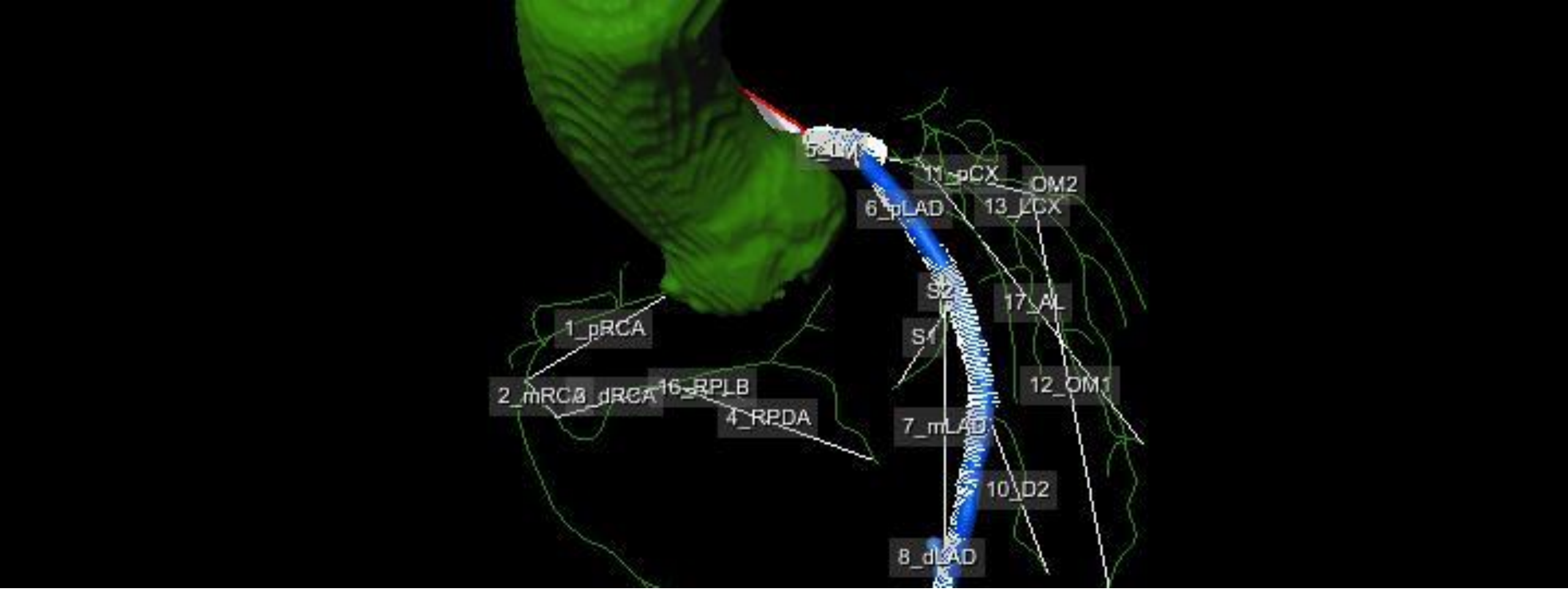


IMAGEN
UNA HERRAMIENTA PARA MEJORAR LA ESTRATIFICACIÓN DEL RIESGO

LEOPOLDO PÉREZ DE ISLA
HOSPITAL CLÍNICO SAN CARLOS
MADRID

Precise Non Invasive diagnosis of subclinical and mild coronary artery disease improves the rationale use of statins and outcomes in hypercholesterolemic patients.

P Marcos-Alberca, C Sánchez, B Ibañez, JA De Agustín, JJ Gómez-Diego, M Luaces, MA García-Fernández, J Arrazola, L Pérez-Isla, C Macaya

Cardiovascular Institute; CNIC & Diagnostic Imaging Dpt. Hospital Clínico San Carlos. Universidad Complutense. Madrid. Spain

Background

Statin therapy is one of the cornerstones of **primary and secondary prevention** of major cardiovascular events in patients (P) with hypercholesterolemia. It is unknown the impact of the diagnosis of **subclinical and mild coronary artery disease** (CHD) in the **prescribing propensity of a statin therapy** and subsequent **outcomes** in P with hypercholesterolemia.

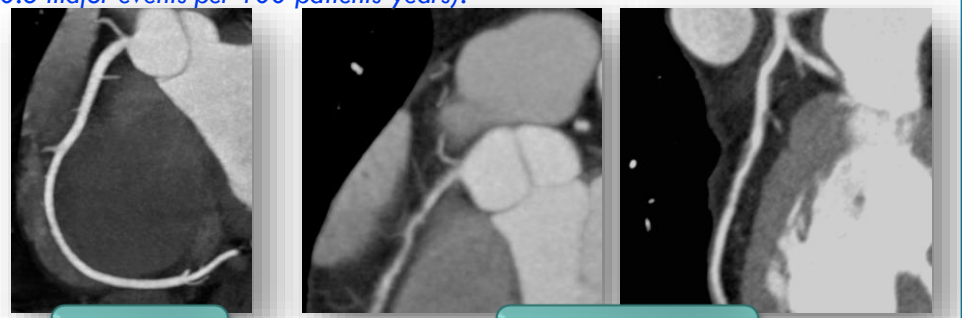
Methods

Prospective and observational study of a cohort of **400 P** screened between 2007 and 2009, without cardiovascular history and submitted to diagnose CHD by means of **non invasive coronary angiography using 64-rows multidetector CT (MDCT)**. Current Appropriateness Criteria and Guidelines for the diagnosis of CHD and the performance of MDCT were strictly observed, including blinded CT review. **Main variables** included were age, sex, major risk factors, CHD status (normal coronary arteries or mild CHD with luminal stenosis <50%), drugs (**statins**, aspirin, ACE inhibitors, ARB, Calcium antagonists agents, diuretics and betablockers) and **outcomes** (total mortality, cardiovascular mortality, non fatal MI, unstable angina, PCI or CABG). The follow up, outcomes collection and prescribing propensity was accomplished through historic controls from Euroaspire Survey and medical records and data collected from a wide Community Database jointly managed by care centers and general practitioners. **The MDCT report did not add advices or recommendations over any drug prescription.**

	EuroAspire II (2001)	EuroAspire III (2009)	HCSC Serie (Global)
Elevated Cholesterol	58%	51%	29%
On Statin previous to diagnose	26%	Not Reported	Not Reported
On Statin after F-U	61%	80%	65%

Results

After a median of 4.6 years, a total of one hundred and forty six P completed the survey: mean age 63±13 yo; M/F ratio 45/55. Prevalence of hypercholesterolemia at inclusion was 29%. **Subclinical and mild CHD was diagnosed in 49%**. After the follow up, in hypercholesterolemic P, **statin prescription** was **50%** when the diagnosis was of **normal coronary arteries,** increasing to **84%** when the diagnosis was **subclinical and mild CHD** *(Odds Ratio 5.3; 95% CI 1.2-23.1; p=0.02)*. Hence, the prescription propensity after MDCT resulted in **5 vs. 3 additional treatments with statin per 100 patients-years** compared with hypercholesterolemic P and normal coronary arteries. **Outcomes** were very low and similar to P with normal coronary arteries *(0.3 vs. 0.6 major events per 100 patients-years)*.



Normal Coronary Artery

Mild Subclinical Coronary Artery Disease

Conclusion

Non Invasive diagnosis of subclinical and mild CHD: **1) increase the prescription of a statin** in hypercholesterolemic patients; **2)** enhancing the adherence, and perhaps the targets in evidence based preventive therapies resulted in a **very low incidence of major CV events** at long term follow up.

Conflict of Interest: Exhibit supported with a travel and accommodation grant only for ESC 2014 days from Alter España and Abbott España. Inscription fees paid by the 1st author: P M-A (MD, PhD, FESC)

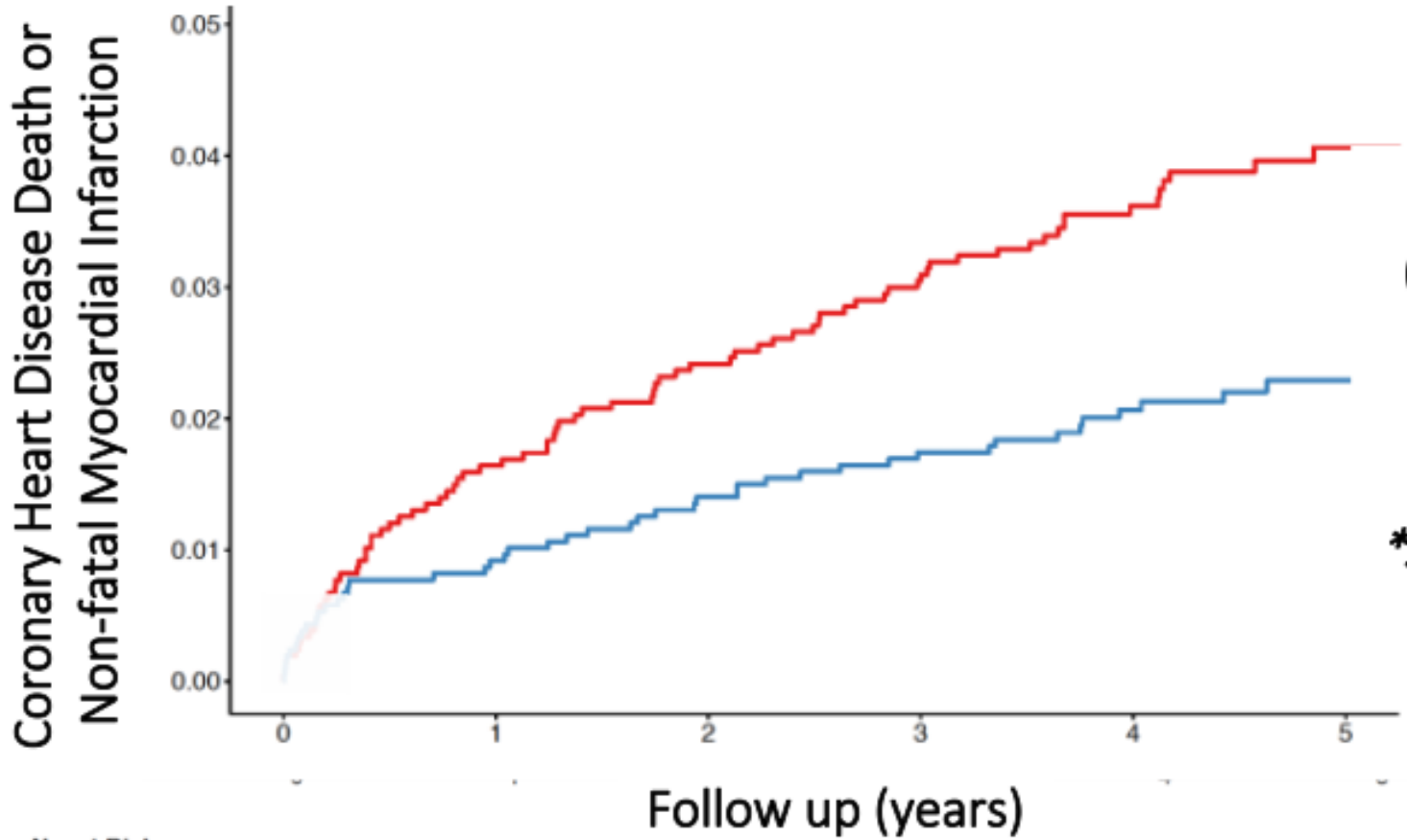
Conclusion

Non Invasive diagnosis of subclinical and mild CHD: **1) increase the prescription of a statin** in hypercholesterolemic patients; **2)** enhancing the adherence, and perhaps the targets in evidence based preventive therapies resulted in a **very low incidence of major CV events** at long term follow up.

Marcos-Alberca P et al. ESC Congress 2014

Primary Clinical End Point

*Excluding the 50-day treatment delay**



Hazard Ratio 0.53
(95% CI, 0.36 to 0.78)
P=0.001

**JACC 2016;67:1759-1768*

No. at Risk						
Standard Care	2073	2033	2008	1994	1572	856
CCTA	2073	2051	2029	2015	1588	872

Standard Care Alone — CTCA + Standard Care

Statin Therapy Use over 5 Years

The Right Patient Gets the Right Treatment

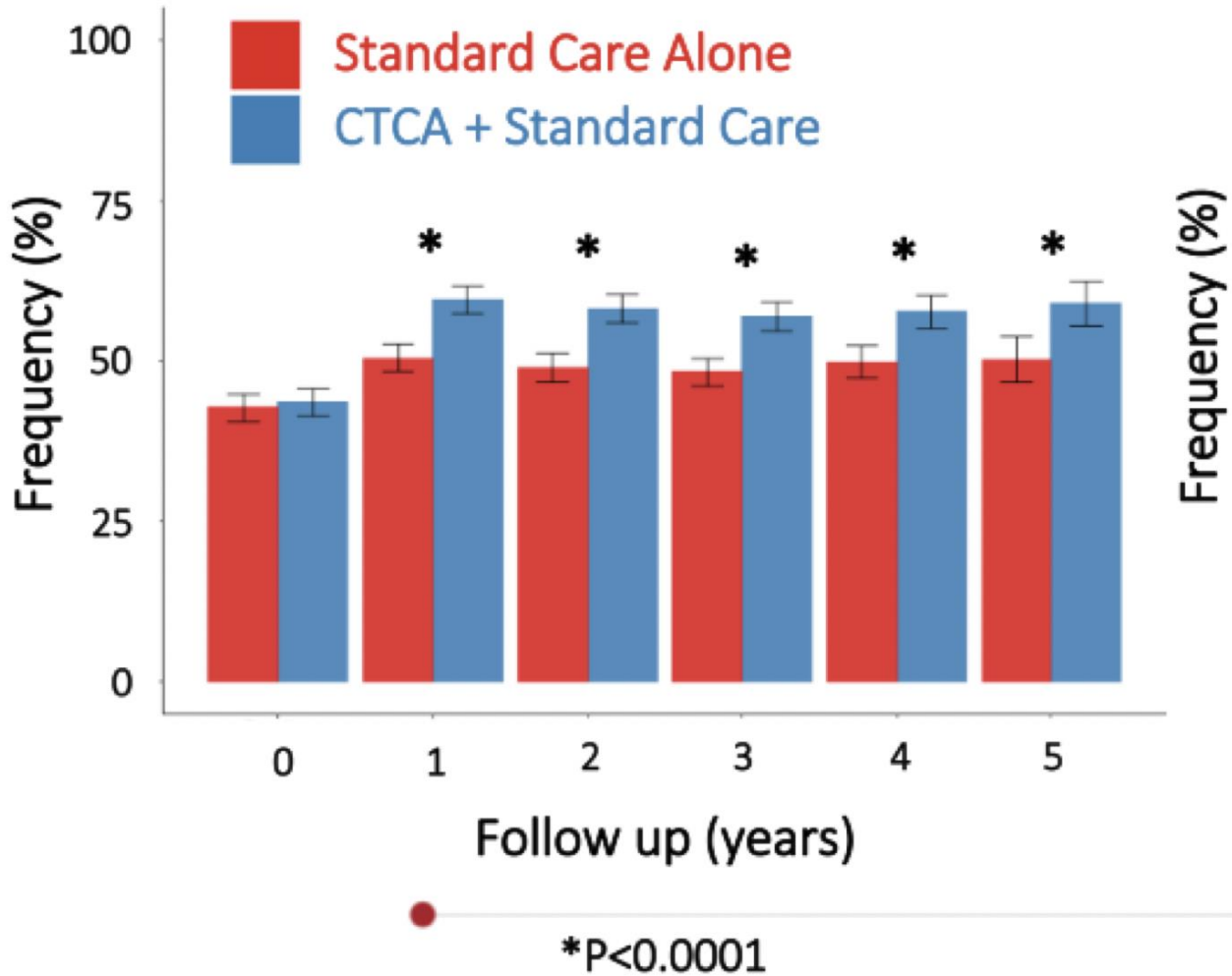
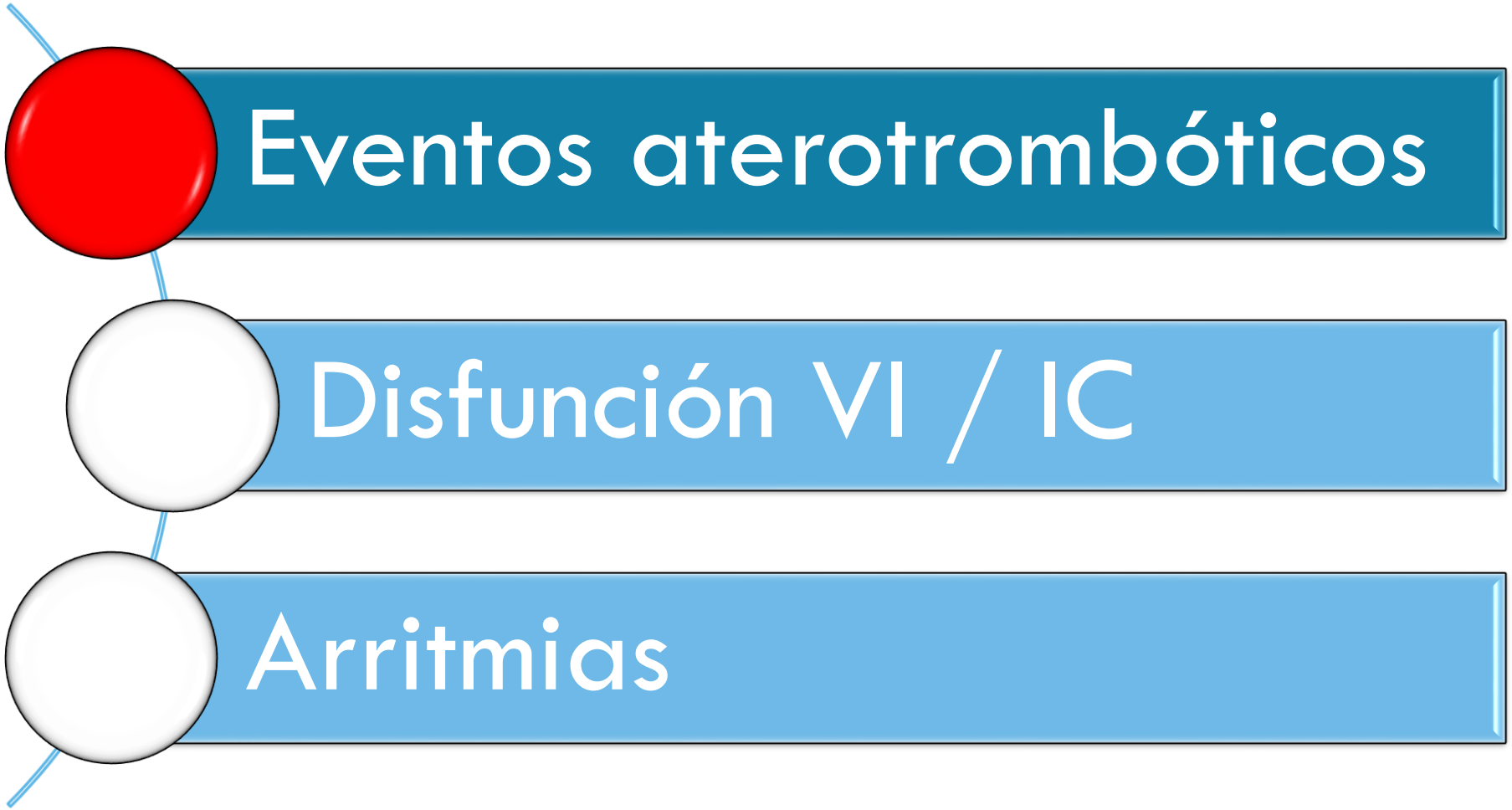



Imagen
Estratificación
Riesgo CV
Cambio
manejo

RIESGO

- Eventos aterotrombóticos
- Disfunción VI / IC
- Arritmias

RIESGO



Am J Roentgenol Radium Ther Nucl Med. 1959 May;81(5):772-7.

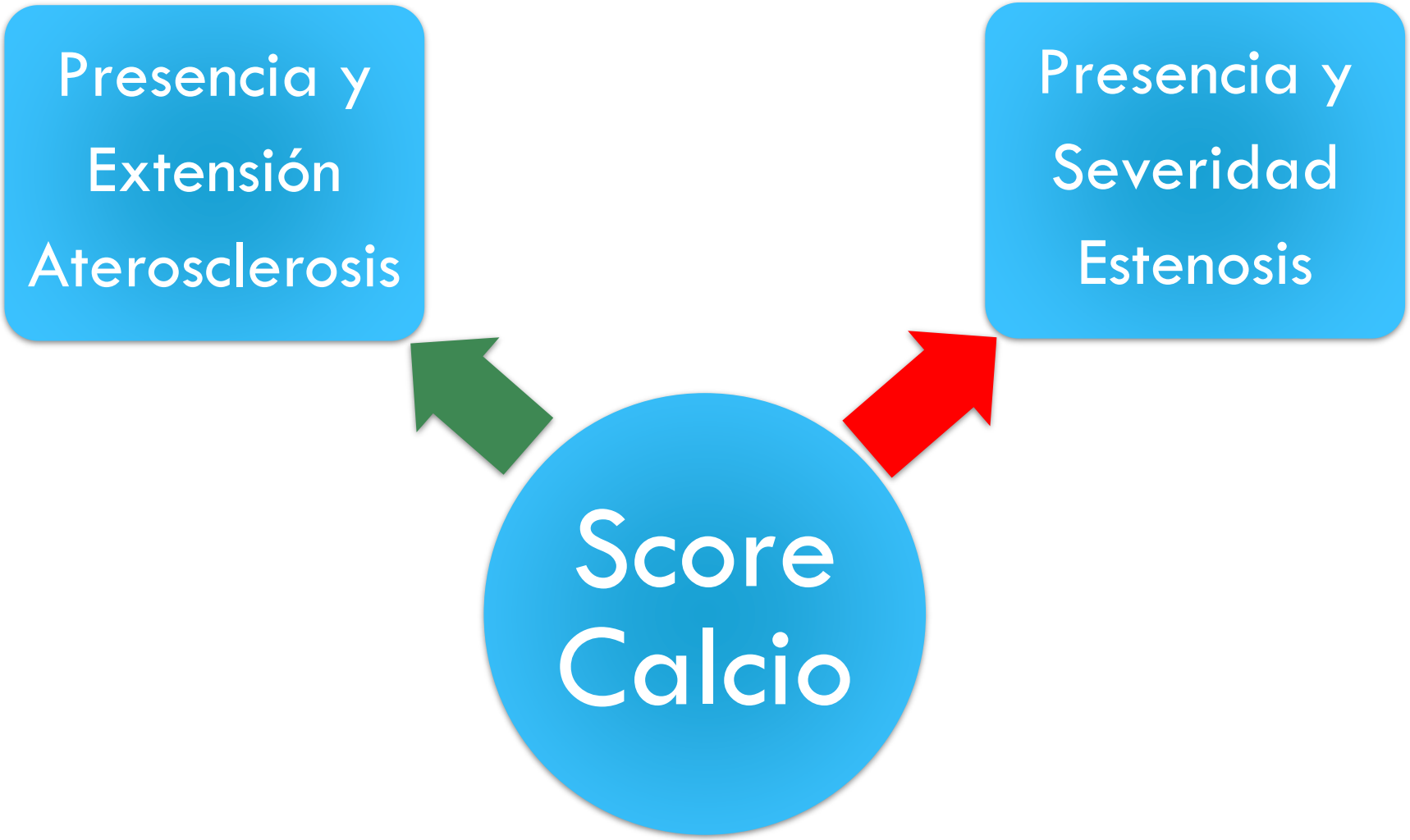
Calcification of the coronary arteries.

BLANKENHORN DH, STERN D.

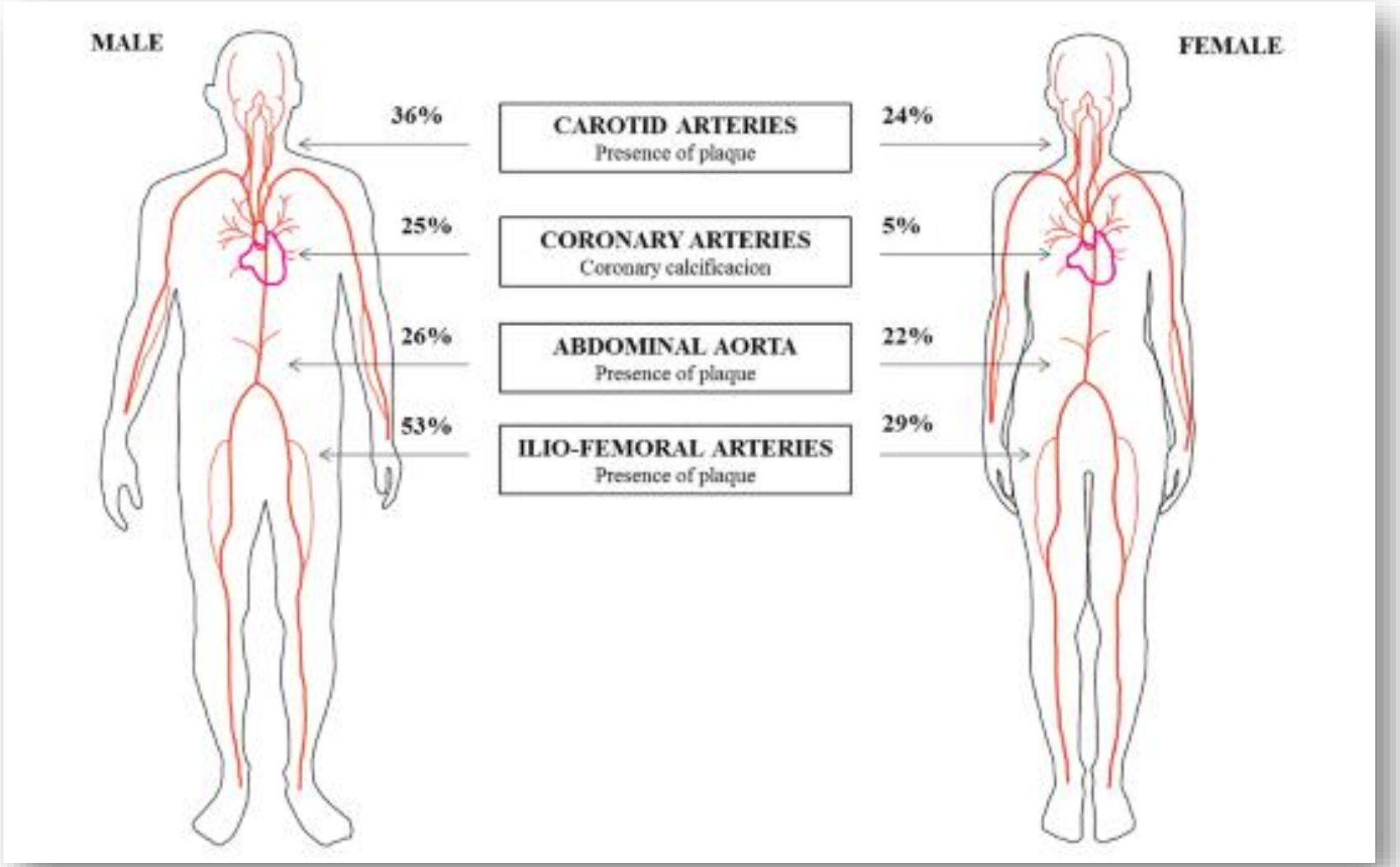
SCORE CALCIO CORONARIO

SCORE CALCIO CORONARIO

CALCIO SCORE CORONARIO



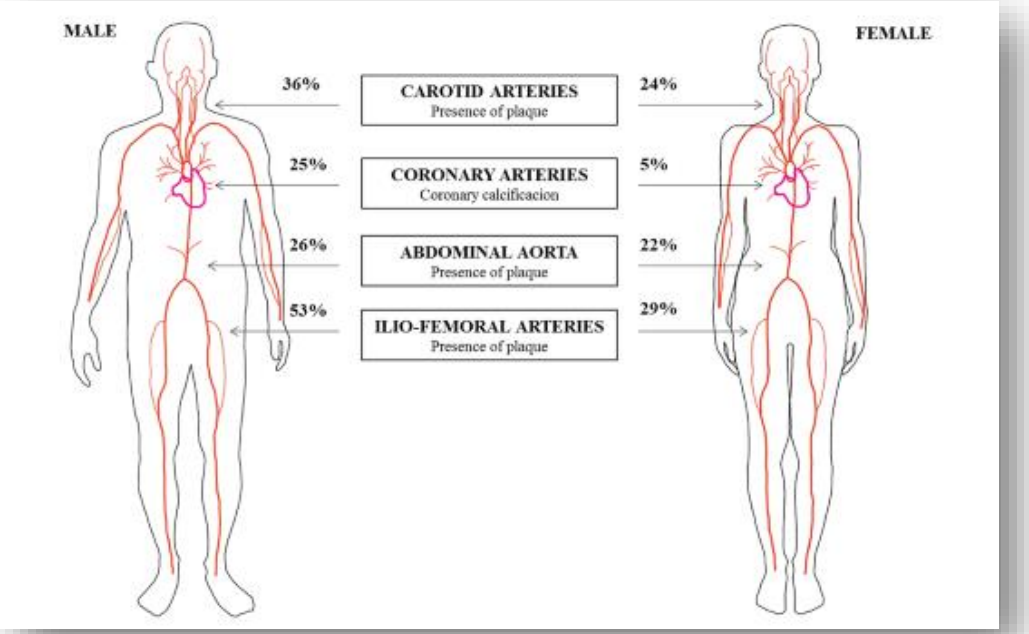
Progression of Early Subclinical Atherosclerosis Study



Fernández-Friera L et al. The PESA study. Circulation. 2015 Jun 16;131(24):2104-13.

ATEROSCLEROSIS CORONARIA SUBCLÍNICA

PESA



Fernández-Friera L et al. The PESA study. Circulation. 2015 Jun 16;131(24):2104-13.

SAFEHEART

Coronary disease (Cardiac CT)

60,5%

♂70,3% ♀51,5%

Pérez de Isla L, et al.
J Clin Lipidol. 2018 Jul - Aug;12(4):948-957

SCORE CALCIO CORONARIO

The diagnostic and prognostic significance of coronary artery calcification. A report of 800 cases.

Margolis JR, Chen JT, Kong Y, Peter RH, Behar VS, Kisslo JA

Radiology. 1980;137(3):609.

ESTRATIFICACIÓN ESC 2016

- Muy alto riesgo
  - Enfermedad CV
    - Clínica
    - **Imagen (Placas; no GIM)**
  - DM con:
    - LOD
    - Otro FRCV (HTA, Tab, HL)
  - Filtrado glomerular < 30
  - SCORE ≥ 10%

- Alto riesgo
  - FR marcado
    - CT > 310 mg/dl
    - TA > 180/100 mm Hg
  - DM (Excepto DM-1 sin FR)
  - Filtrado glomerular 30-59
  - SCORE ≥ 5 % y <10%

- Riesgo moderado
  - SCORE ≥ 1 % y <5%

SCORE CALCIO PARA ESTRATIFICACIÓN PRONÓSTICA

- Score
- Score + Escala de riesgo
- Score + marcador

SCORE CALCIO PARA ESTRATIFICACIÓN PRONÓSTICA

- Score
- Score + Escala de riesgo
- Score + marcador

SCORE SE ASOCIA A RIESGO

- 5635 pacientes asintomáticos
- 30-76 años
- Score>0 se asocia a riesgo ↑:
  - X 6,1 en varones
  - X 3,3 en mujeres

TABLE 1. Event Rates for Men and Women With Detectable CAC Compared to No Detectable CAC

	CAC Present	No CAC	*P*
Men			
Total No.	3065	1086	
Hard events, %	1.6	0.3	0.001
Soft events, %	4.5	0.1	<0.001
All events, %	6.1	0.4	<0.001
Women			
Total No.	754	730	
Hard events, %	0.5	0.3	0.4
Soft events, %	2.8	0.7	0.002
All events, %	3.3	1	0.002

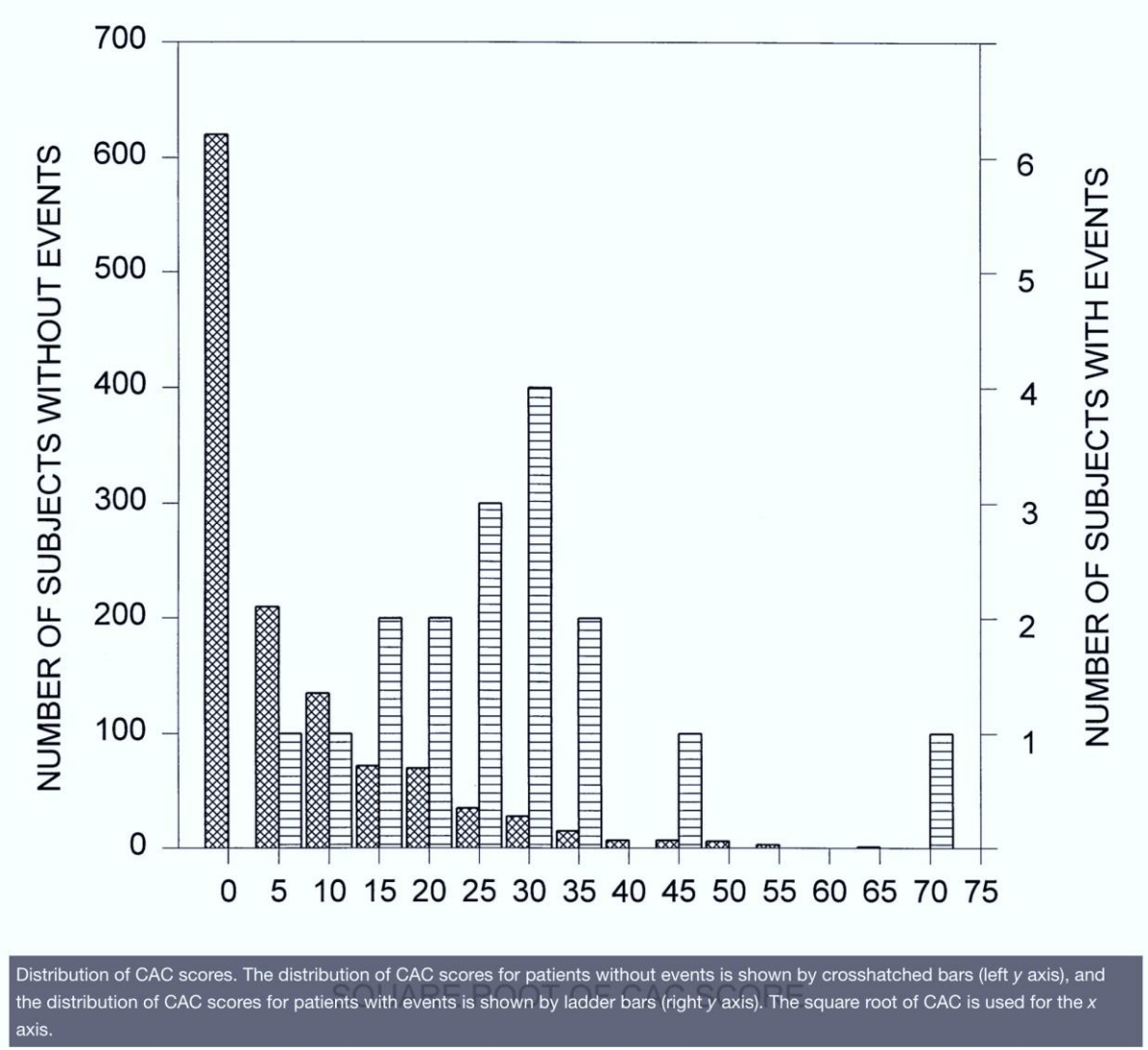
Condos GT et al. Circulation 2003. 107,2751

> SCORE > RIESGO

- 1173 pacientes asintomáticos

Score calcio	100	160	680
Sensibilidad*	89	89	53
Especificidad*	77	82	95

* Para IAM o muerte CV



Distribution of CAC scores. The distribution of CAC scores for patients without events is shown by crosshatched bars (left *y* axis), and the distribution of CAC scores for patients with events is shown by ladder bars (right *y* axis). The square root of CAC is used for the *x* axis.

Arad et al. Circulation 1996; 93:1951.

SAFEHEART-RE

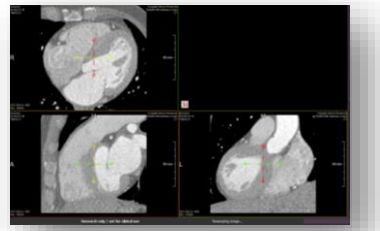
- **5-year risk** = $100 *(1-0.9532^{\exp((0.70*A+1.07*B+1.45*C+0.69*D+1.42*E+0.48*F+0.88*G+0.98*H+0.92*I+1.57*J+0.42*K)-5.4078)})$
- **10-year risk** = $100 *(1-0.9025^{\exp((0.70*A+1.07*B+1.45*C+0.69*D+1.42*E+0.48*F+0.88*G+0.98*H+0.92*I+1.57*J+0.42*K)-5.4078)})$

Índice C de Harrel: 0,85

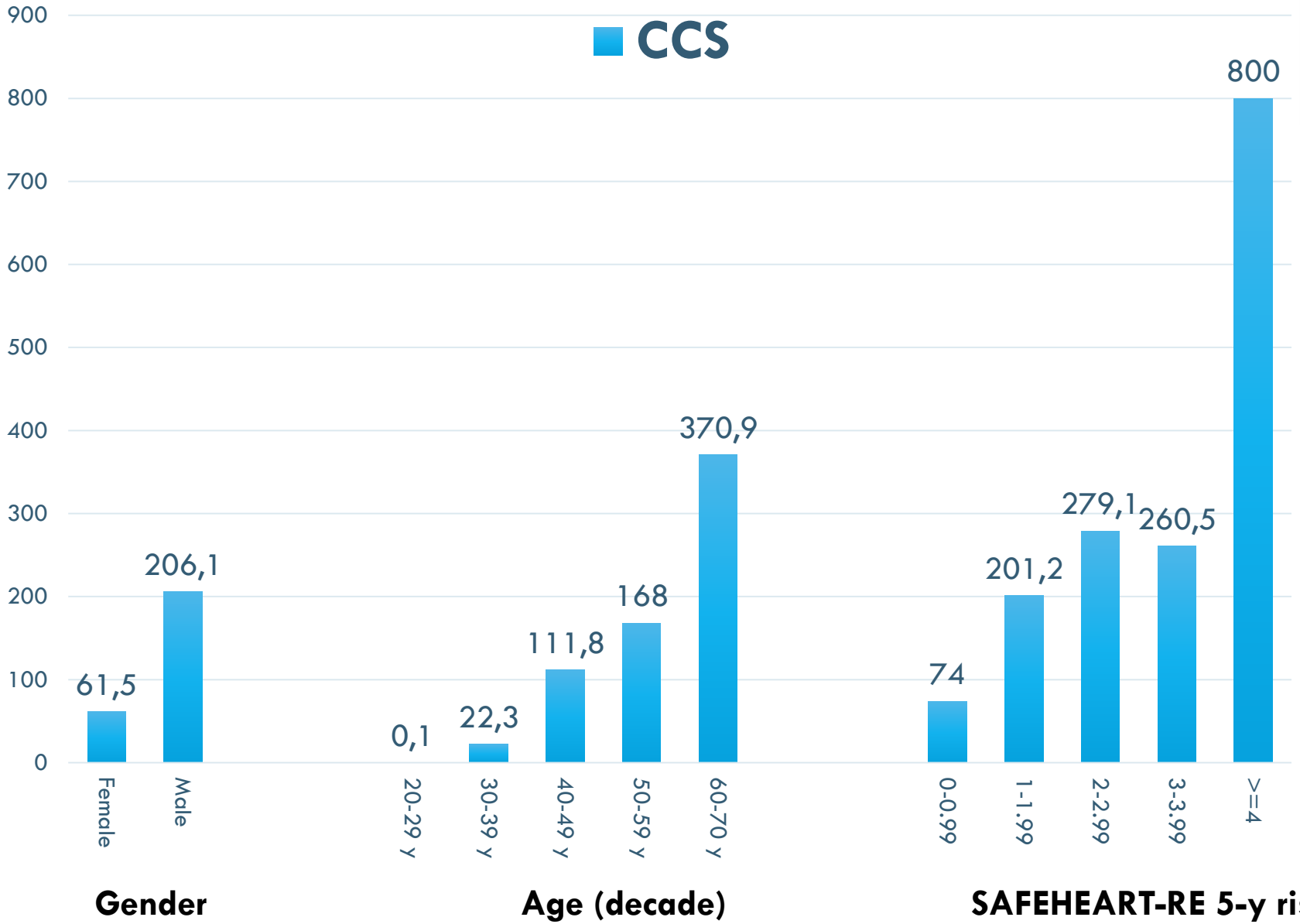
Male		Female: A=0 Male: A=1
Age	< 30 y	B=0 & C=0
	30-59 y	B=1 & C=0
	≥ 60 y	B=0 & C=1
High blood pressure		No: D=0 Yes: D=1
History of ASCVD		No: E=0 Yes: E=1
Active smoking		No: F=0 Yes: F=1
BMI	Normal weight	G=0 & H=0
	Overweight	G=1 & H=0
	Obesity	G=0 & H=1
LDL-C	<100 mg/dl	I=0 & J=0
	100-159 mg/dl	I=1 & J=0
	≥ 160 mg/dl	I=0 & J=1
Lp(a) > 50 mg/dl		No: K=0 Yes: K=1

Pérez de Isla L, et al. The SAFEHEART Registry. Circulation. 2017 May 30;135(22):2133-2144.

Coronary Calcium Score; n = 440 FH



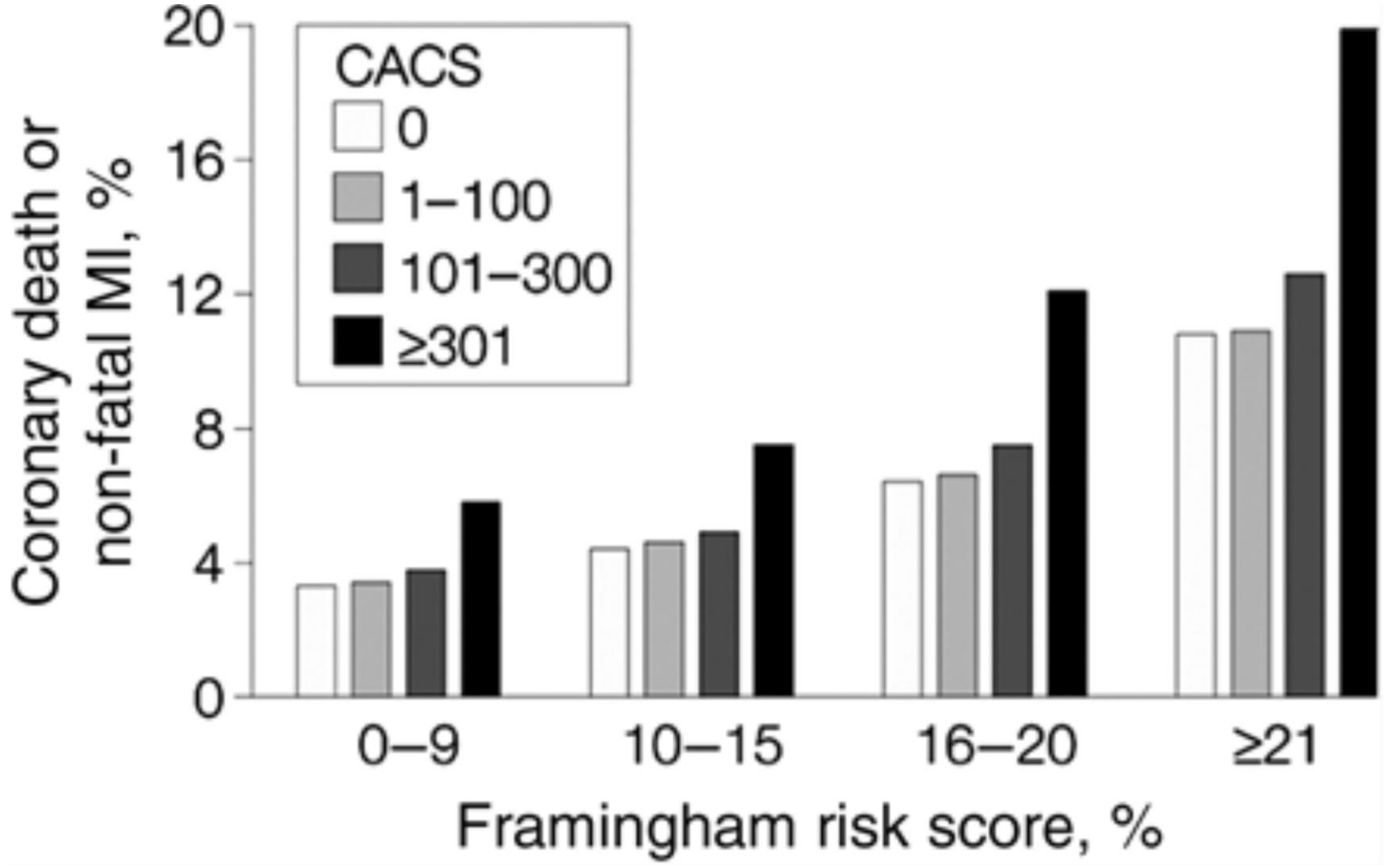
SAFEHEART



Pérez de Isla L, et al. On-going evaluation.

SCORE CALCIO PARA ESTRATIFICACIÓN PRONÓSTICA

- Score
- Score + Escala de riesgo
- Score + marcador



Greenland P, et al. JAMA , 2004, vol. 291 (pg. 210-215)

SCORE CALCIO PARA ESTRATIFICACIÓN PRONÓSTICA

- Score
- Score + Escala de riesgo
- Score + marcador

SCORE + MARCADOR

- N = 1461 sin ECV
- Seguimiento medio 6,4 años
- Riesgo relativo 7,5 veces mayor que para niveles más bajos

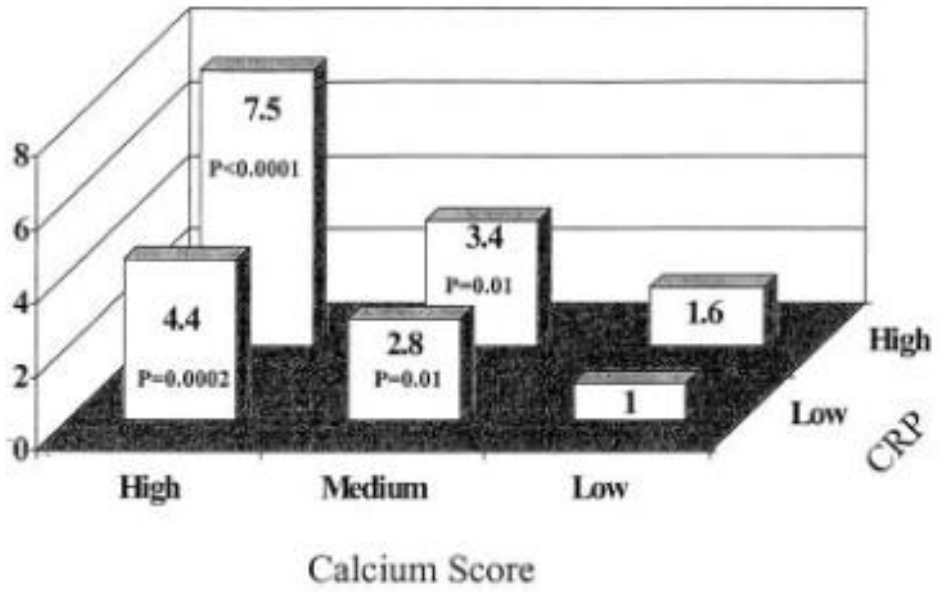


Figure 2. RRs of nonfatal MI, coronary death, PTCA, CABG, or stroke associated with high (≥75th percentile=4.05 mg/L) and low (<4.05 mg/L) levels of CRP and high (>142.1, medium (3.7 to 142.1) and low (<3.7) tertiles of calcium scores.

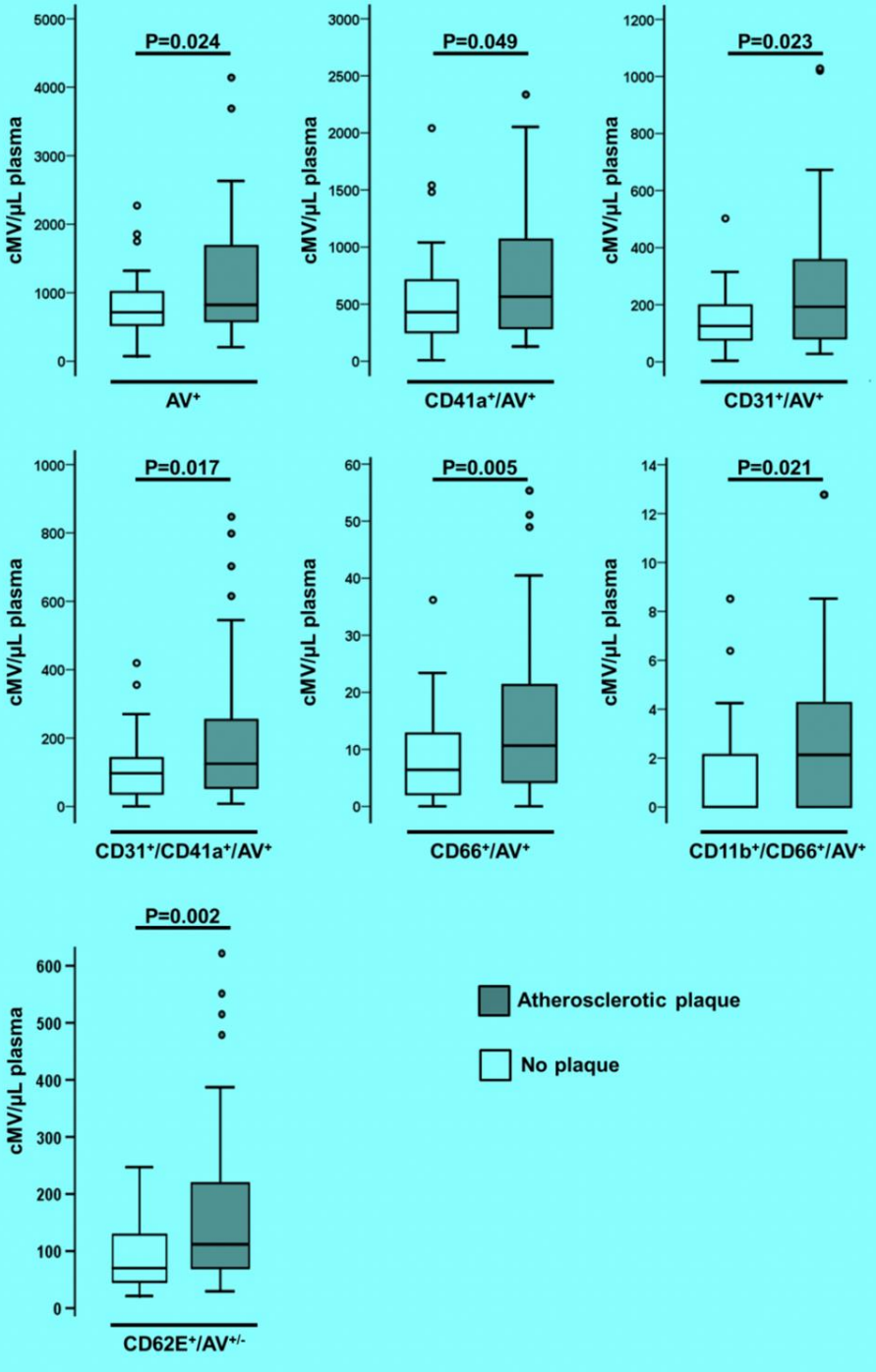
Park R, et al Circulation 2002; 106:2073.

Liquid biopsy of endothelial cells, platelets, granulocytes, and neutrophils by released microvesicles map coronary calcification and atherosclerotic plaque in asymptomatic patients with familial hypercholesterolemia- A CTA imaging study.

Gemma Chiva-Blanch[1], Teresa Padró[1,2], Javier Crespo[1], Leopoldo Perez de Isla[3], Mata P[4], Lina Badimon[1,2*].

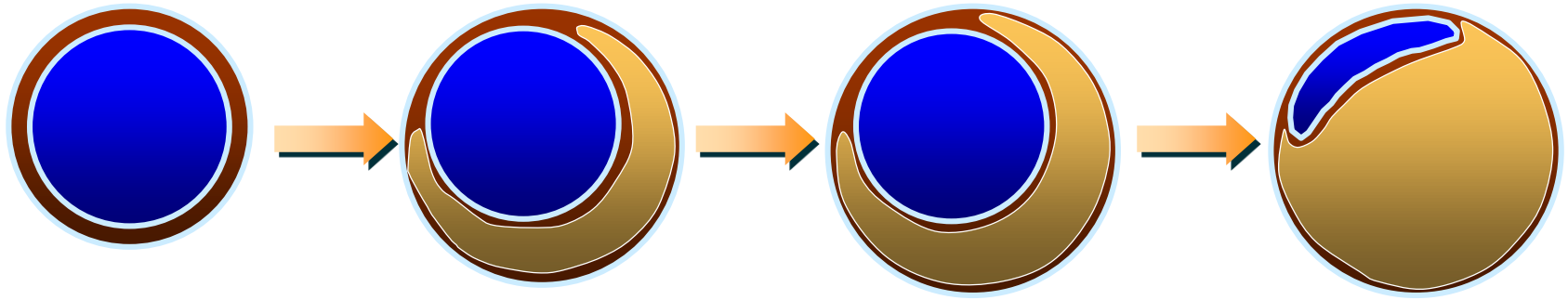
"Circulating microvesicles (cMV) are released when cells are activated"

Ongoing evaluation



Glagov S, et al. N Engl J Med. 1987;316:1371-1375.

Rumberger JA, et al. Circulation 1995; 92:2157.



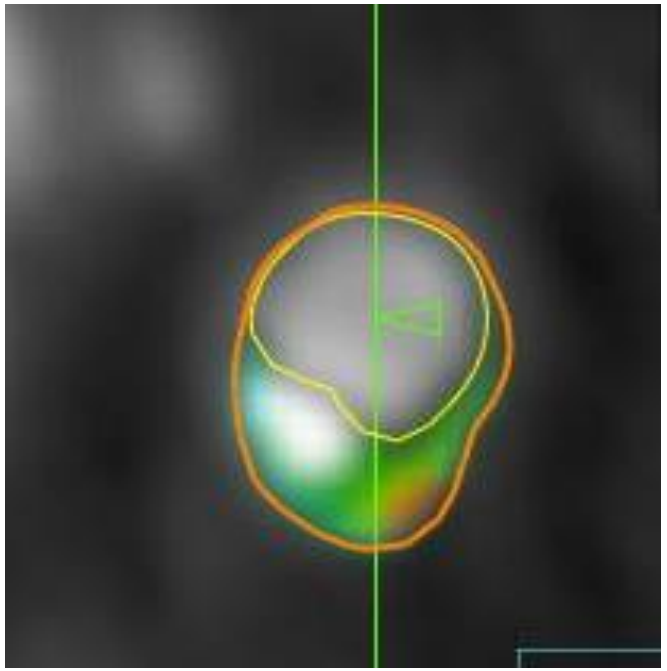
Calcio → Volumen de placa → Riesgo CV

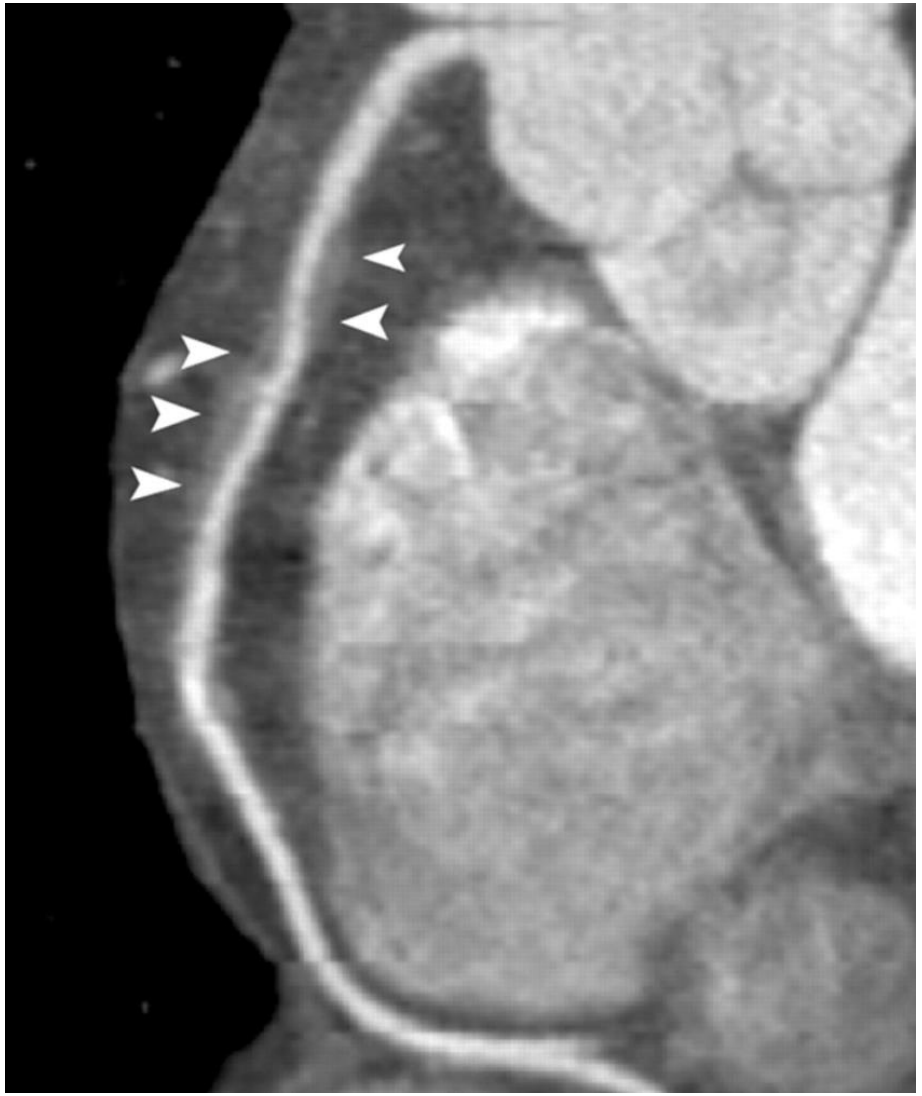
20%

Glagov S, et al. N Engl J Med. 1987;316:1371-1375.

Rumberger JA, et al. Circulation 1995; 92:2157.

MÁS ALLÁ DEL CALCIO…

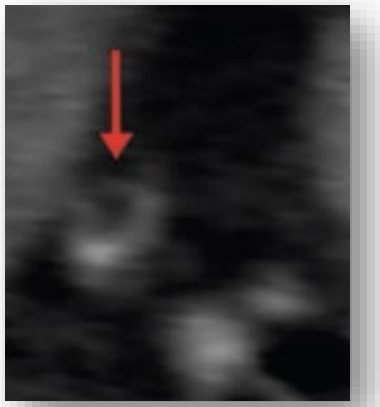




Baumgart D, Schmermund A, Goerge G, Haude M, Ge J, Adamzik M, Sehnert C, Altmaier K, Groenemeyer D, Seibel R, Erbel R J Am Coll Cardiol. 1997;30(1):57.

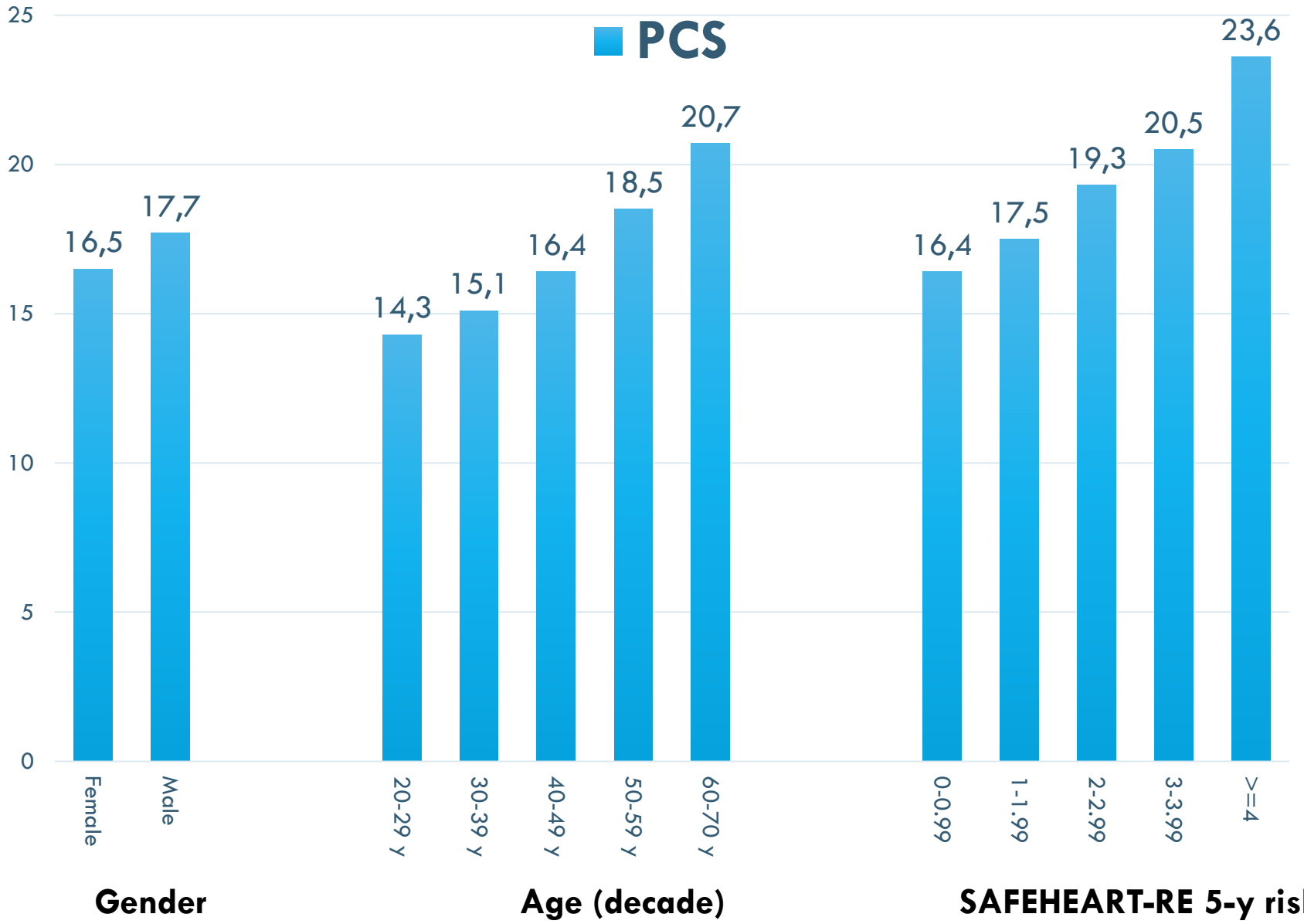
PLACA VULNERABLE

- Remodelado positivo
- Calcificación puntiforme
- Baja atenuación
- Signo del servilletero



Plaque composition sum; n = 440 FH

SAFEHEART



Pérez de Isla L, et al. On-going evaluation.

Liquid biopsy of endothelial cells, platelets, granulocytes, and neutrophils by released microvesicles map coronary calcification and atherosclerotic plaque in asymptomatic patients with familial hypercholesterolemia- A CTA imaging study.

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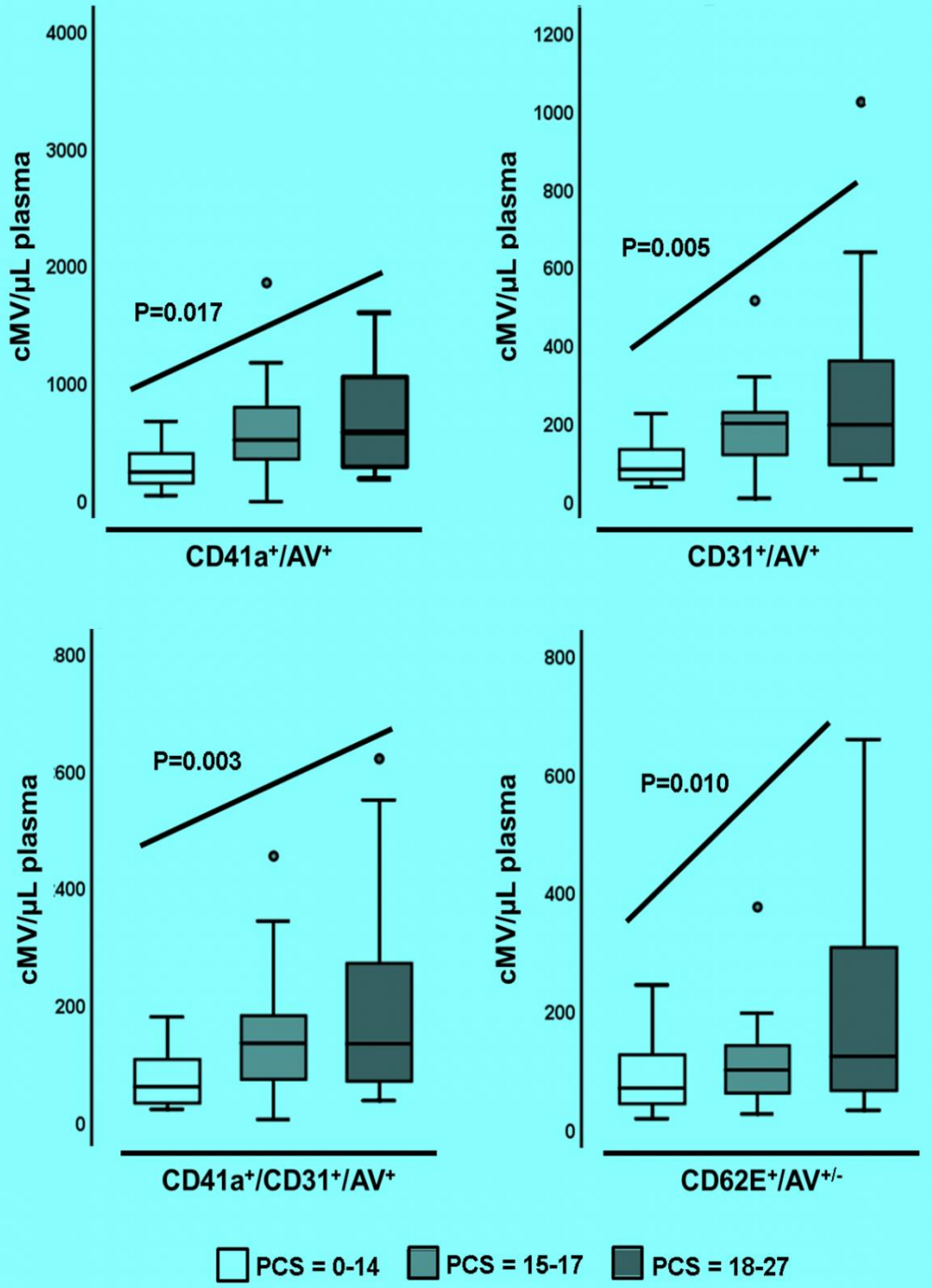
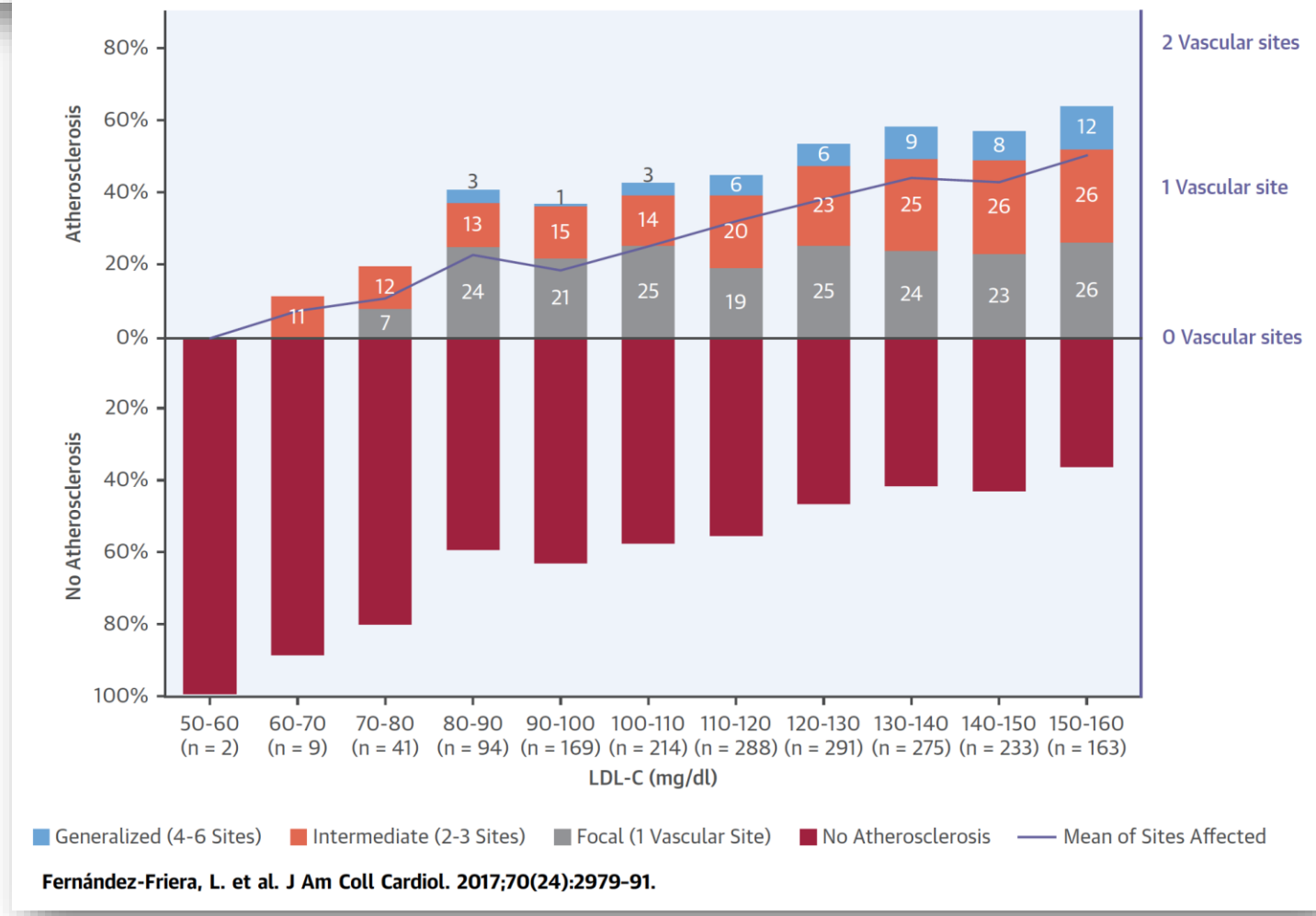
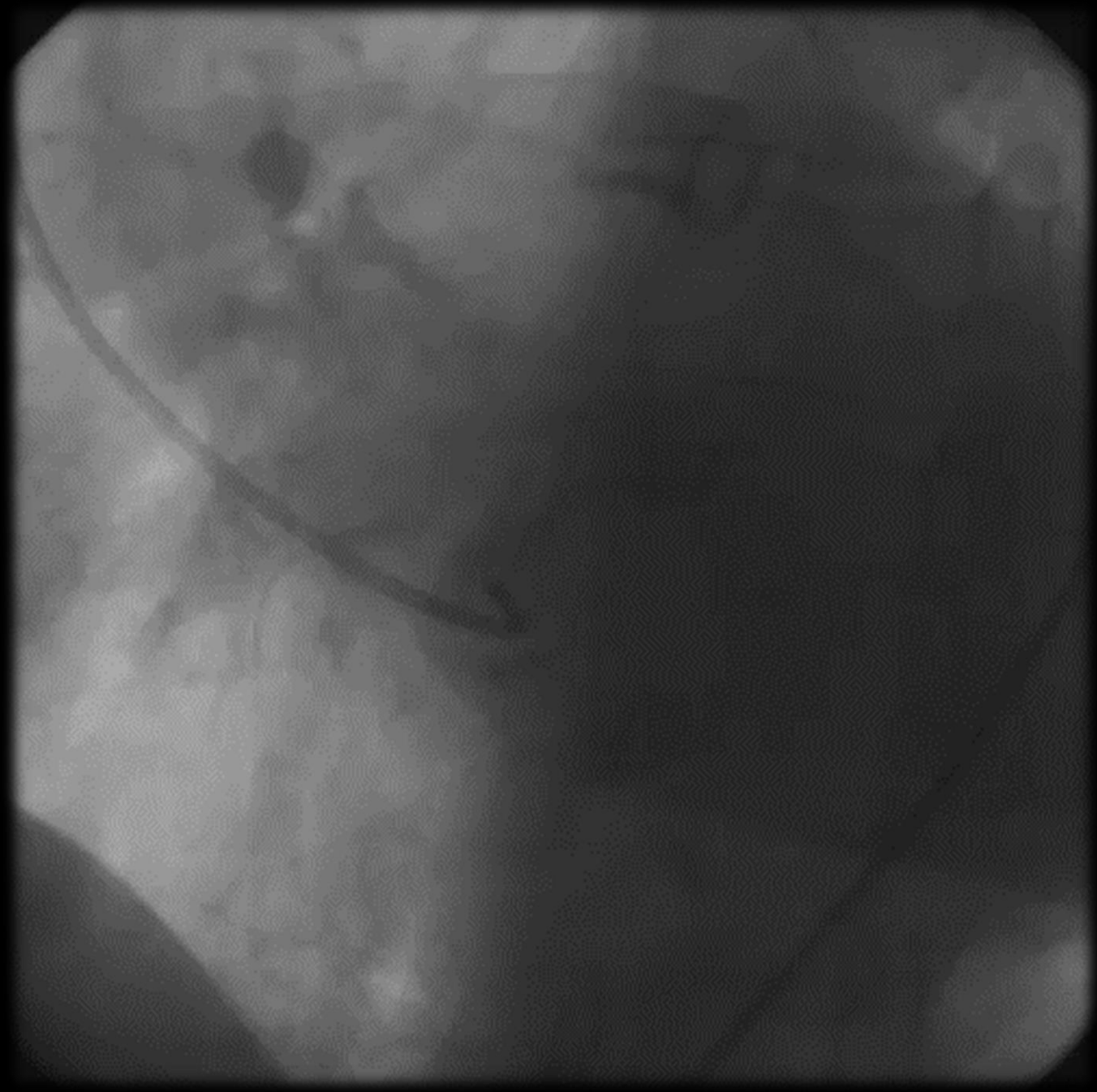


Normal LDL-Cholesterol Levels Are Associated With Subclinical Atherosclerosis in the Absence of Risk Factors

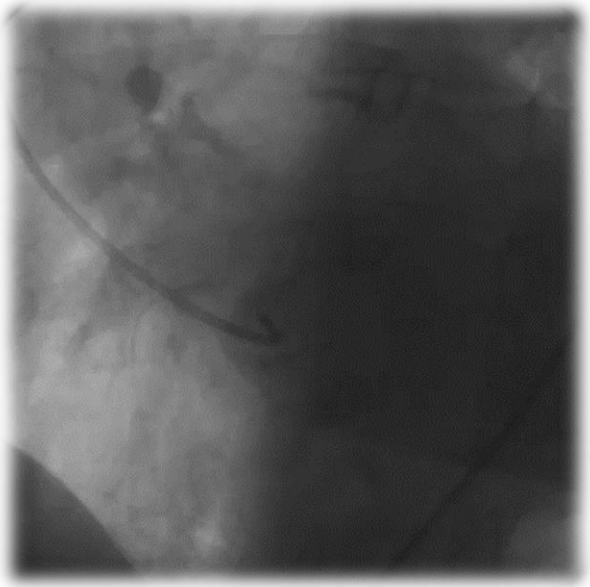
CENTRAL ILLUSTRATION **Relation Between LDL-Cholesterol Levels and Atherosclerosis**

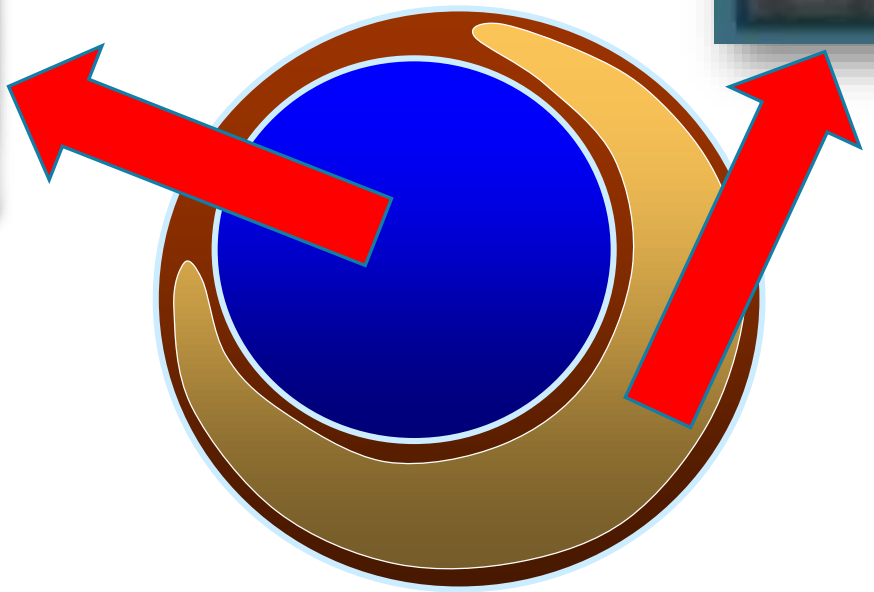


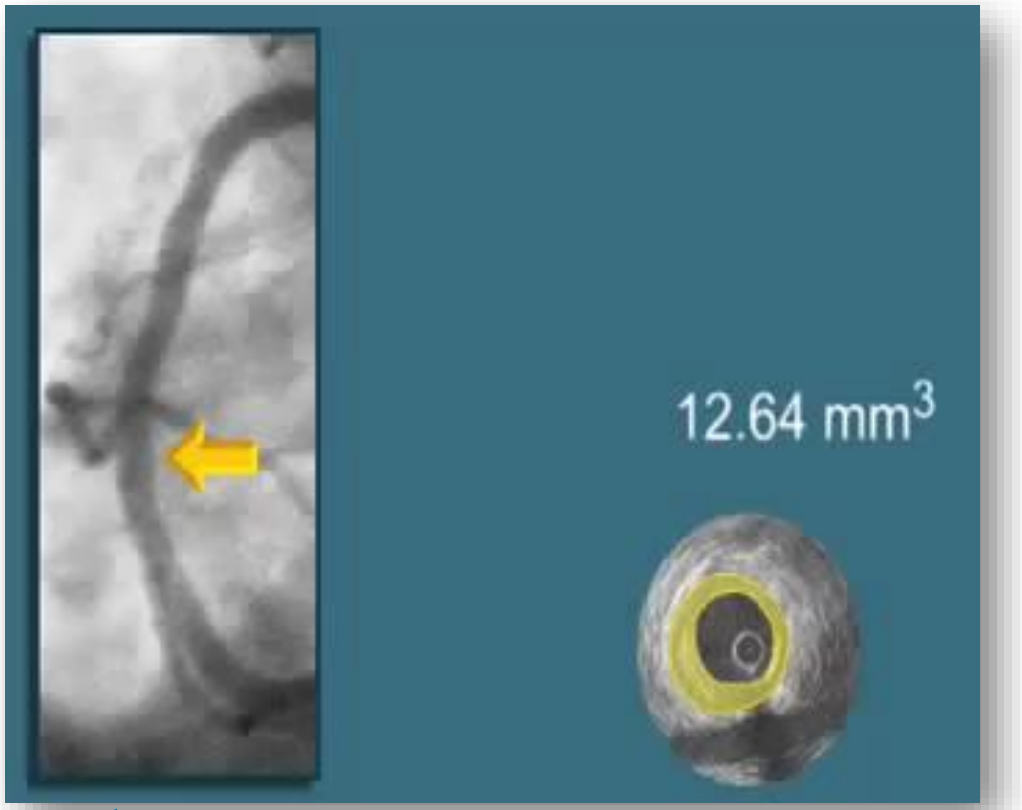
Fernández-Friera, L. et al. J Am Coll Cardiol. 2017;70(24):2979-91.

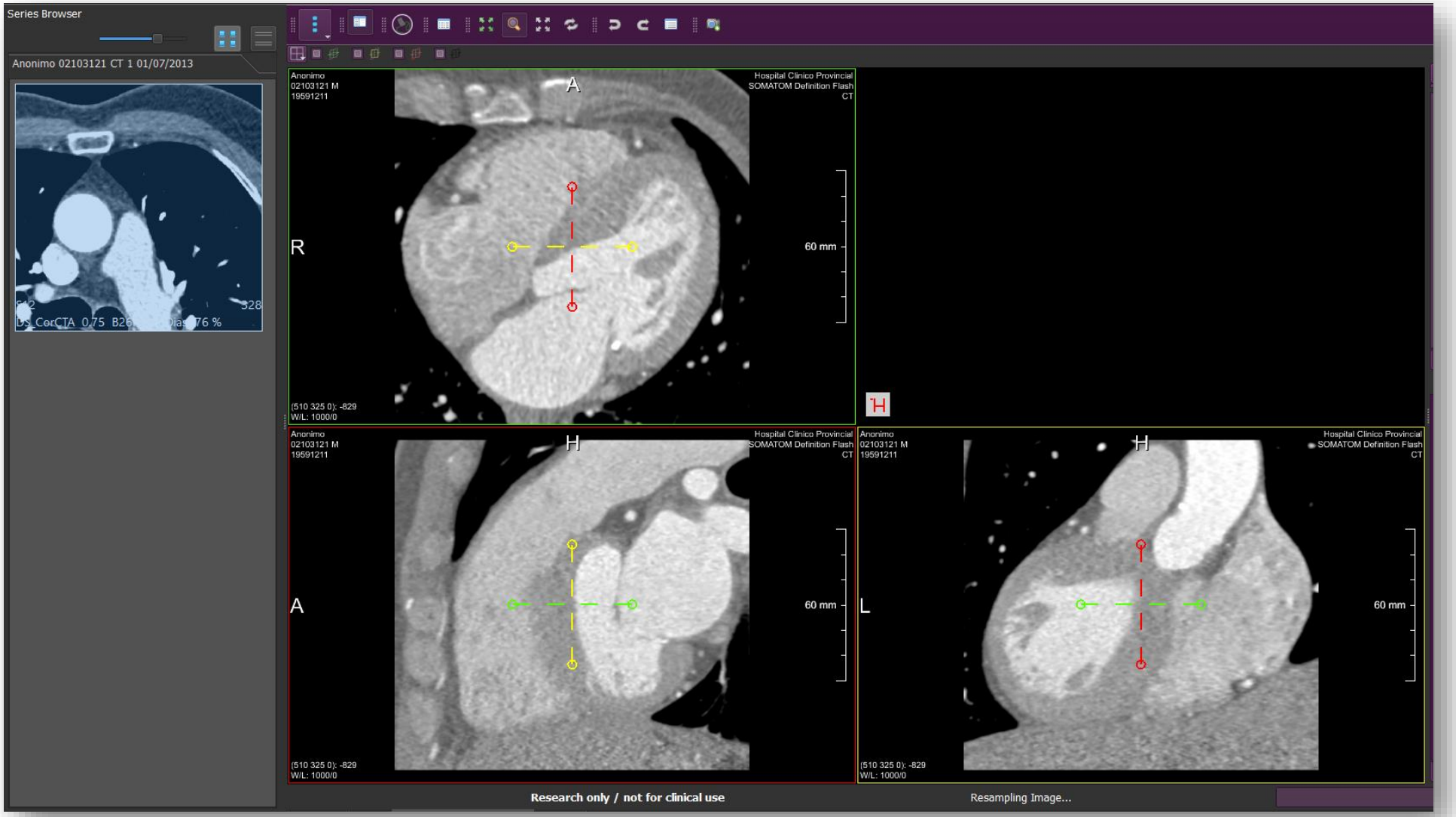


IVUS





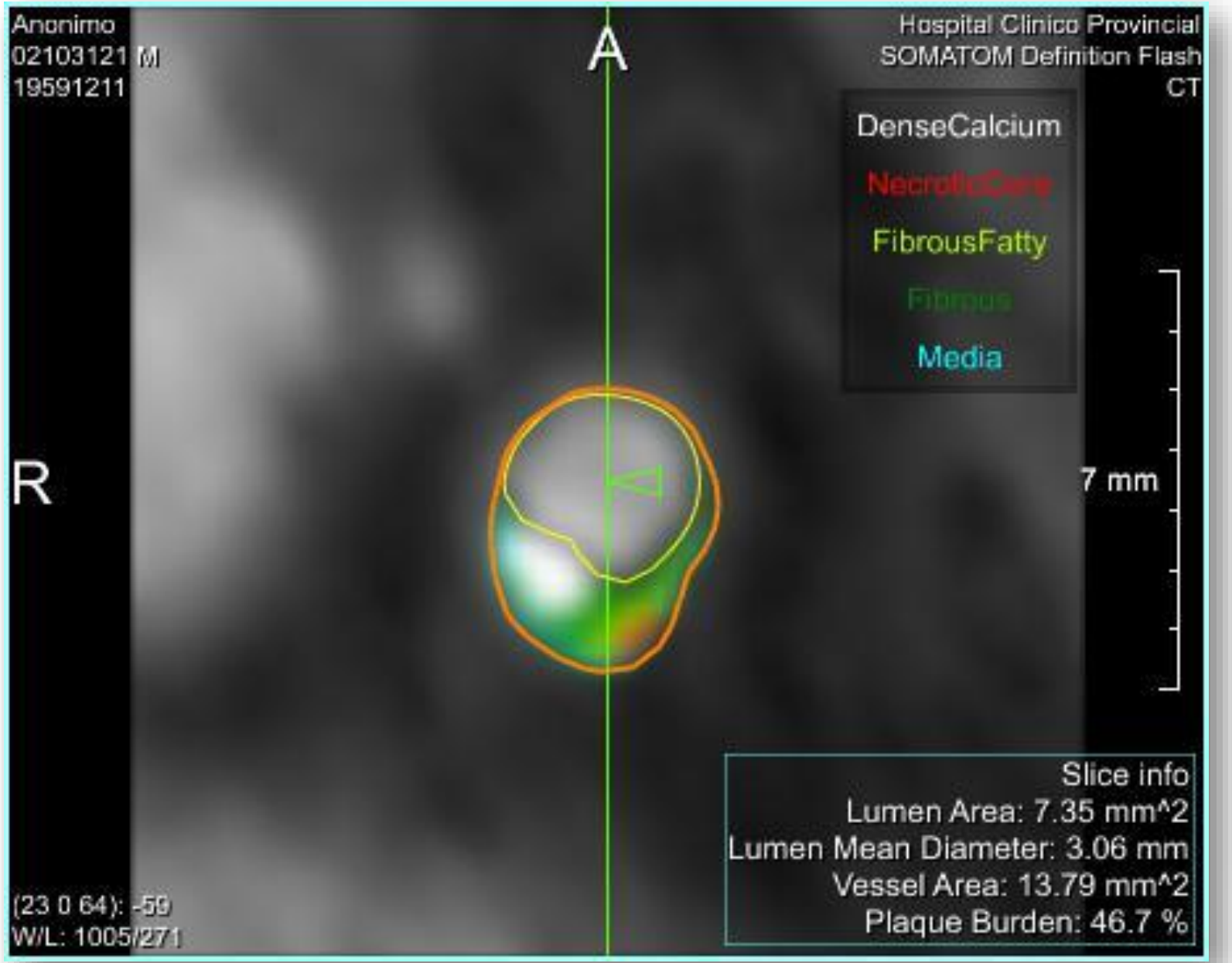


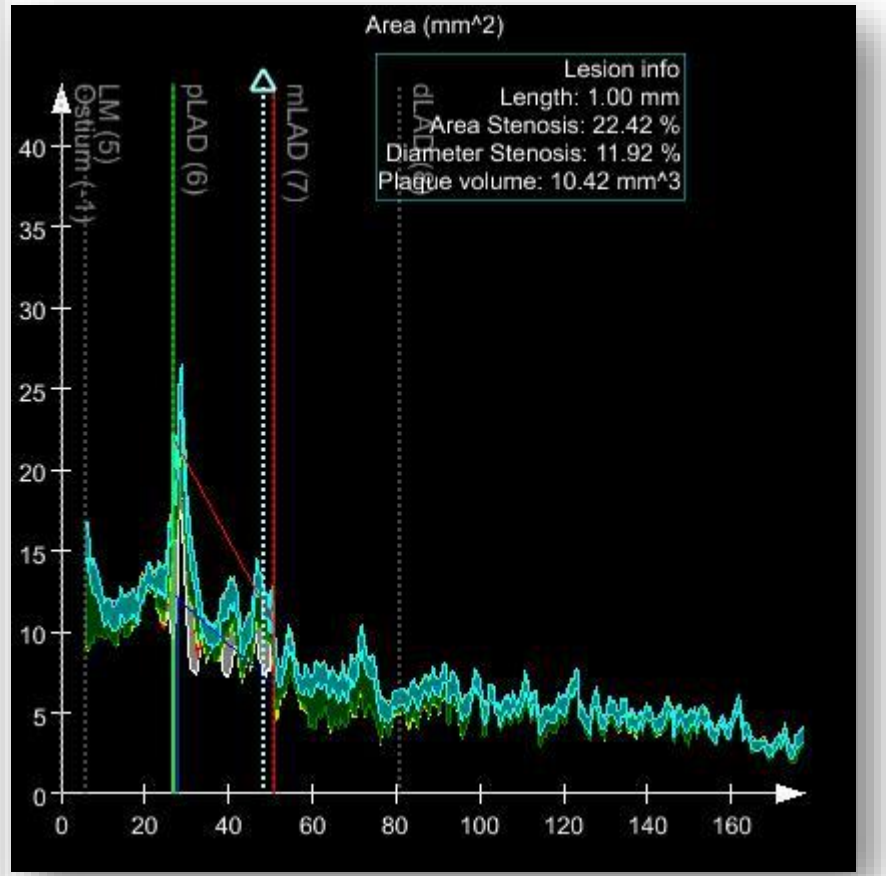


Atherosclerotic cardiovascular disease risk assessment in familial hypercholesterolemia: does one size fit all?

Mata, Pedro[a]; Alonso, Rodrigo[a,b]; Pérez de Isla, Leopoldo[a,c]

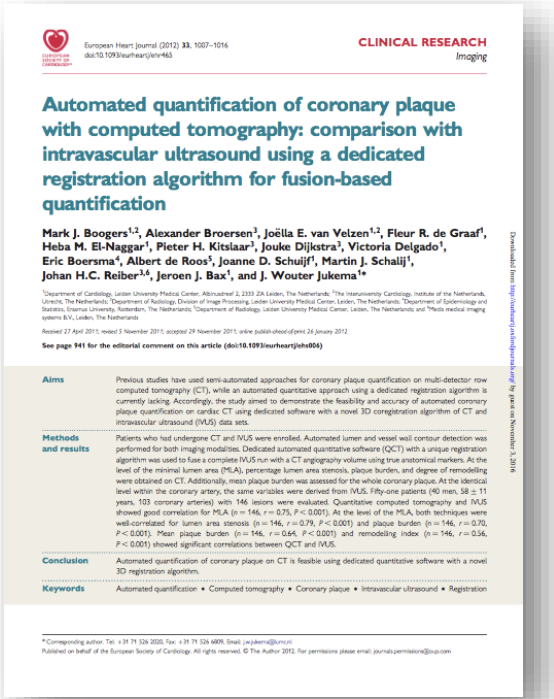
Current Opinion in Lipidology: September 18, 2018 - Volume Publish Ahead of Print - Issue - p
doi: 10.1097/MOL.0000000000000553


Anonimo
02103121 M
19591211
A
Hospital Clinico Provincial
SOMATOM Definition Flash
CT
DenseCalcium
NecroticCore
FibrousFatty
Fibrous
Media
R
7 mm
Slice info
Lumen Area: 7.35 mm^2
Lumen Mean Diameter: 3.06 mm
Vessel Area: 13.79 mm^2
Plaque Burden: 46.7 %
(23 0 64): -59
W/L: 1005/271


Area (mm^2)
LM (5)
Ostium (-1)
pLAD (6)
mLAD (7)
dLAD (8)
Lesion info
Length: 1.00 mm
Area Stenosis: 22.42 %
Diameter Stenosis: 11.92 %
Plaque volume: 10.42 mm^3
40
35
30
25
20
15
10
5
0
0
20
40
60
80
100
120
140
160

QCT

Preciso



European Heart Journal (2012) **33**, 1007–1016
doi:10.1093/eurheartj/ehr463

CLINICAL RESEARCH
Imaging

Automated quantification of coronary plaque with computed tomography: comparison with intravascular ultrasound using a dedicated registration algorithm for fusion-based quantification

Mark J. Boogers[1,2], Alexander Broersen[3], Joëlla E. van Velzen[1,2], Fleur R. de Graaf[1], Heba M. El-Naggar[1], Pieter H. Kitslaar[3], Jouke Dijkstra[3], Victoria Delgado[1], Eric Boersma[4], Albert de Roos[5], Joanne D. Schuijf[1], Martin J. Schalij[1], Johan H.C. Reiber[3,6], Jeroen J. Bax[1], and J. Wouter Jukema[1]*

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Aims Previous studies have used semi-automated approaches for coronary plaque quantification on multi-detector row computed tomography (CT), while an automated quantitative approach using a dedicated registration algorithm is currently lacking. Accordingly, the study aimed to demonstrate the feasibility and accuracy of automated coronary plaque quantification on cardiac CT using dedicated software with a novel 3D coregistration algorithm of CT and intravascular ultrasound (IVUS) data sets.

Methods and results Patients who had undergone CT and IVUS were enrolled. Automated lumen and vessel wall contour detection was performed for both imaging modalities. Dedicated automated quantitative software (QCT) with a unique registration algorithm was used to fuse a complete IVUS run with a CT angiography volume using true anatomical markers. At the level of the minimal lumen area (MLA), percentage lumen area stenosis, plaque burden, and degree of remodelling were obtained on CT. Additionally, mean plaque burden was assessed for the whole coronary plaque. At the identical level within the coronary artery, the same variables were derived from IVUS. Fifty-one patients (40 men, 58 ± 11 years, 103 coronary arteries) with 146 lesions were evaluated. Quantitative computed tomography and IVUS showed good correlation for MLA ($n = 146$, $r = 0.75$, $P < 0.001$). At the level of the MLA, both techniques were well-correlated for lumen area stenosis ($n = 146$, $r = 0.79$, $P < 0.001$) and plaque burden ($n = 146$, $r = 0.70$, $P < 0.001$). Mean plaque burden ($n = 146$, $r = 0.64$, $P < 0.001$) and remodelling index ($n = 146$, $r = 0.56$, $P < 0.001$) showed significant correlations between QCT and IVUS.

Conclusion Automated quantification of coronary plaque on CT is feasible using dedicated quantitative software with a novel 3D registration algorithm.

Keywords Automated quantification • Computed tomography • Coronary plaque • Intravascular ultrasound • Registration

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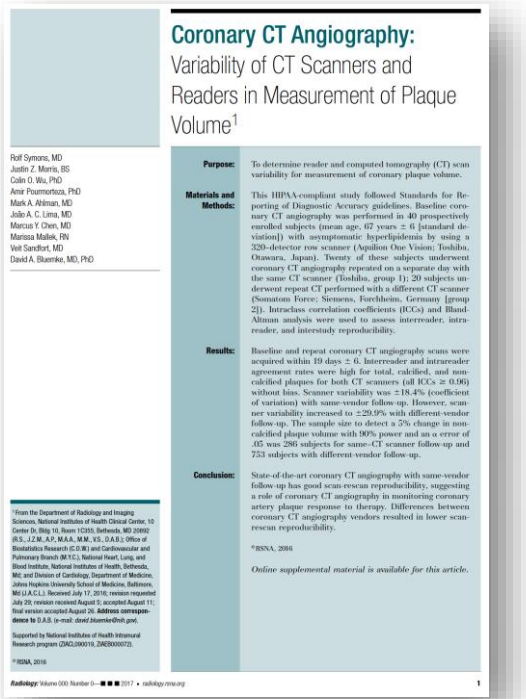
Reproducible



Coronary CT Angiography: Variability of CT Scanners and Readers in Measurement of Plaque Volume[1]

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Purpose: To determine reader and computed tomography (CT) scan variability for measurement of coronary plaque volume.

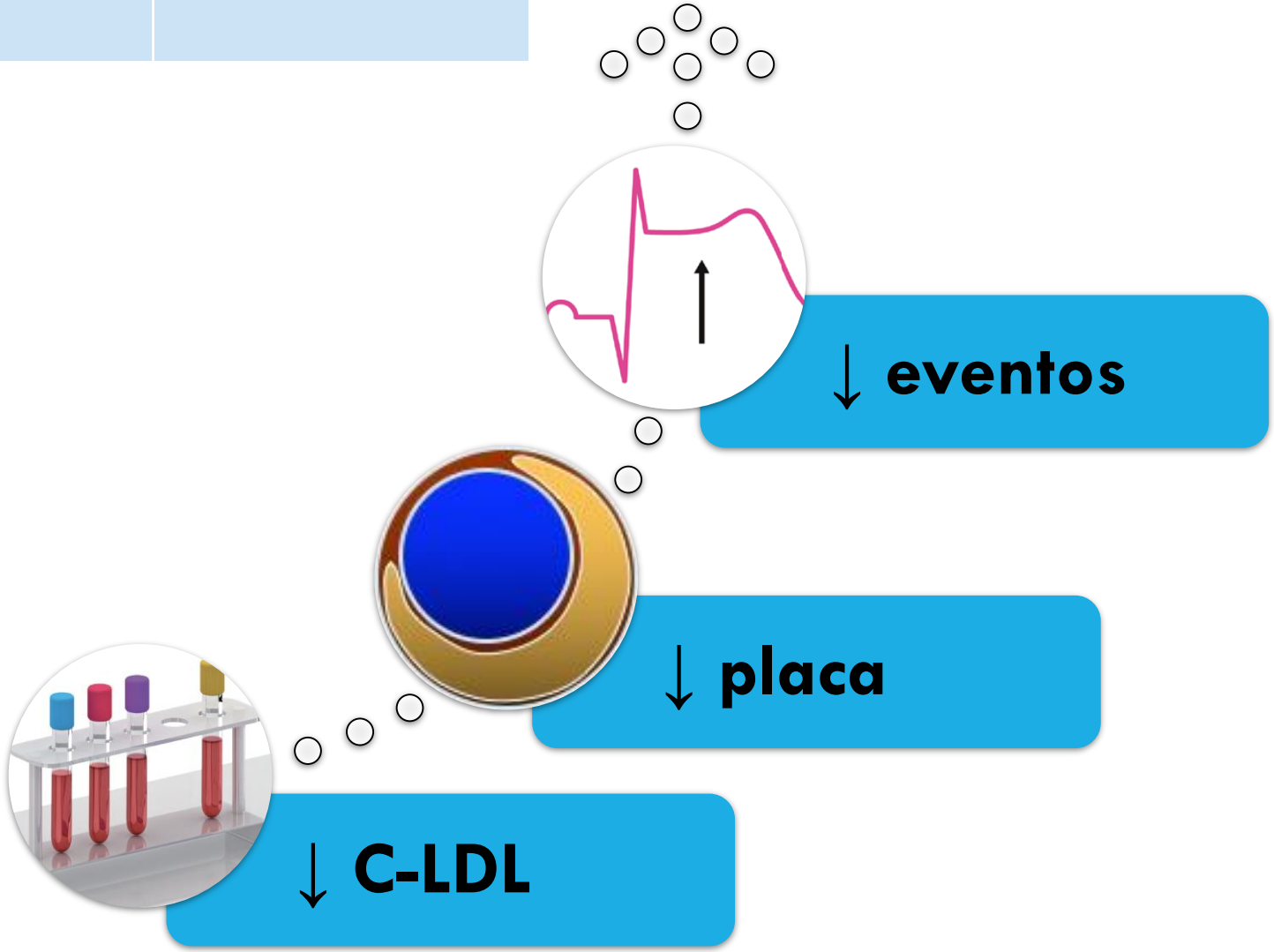
Materials and Methods: This HIPAA-compliant study followed Standards for Reporting of Diagnostic Accuracy guidelines. Baseline coronary CT angiography was performed in 40 prospectively enrolled subjects (mean age, 62 years ± 6 [standard deviation]) with asymptomatic hyperlipidemia by using a 320-detector row scanner (Aquilion One Vision; Toshiba, Otawara, Japan). Twenty of these subjects underwent coronary CT angiography repeated on a separate day with the same CT scanner (Toshiba, group 1); 20 subjects underwent repeat CT performed with a different CT scanner (Somatom Force; Siemens, Forchheim, Germany [group 2]). Intraclass correlation coefficients (ICCs) and Bland-Altman analysis were used to assess interreader, intrareader, and interstudy reproducibility.

Results: Baseline and repeat coronary CT angiography scans were acquired within 19 days ± 6. Interreader and intrareader agreement rates were high for total, calcified, and noncalcified plaques for both CT scanners (all ICCs ≥ 0.96) without bias. Scanner variability was ±18.4% (coefficient of variation) with same-vendor follow-up. However, scanner variability increased to ±29.9% with different-vendor follow-up. The sample size to detect a 5% change in noncalcified plaque volume with 90% power and an α error of .05 was 286 subjects for same–CT scanner follow-up and 753 subjects with different-vendor follow-up.

Conclusion: State-of-the-art coronary CT angiography with same-vendor follow-up has good scan-rescan reproducibility, suggesting a role of coronary CT angiography in monitoring coronary artery plaque response to therapy. Differences between coronary CT angiography vendors resulted in lower scan-rescan reproducibility.

Online supplemental material is available for this article.

Estatinas	Inh. Absorción	iPCSK9
• Atorvastatina • Rosuvastatina • Pitavastatina	• Ezetimibe	• Evolocumab



A QUIÉN

EACVI 2011 POSITION STATEMENT

- Score calcio debe ser considerado en pacientes de riesgo intermedio seleccionados
- Puede reclasificar a alto riesgo y modificar su tratamiento (Recomendación IIa).

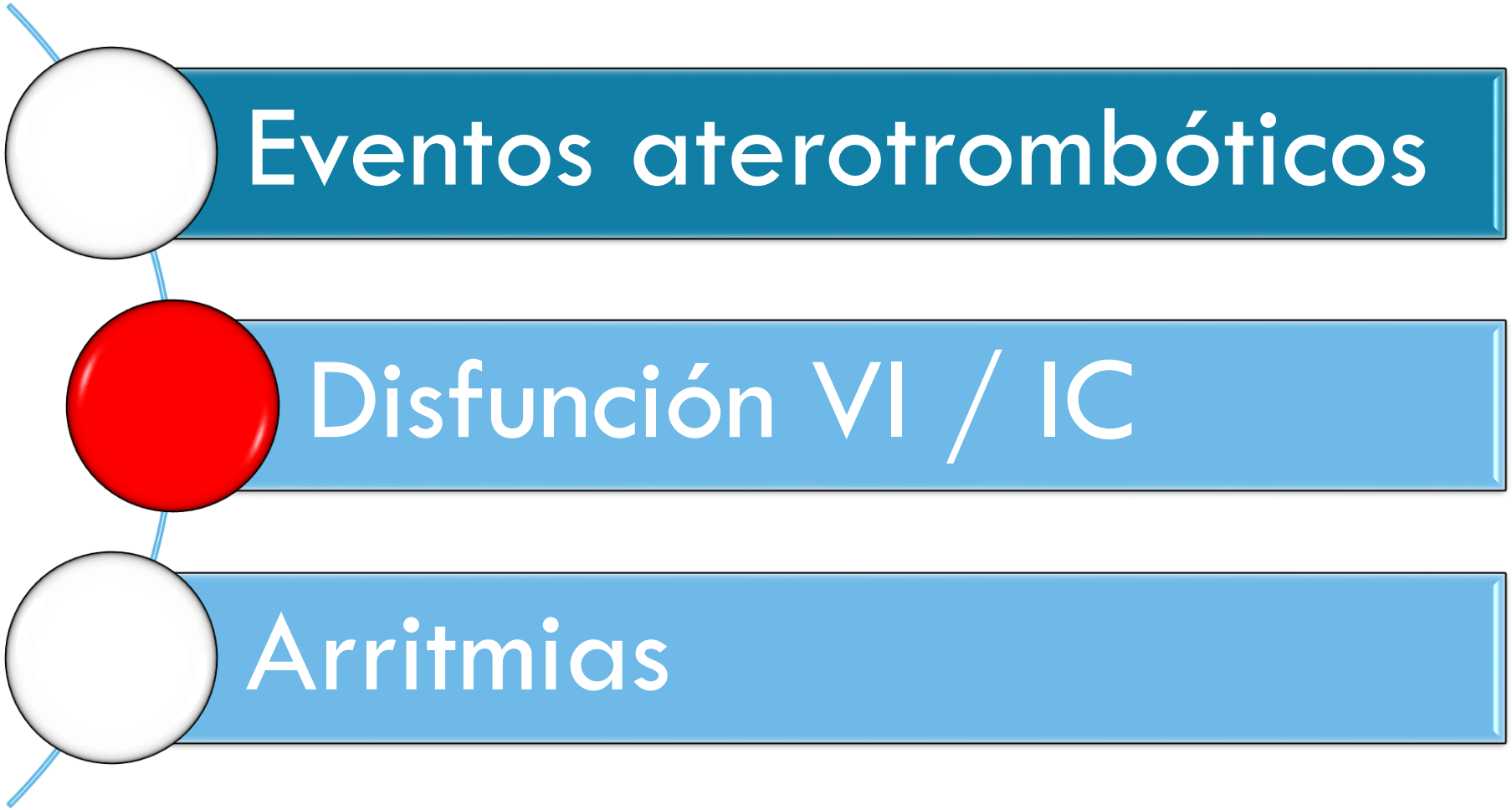
Top 10 Take Home Messages

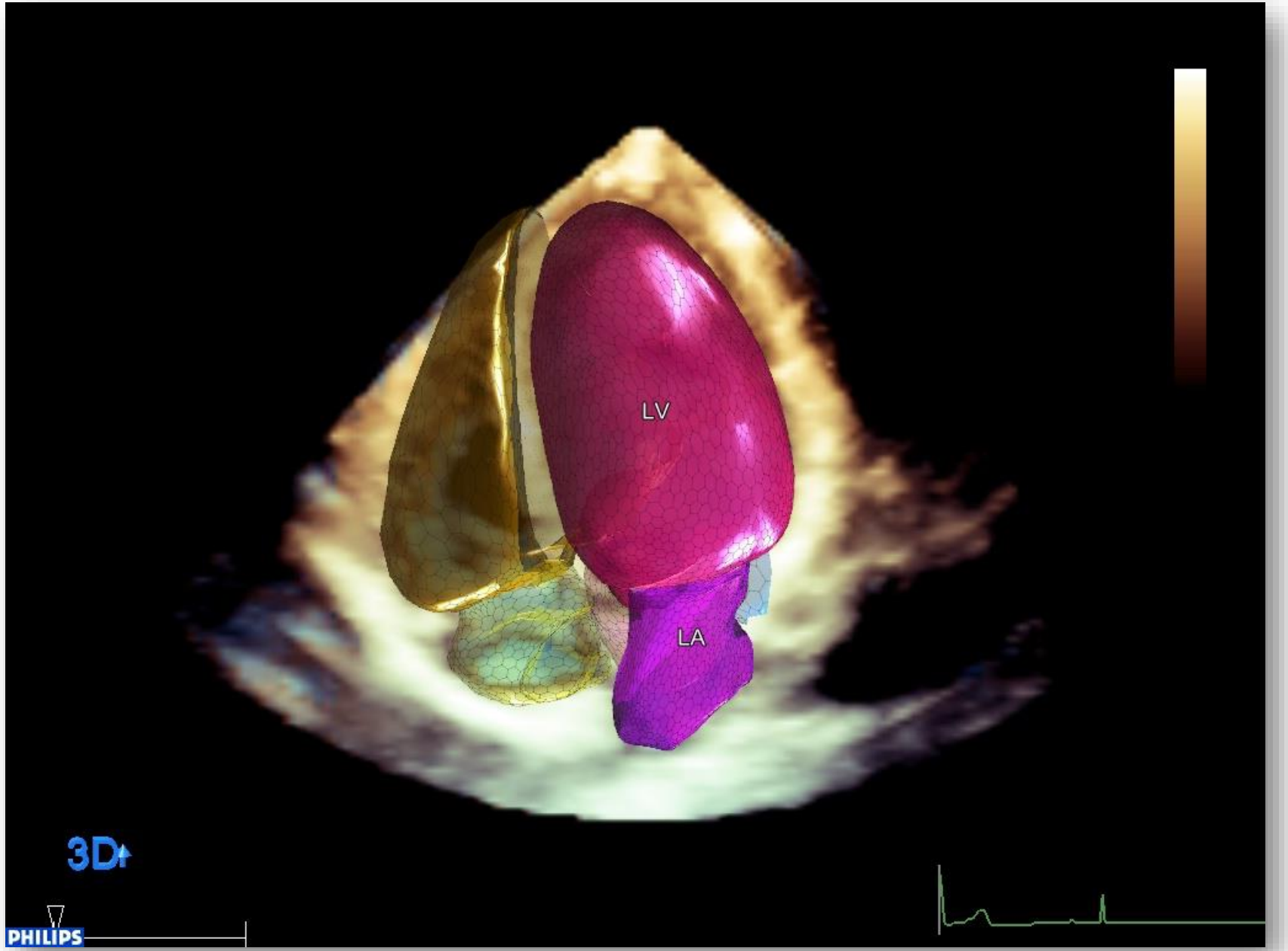
7. **In adults 40 to 75 years of age without diabetes mellitus and with LDL-C levels ≥70 mg/dL (≥1.8 mmol/L), at a 10-year ASCVD risk of ≥7.5%, start a moderate-intensity statin if a discussion of treatment options favors statin therapy.**

   Risk-enhancing factors favor statin therapy (see No. 8).

   If risk status is uncertain, consider using coronary artery calcium (CAC) to improve specificity (see No. 9). If statins are indicated, reduce LDL-C levels by ≥30%, and if 10-year risk is ≥20%, reduce LDL-C levels by ≥50%.

RIESGO




LV
LA
3D
PHILIPS

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ORIGINAL RESEARCH

Inotropic Contractile Reserve Can Risk-Stratify Patients With HIV Cardiomyopathy

A Dobutamine Stress Echocardiography Study

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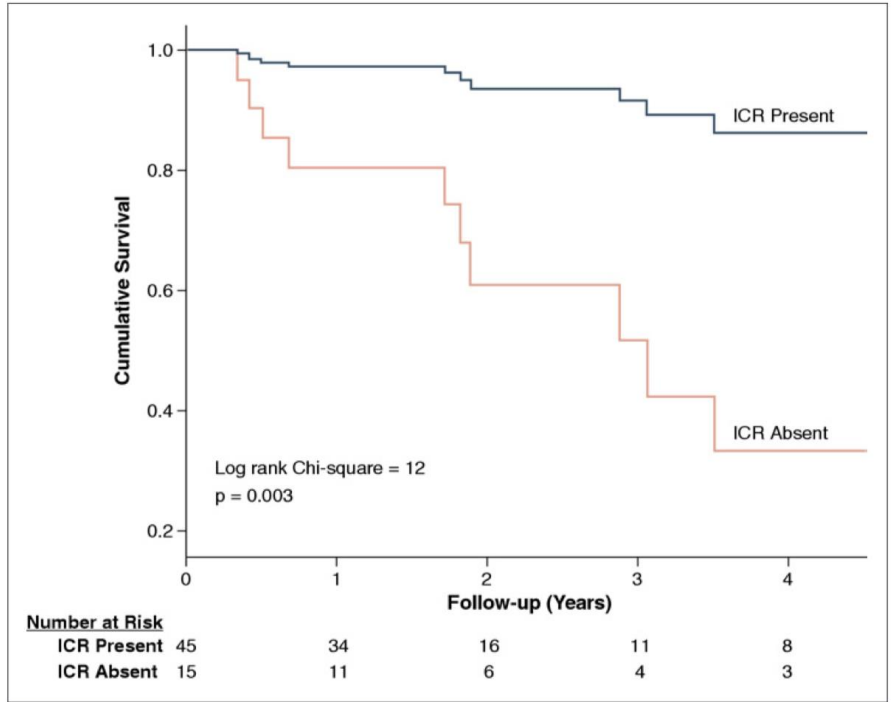


Figure 1. Cumulative Survival as a Function of the Presence of ICR

Inotropic contractile reserve (ICR) risk-stratified patients with human immunodeficiency virus cardiomyopathy into high-risk and low-risk groups. The number of patients at risk for each follow-up period is given **below the graph**.

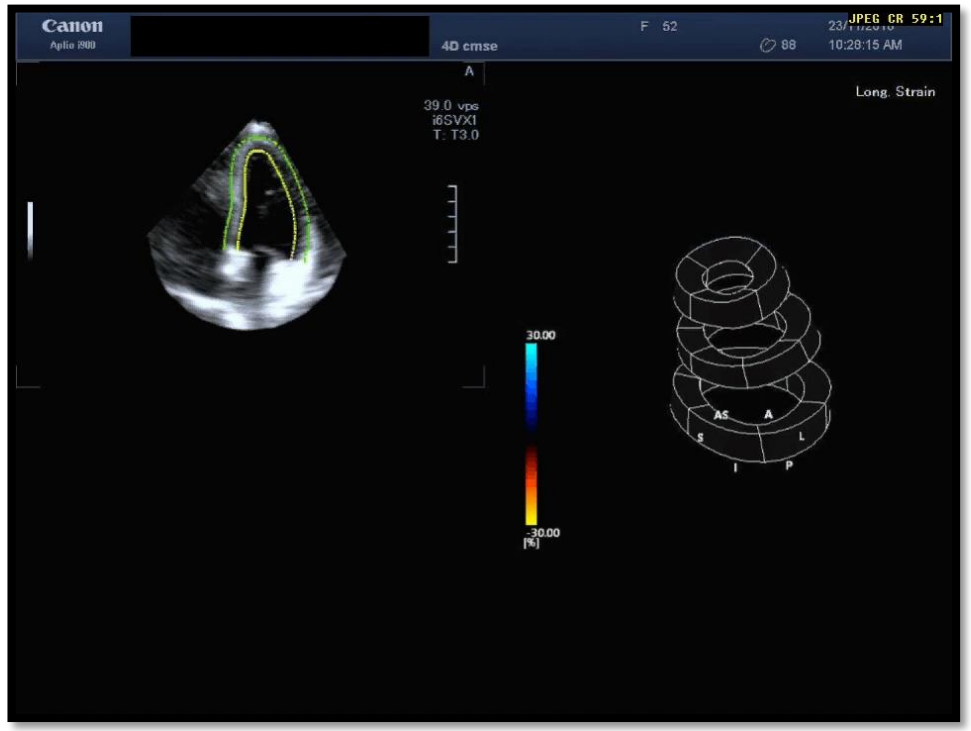
CONCLUSIONS The presence of ICR during DSE can risk-stratify and predict subsequent improvement in LVEF in patients with HIV cardiomyopathy. (J Am Coll Cardiol Img 2011;4:1231–8)

CARDIOTOXICIDAD
STRAIN LONGITUDINAL GLOBAL DEL VI (SLGVI)

Mejor parámetro para detección precoz de disfunción subclínica del VI

Reducción de SLGVI respecto al basal:

- < 8% sin importancia
- >15% alta probabilidad de alteración



SLGVI

Detección más precoz daño miocárdico

Mejora estratificación riesgo disfunción VI

Menos variabilidad que FEVI:

- Intraobservador < 4%
- Interobservador < 6%

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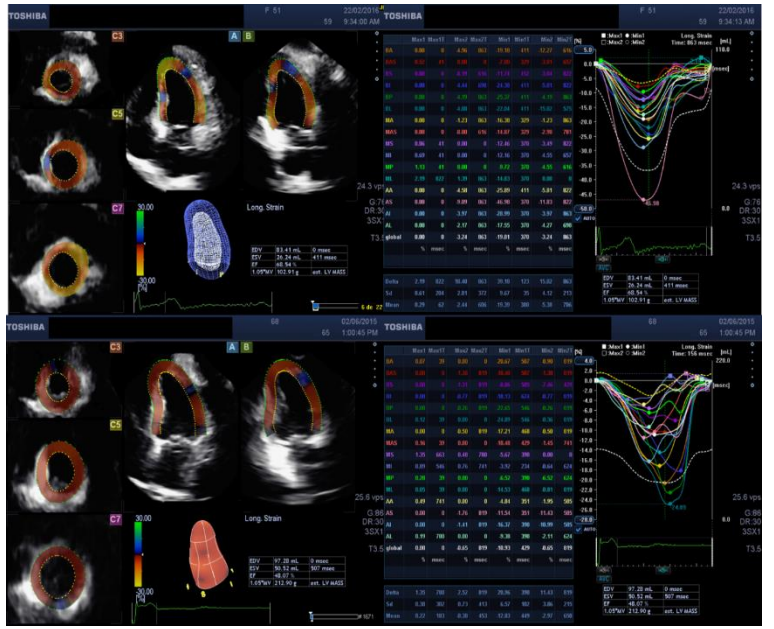
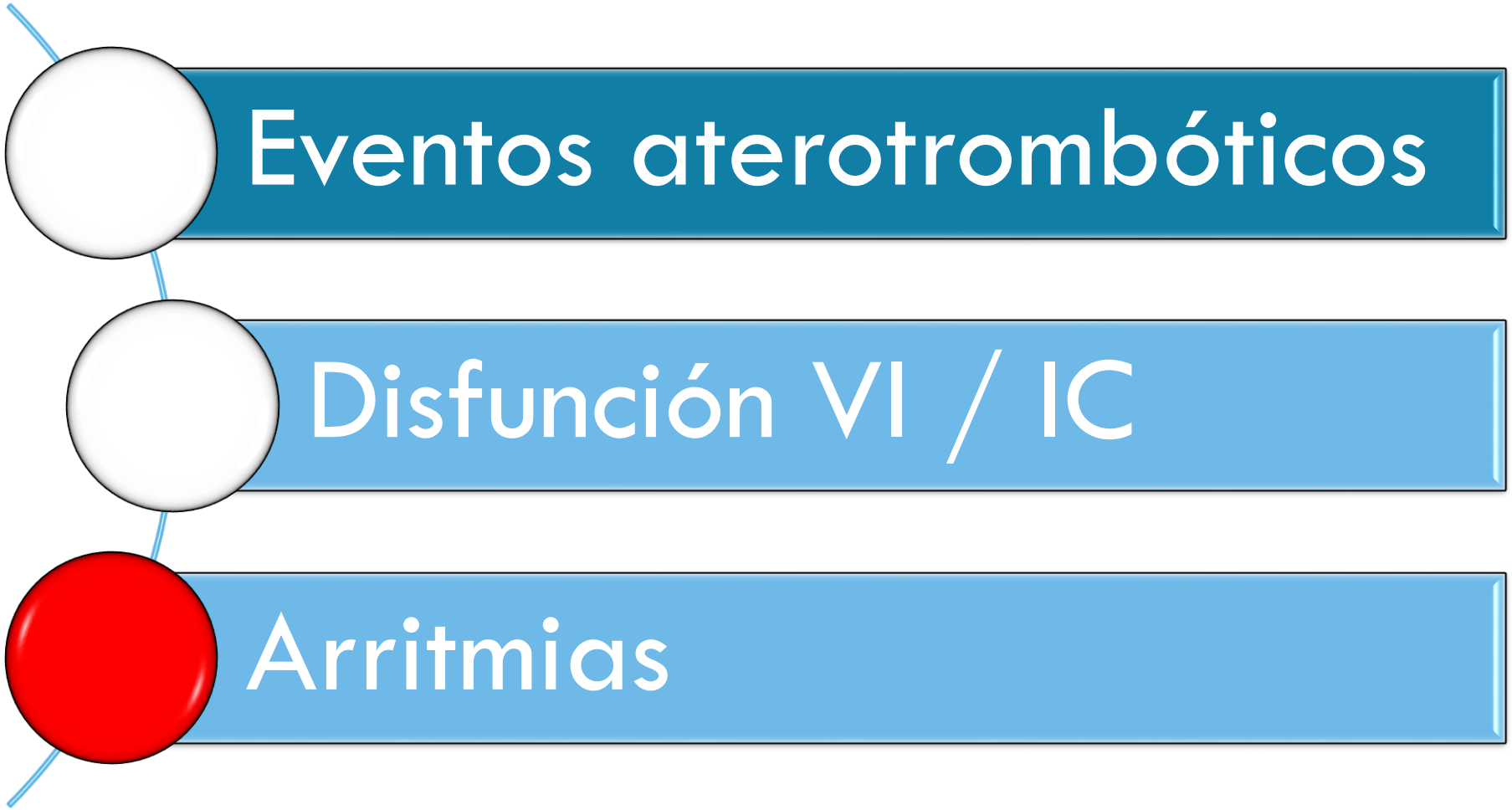
LESOD



	HIV (+) Mean (SD) / n (%)	HIV (-) Mean (SD) / n (%)	p
Indexed LVM (g/m2)	105.64 (17.87)	100.27 (23.64)	0.19
RWT	0.49 (0.09)	0.48 (0.07)	0.59
LVEF (%)	65.91 (5.17)	65.78 (4.87)	0.90
LVGLS (%)	**-14.70 (3.61)**	**-16.43 (2.91)**	**0.02**
TAPSE (mm)	**21.69 (3.03)**	**25.12 (3.22)**	**<0.001**
PASP (mm Hg)	26.11 (4.7)	24.28 (5.28)	0.24
Mitral E wave peak velocity / E´	7.19 (1.81)	7.36 (1.41)	0.60
LAVI (ml/ m2)	24.31 (6.12)	25.41 (6.86)	0.39
LAEF (%)	46.42 (12.63)	45.66 (11.61)	0.78
LAGLS (%)	24.12 (7.91)	24.37 (7.81)	0.88

Islas F et al. On going evaluation

RIESGO



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Prognostic Value of LGE-CMR in HCM

A Meta-Analysis

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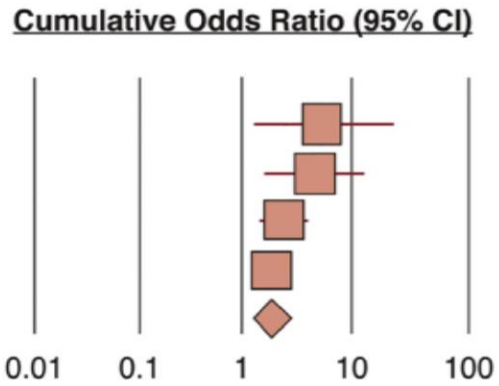
FIGURE 5 Cumulative Analysis of All-Cause Mortality

Study Name	Cumulative Statistics			
	Point	Lower Limit	Upper Limit	p-Value
Bruder et al (2010)	5.469	1.242	24.083	0.025
Rubinshtein et al (2010)	4.464	1.532	13.006	0.006
Chan et al (2014)	2.379	1.395	4.058	0.001
Ismail et al (2014)	1.803	1.208	2.689	0.004
Pooled	1.803	1.208	2.689	0.004



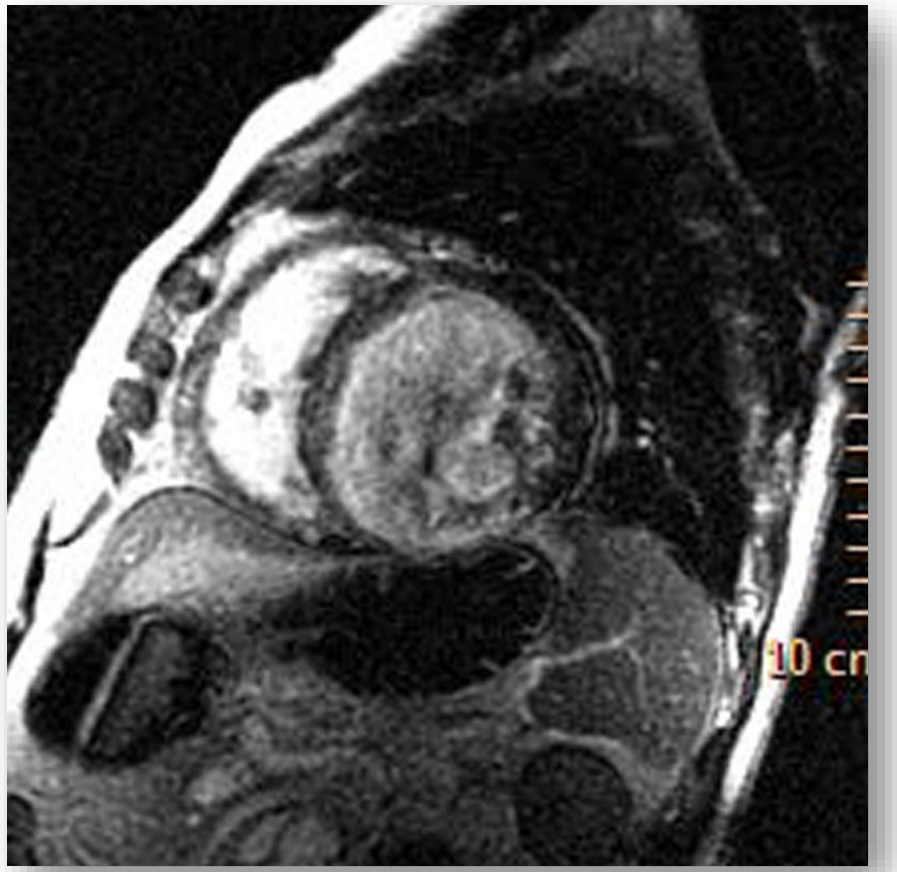
CONCLUSIONS Quantitative LGE by CMR exhibited a substantial prognostic value in SCD events prediction, independent of baseline characteristics. Assessment of LGE can be used as an effective tool for risk stratifying patients with HCM. (J Am Coll Cardiol Img 2016;■:■-■) © 2016 by the American College of Cardiology Foundation.

MÁS ALLÁ DE LA FEVI

Realce tardío

Predictor de arritmias ventriculares en:

- **Miocardiopatía isquémica**
- **Miocardiopatía no isquémica**



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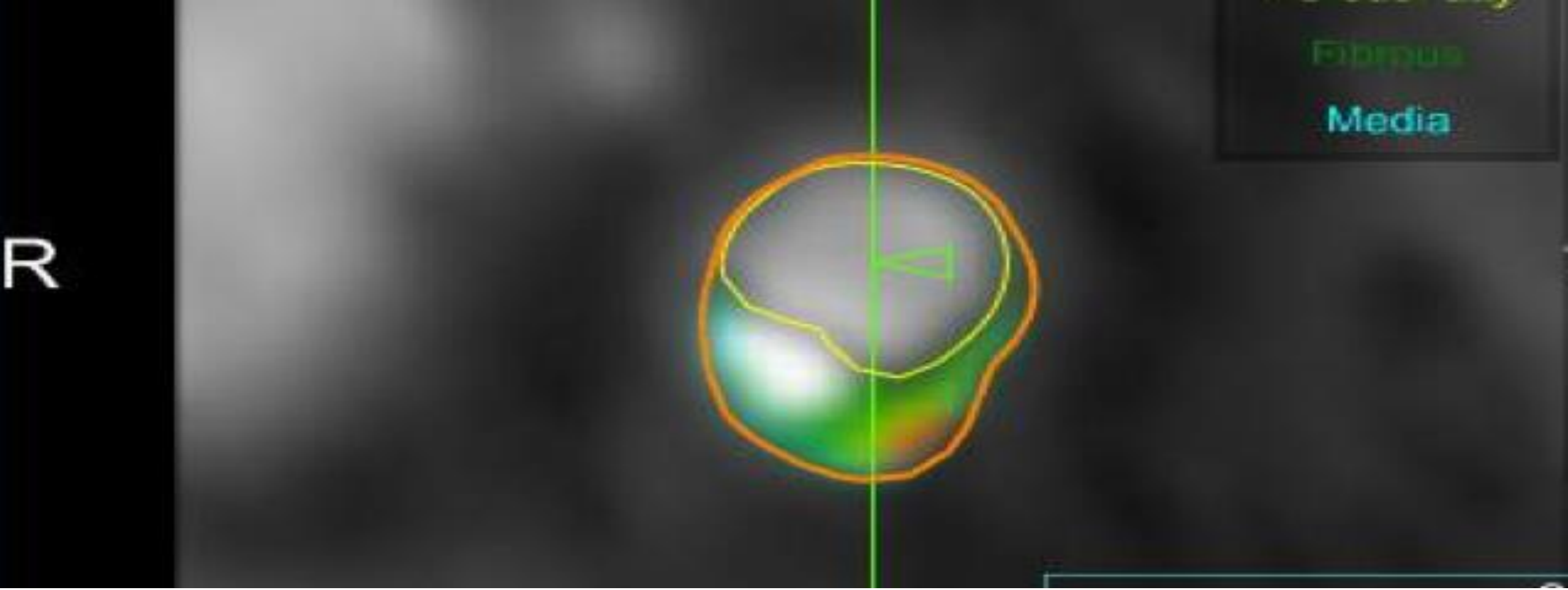

CONCLUSIONES

Gracias!