PAPEL DE LAS ESTATINAS EN EL TRATAMIENTO INTERVENCIONISTA DE LOS SINDROMES CORONARIOS AGUDOS

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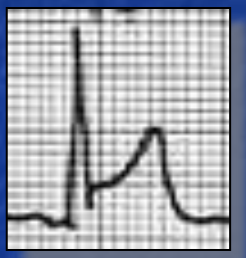
Centro Medico Docente La Trinidad

SOVECI

2013

IMEST anterolateral con 4 horas de evolucion y tiempo de puerta balon de 40 minutos

IM CON elevación ST



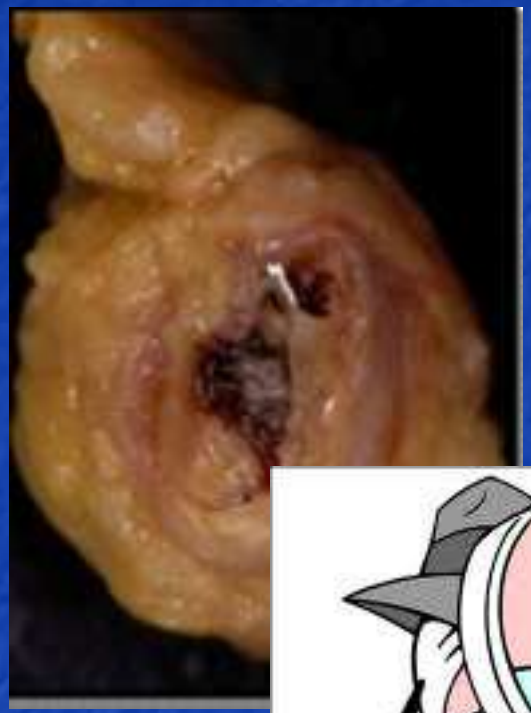
“Abrir la arteria”

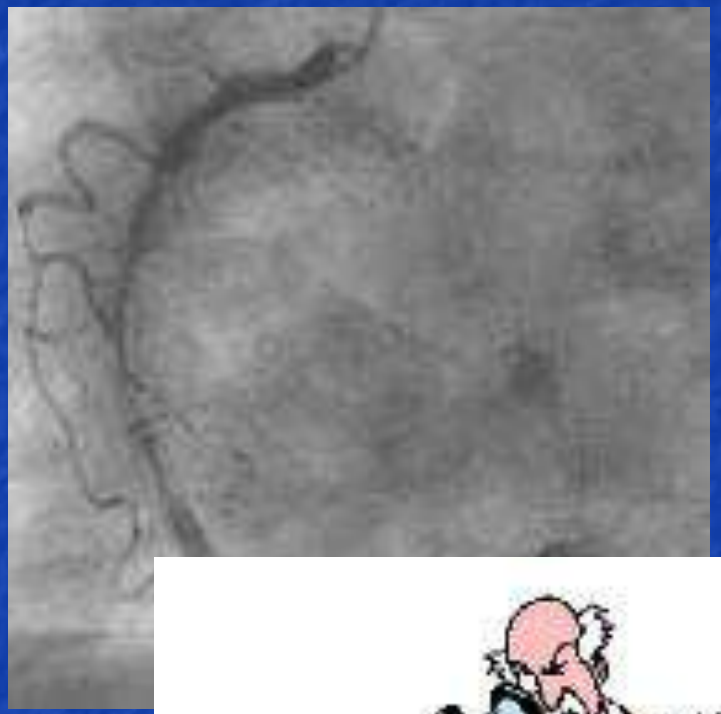
Para ver esta película, debe disponer de QuickTime™ y de un descompresor .

Para ver esta película, debe disponer de QuickTime™ y de un descompresor .

1. Reperfusión farmacológica
2. Reperfusión mecánica

OPTIMIZANDO EL TRATAMIENTO EN LOS SCA





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STATE-OF-THE-PAPERS

Pathogenesis of Acute Coronary Syndromes

Filippo Crea, MD, Giovanna Liuzzo, MD, PHD

Rome, Italy

Experimental models of atherogenesis have provided a growing body of information about molecular mechanisms of plaque growth; however, transition from coronary stability to instability is less well understood due to the lack of animal models reflective of human disease. The abrupt clinical presentation of acute coronary syndromes gives a strong signal of discontinuity in the natural history of atherothrombosis. The causes of such discontinuity are complex, probably multiple, and still largely unknown. A better knowledge of the causes of coronary instability might allow identification of new therapeutic targets aimed at the preservation of plaque stability in those subjects in whom primary prevention fails to prevent plaque growth. The goal of this review was to propose a pathogenetic classification of acute coronary syndromes that might help in the search of new diagnostic algorithms and therapeutic targets. (J Am Coll Cardiol 2013;61:1–11) © 2013 by the American College of Cardiology Foundation

Crea F.JACC. 2013. 61; 1 : 1-11.

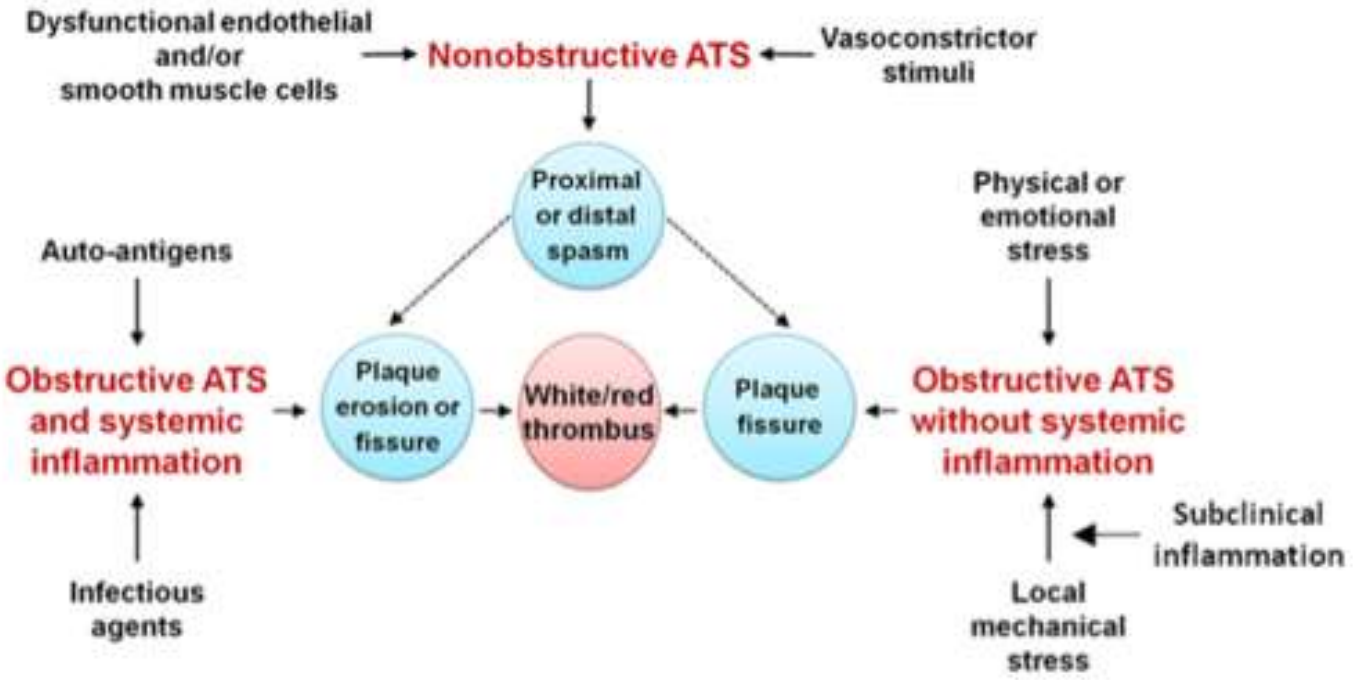
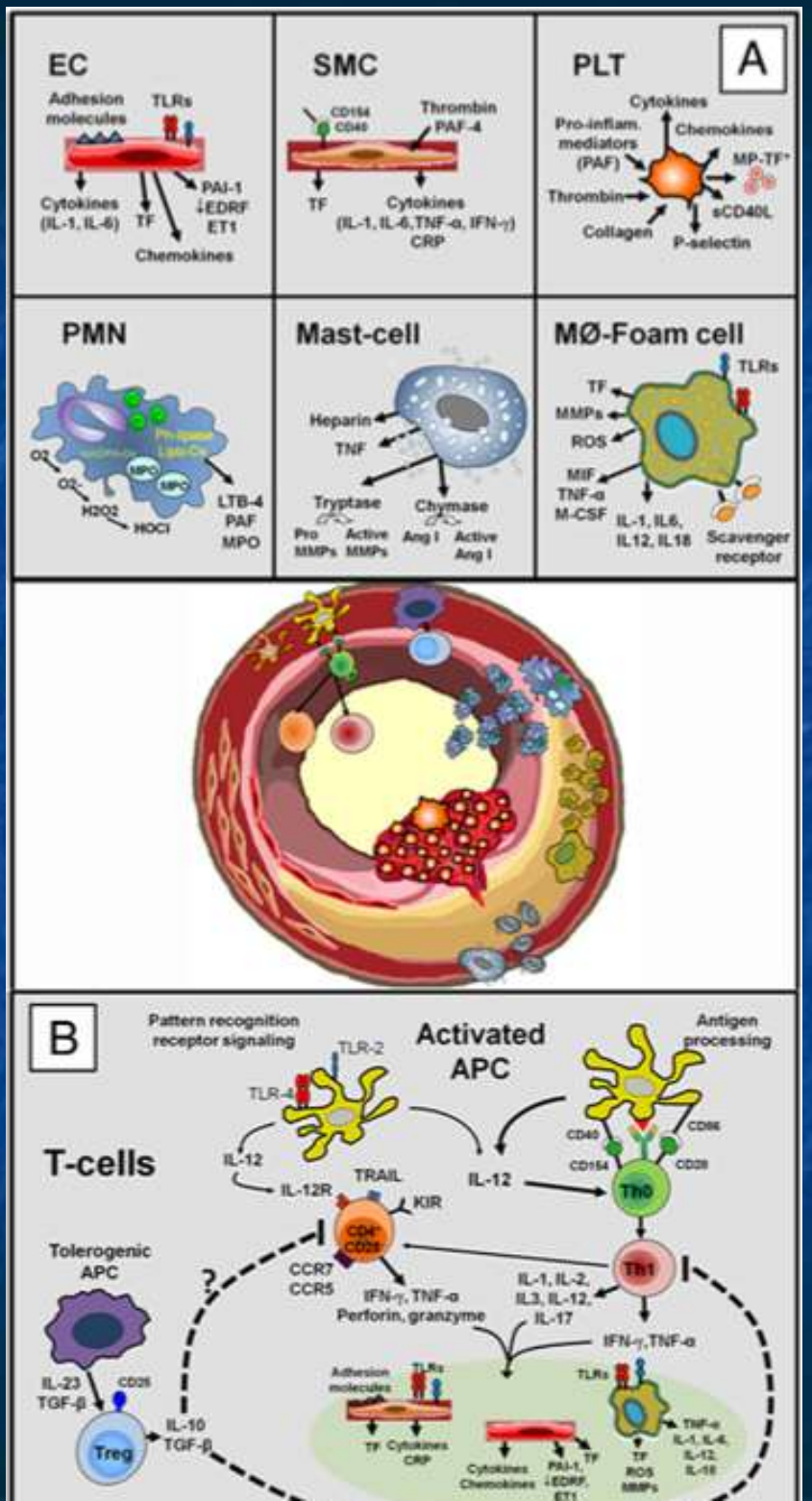


Figure 1 Classification of Acute Coronary Syndromes

Crea F.JACC. 2013. 61; 1 : 1-11.



Crea F.JACC. 2013. 61; 1 : 1-11.

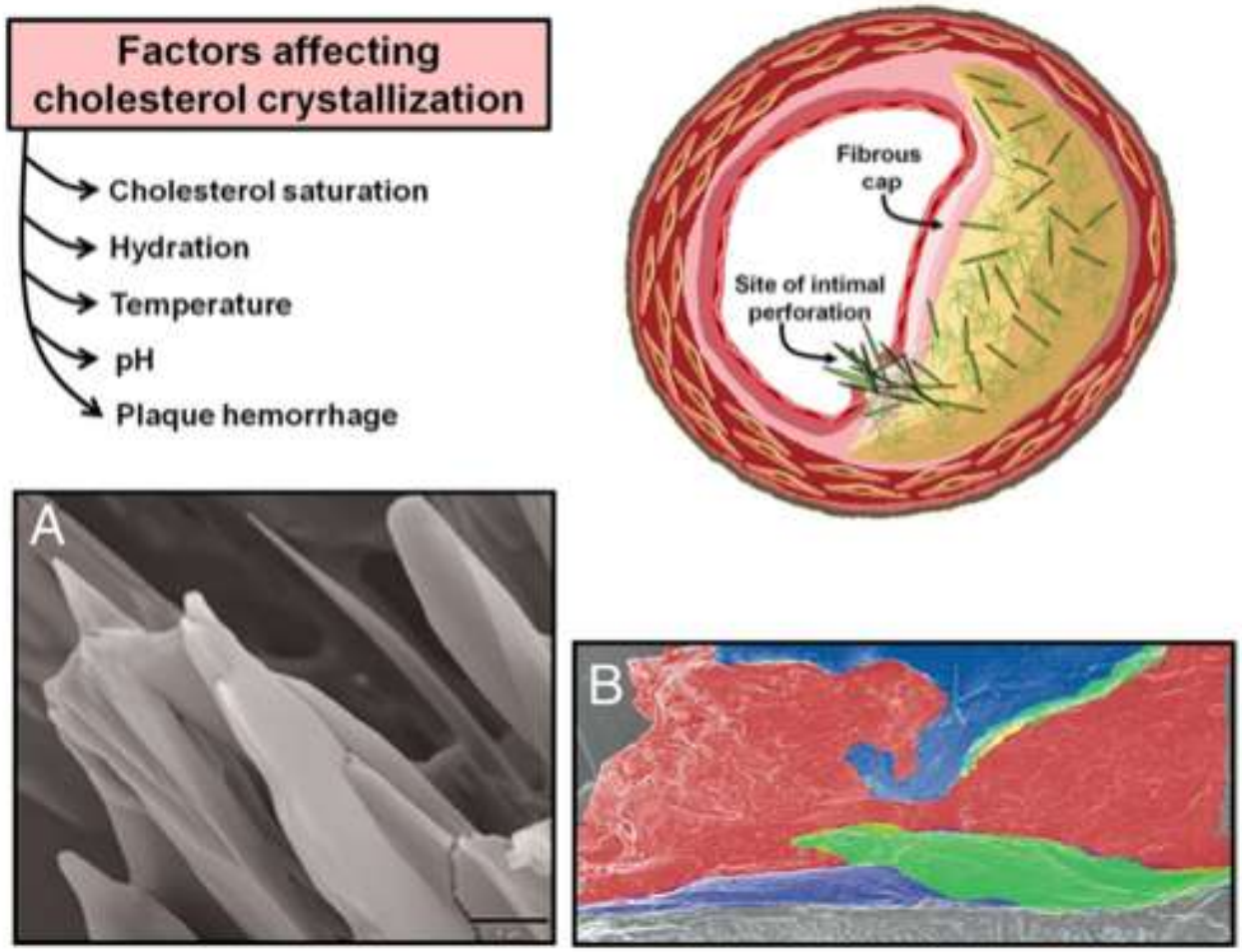
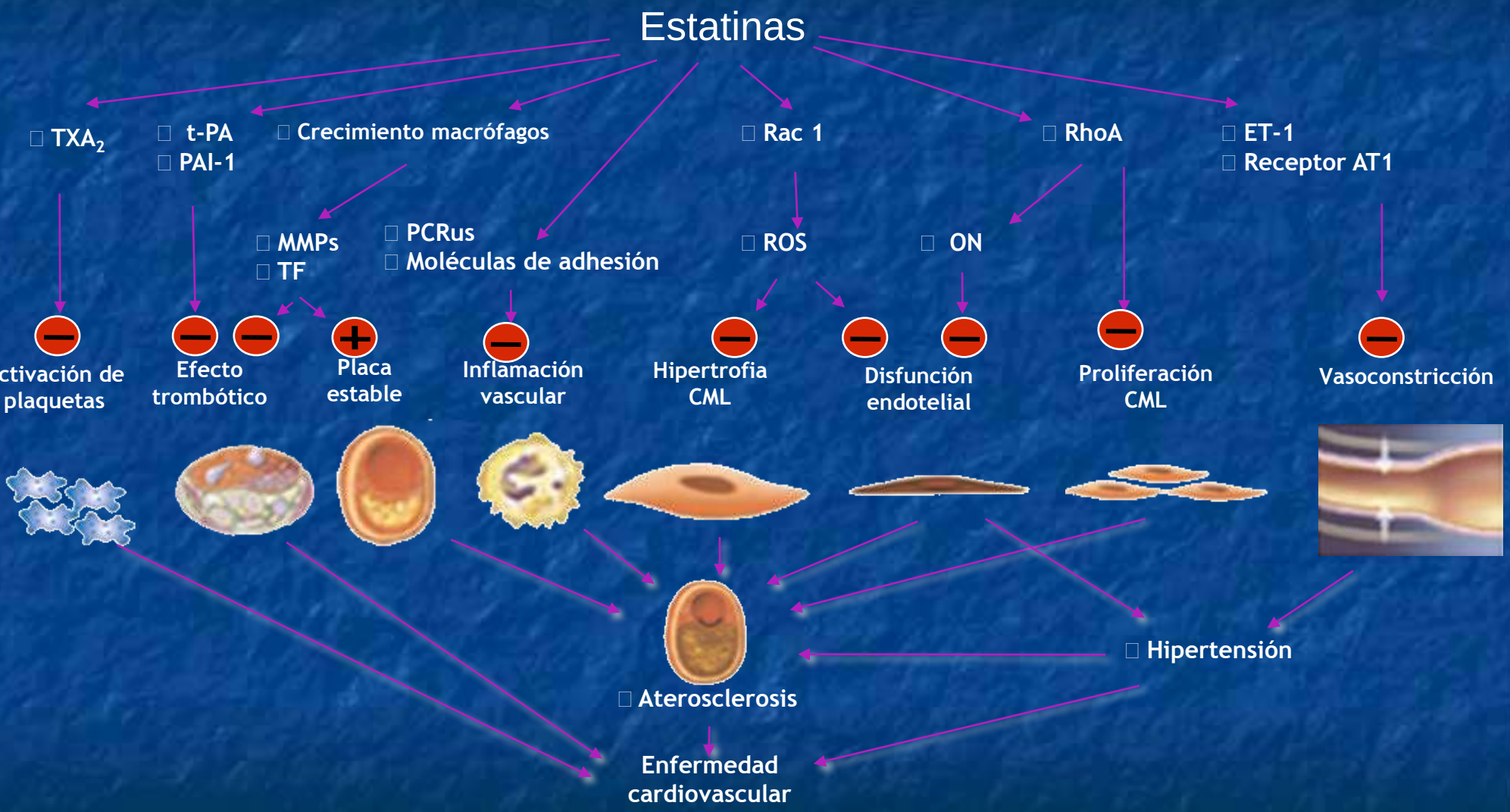


Figure 3 **Physical–Chemical Alterations of Plaque Composition May Cause ACS in Patients Without Systemic Evidence of Inflammation**

Effects of cholesterol crystals on plaque integrity in coronary arteries of patients who died of acute coronary syndrome (ACS) assessed by using light and scanning electron microscopy. **A and B** show scanning electron microscopy results of the culprit stenosis from the left anterior descending artery of a 57-year-old woman who died of ACS. **(A)** Example of cholesterol crystals perforating the intimal surface at the plaque shoulder (bar = 10 μm). **(B)** A color-coded image defines thrombus **(red)**, fissured plaque **(blue)**, and the site of a cholesterol crystal perforating the intima **(green-yellow)**. Modified, with permission, from Abela et al. (59).

Crea F.JACC. 2013. 61; 1 : 1-11.

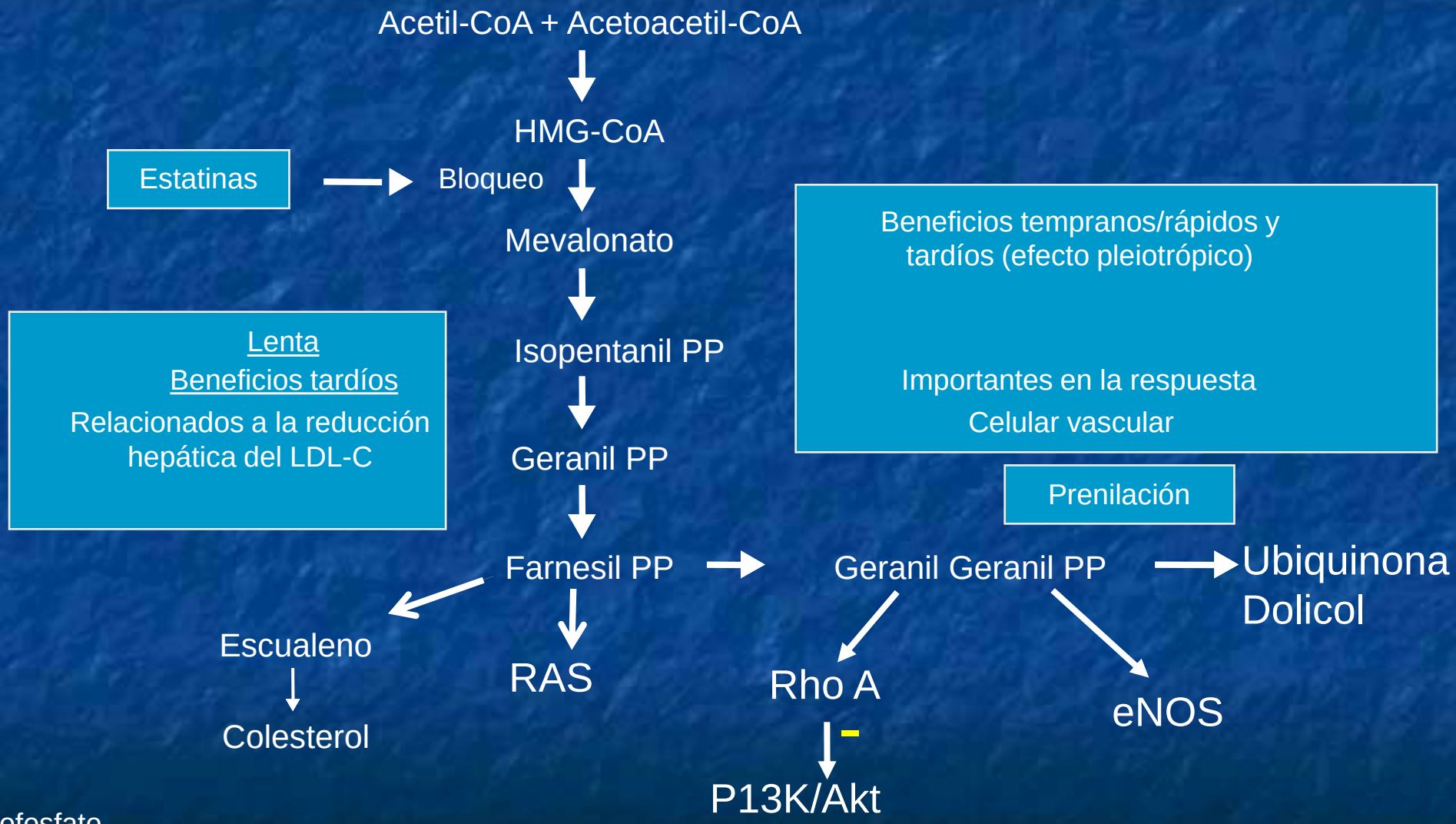
Efectos independientes del colesterol (pleiotrópicos) de las estatinas



AT1 = receptor AT1 de angiotensina; ET-1 = endotelina 1; PCRus = Proteína C reactiva ultrasensible; MMPs = metaloproteinas de la matriz; PAI-1 = inhibidor-1 del activador del plasminógeno; ROS = especies reactivas de oxígeno; CML = célula del músculo liso; TF = factor tisular; t-PA = activador del plasminógeno tisular; TXA_2 = tromboxano A_2..

Adaptado de Takemoto and Liao. Arterioscler Thromb Vasc Biol. 2001;21:1712; Liao. Am J Cardiol. 2005;96(suppl):24F.

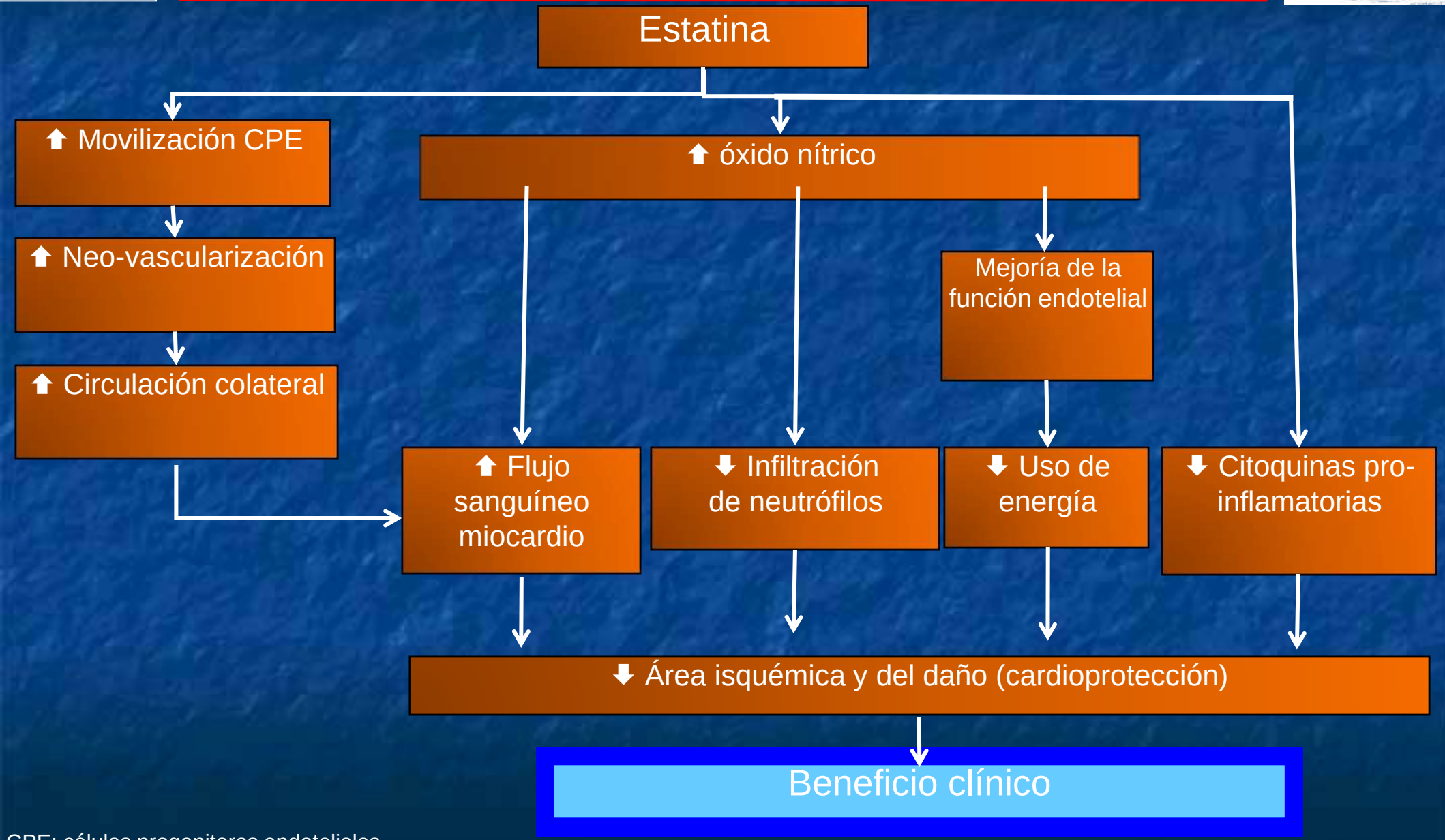
Vías metabólicas bloqueadas por las estatinas



PP = pirofosfato
RAS
RhoA.

Ray KR, Cannon CP. Am J Cardiol. 2005;96(suppl):54F
Merla M et al. Am Heart J 2007;154:391-402

Mecanismos potenciales del beneficio de las estatinas en el proceso de la isquemia-reperfusión



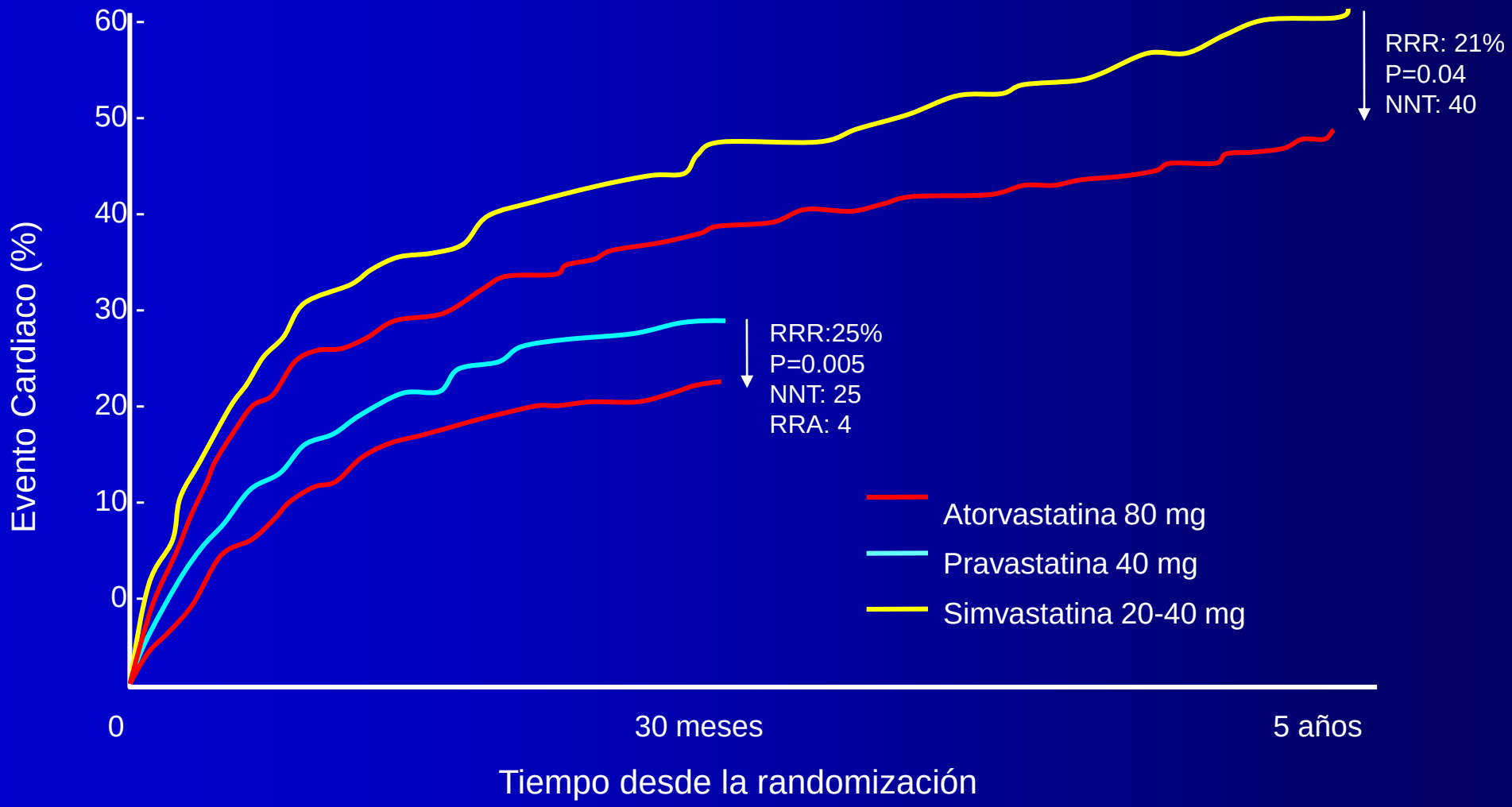
CPE: células progenitoras endoteliales

Modificado de Scalia R. Am J Cardiovasc Drugs 2005;5:163-70

Resumen: 5 años de seguimiento en IDEAL es el mayor periodo de seguimiento de pacientes SCA con terapia de estatinas

PROVE IT
IM o AI

IDEAL
Todos los IM



ESTATINAS EN ICP

- La administración de una estatina horas o días antes de una ICP estuvo asociada a:
  - Menor incidencia temprana de IM[1,2]
  - Menor mortalidad y eventos clínicos a los 30 días y 6 meses[3]
  - Menor mortalidad al cabo de un año[4]
- Dos meta-análisis demostraron
  - Disminución absoluta de riesgo de mortalidad temprana[5]
  - Menor incidencia de fibrilación auricular y ACV[6]

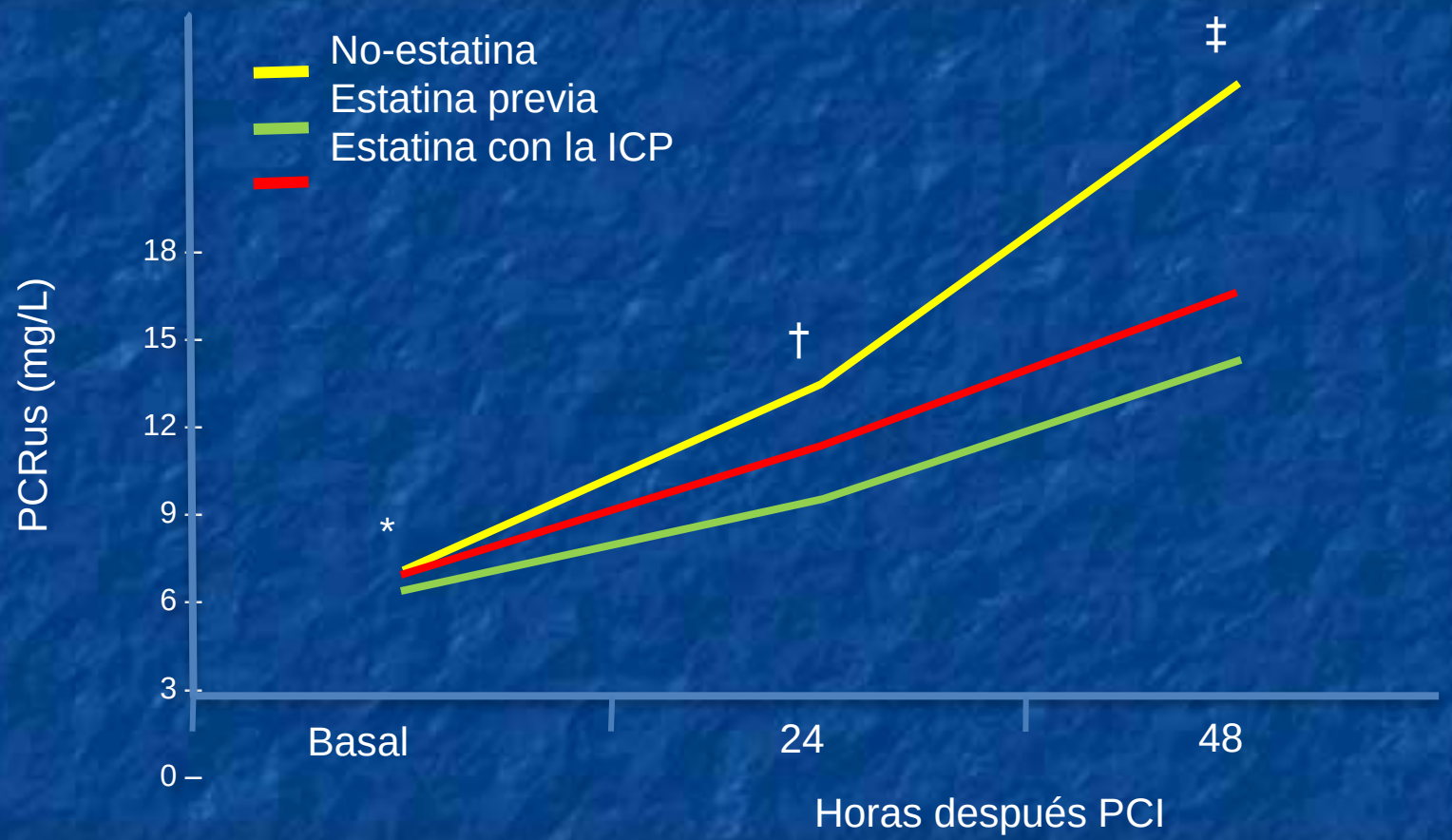
1. Herrmann J et al. Circulation 2002;106: 2180–83
2. Briguori C et al. Eur Heart J 2004;25:1822-28
3. Chan AW et al. Circulation 2002;105: 691–696.
4. Chan AW et al. Circulation 2003;107:1750-56.
5. Merla R et a. Am J Cardiol 2007;100:770-776.
6. Liakopoulos OJ et al. Eur Heart J 2008;29:1548-59

ESTATINAS EN ICP

- Estudio en 223 pacientes consecutivos con angina crónica estable y PCRus <5 mg/dL destinados a implantación de stent en un vaso.
- Tres grupos de observación
  - En tratamiento con estatinas por 6 meses o más antes ICP (n=85)
  - Atorvastatina 80 mg inmediatamente después de la implantación del stent hasta por un mes y seguido con 20 mg indefinidamente (n=62)
  - Sin recibir estatina (n=76)

Gaspardone A et al. Am J Cardiol 2002;90:786-89

Modificación de la PCRus a las 24 y 48 horas post-ICP en los tres grupos



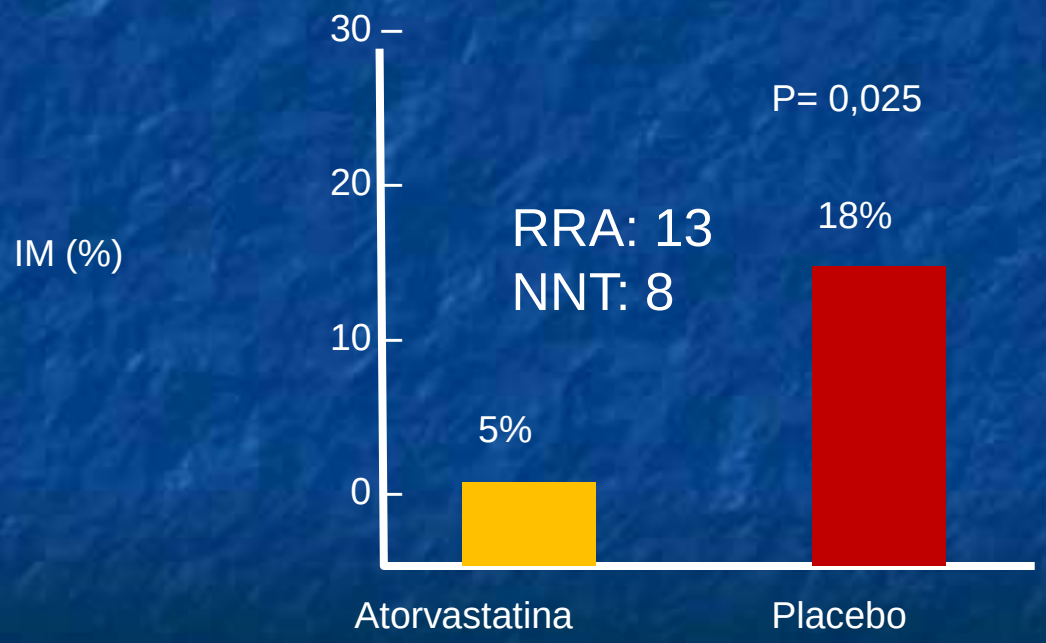
*: p<0,05 grupo pre-tratado con estatinas versus los otros grupos
†p<0,02 grupo pretratado con estatina versus no estatinas
‡ p<0,01 grupo no estatina versus los otros grupos

Gaspardone A et al. Am J Cardiol 2002;90:786-89

ARMYDA

- 153 pacientes asignados a 40 mg de atorvastatina (n=76) o placebo (n=77) siete días antes de la intervención coronaria percutánea (ICP) con determinación de enzimas (CK-MB, troponina I y mioglobina a las 8 y 24 horas posteriores

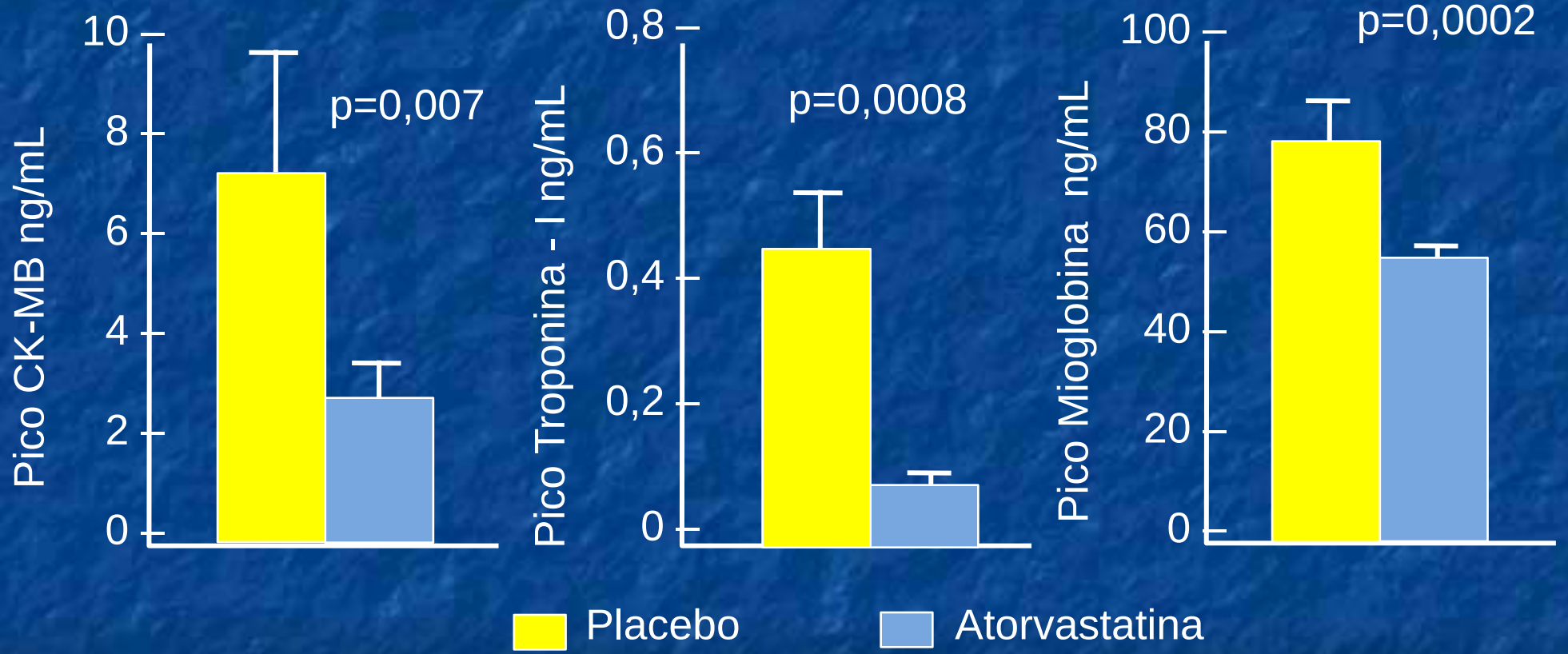
Punto final primario: Incidencia de IM (por CK-MB)



Pasceri V et al. Circulation 2004;110:674-78

ARMYDA.
Valores pico de la CK-MB, troponina I y mioglobina después de la ICP

Media ± EEM



Pasceri V et al. Circulation 2004;110:674-78

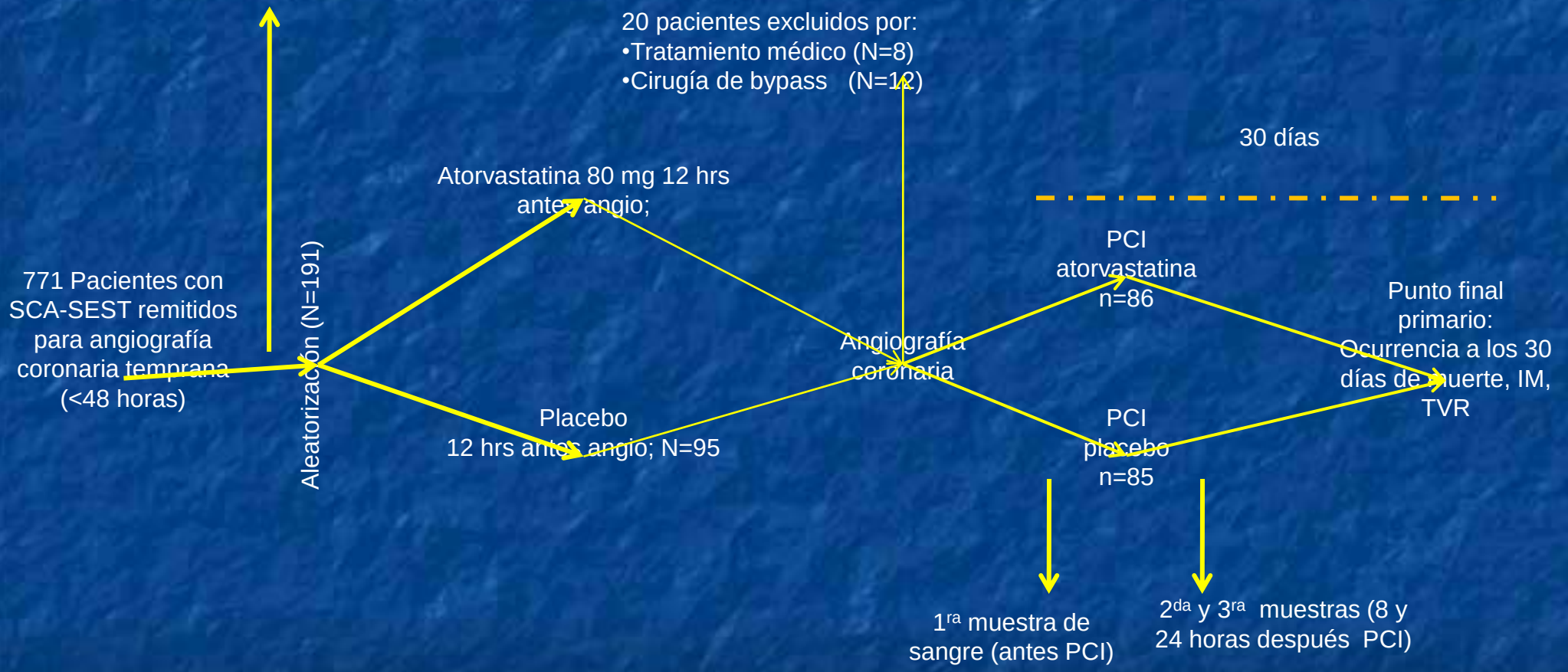
ARMYDA-CAMs
Subestudio del ARMYDA

- Cuantificación de niveles plasmáticos de VCAM-1, ICAM-1 y selectina E en 76 pacientes (38 en cada grupo) siete días antes ICP, inmediata a la ICP y luego a 8 y 24 horas post-ICP
- Resultado: Atenuación en el incremento de la ICAM-1 y selectina E en el grupo atorvastatina

Patti G et al. J Am Coll Cardiol 2006;48:1560-66

ARMYDA-ACS
Diseño del estudio

580 pacientes excluidos por:
- 451 tratamiento con estatina
- 41 angio de emergencia(<48h)
- 43 fracción de eyección <30%
- 30 contraindicación a estatina
- 15 insuficiencia renal severa

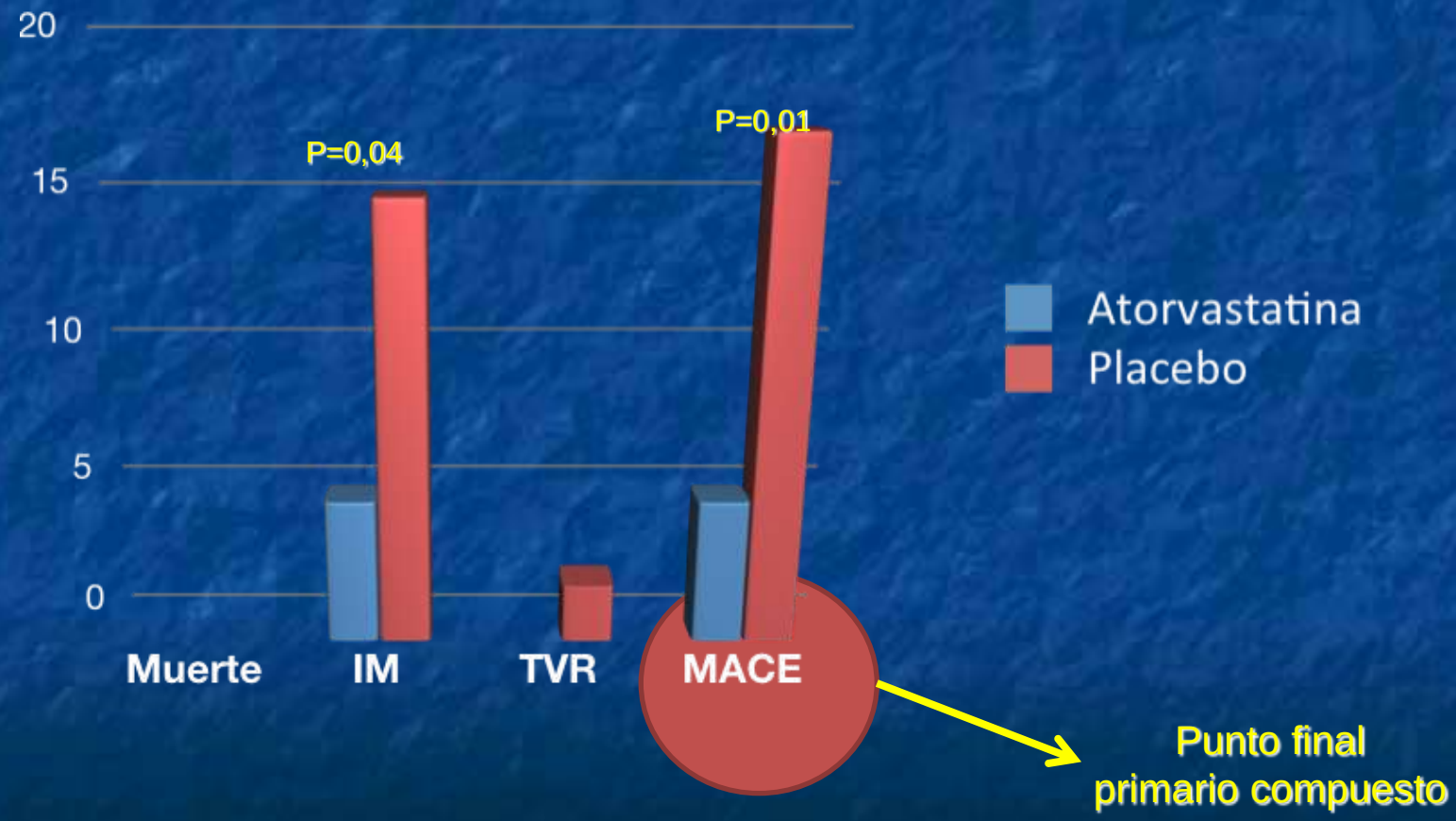


PCI: intervención coronaria percutánea
SCA: síndrome coronario agudo
SEST: sin elevación segmento ST
IM: infarto del miocardio
TVR: Revascularización del vaso diana

Patti G et al. J Am Coll Cardiol 2007;49:1272-78

ARMYDA-ACS
Resultados

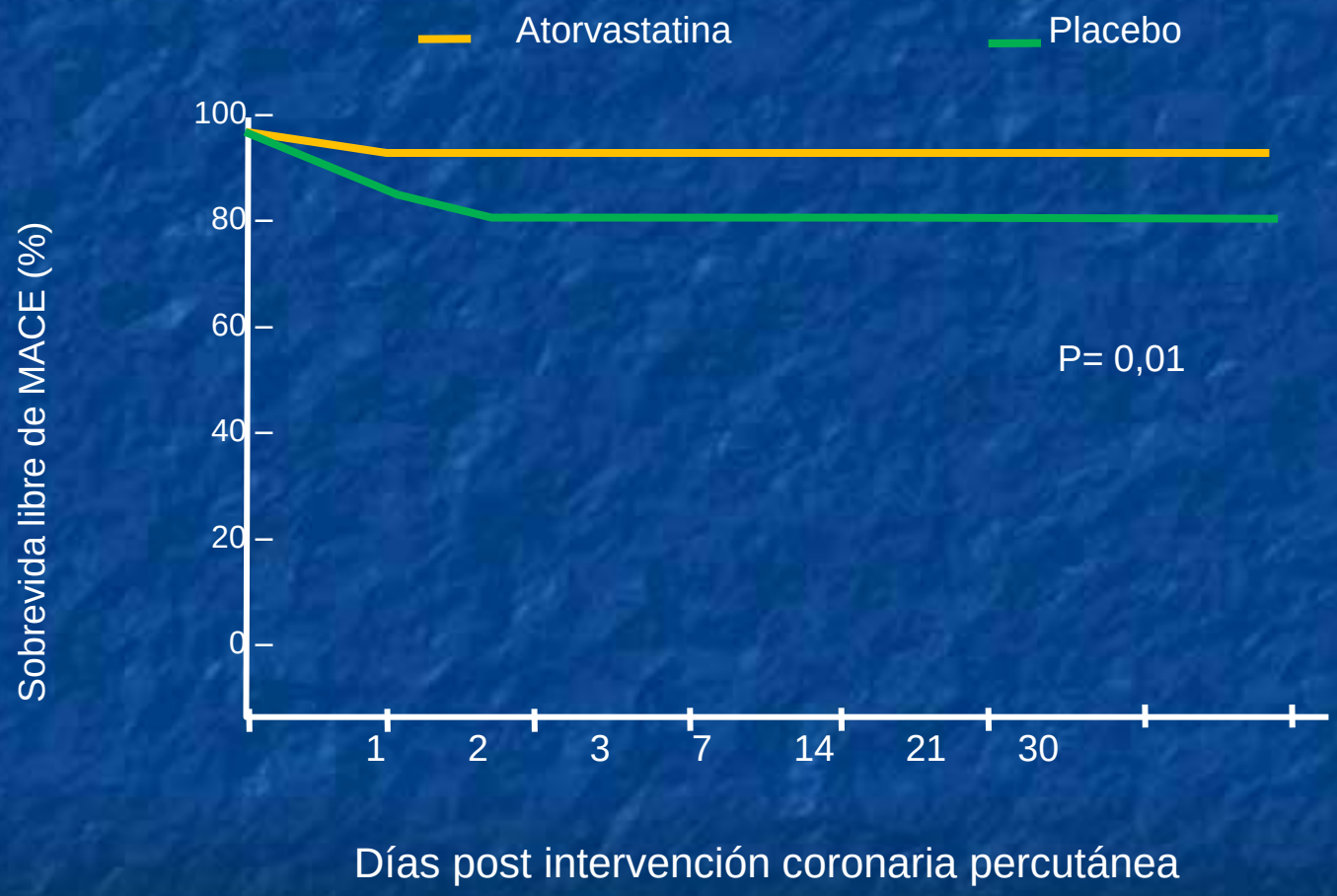
- Desenlaces individuales y combinados del punto final primario a los 30 días



MACE: Major Adverse Cardiac Events
TVR: Revascularización del vaso diana

Patti G et al. J Am Coll Cardiol 2007;49:1272-78

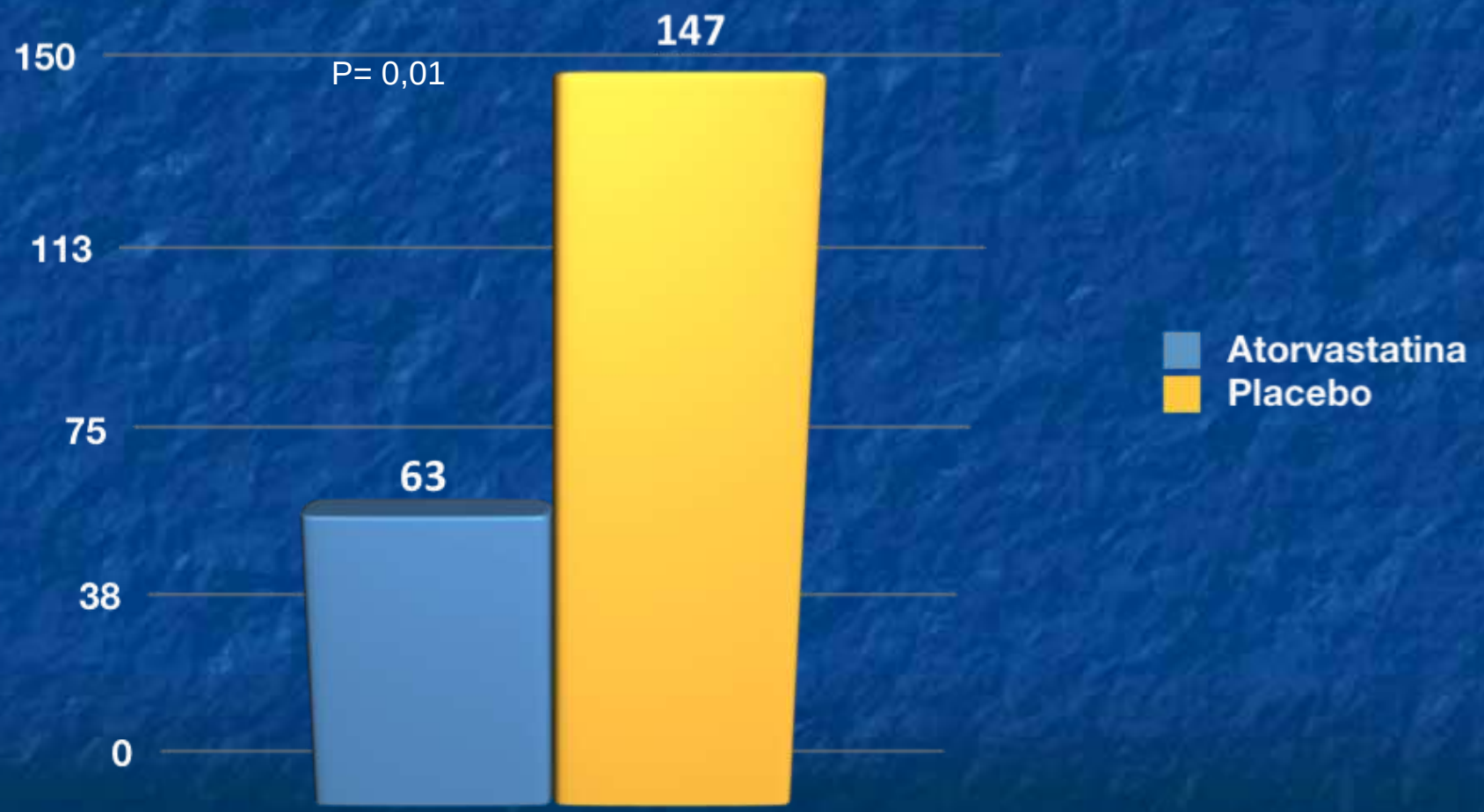
ARMYDA-ACS: Curva de sobrevida a los 30 días



MACE: Major Adverse Cardiac Events

Patti G et al. J Am Coll Cardiol 2007;49:1272-78

ARMYDA-ACS
Punto final secundario: incremento porcentual de la PCR post-PCI a partir del valor basal



Patti G et al. J Am Coll Cardiol 2007;49:1272-78

ARMYDA-ACS Resultados

- Desenlaces individuales y combinados del punto final primario a los 30 días en los grupos atorvastatina y placebo

	Atorvastatina n=86 (%)	Placebo n=85 (%)	RRA NNT	p
Muertes	-	-		-
Infarto del miocardio	4 (5%)	13 (15%)	10 10	0,04
Revascularización vaso diana	-	1 (2%)		1
Total MACE	4 (5%)	14 (17%)	12 8	0,01

Patti G et al. J Am Coll Cardiol 2007;49:1272-78

ARMYDA-RECAPTURE
Diseño del estudio

391 pacientes excluidos por:
- 254 sin tratamiento crónico con estatina
- 40 angio de emergencia
- 86 fracción de eyección <30%
- 11 insuficiencia renal severa

74 pacientes excluidos por:
- Tratamiento médico (N=32)
- Cirugía de bypass (N=42)

848 Pacientes con angina estable o SCA-SEST sometidos a angiografía coronaria

Aleatorización (N=457)

Atorvastatina 80 mg 12 hrs antes angio; 40 mg adicionales 2 hrs antes N=229

Placebo 12 hrs antes angio; dosis adicional 2 hrs antes N=228

Angiografía coronaria

30 días

PCI atorvastatina n=192

PCI placebo n=191

Punto final primario: Ocurrencia a los 30 días de muerte, IM, TVR

1ra muestra de sangre (antes PCI)

2da y 3ra muestras (8 y 24 horas después PCI)

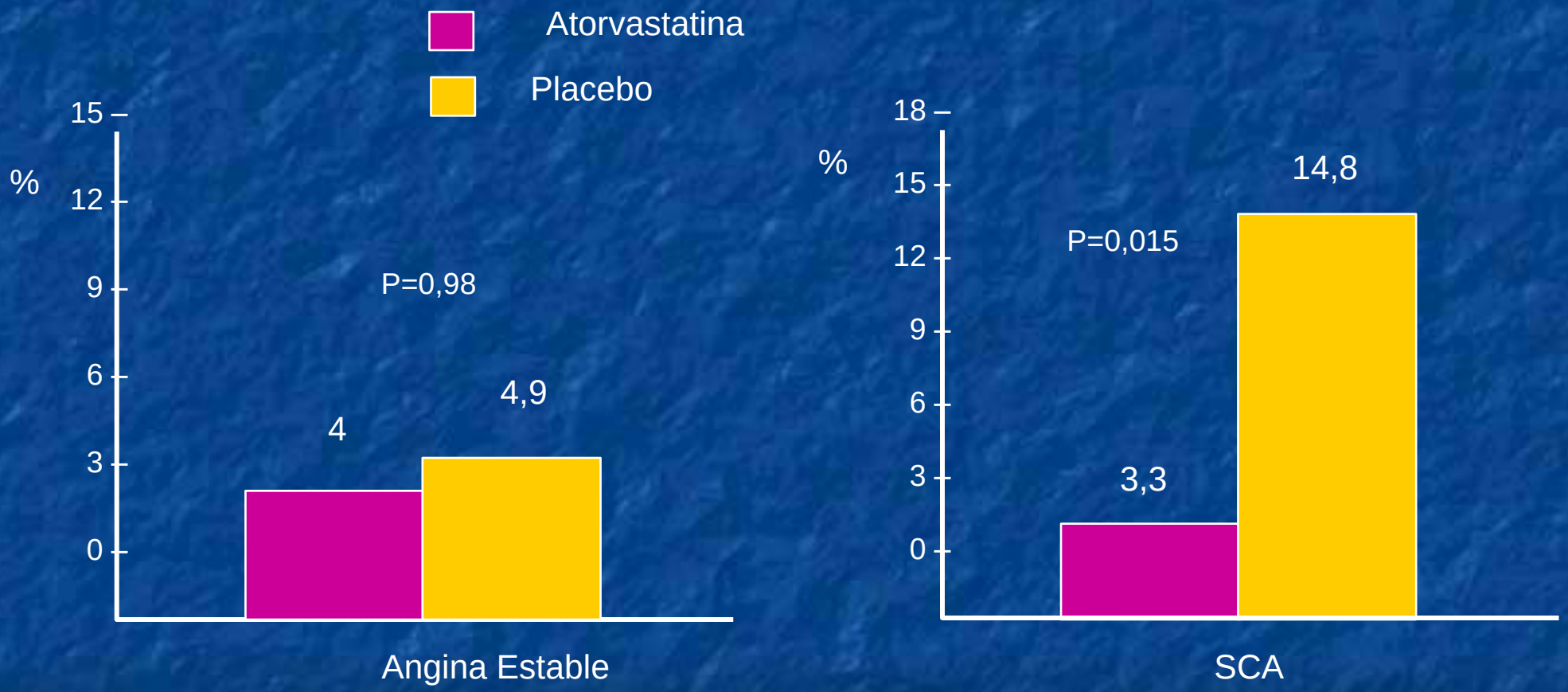
CK-MB, troponina, PCR

PCI: intervención coronaria percutánea
SCA: síndrome coronario agudo
SEST: sin elevación segmento ST
IM: infarto del miocardio
TVR: Revascularización del vaso diana

Di Sciascio G et al. J Am Coll Cardiol 2009; 54:558-65.

ARMYDA-RECAPTURE

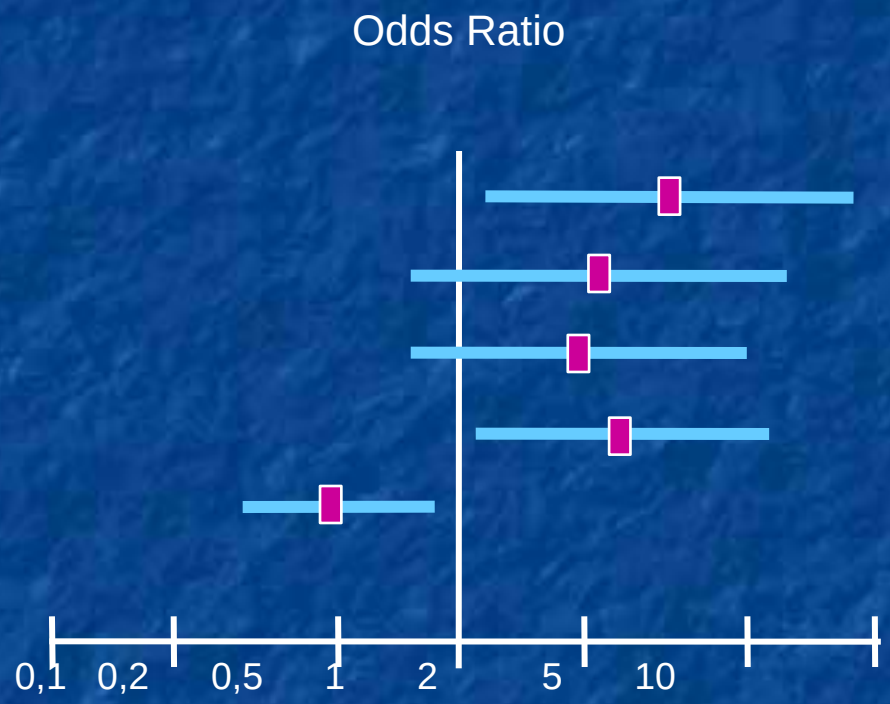
Incidencia de eventos cardíacos mayores a los 30 días de acuerdo a la presentación clínica (angina estable versus síndrome coronario agudo [SCA])



Di Sciascio G et al. J Am Coll Cardiol 2009;54:558-65

ARMYDA-RECAPTURE
Eventos cardíacos mayores a los 30 días (análisis por múltiples variables)

Inhibidores IIb/IIIa
FEVI < 40%
Síndrome coronario agudo
Múltiples stent
Recarga de atorvastatina



Di Sciascio G et al. J Am Coll Cardiol 2009;54:558-65

ARMYDA-RECAPTURE
Resultados

- Desenlaces individuales y combinados del punto final primario a los 30 días en los grupos atorvastatina y placebo

	Atorvastatina n=192 (%)	Placebo n=191 (%)	RRA	NNT	p
Muerte cardíaca	0	1 (0,5)			NS
Infarto del miocardio	7 (3,7)	17 (8,9)	5,2	19	0,056
Trombosis del stent	0	1 (0,5)			NS
Revascularización vaso diana	0	1 (0,5)			NS
Total MACE	7 (3,7)	18 (9,4)	5,7	18	0,037

Di Sciascio G et al. J Am Coll Cardiol 2009;54:558-65

ARMYDA-RECAPTURE

Conclusiones

- En este estudio se respalda que el pretratamiento a corto plazo con una carga de dosis alta de atorvastatina antes de la ICP mejora los desenlaces de los pacientes que ya estaban recibiendo terapia crónica con estatinas.
- Una dosis de 80 mg de atorvastatina administrada 12 horas antes de la intervención seguida por 40 mg adicionales dos horas antes estuvo asociada con una RRR del 50%, RRA 6, NNT 18 de MACE a los 30 días en comparación a los eventos ocurridos en el grupo placebo.

Di Sciascio G et al. J Am Coll Cardiol 2009;54:558-65

Novel Approaches for Preventing or Limiting Events (NAPLES II) Trial

- Población: Pacientes referidos para coronariografía electiva por EAC sintomática o ICP en lesiones de novo en arteria coronaria nativa
- Se asignaron al azar a atorvastatina (dosis única de 80 mg, dentro de las 24 horas previas a la intervención) o placebo.

Brigouri C et al. J Am Coll Cardiol 2009;54:

Novel Approaches for Preventing or Limiting Events (NAPLES II) Trial

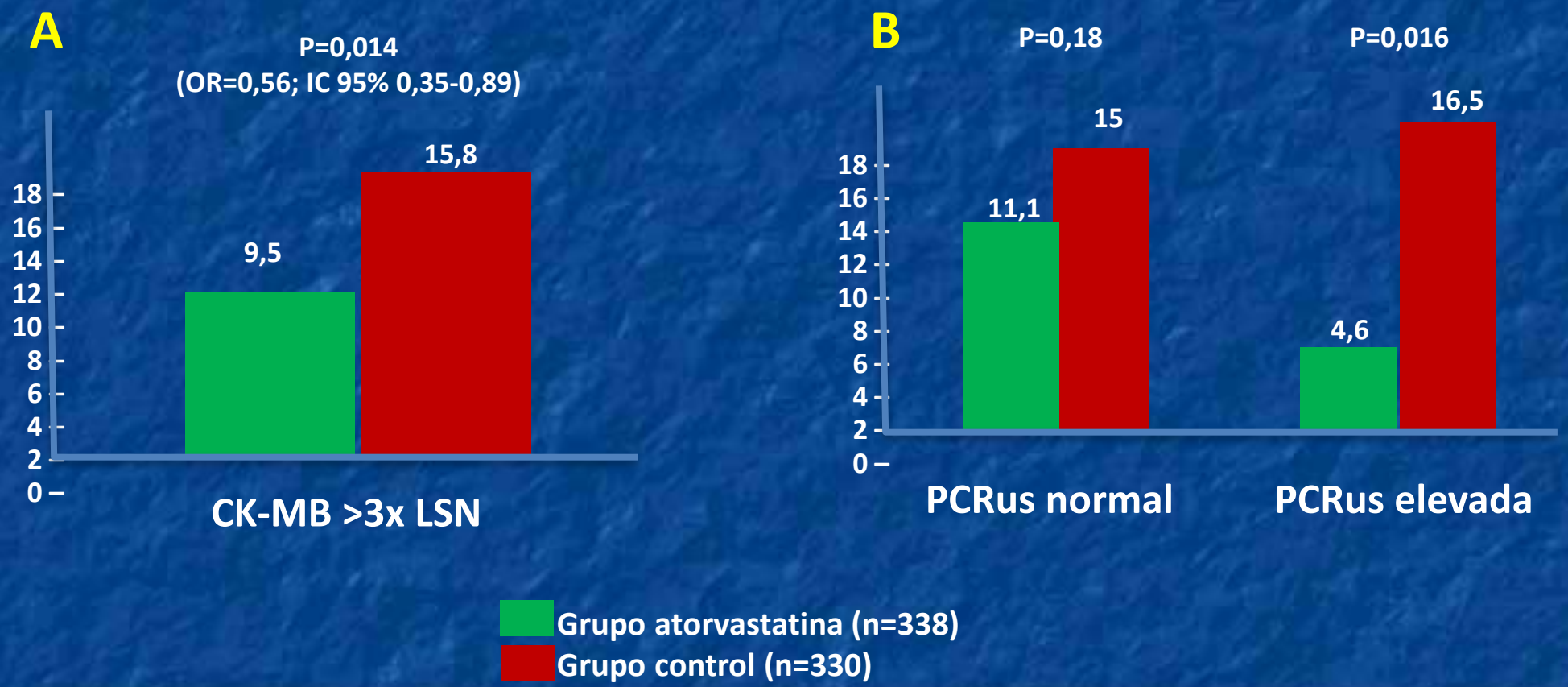
- Punto final primario: Tasa de IM periprocedimiento definido como elevación 3 LSN de CK-MB sola o asociada con dolor torácico, elevación del segmento ST o anormalidades en la onda T.
- Puntos finales secundarios:
  1) Frecuencia en elevación 3 LSN de troponina I y
  2) Eventos intrahospitalarios compuestos (muerte, IM, repetición de revascularización

Brigouri C et al. J Am Coll Cardiol 2009;54:

NAPLES II
Cambios en las enzimas cardíacas

	Atorvastatina n=338 (%)	Placebo n=330 (%)	p
Pico CK-MB, pg/mL	2,10 (0,10-12,50)	3,20 (1,27-16,07)	0,014
Cualquier incremento en CK-MB mayor al LSN (%)	23	37	0,001
Pico troponina I, pg/mL	0,10 (0,03-0,54	0,20 (0,05-0,73)	0,004
Cualquier incremento en troponina I mayor al LSN (%)	42	52,6	<0,001

Incremento en la CK-MB en ambos grupos del estudio NAPLE II



A) Incidencia en la elevación de la CK-MB tres veces por encima del límite superior de lo normal (LSN) en los grupos atorvastatina y control.

B) Incidencia en la elevación de la CK-MB tres veces del LSN en el subgrupo de pacientes con PCR ultrasensible normal y elevada en ambos grupos.

Modificado de Briguori C et al. J Am Coll Cardiol doi:10.1016/ (Published online 5 August 2009).

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PRACTICE GUIDELINE

2013 ACCF/AHA Guideline for the Management of ST-Elevation Myocardial Infarction

A Report of the American College of Cardiology Foundation/
American Heart Association Task Force on Practice Guidelines

Developed in Collaboration With the American College of Emergency Physicians and Society for Cardiovascular Angiography and Interventions

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8.3. Lipid Management: Recommendations

CLASS I

1. **High-intensity statin therapy should be initiated or continued in all patients with STEMI and no contraindications to its use (434–436). (*Level of Evidence: B*)**

points (434,436,439). Among currently available statins, only high-dose atorvastatin (80 mg daily) has been shown to reduce death and ischemic events among patients with ACS (436,440). Approximately one third of patients in the PROVE-IT TIMI 22 (Pravastatin or Atorvastatin Evaluation and Infection Therapy—Thrombolysis in Myocardial Infarction 22) trial had STEMI (436). Cardiovascular event rates were not significantly reduced with a tiered strategy of simvastatin (40-mg daily for 1 month followed by 80 mg daily) in the A to Z Trial (Aggrastat to Zocor) (439), and concerns have been raised recently about the safety of high-dose simvastatin (i.e., 80 mg daily) (441). Although the

European Heart Journal
doi:10.1093/eurheartj/ehr236

ESC GUIDELINES

ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation

The Task Force for the management of acute coronary syndromes (ACS) in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC)

Authors/Task Force Members: Christian W. Hamm (Chairperson) (Germany)*, Jean-Pierre Bassand (Co-Chairperson)*, (France), Stefan Agewall (Norway), Jeroen Bax (The Netherlands), Eric Boersma (The Netherlands), Hector Bueno (Spain), Pio Caso (Italy), Dariusz Dudek (Poland), Stephan Gielen (Germany), Kurt Huber (Austria), Magnus Ohman (USA), Mark C. Petrie (UK), Frank Sonntag (Germany), Miguel Sousa Uva (Portugal), Robert F. Storey (UK), William Wijns (Belgium), Doron Zahger (Israel).

Statin therapy with target LDL-C levels <1.8 mmol/L (<70 mg/dL) initiated early after admission is recommended.	I	B	313

Table 39 Long-term medical therapy after myocardial revascularization

	Class[a]	Level[b]
• ACE inhibitors should be started and continued indefinitely in all patients with LVEF ≤40% and for those with hypertension, diabetes, or CKD, unless contraindicated.	I	A
• ACE inhibitors should be considered in all patients, unless contraindicated.	IIa	A
• Angiotensin receptor blockers are indicated in patients who are intolerant of ACE inhibitors and have HF or MI with LVEF ≤40%.	I	A
• Angiotensin receptor blockers should be considered in all ACE-inhibitor intolerant patients.	IIa	A
• It is indicated to start and continue ß-blocker therapy in all patients after MI or ACS or LV dysfunction, unless contraindicated.	I	A
• High-dose lipid lowering drugs are indicated in all patients regardless of lipid levels, unless contraindicated.	I	A

Wijns V , et al. Eur Heart J 2010;31:2501-55

SOVECI

European Heart Journal (2011) **32**, 1769–1818
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ESC/EAS GUIDELINES

ESC/EAS Guidelines for the management of dyslipidaemias

The Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and the European Atherosclerosis Society (EAS)

Developed with the special contribution of: European Association for Cardiovascular Prevention & Rehabilitation†

Guidelines Europeos de Hiperlipidemias

- Dosis altas de estatinas deben ser inciadas durante el primero al cuarto dia de hospitalizacion en SCA y debe alcanzar posteriormente un LDL meta de 70 mg/dl. Clase I. Nivel de Evidencia B.
- La recarga con dosis altas de estatinas reduce la frecuencia de IM periprocedimiento, aun en pacientes con terapia cronica de estatinas que vayan a una ICP para e manejo de angina estable o SCA. Clase IIb. Nivel de evidencia B.

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STATE-OF-THE-ART PAPER

The Controversies of Statin Therapy

Weighing the Evidence

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The debate whether statins, 3-hydroxymethyl-3-methylglutaryl coenzyme A reductase inhibitors, are safe to use has been raging since their introduction in 1987. Statins are generally well tolerated and are believed to have minimal adverse effects. However, individual, specific rare adverse events have been reported, such as elevations of liver enzymes, muscle aches, and very rarely, rhabdomyolysis. Discontinuation and/or reduction in the dose of the statin usually leads to resolution of these side effects. Recently, however, debate has focused on the possible negative long-term effects of statin treatment on cognitive decline, the incidence of cancer, and the development of diabetes mellitus. Recently, the U.S. Food and Drug Administration has expanded the warning for statins with a statement that statin use may lead to cognitive impairment. In this review, we discuss all levels of evidence, from case reports to large randomized controlled clinical trials, for the possible adverse effects of statins on cognitive decline, cancer, and diabetes. After careful consideration of all discussed scientific evidence, we conclude that there is no increased risk of cognitive decline or cancer with statin use. However, statin use is related to a small increased risk of type 2 diabetes mellitus. In view of the overwhelming benefit of statins in the reduction of cardiovascular events, we believe the small absolute risk for development of diabetes is outweighed by the cardiovascular benefits in patients for whom statin therapy is recommended. We, therefore, suggest that clinical practice for statin therapy should not be changed on the basis of the most recent Food and Drug Administration informational warnings. (J Am Coll Cardiol 2012;60:875–81) © 2012 by the American College of Cardiology Foundation

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