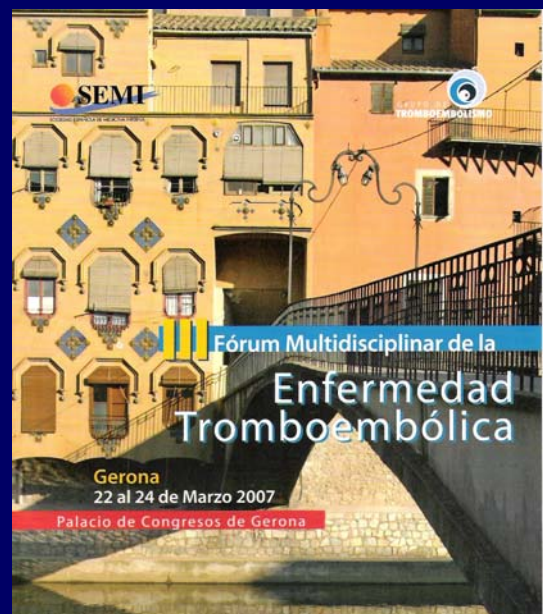
Caso clínico III:
Embolia pulmonar hemodinámicamente inestable

FJ Muñoz
Medicina Interna
Hospital de Mollet



Caso clínico

- Hombre de 34 años.
- No antecedentes familiares de interés.
- Profesión: profesor.
- Reside en Cartagena y realiza frecuentes viajes a Madrid en coche.
- Fumador activo de 10 cig/día.
- AP: IQ por fractura traumática de antebrazo hace años.

Caso clínico

- Enfermedad actual: disnea progresiva de 1 mes de evolución hasta hacerse de mínimos esfuerzos. El 29/12/2005 sensación de muerte inminente.
- Urgencias: TA 85/40 mmHg, FC 90lpm, obnubilación y relajación de esfínteres.
- UCI: shock cardiogénico con PCR, IOT con maniobras de RCP y drogas vasoactivas.

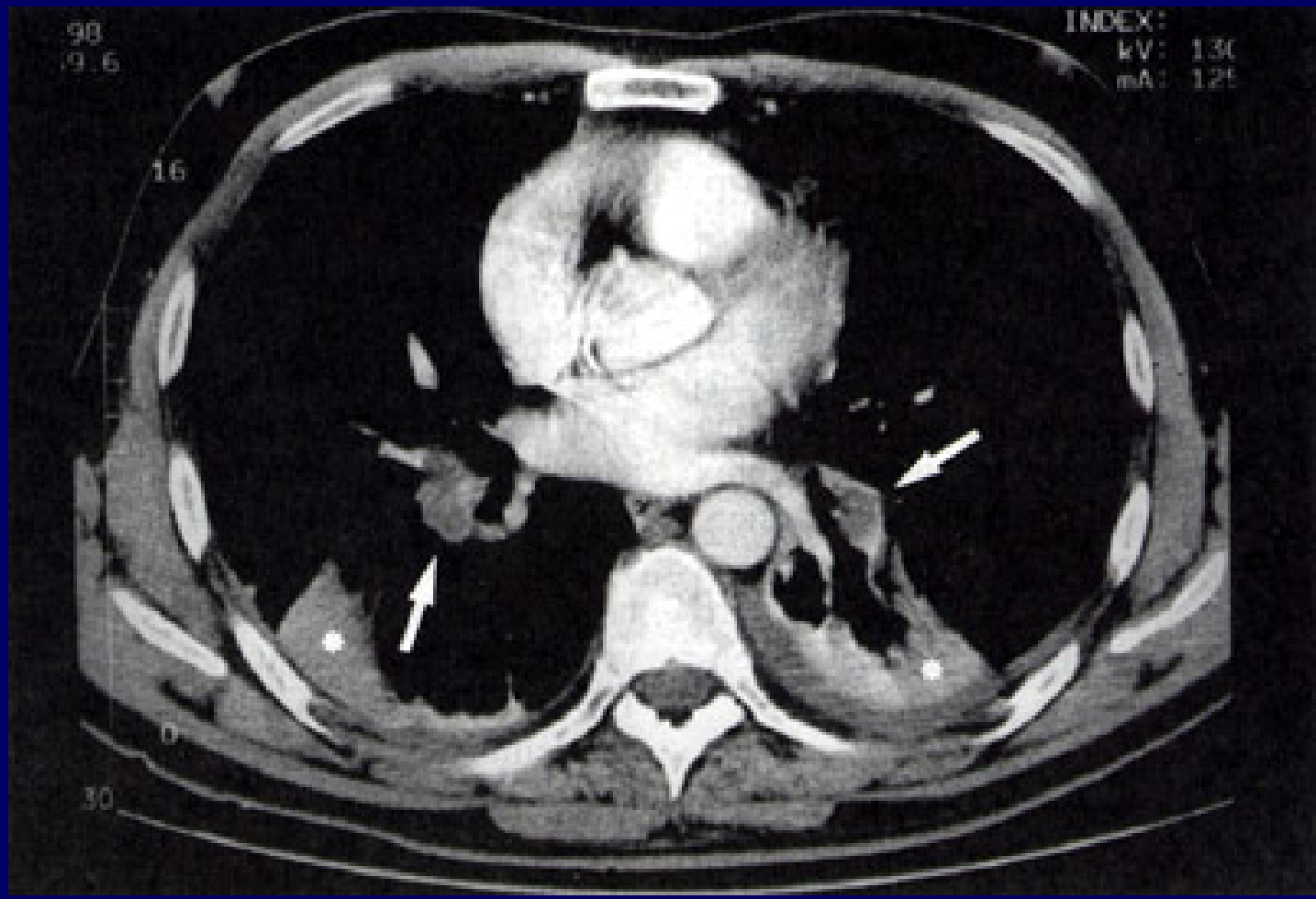
Caso clínico

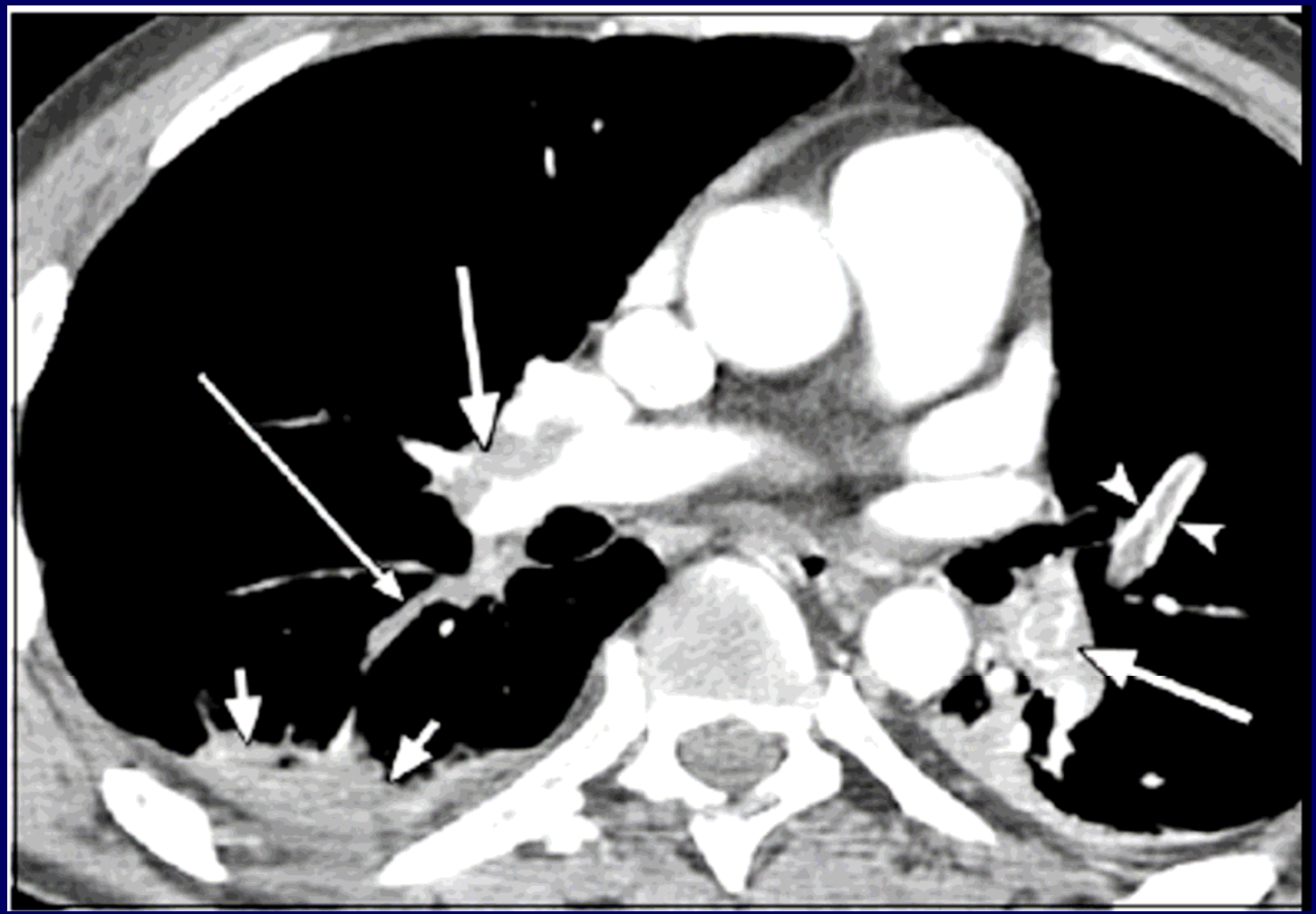
- Analítica: Hb 16g/dl, leucocitos 17.000/mm^3, plaquetas 209.000/mm^3, tasa de protrombina 69%, creatinina normal, dímero-D no realizado, pO2 20mmHg, pCO2 89mmHg.
- RX tórax: normal.
- ECG: ritmo sinusal con Q en DIII y T- en DIII y precordiales derechas.

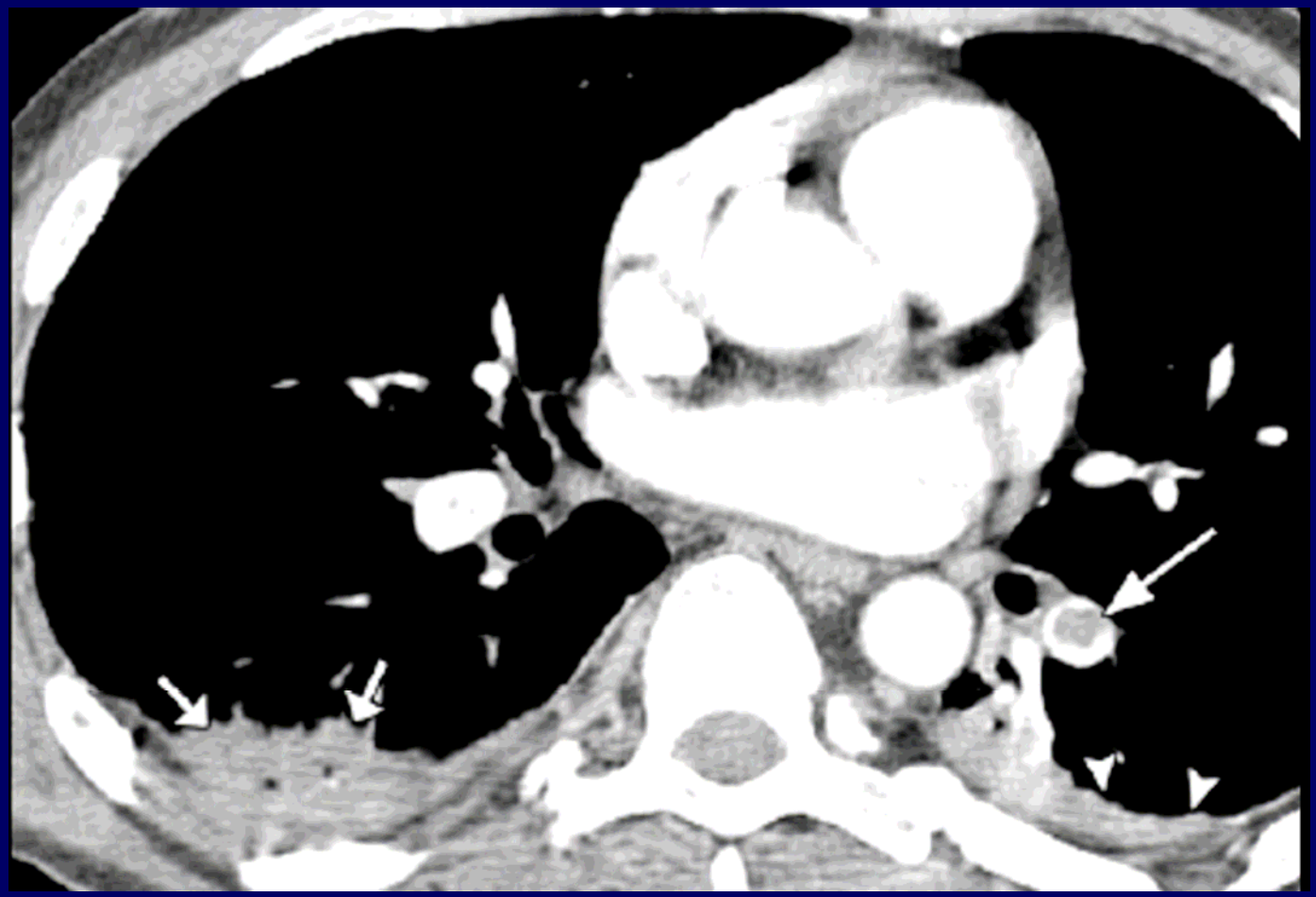
Caso clínico

Exploraciones complementarias:

- Ecocardiografía: dilatación de VD con HTp.
- Angio-TAC: trombos en ambas arterias pulmonares principales, arterias lobares de ambos lóbulos superiores y lóbulo medio, y segmentarias de ambos lóbulos inferiores.
- Eco-doppler venoso de MMII: TVP en EII a nivel poplíteo.


98
9.6
INDEX:
kV: 13(
mA: 12(
16
30





Caso clínico

- Evolución hospitalaria:
  1. Fibrinolisis con T-NK.
  2. Anticoagulación con HNF durante 20 días.
  3. Paso a ACO.

Caso clínico

- Evolución posthospitalaria:
  - 6 meses con ACO con mejoría clínica.
  - Suspensión del tratamiento tras realizar angio-TAC de control (normal) y estudio de trombofilia (negativo).

1. ¿Cuál es la mejor técnica para el diagnóstico del EP masivo?
2. ¿Cómo podemos estratificar mejor el riesgo del EP?
3. ¿Cuál es el mejor tratamiento inicial del EP hemodinámicamente inestable?
4. ¿Cuánto tiempo debe prolongarse el tratamiento anticoagulante?

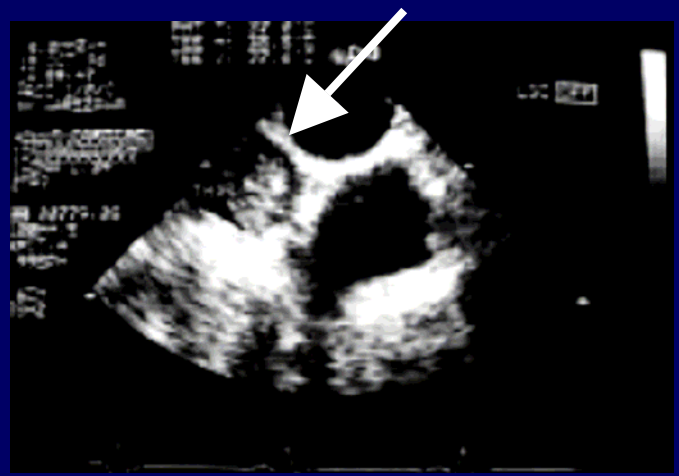
¿Cuál es la mejor prueba para el diagnóstico del EP inestable?

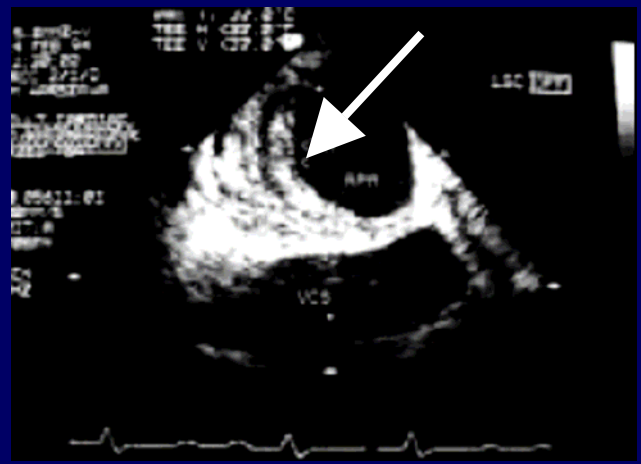
- No existe ningún algoritmo diagnóstico validado.
- Las exploraciones más utilizadas para el diagnóstico son:
  1. Ecocardiografía.
  2. Angio-TAC torácica.

Ecocardiografía transtorácica

- Tiene un claro valor pronóstico.
- Signos indirectos de TEP masivo:
  - Disfunción de VD (hipocinesia grave).
  - Detección de HTp.
  - Detección de trombos móviles en cavidades derechas.
  - Persistencia de foramen oval abierto.

Ecocardiografía transesofágica





Ecocardiografía transesofágica

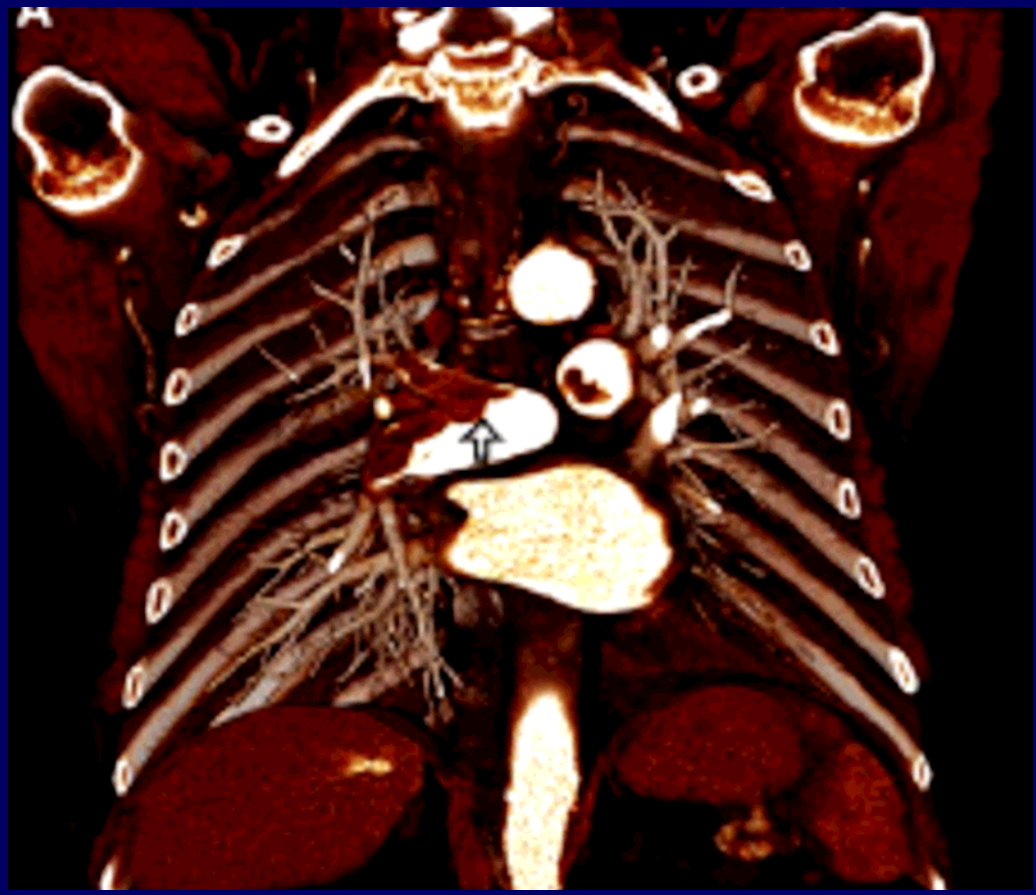
	Total TEP	Agudo	Crónico
Sensibilidad (%)	80,5	76,1	85,7
Especificidad (%)	97,2	100	96,3
VPP (%)	98,4	100	96,7
VPN (%)	70	47,3	83,8

Pruszczyk P et al. Heart 2001

Angio-TAC torácica

- Ventajas:
  - Visualización directa del trombo.
  - Diagnósticos alternativos.
  - Coste-efectiva.
  - Alto VPN para EP.

- Limitaciones:
  - Necesidad de contraste yodado.
  - Exposición a la radiación.
  - Dificultad para detectar émbolos periféricos.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The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 1, 2006 VOL. 354 NO. 22

Multidetector Computed Tomography for Acute Pulmonary Embolism

Paul D. Stein, M.D., Sarah E. Fowler, Ph.D., Lawrence R. Goodman, M.D., Alexander Gottschalk, M.D., Charles A. Hales, M.D., Russell D. Hull, M.B., B.S., M.Sc., Kenneth V. Leeper, Jr., M.D., John Popovich, Jr., M.D., Deborah A. Quinn, M.D., Thomas A. Sos, M.D., H. Dirk Sostman, M.D., Victor F. Tapson, M.D., Thomas W. Wakefield, M.D., John G. Weg, M.D., and Pamela K. Woodard, M.D., for the PIOPED II Investigators*

Table 5. Positive and Negative Predictive Values of CTA, as Compared with Previous Clinical Assessment.*

Variable	High Clinical Probability		Intermediate Clinical Probability		Low Clinical Probability	
	No./Total No.	Value (95% CI)	No./Total No.	Value (95% CI)	No./Total No.	Value (95% CI)
Positive predictive value of CTA	22/23	96 (78–99)	93/101	92 (84–96)	22/38	58 (40–73)
Positive predictive value of CTA or CTV	27/28	96 (81–99)	100/111	90 (82–94)	24/42	57 (40–72)
Negative predictive value of CTA	9/15	60 (32–83)	121/136	89 (82–93)	158/164†	96 (92–98)
Negative predictive value of both CTA and CTV	9/11	82 (48–97)	114/124	92 (85–96)	146/151†	97 (92–98)

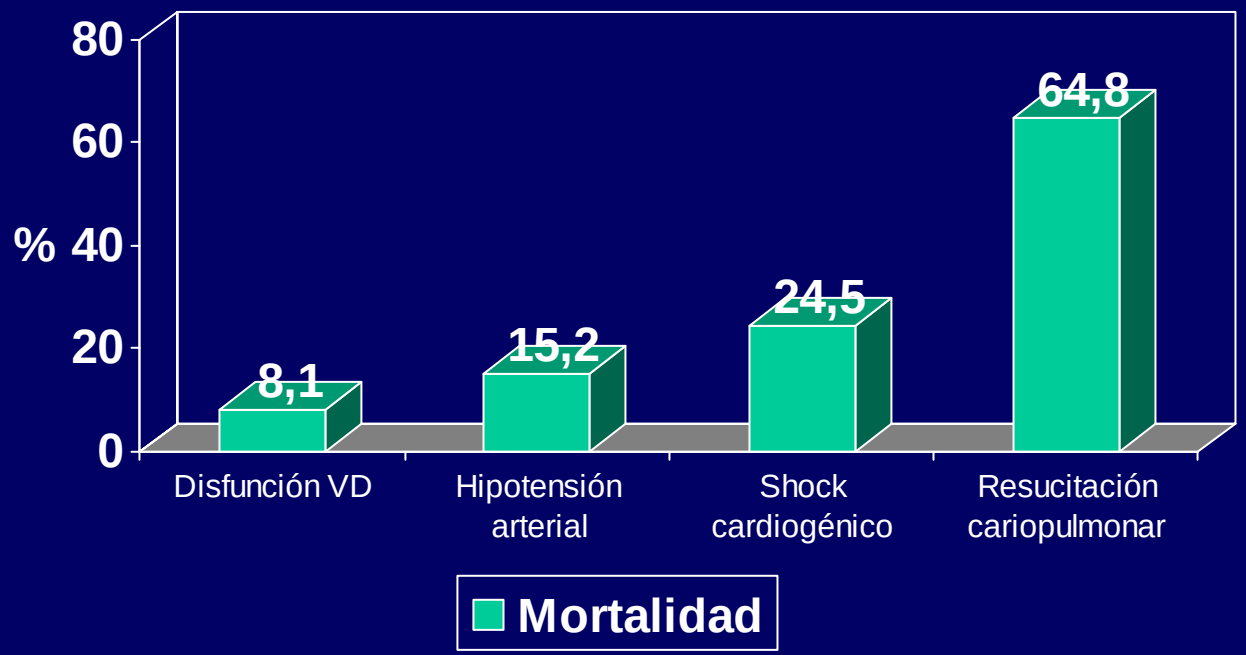
The PIOPED II study. N Engl J Med 2006

Reference	Year	Journal	Patients Without Anticoagulation Based on Normal CT, n	Follow-Up Period	Documented DVT/PE in Patients Without Anticoagulation, n	Negative Predictive Value of Normal CT for Ruling out PE, %
Garg[51]	1999	*AJR Am J Roentgenol*	78	6 mo	1	99
Lomis[52]	1999	*J Vasc Interv Radiol*	100	6–24 mo	0	100
Goodman[53]	2000	*Radiology*	198	3 mo	2	99
Blachere[29]	2000	*AJR Am J Roentgenol*	104	124–479 d	3	96.2
Gottsater[54]	2001	*Eur Radiol*	215	3 mo	3	99.1
Ost[55]	2001	*Am J Med*	71	6 mo	3	96
Tillie-Leblond[56]	2002	*Radiology*	185	12 mo	3	98
Swensen[57]	2002	*Mayo Clin Proc*	993	3 mo	8	99
Nilsson[58]	2002	*Acta Radiol*	441	3 mo	4	99.1
Musset[59]	2002	*Lancet*	507	3 mo	9	98.8
Van Strijen[60]	2003	*Ann Intern Med*	246	3 mo	1	99.2

Schoepf UJ et al. Circulation 2004

¿Qué variables nos ayudan a estratificar el riesgo en pacientes con TEP masivo?

Situación hemodinámica



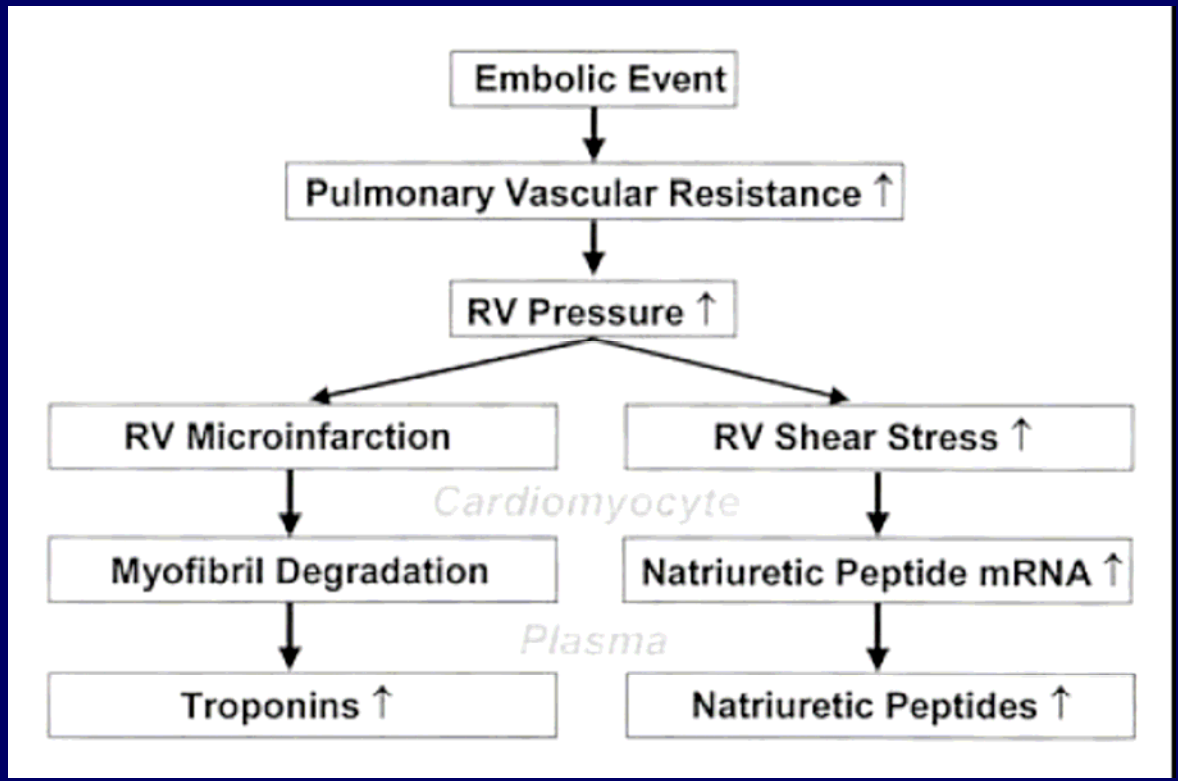
Kasper W et al. J Am Coll Cardiol 1997

Biomarcadores cardiacos

- Troponina:
  - Sensible y específico de daño miocárdico.
  - Elevación ligera y de corta duración.
  - Correlaciona con el grado de disfunción de VD.

- BNP o pro-BNP:
  - Marcador útil para el diagnóstico y pronóstico de ICC.
  - Producido por los miocitos ventriculares en respuesta al *stress* de la pared.

Biomarcadores cardiacos



Kucher N et al. Circulation2003

Biomarcadores cardiacos

Accuracy of Cardiac Biomarkers for the Prediction of In-Hospital Death in Pulmonary Embolism

Reference	n	Biomarker	Assay	Cut-Off Level	Test +, %	NPV, %	PPV, %
Konstantinides et al[11]	106	cTnI	Centaur (Bayer)	0.07 ng/mL	41	98	14
Konstantinides et al[11]	106	cTnT	Elecsys (Roche Pharmaceuticals)	0.04 ng/mL	37	97	12
Giannitsis et al[12]	56	cTnT	TropT (Roche Pharmaceuticals)	0.10 ng/mL	32	97	44
Janata et al[24]	106	cTnT	Elecsys (Roche Pharmaceuticals)	0.09 ng/mL	11	99	34
Pruszczyk et al[13]	64	cTnT	Elecsys (Roche Pharmaceuticals)	0.01 ng/mL	50	100	25
ten Wolde et al[25]	110	BNP	Shionoria (CIS Bio International)	21.7 pmol/L	33	99	17
Kucher et al[18]	73	NT-proBNP	Elecsys (Roche Pharmaceuticals)	500 pg/mL	58	100	12
Kucher et al[17]	73	BNP	Triage (Biosite Technologies)	50 pg/mL	58	100	12
Pruszczyk et al[26]	79	NT-proBNP	Elecsys (Roche Pharmaceuticals)	153 to 334* pg/mL	66	100	23

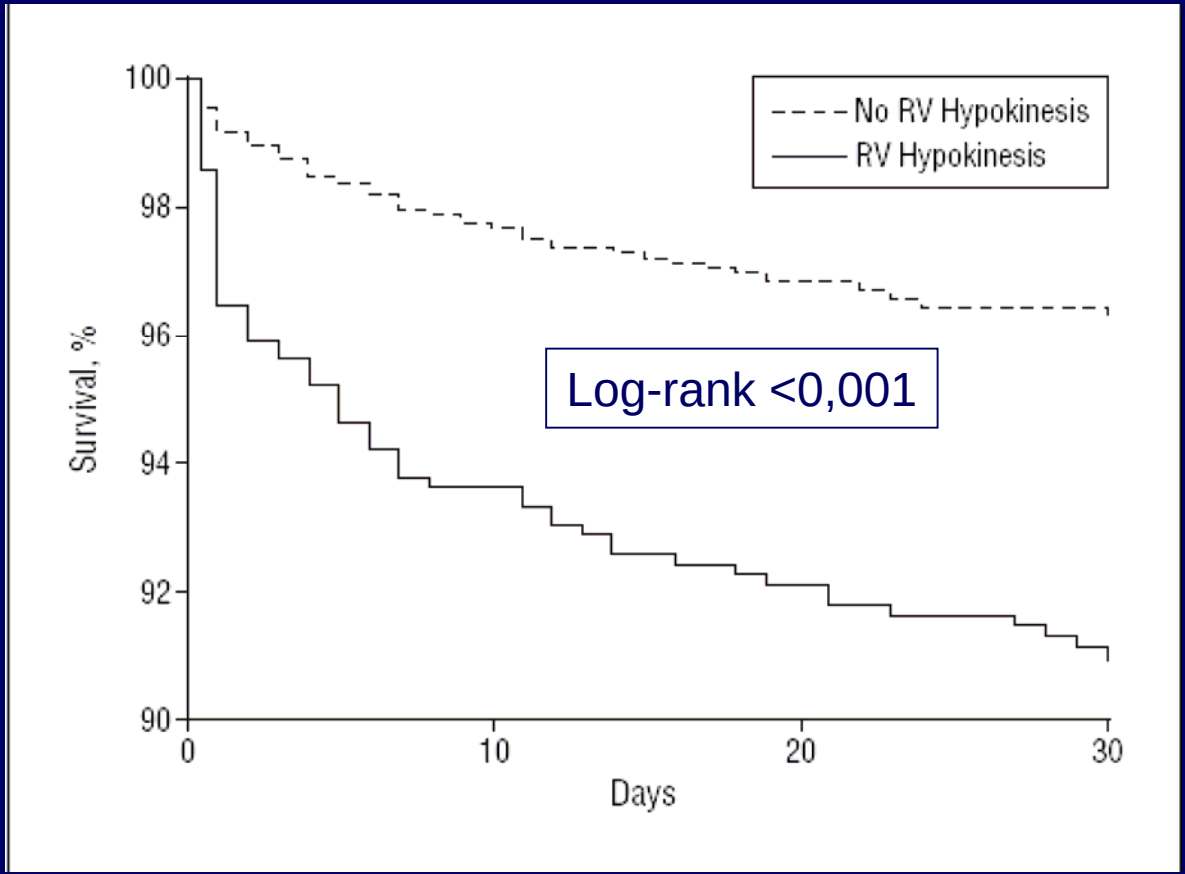
NPV indicates negative predictive value; PPV, positive predictive value.
*Age and gender adjusted cut-off levels according to the manufacturer.

Kucher N et al. Circulation2003

Clasificación pronóstica de EP

1. EP de bajo riesgo:
   - Sin disfunción de VD.
   - Mortalidad intrahospitalaria <4%.
2. EP submasivo:
   - Disfunción de VD sin hipotensión arterial.
   - Mortalidad intrahospitalaria 5-10%.
3. EP masivo:
   - Disfunción de VD y shock cardiogénico.
   - Mortalidad intrahospitalaria 30%.

Valor pronóstico de la ETT en EP con TA>90 mmHg



Kucher N et al. Arch Intern Med 2005

Valor pronóstico de la ETT en EP con TA>90 mmHg

Table 3. Multivariable Analysis of Univariately Significant Variables for Predicting Mortality at 30 Days, Stratified by the International Cooperative Pulmonary Embolism Registry Institution

Variable	Adjusted Hazard Ratio (95% Confidence Interval)
Right ventricular hypokinesis	1.94 (1.23-3.06)
Cancer	2.31 (1.52-3.51)
Congestive heart failure	1.92 (1.18-3.11)
Chronic lung disease	1.77 (1.11-2.83)
Age >70 y	1.70 (1.15-2.52)
Systolic arterial pressure ≤100 mm Hg	1.58 (0.98-2.54)
Heart rate >100 beats per min	1.42 (0.95-2.12)
Right heart thrombus	1.11 (0.52-2.33)
Thrombolysis	1.33 (0.81-2.17)

Kucher N et al. Arch Intern Med 2005

TABLE 4. Sensitivity, Specificity, and Predictive Value of Echocardiographic Signs of RV Dysfunction as Predictors of In-Hospital Mortality in 209 Patients With PE

	All Patients (n=209), %		Normotensive Patients (n=162), %	
	PE Related	All Causes	PE Related	All Causes
Sensitivity	100	82	100	57
Specificity	52	51	61	61
Positive predictive value	12	13	5	6
Negative predictive value	100	97	100	97

Grifoni S et al. Circulation 2000

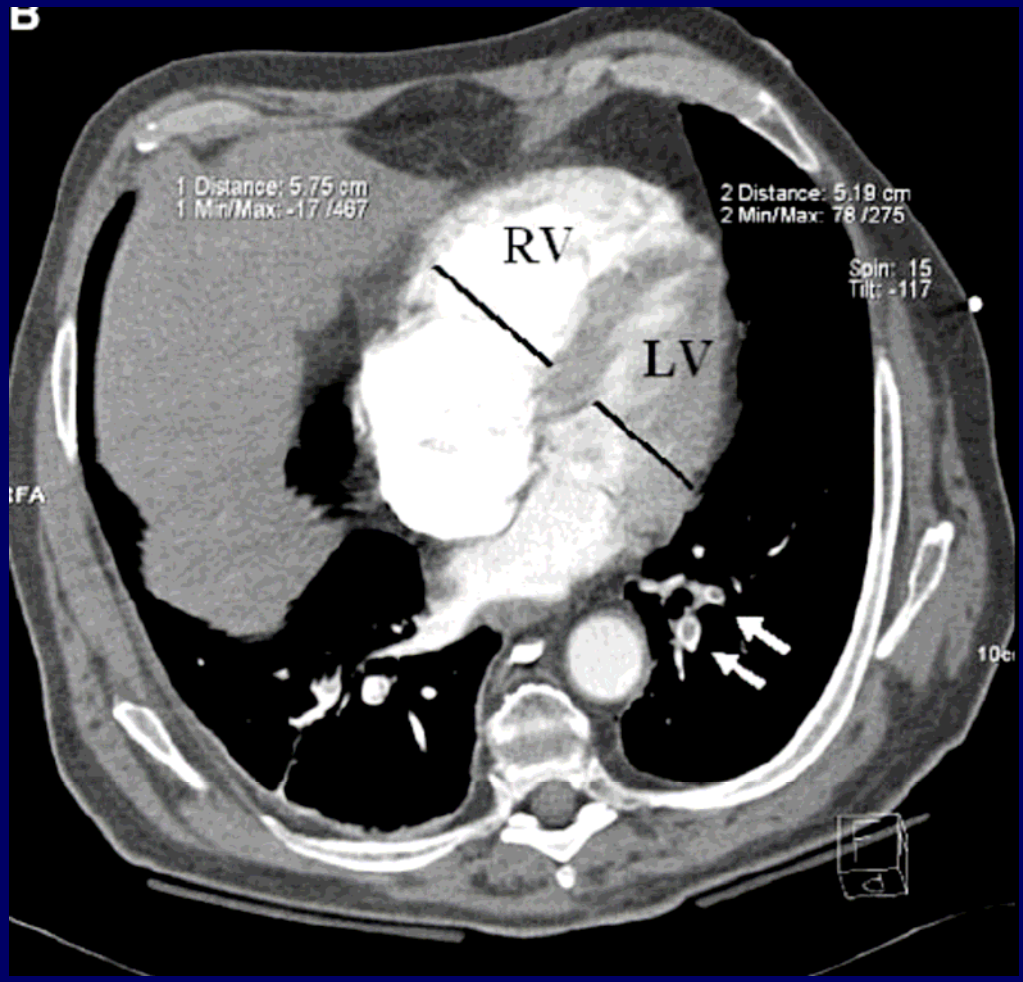
Vascular Medicine

Right Ventricular Enlargement on Chest Computed Tomography

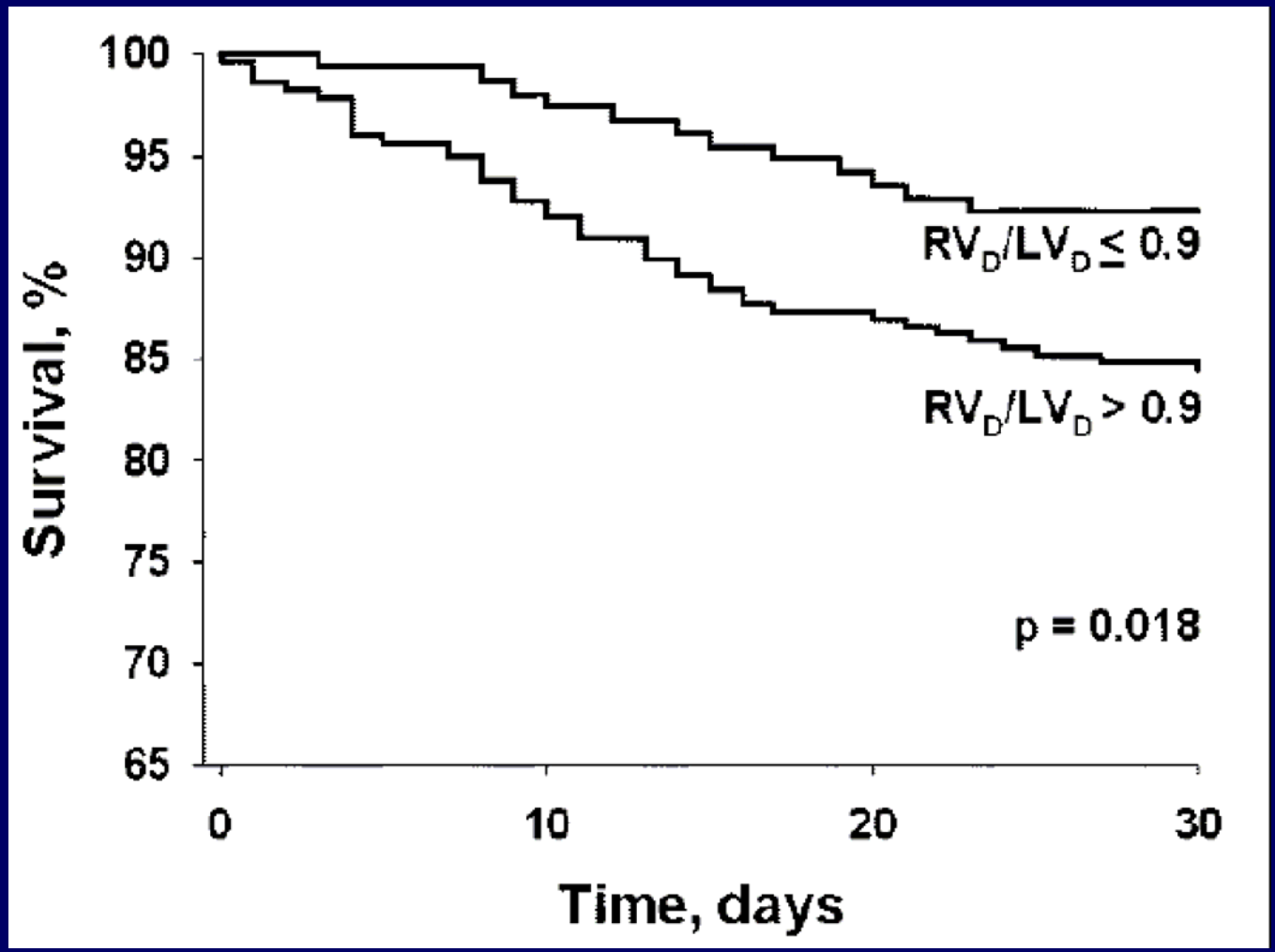
A Predictor of Early Death in Acute Pulmonary Embolism

U. Joseph Schoepf, MD*; Nils Kucher, MD*; Florian Kipfmueller, BS; Rene Quiroz, MD, MPH; Philip Costello, MD; Samuel Z. Goldhaber, MD

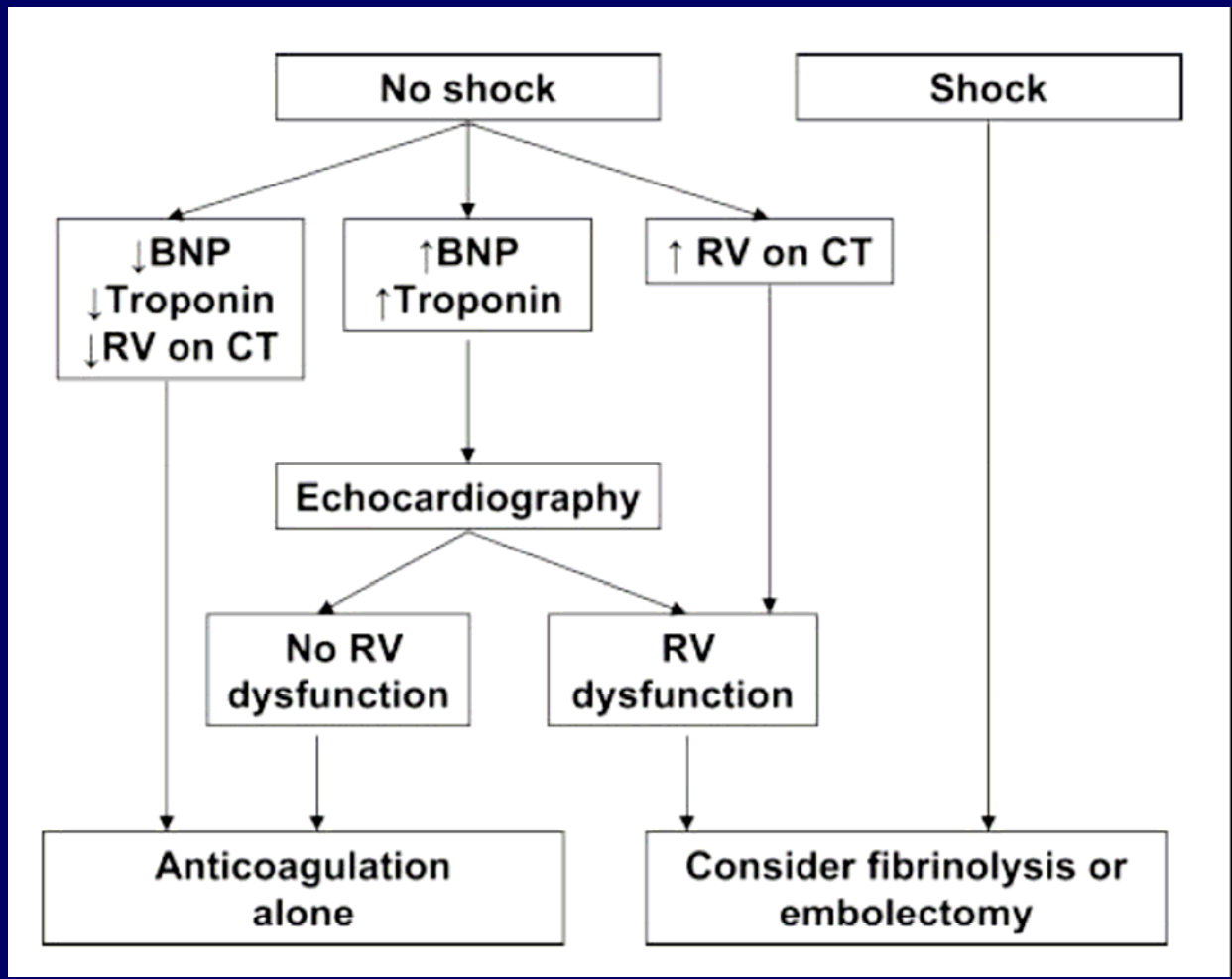
Circulation 2004


1 Distance: 5.75 cm
1 Min/Max: -17 /467
2 Distance: 5.19 cm
2 Min/Max: 78 /275
RV
LV
Spin: 15
Tilt: -117

RV_D/LV_D >0.9


100
95
90
85
80
75
70
65
Survival, %
RV$_D$/LV$_D$ ≤ 0.9
RV$_D$/LV$_D$ > 0.9
p = 0.018
0
10
20
30
Time, days

Algoritmo de manejo clínico del EP



Piazza G et al. Circulation 2006

¿Cuál es el mejor tratamiento inicial para el EP hemodinámicamente inestable?

Fibrinolisis vs Heparina

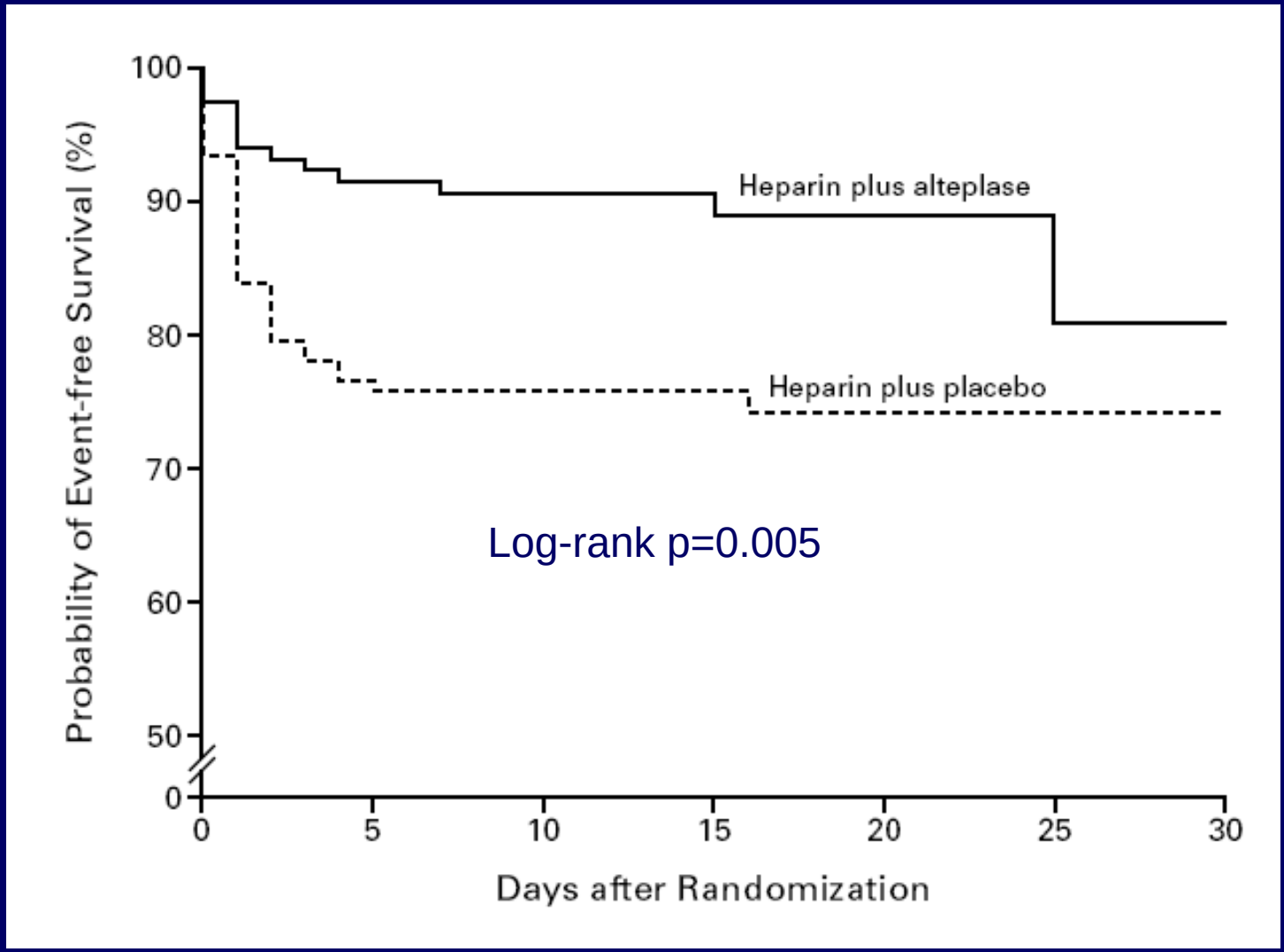
ALTEPLASE IN PULMONARY EMBOLISM

HEPARIN PLUS ALTEPLASE COMPARED WITH HEPARIN ALONE IN PATIENTS WITH SUBMASSIVE PULMONARY EMBOLISM

STAVROS KONSTANTINIDES, M.D., ANNETTE GEIBEL, M.D., GERHARD HEUSEL, PH.D., FRITZ HEINRICH, M.D., AND WOLFGANG KASPER, M.D., FOR THE MANAGEMENT STRATEGIES AND PROGNOSIS OF PULMONARY EMBOLISM-3 TRIAL INVESTIGATORS*

Objetivo primario: muerte o deterioro clínico que requiere escalada terapéutica

N Engl J Med 2002


Probability of Event-free Survival (%)
100
90
80
70
60
50
0
0
5
10
15
20
25
30
Days after Randomization
Heparin plus alteplase
Heparin plus placebo
Log-rank p=0.005

Thrombolysis Compared With Heparin for the Initial Treatment of Pulmonary Embolism

A Meta-Analysis of the Randomized Controlled Trials

Susan Wan; Daniel J. Quinlan, MBBS; Giancarlo Agnelli, MD; John W. Eikelboom, MBBS

Circulation 2004

Trial, Year	Eligibility	n	Randomized Treatment		Subsequent Anticoagulation		Follow-Up*
			Thrombolysis	Heparin	Thrombolysis	Heparin	
UPET trial, 1973	Acute PE,† symptoms ≤5 days	160	Urokinase 12 hours	Heparin	Heparin, warfarin	Heparin, warfarin	14 days
Tibbutt et al, 1974	Acute life-threatening PE†	30	Streptokinase‡ 72 hours	Heparin‡	Warfarin (started at 60 hours)	Warfarin (started at 60 hours)	72 hours
Ly et al, 1978	Acute major PE†, symptoms <5 days	25§	Streptokinase 72 hours	Heparin (7 days)	Warfarin, heparin if TCT <2× control	Heparin, warfarin	10 days
Dotter et al, 1979	Acute PE†	31	Streptokinase 18–72 hours	Heparin (5 days)	Heparin, warfarin	Heparin, warfarin	In hospital
Marini et al, 1988	Acute PE, symptoms ≤7 days	30	Urokinase, 12 hours or 3 days	Heparin (7 days)	Warfarin	Heparin, warfarin	7 days
Levine et al, 1990	Acute PE, symptoms ≤14 days	58	tPA 2 minutes	Heparin	Heparin, warfarin	Heparin, warfarin	10 days
PIOPED, 1990	Acute PE, symptoms ≤7 days	13	tPA 40 to 90 minutes	Heparin	Heparin, warfarin	Heparin, warfarin	7 days
Dalla-Volta et al, 1992	Acute PE, symptoms ≤10 days	36	tPA 2 hours	Heparin	Heparin, warfarin	Heparin, warfarin	30 days
Goldhaber et al, 1993	Acute PE, symptoms ≤14 days	101	tPA 2 hours	Heparin	Heparin, warfarin	Heparin, warfarin	In hospital or 14 days
Jerjes-Sanchez et al, 1995	Acute massive PE,† symptoms ≤14 days	8	Streptokinase 2 hours	Heparin	Heparin, warfarin	Heparin, warfarin	In hospital
Konstantinides et al, 2002	Acute PE, symptoms ≤4 days	256	tPA 2 hours	Heparin	Heparin, warfarin	Heparin, warfarin	In hospital or 30 days

Thrombolysis Compared With Heparin for the Initial Treatment of Pulmonary Embolism

A Meta-Analysis of the Randomized Controlled Trials

Susan Wan; Daniel J. Quinlan, MBBS; Giancarlo Agnelli, MD; John W. Eikelboom, MBBS

Seguimiento	Trombolisis	Heparina	OR (IC 95%)
EP recurrente o muerte	6,7%	9,6%	0,67 (0,4-1,12)
EP recurrente	2,7%	4,3%	0,67 (0,33-1,37)
Muerte	4,3%	5,9%	0,7 (0,37-1,3)
Hemorragias:			
Graves	9,1%	6,1%	1,42 (0,81-2,46)
No graves	22,7%	10%	2,63 (1,53-4,54)
Intracraneales	0,5%	0,3%	1,04 (0,36-3,04)

Thrombolysis Compared With Heparin for the Initial Treatment of Pulmonary Embolism

A Meta-Analysis of the Randomized Controlled Trials

Susan Wan; Daniel J. Quinlan, MBBS; Giancarlo Agnelli, MD; John W. Eikelboom, MBBS

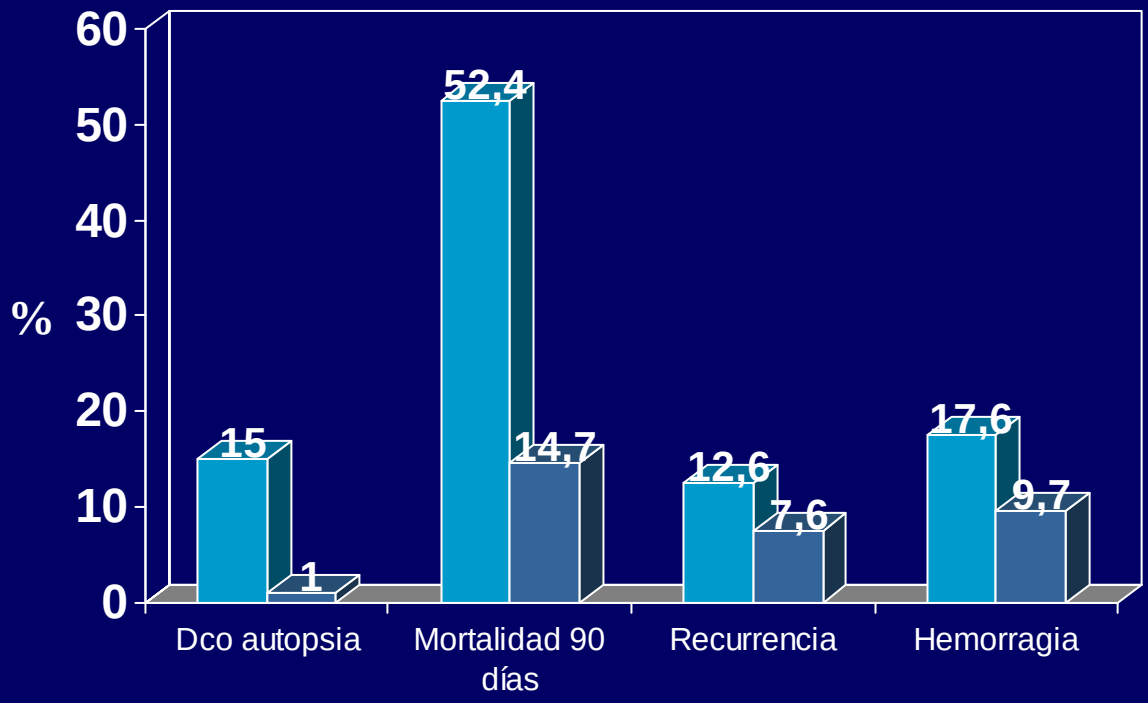
Seguimiento*	Trombolisis	Heparina	OR (IC 95%)
EP recurrente o muerte	9,4%	19%	0,45 (0,22-0,92)
EP recurrente	3,9%	7,1%	0,61 (0,23-1,62)
Muerte	6,2%	12,7%	0,47 (0,2-1,1)
Hemorragias: Graves	21,9%	11,9%	1,98 (1,00-3,92)

*Estudios que incluían pacientes con EP masivo

Vascular Medicine

Massive Pulmonary Embolism

Nils Kucher, MD; Elisa Rossi, BS; Marisa De Rosa, PhD; Samuel Z. Goldhaber, MD

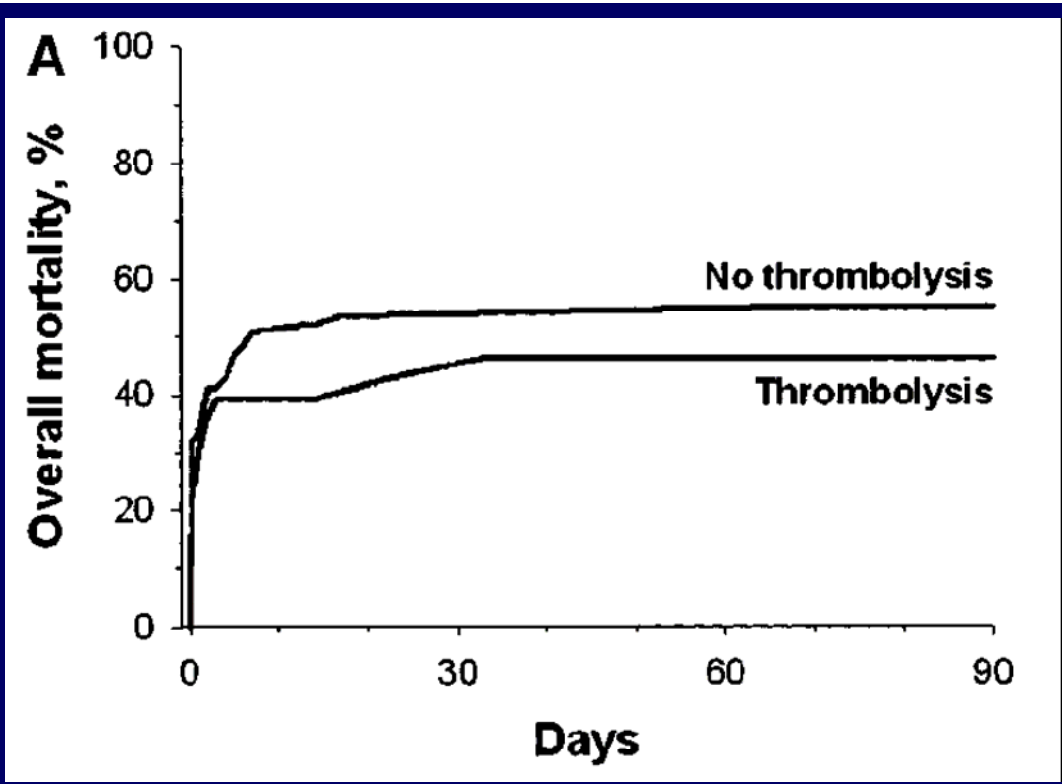


Circulation 2006.
ICOPER

Vascular Medicine

Massive Pulmonary Embolism

Nils Kucher, MD; Elisa Rossi, BS; Marisa De Rosa, PhD; Samuel Z. Goldhaber, MD



Circulation 2006. ICOPER

Antithrombotic Therapy for Venous Thromboembolic Disease: The Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy

Recomendaciones sobre terapia trombolítica en el EP

4.2.1. For most patients with PE, we recommend clinicians **not** use systemic thrombolytic therapy (**Grade 1A**). In selected patients, we suggest systemic administration of thrombolytic therapy (**Grade 2B**). For patients who are hemodynamically unstable, we suggest use of thrombolytic therapy (**Grade 2B**).

Antithrombotic Therapy for Venous Thromboembolic Disease: The Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy

Recomendaciones sobre terapia trombolítica en el EP

4.2.2. We suggest clinicians **not** use local administration of thrombolytic therapy via a catheter (**Grade 1C**).

4.2.3. For patients with PE who receive thrombolytic regimens, we suggest use of thrombolytic regimens with a short infusion time over those with prolonged infusion times (**Grade 2C**).

Antithrombotic Therapy for Venous Thromboembolic Disease: The Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy

Recomendaciones sobre embolectomía percutánea en el EP

4.3.1. For most patients with PE, we recommend **against** use of mechanical approaches (**Grade 1C**). In selected highly compromised patients who are unable to receive thrombolytic therapy or whose critical status does not allow sufficient time to infuse thrombolytic therapy, we suggest use of mechanical approaches (**Grade 2C**).

Antithrombotic Therapy for Venous Thromboembolic Disease: The Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy

Recomendaciones sobre embolectomía quirúrgica en el EP

4.4.1. For most patients with PE, we recommend **against** pulmonary embolectomy (**Grade 1C**). In selected highly compromised patients who are unable to receive thrombolytic therapy or whose critical status does not allow sufficient time to infuse thrombolytic therapy, we suggest pulmonary embolectomy (**Grade 2C**).

¿Cuánto tiempo debe prolongarse el tratamiento anticoagulante?

EP idiopático

Factores asociados con ETV recurrente

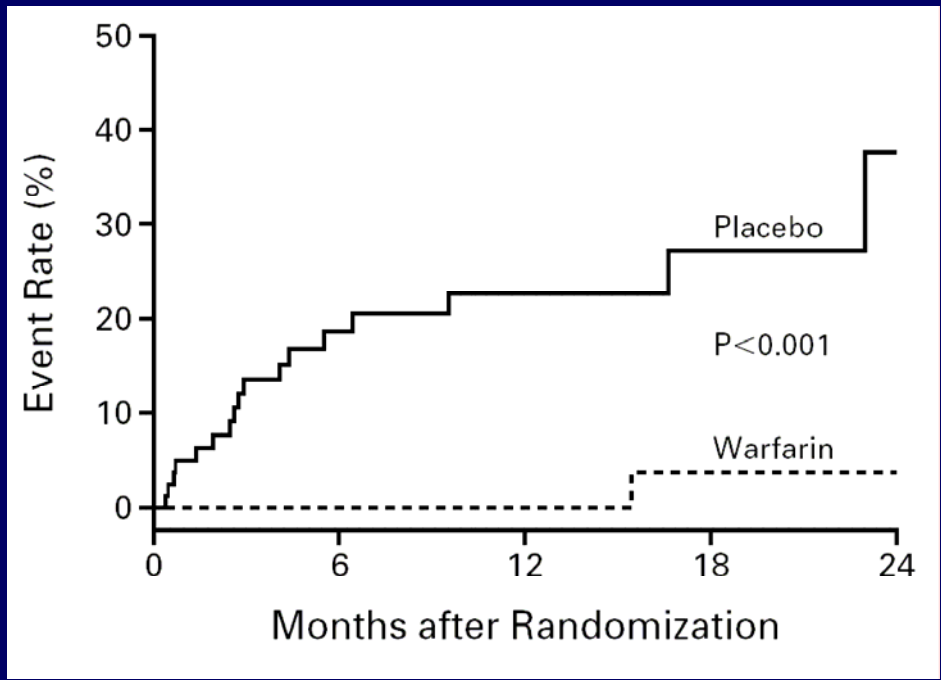
- ETV idiopática *vs* secundaria.
- EP *vs* TVP como primer episodio.
- Trombofilia congénita o adquirida.
- Trombosis venosa residual.
- Antecedentes de ETV.
- Portador de un filtro de vena cava.
- Dímero-D elevado tras finalizar el tto.
- Cáncer.

Consideraciones

- ACO reduce el riesgo de recurrencia >90%
- Riesgo de recurrencia tras la retirada de ACO en casos de ETV idiopática:
  - 10% en el primer año.
  - 30% a los 5 años
- Riesgo de sangrado:
  - Grave 2% anual.
  - Fatal 0,2% anual.

A COMPARISON OF THREE MONTHS OF ANTICOAGULATION WITH EXTENDED ANTICOAGULATION FOR A FIRST EPISODE OF IDIOPATHIC VENOUS THROMBOEMBOLISM

CLIVE KEARON, M.B., PH.D., MICHAEL GENT, D.SC., JACK HIRSH, M.D., JEFFREY WEITZ, M.D., MICHAEL J. KOVACS, M.D., DAVID R. ANDERSON, M.D., ALEXANDER G. TURPIE, M.B., DAVID GREEN, M.D., PH.D., JEFFREY S. GINSBERG, M.D., PHILIP WELLS, M.D., BETSY MACKINNON, M.SC., AND JIM A. JULIAN, M.MATH.



Extended Oral Anticoagulant Therapy after a First Episode of Pulmonary Embolism

Giancarlo Agnelli, MD; Paolo Prandoni, MD, PhD; Cecilia Becattini, MD; Mauro Silingardi, MD; Maria Rita Taliani, MD; Maddalena Miccio, MD; Davide Imberti, MD; Renzo Poggio, MD; Walter Ageno, MD; Enrico Pogliani, MD; Fernando Porro, MD; and Pietro Zonzin, MD, for the Warfarin Optimal Duration Italian Trial Investigators*

	Recurrencia (%)	Incidencia (%paciente-año)	Seguimiento (meses)	RR (IC 95%)
EP idiopático:				
ACO 3 m	12,1	4,6	31,7	0,99
ACO 12 m	12,2	4,2	34,8	(0,45-2,16)
EP secundario:				
ACO 3 m	10	3,5	33,9	0,53
ACO 6 m	5,3	1,8	35	(0,16-1,74)

Ann Intern Med 2003

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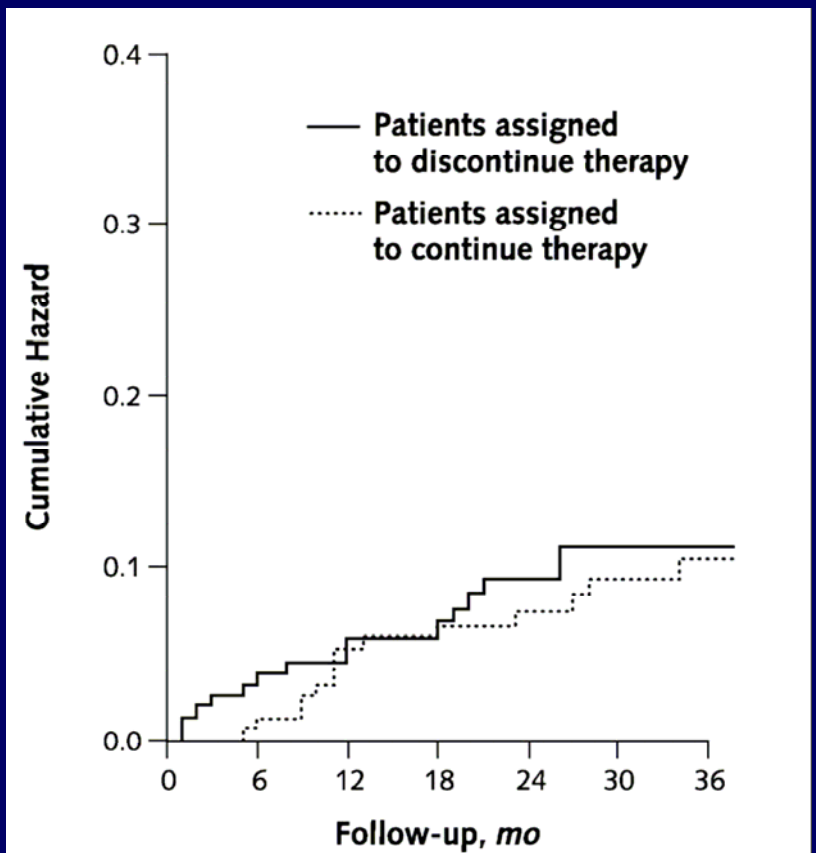
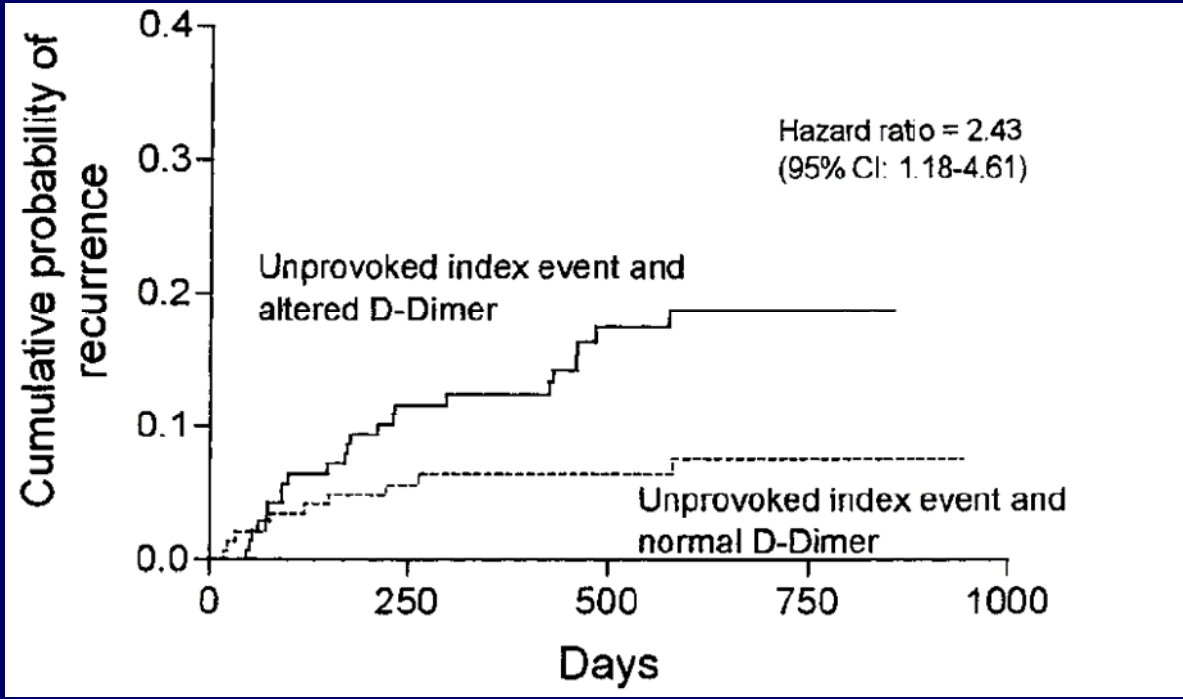


Ann Intern Med 2003

Predictive Value of D-Dimer Test for Recurrent Venous Thromboembolism After Anticoagulation Withdrawal in Subjects With a Previous Idiopathic Event and in Carriers of Congenital Thrombophilia

Gualtiero Palareti, MD; Cristina Legnani, MS; Benilde Cosmi, MD; Lelia Valdré, MD; Barbara Lunghi, MS; Francesco Bernardi, MS; Sergio Coccheri, MD



Circulation 2003

Antithrombotic Therapy for Venous Thromboembolic Disease: The Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy

5.1.2. For patients with a first episode of idiopathic PE, we recommend treatment with a VKA at least 6 to 12 months (**Grade 1A**).

5.1.3. We suggest that patients with first-episode idiopathic PE be considered for indefinite anticoagulant therapy **(Grade 2A).**