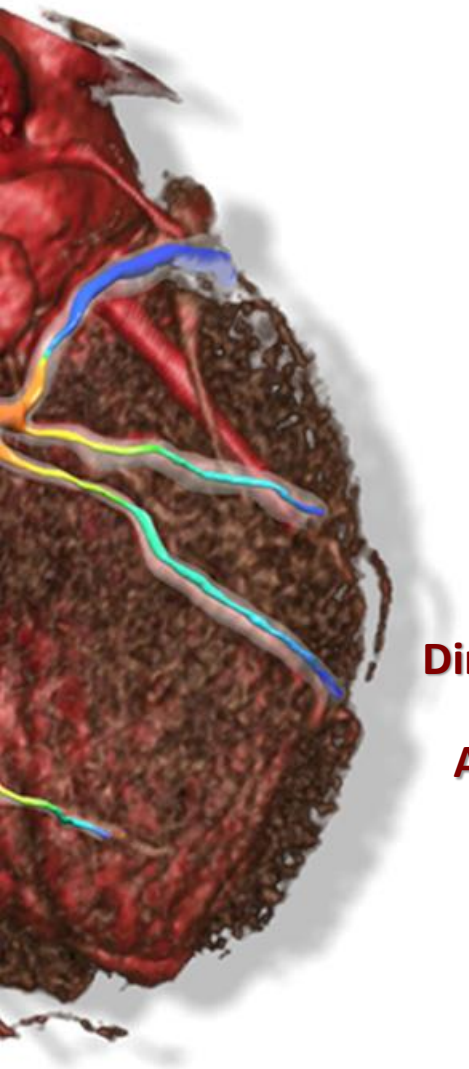
A SMARTool project workshop

CAD RISK PREDICTION AND STRATIFICATION: THE ICT APPROACH



CT Imaging of coronary atherosclerosis. State-of-the-art and beyond

Daniele Andreini, MD, PhD, FESC, FSCCT

Director, Cardiovascular CT Unit, Centro Cardiologico Monzino, Milan, Italy

Associate Professor of CV Disease, University of Milan, Italy

Tuesday 6th November 2018

CNR Research Area Campus
Building A, Room 27
via Moruzzi, 1 Pisa - Italy

Horizon 2020
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http://dx.doi.org/10.1016/j.jcmg.2012.03.009

A Long-Term Prognostic Value of Coronary CT Angiography in Suspected Coronary Artery Disease

Daniele Andreini, MD,* Gianluca Pontone, MD,* Saima Mushtaq, MD,*
Antonio L. Bartorelli, MD,*† Erika Bertella, MD,* Laura Antonioli, MD,*
Alberto Formenti, MD,* Sarah Cortinovis, MD,* Fabrizio Veglia, PHD,*
Andrea Annoni, MD,* Piergiuseppe Agostoni, MD, PHD,*† Piero Montorsi, MD,*†
Giovanni Ballerini, MD,* Cesare Fiorentini, MD,*† Mauro Pepi, MD*

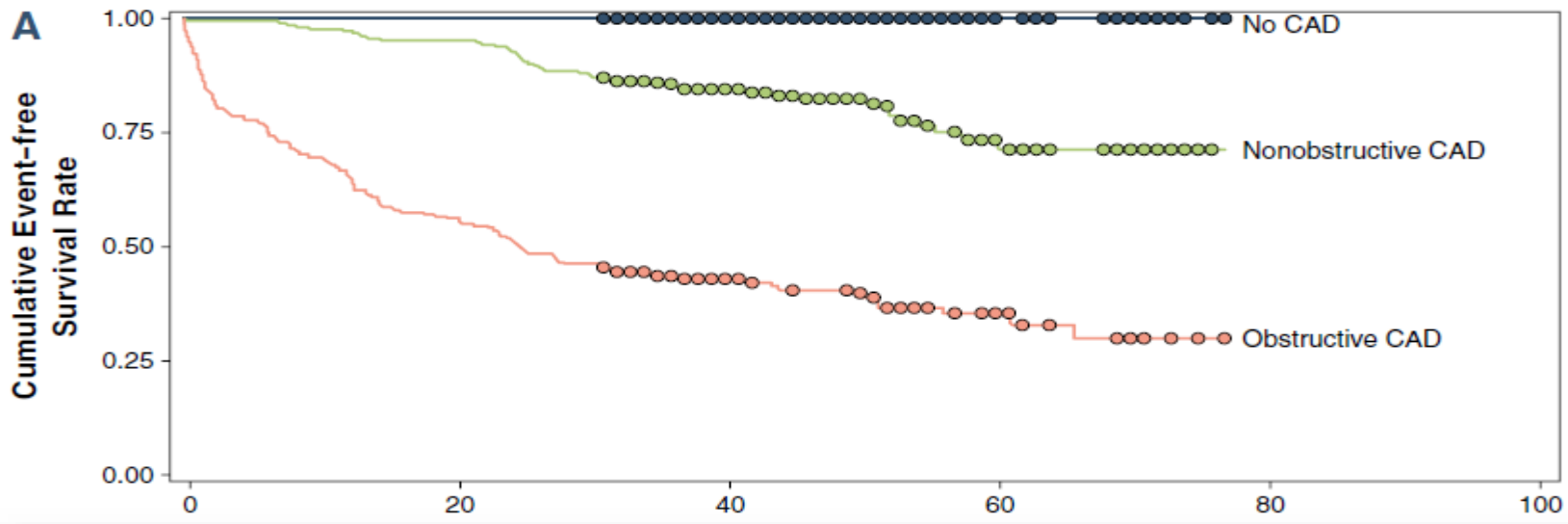

Figure 1. Kaplan-Meier Survival Curves in Patients With Normal and Abnormal Coronary Arteries

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Sex-Specific Associations Between Coronary Artery Plaque Extent and Risk of Major Adverse Cardiovascular Events

The CONFIRM Long-Term Registry

Joshua Schulman-Marcus, MD,[a] Bríain ó Hartaigh, PhD,[a] Heidi Gransar, MS,[b] Fay Lin, MD,[a] Valentina Valenti, MD,[a] Iksung Cho, MD,[a] Daniel Berman, MD,[b] Tracy Callister, MD,[c] Augustin DeLago, MD,[d] Martin Hadamitzky, MD,[e] Joerg Hausleiter, MD,[e] Mouaz Al-Mallah, MD,[f] Matthew Budoff, MD,[g] Philipp Kaufmann, MD,[h] Stepha[illegible]MD,[k] Todd V[illegible]MD,[p] Gianluc[illegible]

TABLE 3 Adjusted Hazards of MACE and MACE Components by CAD Extent, Stratified by Sex

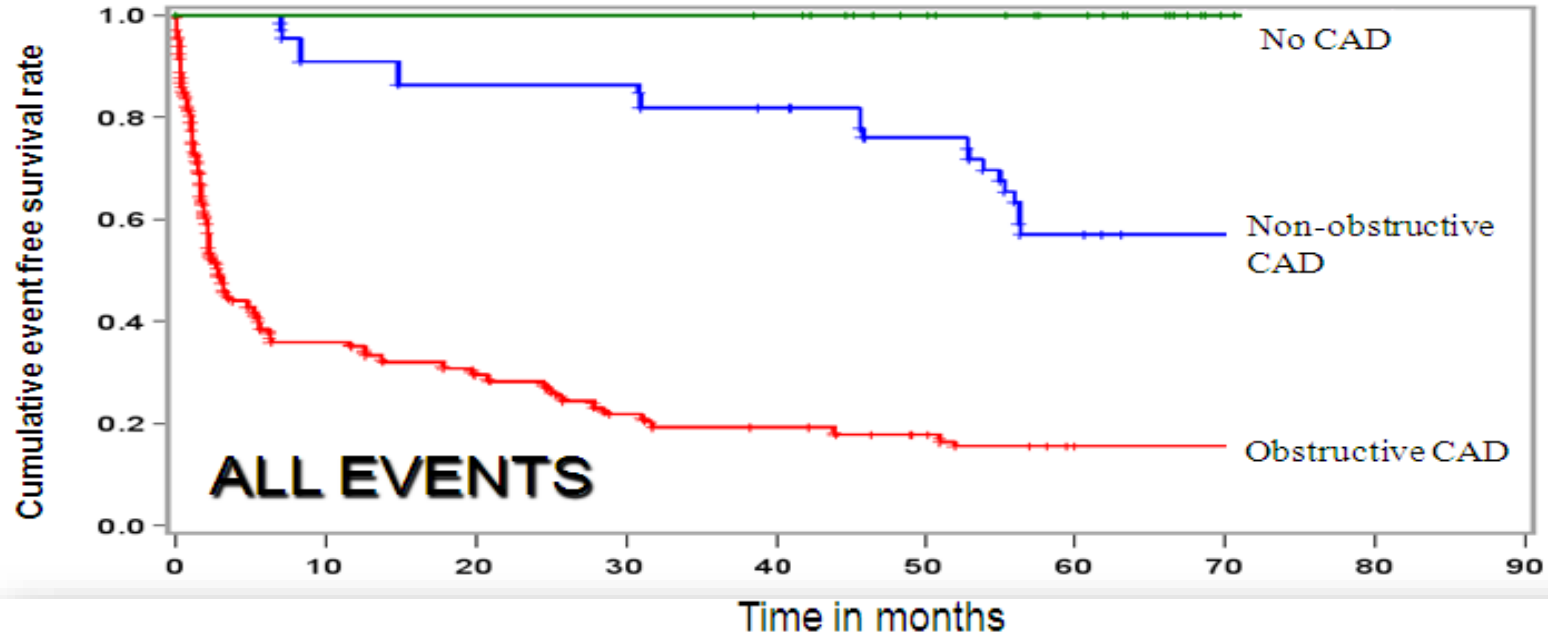
	Women		Men	
	Adjusted HR (95% CI)	p Value	Adjusted HR (95% CI)	p Value
Total MACE				
Normal	Ref	Ref	Ref	Ref
Nonobstructive	2.16 (1.41-3.29)	<0.001	2.56 (1.62-4.04)	<0.001
1-vessel obstructive	3.69 (2.35-5.78)	<0.001	2.66 (1.66-4.26)	<0.001
2-vessel obstructive	3.92 (2.24-6.85)	<0.001	3.55 (2.17-5.79)	<0.001
3-vessel obstructive/LM	5.94 (3.47-10.17)	<0.001	4.44 (2.73-7.22)	<0.001

Diabetes Care Symposium
ORIGINAL ARTICLE

Prognostic Value of Multidetector Computed Tomography Coronary Angiography in Diabetes

Excellent long-term prognosis in patients with normal coronary arteries

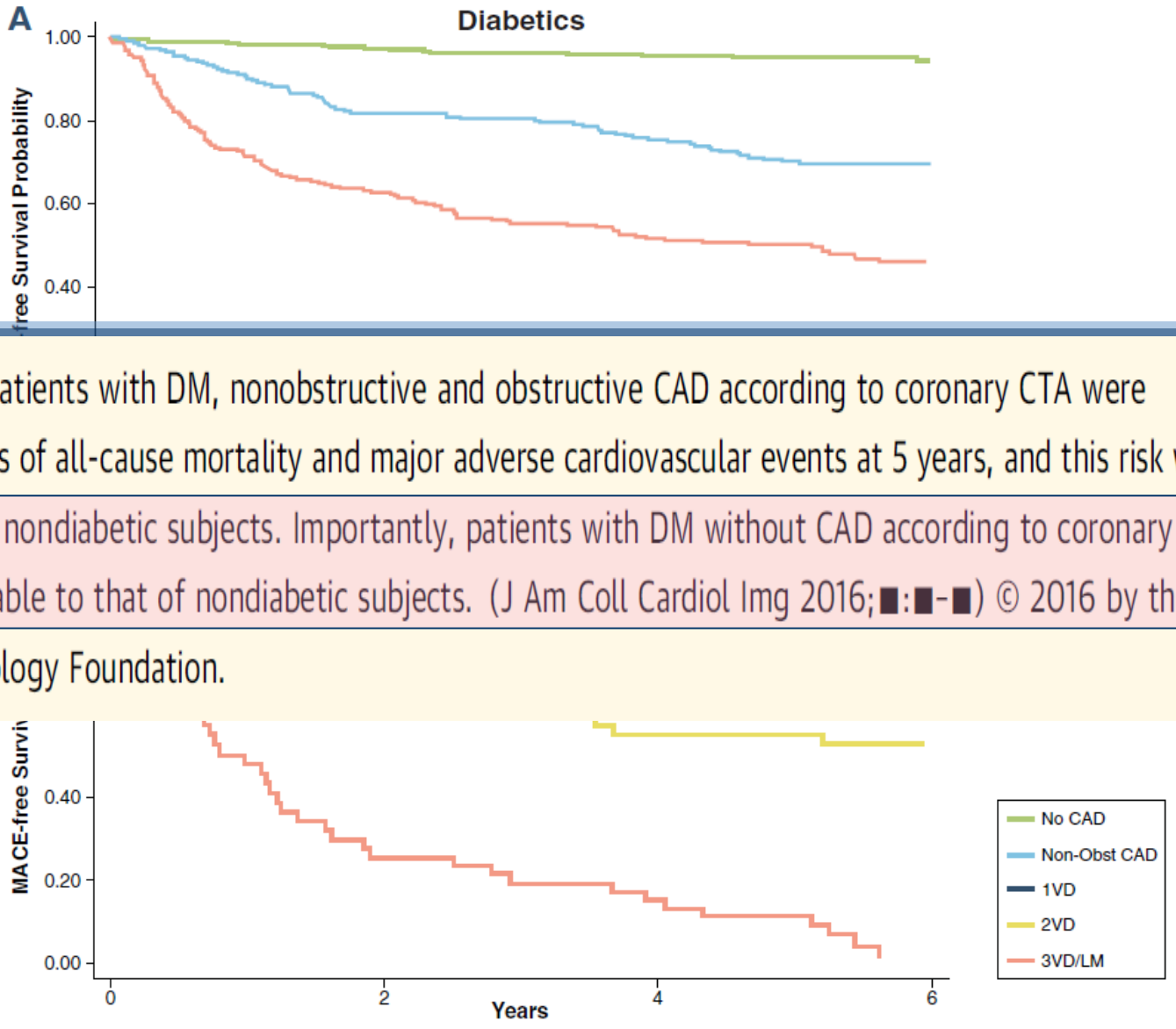
DANIELE ANDREINI, MD[1,2]
GIANLUCA PONTONE, MD[1]
SAIMA MUSHTAQ, MD[1]
ERIKA BERTELLA, MD[1]
EDOARDO CONTE, MD[1]
ANDREA BAGGIANO, MD[1]
FABRIZIO VEGLIA, PHD[1]
PIERGIUSEPPE AGOSTONI, MD, PHD[1,2]
ANDREA ANNONI, MD[1]
ALBERTO FORMENTI, MD[1]
PIERO MONTORSI, MD[1,2]
GIOVANNI BALLERINI, MD[1]
ANTONIO L. BARTORELLI, MD[1,2]
CESARE FIORENTINI, MD[1,2]
MAURO PEPI, MD[1]



Long-Term Coronary C Patients W

Philipp Blanke, MD,[a] Christ
Jeanette Soon, MBBS,[a] Ches),[c]
Matthew J. Budoff, MD,[e] Ti
Kavitha Chinnaiyan, MD,[i] R

FIGURE 4 Risk-Adjusted Kaplan-Meier Curve for Event-Free Survival Stratified According to CAD



CONCLUSIONS Among patients with DM, nonobstructive and obstructive CAD according to coronary CTA were associated with higher rates of all-cause mortality and major adverse cardiovascular events at 5 years, and this risk was significantly higher than in nondiabetic subjects. Importantly, patients with DM without CAD according to coronary CTA were at a risk comparable to that of nondiabetic subjects. (J Am Coll Cardiol Img 2016;■:■-■) © 2016 by the American College of Cardiology Foundation.

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EDITORIAL COMMENT

Screening CT Angiography in Asymptomatic Diabetes Mellitus?*

Daniele Andreini, MD, PhD

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Vol. 58, No. 8, 2011
ISSN 0735-1097/$36.00
doi:10.1016/j.jacc.2011.02.074

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

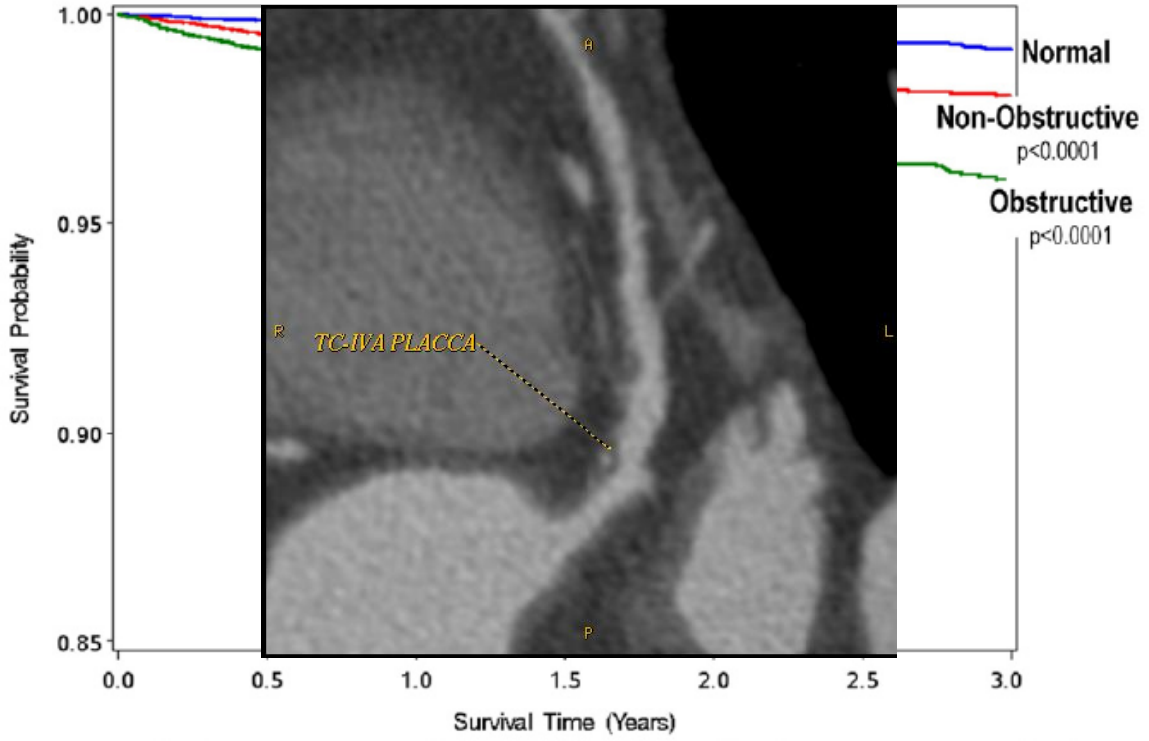
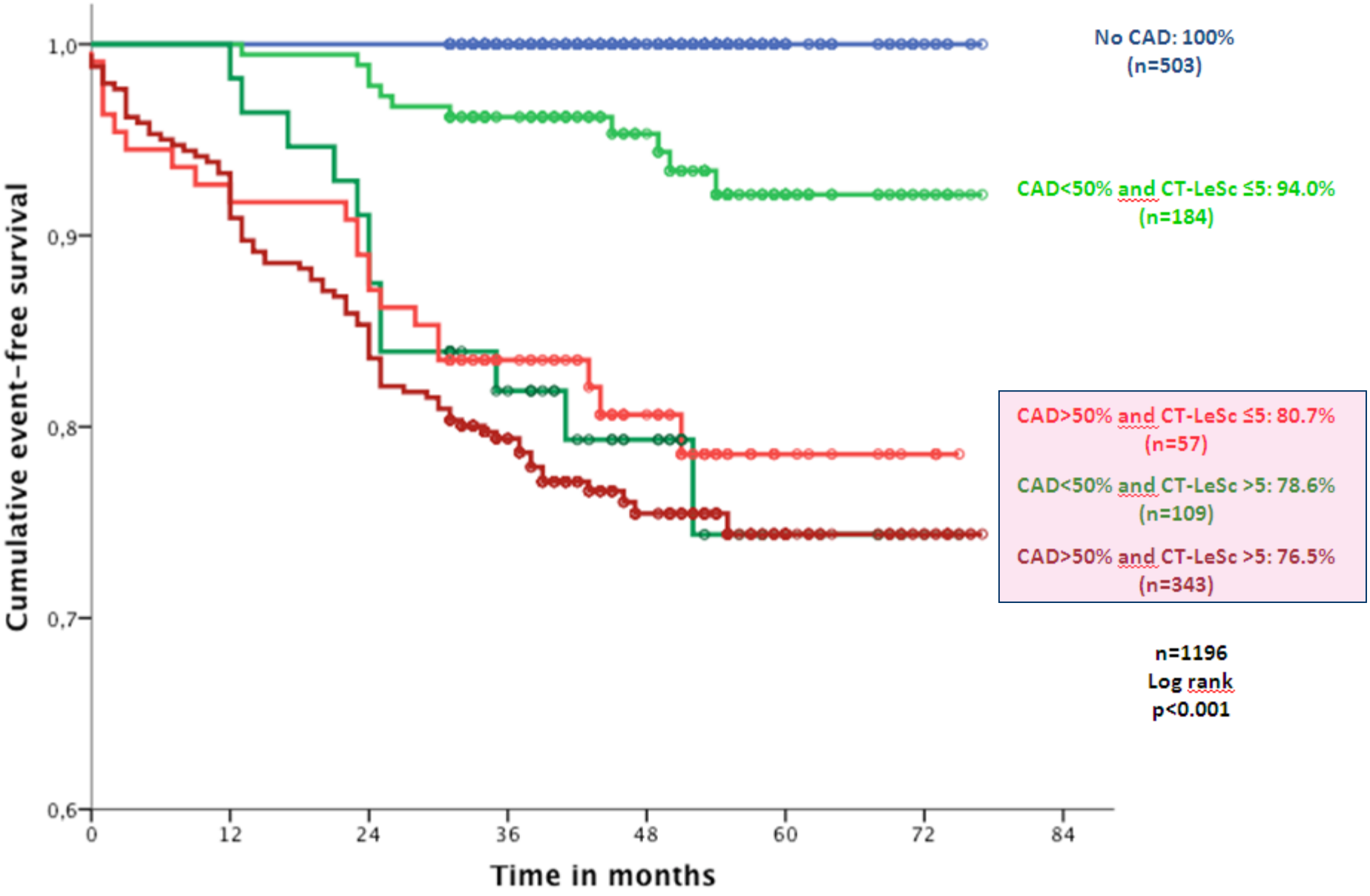


Table 1: CT-adapted Leaman Score (CT-LeSc) weighting factors

Localization			
Segment	**Right dominance**	**Left dominance**	**Balanced**
RCA proximal	1	0	0.5
RCA mid	1	0	0.5
RCA distal	1	0	0.5
PDA	1	na	0.5
Left main	5	6	5.5
LAD proximal	3.5	3.5	3.5
LAD mid	2.5	2.5	2.5
LAD distal	1	1	1
1st Diagonal	1	1	1
2nd Diagonal	0.5	0.5	0.5
LCx proximal	1.5	2.5	2.0
1st Obtuse marginal	1	1	1
LCx distal	0.5	1.5	1
2nd Obtuse marginal	1	1	1
PDA from LCA	na	1	na
PL branch from LCA	na	0.5	0.5
PL branch from RCA	0.5	na	na
Intermediate branch	1	1	1

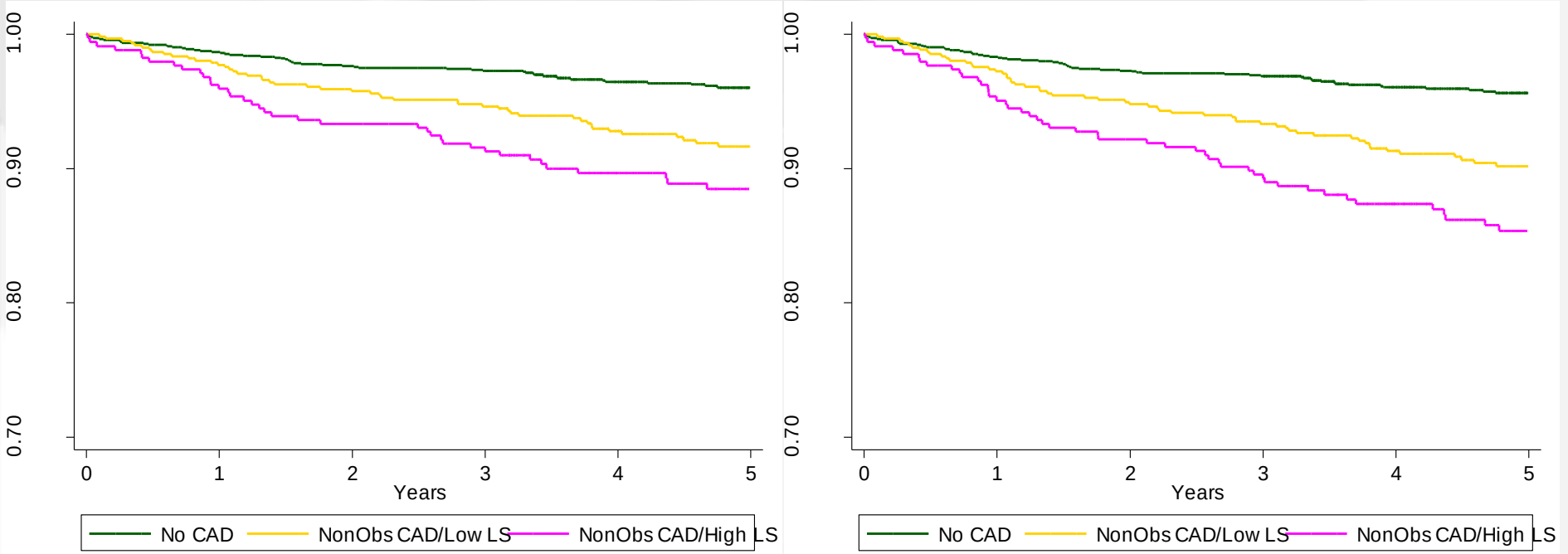
Stenosis severity‡	
Obstructive CAD	1
Nonobstructive CAD	0.615

Plaque composition*	
Non-calcified or mixed	1.5
Calcified	1


Cumulative event-free survival
1,0
0,9
0,8
0,7
0,6
0
12
24
36
48
60
72
84
Time in months
No CAD: 100%
(n=503)
CAD<50% and CT-LeSc ≤5: 94.0%
(n=184)
CAD>50% and CT-LeSc ≤5: 80.7%
(n=57)
CAD<50% and CT-LeSc >5: 78.6%
(n=109)
CAD>50% and CT-LeSc >5: 76.5%
(n=343)
n=1196
Log rank
p<0.001

Long-term prognostic impact of CT-Leaman score in patients with non-obstructive CAD: Results from the COronary CT Angiography EvaluatioN For Clinical Outcomes InteRnational Multicenter (CONFIRM) study☆

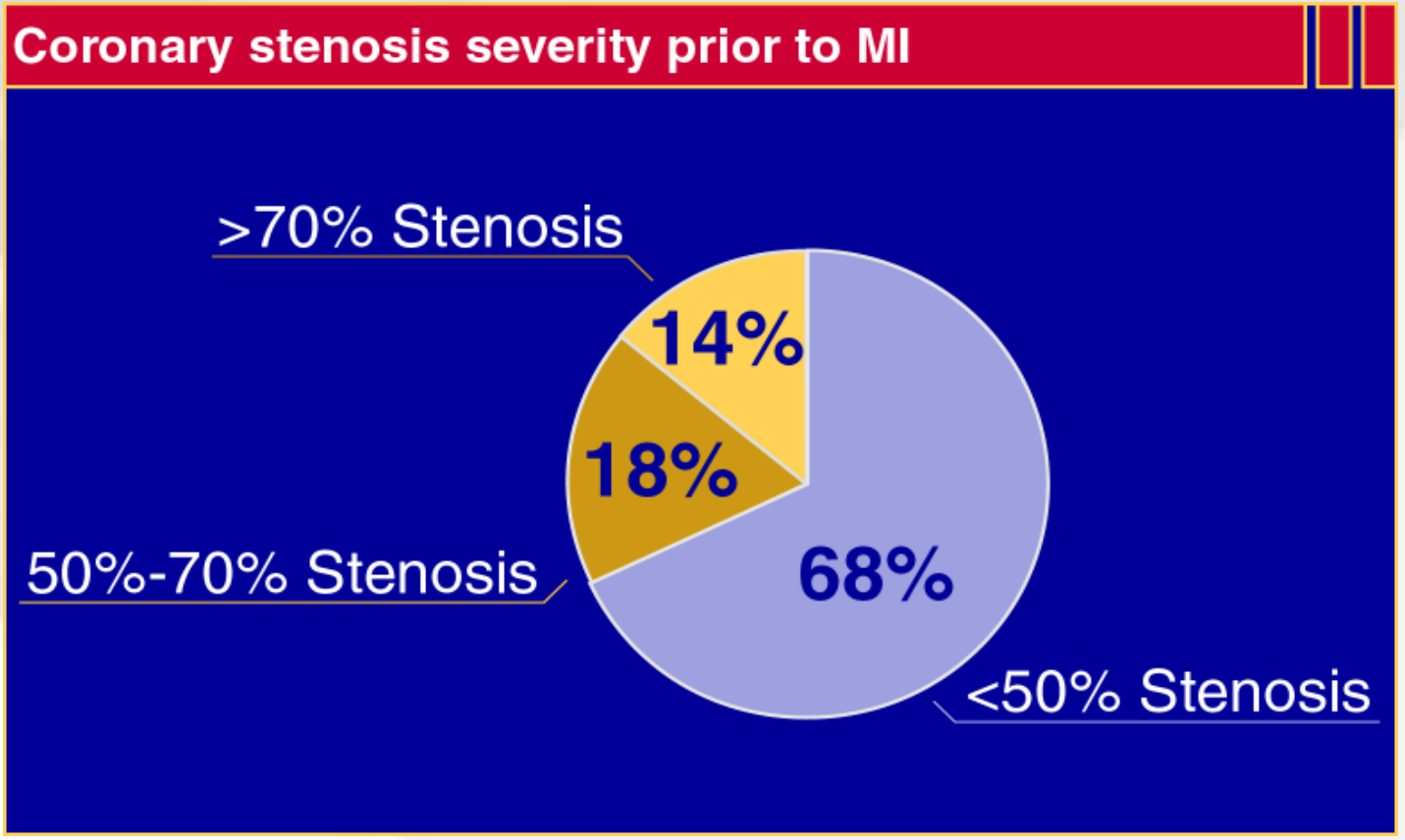
Daniele Andreini [i,*], Gianluca Pontone [i], Saima Mushtaq [i], Heidi Gransar [d], Edoardo Conte [i], Antonio L. Bartorelli [i], Mauro Pepi [i], Maksymilian P. Opolski [a], Bríain ó Hartaigh [b], Daniel S. Berman [d], Matthew J. Budoff [e], Stephan Achenbach [f], Mouaz Al-Mallah [g], Filippo Cademartiri [j,y], Tracy Q. Callister [k], Hyuk-Jae Chang [l], Kavitha Chinnaiyan [m], Benjamin J.W. Chow [n], Ricardo Cury [o], Augustin Delago [q], Martin Hadamitzky [r], Joerg Hausleiter [s], Gudrun Feuchtner [t], Yong-Jin Kim [u], Philipp A. Kaufmann [v], Jonathon Leipsic [w], Fay Y. Lin [b], Erica Maffei [y], Gilbert Raff [m], Leslee J. Shaw [z], Todd C. Villines [aa], Allison Dunning [c], Hugo Marques [h], Ronen Rubinshtein [p], Niree Hindoyan [x], Millie Gomez [x], James K Min [b]



Centro Cardiologico Monzino

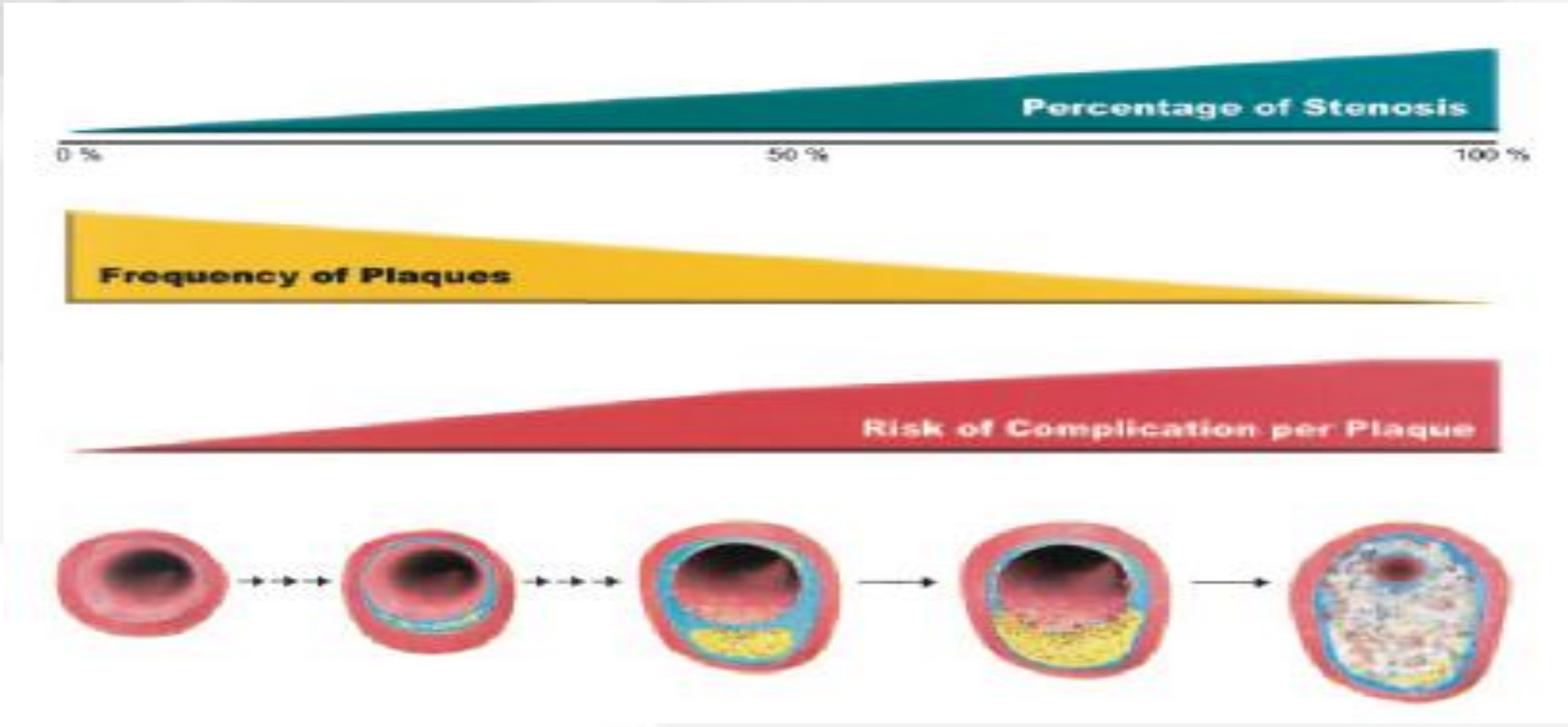
D. Andreini et al, Int J Cardiol 2017

The most of AMI from <50% stenosis



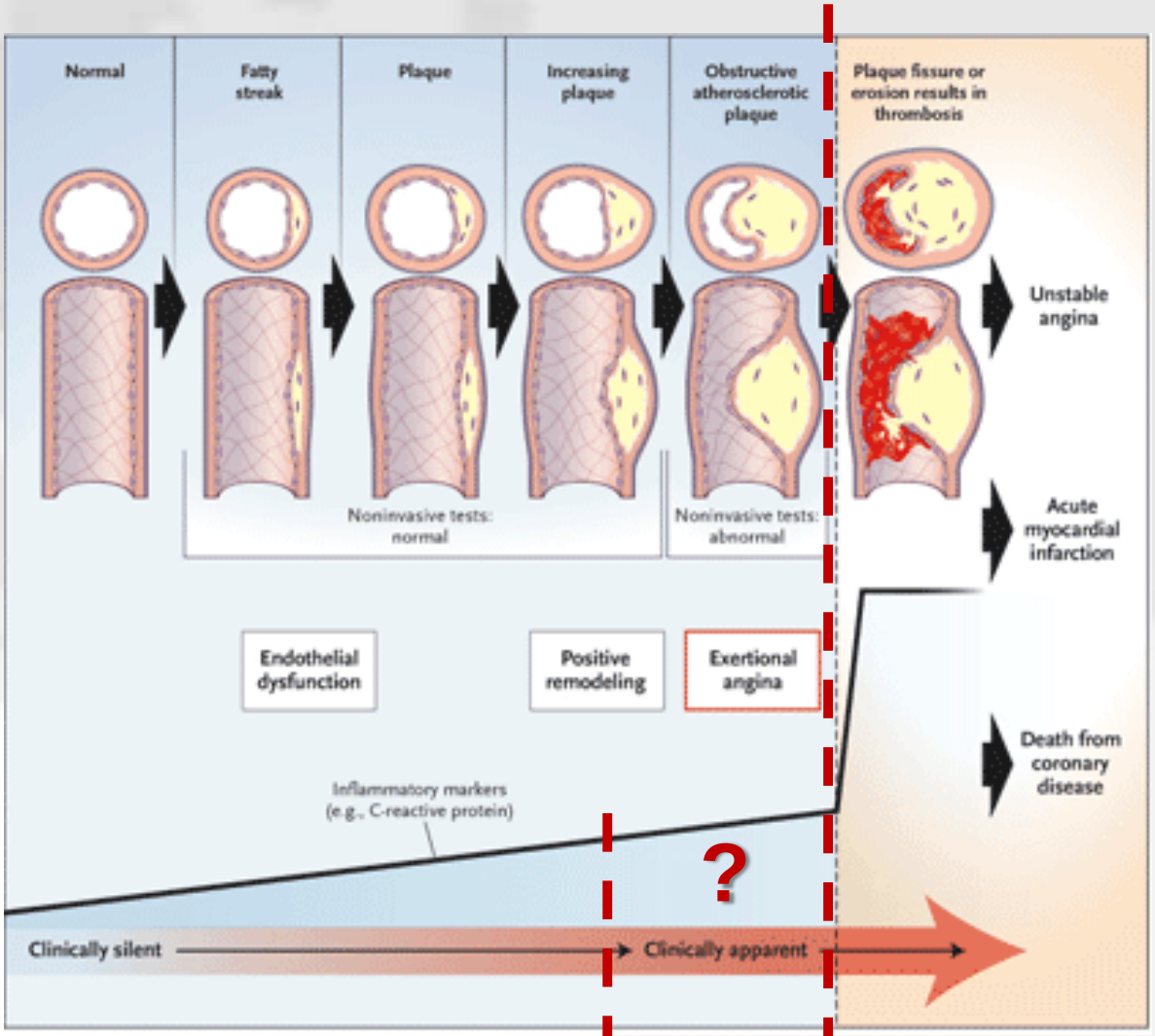
Pooled data from 4 studies: Ambrose et al., 1988; Little et al., 1988; Nobuyoshi et al., 1991; and Giroud et al., 1992.

Frequency vs. grade of stenosis and rate of complication



Naghavi M., Circulation 2003

Background



2014 AHA/ACC Guideline for the Management of Patients With Non–ST-Elevation Acute Coronary Syndromes

First Evidence …

Vol. 316 No. 22 HUMAN ATHEROSCLEROTIC CORONARY ARTERIES — GLAGOV ET AL.

COMPENSATORY ENLARGEMENT OF HUMAN ATHEROSCLEROTIC CORONARY ARTERIES

SEYMOUR GLAGOV, M.D., ELLIOT WEISENBERG, B.A., CHRISTOPHER K. ZARINS, M.D., REGINA STANKUNAVICIUS, M.P.H., AND GEORGE J. KOLETTIS, B.A.

- We studied histologic sections of the left main coronary artery in 136 hearts obtained at autopsy to determine whether atherosclerotic human coronary arteries enlarge in relation to plaque (lesion) area and to assess whether such enlargement preserves the cross-sectional area of the lumen.

- We conclude that human coronary arteries enlarge in relation to plaque area and that functionally important lumen stenosis may be delayed until the lesion occupies 40 percent of the internal elastic lamina area. The preservation of a nearly normal lumen cross-sectional area despite the presence of a large plaque should be taken into account in evaluating atherosclerotic disease with use of coronary angiography

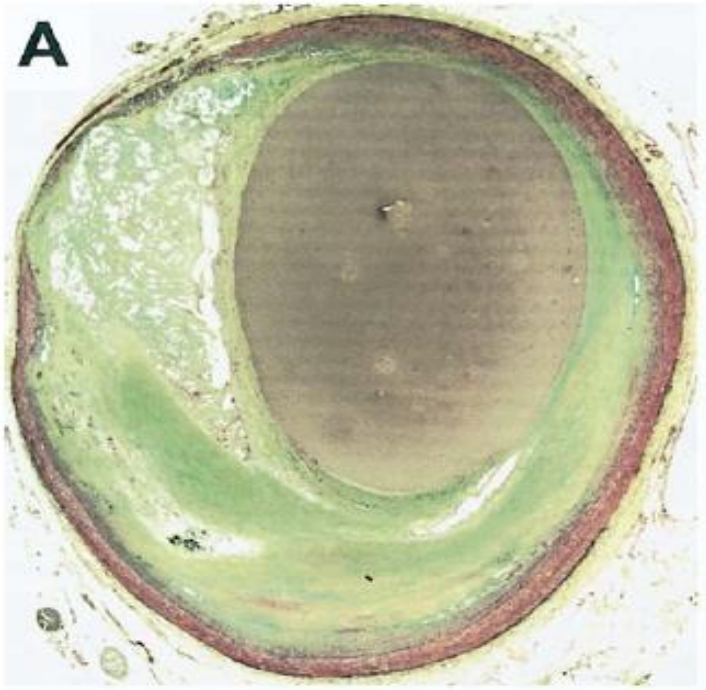
N Engl J Med 1987; 316:1371-1375 May 28, **1987**

Pathology of the Vulnerable Plaque

Renu Virmani, MD,* Allen P. Burke, MD,* Andrew Farb, MD,† Frank D. Kolodgie, PHD*
Gaithersburg and Rockville, Maryland

- The most common cause of coronary syndrome is plaque rupture with subsequent thrombosis….

- The non-thrombosed lesion that most resembles the acute plaque rupture is the thin cap fibroatheroma (TCFA).
- Vessels demonstrating TCFA do not usually show severe luminal narrowing but show positive remodeling.
- Cross-sectional area narrowing in over 75% of TCFA cases is lower than 75%.



J Am Coll Cardiol 2006;47:C13–8

JACC: CARDIOVASCULAR INTERVENTIONS

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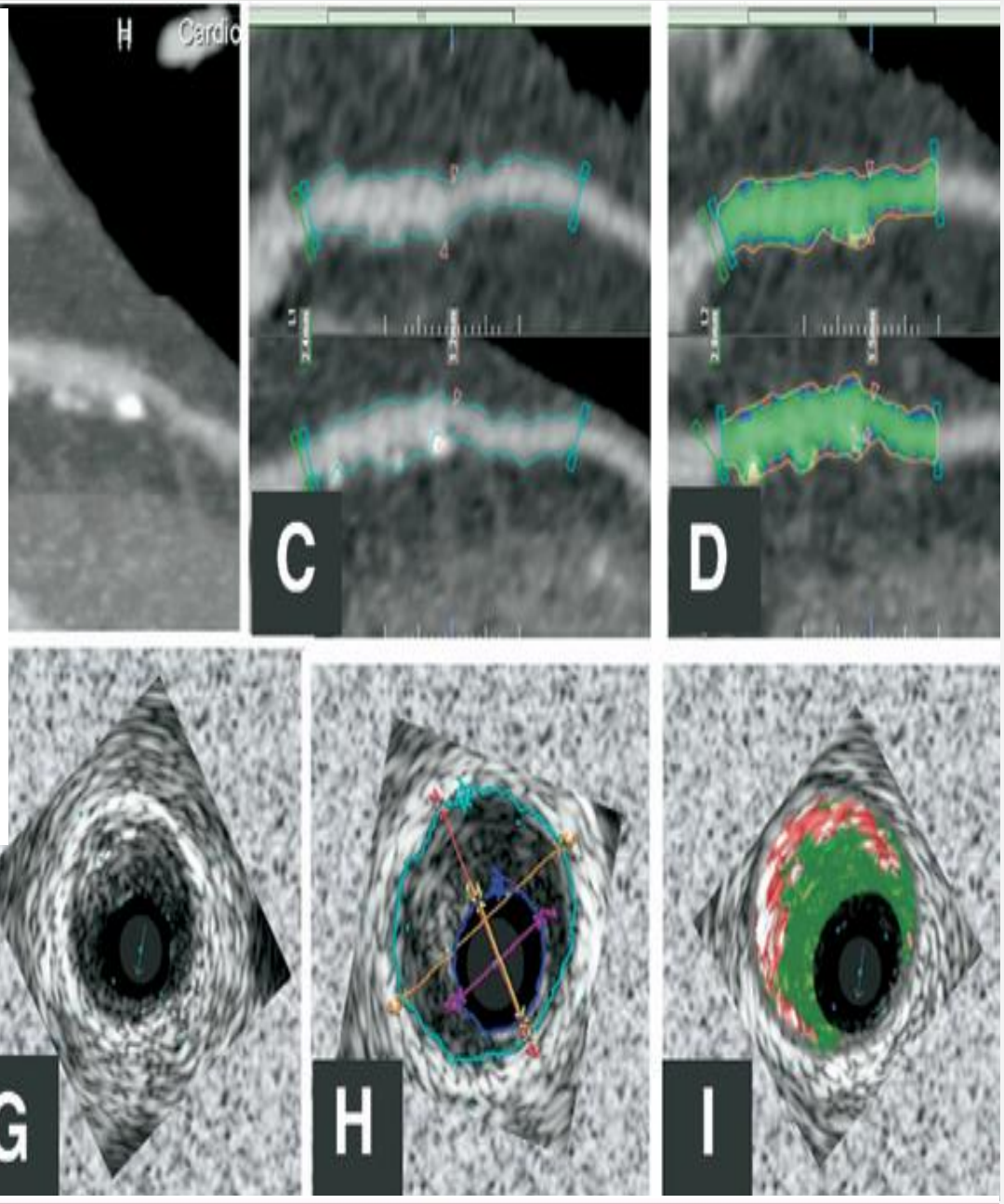
EDITORIAL COMMENT

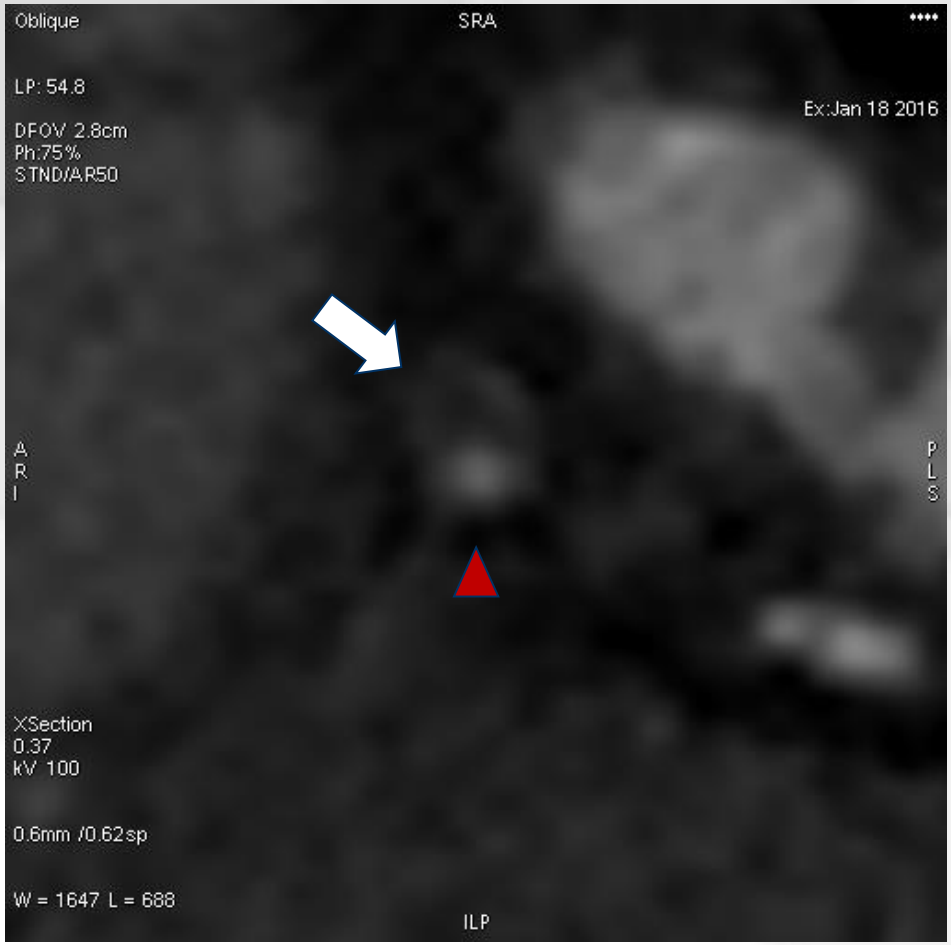
Can Computed Tomography Angiography of the Coronary Arteries Characterize Atherosclerotic Plaque Composition?

Is the CAT (Scan) Out of the Bag?*

Szilard Voros, MD, FACC



Low attenuation plaques (LAP) / Positive Remodelling

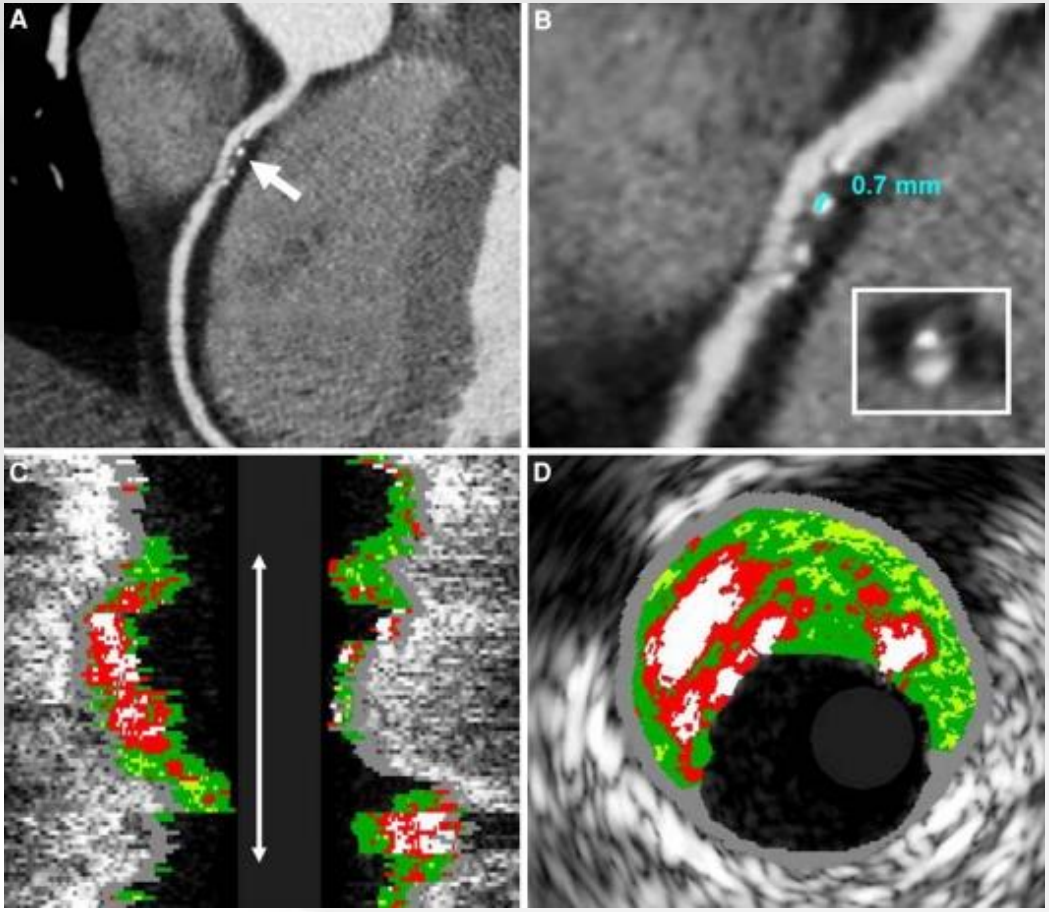


LAP (plaque with 30 – 50 HU) or intermediate-attenuation plaques (plaque between 50 and 150 HU)

ratio of the vessel diameter/area at the plaque site to a reference diameter /area proximal to the lesion in a normal-appearing vessel segment.
RI>1.1

JACC:CARDIOVASCULARIMAGING,VOL.6,NO.4,2013

Spotty Calcifications (SCPs)



small calcified nodules with length <3 mm

J Nucl Cardiol. 2011 Oct; 18(5): 893–903.

Napkin-ring sign

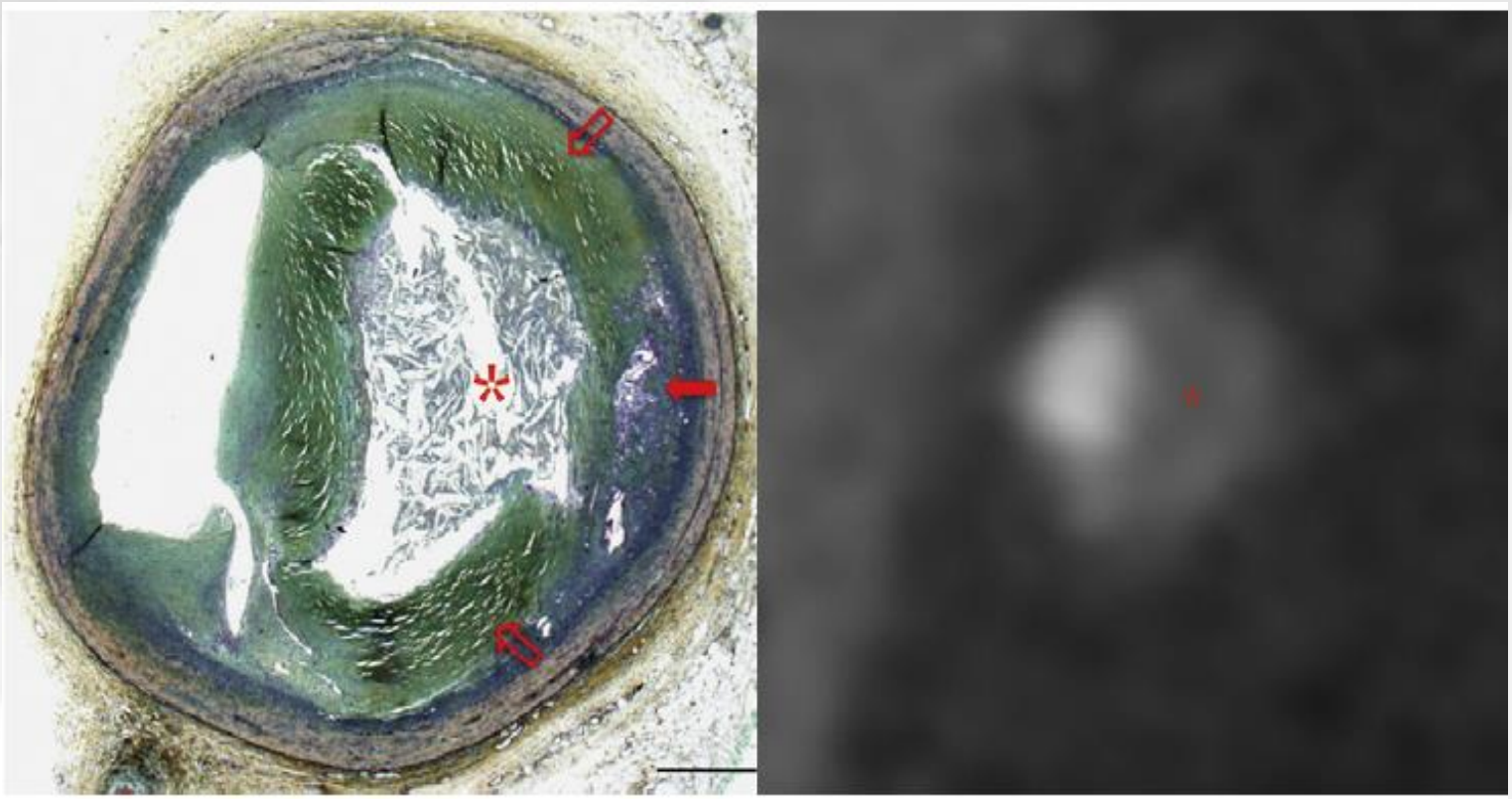


Fig. 1. Late fibroatheroma as classified by histology (left image) Note the large necrotic core (*) in the center of the plaque, which correlates with the hypodense center of the plaque (*) in CT (right image). The core is surrounded by prominent fibrotic tissue (open arrows), which appears as a hyperdense ring around the core in CT. Thus the plaque has a ring-like appearance in coronary CT angiography which was coined as napkin-ring sign. Additionally neovascularization is present within the plaque (closed arrow).

H. Seifarth et al. / Atherosclerosis 224 (2012) 90e96

Contents lists available at ScienceDirect

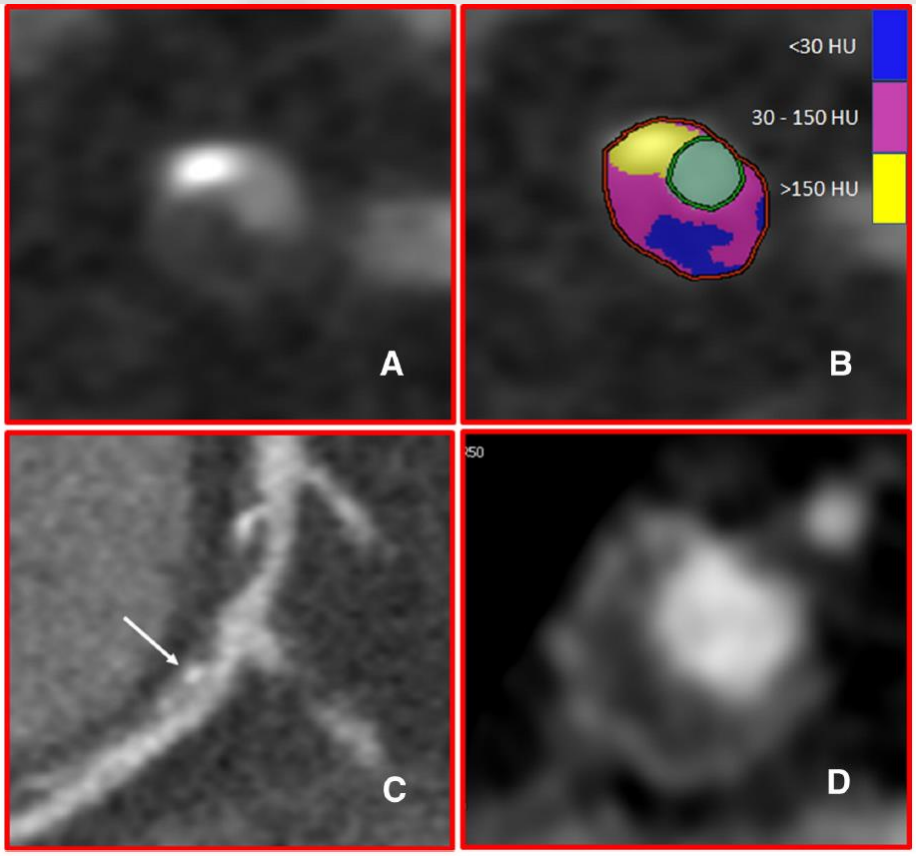
International Journal of Cardiology

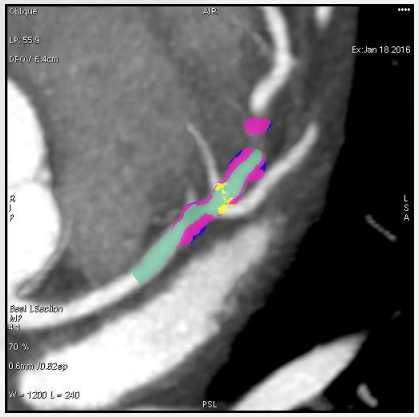
journal homepage: www.elsevier.com/locate/ijcard

Review

Role of new imaging modalities in pursuit of the vulnerable plaque and the vulnerable patient

Paolo Raggi [a,b,*], Gianluca Pontone [c,d], Daniele Andreini [c,e]



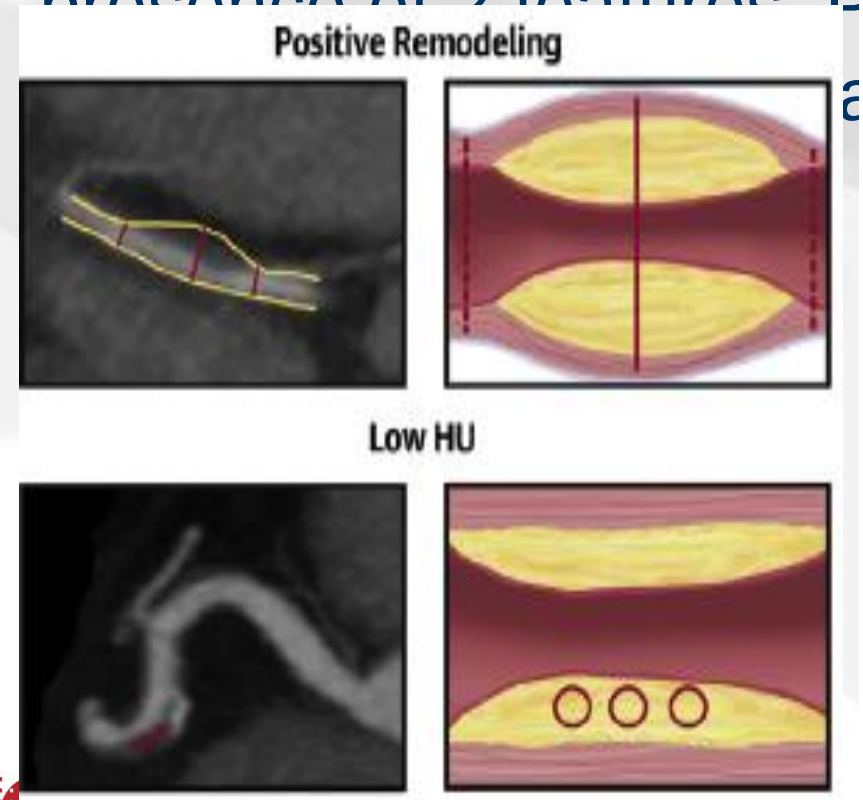


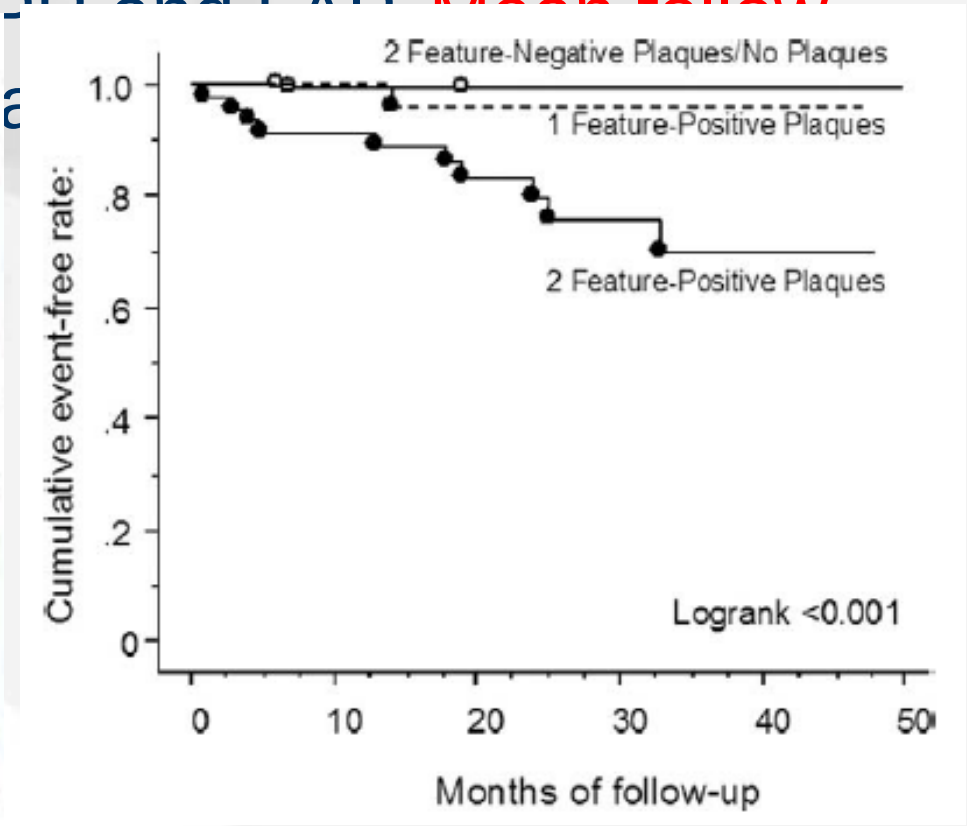
Centro Cardiologico Monzino

IJC 2017

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

In 1,059 unselected patients who underwent CCTA, atherosclerotic lesions were analyzed for the presence of 2 features: RR and LAP. Mean follow-





Motoyama et al. J Am Coll Cardiol 2009;54:49–57

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ORIGINAL INVESTIGATIONS

Plaque Characterization by Coronary Computed Tomography Angiography and the Likelihood of Acute Coronary Events in Mid-Term Follow-Up

Sadako Motoyama, MD, PhD,*† Hajime Ito, MD, PhD,* Masayoshi Sarai, MD, PhD,* Takeshi Kondo, MD, PhD,* Hideki Kawai, MD, PhD,* Yasuomi Nagahara, MD,* Hiroto Harigaya, MD, PhD,*‡ Shino Kan, MD,*‡ Hirofumi Anno, MD, PhD,§ Hiroshi Takahashi, BSc,‖ Hiroyuki Naruse, MD, PhD,* Junichi Ishii, MD, PhD,* Harvey Hecht, MD,† Leslee J. Shaw, PhD,¶ Yukio Ozaki, MD, PhD,* Jagat Narula, MD, PhD†

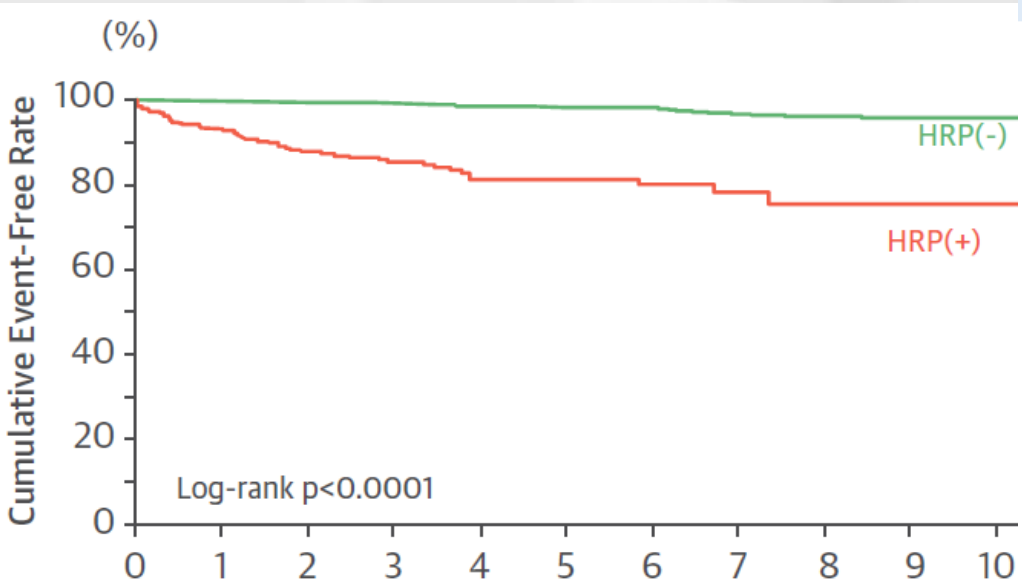
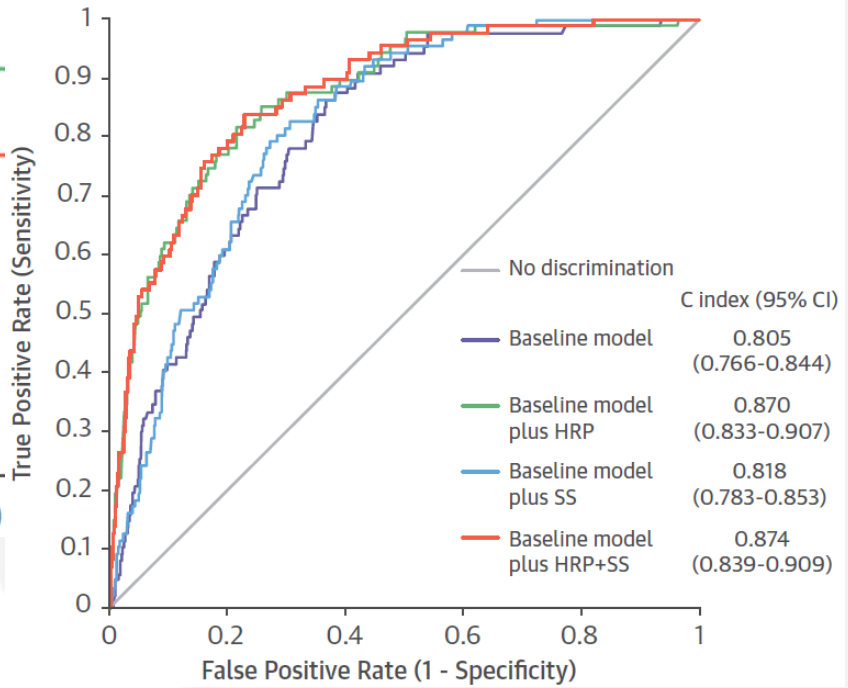


FIGURE 3 Incremental Value of CTA to Detect ACS



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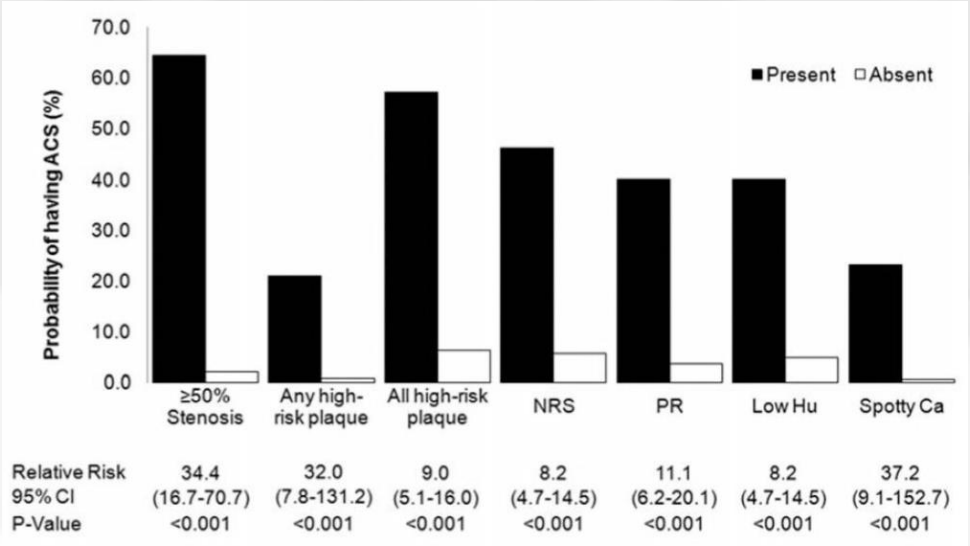
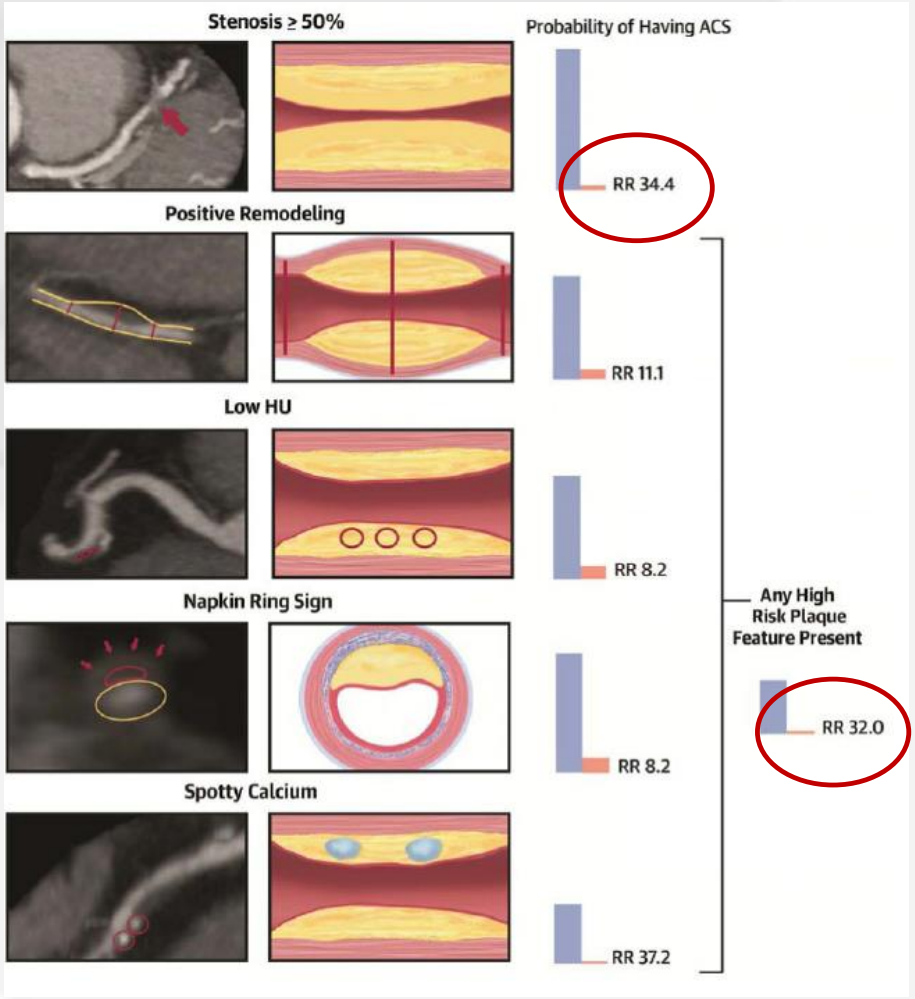
High-risk Plaque Detected on Coronary Computed Tomography Angiography Predicts Acute Coronary Syndrome Independent of Significant Stenosis in Patients with Acute Chest Pain – Results from ROMICAT II Trial





Centro Cardiologico Monzino

Puchner et al. J Am Coll Cardiol. 2014 Aug 19; 64(7): 684–692

European Heart Journal – Cardiovascular Imaging
doi:10.1093/ehjci/jew200

Evaluation of coronary plaque characteristics with coronary computed tomography angiography in patients with non-obstructive coronary artery

Table 4 Multivariate analysis of CCTA characteristics combined endpoints adjusted for clinical variables.

	Cardiac death + ACS[a]		Cardiac death + ACS + vl-ER[a]	
	HR (95% CI)	P	HR (95% CI)	P
≥1 plaque with PRI > 1.4	3.31 (1.11.9.91)	0.0392	2.34 (1.04–5.23)	0.0403
≥1 plaque with LAP < 30	8.45 (2.22–32.21)	0.0019	5.30 (1.52–18.54)	0.0094
≥1 plaque with PB > 0.7	5.25 (1.45–19.03)	0.0120	4.89 (1.65–14.56)	0.0045
≥1 plaque with NRS	12.52 (1.51–103.90)	0.0198	-	-
≥2 high-risk plaque characteristics	7.54 (2.43–23.34)	0.0005	5.49 (2.11–14.26)	0.0005
	All cause of death + ACS[b]		**All cause of death + ACS + vl-ER[b]**	
	HR (95% CI)	P	HR (95% CI)	P
≥1 plaque with PRI > 1.4	2.98 (1.16–7.69)	0.0245	2.39 (1.11–4.92)	0.0260
≥1 plaque with LAP < 30	9.49 (2.59–34.72)	0.0007	6.47 (1.88–22.32)	0.0033
≥1 plaque with PB > 0.7	6.60 (1.88–23.18)	0.0034	5.29 (1.82–15.38)	0.0023
≥2 high-risk plaque characteristics	7.45 (2.61–21.28)	0.0002	5.50 (2.20–13.74)	0.0003

As for *Table 2*.
[a]Adjusted for β-blockers use.
[b]Adjusted for age and current smoke.

EHJ im 2016

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ORIGINAL RESEARCH

Atherosclerotic Plaque Characteristics by CT Angiography Identify Coronary Lesions That Cause Ischemia

A Direct Comparison to Fractional Flow Reserve

Hyung-Bok Park, MD,*†‡ Ran Heo, MD,*† Bríain ó Hartaigh, PHD,* Iksung Cho, MD,*† Heidi Gransar, MSc,§ Ryo Nakazato, MD,‖ Jonathon Leipsic, MD,¶ G.B. John Mancini, MD,# Bon-Kwon Koo, MD,** Hiromasa Otake, MD,†† Matthew J. Budoff, MD,‡‡ Daniel S. Berman, MD,§ Andrejs Erglis, MD,§§ Hyuk-Jae Chang, MD,† James K. Min, MD*

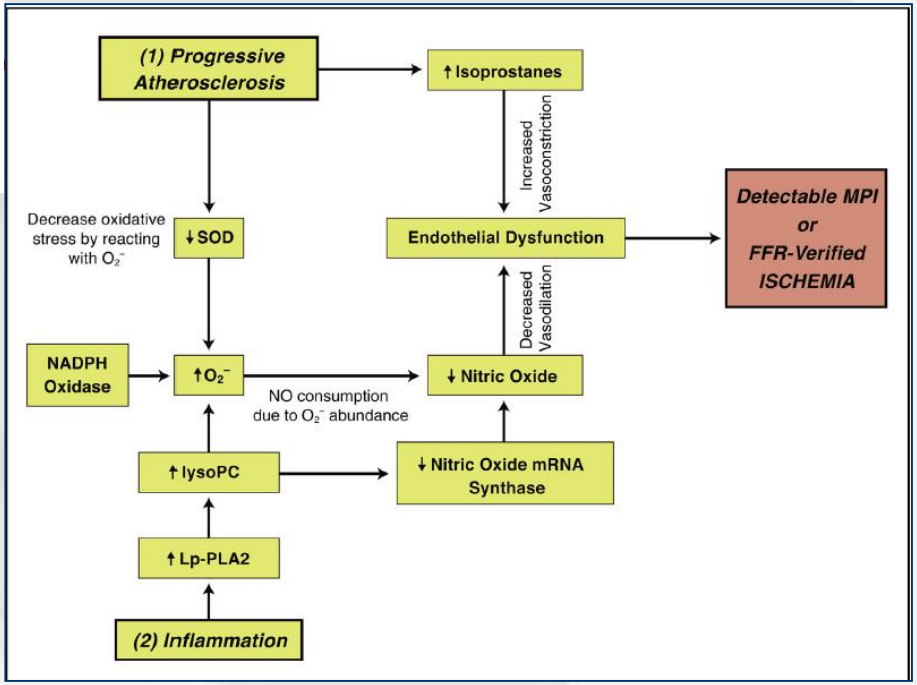
TABLE 4 Multivariable Analysis of APCs in Obstructive Lesions (≥50%) and Nonobstructive Lesions (<50%) for Ischemia Detection

Obstructive Lesions (≥50%)			Nonobstructive Lesions (<50%)		
	OR (95% CI)	p Value		OR (95% CI)	p Value
Model 1			Model 3		
Lumen area stenosis (per 5%)	1.1 (0.99-1.3)	0.07	Lumen area stenosis (per 5%)	1.3 (1.06-1.6)	0.01
Lesion length	1.03 (1.01-1.06)	0.01	Lesion length	1.02 (0.97-1.07)	0.44
PR	3.6 (1.8-7.2)	<0.001	PR	10.5 (3.1-36.4)	<0.001
LAP	2.5 (1.2-5.3)	0.018	LAP	1.3 (0.3-5.6)	0.74
SC	1.4 (0.6-3.2)	0.42	SC	1.8 (0.5-7.3)	0.40
Model 2			Model 4		
Lumen area stenosis (per 5%)	1.1 (0.97-1.3)	0.12	Lumen area stenosis (per 5%)	1.3 (1.02-1.6)	0.03
% APV (per 5%)	1.8 (1.4-2.2)	<0.001	%APV (per 5%)	1.3 (0.9-1.9)	0.24
0 APC	1.0 (reference)	—	0 APC	1.0 (reference)	
1 APC	2.3 (1.1-5.1)	0.037	1 APC	7.8 (1.9-31.6)	0.004
>2 APCs	8.6 (3.8-19.3)	<0.001	≥2 APCs	25.2 (3.1-207.4)	0.003

Discordance Between Ischemia and Stenosis, or PINSS and NIPSS

Are We Ready for New Vocabulary?*

- Presence of ischemia in not significant stenosis
- No ischemia in presence of significant stenosis



- Features of CTA-verified high-risk plaques (HRPs), including positive remodeling (PR) and low attenuation plaque (LAP), were examined for their relationship to the invasive FFR-verified lesion-specific ischemia. **The presence of PR and LAP was highly predictive of ischemia independent of the severity of stenosis.**
- Most myocardial infarctions are caused by large volume HRP with large necrotic core and PR, regardless of the extent of luminal stenosis. Here, we propose that large volume HRP can be ischemic, independent of the degree of luminal stenosis. **Could the strong predictive value of ischemia testing be a result of indirectly screening for HRP?**

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Ahmadi et al. j a c c : c a r d i o v a s c u l a r ima g i n g , v o l . 8 , no. 1 , 2 0 1 5

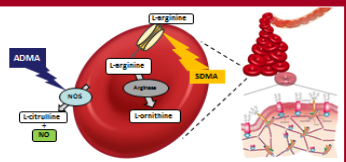
Translational Research: MERCAD project

Morphological alterations of erythrocyte in Coronary Artery Disease patients

B. Porro[1], D.Andreini[1,3], A. Zaninoni[2], E. Conte[1], S. Fiorelli[1], P. Bianchi[2], L. Cantù[4], L. Turnu[1], A. Di Minno[1], C. Manega[1], E. Tremoli[1], V. Cavalca[1]

[1]Centro Cardiologico Monzino IRCCS, Milan, Italy; [2]UO Oncoematologia, UOS Fisiopatologia delle Anemie, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico; [3]Dipartimento di Scienze Cliniche e di Comunità, [4]Dipartimento di Biotecnologie Mediche e Medicina Traslazionale,Università degli Studi di Milano, Milan, Italy.

Among circulating cells, erythrocytes (RBCs) exhibit a unique ability to deform, which enables them to change their shape reversibly in response to an external force. This property allows RBCs to flow in microvessels while transporting oxygen and carbon dioxide. In these cells nitric oxide (NO), which can be produced by the activity of a constitutive type of NO synthase (RBC-NOS), has been proven to hold a regulatory role in their deformability and aggregation. In this context, our group highlighted a reduced ability of coronary artery disease (CAD) RBCs to synthetize NO [1].



[1] Eligini S, Porro B, Lualdi A, et al. PLoS One. 2013;8(8):e66945.

PURPOSE

To characterize morphological and functional properties of RBC from CAD patients in comparison to healthy controls (Ctrl).

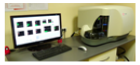
METHODS

Table 1: Demographic and clinical characteristics of the two study groups.

Variable	CAD (n=13)	Ctrl (n=15)	*p value*
Age (years)	60.0±2.1	50.0±2.1	0.060
Male gender (%)	12 (92.3)	6(40.0)	*0.006*
BMI	27.4±0.7	24.3±1.0	0.106
Total cholesterol (mg/dL)	194.0±16.3	190.0±10.2	0.710
HDL-cholesterol (mg/dL)	40.0±2.7	59.0±2.4	*0.001*
LDL-cholesterol (mg/dL)	121.0±11.1	112.0±8.9	0.467
Triglycerides (mg/dL)	129.0±9.2	87.0±11.2	*0.049*
Current Smoker	1(7.7)	1(6.7)	1.0
Hypercholesterolemia	9(69)	6(33)	0.128
Hypertriglyceridemia	2(15)	0(0)	0.206
Hypertension	10(77)	7(47)	0.137
Pharmacological treatments			
Converting enzyme inhibitors	6(46)	3(20)	0.227
Aspirin	7(54)	5(33)	0.445
Antithrombotics	2(15)	0(0)	0.206
Beta-Blockers	6(46)	3(20)	0.227
Calcium channel blockers	5(38)	2(13)	0.198
Diuretics	3(23)	0(0)	0.087
Statins	5(38)	3(20)	0.410
Hypoglycemics	0(0)	0(0)	-
Angiotensin receptor blockers	2(15)	2(13)	1.00

Quantitative variables were expressed as mean±SD and categorical variables as n(%).

✓Deformability
✓Aggregation

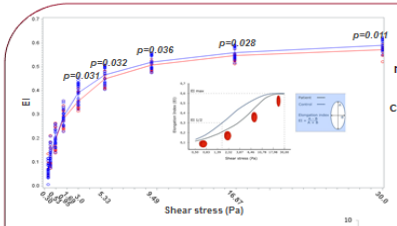


✓Phosphatidylserine exposure

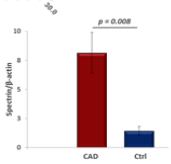
✓Spectrin quantification

✓Synchrotron X-ray spectroscopy of RBC cytoskeleton

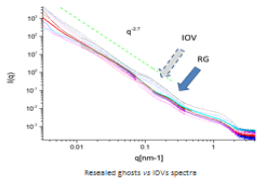
RESULTS



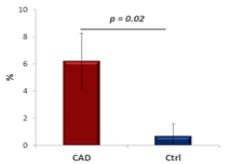
RBC deformability. RBC membranes of CAD patients had a reduced capacity to warp in response to increasing shear stress. Individual data are expressed as geometric means.



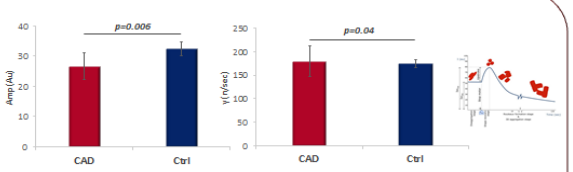
Spectrin expression in RBCs. Spectrin content is higher in RBC membranes from CAD patients than in Ctrl.
Data are expressed as median±SE.



Synchrotron X-ray spectroscopy of RBC cytoskeleton. RBCs of CAD patients are unable to disassemble the spectrin-actin cytoskeleton.



Phosphatidylserine (PS) exposure in RBCs. PS exposure on RBC membrane is higher in CAD patients than in Ctrl.
Data are expressed as median±SE of the % of positive cells.



RBC aggregation. RBC of CAD patients are able to form aggregates smaller and more stable than that developed in Ctrl.

CONCLUSIONS

In RBCs from CAD patients we evidenced an alteration of membrane deformability in response to increased shear stress in parallel to an imbalance in the spectrin protein content. The increased exposure of PS, in addition to the greater minimal shear rate value required to disperse pre-formed CAD RBC aggregates, could have a pivotal role in modulating blood flow dynamics in the microcirculation.

Conflict of interest: nothing to disclose.

ESC Congress, 26-30 August 2017 - Barcelona

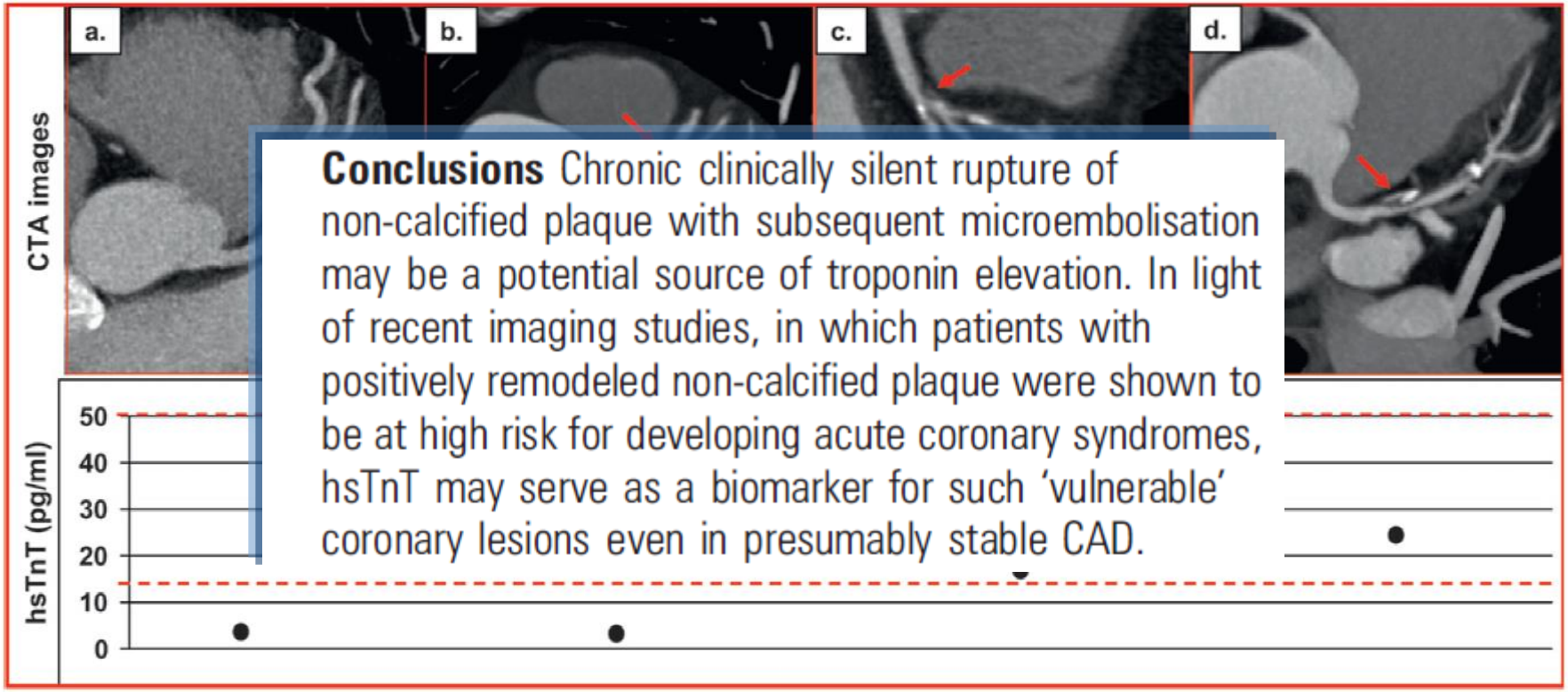
Author's e-mail benedetta.porro@ccfm.it

Centro Cardiologico Monzino

B. Porro et al, ESC 2017

Determinants of troponin release in patients with stable coronary artery disease: insights from CT angiography characteristics of atherosclerotic plaque

Grigorios Korosoglou,[1] Stephanie Lehrke,[1] Dirk Mueller,[2] Waldemar Hosch,[3] Hans-Ulrich Kauczor,[3] Per M Humpert,[4] Evangelos Giannitsis,[1] Hugo A Katus[1]



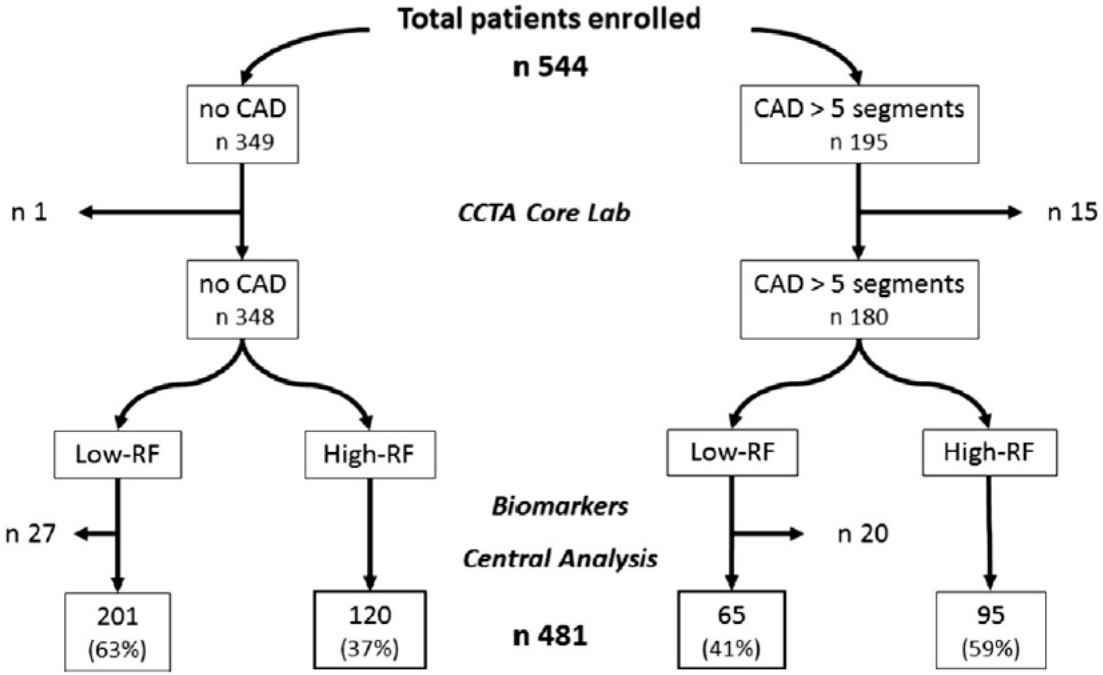
Conclusions Chronic clinically silent rupture of non-calcified plaque with subsequent microembolisation may be a potential source of troponin elevation. In light of recent imaging studies, in which patients with positively remodeled non-calcified plaque were shown to be at high risk for developing acute coronary syndromes, hsTnT may serve as a biomarker for such 'vulnerable' coronary lesions even in presumably stable CAD.

Figure 4 Representative images of patients with normal vessels (A), calcified plaque (B), mixed plaque (C) and remodeled mixed plaque (D) with their corresponding high sensitive troponin (hsTnT) values. CTA, computed tomography angiography.

Coronary atherosclerosis in outlier subjects at the opposite extremes of traditional risk factors: Rationale and preliminary results of the Coronary Atherosclerosis in outlier subjects: Protective and novel Individual Risk factors Evaluation (CAPIRE) study

Marco Magnoni, MD,[a] Daniele Andreini, MD,[b] Marco Gorini, MS,[c] Tiziano Moccetti, MD,[d] Maria Grazia Modena, MD,[e] Maur... Paolo Marra... and Attilio M... ggioni, MD,[c] ...dena, Fano, Massa, Lid...

Figure 1



Usefulness of High-Sensitivity Cardiac Troponin T for the Identification of Outlier Patients With Diffuse Coronary Atherosclerosis and Low-Risk Factors

Marco Magnoni, MD[a,*], Serge Masson, PhD[b], Daniele Andreini, MD[c], Tiziano Moccetti, MD[d], Maria Grazia Modena, MD[e], Mauro Canestrari, MD[f], Sergio Berti, MD[g], Giancarlo Casolo, MD[h], Domenico Gabrielli, MD[i], Paolo Marraccini, MD[j], Gianluca Pontone, MD[c], Roberto Latini, MD[b], Aldo Pietro Maggioni, MD[k], and Attilio Maseri, MD[a], on behalf of the CAPIRE Study Group

Am J Cardiol 2016

Univariate and multivariate regression analysis for the association with diffuse CAD

Variable	Low RF					
	Univariate			Multivariate		
	OR	95% CI	P value	OR	95% CI	p value
Age (years)						
< 55	Ref.			Ref		
55-64	3.61	1.61-8.54	0.0016	5.77	2.26-15.82	0.0002
≥ 65	5.20	2.45-11.91	<0.0001	7.29	2.81-20.46	<0.0001
Gender						
Male	Ref.			Ref		
Female	0.07	0.02-0.17	<0.0001	0.03	0.01-0.13	<0.0001
BMI (Kg/m^2)						
< 25	Ref.			Ref		
25-29.9	1.69	0.90-3.22	0.11	-	-	ns
≥ 30	2.65	1.18-5.85	0.018	-	-	ns
HDL-cholesterol (mg/dl)						
≤ 50	Ref.			Ref		
> 50	0.25	0.13-0.46	<0.0001	0.28	0.12-0.62	0.0017
hs-cTnT(ng/L)						
≤ 3.0	Ref.			Ref		
3.0-6.0	4.43	1.43-19.45	0.0081	2.81	0.77-13.68	0.124
> 6.0	13.44	4.55-57.64	<0.0001	6.72	1.81-33.29	0.0035
Serum creatinine* (mg/dl)						
≤ 0.73	Ref.			Ref.		
0.73-0.91	2.08	0.99-4.55	0.0546	-	-	ns
> 0.91	3.13	1.52-6.76	0.0018	-	-	ns

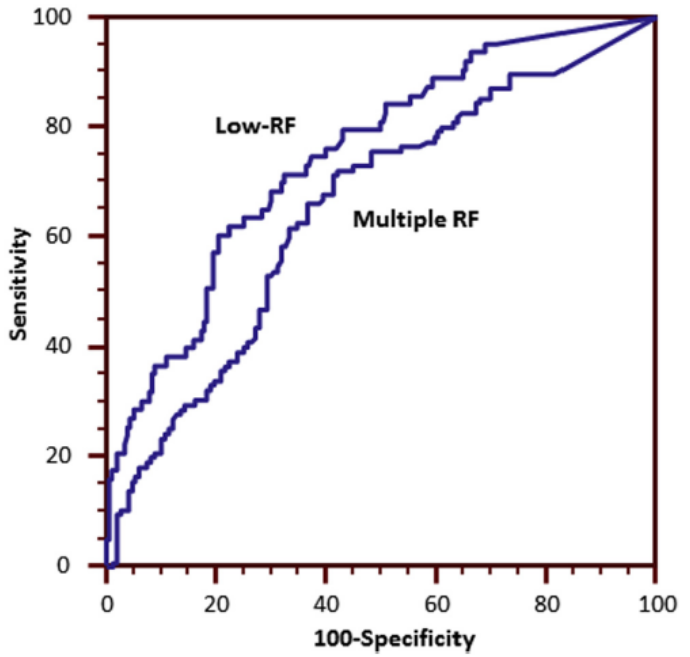
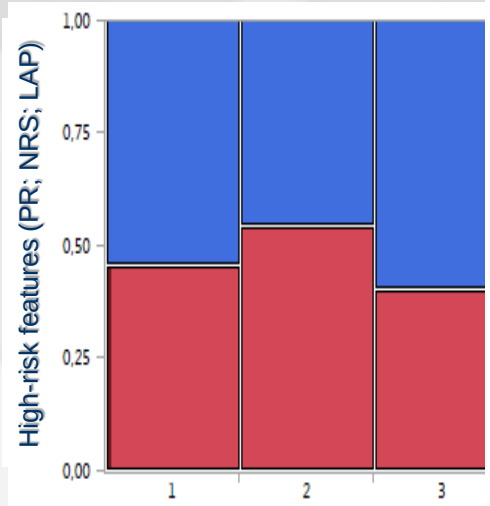


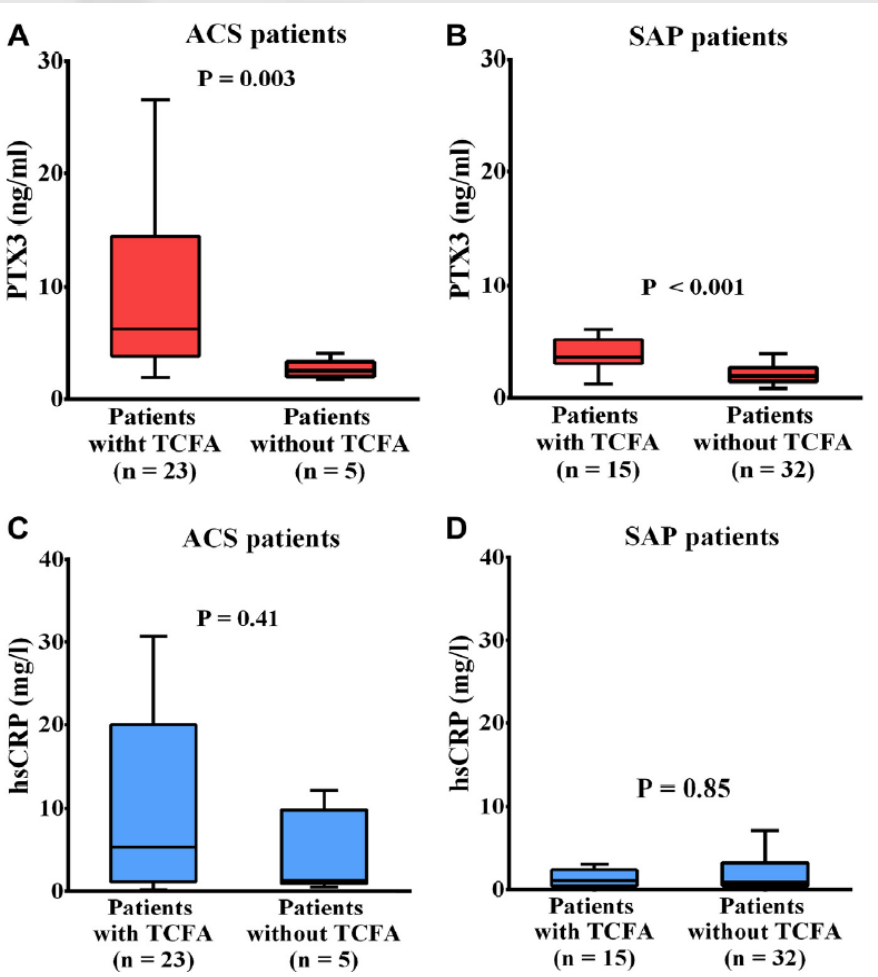
Figure 3. Area under the curve of hs-cTnT ability to predict CAD in low-RF and multiple-RF groups.

CAPIRE: Plaque features, Biomarkers and Prognosis



IL-6

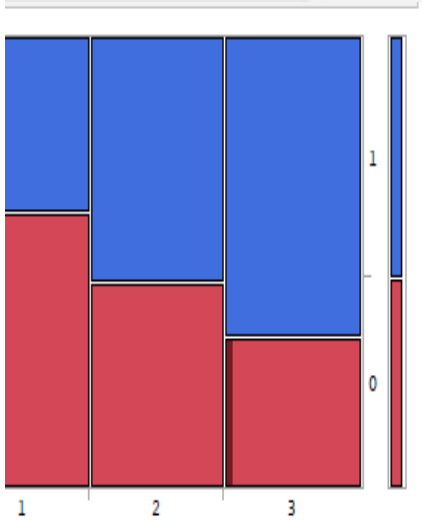
P value (Pearson): 0.29



Elevated Levels of Systemic Pentraxin 3 Are Associated With Thin-Cap Fibroatheroma in Coronary Culprit Lesions

Assessment by Optical Coherence Tomography and Intravascular Ultrasound

Seiji Koga, MD,* Satoshi Ikeda, MD,* Takeo Yoshida, MD,* Tomoo Nakata, MD,* Masayoshi Takeno, MD,* Nobuhito Masuda, PHD,† Yuji Koide, MD,* Hiroaki Kawano, MD,* Koji Maemura, MD*



Pentraxin3

0.01

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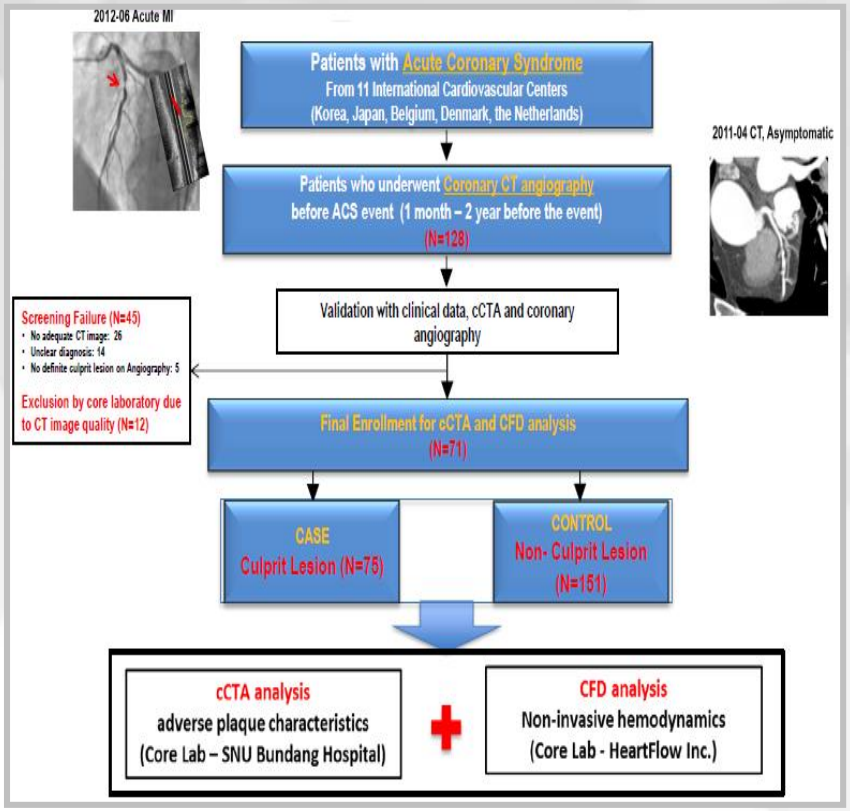
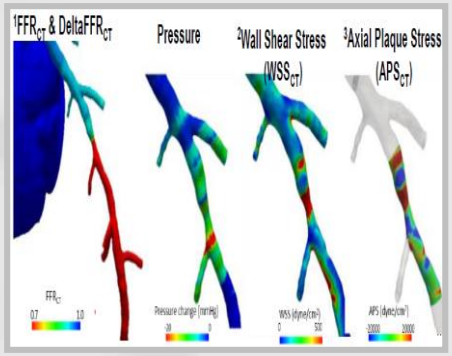
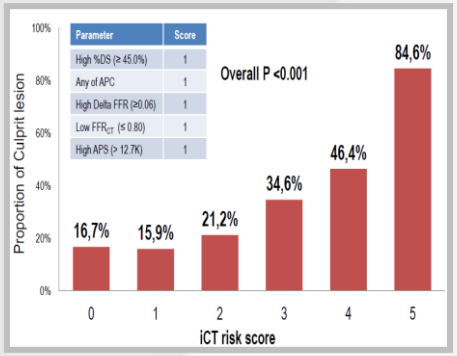
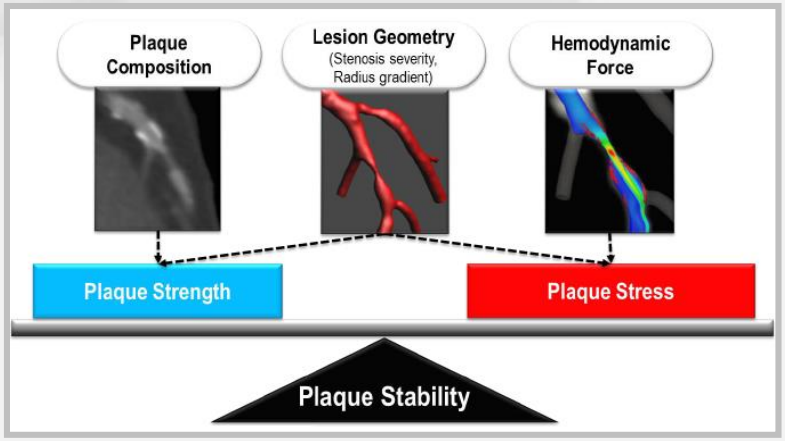
I. Unpublished data

New perspectives: the EMERALD study









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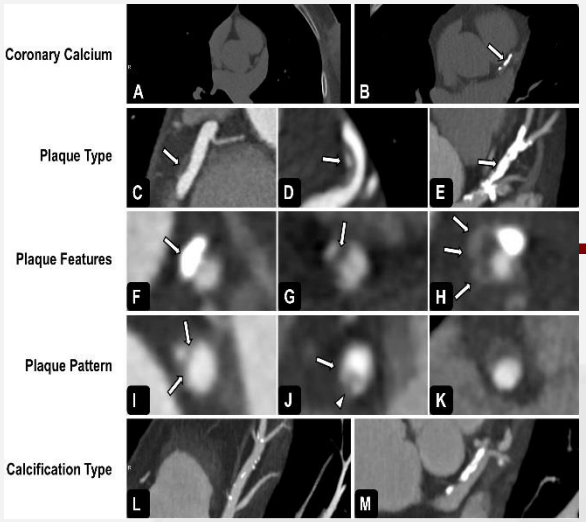
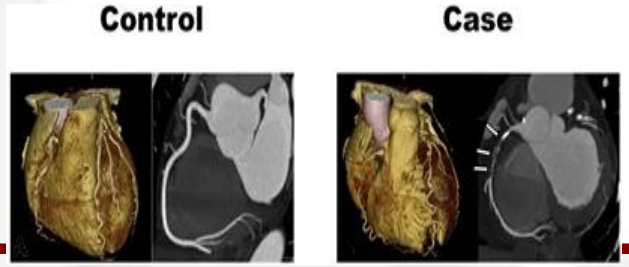
"EPIFANIA" study

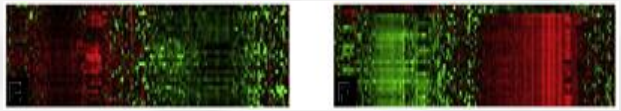
(**È** **P**revedibile **I**n quale **F**orma **A**vverrà la prima manifestazione clinica **N**ell'**I**ndividuo con **A**terosclerosi coronarica non ostruttiva?)



Coronary CTA



Genomic profile



Integration of *coronary imaging* (**Coronary CTA**) and *genomic assessment* (**circulating transcriptome**) for the identification of ***non invasive biomarkers:***

- New risk scores

- Targeted treatment or follow-up

- **2000 patients: case-controls**
- **CTA and Molecular profile**
- **At baseline and 2 years f-up**
- **Clinical follow-up of 5 years**

Coronary ATS as acute (AMI), stable (angina) or silent presentation: its "epifania" is crucial for prognosis; is it possible to predict what's happen as first?

Journal of the American College of Cardiology
Volume 71, Issue 5, 6 February 2018, Pages 499-509

Original Investigation

Effect of Plaque Burden and Morphology on Myocardial Blood Flow and Fractional Flow Reserve

Roel S. Driessen MD [a], Wijnand J. Stuijfzand MD [a], Pieter G. Raijmakers MD, PhD [b], Ibrahim Danad MD [a], James K. Min MD, PhD [c], Jonathon A. Leipsic MD, PhD [d], Amir Ahmadi MD, PhD [e], Jagat Narula MD, PhD [e], Peter M. van de Ven PhD [f], Marc C. Huisman PhD [b], Adriaan A. Lammertsma PhD [b], Albert C. van Rossum MD, PhD [a], Niels van Royen MD, PhD [a], Paul Knaapen MD, PhD [a]

CENTRAL ILLUSTRATION: Plaque Morphology Associated With Myocardial Perfusion

	Predictor of impaired MBF	CT derived plaque characteristics	Predictor of impaired FFR	
p=0.001	+ + +	>70% Luminal Stenosis	+ + +	P<0.001
p=0.004	+	Positive Remodeling	+	p=0.007
p<0.001	+	Noncalcified Plaque Volume	+	p=0.01
	–	Spotty Calcification	+	
	–	Low Attenuation Plaque	+	

Driessen, R.S. et al. J Am Coll Cardiol. 2018;71(5):499-509.

Multivariable analysis:

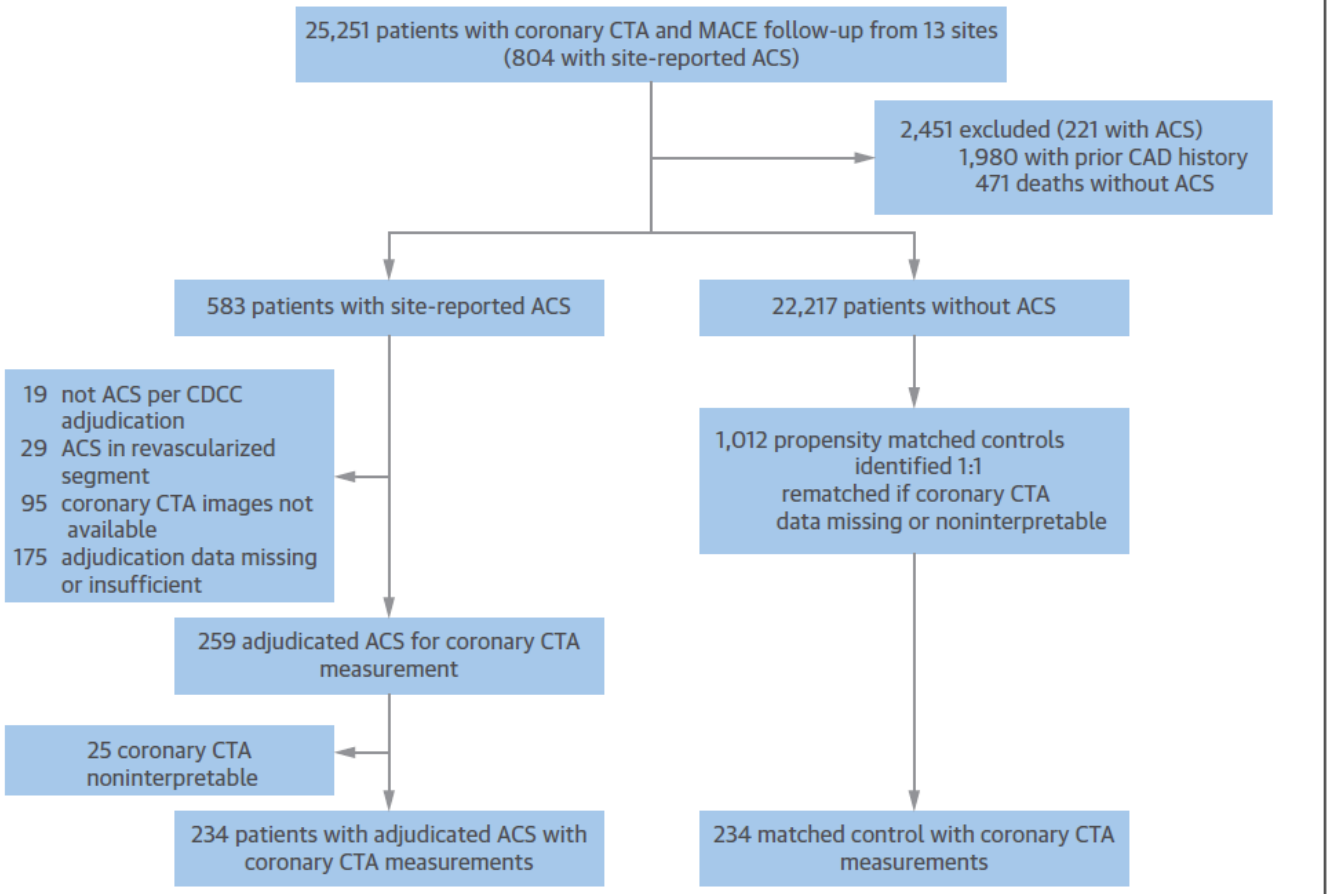
PR was independently related to impaired hyperemic MBF as well as an unfavorable FFR (p=0.004 and p=0.007, respectively), next to stenosis percentage (p=0.001 and p < 0.001, respectively) and noncalcified plaque volume (p<0.001 and p=0.010, respectively).

Coronary Atherosclerotic Precursors of Acute Coronary Syndromes

Hyuk-Jae Chang
Jeroen Bax, MD,
Edoardo Conte,
Jonathon Leipsi
Gilbert L. Raff, I
Subhi J. Al'Aref,
Ran Heo, MD,[r] Ji
Ji Min Sung, PhI
Leslee J. Shaw,

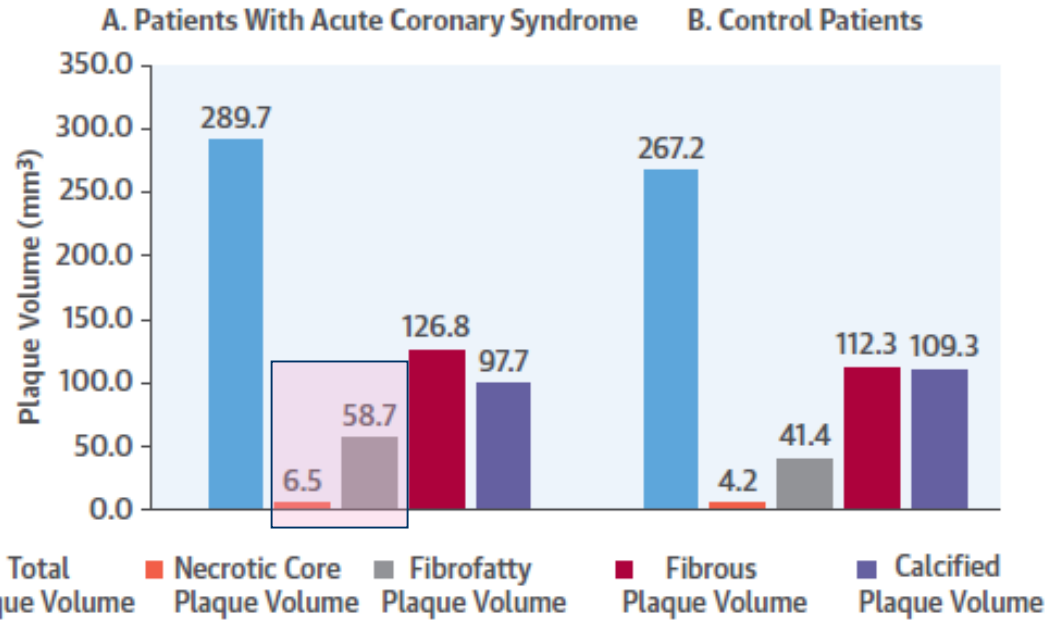
),[g]
im, MD,[k]
), PhD,[c]
, MD,[a,b]
Lu, MSc,[b]
, MD,[v]
D[b]

FIGURE 1 CONSORT Diagram for the ICONIC study



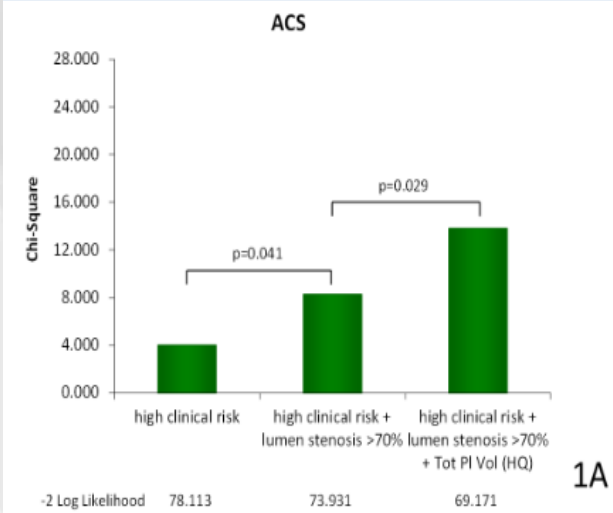
CENTRAL ILLUSTRATION Precursors of Acute Coronary Syndrome and Control Subjects as Identified by Coronary CTA

PER PATIENT PRECURSORS OF ACUTE CORONARY SYNDROME

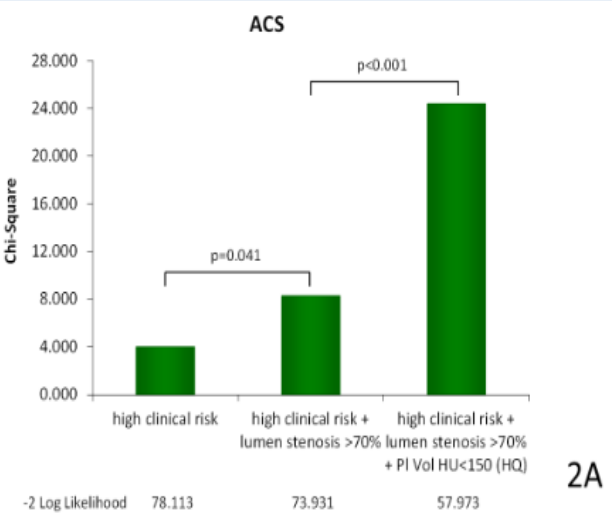


Chang, H.-J. et al. J Am Coll Cardiol. 2018;71(22):2511-22.

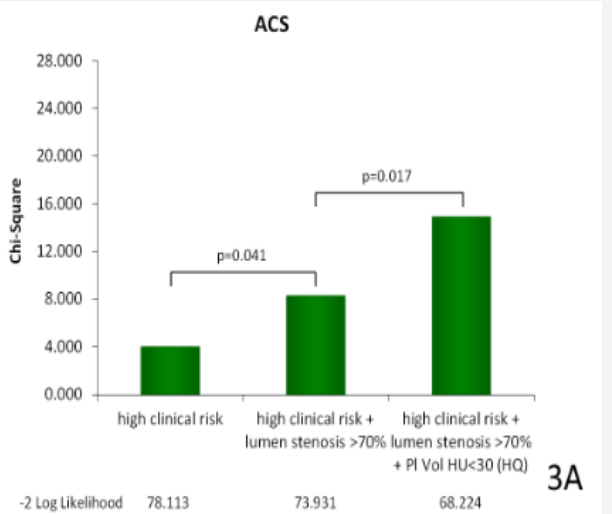
CAPIRE: Plaque features, Biomarkers and Prognosis



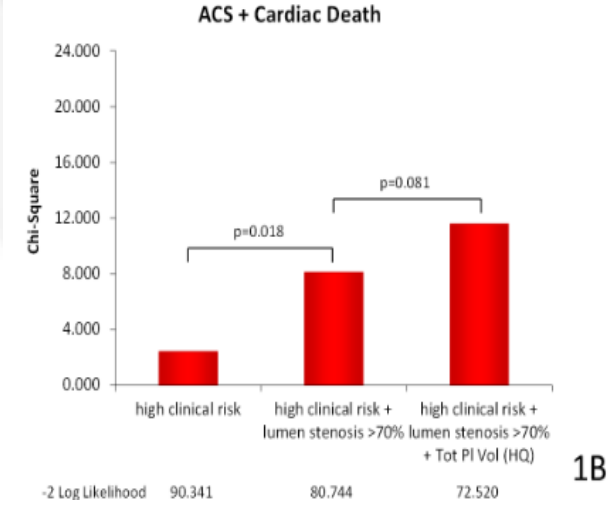
1A



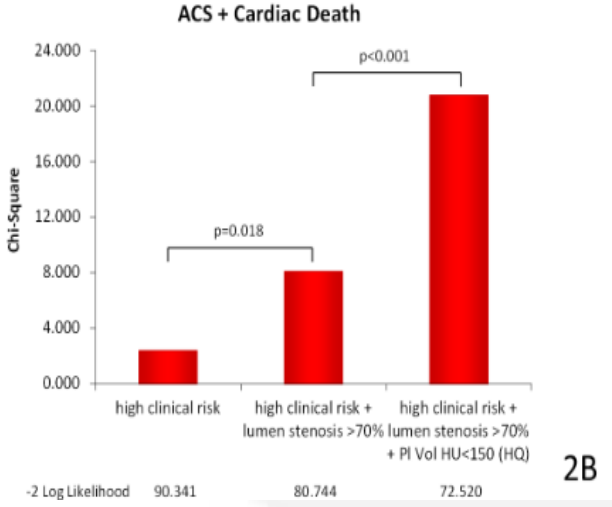
2A



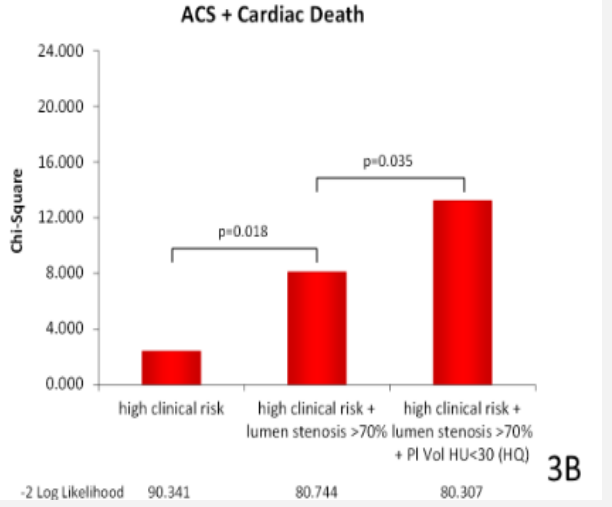
3A



1B



2B



3B

Centro Cardiologico Monzino

Andreini D et al. Unpublished data

Prognostic and Therapeutic Implications of Statin and Aspirin Therapy in Individuals With Nonobstructive Coronary Artery Disease

Results From the CONFIRM (Coronary CT Angiography Evaluation For Clinical Outcomes: An International Multicenter Registry) Registry

Table 4. Cox Models for All-Cause Mortality in Patients With Nonobstructive CAD

Models	Hazard Ratio* (95% CI)	*P* Value
All patients (n=10 418)		
Statin therapy	0.52 (0.34–0.79)	0.002
ASA therapy	0.77 (0.53–1.12)	0.173
Nonobstructive CAD (n=4706)		
Statin therapy	0.39 (0.23–0.65)	<0.001
ASA therapy	0.66 (0.42–1.04)	0.070
No coronary plaque (n=5712)		
Statin therapy	0.64 (0.30–1.37)	0.252
ASA therapy	0.73 (0.37–1.47)	0.384

CAD indicates coronary artery disease; and CI, confidence interval.
*Adjusted for National Cholesterol Education Program/Adult Treatment Program III risk.

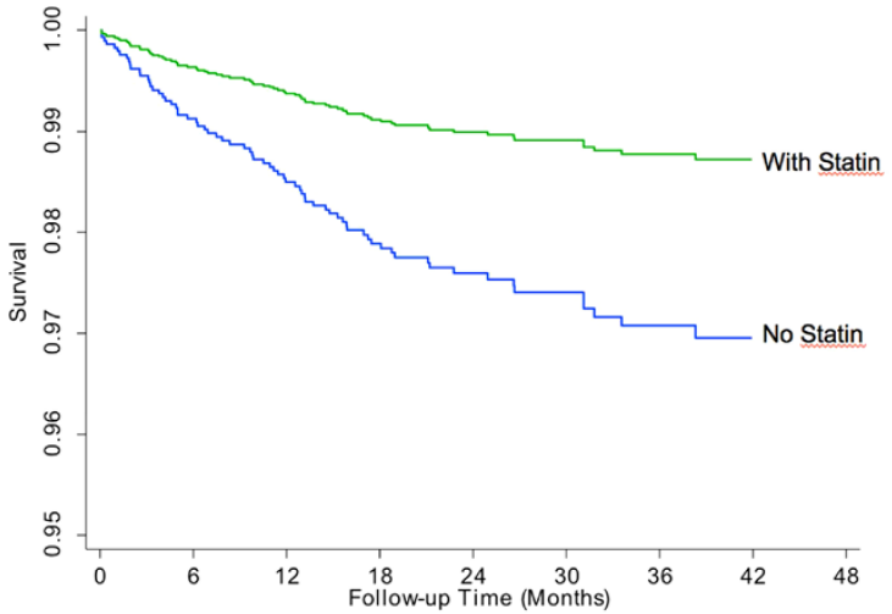


Figure 3. Kaplan–Meier survival curves as a function of statin use in patients with coronary plaque.

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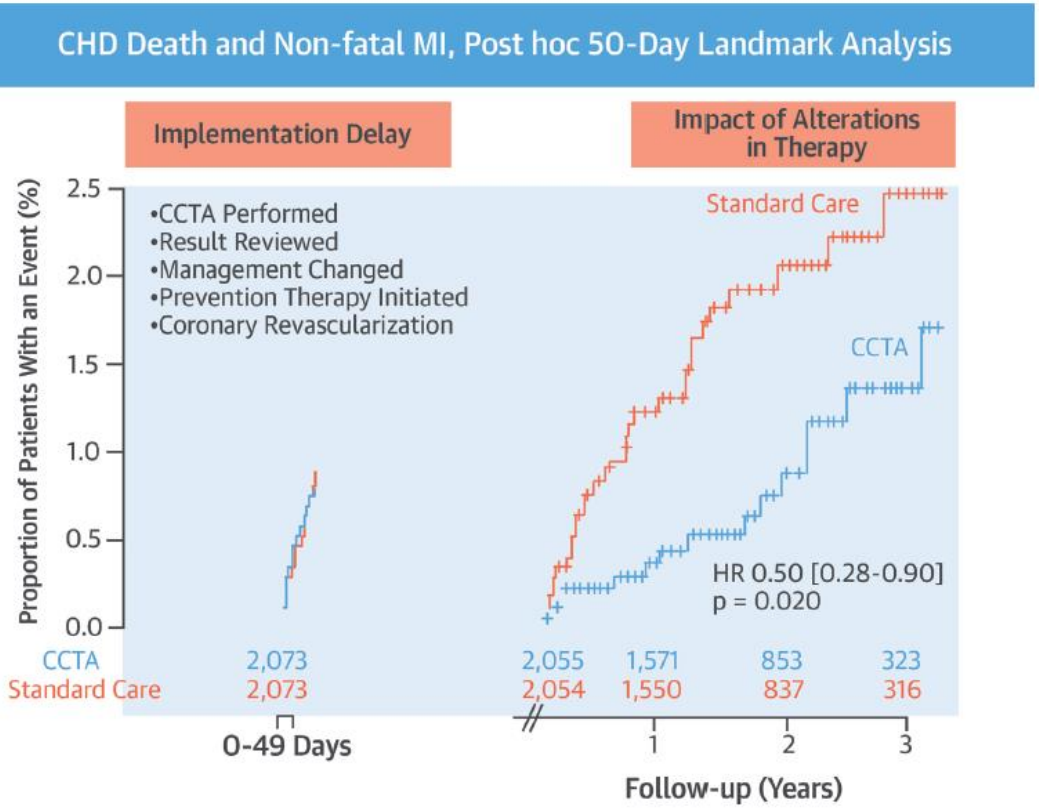
Chow et al, *Arterioscler Thromb Vasc Biol 2015*

Use of Coronary Computed Tomographic Angiography to Guide Management of Patients With Coronary Disease

Michelle C. Wil[illegible],[b]
Stephanie Lew[illegible] Clark,[a]
Marcus Flather[illegible] an Beek, MD,[a]
Adam D. Timm[illegible]

CENTRAL ILLUSTRATION Clinical Effect of CCTA in Suspected Angina Pectoris: Coronary Heart Disease Death and Nonfatal Myocardial Infarction

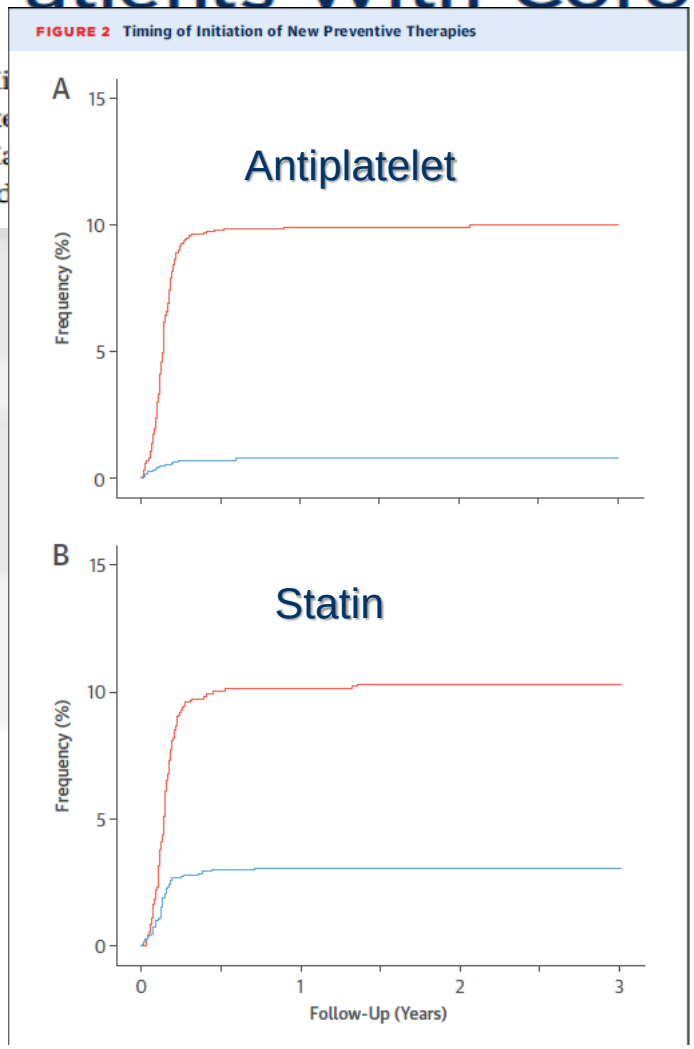


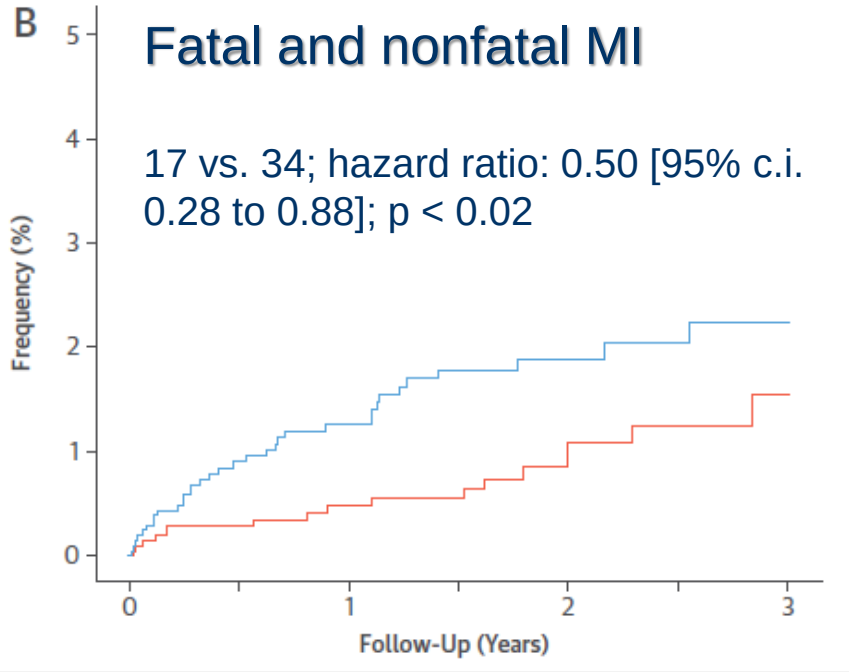
Williams, M.C. et al. J Am Coll Cardiol. 2016;67(15):1759-68.

Post hoc landmark analysis at 50 days to account for the implementation and treatment delay consequent on the conduct, reporting, and communication of the coronary computed tomography angiography (CCTA) findings. HR = hazard ratio.

Jacc 2016

Use of Coronary Computed Tomographic Angiography to Guide Management of Patients With Coronary Disease





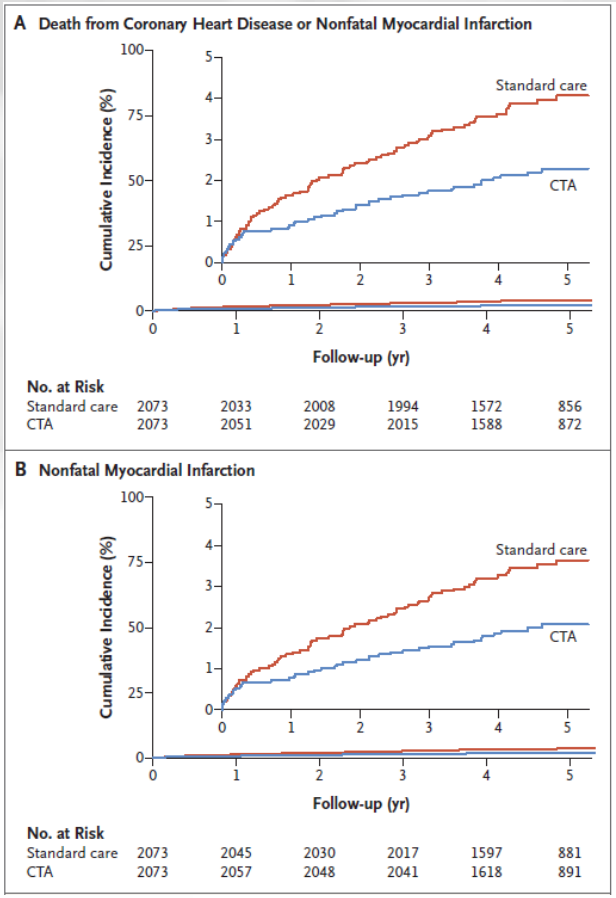
-Red line: CTA
-Blue line: SOC

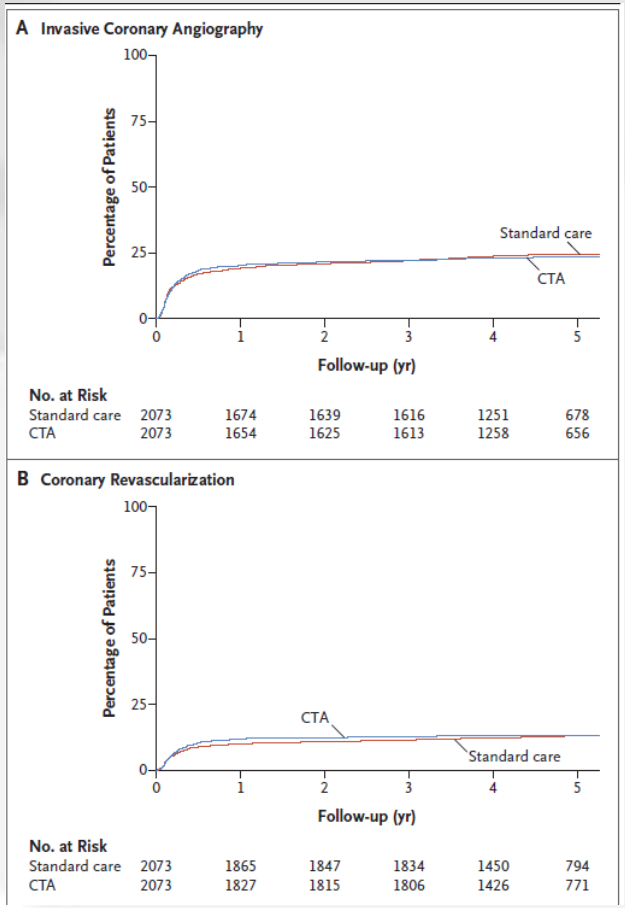
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Coronary CT Angiography and 5-Year Risk of Myocardial Infarction

The SCOT-HEART Investigators*





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Newby et al. NEJM 2018

Rationale and design of the *Progression of AtheRosclerotic PlAque DetermIned by Computed TomoGraphic Angiography IMaging (PARADIGM) registry: A comprehensive exploration of plaque progression and its impact on clinical outcomes from a multicenter serial coronary computed tomographic a*

San
Edo
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Hug
and
Jan

Study Design and Population

- **Dynamic multi-national observational prospective registry**

Inclusion criteria

- Consecutive patients without prior history of CAD, undergoing 'clinically-indicated' serial coronary CTAs at a ≥2 years inter-scan interval

Exclusion criteria

- No information on statin use at both baseline (CTA-1) and follow-up CTA (CTA-2)
- Patients who discontinued statin use after the CTA-1
- Patients with non-interpretable CTA for all coronary vessels

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Am H J 2017

JACC: CARDIOVASCULAR IMAGING
VOL. ■, NO. ■, 2018

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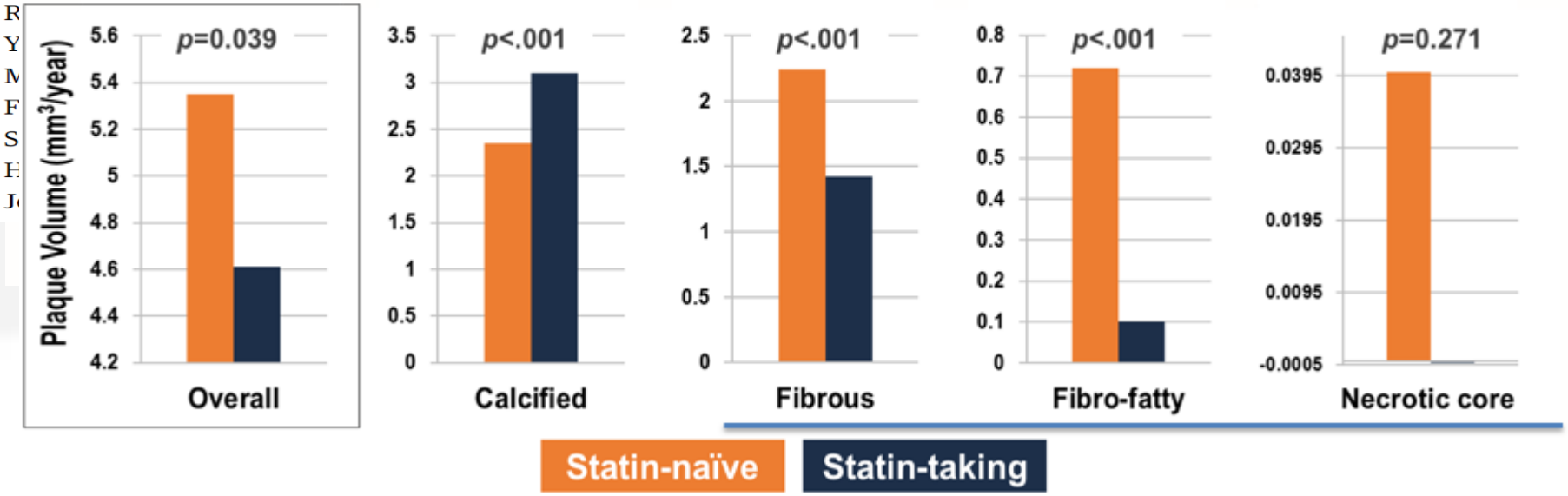
Effects of Statins on Coronary Atherosclerotic Plaques

Annualized Change in Plaque Volume According to Statin Treatment



Reducing in Overall / Non-calcified, but Increasing Calcified components of plaque

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Lee at al, JACC img 2018

Temporal Change in Plaque Characteristics According to Statin Treatment

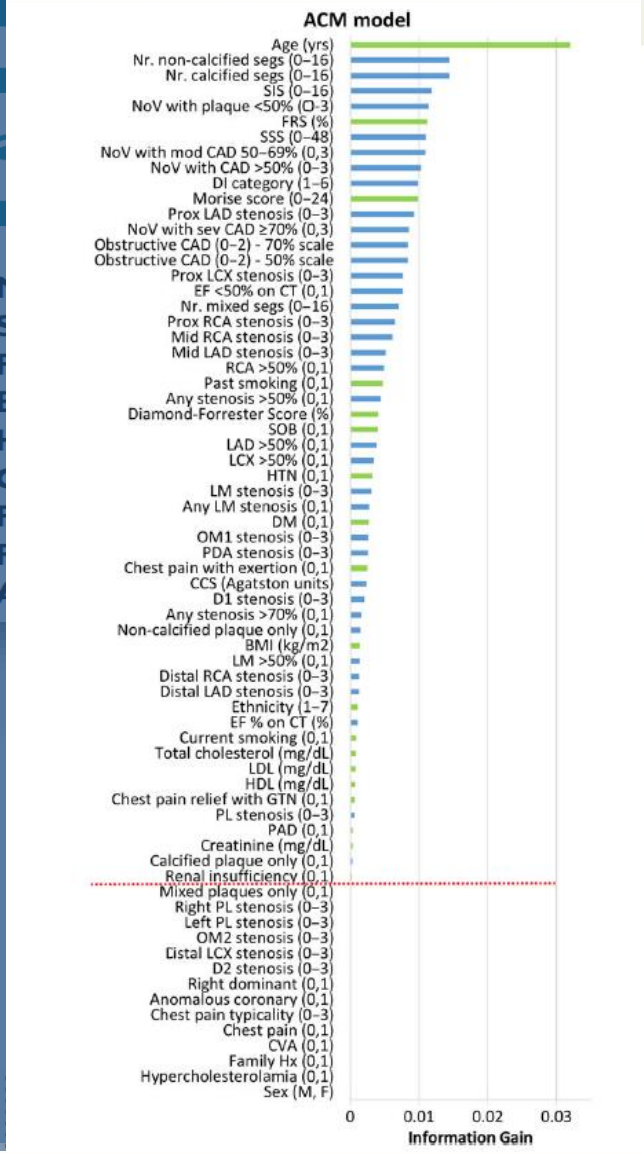
Summary

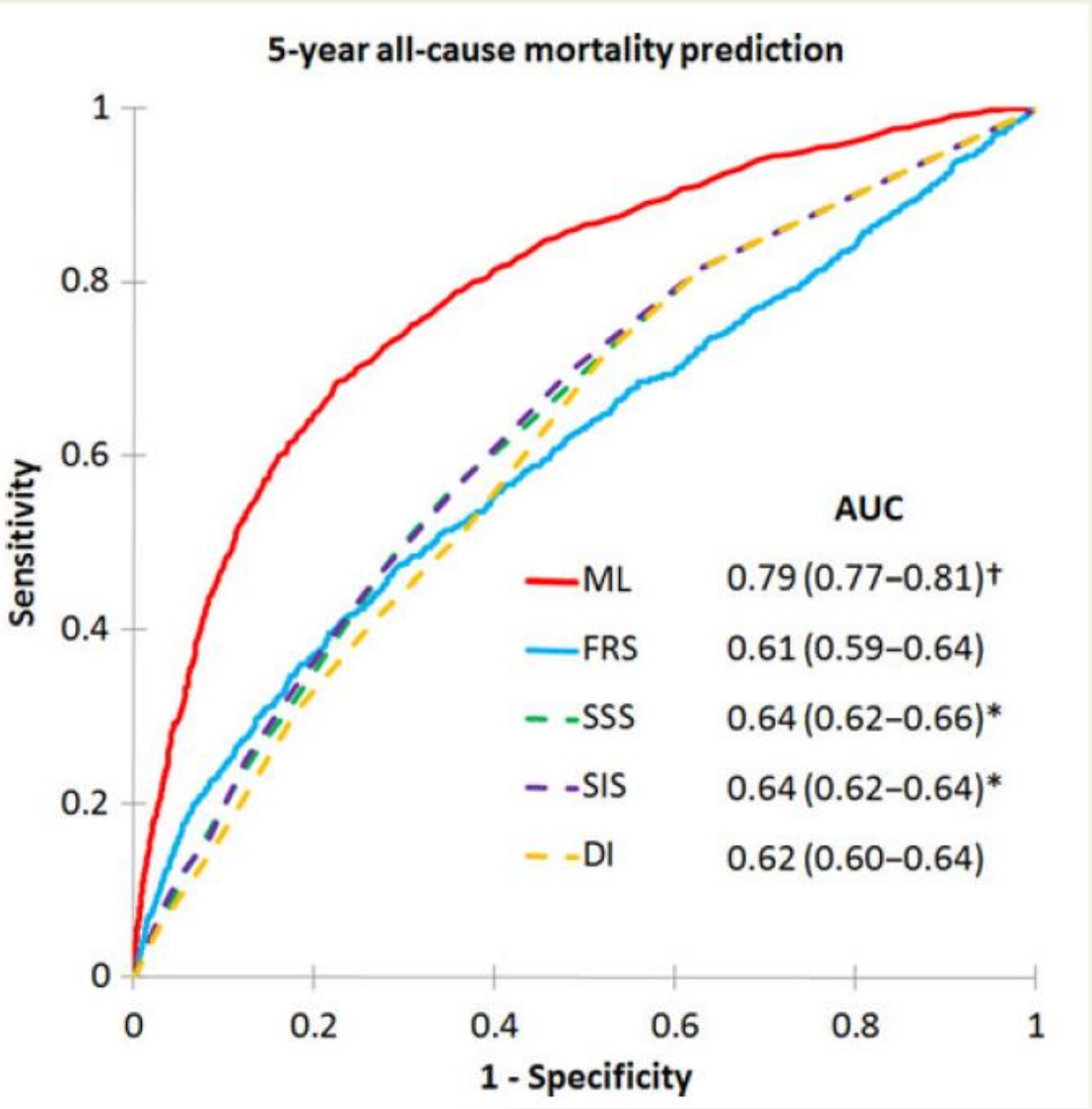
- Statins are associated with
  - Slower progression of overall coronary atherosclerosis volume (PV, total: 5.4±10.1 vs 4.6±9.7 mm^3/year)
  - Increased plaque calcification (calcified PV: 7.9±17.7 vs. 11.3±23.1 mm^3/year)
  - Reduction of high-risk plaque (annual incidence: 1.6 vs 0.9 %/year) and its constituents
- Statins are not associated with lesions progressing to high-grade stenoses (annual incidence: 2.8 vs. 3.2 %/year, *p*=NS)

Lee at al, JACC img 2018

European Heart Journal Advance Access published June 1, 2016

European Heart Journal
doi:10.1093/eurheartj/ehw188





Contents lists available at ScienceDirect

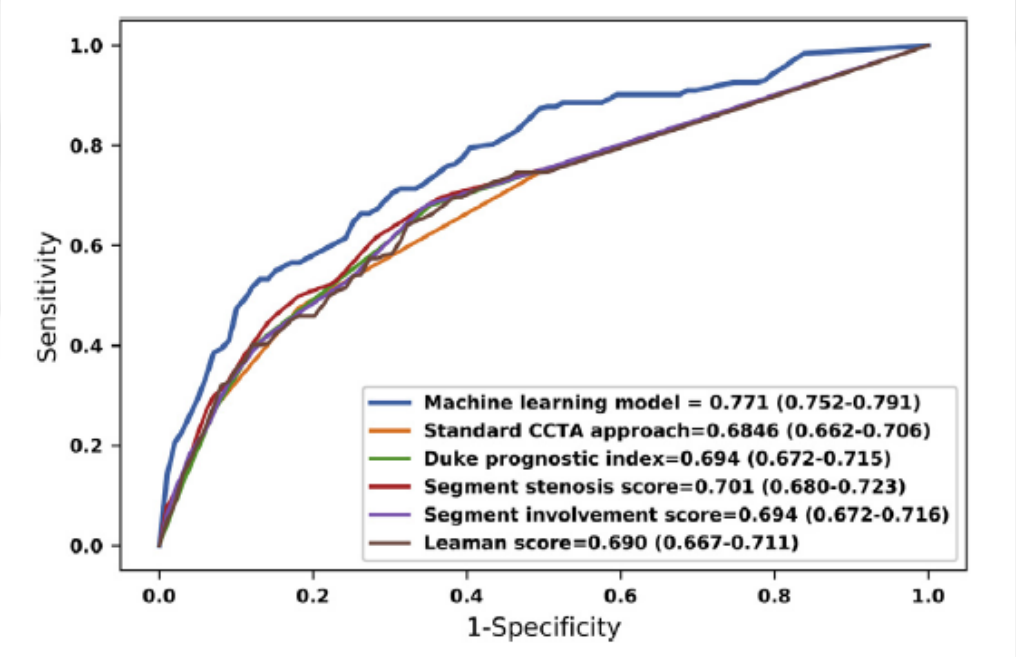
Journal of Cardiovascular Computed Tomography

journal homepage: www.elsevier.com/locate/jcct

Research paper

Maximization of the usage of coronary CTA derived plaque information using a machine learning based algorithm to improve risk stratification; insights from the CONFIRM registry

Alexander R. van Rosendael[a], Gabriel Maliakal[a], Kranthi K. Kolli[a], Ashley Beecy[a], Subhi J. Al'Aref[a], Aeshita Dwivedi[a], Gurpreet Singh[a], Mohit Panday[a], Amit Kumar[a], Xiaoyue Ma[a], Stephan Achenbach[b], Mouaz H. Al-Mallah[c], Daniele Andreini[d], Jeroen J. Bax[e], Daniel S. Berman[f], Matthew J. Budoff[g], Filippo Cademartiri[h], Tracy Q. Callister[i], Hyuk-Jae Chang[j], Kavitha Chinnaiyan[k], Benjamin J.W. Chow[l], Ricardo C. Cury[m], Augustin DeLago[n], Gudrun Feuchtner[o], Martin Hadamitzky[p], Joerg Hausleiter[q], Philipp A. Kaufmann[r], Yong-Jin Kim[s], Jonathon A. Leipsic[t], Erica Maffei[u], Hugo Marques[v], Gianluca Pontone[d], Gilbert L. Raff[k], Ronen Rubinshtein[w], Leslee J. Shaw[x], Todd C. Villines[y], Heidi Gransar[z], Yao Lu[aa], Erica C. Jones[a], Jessica M. Peña[a], Fay Y. Lin[a], James K. Min[a,*]



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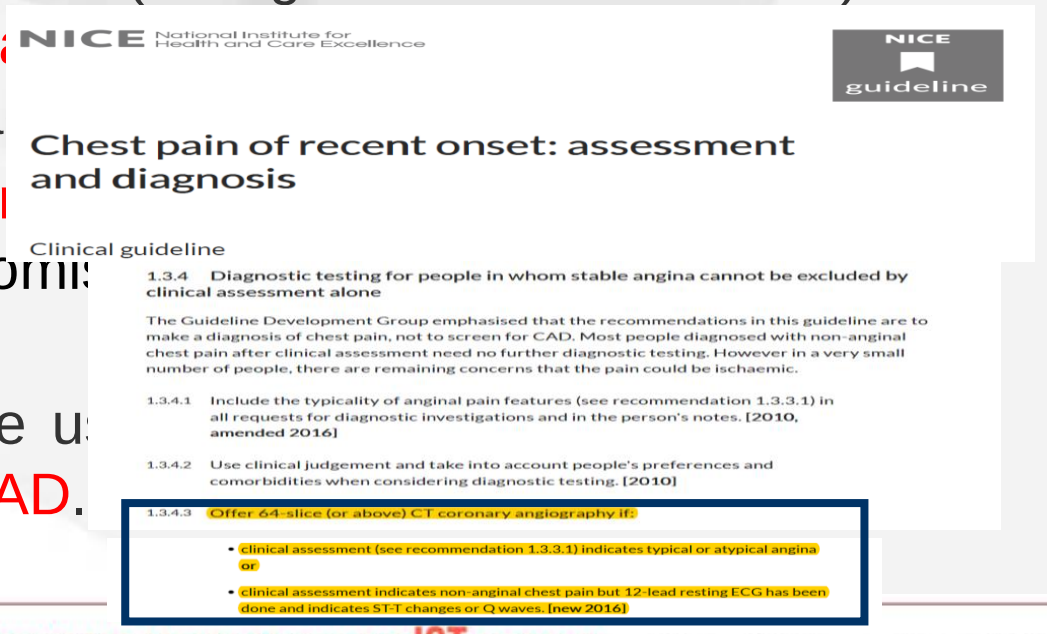
CONCLUSIONS

- Before the “CCTA era”, patients with non-obstructive CAD, in the absence of inducible ischemia, were included in the same group of those without CAD.
- Patients with non-obstructive CAD may be divided into two groups, those with low-risk plaque morphology and those in whom plaque characteristics (i.e.higher PRI and/or LAP) are associated with an increa
could benefit from more a
- Biomarkers as hsTr (silen
inflammation) seems promis
together with CCTA.
- These results support the us
patients without known CAD.


NICE National Institute for Health and Care Excellence

NICE guideline

Chest pain of recent onset: assessment and diagnosis

Clinical guideline

1.3.4 Diagnostic testing for people in whom stable angina cannot be excluded by clinical assessment alone

The Guideline Development Group emphasised that the recommendations in this guideline are to make a diagnosis of chest pain, not to screen for CAD. Most people diagnosed with non-anginal chest pain after clinical assessment need no further diagnostic testing. However in a very small number of people, there are remaining concerns that the pain could be ischaemic.

1.3.4.1 Include the typicality of anginal pain features (see recommendation 1.3.3.1) in all requests for diagnostic investigations and in the person's notes. [2010, amended 2016]

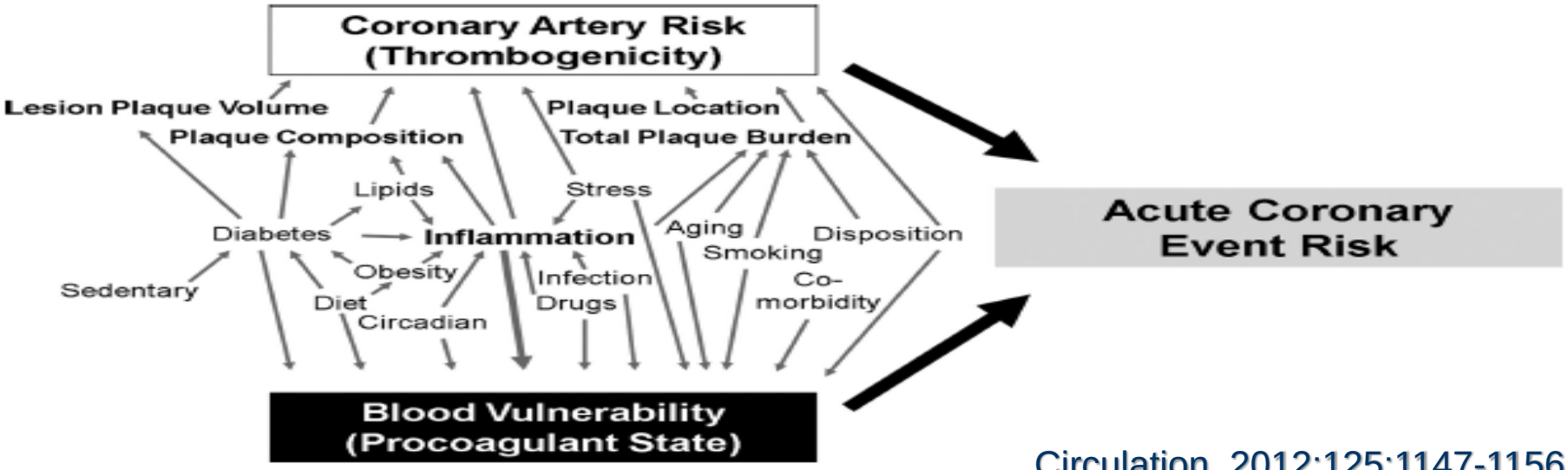
1.3.4.2 Use clinical judgement and take into account people's preferences and comorbidities when considering diagnostic testing. [2010]

1.3.4.3 Offer 64-slice (or above) CT coronary angiography if:

- clinical assessment (see recommendation 1.3.3.1) indicates typical or atypical angina or
- clinical assessment indicates non-anginal chest pain but 12-lead resting ECG has been done and indicates ST-T changes or Q waves. [new 2016]

CONCLUSIONS

- We are quite far from early identification of vulnerable plaque and vulnerable patient.
- Acute coronary events results from a complex interplay in which atherosclerotic plaque is only one actor toghether with pro-thrombotic factors.
- It is time to go outside the lumen looking for atherosclerosis.



Circulation. 2012;125:1147-1156

The Future From the Past

A Chance for Change*

James K. Min, MD, Erica C. Jones, MD, Jessica M. Peña, MD, MPH

This “new” paradigm is not actually new, but simply encourages diagnostic CAD evaluation by a forward rather than backward-looking stance, reflecting the natural history of atherosclerosis progression; namely, that disease severity should be gauged hierarchically:

-plaque versus no plaque;

-high-risk plaque features versus non-high-risk plaque features; ←

-high-grade stenosis versus non–high-grade stenosis;

-ischemia versus no ischemia ←

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THE PRESENT AND FUTURE

REVIEW TOPIC OF THE WEEK

The Risk Continuum of Atherosclerosis and by C

Armin Arba

FIGURE 1 Nonobstructive Coronary Atherosclerotic Disease by Computed Tomography Angiography