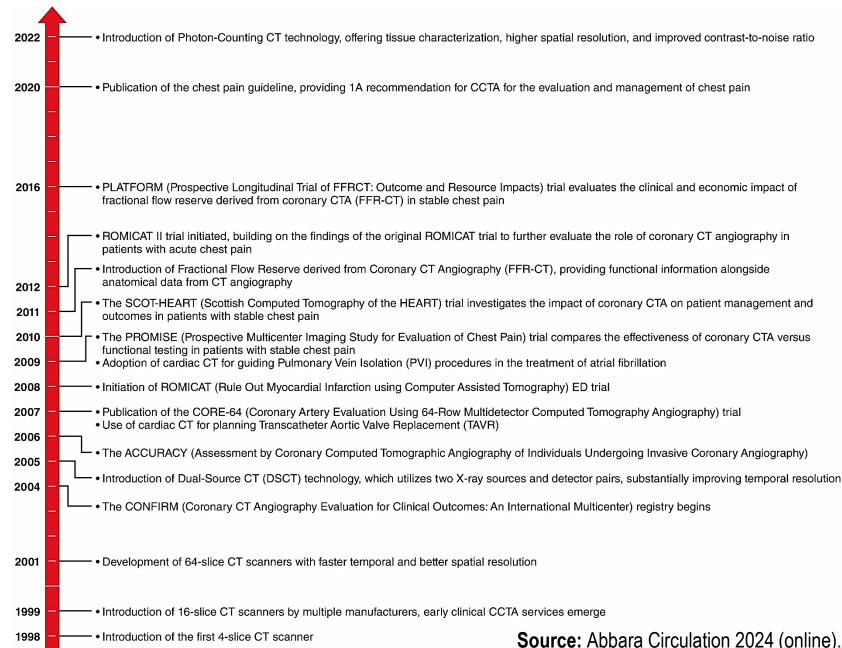
- U01HL10556 ISCHEMIA Trial Imaging Coordinating Center
- R01HL159433 Atherosclerotic Plaque Progression with COVID-19
- U01HL088942 Multiparametric Imaging to Understand Mechanisms of Post-Intervention Benefit in the Percutaneous or Surgical Repair In Mitral Prolapse & Regurgitation Trial for ≥60 Year Olds

DOD Women's Ischemia TRial to Reduce Events In NonObstRuctive CAD (WARRIOR) Trial

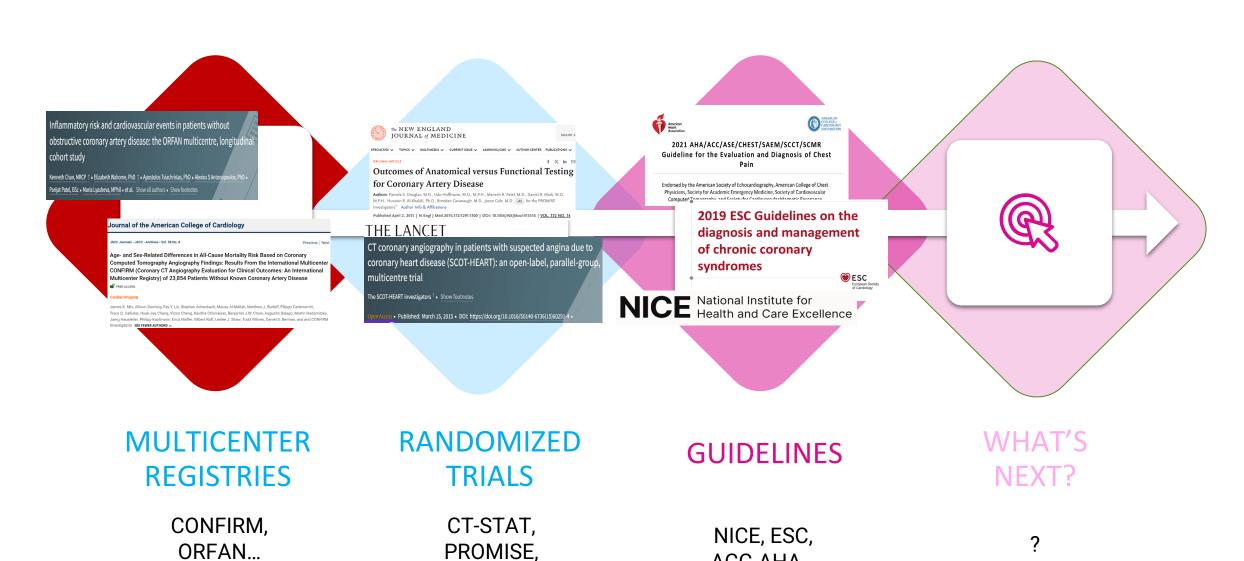
Invited Speaker / Unrestricted Grant Support Heartflow

Past, Present, & Future

"After remarkable developments in recent decades, we seem to unlocked but a small portion of the enormous potential of cardiac CT."



The CCTA Revolution!

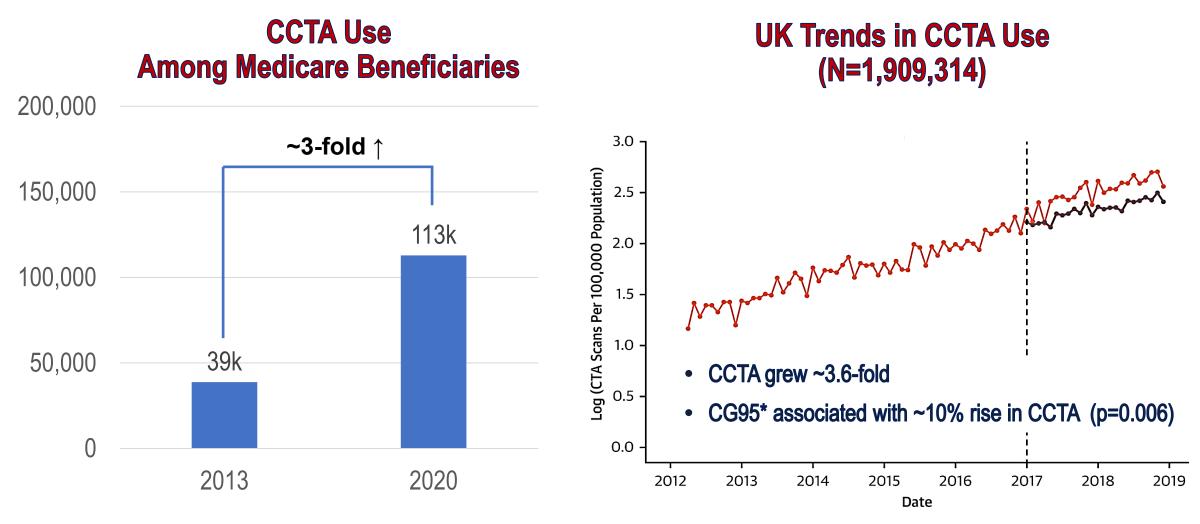


SCOT-HEART...

ACC-AHA...

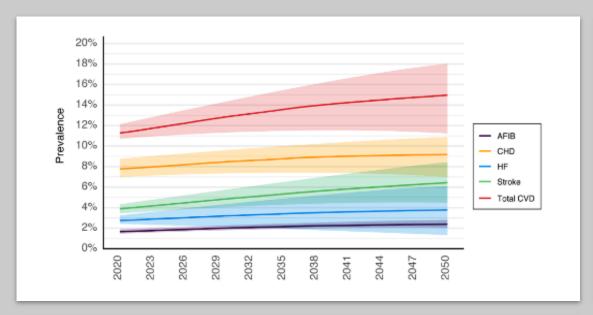
Rising Demand for CCTA

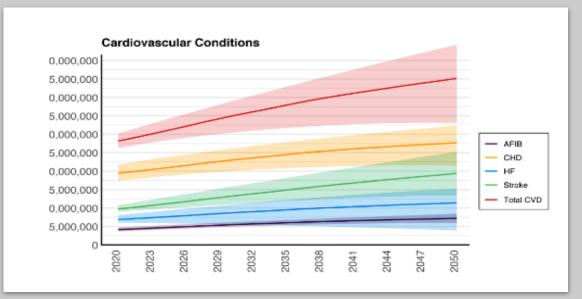
Rising CCTA demand - 2⁰ to ↑ CAD risk worldwide combined with substantive research + supportive guidelines

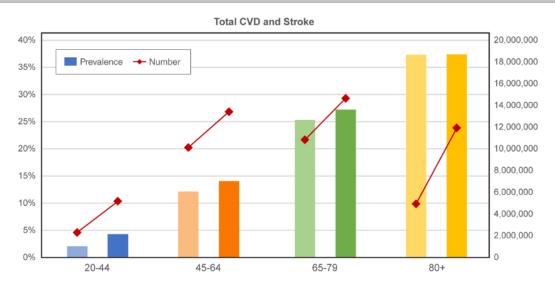


...CCTA market is growing with compounded annual growth rate ~6%

Source: Reeves Radiol: Cardiothoracic Imaging 2023;3:5., https://www.databridgemarketresearch.com, Al-Ogaili RSNA 2023., Weir-McCall JACC Imag 2023;16:659-671.







- Prevalence of <u>Hypertension</u> (51% in 2020 → 61.0% in 2050), <u>Diabetes</u> (16%→27%),
 <u>Obesity</u> (43%→61%)
- Prevalence of <u>CAD</u> (8%→9%), <u>HF</u> (3%→ 4%),
 <u>Total CVD</u> (11%→15%)
- CVD-related costs expected to triple to \$1.8 trillion by 2050

Source: Joynt Maddox Circulation 2024;149:e00-e00.

Risk Factor Burden at Younger Ages is Shocking

- High incidence of traditional risk factors early in life (age <50 years)
 - e.g., Age 20-40 years 1 in 8 are hypertensive
 - Even higher rates among African American Individuals
 - African American women are at High Risk for Preeclampsia!
 - 40% of Ages 20-40 years are obese and 4% are diabetic (↑ type 2 DM)
- Cumulative exposure of risk factors leads to greater rates of progression & increased CVD event risk
- High rates of progression elevate ASCVD event risk

Source: PESA Circulation 2015;131:2104., Domanski J Am Coll Cardiol 2023;12:1151-.

Global Burden of Cardiovascular Disease

9,440,000 Deaths Related to CAD

1990 rank

• Worldwide patterns emerge - massive population shifts to more urban environments Changing (and poor) dietary patterns, more physical inactivity,

What Would Change with Improved Risk Factor Control?

1 Cardiovascular diseases 1 Neoplasms 2 Neoplasms 2 Cardiovascular diseases 3 Respiratory infections & TB 3 Chronic respiratory 4 Maternal & neonatal 4 Neurological disorders 5 Respiratory infections & TB 5 Enteric infections 6 Chronic respiratory 6 Digestive diseases 7 Other infectious 7 Unintentional ini 8 Other non-communicable 8 Digestive diseases 9 Unintentional inj 9 Enteric infections 10 Other non-communicable 10 Transport injuries 11 Self-harm & violence 11 Diabetes & CKD 12 Self-harm & violence 12 Maternal & neonatal 13 Transport injuries 13 Diabetes & CKD 14 Neurological disorders 14 Other infectious 15 NTDs & malaria 15 NTDs & malaria 16 Skin diseases 16 Nutritional deficiencies 20 Skin diseases 18 Nutritional deficiencies

Source: Vaduganathan J Am Coll Cardiol 2022;80:2361-2371., Institute for Health Metrics and Evaluation.

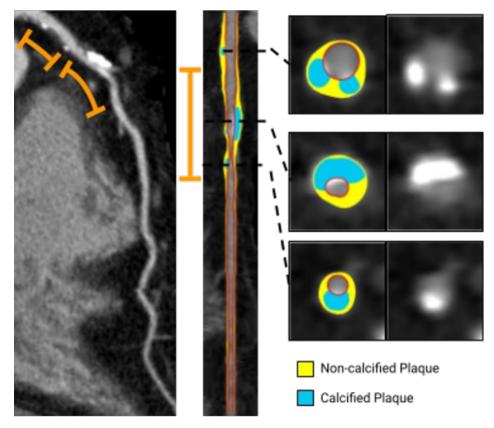
2050 rank

Challenge Longstanding Public Policy

- Screening Beyond ASCVD Risk Scores Not Accepted*
 - Suboptimal Accuracy of Risk Scores Across Diverse Populations of Women and Men Throughout the Continuum of Risk
 - Limited validation, Lack of Novel Risk Measures
 - Epidemic of obesity, HTN, diabetes, poor diet, physical inactivity...
 - Clinical & public health interventions are needed to effectively manage, stem, and even reverse these adverse trends
 - Evidence is Substantial that CT-Based Imaging (CAC) Can Improve Risk Detection among Large Sectors of At-Risk Asymptomatic Individuals

Detecting Early Atherosclerosis

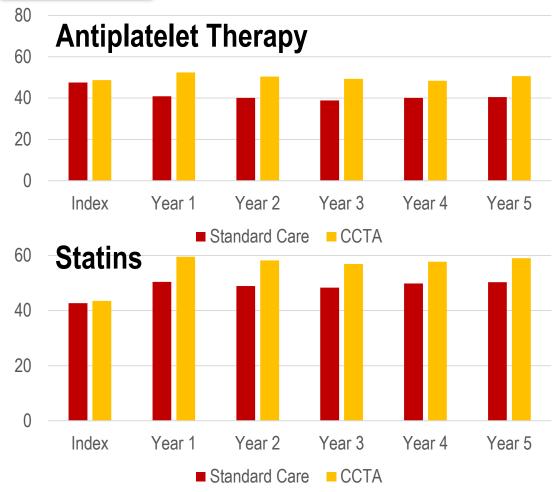
- With the introduction of plaque imaging into clinical practice, it is abundantly clear that basing CAD diagnosis on inducible myocardial ischemia is fundamentally flawed
- It is recognizing a problem too late along the disease continuum by detecting advanced atherosclerosis
- Our next challenge is to target early atherosclerotic plaque that is amenable to regression / averting ACS



Source: Koo JACC lmg 2024:S1936-878X(24)00130-X.

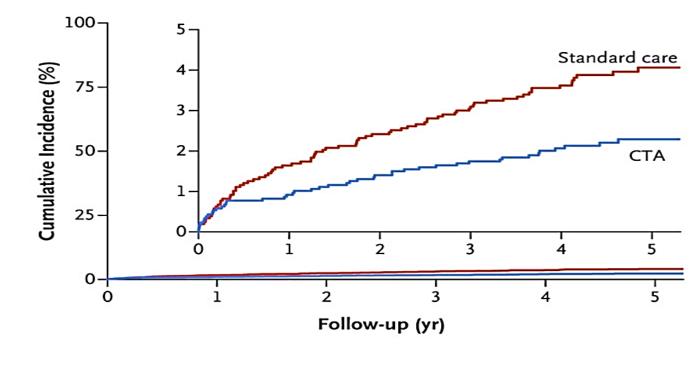


SCOT-HEART: CT-Prompted Preventive Care



Protocol Prompted Preventive Care for Patients with Nonobstructive / Obstructive CAD

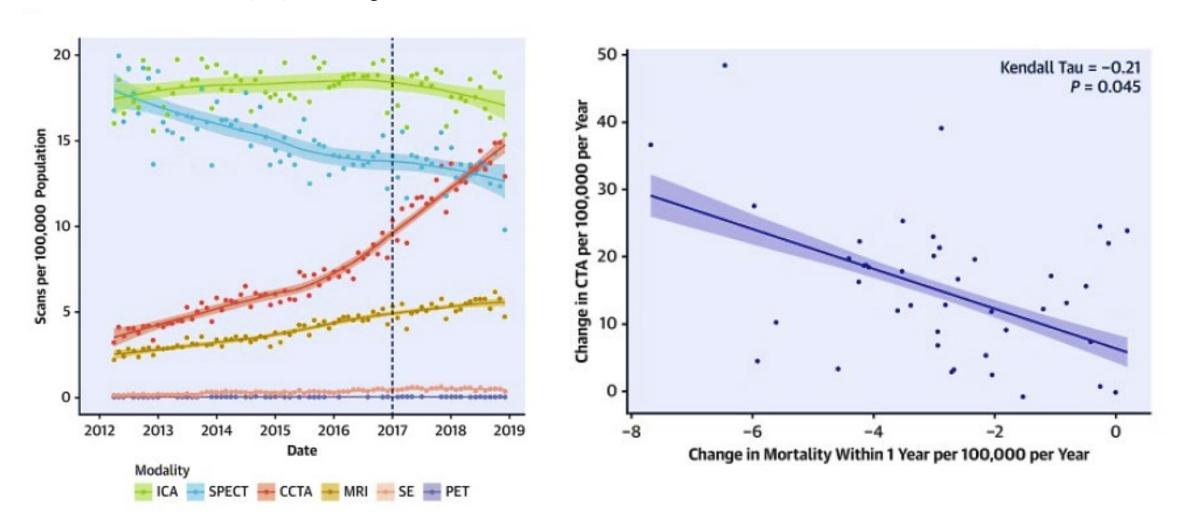
■ ↑ Use of Antiplatelet / Statin Therapy



Source: SCOT-HEART NEJM 2018;379:924-933.

Does CCTA Improve Outcomes?

UK National Health Service - 1,909,314 investigations for CAD

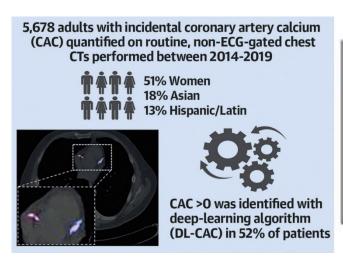


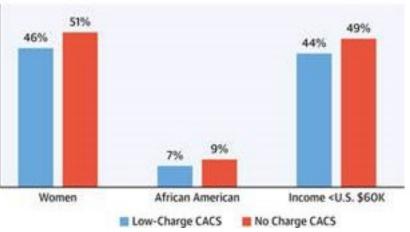
Source: Weir-McCall JACC Imag 2023;16:659-671.

Scalability Across the Globe - Finding Solutions for Limited Resource Settings

Low-Middle Income Countries + Equally Challenging Rural + Urban Areas in the US

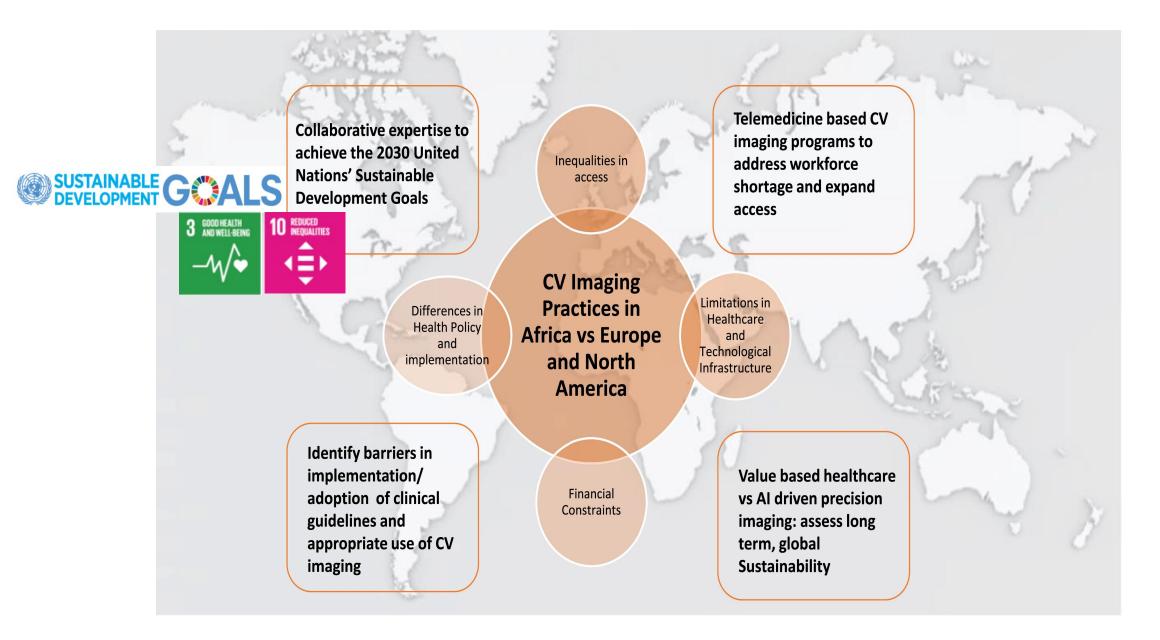
- Public policies must provide adequate funding to address the burden of atherosclerosis
 - Promote CCTA use to promote timely & equitable access
 - Cost effectiveness will be key
 - Varied CT approaches may be needed to characterize plaque CAC, SIS...
 - No cost scanning
 - Low-cost Al approaches integrating Imaging with EHR







Fource: Al-Kindi JACC 2020;76:1259-1262., CAD-RADS 2.0™ app.

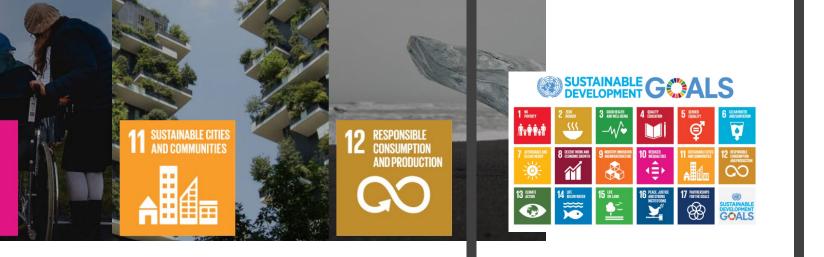


Source: Lakshmanan Eur Heart J - Imaging Methods Practice, 2023;1(1):qyad005.

A Call to Action!

- Novel CCTA strategies should expand focus toward early forms of atherosclerosis prior to functional ischemia with obstructive stenosis
- Atherosclerosis detection should target disease states + treatments capable of halting progressive atherosclerosis / reducing later stage complications of atherosclerosis
- Improve implementation and scalability of high quality CCTAguided care around the world











FULL TEXT ARTICLE

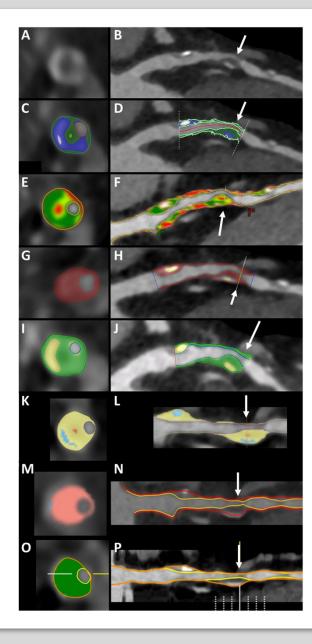
Standards for quantitative assessments by coronary computed tomography angiography (CCTA)

Article in Press: Corrected Proof

Koen Nieman, Hector M. García-García, Alexandre Hideo-Kajita, Carlos Collet, Damini Dey, Francesca Pugliese, Gaby Weissman, Jan G.P. Tijssen, Jonathon Leipsic, Maksymilian P. Opolski, Maros Ferencik, Michael T. Lu, Michelle C. Williams, Nico Bruining, Pablo Javier Blanco, Pal Maurovich-Horvat and Stephan Achenbach

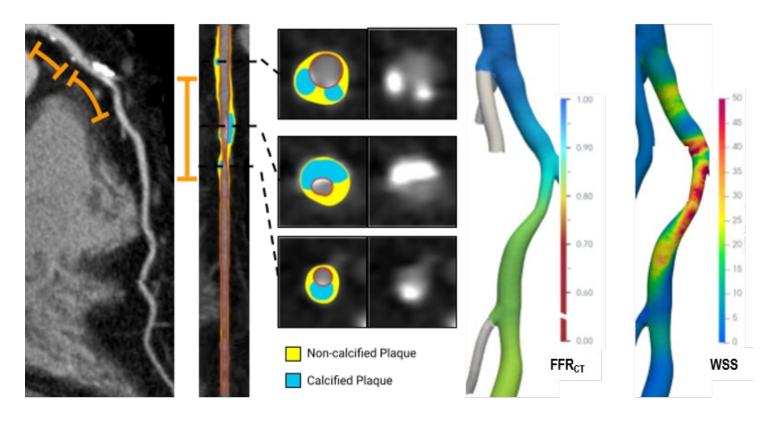
Journal of Cardiovascular Computed Tomography, Copyright © 2024 Society of Cardiovascular Computed Tomography

Source: Nieman JCCT 2024 (online).





Exploring the Mechanism of Plaque Rupture in ACS using CCTA & Computational Fluid Dynamics II) Study (EMERALD II Study)



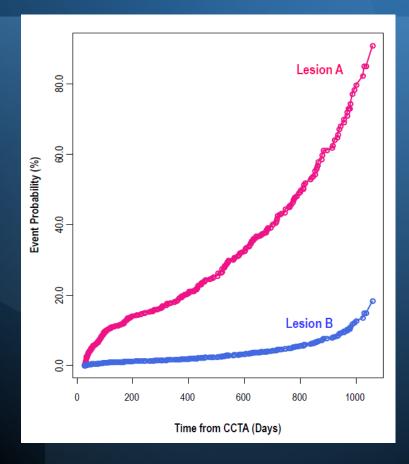
TPV: Total plaque volume, NCPV: Noncalcified plaque volume, LAPV: Low attenuation plaque volume, WSS: Wall shear stress; APS: Axial plaque stress, MBF: Myocardial blood flow, Plaque burden (cross-sectional plaque area/vessel area @ minimum lumen area site

351 Patients with Definite ACS Culprit Lesions





ACS Precision Risk Assessment



Exploring the Mechanism of Plaque Rupture in ACS using CCTA & Computational Fluid Dynamics II) Study

(EMERALD II Study) Lesion A Lesion B Lesion-specific prediction = 0.07 Lesion-specific prediction = 0.60 $\Delta FFR_{CT} = 0.02$ $\Delta FFR_{cr} = 0.14$ +0.21 Plaque Burden Averaged +0.08 % Total MBF = 28.3 =58.4% CAD RADS = 1 +0.05 TPV = 151 mm³ 1-24% Stenosis +0.04 CAD RADS = 3 -0.01 $TPV = 63.7 \text{ mm}^3$ 50-69% Stenosis Plaque Burden +0.04 -0.01 HRP (-) =88.6% Averaged LAPV lesion +0.03 +0.01 = 10.6 mm³ % Total MBF = 24.3 LAPV_lesion -0.01 -0.01 HRP (-) $= 0.60 \, \text{mm}^3$

0.00

0.05

0.10

Probability

351 Patients with Definite ACS Culprit Lesions

Probability

Source: Koo JACC Img 2024:S1936-878X(24)00130-X.

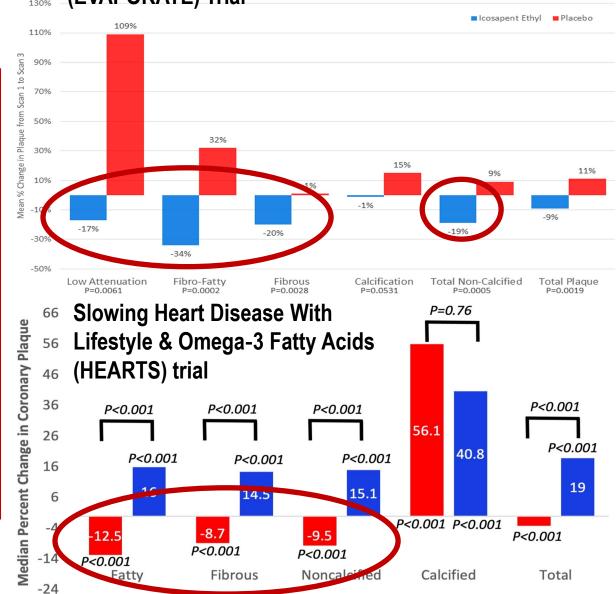
0.15

0.20

Treatment-Induced Regression of Atherosclerotic Plaque

Plaque Regression Strategies CETP Inhibitors reduces transfer of cholesterol Statins from HDL-C to LDL-C **HMG-CoA** reductase inhibitor PCSK9 Inhibitors Ezetimibe = Reduced cholesterol inhibits intestinal increases hepatocyte deposition and biliary cholesterol uptake of LDL-C absorption Enhanced endothelial repair Reduced cholesterol inflammation Exercise Eicosapentaenoic Colchicine inhibits Acid microtubule modulators that dampen inflammatory formation response

Effect of Vascepa on Improving Atherosclerosis in People with Elevated Triglycerides on Statin Therapy (EVAPORATE) Trial

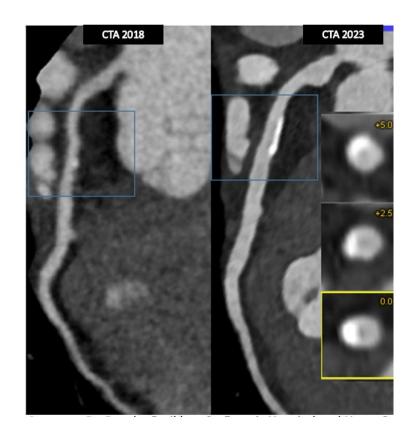


Source: Dawson JACC 2022;79:66-82., Budoff Eur Heart J 2020;41:3925-3932., Welty JAHA 2023;12:e030071.

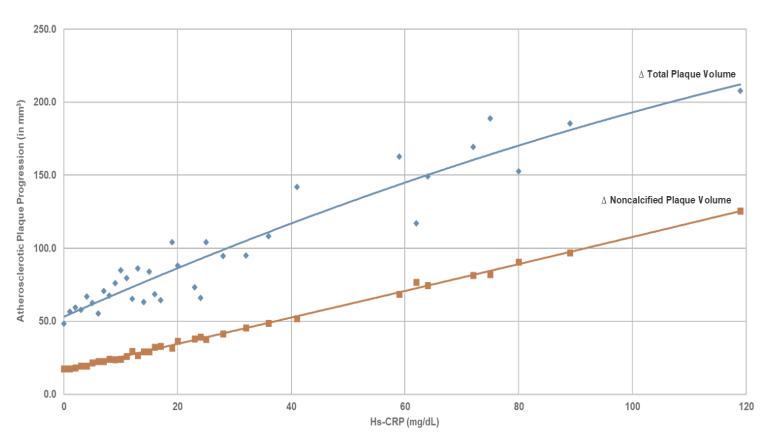


- Standards for Regression / Progression
 - Beyond Repeatability
 - Clinically Meaningful Change in Prognosis
- Optimal Timing for Risk and/or Treatment Effect
- Issues Specific to CCTA*





Atherosclerotic Plaque Progression and Inflammation



- Plaque progression >2-fold ↑ with Hs-CRP ≥2 mg/dL for <u>Total</u> and <u>Noncalcified</u> (necrotic core and fibrofatty) plaque (p<0.01); even when controlling for risk factors & statin use
- Calcified plaque progression was unrelated to Hs-CRP (p=0.3)
- Associations between HIV infection and a greater burden of noncalcified plaque are also reported

Concluding Remarks

- Growing Evidence for Plaque Assessment with CCTA
- More Prognostic Data is Needed
- A lot we do not know, factors that will be essential for regression & links to improved patient outcomes



