

Nuevas Estrategias de Reperfusión Miocárdica en el IAM con Elevación del Segmento ST. Consenso e Interrogantes



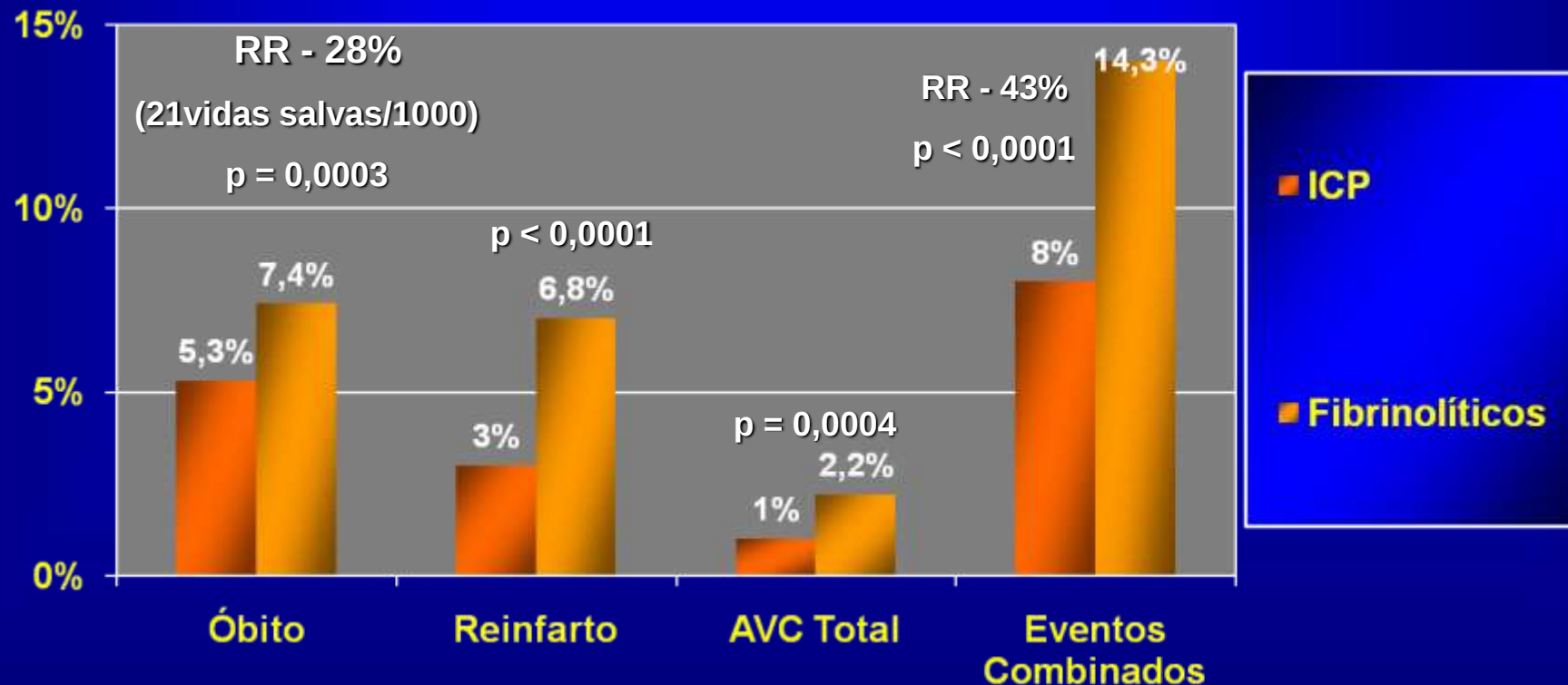
XXII Jornadas SOLACI
La Paz – Bolivia
Noviembre/2013

23 Estudios Randomizados

ICP Primaria vs Fibrinolíticos

n = 7.739

Resultados 30 días

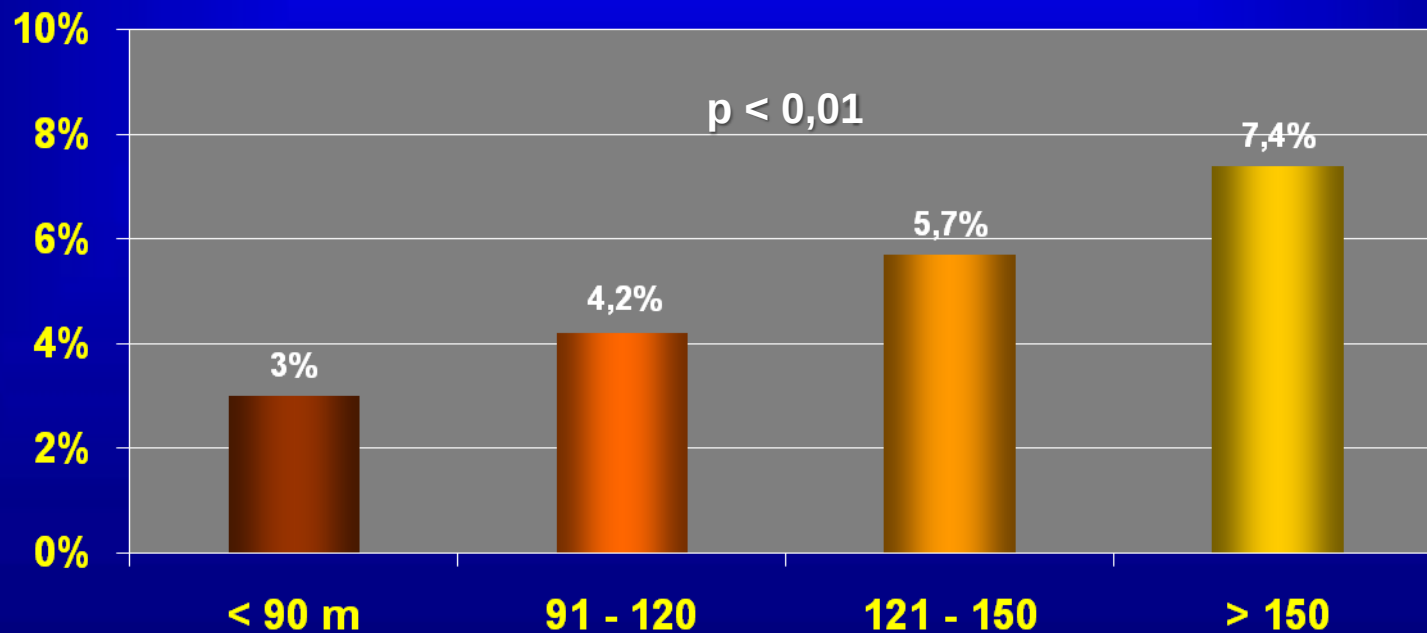


Mortalidad 30 días

Influencia del Retardo Puerta - Balón

Registro NRMI 3 – 4 (EUA)

1999 a 2006 n = 29.222 SCACST < 6 h → ICP



Puerta-balón > 90 m

OR 1,42; 95% IC 1,24 to 1,62

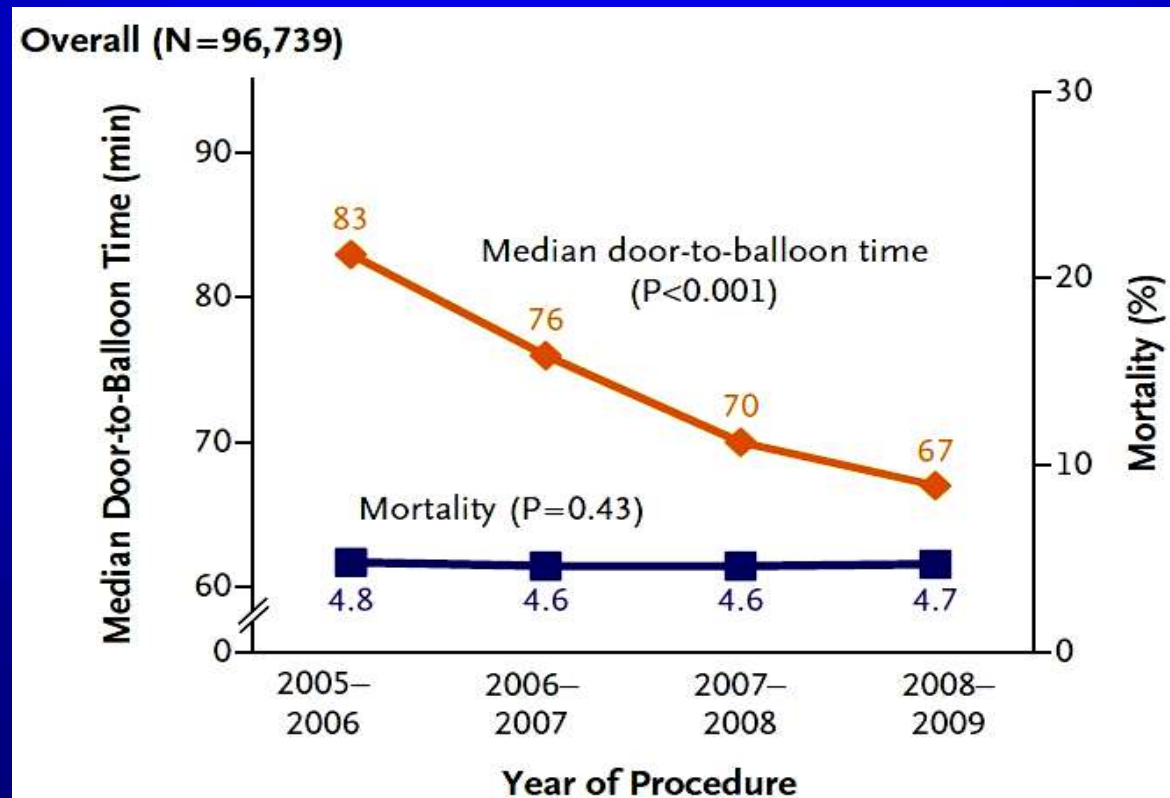
McNamara RL. J Am Coll Cardiol 2006;47:2180-86

Tiempo Puerta – Balón < 90 m

Mortalidad

Cathregistry (NRFMI) – EUA Julio/2005 a Junio/2009

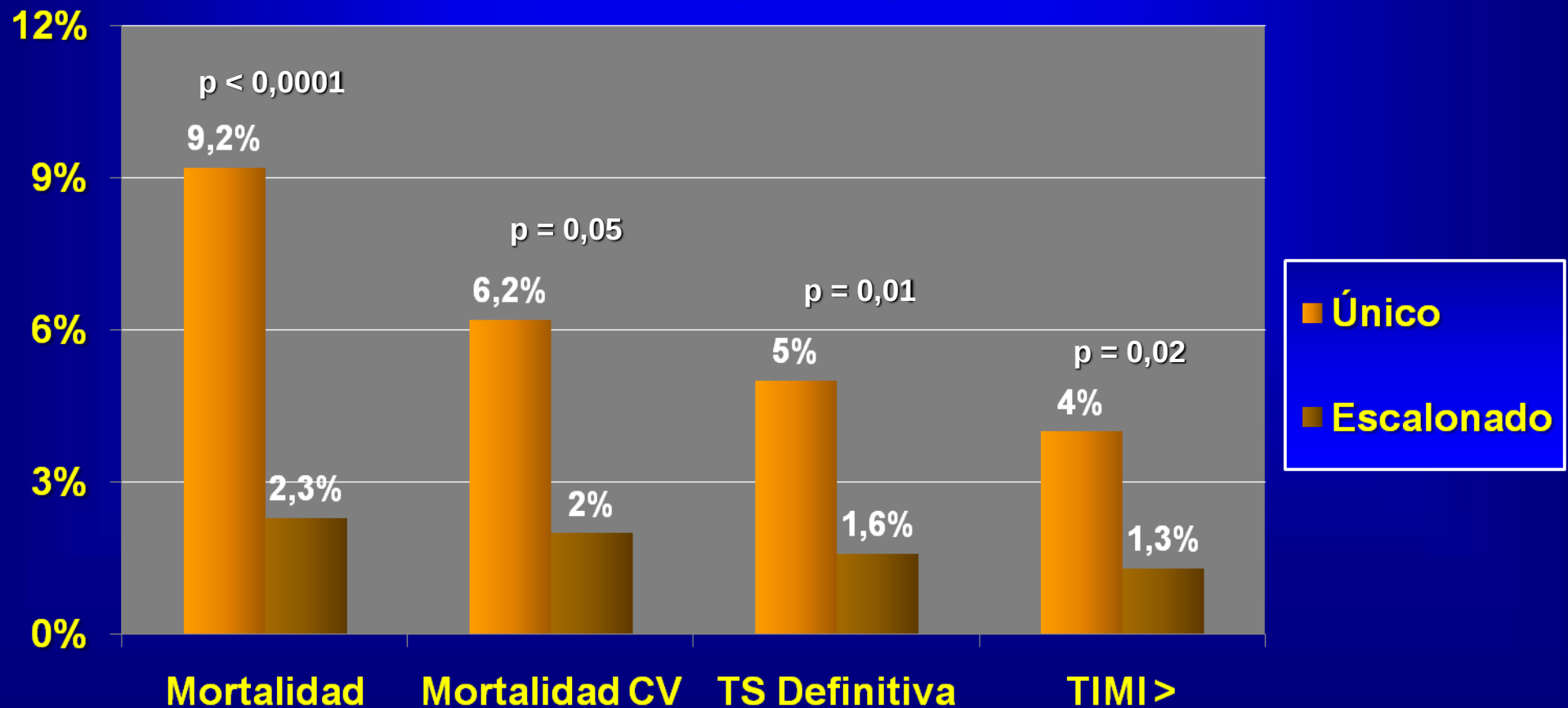
n = 96.739 ICP → STEMI 515 centros



HORIZONS TRIAL

Procedimiento Único vs Escalonado

Multiarteriales n = 668 (18,5%) Resultados 1 año



Registro Estado de Nueva York

Mortalidad

n = 4.024 Enero/2003 a Junio/2006 ICP - IAM con ST Elevado ≤ 24 h

Amuestras con Propensión de Semejanza

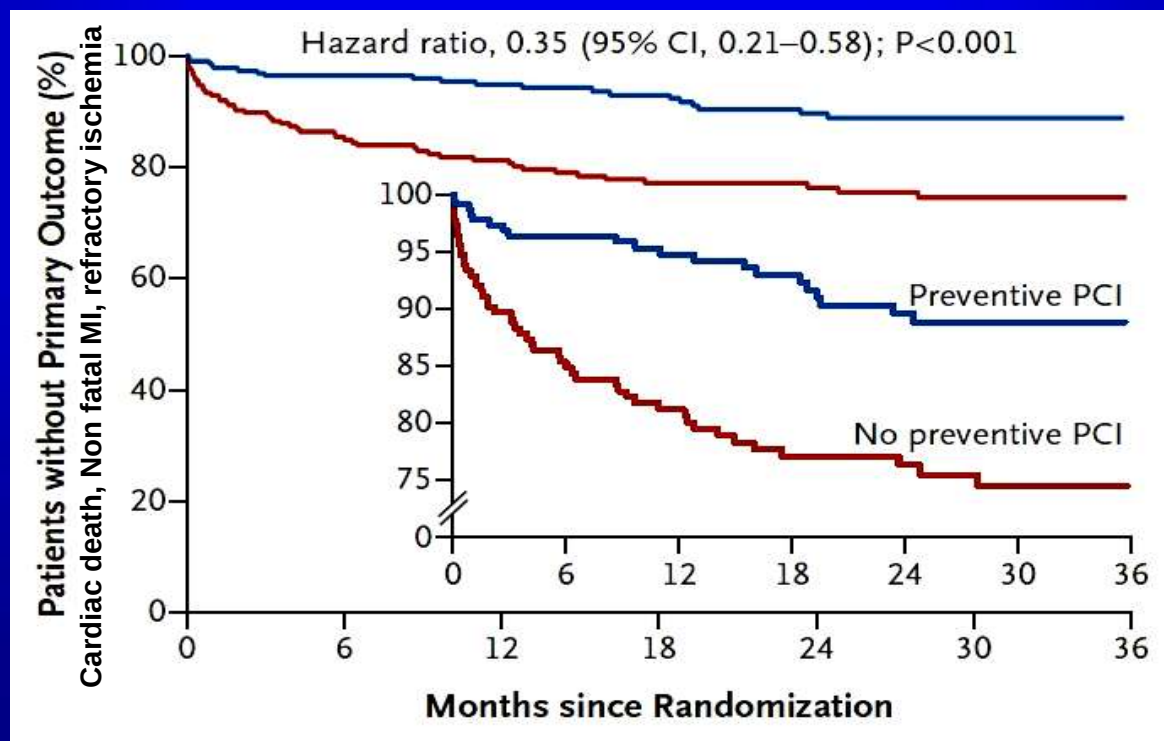
Mortalidad Excepto: Inestabilidad Hemodinámica, FE < 20%, Arritmia Ventricular Grave	Vaso Culpable n = 458	Multiarterial n = 458	p
Hospitalaria	0,9%	2,4%	0,04
12 m	4,2%	5,8%	0,13
24 m	4,9%	7,2%	0,07
42 m	6,75	10,4%	0,08

PRAMI TRIAL

ICP Preventiva en el IAM

Estudio Randomizado 5 Centros Reino Unido 2008-2013

n = 465 → Multiarteriales ($\geq 50\%$ en otras arterias) Follow-up (medio) 23 sem



- No preventiva – ICP → angina refractaria con evidencia objetiva de ischemia
- Interrupción precoz

PRAMI TRIAL

ICP Preventiva en el IAM

Outcome	Preventive PCI (N = 234) <i>no. of events</i>	No Preventive PCI (N = 231) <i>no. of events</i>	Hazard Ratio (95% CI)	P Value
Primary outcome				
Death from cardiac causes, nonfatal myocardial infarction, or refractory angina†	21	53	0.35 (0.21–0.58)	<0.001
Death from cardiac causes or nonfatal myocardial infarction†	11	27	0.36 (0.18–0.73)	0.004
Death from cardiac causes	4	10	0.34 (0.11–1.08)	0.07
Nonfatal myocardial infarction	7	20	0.32 (0.13–0.75)	0.009
Refractory angina	12	30	0.35 (0.18–0.69)	0.002
Secondary outcomes				
Death from noncardiac causes	8	6	1.10 (0.38–3.18)	0.86
Repeat revascularization	16	46	0.30 (0.17–0.56)	<0.001

IMA con ST Elevado

Directrices ACCF/AHA

Procedural aspects of primary PCI

Primary PCI should be limited to the culprit vessel with the exception of cardiogenic shock and persistent ischaemia after PCI of the supposed culprit lesion.

Ila

B

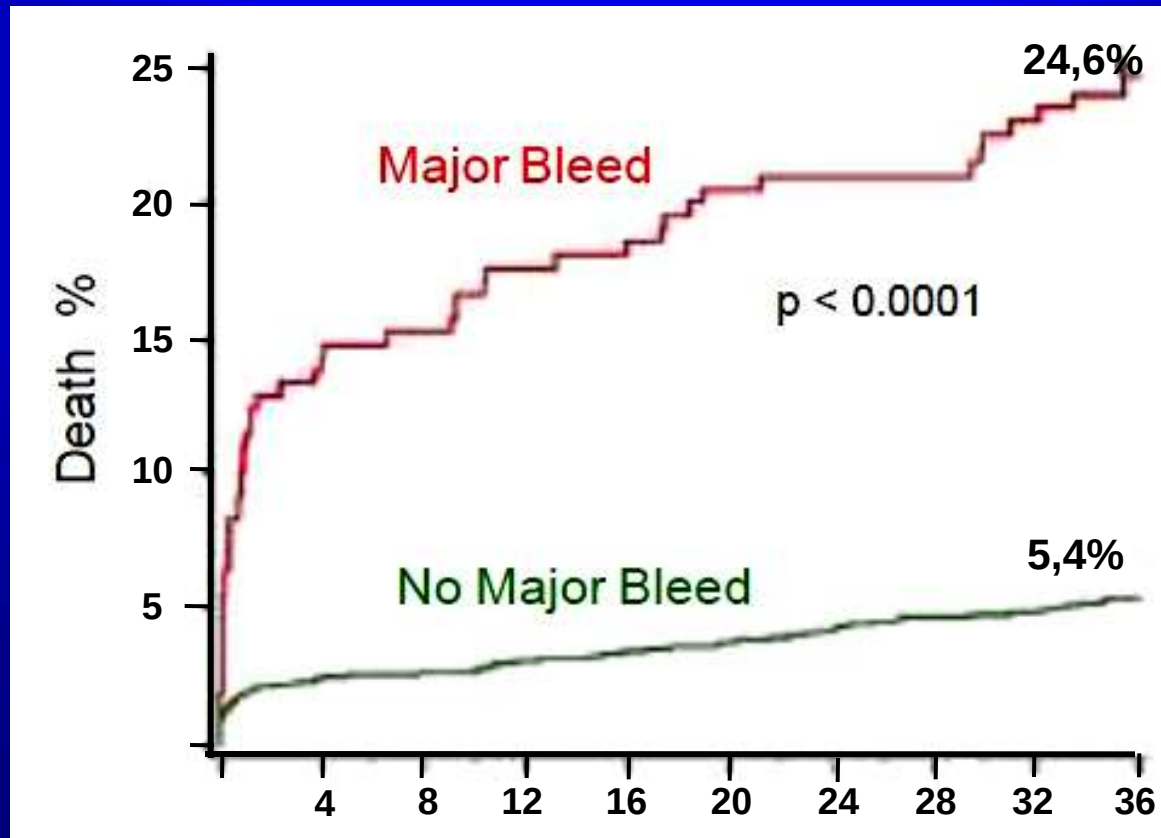
	COR	LOE
Ischemic symptoms <12 h	I	A
Ischemic symptoms <12 h and contraindications to fibrinolytic therapy irrespective of time delay from FMC	I	B
Cardiogenic shock or acute severe HF irrespective of time delay from MI onset	I	B
Evidence of ongoing ischemia 12 to 24 h after symptom onset	Ila	B
PCI of a noninfarct artery at the time of primary PCI in patients without hemodynamic compromise	III: Harm	B

Sangrados > Hospitalización

Mortalidad

HORIZONS AMI TRIAL (HNF + IGP IIb/IIIa vs Bivalirudina)

n = 3.602 STEMI ≤ 12 h ICP Primária

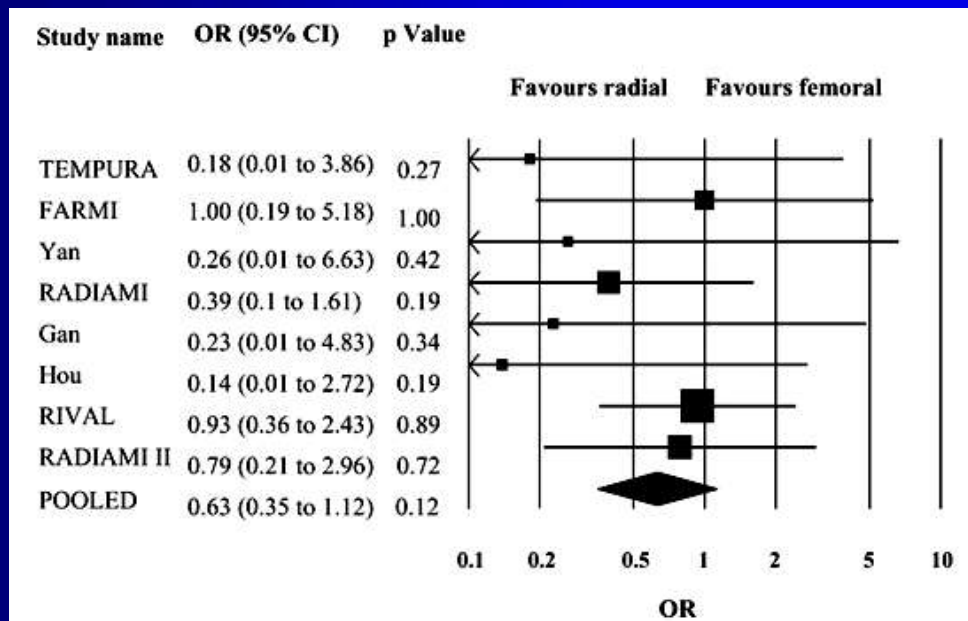


Radial vs Femoral

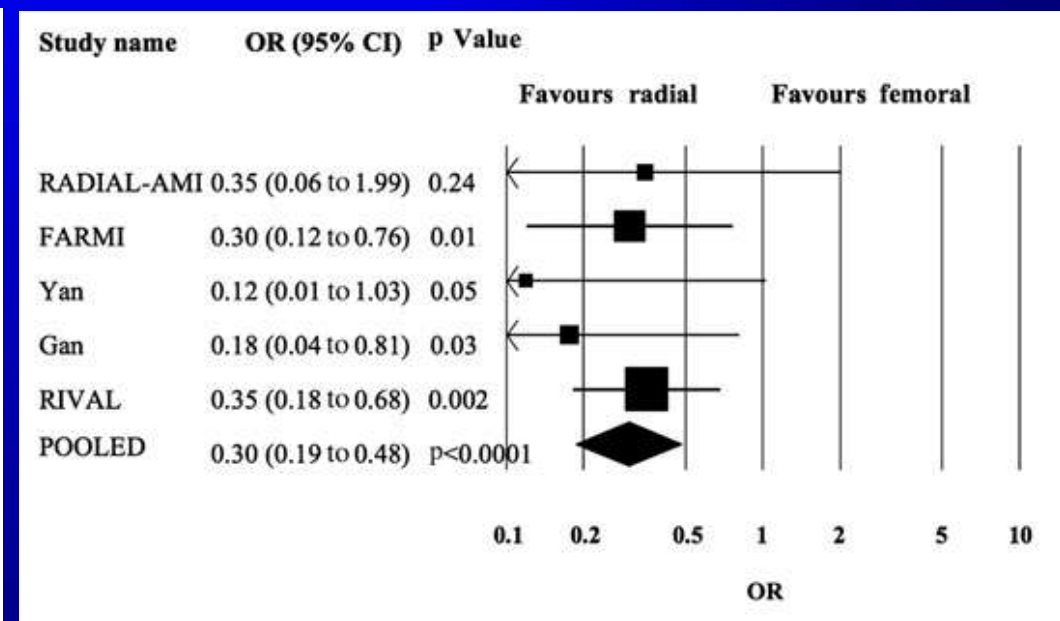
Complicaciones Vasculares/Sangrados >

8 Estudios Randomizados
2003 a 2011

ICP IAM con ST Elevado
n = 2.977



Sangrados >



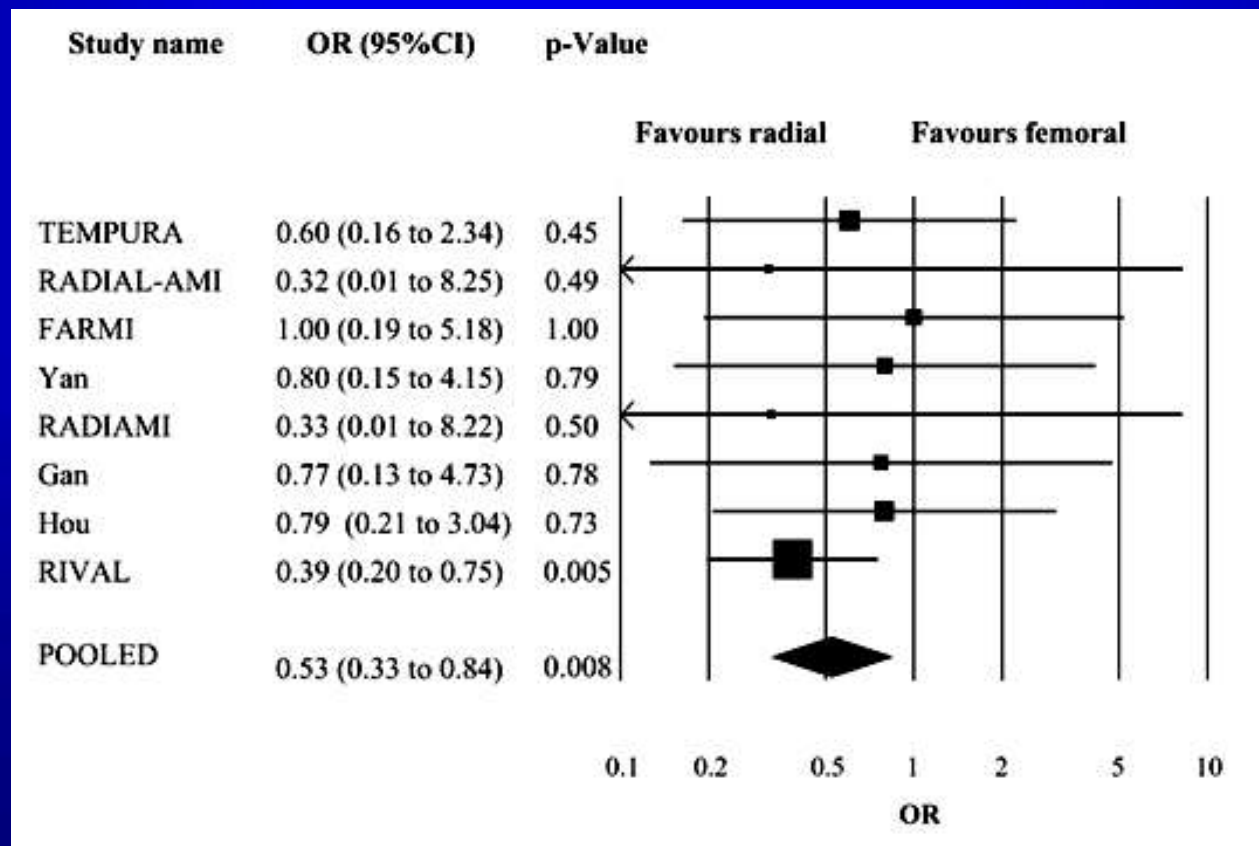
Complicaciones Vasculares

Mortalidad

Radial vs Femoral

9 Estudios Randomizados
2003 a 2011

ICP IAM con ST Elevado
n = 2.977

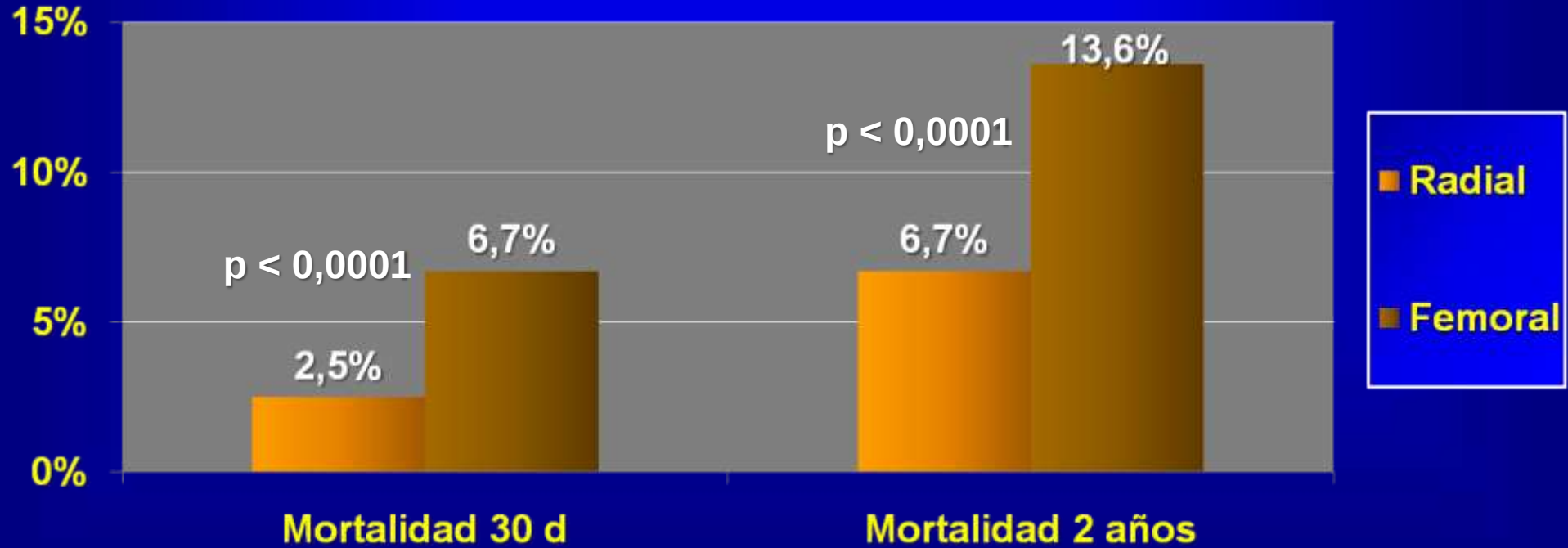


Radial vs Femoral

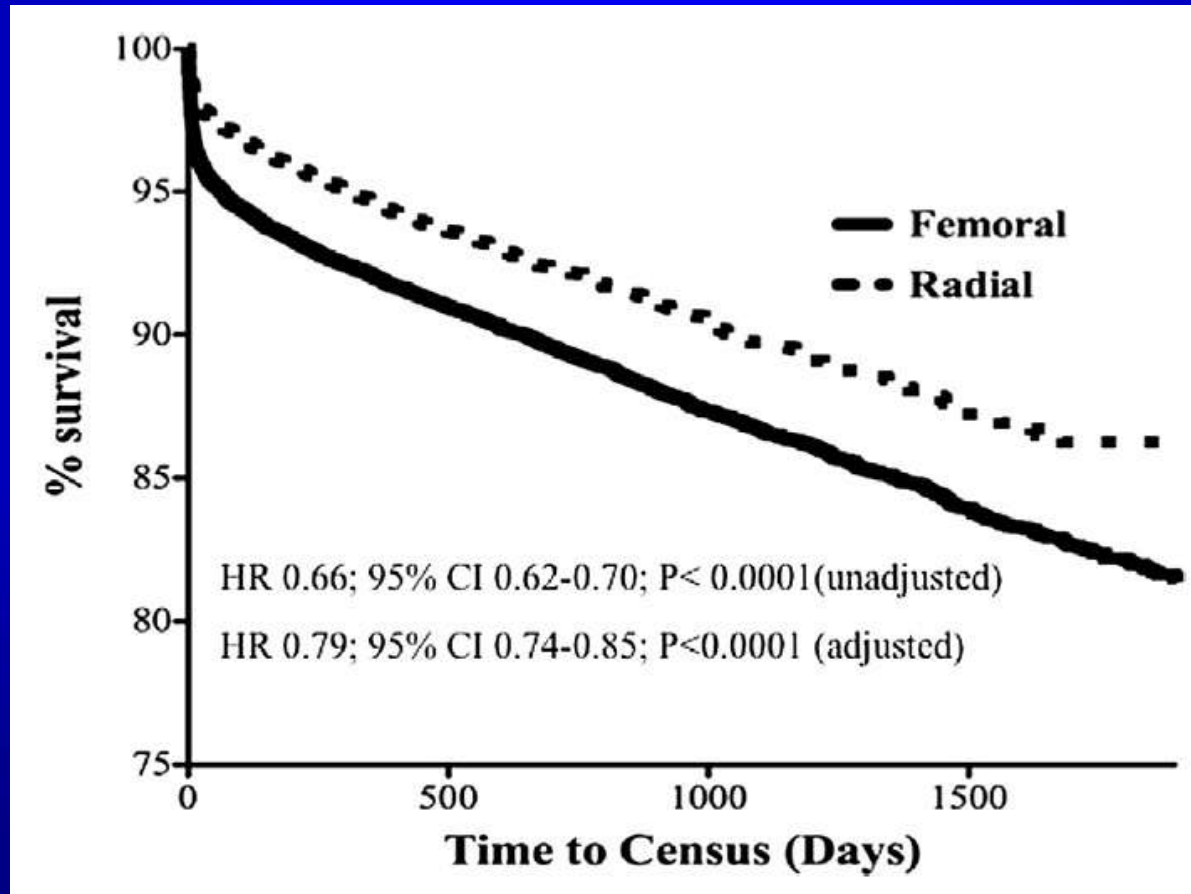
Práctica Clínica

2006 a 2010 Reino Unido n = 46.128 ICP IAM

Femoral n = 28.091 (60,9%) **Radial** n = 18.037 (39,1%)



Radial vs Femoral *Supervivencia*



Técnica Radial

Directrices Europea

Recommendations	Class	Level
Indications for primary PCI		
Primary PCI is the recommended reperfusion therapy over fibrinolysis if performed by an experienced team within 120 min of FMC.	I	A
Primary PCI is indicated for patients with severe acute heart failure or cardiogenic shock, unless the expected PCI related delay is excessive and the patient presents early after symptom onset.	I	B
Procedural aspects of primary PCI		
Stenting is recommended (over balloon angioplasty alone) for primary PCI.	I	A
Primary PCI should be limited to the culprit vessel with the exception of cardiogenic shock and persistent ischaemia after PCI of the supposed culprit lesion.	IIa	B
If performed by an experienced radial operator, radial access should be preferred over femoral access.	IIa	B
If the patient has no contraindications to prolonged DAPT (indication for oral anticoagulation, or estimated high long-term bleeding risk) and is likely to be compliant, DES should be preferred over BMS.	IIa	A
Routine thrombus aspiration should be considered.	IIa	B
Routine use of distal protection devices is not recommended.	III	C
Routine use of IABP (in patients without shock) is not recommended.	III	A

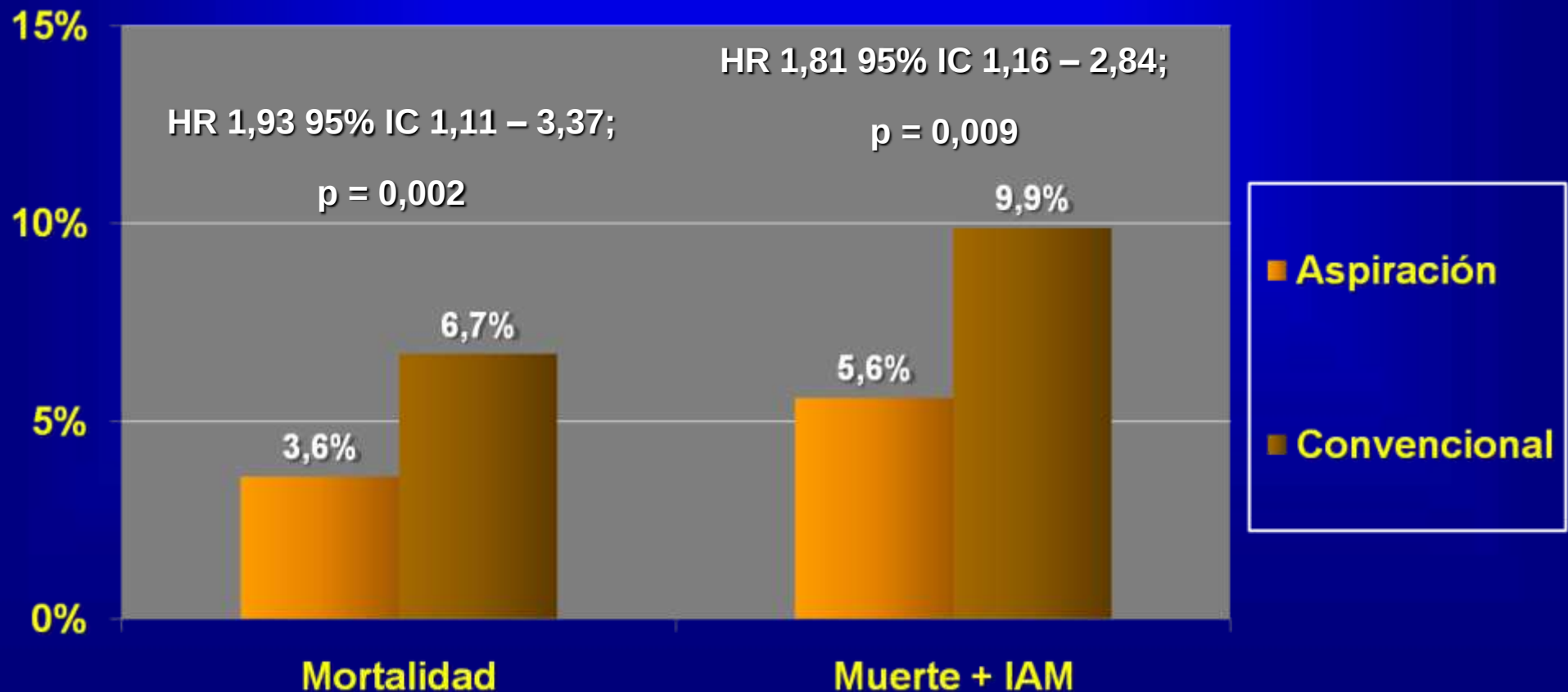
TAPAS TRIAL

Resultados 1 año

Export®

n = 1.701 IAM c/ Supra ST

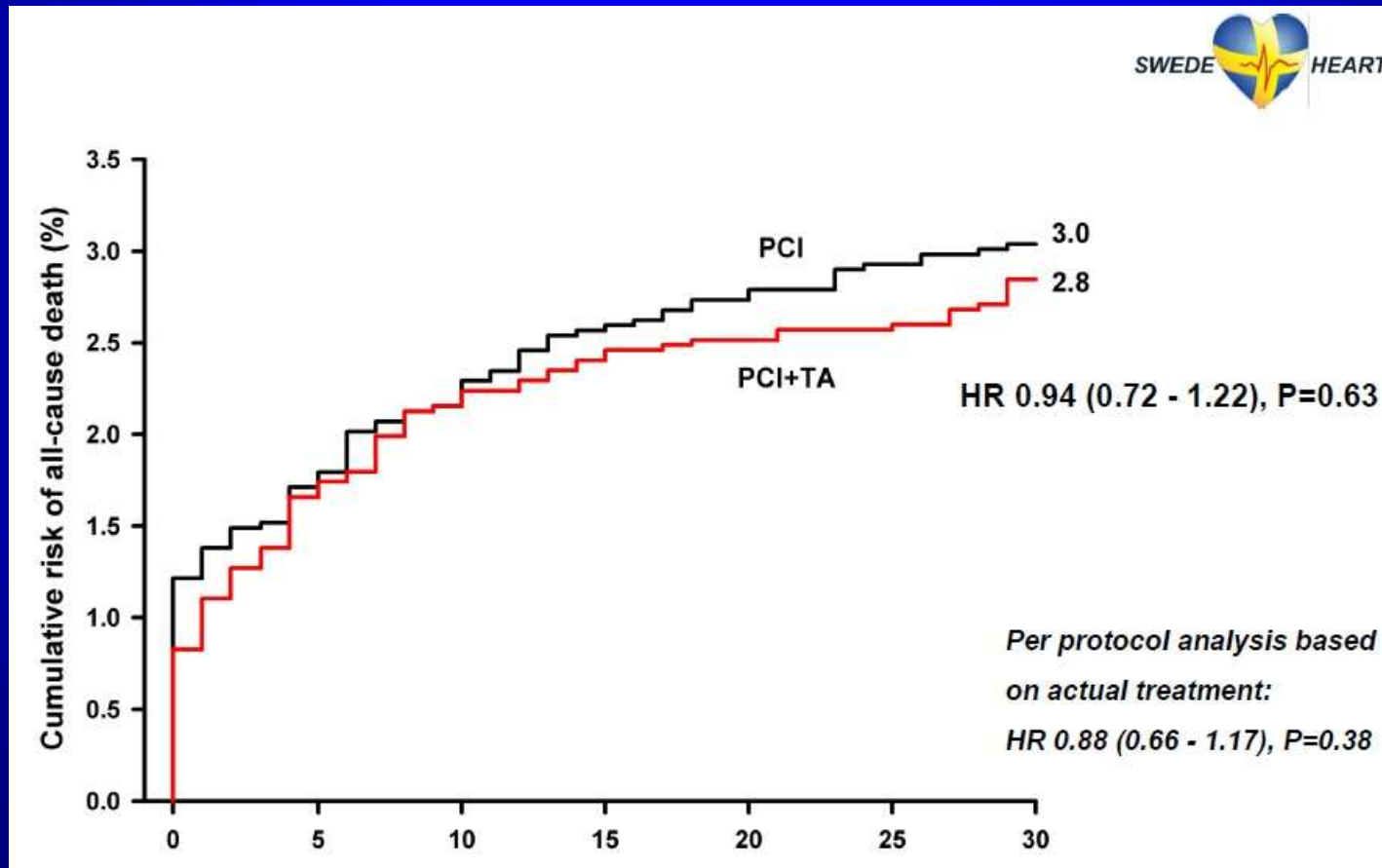
Enero/2005 a Diciembre/2006 Universidad Groningen/Holanda



TASTE TRIAL

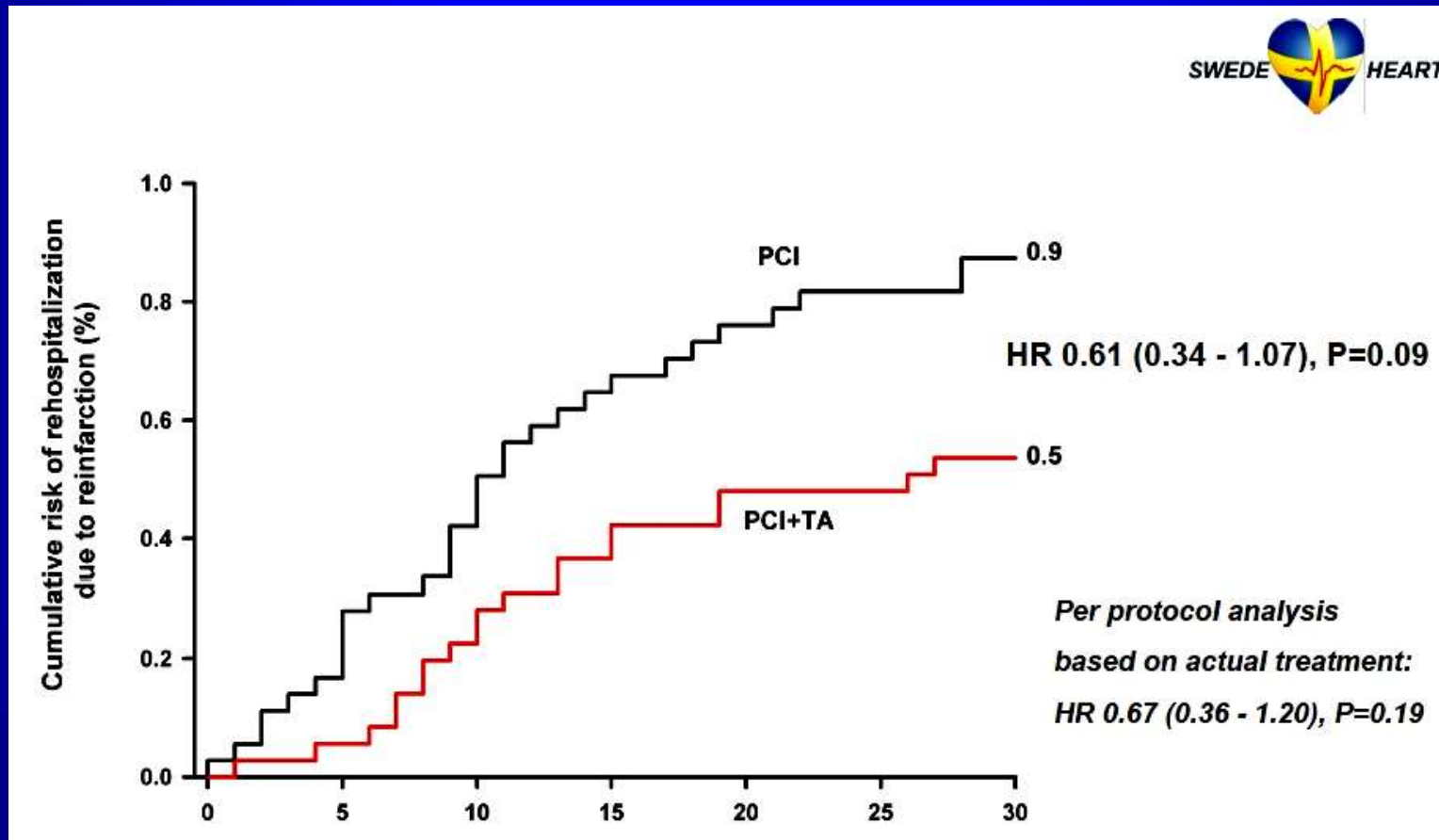
Mortalidad – 30 días

n = 7.244 STEMI < 24 h Aspiración Manual



TASTE TRIAL

Reinfarto – 30 días



Trombosis del Stent – ICP 0,5% vs ICP + TA 0,2% - p = 0,06

Frobert O. N Engl J Med 2013;369:1587-1597

Aspiración en la ICP Primaria

Directrices

Procedural aspects of primary PCI

Routine thrombus aspiration should be considered.	IIa	B
Routine use of distal protection devices is not recommended.	III	C
Routine use of IABP (in patients without shock) is not recommended.	III	A

3.2. Aspiration Thrombectomy

Class IIa

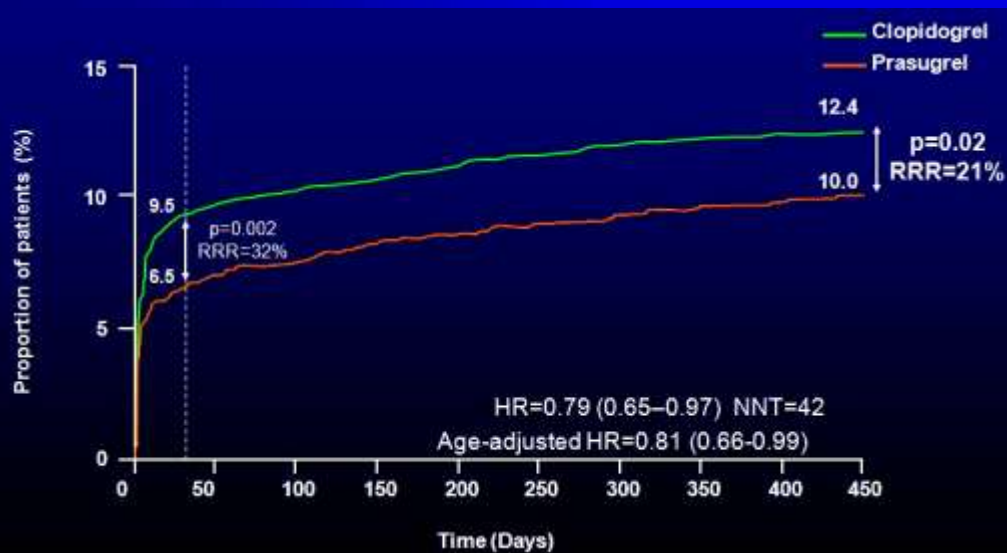
1. Manual aspiration thrombectomy is reasonable for patients undergoing primary PCI.⁶¹⁻⁶⁴ (*Level of Evidence: B*)

TRITON – TIMI 38

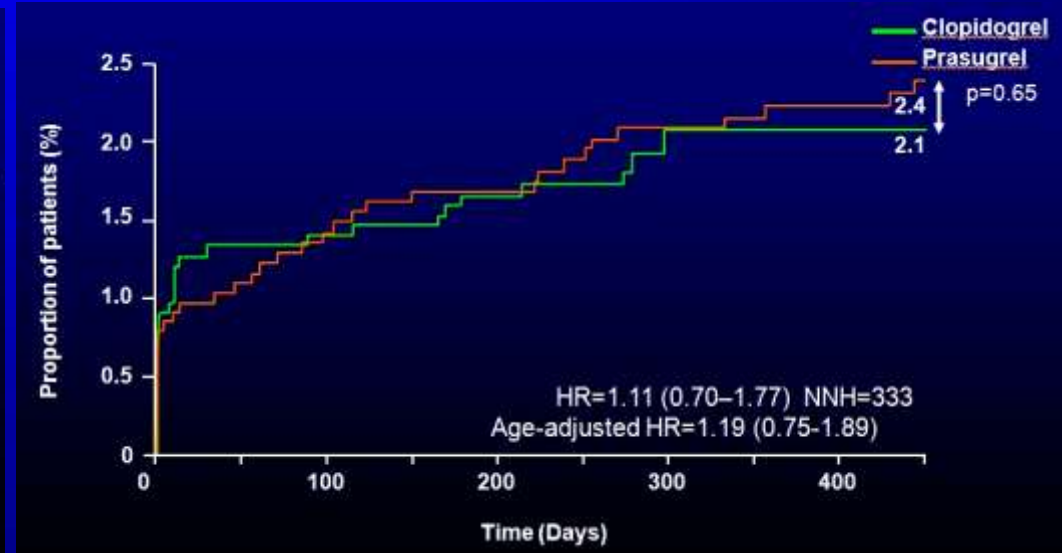
Prasugrel - Resultados

IAM com Supra ST

n = 3.534



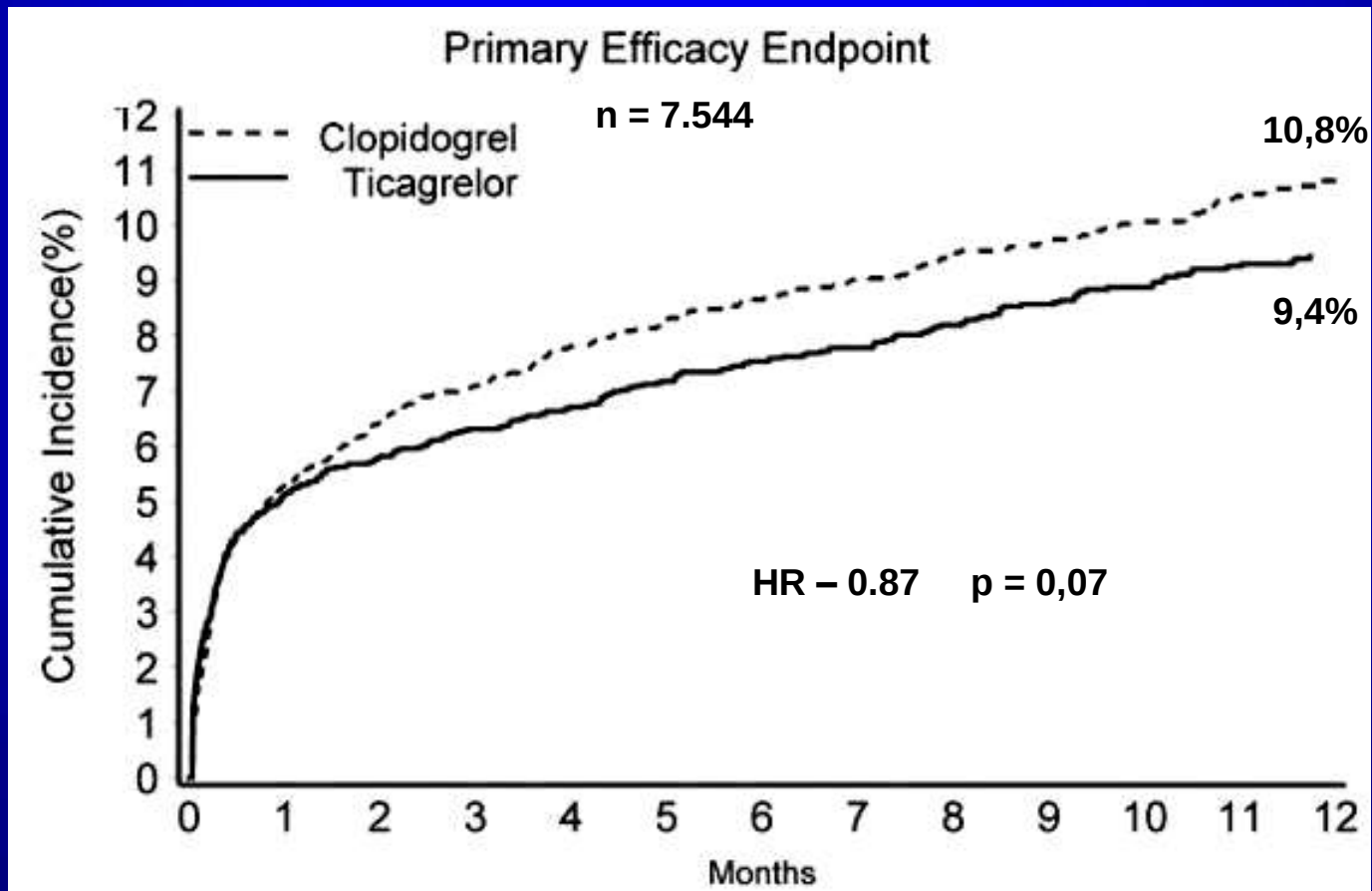
Muerte CV, IAM, AVC



Sangrado >

PLATO Trial

IAM com Supra de ST



IMA con ST Elevado

Directrices P2Y₁₂

P2Y₁₂ inhibitors

Loading doses

- Clopidogrel: 600 mg as early as possible or at time of PCI
- Prasugrel: 60 mg as early as possible or at time of PCI
- Ticagrelor: 180 mg as early as possible or at time of PCI

I	B
I	B
I	B

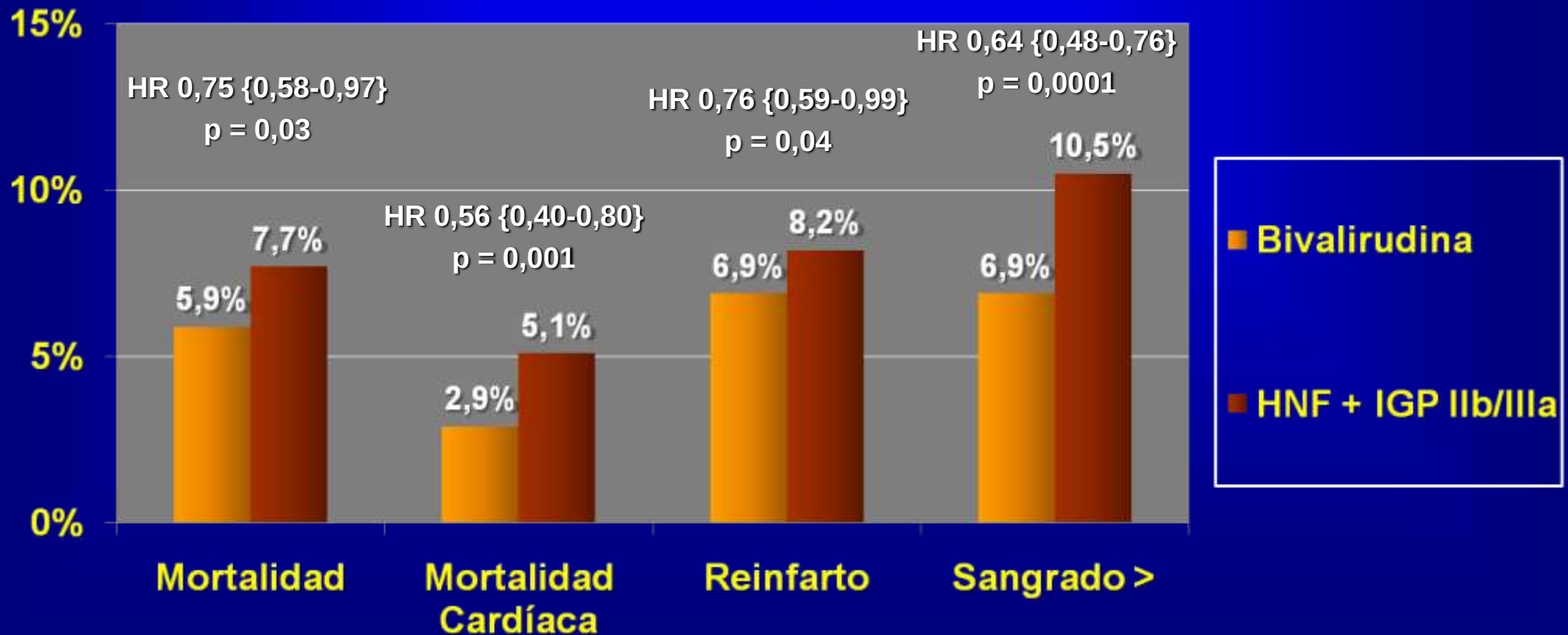
Recommendations	Class	Level
Antiplatelet therapy		
Aspirin oral or i.v. (if unable to swallow) is recommended	I	B
An ADP-receptor blocker is recommended in addition to aspirin. Options are:	I	A
• Prasugrel in clopidogrel-naïve patients, if no history of prior stroke/TIA, age < 75 years.	I	B
• Ticagrelor.	I	B
• Clopidogrel, preferably when prasugrel or ticagrelor are either not available or contraindicated.	I	C

HORIZONS TRIAL

Resultados 3 años

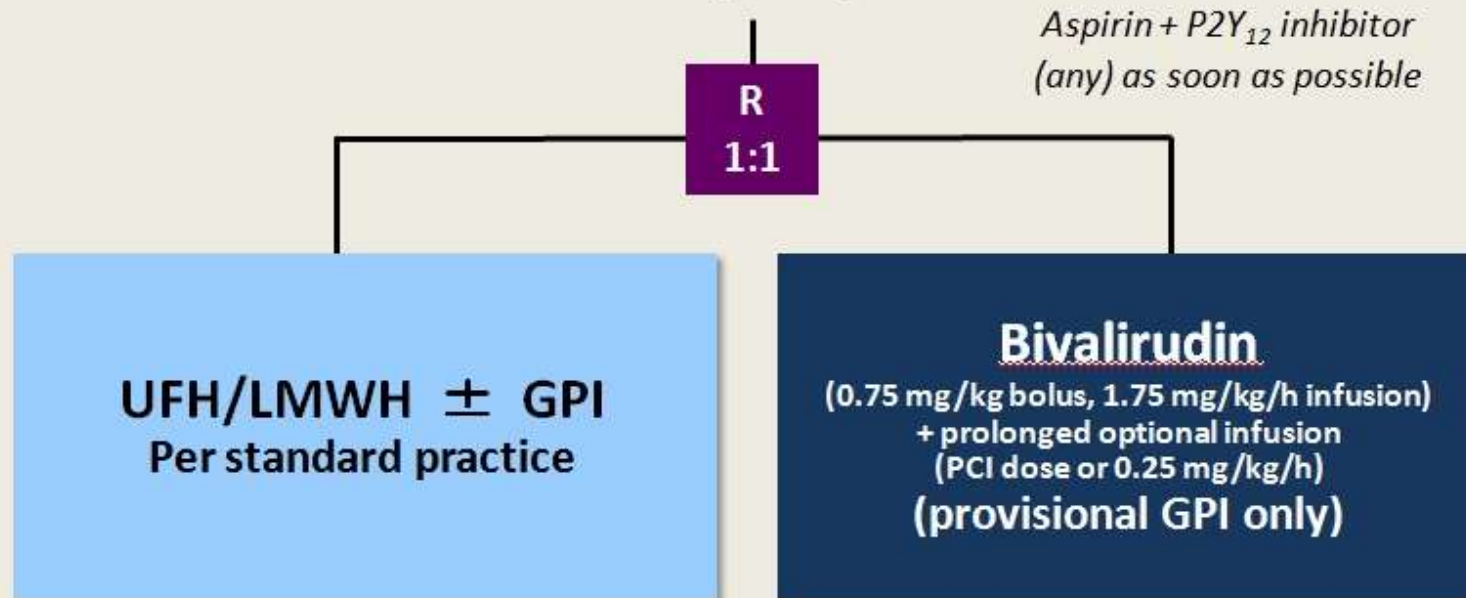
n = 3.602 123 centros

IAM c/ ST $\leq$ 12h $\rightarrow$ Coronariografía (83% ICP con Stent)



EUROMAX Trial Design

2218 patients with STEMI with symptom onset >20 min and ≤12h
Randomized in ambulance or non-PCI hospital
Intent for primary PCI



Primary endpoint: 30-day death or non-CABG related major bleeding

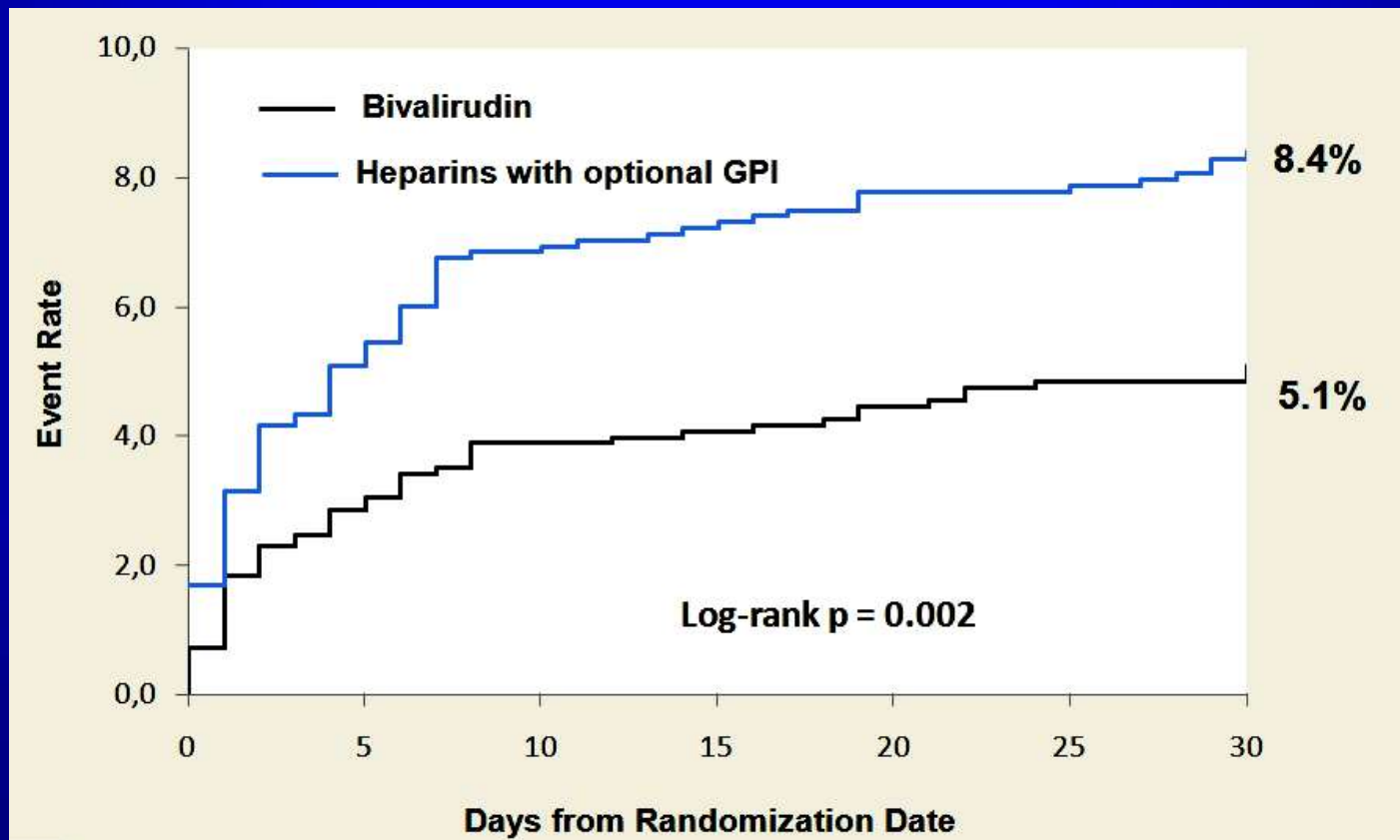
Key Secondary endpoint: Death, Re-infarction or non-CABG major bleeding at 30 days

Clinical FU at 30 days and 1 year

Euromax Trial

Muerte o Sangrado > - 30 días

Endpoint Primario



Euromax Trial

Evolución Clínica - 30 d

	Bivalirudin (N=1089)	Heparins with optional GPI (N=1109)	Relative risk [95% CI]	P Value
Death or major bleeding (non-CABG) (primary outcome)	55 (5.1)	94 (8.5)	0.60 (0.43–0.82)	0.001
Death, reinfarction, or major bleeding (non-CABG) (key secondary outcome)	72 (6.6)	102 (9.2)	0.72 (0.54–0.96)	0.02
Death	32 (2.9)	34 (3.1)	0.96 (0.60–1.54)	0.86
Cardiac causes	27 (2.5)	33 (3.0)	0.83 (0.50–1.38)	0.48
Noncardiac causes	5 (0.5)	1 (0.1)	5.09 (0.60–43.51)	0.12
Major bleeding (non-CABG)	28 (2.6)	67 (6.0)	0.43 (0.28–0.66)	<0.001
Major adverse cardiovascular events*	65 (6.0)	61 (5.5)	1.09 (0.77–1.52)	0.64
Net adverse clinical events *	85 (7.8)	118 (10.6)	0.73 (0.56–0.96)	0.02

Euromax Trial

Evolución Clínica - 30 d

	Bivalirudin (N=1089)	Heparins with optional GPI (N=1109)	Relative risk [95% CI]	P Value
Reinfarction	19 (1.7)	10 (0.9)	1.93 (0.90–4.14)	0.08
Q-wave	3 (0.3)	2 (0.2)	1.53 (0.26–9.12)	0.68
Non-Q-wave	16 (1.5)	8 (0.7)	2.04 (0.88–4.74)	0.09
Stent thrombosis (ARC definition)	17 (1.6)	6 (0.5)	2.89 (1.14–7.29)	0.02
Definite	17 (1.6)	6 (0.5)	2.89 (1.14–7.29)	0.02
Probable	0 (0)	0 (0)	–	n/a
Acute (≤24 hours)	12 (1.1)	2 (0.2)	6.11 (1.37–27.24)	0.007
Subacute (>24 hours to 30 days)	5 (0.5)	4 (0.4)	1.27 (0.34–4.73)	0.75
Ischemia-driven revascularization	24 (2.2)	17 (1.5)	1.44 (0.78–2.66)	0.25
Reinfarction, ischemia-driven revascularization or stent thrombosis	29 (2.7)	21 (1.9)	1.41 (0.81–2.45)	0.23
Any stroke	6 (0.6)	11 (1.0)	0.56 (0.21–1.50)	0.24
Ischemic	6 (0.6)	9 (0.8)	0.68 (0.24–1.9)	0.46
Hemorrhagic	0	2 (0.2)	Not applicable	0.50
Acquired thrombocytopenia	7 (0.7)	14 (1.4)	0.50 (0.20–1.24)	0.13

Recomendaciones Bivalirudina

Directrices

Anticoagulant therapy

- UFH:
 - With GP IIb/IIIa receptor antagonist planned: 50- to 70-U/kg IV bolus to achieve therapeutic ACT $\ddagger$
 - With no GP IIb/IIIa receptor antagonist planned: 70- to 100-U/kg bolus to achieve therapeutic ACT $\S$
- Bivalirudin: 0.75-mg/kg IV bolus, then 1.75-mg/kg/h infusion with or without prior treatment with UFH. An additional bolus of 0.3 mg/kg can be given if needed.
 - Reduce infusion to 1 mg/kg/h with estimated CrCl <30 mL/min
 - Preferred over UFH with GP IIb/IIIa receptor antagonist in patients at high risk of bleeding
- Fondaparinux: Not recommended as sole anticoagulant for primary PCI

I	C
I	C
I	B
IIa	B
III: Harm	B

Recommendations	Class	Level
Anticoagulants		
An injectable anticoagulant must be used in primary PCI.	I	C
Bivalirudin (with use of GP IIb/IIIa blocker restricted to bailout) is recommended over unfractionated heparin and a GP IIb/IIIa blocker.	I	B
Enoxaparin (with or without routine GP IIb/IIIa blocker) may be preferred over unfractionated heparin.	IIb	B
Unfractionated heparin with or without routine GP IIb/IIIa blocker must be used in patients not receiving bivalirudin or enoxaparin.	I	C
Fondaparinux is not recommended for primary PCI.	III	B
The use of fibrinolysis before planned primary PCI is not recommended.	III	A

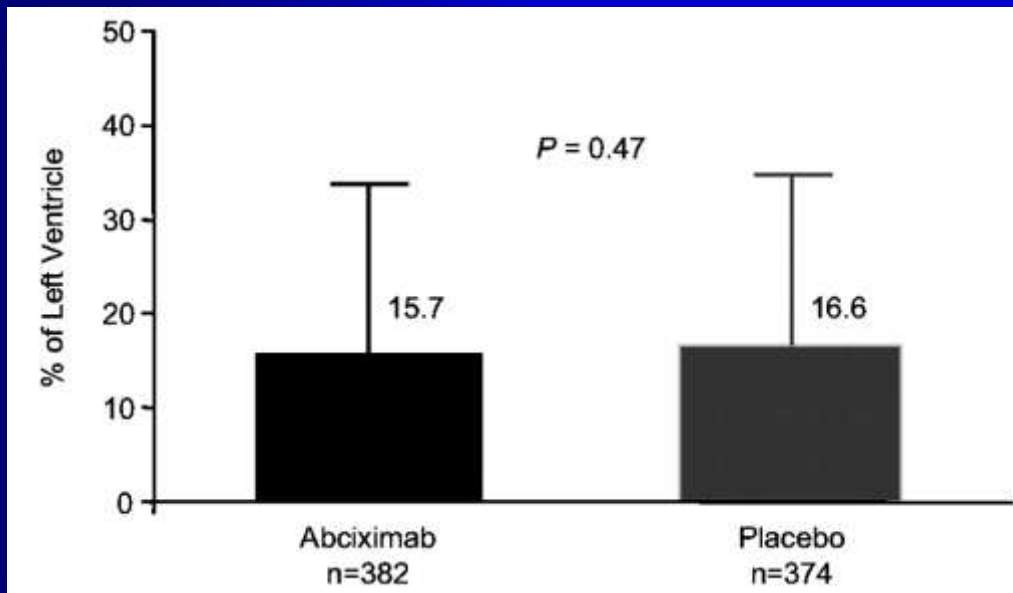
BRAVE 3 TRIAL

Endpoint Primario

n = 800

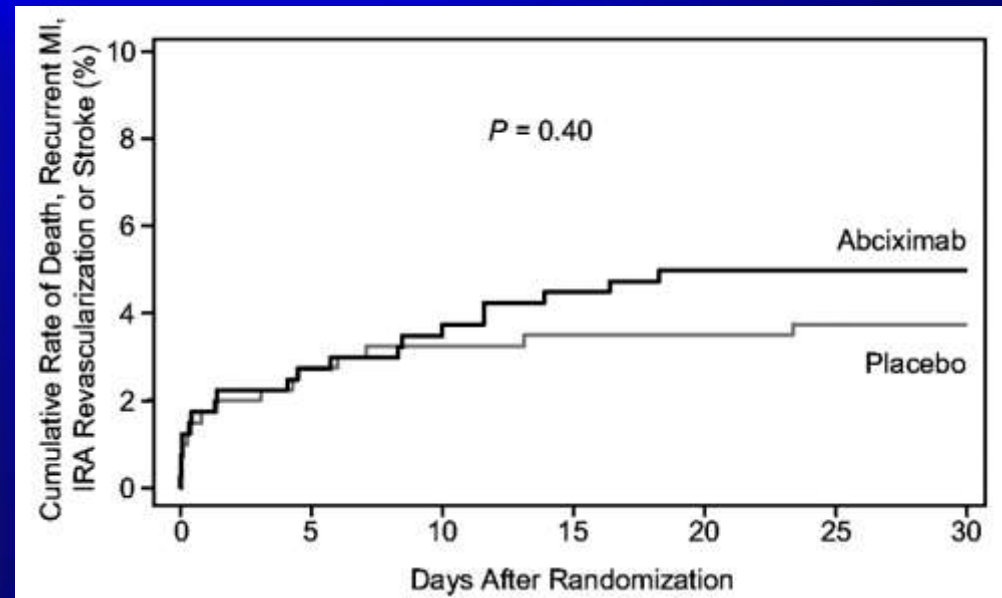
IAM < 24 h → ICP

Clopidogrel 600mg + AAS 500mg + Heparina 5000u



Enpoint Primario

Extensión del Infarto (SPECT)



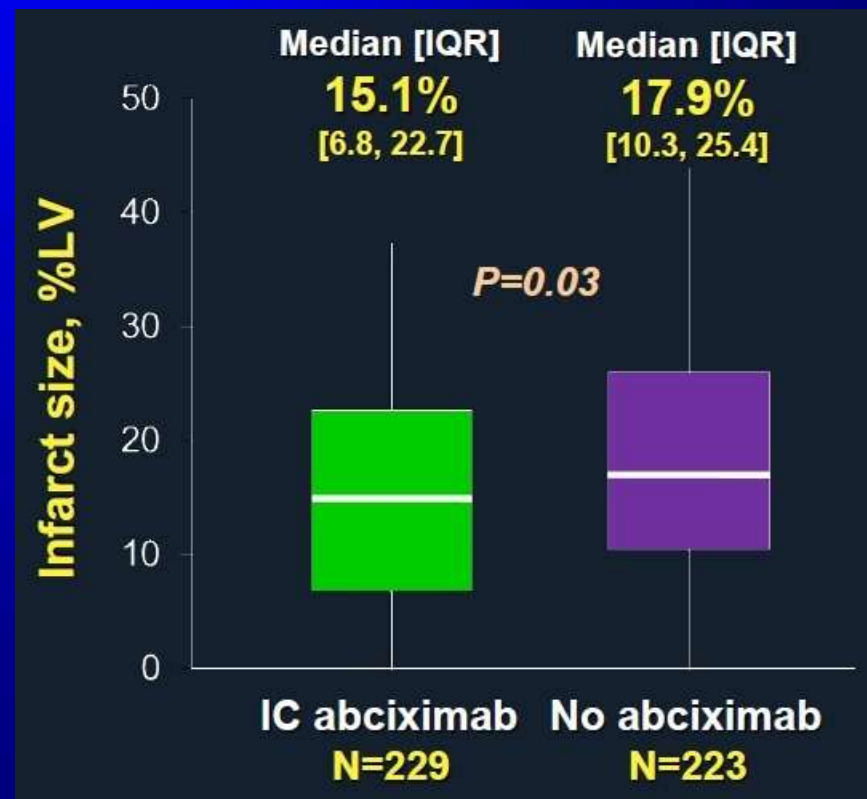
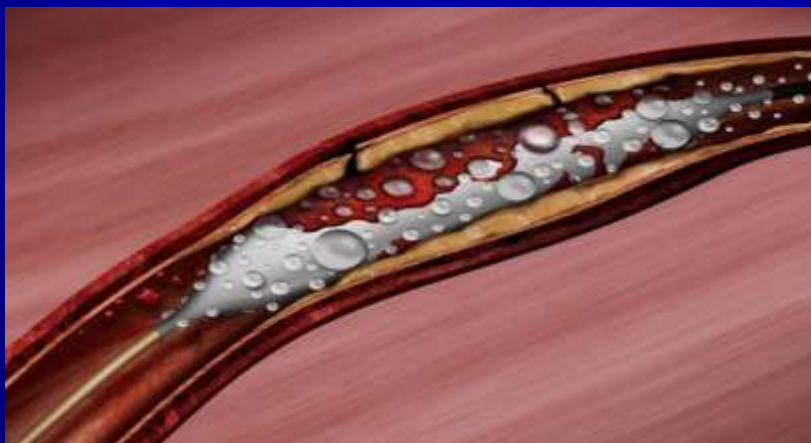
Mehilli J. Circulation 2009;119:1933-40

INFUSE – AMI

Abciximab Intracoronario

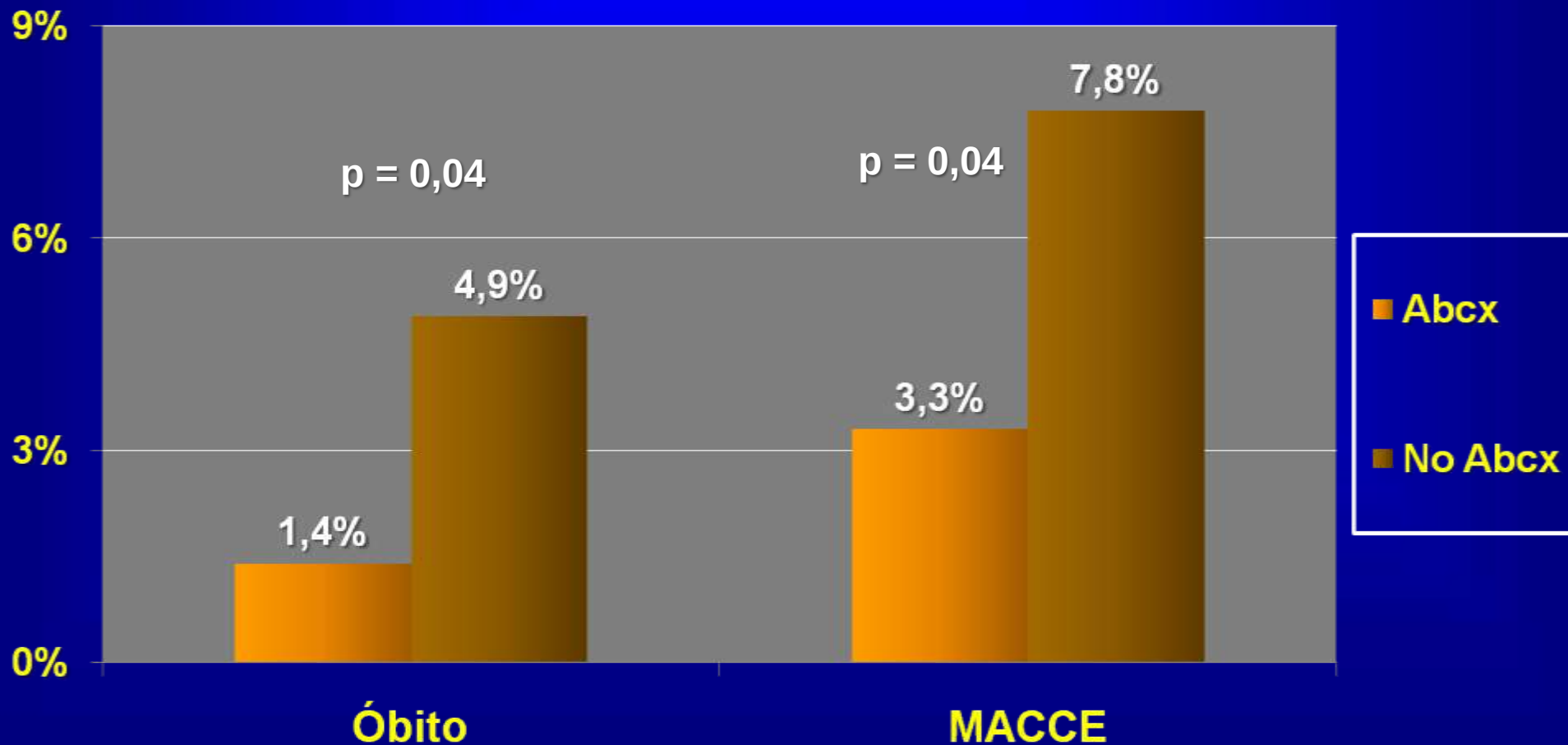
ICP Primaria Bivalirudina n = 452

STEMI Anterior < 5 h



INFUSE – AMI

Resultados – 30 dias a 1 ano



IMA con ST Elevado

Directrices ACCF/AHA

IV GP IIb/IIIa receptor antagonists in conjunction with UFH or bivalirudin in selected patients

- Abciximab: 0.25-mg/kg IV bolus, then 0.125 mcg/kg/min (maximum 10 mcg/min)
- Tirofiban: (high-bolus dose): 25-mcg/kg IV bolus, then 0.15 mcg/kg/min
 - In patients with CrCl <30 mL/min, reduce infusion by 50%
- Eptifibatide: (double bolus): 180-mcg/kg IV bolus, then 2 mcg/kg/min; a second 180-mcg/kg bolus is administered 10 min after the first bolus
 - In patients with CrCl <50 mL/min, reduce infusion by 50%
 - Avoid in patients on hemodialysis
- Pre-catheterization laboratory administration of IV GP IIb/IIIa receptor antagonist
- Intracoronary abciximab 0.25-mg/kg bolus

Ila	A
Ila	B
Ila	B
Ilb	B
Ilb	B

CARESS-IN-AMI

Diseño del Estudio

n = 600 3 Países (Francia, Italia e Polonia)

Centros s/ Laboratorio de Hemodinámica

IAMCEST ≤ 12 h Alto Risco:

**≤ 75 años con ≥ 1 criterio: Elevación ST Extensa, BRE nuevo, IAM previo,
Killip ≥ 2 , FEVE $\leq 35\%$**

Reteplase $\frac{1}{2}$ doses + AAS + Heparina + Abciximab

n = 1593

ICP Precoz ≤ 6 h

n = 1438

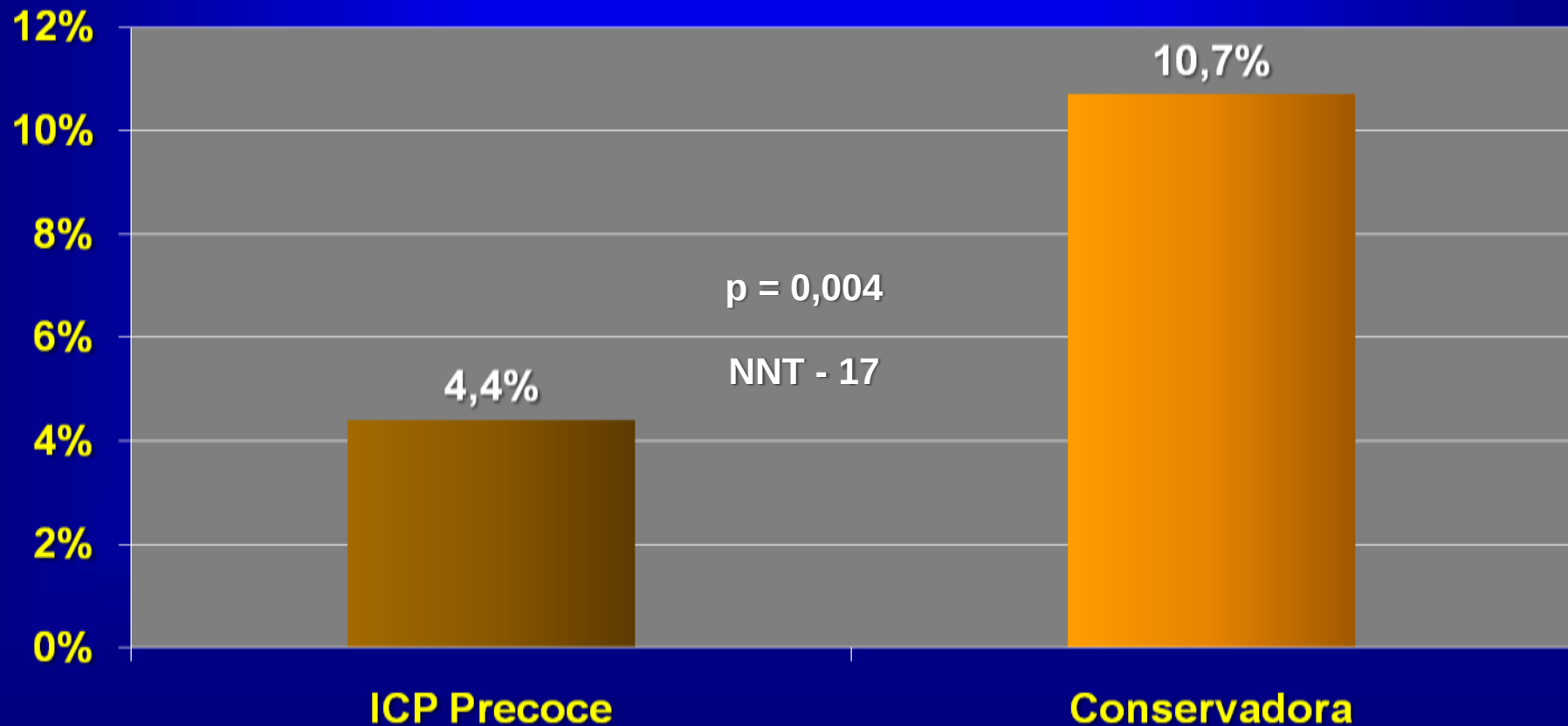
Conservadora

Transferencia ICP Rescate

CARESSS-IN-AMI

Objetivo Primario

Muerte, Reinfarto, Isquemia Recurrente – 30 días



TRANSFER - AMI

Diseño del Estudio

n = 1.059 Centros s/ Laboratorio de Hemodinámica

IAMCEST ≤ 12 h Alto Riesgo:

**IAM anterior o IAM inferior + 1 criterio: PAS < 100 mmHg, FC > 100 bpm,
Killip II/III, Depresión ST ≥ 2 mm anterior, Elevación ST V₄R**

TNK + AAS + Heparina + Clopidogrel (encorajado)

n = 1593

ICP Precoz ≤ 6 h

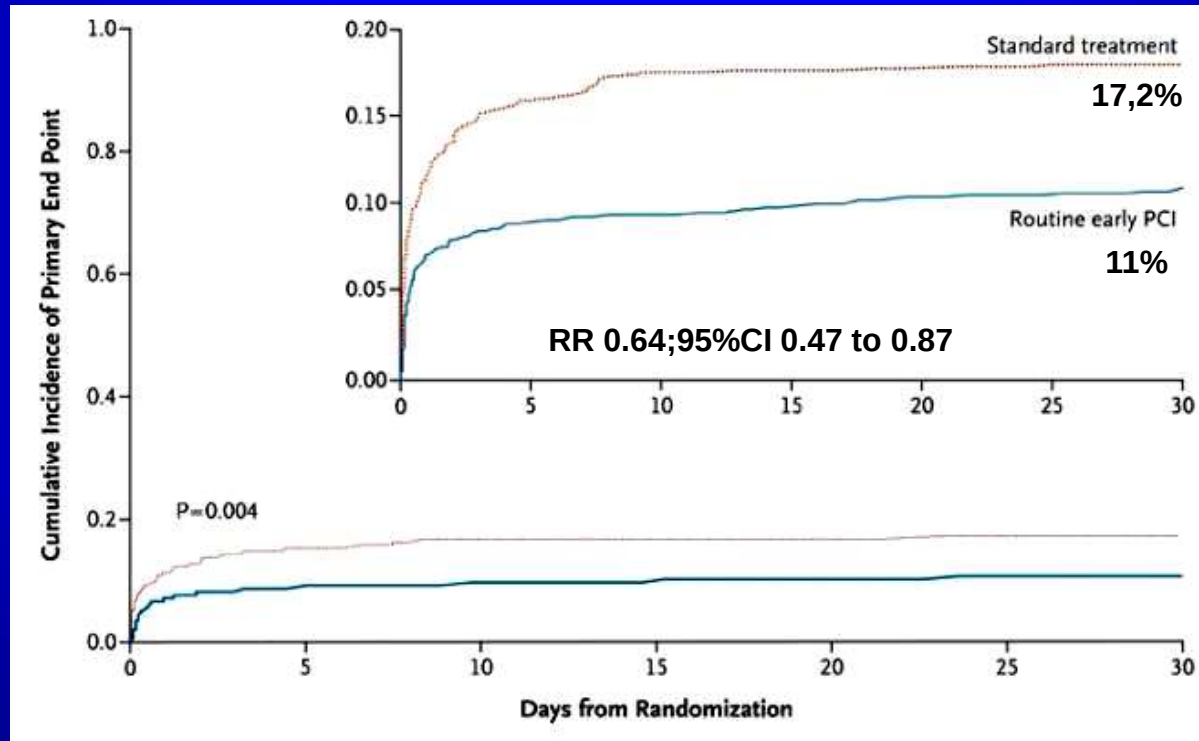
n = 1438

Conservadora (angiografía ≤ 2 sem)

ICP rescate/salvamento

TRANSFER - AMI

Desfecho Primário



Óbito, Reinfarto, Isq. Recorrente, IC nova ou piora, Choque Cardiogênico

Sangramento > TIMI ou GUSTO

ICP Precoce 7,4% vs Conservadora 9% (p = 0,36)

Cantor WJ N Engl J Med 2009;360:2705-18

Transferencia para ICP Pos Fibrinólisis

Directrices

Transfer to a PCI-capable centre following fibrinolysis		
Is indicated in all patients after fibrinolysis.	I	A
Interventions following fibrinolysis		
Rescue PCI is indicated immediately when fibrinolysis has failed (<50% ST-segment resolution at 60 min).	I	A
Emergency PCI is indicated in the case of recurrent ischaemia or evidence of reocclusion after initial successful fibrinolysis.	I	B
Emergency angiography with a view to revascularization is indicated in heart failure/shock patients.	I	A
Angiography with a view to revascularization (of the infarct-related artery) is indicated after successful fibrinolysis.	I	A
Optimal timing of angiography for stable patients after successful lysis: 3–24 h.	IIa	A

Class IIa

Transfer to a PCI-capable hospital for coronary angiography is reasonable for patients with STEMI who have received fibrinolytic therapy even when hemodynamically stable[§] and with clinical evidence of successful reperfusion. Angiography can be performed as soon as logistically feasible at the receiving hospital, and ideally within 24 hours, but should not be performed within the first 2 to 3 hours after administration of fibrinolytic therapy.^{133–138} (*Level of Evidence: B*)

IAM com Supra de ST

Stents Farmacológicos vs No Farmacológicos

n = 6.026

Seguimiento Clínico 3 a 5 anos

<u>DEATH</u>	DES	BMS	OR [95%CI]	P
DEDICATION	10.5%	6.4%	1.73 [0.97, 3.08]	0.06
PASEO	8.3%	12.2%	0.65 [0.29, 1.49]	0.31
STRATEGY	18.4%	15.9%	1.19 [0.54, 2.62]	0.66
SESAMI	3.2%	5.0%	0.61 [0.20, 1.92]	0.40
MISSION	4.4%	6.6%	0.69 [0.25, 1.85]	0.46
TYPHOON	4.0%	6.6%	0.61 [0.27, 1.36]	0.23
PASSION	8.9%	11.5%	0.75 [0.45, 1.27]	0.29
HORIZONS-AMI	5.6%	6.6%	0.84 [0.60-1.17]	0.33
META-ANALYSIS			0.88 [0.68-1.11]	0.27

<u>Stent thrombosis</u>	DES	BMS	OR [95%CI]	P
DEDICATION	2.9%	3.2%	0.90 [0.36, 2.24]	0.82
PASEO	1.1%	2.2%	0.49 [0.07, 3.57]	0.48
STRATEGY	6.9%	7.9%	0.86 [0.28, 2.66]	0.79
SESAMI	5.1%	5.1%	1.00 [0.37, 2.73]	1.00
MISSION	3.1%	2.0%	1.69 [0.40, 7.20]	0.48
TYPHOON	5.3%	5.5%	0.90 [0.42, 2.00]	0.83
PASSION	4.2%	3.4%	1.19 [0.52, 2.69]	0.68
HORIZONS-AMI	5.1%	4.4%	1.15 [0.77-1.72]	0.50
META-ANALYSIS			1.06 [0.81-1.39]	0.67

IAM com Supra de ST

Stents Farmacológicos vs No Farmacológicos

n = 6.026

Seguimiento Clínico 3 a 5 años

<u>TVR</u>	DES	BMS	OR [95%CI]	P
DEDICATION	8.9%	19.8%	0.40 [0.25, 0.64]	<0.01
PASEO	6.1%	21.1%	0.24 [0.11, 0.54]	<0.01
STRATEGY	10.3%	26.1%	0.33 [0.14, 0.75]	0.01
SESAMI	8.3%	16.0%	0.46 [0.23, 0.92]	0.03
MISSION	8.9%	15.8%	0.54 [0.27, 1.09]	0.09
TYPHOON	11.9%	21.5%	0.49 [0.30, 0.80]	<0.01
PASSION	7.7%	10.5%	0.73 [0.42, 1.26]	0.26
HORIZONS-AMI	12.5%	17.7%	0.67 [0.53-0.84]	0.001
META-ANALYSIS			0.50 [0.40-0.64]	<0.001

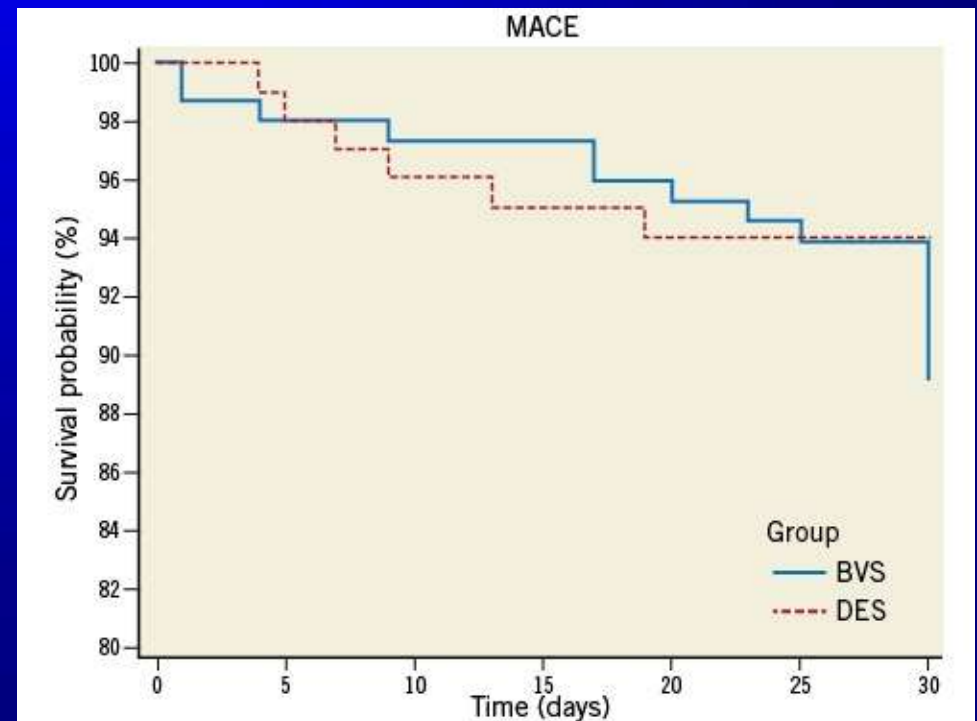
Síndrome Coronaria Aguda

Soporte Vascular Bioabsorbible (BVS)

Universidad de Mainz – Alemania Mayo/2012 a Junio/2013

n = 253 (STEMI 41%)

	BVS	DES *	p
In-hospital outcome	n = 150	n = 103	
Death	1 (0.7%)	1 (1%)	1
Non-fatal MI	3 (2.1%)	1 (1%)	0.63
Non-target lesion revascularisation	0	0	1
Definite in-stent/scaffold thrombosis	2 (1.4%)	1 (1%)	0.77
Hospital stay, days	4.9±2.7	4.7±2.6	0.8
One-month outcome			
Death	2 (1.4%)	3 (2.9%)	0.66
Non-fatal MI	6 (4.0%)	4 (3.9%)	1
Non-target lesion revascularisation	10 (6.6%)	7 (6.9%)	1
Definite in-stent/scaffold thrombosis	3 (2.0%)	2 (1.9%)	1
Probable in-stent/scaffold thrombosis	1 (0.7%)	1 (1%)	1



Stents Farmacológicos no IAM

Directrices AHA/ACC

3.3. Use of Stents in Patients With STEMI

Class I

- 1. Placement of a stent (bare-metal stent or drug-eluting stent) is useful in primary PCI for patients with STEMI.^{65,66} (*Level of Evidence: A*)**
- 2. Bare-metal stents[†] should be used in patients with high bleeding risk, inability to comply with 1 year of dual antiplatelet therapy (DAPT), or anticipated invasive or surgical procedures in the next year. (*Level of Evidence: C*)**

ICP no IAM

Conclusiones

- **Porque** - > Eficacia e Seguridad comparada a los fibrinolíticos
 - **Cuando** - + precoz (< 90m)
 - **Técnicas** - Acceso Radial Preferencial
- Tromboaspiración - > carga de trombos, choque cardiogénico
 - Stents Farmacológicos – ↓ RVA; Seguridad ≈ BMS
 - **Farmacología Adjunta**
Prasugrel, Ticagrelor – Mejores resultados
Bivalirudina - ↓ Sangrado (Pacientes de alto riesgo)
> Trombosis do Stent