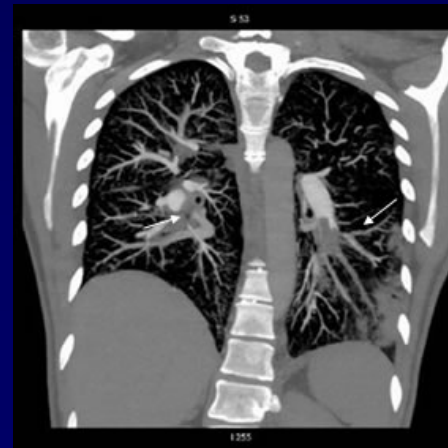


*VI Fórum multidisciplinar  
de la  
Enfermedad Tromboembólica*

*“ Predicción de muerte por sangrado “*

Dr. José Antonio Nieto Rodríguez  
Servicio de Medicina Interna  
Hospital Virgen de la Luz  
Cuenca



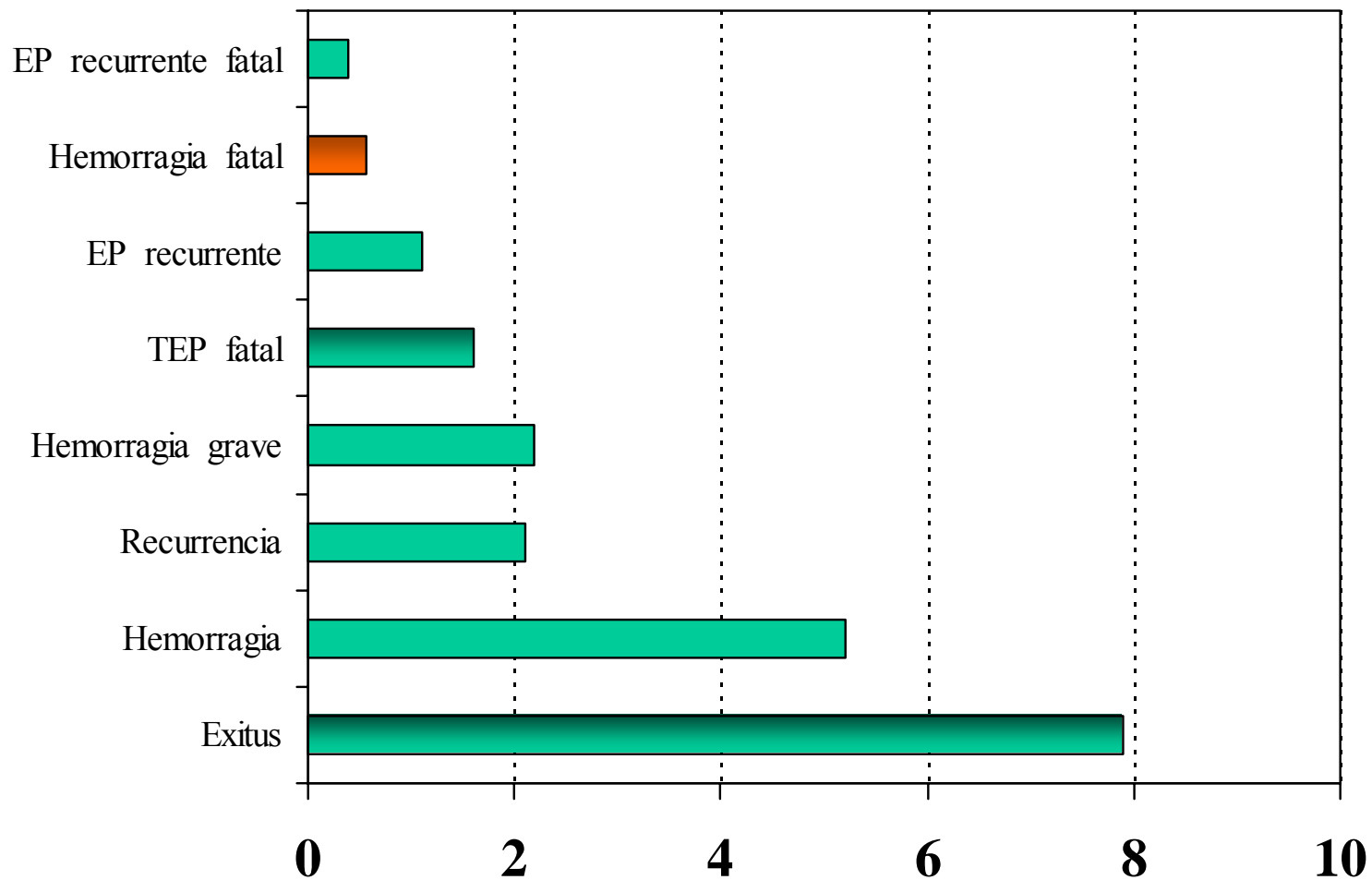
**ORIGINAL ARTICLE**

## **Fatal bleeding in patients receiving anticoagulant therapy for venous thromboembolism: findings from the RIETE registry**

J. A. NIETO,\* R. SOLANO,\* M. D. RUIZ-RIBÓ,\* N. RUIZ-GIMENEZ,† P. PRANDONI,‡ C. KEARON§ and M. MONREAL¶ FOR THE RIETE INVESTIGATORS<sup>1</sup>

*Journal of Thrombosis and Hemostasis* 2010; 8: 1216-1222

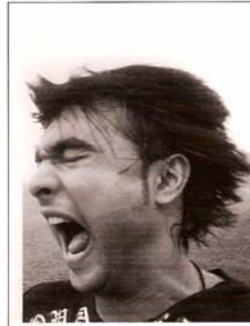
# Principales eventos en 27.029 pacientes con TVP / EP en 3 meses



# Annals of Internal Medicine

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## REVIEWS

**Systematic Review: Case-Fatality Rates of Recurrent Venous Thromboembolism and Major Bleeding Events Among Patients Treated for Venous Thromboembolism** CARRIER, LE GAL, WELLS, AND RODGER

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CUENCAL6001  
SPAIN

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**The Looming Rash of Herpes Zoster and the Challenge of Adult Immunization** DONAHUE AND BELONGIA 609

## ON BEING A DOCTOR

**A Family Affair—Revisited** HABER 612

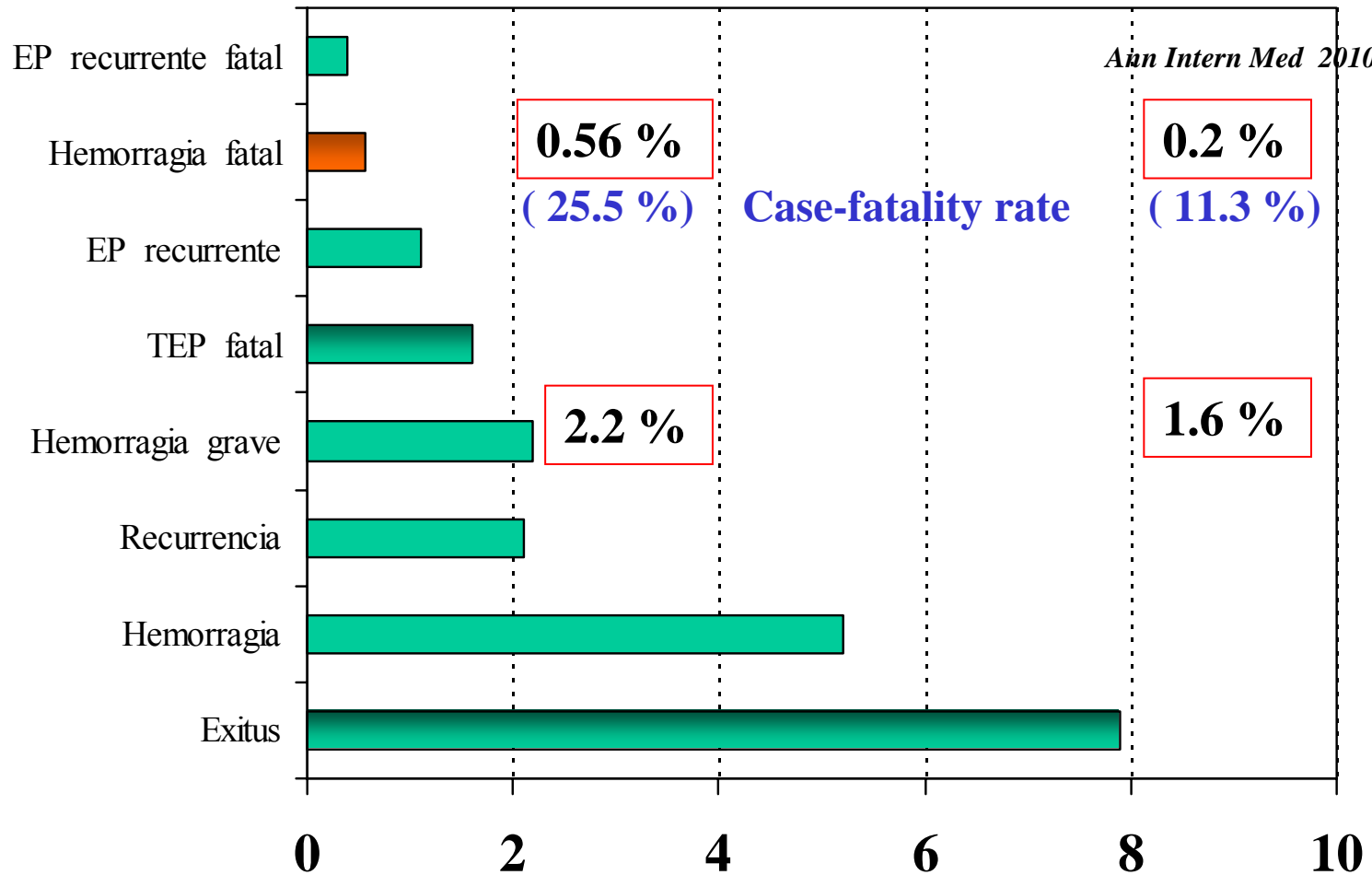
## IN THE CLINIC

**Depression** ITC5-1

*Ann Intern Med 2010; 152: 578-589*

reported (1 fatal) for a case-fatality rate of 15.1% (CI, 0.1% to 38.7%). This low rate of major bleeding is probably due to lack of reporting or follow-up for major bleeding events after completion of anticoagulant therapy in the included studies (81). Sixth, we extracted most patients included in this study from RCTs; as a result, our findings are not generalizable to all patients with VTE because those with additional comorbid conditions are often excluded from clinical trials. Finally, our study does not address other factors, including costs, lifestyle modifications, burden of laboratory monitoring, and patient values and

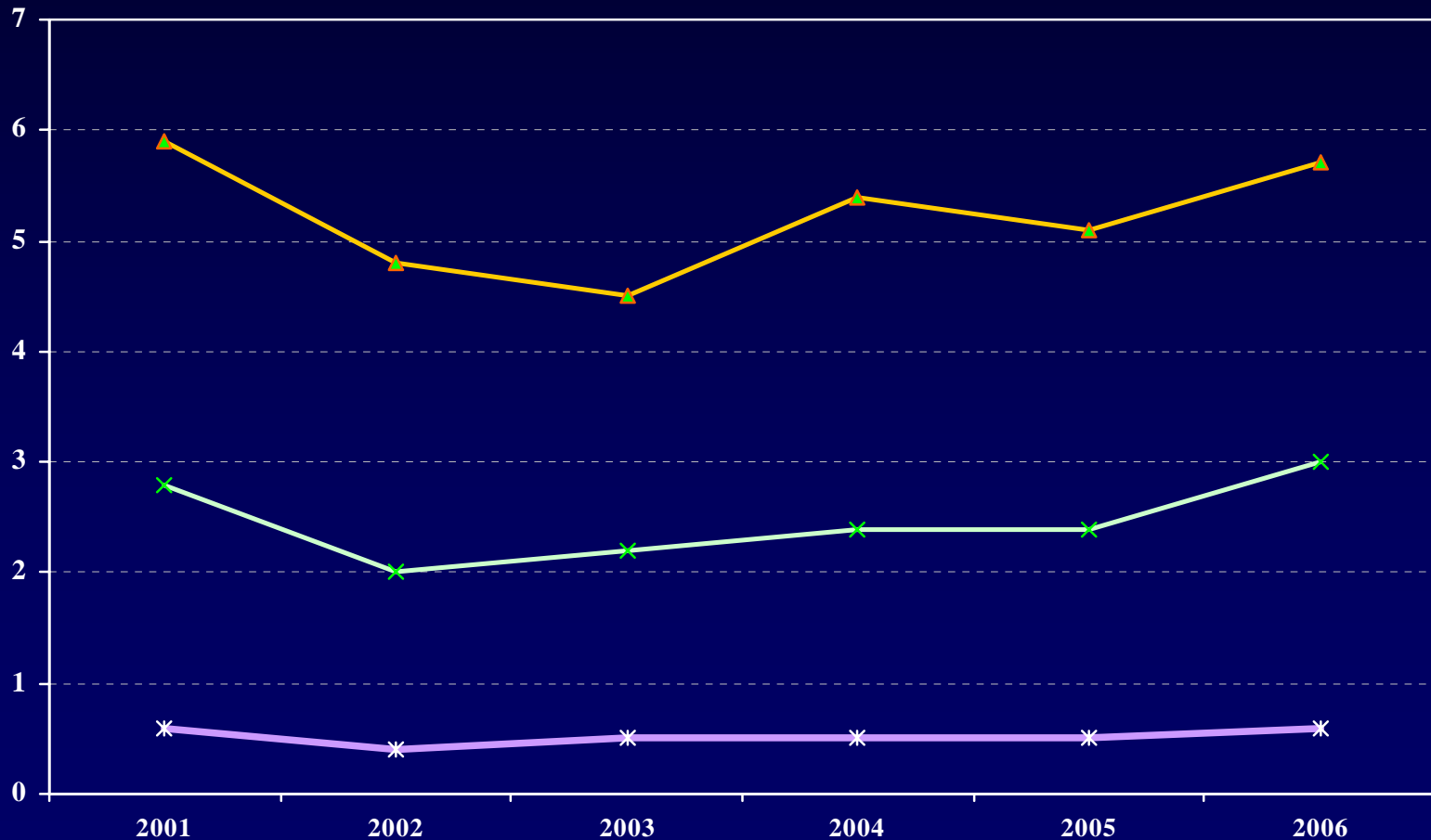
# Principales eventos en 27.029 pacientes con TVP / EP en 3 meses



# RIETE - 17.368 pacientes

## Hemorragias en 90 días. Periodo 2001-2006

—▲— Cualquier hemorragia —×— H grave —\*— H mortal



# Hemorragias por anticoagulantes

	ACO*	ETV	RIETE**
Hemorragia total	9,6 %	22,9 %	5,2 %
Hemorragia mayor	3,0 %	9,47 %	2,2 %
Hemorragia fatal	0,6 %	----	0,6 %

\* Frecuencia media anual (Nº de hemorragias por 100 personas/año )

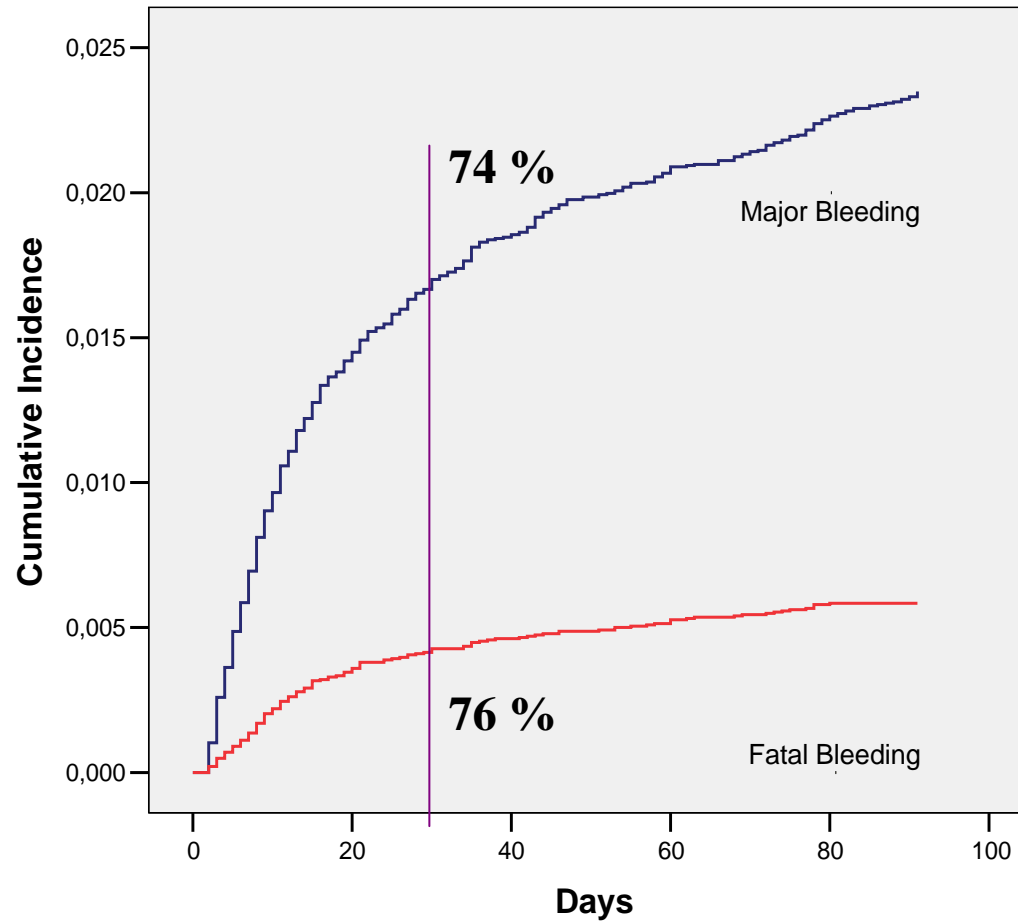
\*\* Incidencia en los tres primeros meses

Riesgo : x 10 en primer mes respecto al resto del año



# Incidencia de hemorragia grave y fatal en pacientes ETV

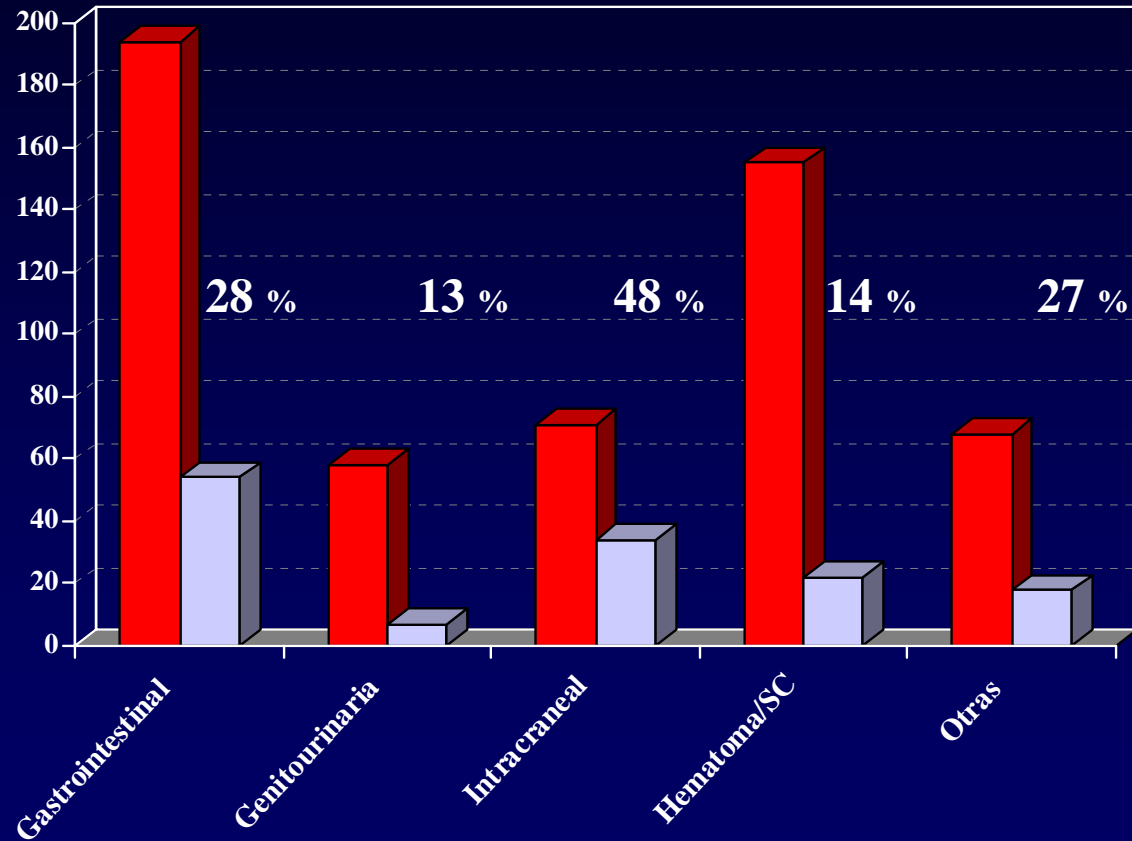
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# RIETE. 24.395 pacientes.

## Hemorragias graves (n, 546) y mortales (n, 135)

■ Graves ■ Mortales



Días hasta hemorragia	10	11	20	9	22
Días hasta fallecimiento	1.5	7	1	2.5	1

# Objetivos

---

¿Es posible identificar en el momento del diagnóstico de ETV a los pacientes anticoagulados que pueden morir de una hemorragia?

Intensidad del tratamiento anticoagulante

Filtro en la cava

Mayor supervisión

Ensayos clínicos: Clasificar a los pacientes

# Principales limitaciones

---

Número pequeño de pacientes (n, 135)

Gran heterogeneidad de las hemorragias

Definición de muerte por hemorragia

Variables limitadas al momento del diagnóstico

Pérdida de pacientes

## Blood Coagulation, Fibrinolysis and Cellular Haemostasis

Predictive variables for major bleeding events in patients presenting with documented acute venous thromboembolism. Findings from the RIETE Registry

Nuria Ruíz-Giménez<sup>1</sup>, Carmen Suárez<sup>1</sup>, Rocío González<sup>2</sup>, José Antonio Nieto<sup>3</sup>, José Antonio Todolí<sup>4</sup>, Ángel Luis Samperiz<sup>5</sup>, Manuel Monreal<sup>6</sup>, and the RIETE Investigators\*

*Thromb Hemost 2008; 100: 26-31*

Puntuación	
Edad > 75 años	1 punto
EP sintomático	1 punto
Cáncer	1 punto
Anemia	1.5 puntos
Hemorragia reciente	2 puntos
Creatinina > 1.2 mg/dl	1.5 puntos

# Características clínicas

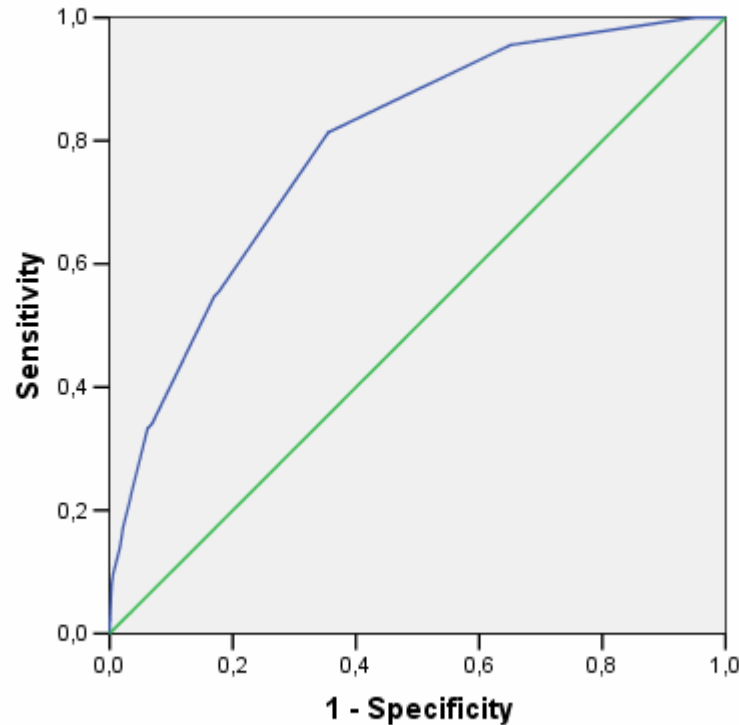
	Si	No	Odds ratio (IC 95%)	p
<b>PACIENTES</b>	<b>135</b>	<b>24216</b>		
Edad >75 años	84 (63%)	9148 (38%)	2.71 (1.91-3.85)	<0.001
Peso <70 kg	69 (51%)	8961 (37%)	1.78 (1.27-2.50)	0.001
Cardiopatía crónica	15 (11%)	1324 (5.7%)	2.16 (1.26-3.71)	0.007
Hemorragia mayor reciente	13 (9.6%)	590 (2.4%)	4.27 (2.40-7.60)	<0.001
Inmovilización ≥ 4días	63 (47%)	6128 (25%)	2.57 (1.83-3.60)	<0.001
Cáncer metastásico	42 (31%)	2174 (9.0%)	4.58 (3.17-6.61)	<0.001
Anemia	77 (57%)	7938 (33%)	2.72 (1.93-3.83)	<0.001
Leucocitos > 11.000 / mm <sup>3</sup>	54 (39%)	6874 (28%)	1.62 (1.15-2.29)	0.007
Plaquetas <100x 10 <sup>9</sup> /L	11 (8.1%)	555 (2.3%)	3.78 (2.03-7.05)	<0.001
Tiempo protrombina alterado	27 (20%)	1601 (6.6%)	3.53 (2.31-5.40)	<0.001
Cr Cl <30 ml/min	37 (27%)	1985 (8.2%)	4.23 (2.89-6.19)	<0.001
Filtro en la cava inferior	10 (7.4%)	528 (2.2%)	3.51 (1.83-6.72)	0.001
TVP distal	5 (3.7%)	2959 (12%)	0.28 (0.11-0.68)	<0.001

# Análisis multivariante

	<b>OR</b>	<b>95% CI</b>	<b>p value</b>	<b>Points</b>
Age >75 years	2.16	1.49-3.16	<0.001	1
Metastatic cancer	3.80	2.56-5.64	<0.001	2
Immobility $\geq$ 4 days	1.99	1.40-2.83	<0.001	1
Recent major bleeding	2.64	1.44-4.83	0.002	1.5
Abnormal prothrombin time	2.09	1.34-3.26	0.001	1
CrCl < 30 ml/min	2.27	1.49-3.44	<0.001	1
Platelet Count <10 <sup>9</sup> /L	2.23	1.16-4.29	0.016	1
Anemia	1.54	1.07-2.22	0.021	1
Distal DVT	0.39	0.16-0.95	0.038	-1

Total

ROC Curve



Diagonal segments are produced by ties

Area Under the Curve

Test Result Variable(s): SCORE 9 variables, cancer metastasico

Area	Std. Error <sup>a</sup>	Asymptotic Sig. <sup>b</sup>	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
,790	,018	,000	,754	,825

The test result variable(s): SCORE 9 variables, cancer metastasico has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased.

a. Under the nonparametric assumption

b. Null hypothesis: true area = 0.5



# Puntuación ( 24.395 pacientes)

■ Proporción de pacientes con hemorragia fatal

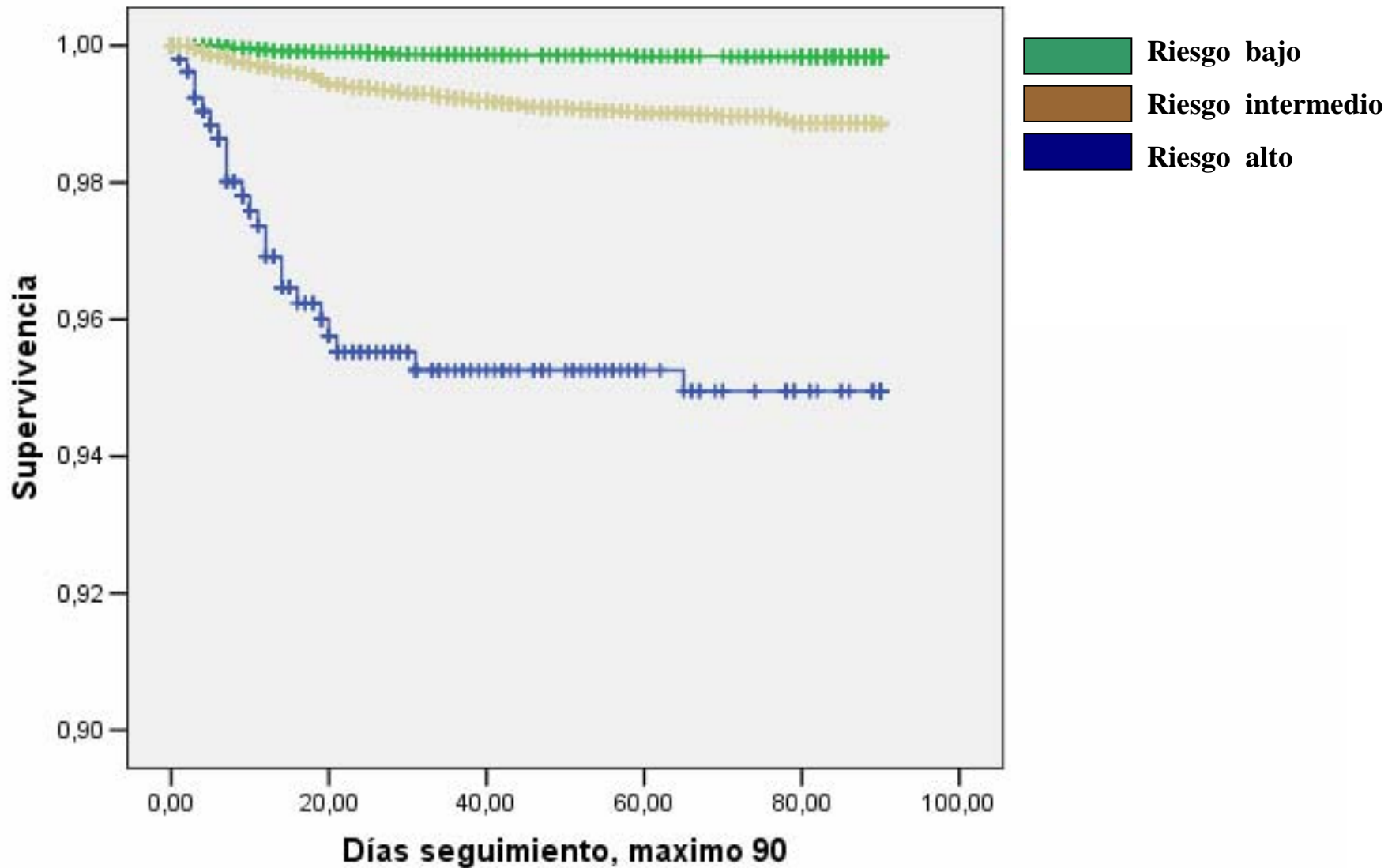


Likelihood ratio

0.29

1.92

7.95



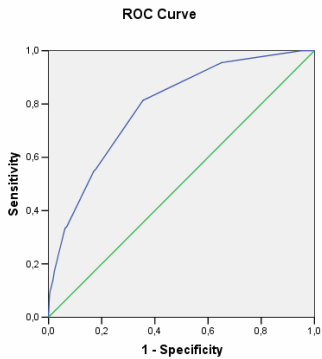
# Categorías de riesgo y localización del sangrado

	<b>Low</b>	<b>Intermediate</b>	<b>High</b>
<i>Gastrointestinal</i>	<b>0.11 (0.06-0.21)</b>	<b>3.68 (2.15-6.30)</b>	<b>39.7 (20.1-78.4)</b>
<i>Intracraneal</i>	0.31 (0.16-0.60)	3.38 (1.72-6.66)	0
<i>Genitourinaria</i>	0.06 (0.01-0.54)	16.0 (1.93-132.8)	0
<i>Haematoma</i>	0.09 (0.03-0.24)	12.0 (4.05-35.4)	0
<i>Otras</i>	<b>0.07 (0.02-0.23)</b>	<b>4.96 (1.98-12.4)</b>	<b>40.7 (13.4-123.1)</b>
<i>Hemorragia no fatal</i>	0.35 (0.29-0.429)	2.75 (2.25-3.35)	2.92 (1.32-6.17)

# Categorías de riesgo y localización del sangrado

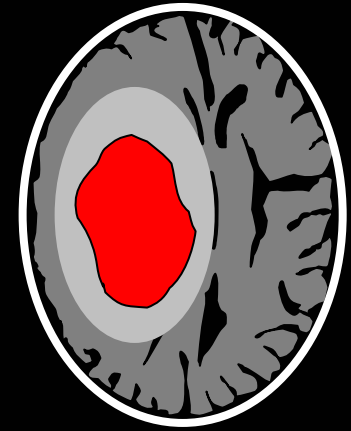
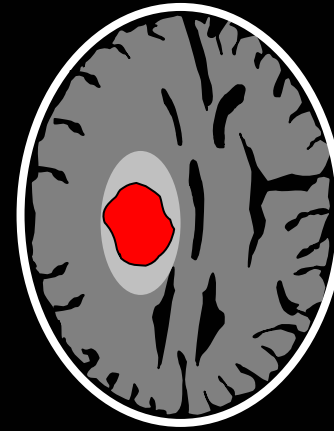
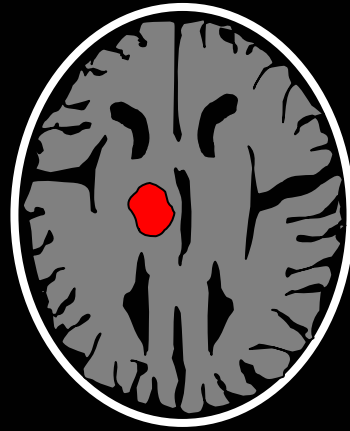
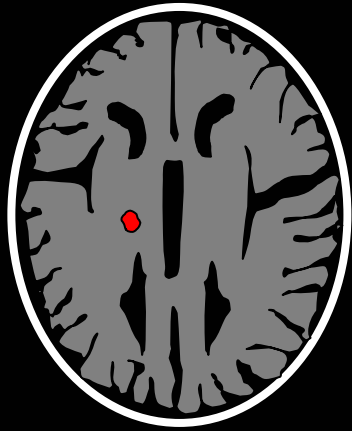
	<b>Low</b>	<b>Intermediate</b>	<b>High</b>
<i>Extracranial fatal</i>	<b>0.09</b> (0.06-0.15)	<b>5.17</b> (3.44-7.77)	<b>26.5</b> (15.0-46.9)
<i>Intracranial fatal</i>	0.31 (0.16-0.60)	3.38 (1.72-6.66)	0
<i>Non fatal major bleeding</i>	0.35 (0.29-0.42)	2.75 (2.25-3.35)	2.92 (1.32-6.17)

OR ( 95% IC )



Diagonal segments are produced by ties.

	<b>AUC</b>	<b>95% IC</b>
<b><i>Extracranial</i></b>	0.83	0.79 - 0.86
Digestiva	0.86	0.81 - 0.91
<b><i>Intracranial</i></b>	0.68	0.60 - 0.76
<b><i>Hemorragia grave no fatal</i></b>	0.68	0.65 - 0.70



Sintomático

6 horas

24 horas

→ 10-15 %

→ 70 %

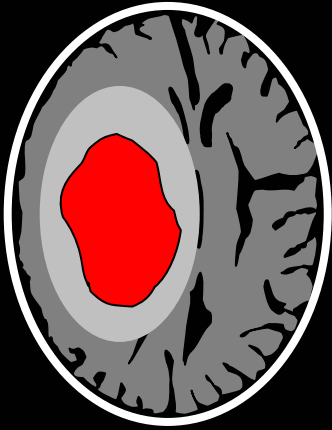
OR 6.2 ; 1.7 - 23

## Anticoagulados

mayor volumen

50% sangrado activo al diagnóstico

45% INR encima del rango



Mal pronóstico



Glasgow 3-4, 5-12, 13-15

Volumen  $\pm$  30 cm<sup>3</sup>

Extensión intraventricular

Origen infratentorial

Edad  $\pm$  80 años

# Conclusiones

---

- 1.- Con variables clínicas y analíticas se pueden identificar a pacientes con riesgo elevado de muerte por hemorragia.
- 2.- El modelo identifica mejor a los pacientes que mueren por hemorragia extracraneal, especialmente por hemorragia digestiva

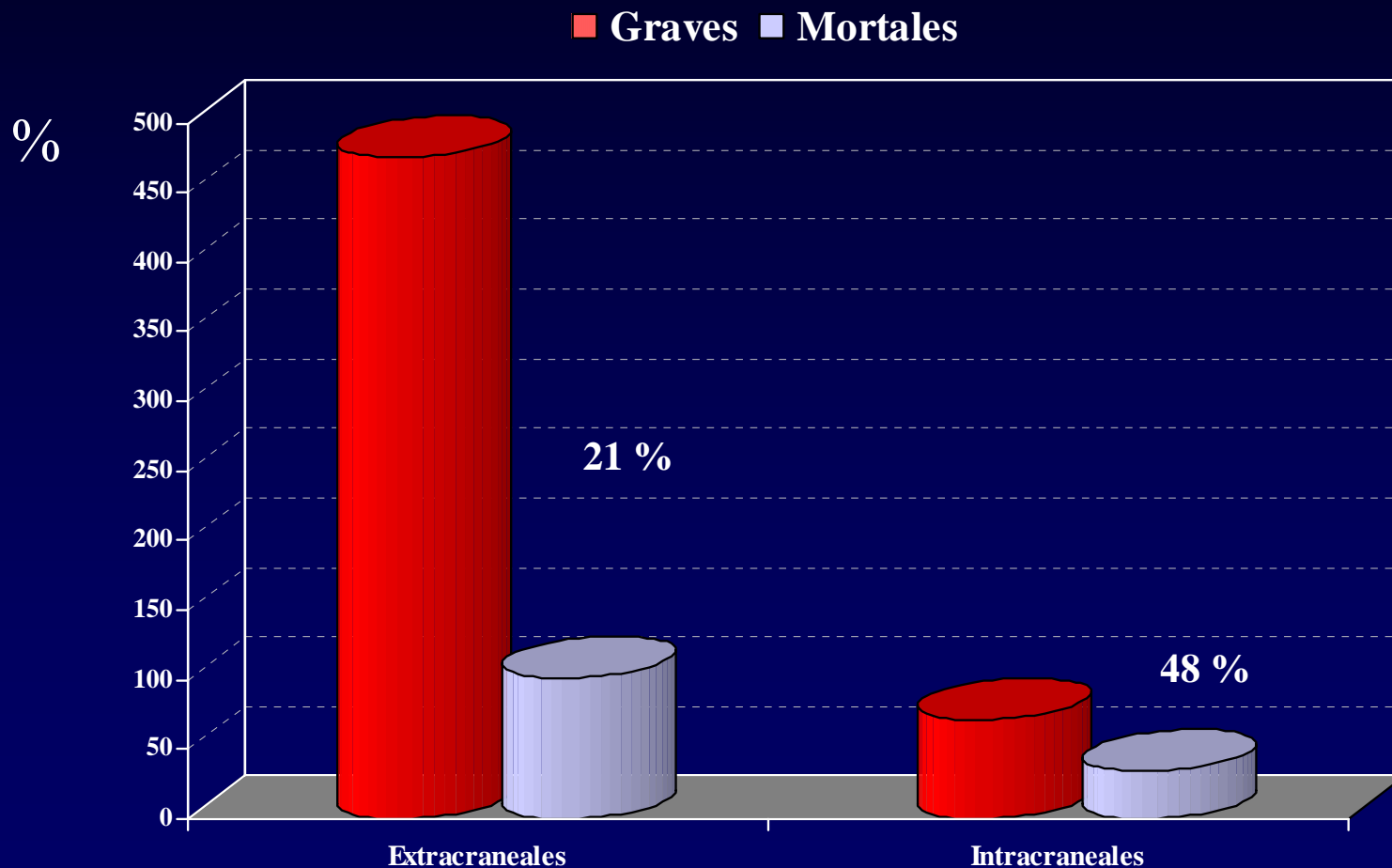


	<b>Fatal Bleeding</b>		<b>Major Bleeding</b>	
	<b>OR</b>	<b>Points</b>	<b>OR</b>	<b>Points</b>
Age >75 years	<b>2.2</b>	1	<b>1.6</b>	1
Metastatic cancer	<b>3.8</b>	2	<b>2.1</b>	1
Immobility $\geq$ 4 days	<b>2.0</b>	1		
Recent major bleeding	<b>2.6</b>	1.5	<b>2.2</b>	2
Abnormal prothrombin time	<b>2.1</b>	1		
CrCl < 30 ml/min	<b>2.3</b>	1	<b>2.4</b>	1.5
Platelet Count <10 <sup>9</sup> /L	<b>2.2</b>	1		
Anemia	<b>1.5</b>	1	<b>2.0</b>	1.5
Distal DVT	<b>0.4</b>	-1		
Pulmonary Embolism			<b>1.4</b>	1

*JTH 2010; 8: 1216-1222*

*Thromb Hemost 2008; 100: 26-31*

RIETE. 24.395 pacientes.  
Hemorragias graves (n, 546) y mortales (n, 135)



$p < 0,001$

# Categorías de riesgo y tipo de sangrado

---

<b>SCORE</b>	<b>Sensitivity</b>	<b>Specificity</b>	<b>PPV</b>	<b>NPV</b>	<b>LR (95%CI)</b>
Low risk (< 1,5)	18.5	35.8	0.2	98.7	0.29 (0.20-0.41)
Intermediate risk (1.5-4)	64.4	66.4	1.1	99.7	1.92 (1.69-2.17)
High risk (>4)	17	97.9	4.2	99.5	7.95 (5.42-11.6)

# Riesgo de hemorragia grave en 3 meses

( % de pacientes )

Riesgo	Derivación N = 9.756	Validación N = 4.773
Bajo (0-1)	0,8 ( 0,6 – 1.1 )	0,6 ( 0,3 – 1.0 )
Intermedio (2-5)	3,3 ( 2,8 – 3,8 )	3,3 ( 2,6 – 4,1 )
Alto (>5)	8,1 ( 6.0 – 11 )	7,7 ( 4,9 – 11 )

*Thromb Hemost 2008; 100: 26-31*