CARDIAC CT FOR RISK STRATIFICATION OF CAD

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September 12, 2021

LEARNING OBJECTIVES & DISCLOSURES

- To understand the contemporary use of CT for the diagnosis and risk stratification of Coronary Heart Disease

- I have no disclosures

AGENDA

- Risk stratification with Coronary Artery Calcium Score
- CT Coronary Angiography
  - Excluding disease
  - Stable and Unstable Chest Pain
  - Plaque characterization
  - Functional assessment

BACKGROUND OF CAC SCREENING

- ASCVD remains a major cause of death globally.
- ASCVD risk assessment and subsequent allocation of interventions guided by demographic characteristics, clinical risk factors, and lab measures
- Clinical risk scores lack accuracy in predicting ASCVD risk
- 2013 ACC/AHA and 2016 ESC guidelines broadened eligibility of statin use -> overtreatment?

thebmj

STATE OF THE ART REVIEW

Role of coronary artery calcium score in the primary prevention of cardiovascular disease

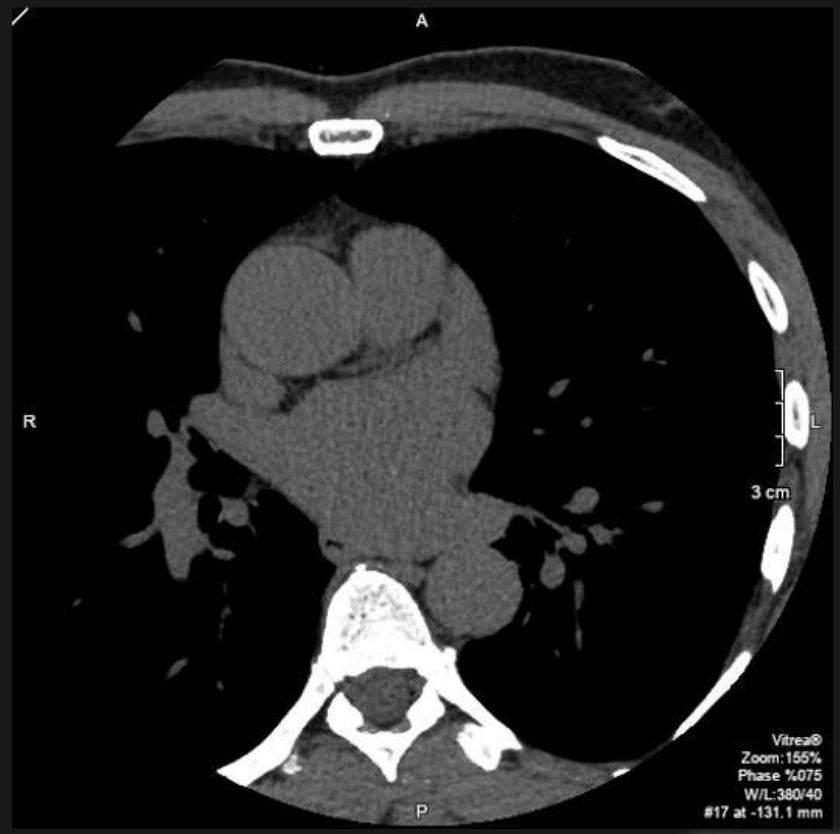
Khurram Nasir,[1,2] Miguel Cainzos-Achirica[1,2]

BMJ 2021; 373 Published 04 May 2021

- Agatston and Janowitz published the first technique for coronary artery calcium (CAC) scoring in **1990**.
- Each lesion with area ≥1mm2 and radiological attenuation >130 HU assigned a score that integrates volume and attenuation/density.
- score as a sum of individual lesions, ranging from 0 to ∞
- simple to quantify, little test time, and interpretation is done in a semi-automated manner
- Standardized acquisition, widespread use, well known CAC thresholds

CORONARY CALCIUM SCORING

- highly sensitive imaging test for detection of Ca2+ dense structures, small calcifications in coronary walls.
- Histopathologic study in 1995 (Rumberger et al) showed CAC area roughly 1/5th total coronary plaque
- Non-calcified plaque may be present in the absence of calcification, severe coronary stenoses are rare.



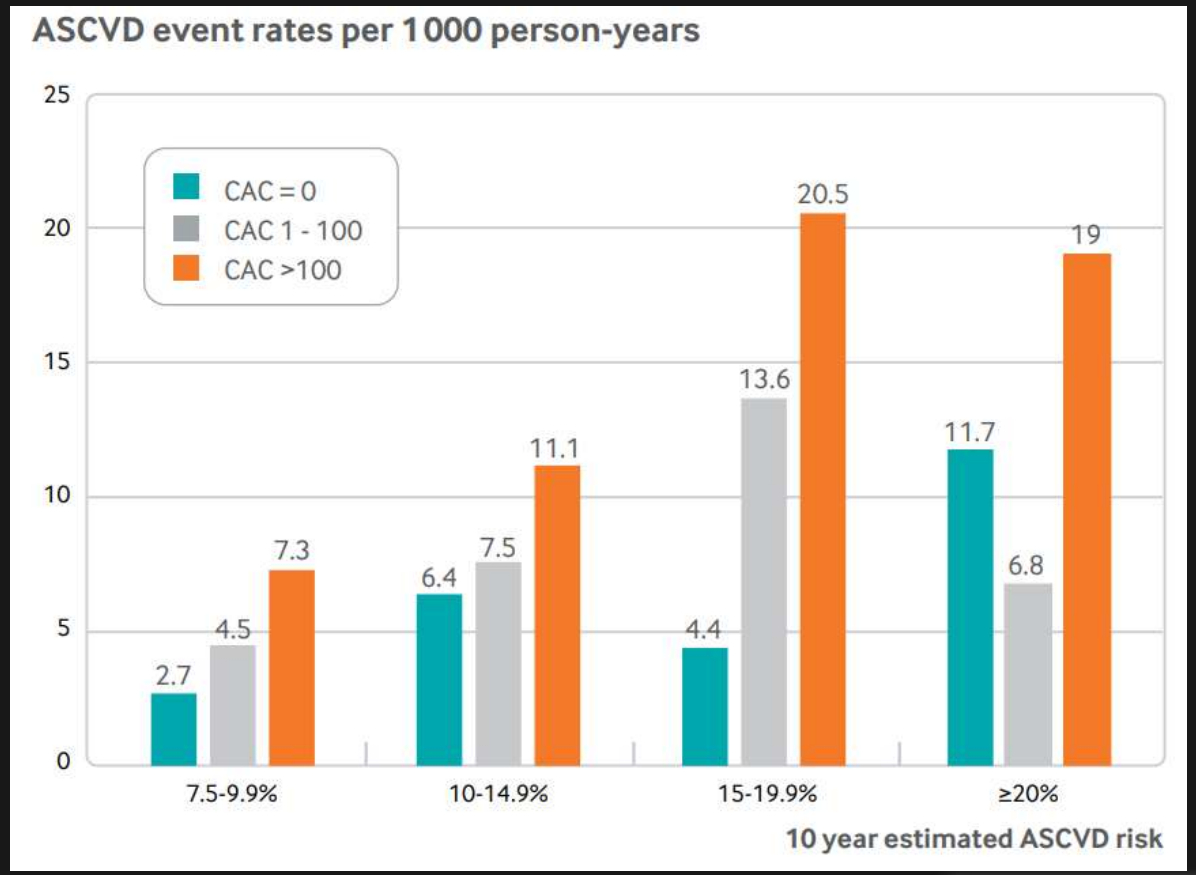
SHOW ME THE DATA!

Study	Year	Patients	Results
Prospective Army CAC Project[5]	2005	2,000	CAC was associated with an increase in coronary event risk by a factor of 12 during 3 years of follow-up.
Rotterdam Study[6]	2005	1,795	Relative risk of coronary events for CAC 101-400, 401-1000, and >1000 (compared with scores of 0-100) were 3.1, 4.6, and 8.3, respectively over 3 years follow up.
Cooper Clinic Cohort[7]	2005	10,746	Age-adjusted rates (per 1,000 person-years) of hard events for no detectable CAC and incremental sex-specific thirds of detectable CAC were 0.4, 1.5, 4.8, and 8.7, respectively over 3.5 years.
St. Francis Heart Study[8]	2005	4,903	Subjects with ASCVD events had higher baseline CAC scores than those without events. Relative risk for all ASCVD events of CAC ≥100 was 11.1 compared to CAC <100.
MESA[9]	2008	6,814	Adjusted risk of a coronary event increased by 7.73 when CAC 101-300 and 9.67 when CAC >300 regardless of ethnicity.
Heinz Nixdorf Recall[10]	2010	4,129	Reclassifying intermediate risk subjects with CAC <100 to the low-risk category and CAC >400 to high-risk yielded a reclassification improvement (NRI) of 21.7% and 30.6% for the FRS, respectively.
Jackson Heart Study[11]	2015	2,944	In African Americans, CAC was associated with prevalent CVD. CAC improved the diagnostic accuracy of the FRS by 14%.
Framingham Offspring[12]	2016	3,486	CAC was most strongly associated with major coronary heart disease independent of Framingham risk factors and improved discriminatory value beyond risk factors for coronary heart disease.
CARDIA[13]	2017	3,043	In adults 32 to 46 years, those with any CAC had a 5-fold increase in CHD events and 3-fold increase in CVD events.
CAC Consortium[14,15]	2020	66,636	CAC was the most reliable predictor for long-term mortality.

Table reproduced from Gagel, et al "The Ever-Growing Role of Coronary Artery Calicum in primary Prevention", www.acc.org, June 21,2021

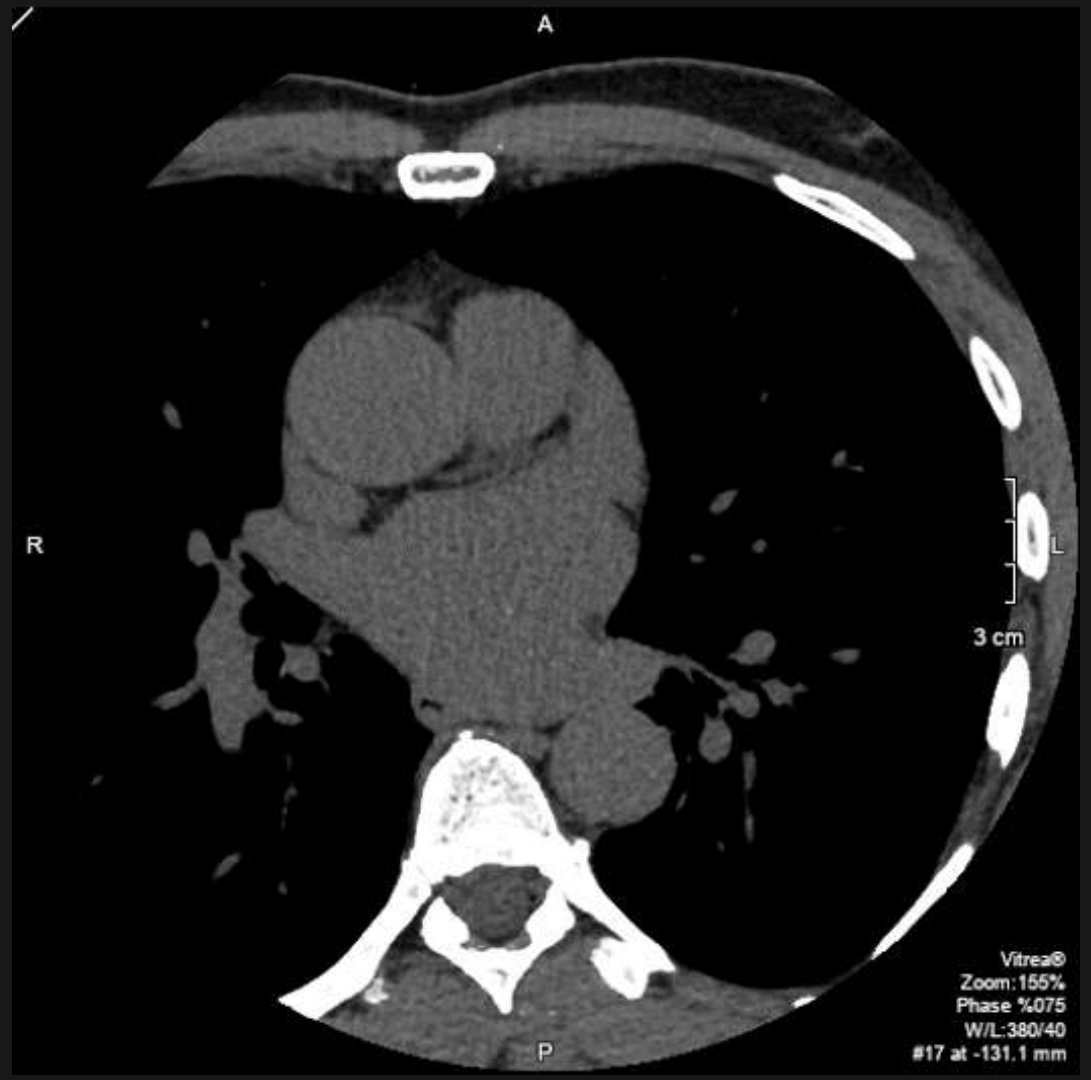
“DE-RISKING” AND THE POWER OF ZERO

- CAC=0 confers a low risk for future CV events and mortality.
- One of the strongest negative risk markers of ASCVD events over 10-15 years, event rates below 2013 guideline threshold for statin benefit in *intermediate and low-risk individuals*
- Sawar et al 2009 Meta-analysis of 13 studies with ~72000 asymptomatic patients showed only 154 individuals had CV event in 3-5 years
- Even among high risk MESA showed significantly lower events in CAC 0 (NNT 549 vs. 42 in patients with hsCRP >2)



CASE EXAMPLE

- 47 Y man with HTN on a lisinopril with BP 135/70, non-smoker who wants to know about his risk in the presence of family history of MI. Should he take a statin?
  - Total Chol 185
  - HDL 44
  - LDL 131
  - Trig 150
- 10 year ASCVD risk of 3.5%



LMA: 43

LAD: 365

LCX: 21

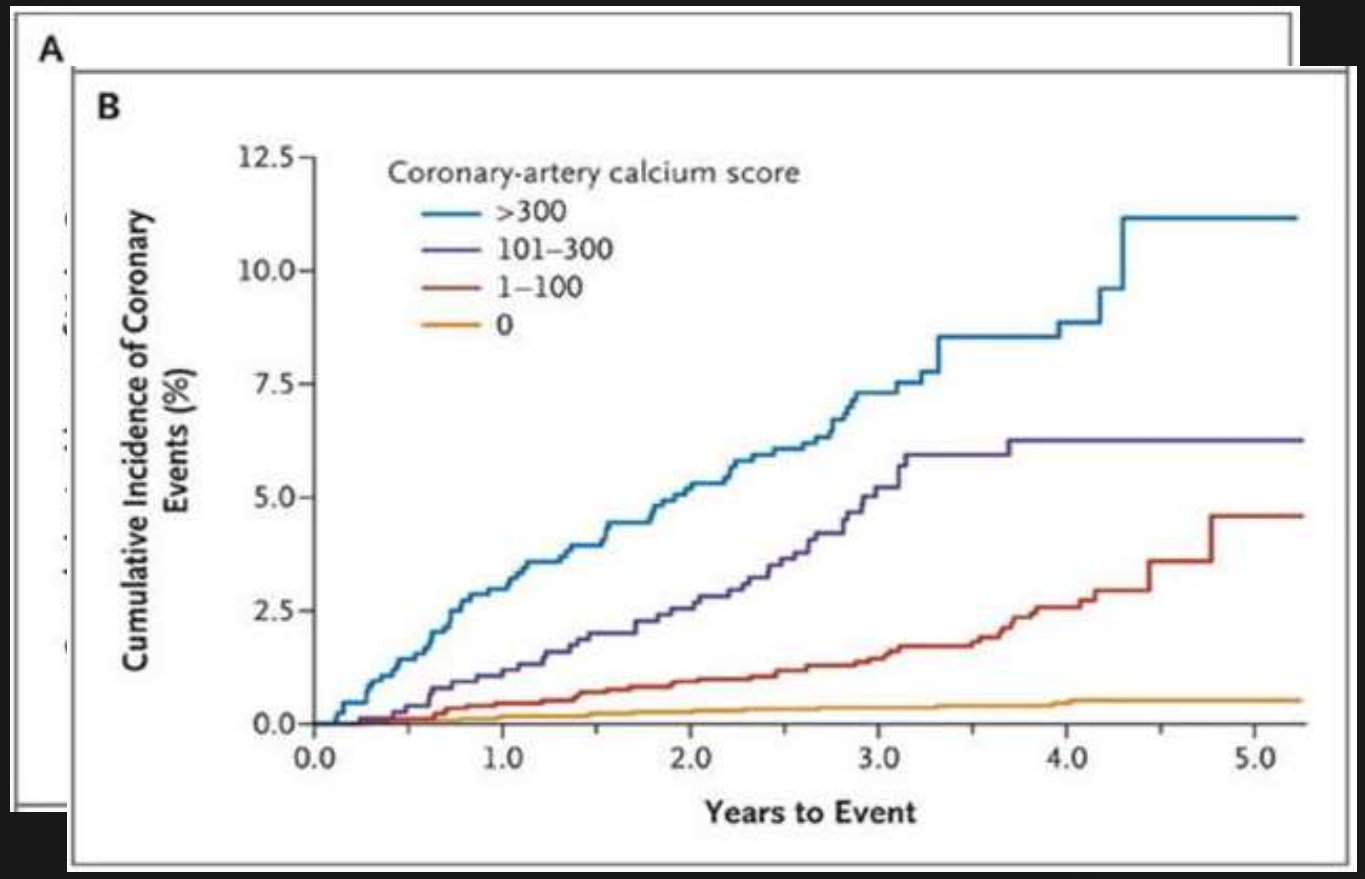
RCA: 76

Total: 595

Percentile: 80%

SO WHAT ABOUT ELEVATED SCORES?

- Elevated CAC Identifies patients who may not have been considered candidate for preventative therapy but may receive a net benefit from treatment
- The number of vessels with coronary calcifications has additive prognostic value
- In MESA population a CAC score of 1-100 was associated with a nearly 4-fold higher risk of hard events (95% CI 1.72, 8.79), while a CAC score >300 was associated with a nearly 7-fold higher hard event risk (95% CI 2.93, 15.99) compared to those who had a CAC score of 0.
- Each doubling of CAC was associated with a 20% increased risk of events (95% CI 1.12, 1.29)



Detrano et al, 2008, NEJM – MESA substudy of CAC -Panel A shows the rates for major coronary events (myocardial infarction and death from coronary heart disease), and Panel B shows the rates for any coronary event. The differences among all curves are statistically significant (P<0.001)

MESA The Multi-Ethnic Study of Atherosclerosis

MESA 10-Year CHD Risk with Coronary Artery Calcification

Back to CAC Tools

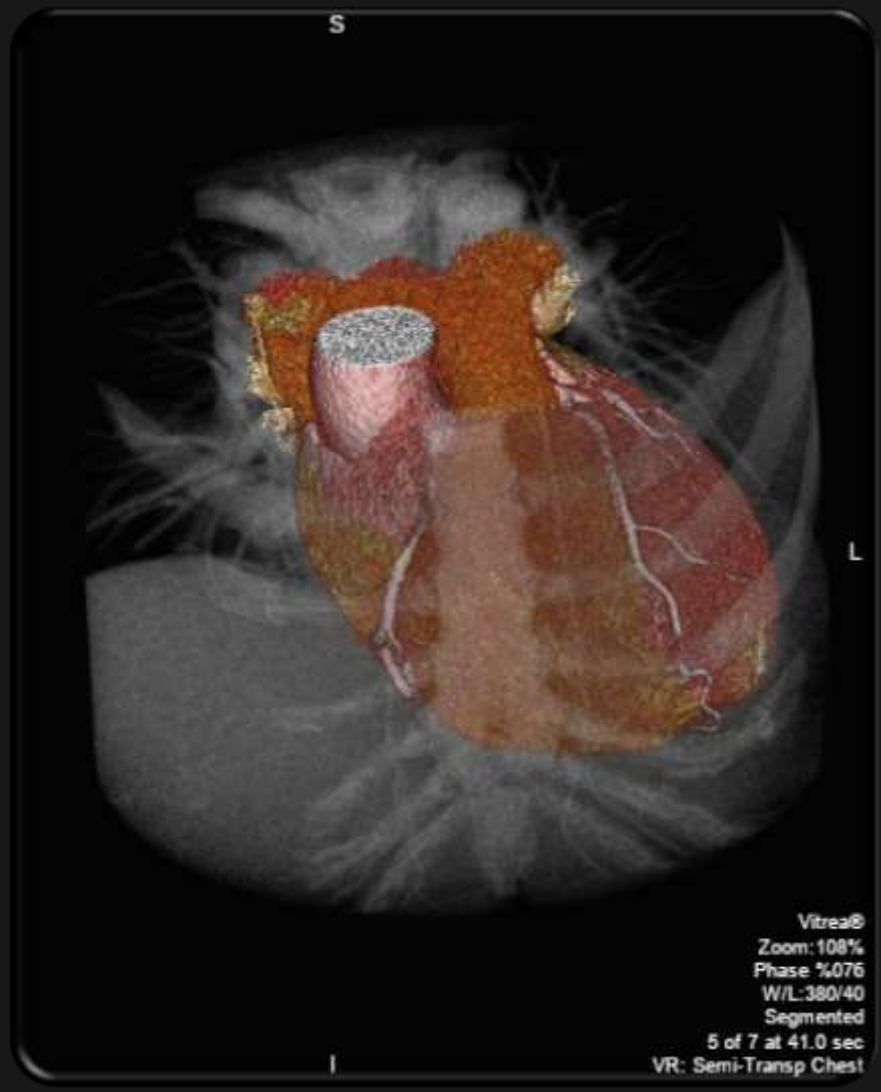
1. Gender	Male ◉	Female ○				
2. Age (45-85 years)	47	Years				
3. Coronary Artery Calcification	595	Agatston				
4. Race/Ethnicity	**Choose One**					
Caucasian	◉					
Chinese	○					
African American	○					
Hispanic	○					
5. Diabetes	Yes ○	No ◉				
6. Currently Smoke	Yes ○	No ◉				
7. Family History of Heart Attack (History in parents, siblings, or children)	Yes ◉	No ○				
8. Total Cholesterol	185	mg/dL	or	4.8	mmol/L	
9. HDL Cholesterol	44	mg/dL	or	1.1	mmol/L	
10. Systolic Blood Pressure	135	mmHg	or	18.0	kPa	
11. Lipid Lowering Medication	Yes ○	No ◉				
12. Hypertension Medication	Yes ◉	No ○				

Calculate 10-year CHD risk

The estimated 10-year risk of a CHD event for a person with this risk factor profile including coronary calcium is 16.9%. The estimated 10-year risk of a CHD event for a person with this risk factor profile if we did not factor in their coronary calcium score would be 6.5%.

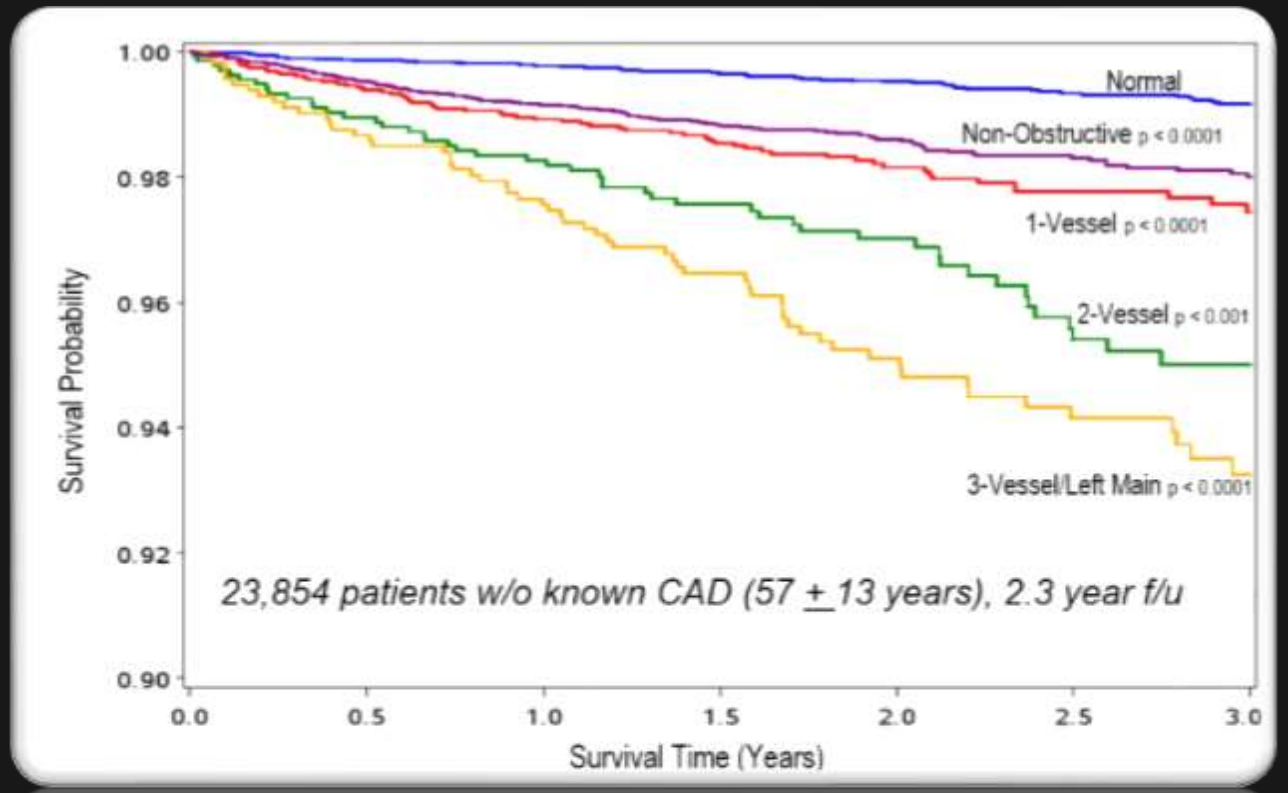
CORONARY CT ANGIOGRAPHY

Is there added benefit of CTA in asymptomatic patients for assessing their risk?



ADDED BENEFIT OF CTA OVER CAC?

- CONFIRM international, multicenter registry of 24,000 asymptomatic patients
- demonstrated progressive increase in mortality from normal -> 3V/LM
- Addition of cCTA to a model with Framingiham + CACS did not lead to a significant improvement for all-cause mortality



Cho, I et al 2012, “Coronary CTA and risk of all-cause mortality and nonfatal MI in subjects without chest pain syndrome from the CONFIRM Registry. *Circulation*, *126*(3), 304-313.

THE POWER OF CTA

- Since 2005 multiple studies have confirmed high accuracy in detection and exclusion of CAD considered obstructive on invasive coronary angio.
- Coronary CTA high unlikely to miss patients with highest risk disease (LM or Prox LAD) -> Very high NPV
- The absence of CAD on CTA is associated with excellent prognosis and very low rate of cardiac events over 5 years – AKA the Warranty Period

STABLE CHEST PAIN

- Evaluation of stable chest pain is common and costly
- Several well studied, prognostically useful methods for CAD
- Current US guidelines favor a functional assessment first

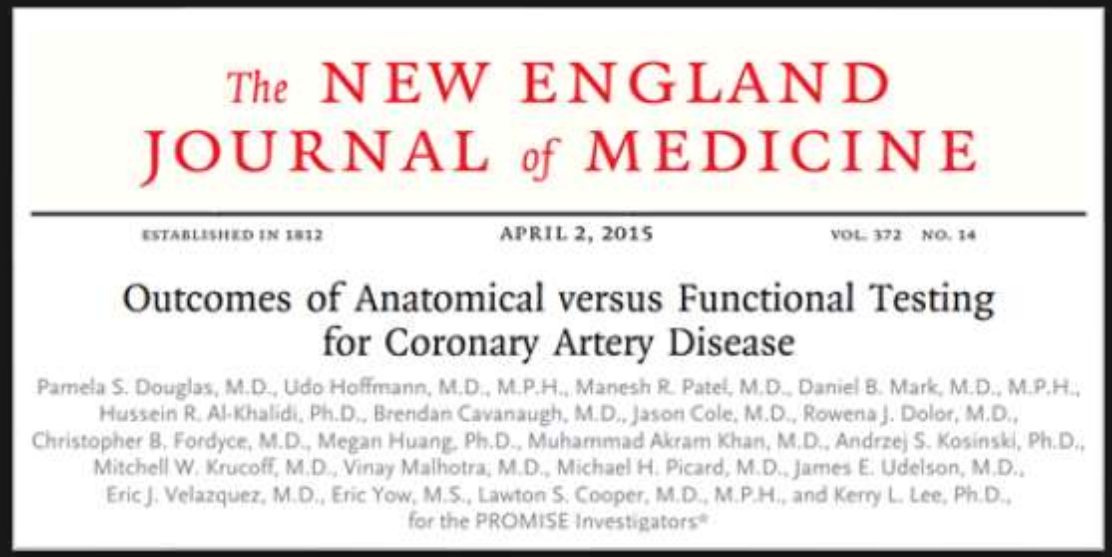
2012 ACC/AHA/ACP GUIDELINE FOR DIAGNOSIS AND MANAGEMENT OF PATIENTS WITH SIHD

- Ischemia tests preferred – stress echo or SPECT were the preferred imaging tests
- Exercise ECG preferred if no prior revasc, non-high pre-test risk
- Pre-Test Risk by Diamond and Forster
- Coronary CTA was a IIA recommendation: Unable to exercise + inconclusive test, inconclusive exercise, unable to undergo stress imaging

Test	Exercise Status		ECG Interpretable		Pretest Probability of IHD			COR	LOE
	Able	Unable	Yes	No	Low	Intermediate	High		
Patients unable to exercise									
Pharmacological stress with nuclear MPI or Echo	X	Any		X		X	X	I	B	(148–150,152–156)
Pharmacological stress Echo	X	Any	X					IIa	C	N/A
CCTA	X	Any	X	X				IIa	B	(158–166)
Pharmacological stress CMR	X	Any		X		X	X	IIa	B	(153,157,158,169–172)
Exercise ECG	X		X	Any				III: No Benefit	C	(91,132,148–156,161)
Other									
CCTA If patient has any of the following: a) Continued symptoms with prior normal test, or b) Inconclusive exercise or pharmacological stress, or c) Unable to undergo stress with MPI or Echo	Any	Any		X				IIa	C	(173)
CAC score	Any	Any	X					IIb	C	(174)

A PARADIGM SHIFT ABROAD

- In 2016 the National Institute for Health and Care Excellence (NICE) updated chest pain guideline
- elevated CTAC to first test of choice in all patients without established CAD who present with typical or atypical angina or with non-anginal chest pain plus an abnormal resting electrocardiogram (ECG).
- What drove the guideline shift?



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 APRIL 2, 2015 VOL. 372 NO. 14

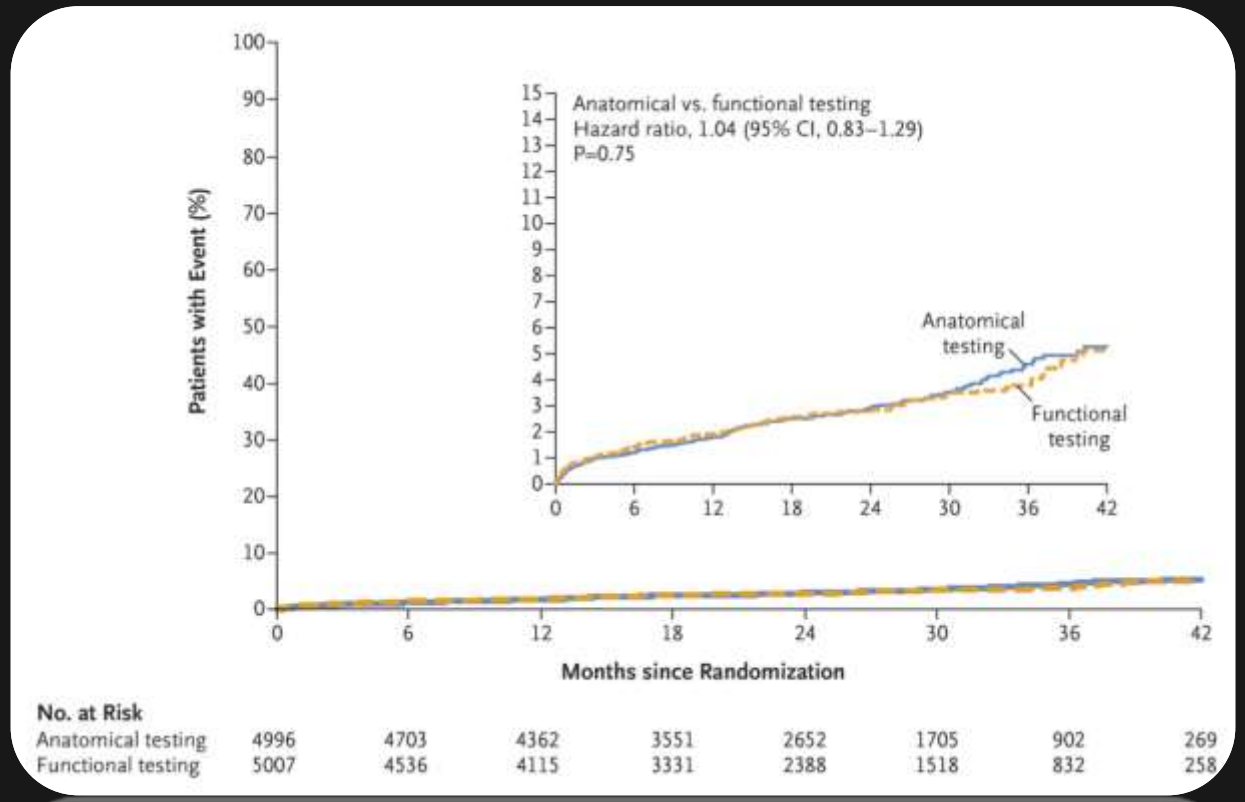
Outcomes of Anatomical versus Functional Testing for Coronary Artery Disease

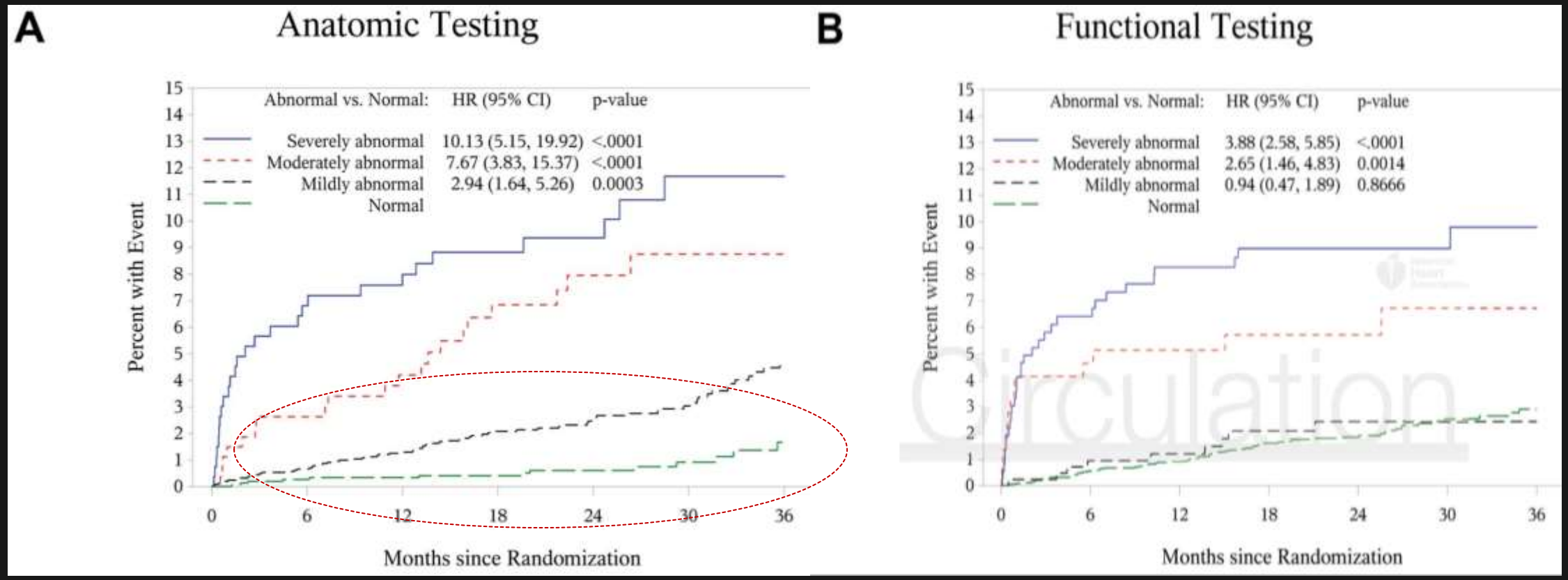
Pamela S. Douglas, M.D., Udo Hoffmann, M.D., M.P.H., Manesh R. Patel, M.D., Daniel B. Mark, M.D., M.P.H., Hussein R. Al-Khalidi, Ph.D., Brendan Cavanaugh, M.D., Jason Cole, M.D., Rowena J. Dolor, M.D., Christopher B. Fordyce, M.D., Megan Huang, Ph.D., Muhammad Akram Khan, M.D., Andrzej S. Kosinski, Ph.D., Mitchell W. Krucoff, M.D., Vinay Malhotra, M.D., Michael H. Picard, M.D., James E. Udelson, M.D., Eric J. Velazquez, M.D., Eric Yow, M.S., Lawton S. Cooper, M.D., M.P.H., and Kerry L. Lee, Ph.D., for the PROMISE Investigators*

- PROMISE – Prospective Multicenter Imaging Study for Evaluation of Chest Pain
  - 10,003 patients age ≥ 45 with suspected CAD to anatomic vs. functional non-invasive testing
  - 64-slice or greater multidetector CT vs exercise ECG (10%), stress echo (22%) or nuclear stress imaging (68%)
  - Primary endpoint: composite all-cause mortality, MI, UA hospitalization, and major complications from CV procedure (stroke, bleeding, renal failure)
  - Follow up of 25 – 50 months

PROMISE TRIAL - *RESULTS*

- No difference in primary outcome between CTA and functional testing (3.3 vs. 3.0%, P= 0.75)
- More patients in CTA group underwent ICA w/i 90 days
- CTA associated with lower rates of non-obstructive CAD on angiography (i.e., higher diagnostic yield) than functional group (3.4% vs. 4.3%, P = 0.022)
- Initial cost of diagnostic CTA was lower, but down stream costs had non-significant increase





The discriminatory ability of CTA in predicting events was significantly better than functional testing (c-index, 0.72; 95% CI, 0.68–0.76 versus 0.64; 95% CI, 0.59–0.69; *P=0.04).*

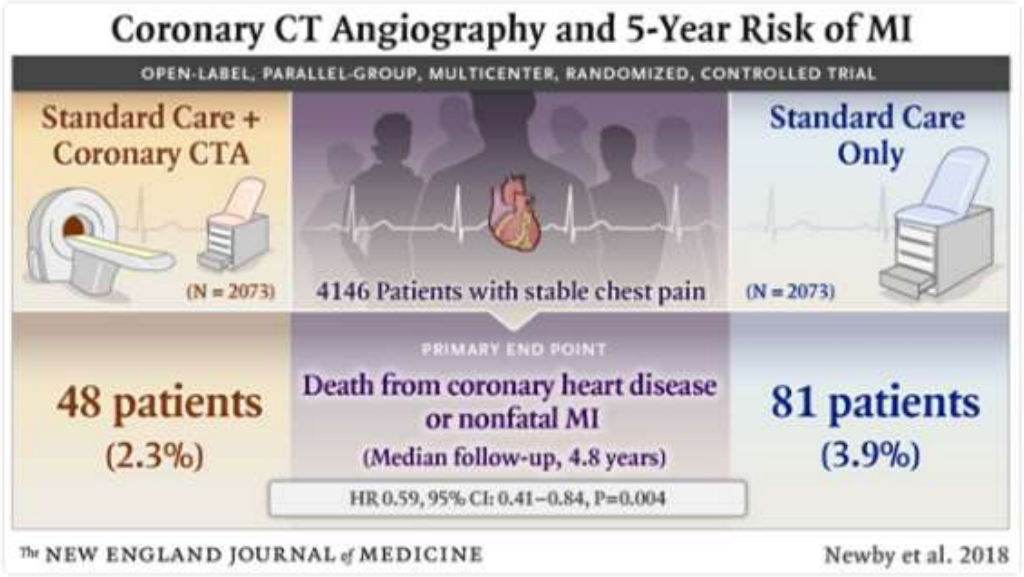
Hoffmann et al. PROMISE TRIAL, *Circulation* 2017

SCOT-HEART

NEJM @NEJM

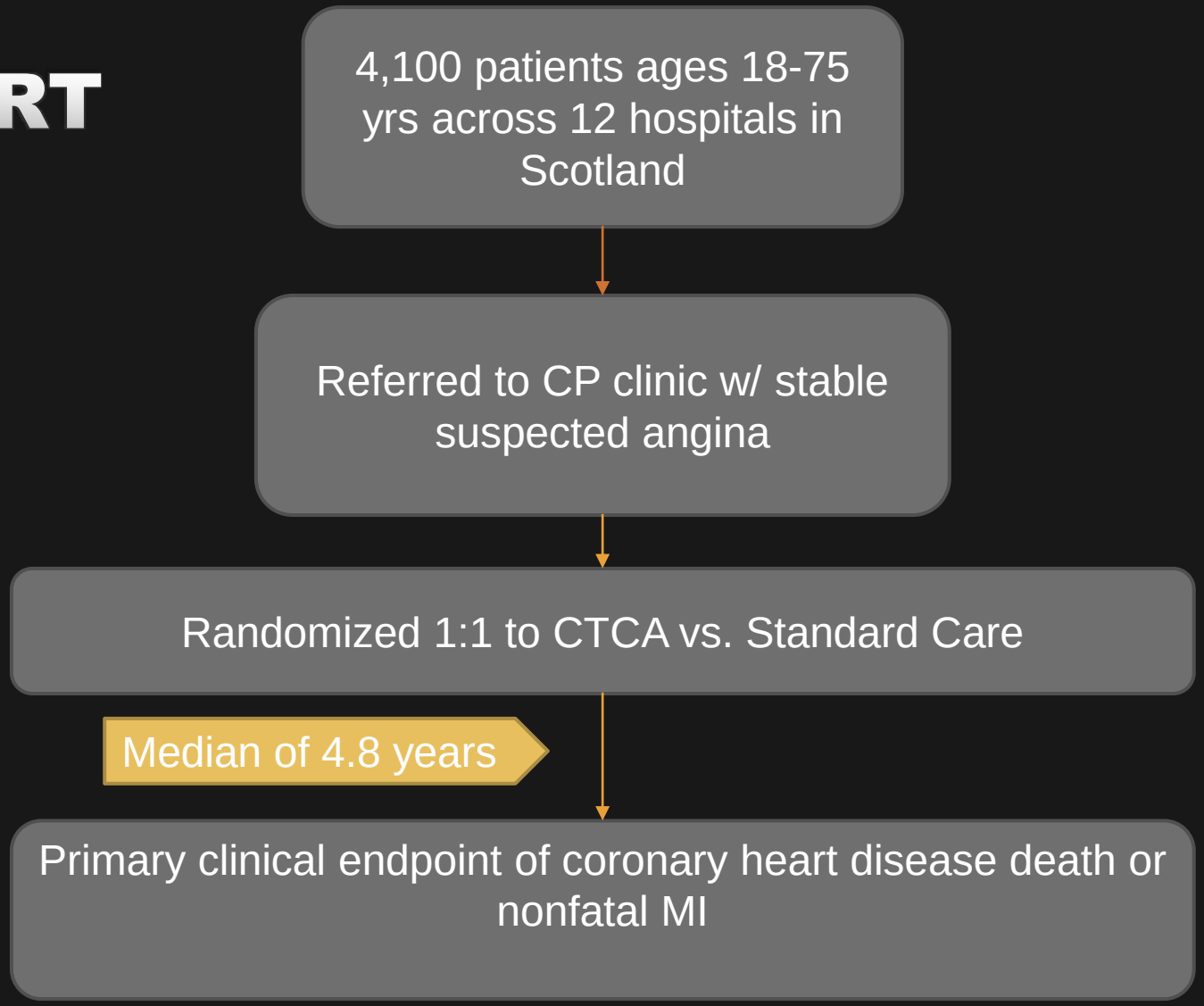
Follow

SCOT HEART: Patients with chest pain assigned to coronary CT angiography have lower rate of CHD death or nonfatal MI at five years than those who didn't receive CTA. nej.md/2OqnL2y #ESCCongress



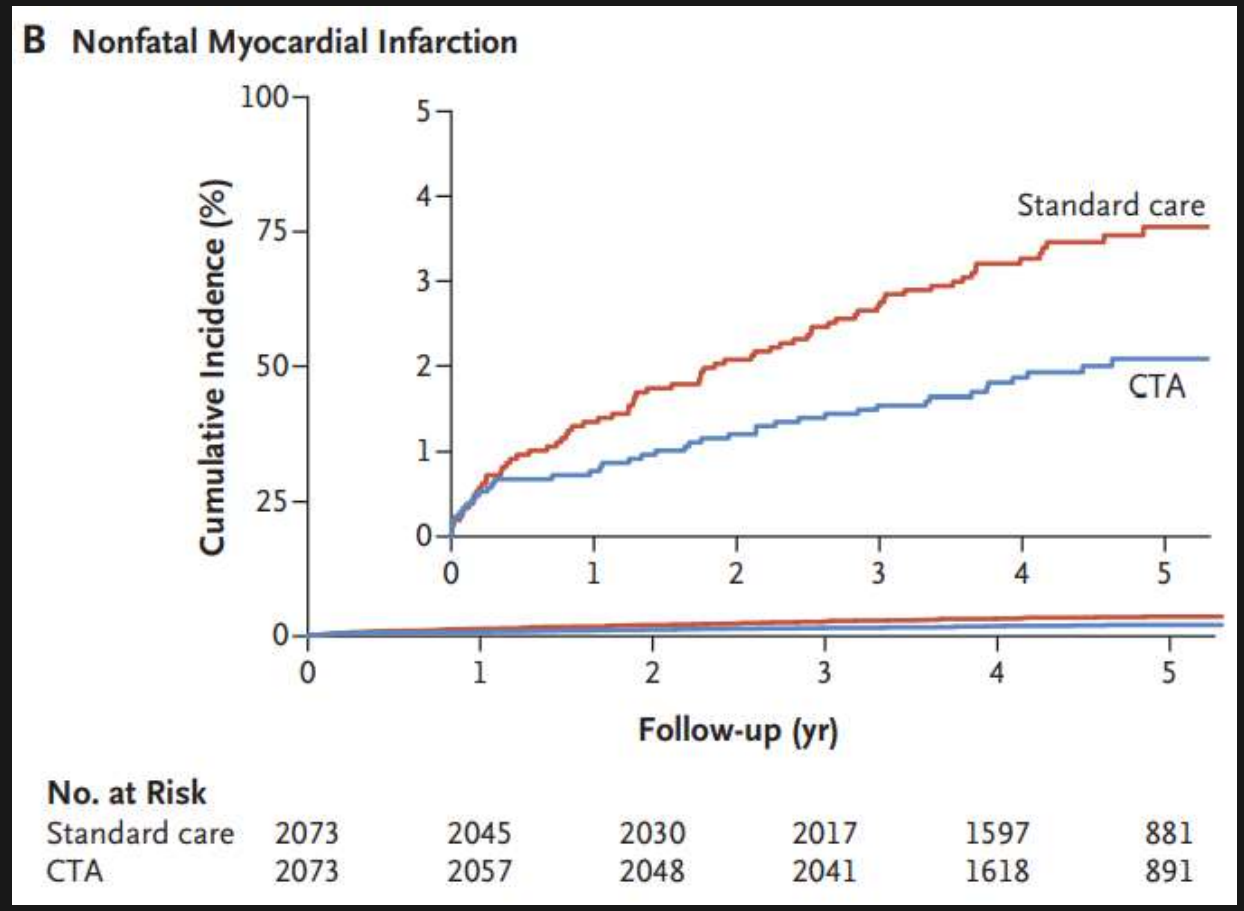
5:40 AM - 25 Aug 2018

SCOT-HEART


4,100 patients ages 18-75 yrs across 12 hospitals in Scotland
Referred to CP clinic w/ stable suspected angina
Randomized 1:1 to CTCA vs. Standard Care
Median of 4.8 years
Primary clinical endpoint of coronary heart disease death or nonfatal MI

SCOT-HEART Events: Median Follow-up of 4.8 Years

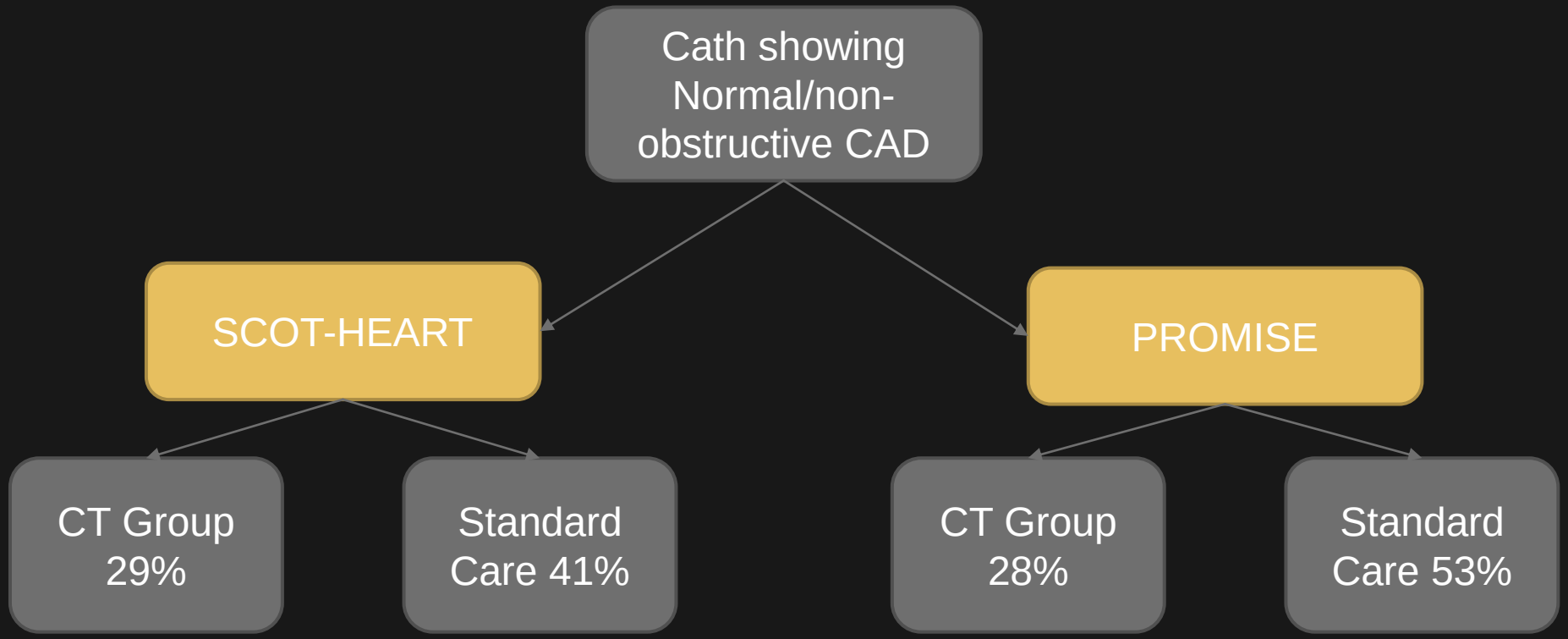
	Standard Care (n = 2,073)	CTA + Standard Care (n = 2,073)	HR (95% CI)
Primary Endpoint	3.9%	2.3%	0.59 (0.41-0.84)
Nonfatal MI	3.5%	2.1%	0.60 (0.41-0.87)
Invasive Angiography	24.2%	23.7%	1.00 (0.88-1.13)
Revascularization	12.9%	13.5%	1.07 (0.91-1.27)



SCOT-HEART AND PROMISE RESULTS

- CTA in patients referred for stable chest pain resulted in lower risk of death from CHD or nonfatal MI than standard care alone
- “Benefits appear attributable to better preventive therapies and coronary revascularization”

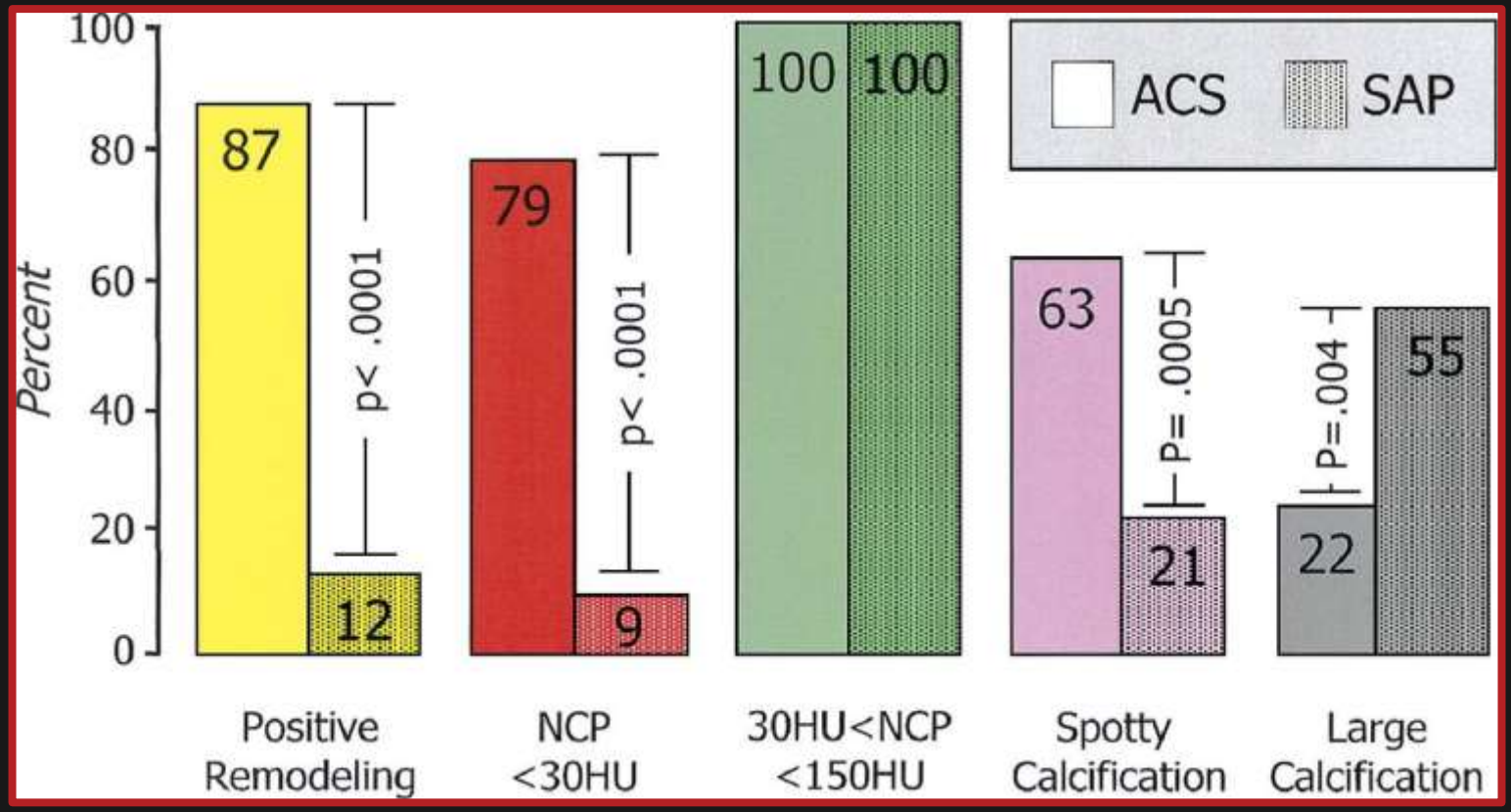
GATEKEEPER FOR CATH LAB?



- *CCTA can be used to select appropriately patients for ICA and can reduce the number performed in patients with normal coronary arteries*

PLAQUE CHARACTERIZATION

- Beyond stenosis severity!
- Motoyama et al. 2007 identified plaque features associated with increased risk of ACS
  - low attenuation plaque (<30 HU)
  - positive remodeling
  - spotty calcification



Motoyama S, et al. J Am Coll Cardiol. 2007 & 2015.

JAMA Cardiology | Original Investigation

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

A Se

Maros Fer
Nandini M
Kerry L. Le

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

Michelle C. Williams, MBChB, PhD,[a,b] Alastair J. Moss, MD,[a] Marc Dweck, MBChB, PhD,[a,b] Philip D. Adamson, MD, PhD,[a,c] Shirjel Alam, MD,[a] Amanda Hunter, MD,[a] Anoop S.V. Shah, MD,[a] Tania Pawade, MD,[a] Jonathan R. Weir-McCall, MBChB, PhD,[d] Giles Roditi, MD,[e] Edwin J.R. van Beek, MD, PhD,[b] David E. Newby, MD, PhD,[a,b] Edward D. Nicol, MD[f,g]

HIGH RISK PLAQUES

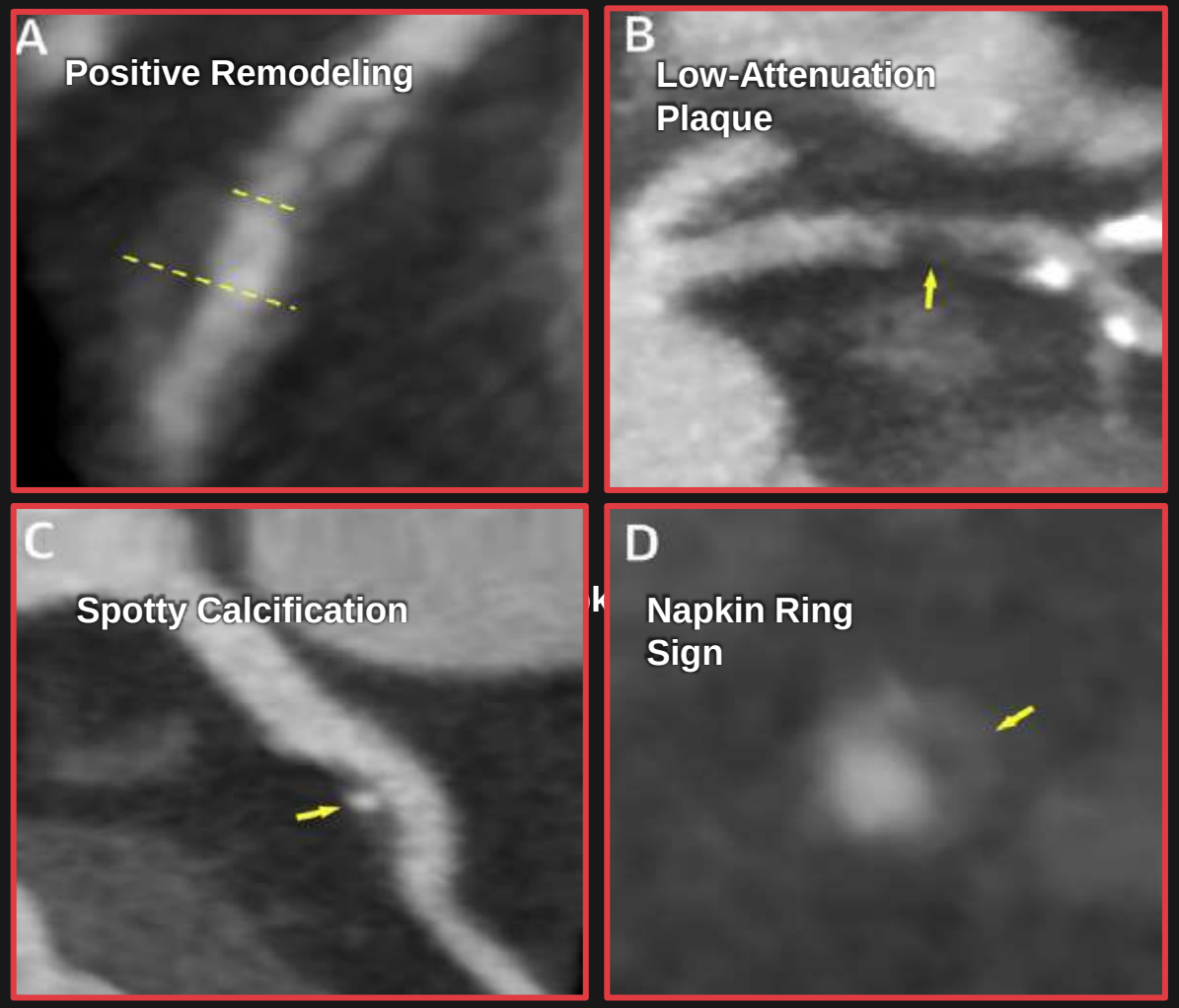
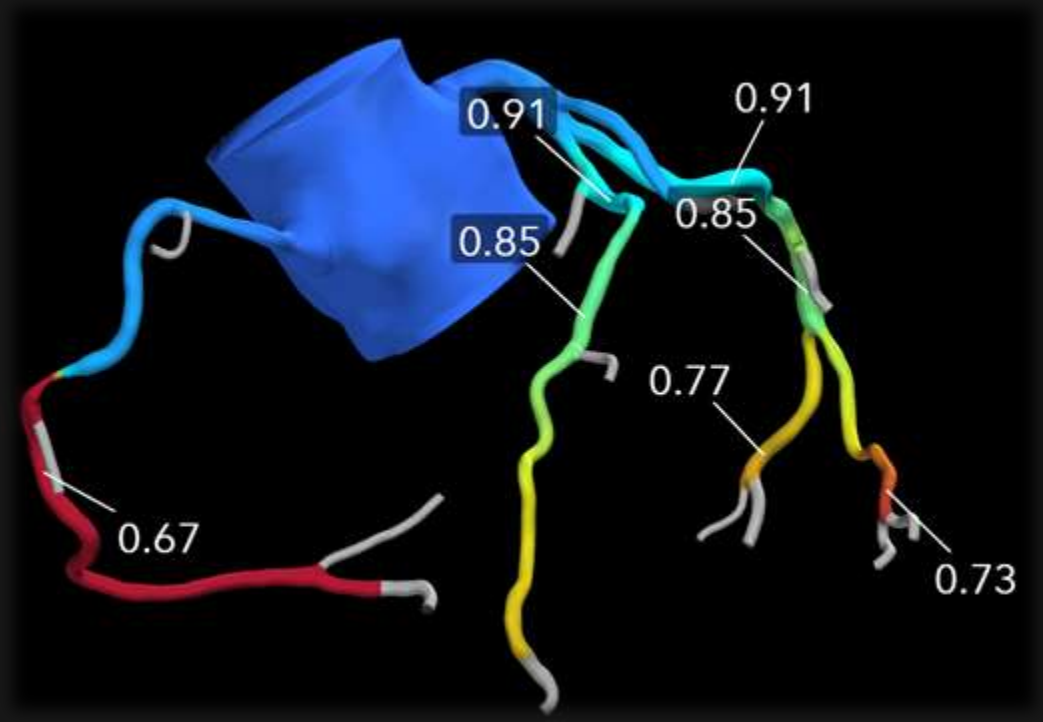


Image from Williams et al. JACC,Jan 2019

- PROMISE: HRPs associated with increased risk of MACE (HR 1.73, 95% CI 1.13-2.62)
  - Prognostic importance especially apparent among low-intermediate risk cohort with non-obstructive CAD (HR 4.31 vs. 2.64)
- SCOT-HEART: HRP increased risk of CHD death or MI 3-fold (p = 0.001).

NOT JUST ANATOMIC DATA!



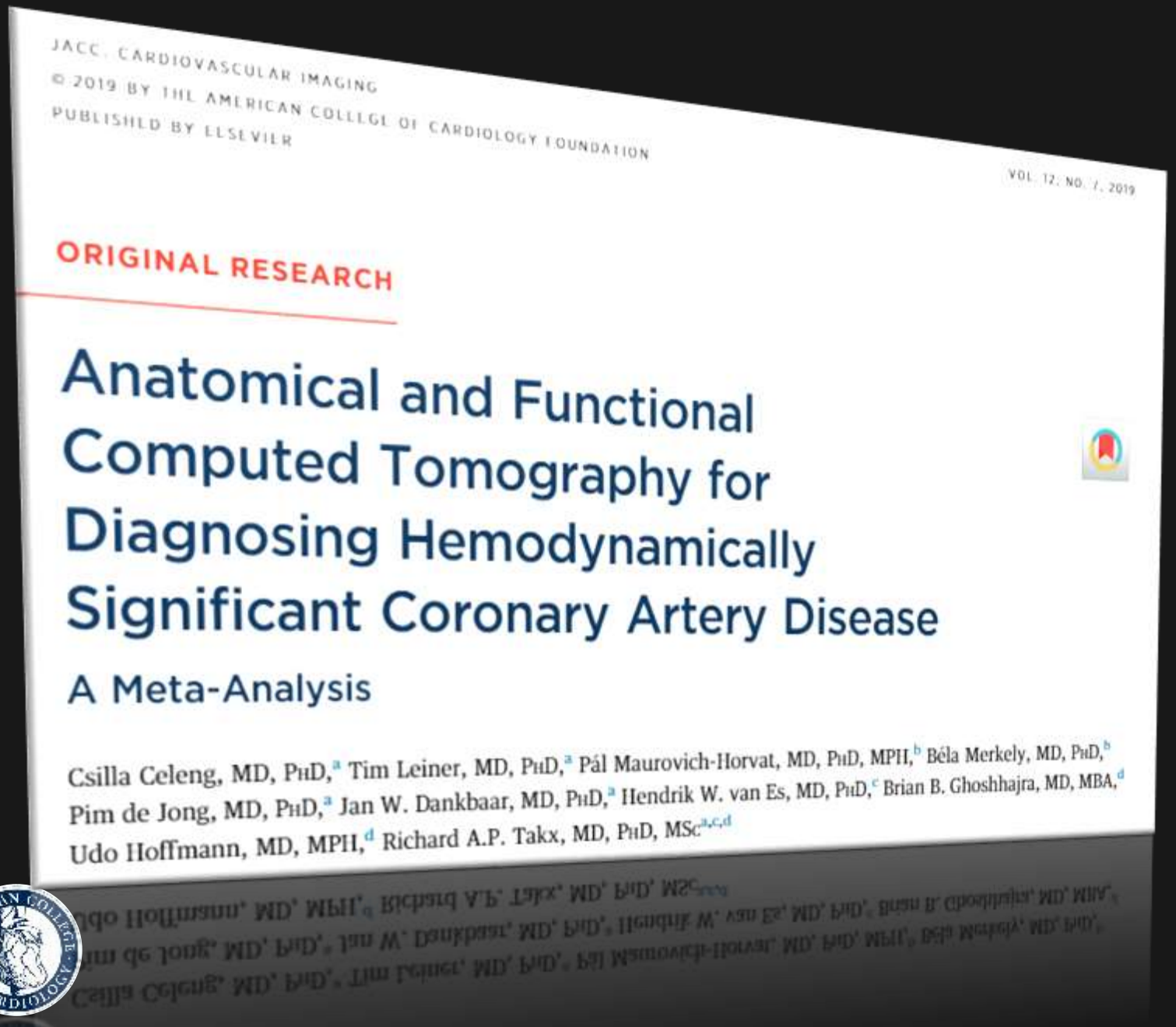
- Computed tomography angiography–derived fractional flow reserve (FFRCT) is calculated using images for CTA.
- Automatically lumen centerline assessment, luminal boundary determination, and myocardial mass assessment.
- Deep learning methods inspected and corrected by trained analysts
- FFR calculated using “a finite element mesh model and computational fluid dynamics methods based on solving the Navier–Stokes equation for flow velocity and pressure.”

Navier-Stokes Equations

The Navier-Stokes equations are the fundamental partial differentials equations that describe the flow of incompressible fluids. Using the rate of stress and rate of strain tensors, it can be shown that the components F_j of a viscous force $\mathbf{F}$ in a nonrotating frame are given by

$$\frac{F_i}{V} = \frac{\partial}{\partial x_j}\left[\eta\left(\frac{\partial u_i}{\partial x_j}+\frac{\partial u_j}{\partial x_i}\right)+\lambda\delta_{ij}\nabla\cdot\mathbf{u}\right] \tag{1}$$

$$= \frac{\partial}{\partial x_j}\left[\eta\left(\frac{\partial u_i}{\partial x_j}+\frac{\partial u_j}{\partial x_i}-\tfrac{2}{3}\delta_{ij}\nabla\cdot\mathbf{u}\right)+\mu_B\delta_{ij}\nabla\cdot\mathbf{u}\right], \tag{2}$$

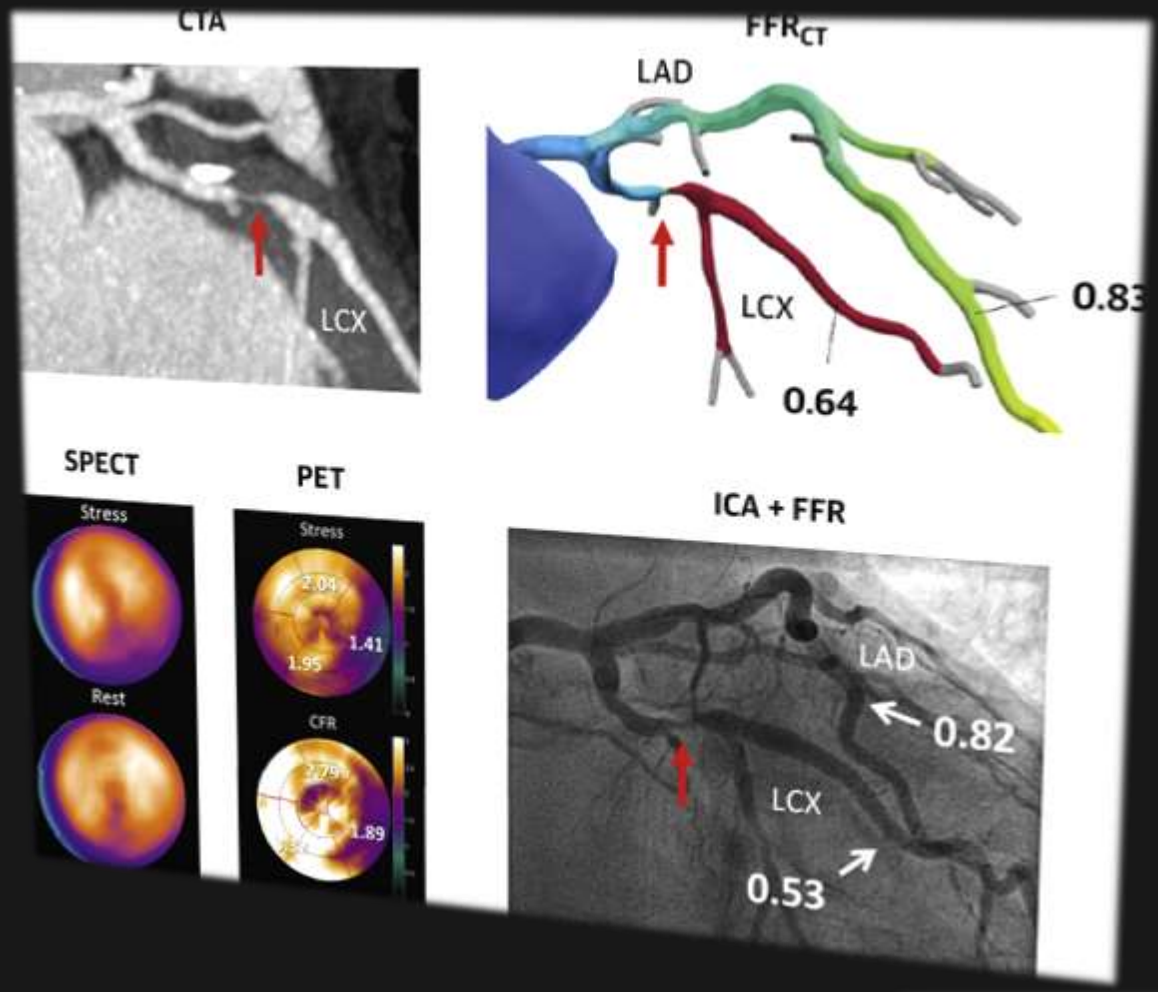


- 6,400 vessels
- invasive FFR used as a reference
- specificity of CTA (61%) remains moderate for the detection of a hemodynamically significant stenosis
- Spec of FFRCT (n= 2,432) and its combined use with CTA (n = 362) were high (78% and 80%, respectively).

PACIFIC TRIAL

Prospective Comparison of Cardiac PET/CT, SPECT/CT Perfusion Imaging and CCTA With Invasive Coronary Angiography

- Compared diagnostic performance of FFRCT, SPECT, and PET for diagnosing ischemia using FFR as the reference.
- AUCs of FFRCT, SPECT, and PET were 0.92, 0.75, and 0.91 at the patient level, and 0.94, 0.70, and 0.87 at the vessel level,
- analyzability of FFRCT was 75% (157 patients in 208 patients) at the patient level and 83% (505 vessels in 612 vessels) at the vessel level (38).
- FFRCT showed the highest diagnostic performance for vessel-specific ischemia, compared with SPECT ($P < 0.001$) and PET ($P < 0.001$) when the vessels were interpretable (83%) by CTA.



WHAT ARE THE BIG CCTA TAKEAWAYS

- CCTA has demonstrated it can lead to improved patient outcomes compared with functional testing
- High diagnostic accuracy! CCTA rarely misses severe or high-risk CA
- CCTA can be a cath lab gatekeeper -> may better select patients who might benefit from revascularization


Thanks for listening!
Any questions?
WISCONSIN
GUADALUPE MOUNTAINS
National Park
No Dogs Allowed