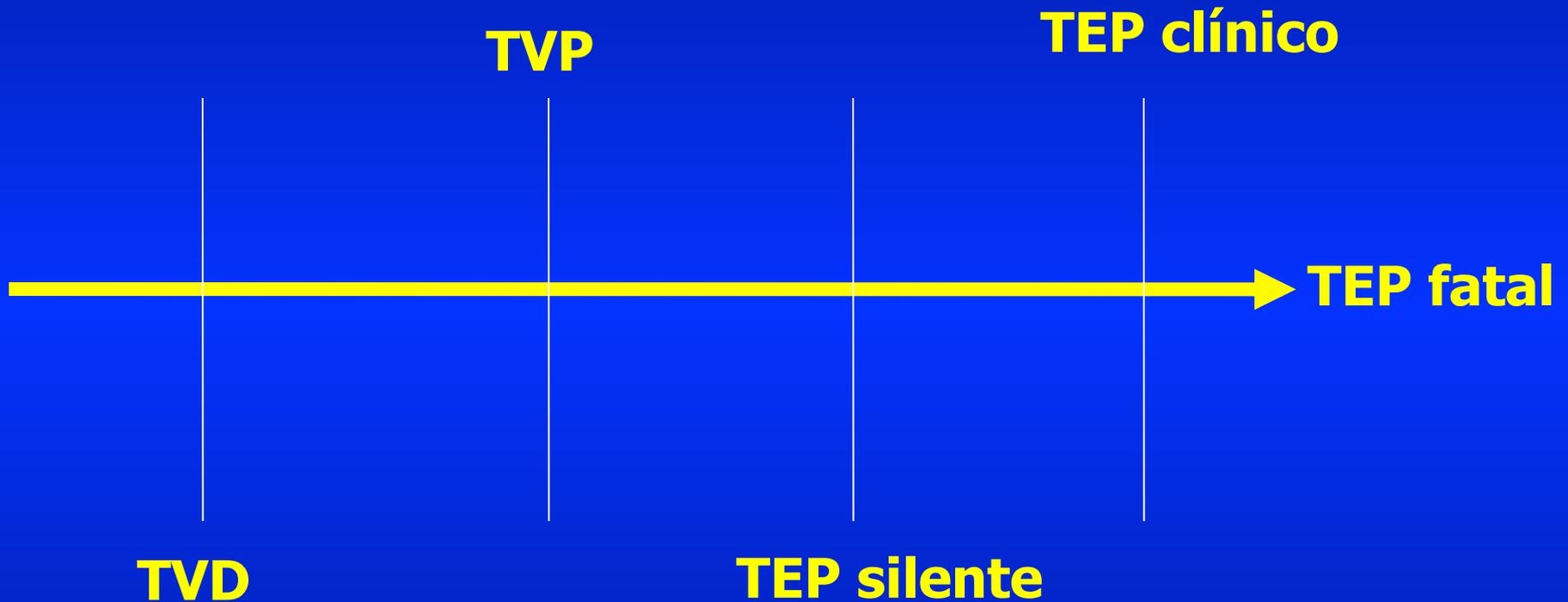


# **Tromboembolismo Venoso (TEV) Diagnóstico y Tratamiento**



**Dardo Riveros**  
**Sección Hematología**  
**Departamento de Medicina Interna**

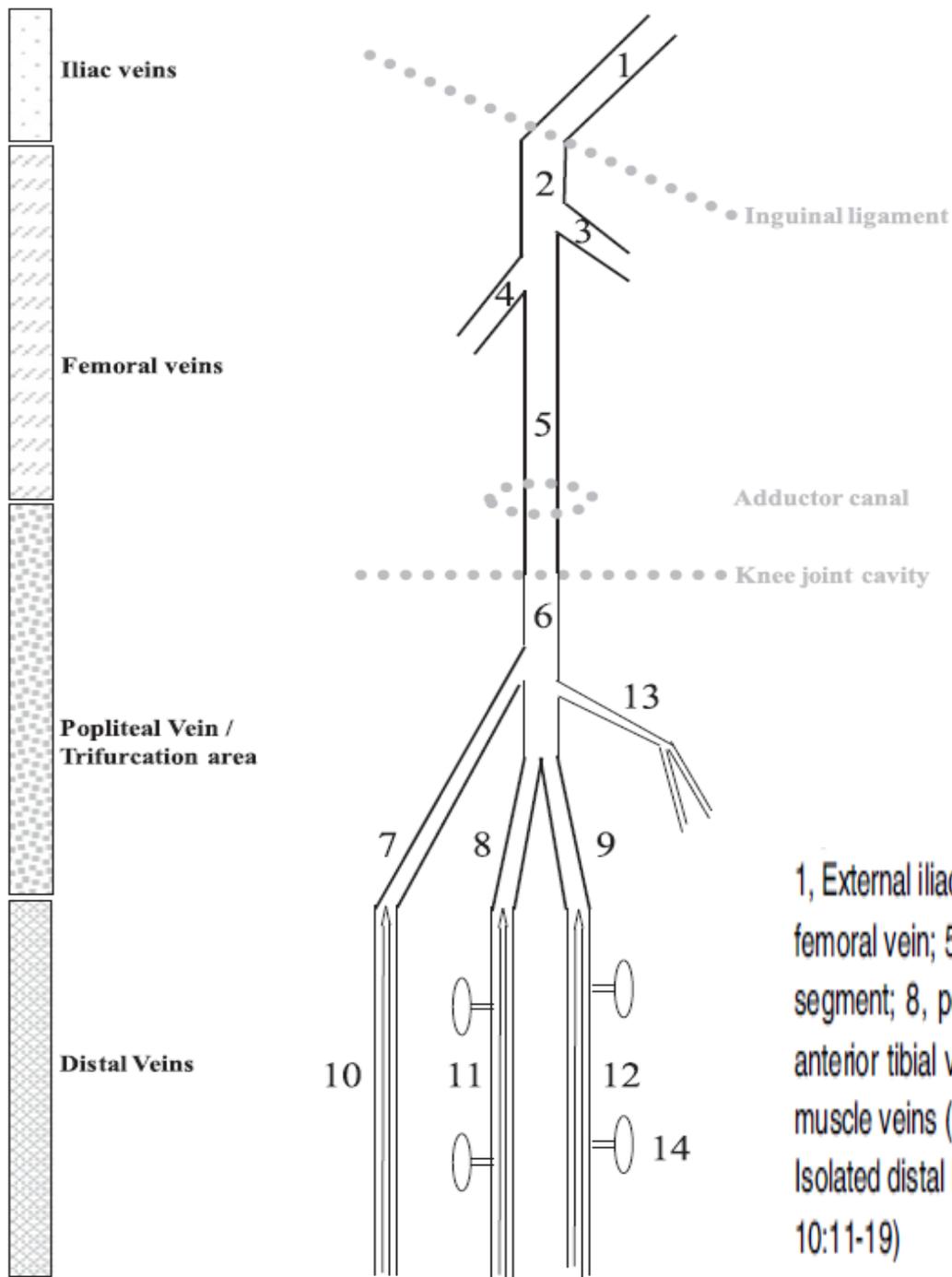
# El TEV como un Proceso con Distintas Expresiones



*TVD: trombosis venosa distal*

*TVP: trombosis venosa proximal*

*TEP: tromboembolismo pulmonar*



# Venas de la Pierna

## Representación Esquemática

1, External iliac vein; 2, common femoral vein; 3, greater saphenous vein; 4, profound femoral vein; 5, (superficial) femoral vein; 6, popliteal vein; 7, anterior tibial confluent segment; 8, posterior tibial confluent segment; 9, peroneal confluent segment; 10, anterior tibial veins; 11, posterior tibial veins; 12, peroneal veins; 13, gastrocnemius muscle veins (medial head); 14, soleus muscle veins. (From Palareti G, Schellong S. Isolated distal DVT: what we know and what we are doing. *J Thromb Haemost.* 2012; 10:11-19)

# Epidemiología

- **Incidencia :** **100-270 /100.000/año**
- **Mortalidad en internación:** **30 %**
- **Recurrencia a los 10 años:** **30 %**
- **Síndrome post- trombótico:** **40 % a los 20 años**
- **Incidencia de hipertensión pulmonar sintomática:** **4% a los 2 años**

## Venous thromboembolism caused 25 000 deaths a year, say MPs

Rebecca Coombes London

Blood clots that develop while patients are in hospital cause deaths on a far larger scale than does methicillin resistant *Staphylococcus aureus* (MRSA), but the extent of the problem is largely unrecognised by doctors, MPs said this week.

In a critical report on the prevention of venous thromboembolism, the health select committee said the condition killed more than 25 000 patients in England each year, more than the combined deaths from breast cancer, AIDS, and road traffic injuries and more than 25 times the number of deaths from MRSA.

However, although many of the deaths from venous thromboembolism are preventable through cheap and effective drug treatment, problems often do not occur until after discharge from hospital, and so physicians and surgeons are left unaware of the problem.

part or all of the clot breaks off and travels through the venous system. In the United Kingdom, pulmonary embolism after deep vein thrombosis is the immediate cause of death of a tenth of all patients who die in hospital.

The MPs' report cited a study of over 4000 patients who died of pulmonary embolism after major surgery; the study showed that the use of perioperative low dose heparin saved seven lives per 1000 patients operated on. The death rate is currently eight per 1000 operated on.

Despite the scale of the problem, doctors will have to wait until May 2007 for clinical guidelines on preventive measures from the National Institute for Clinical Excellence. These guidelines will apply only to surgical patients at high risk of venous thromboembolism.

The select committee condemned this response as "remarkably tardy." It said: "Moreover, the

## Mortalidad por TEV en internación

- 25000 muertes al año (25 veces más que por *S. aureus MR* y más que la combinación de muertes por SIDA, cáncer de mama y accidentes de tránsito.
- 8 c/1000 cirugías
- Heparina salva 7 vidas c/ 1000 cirugías

■ On 19 April 2007, Government announced national VTE strategy, which will require mandatory risk-assessment and prophylaxis in UK hospitals

# Recomendaciones para Profilaxis del TEV

<b>Nivel</b>	<b>Riesgo (%)</b>	<b>Tromboprofilaxis</b>
<b>Bajo</b> Cirugía menor sin factores de riesgo. No quirúrgicos (activos)	<10	<i>Ambulación precoz</i>
<b>Moderado</b> Cirugía mayor No quirúrgicos (en reposo)	30	<i>HBPM, HNF x 2 fondaparinux</i>
<b>Alto-Muy alto</b> Ortopedia-Oncología Trauma-Trombofilia	40-80	<i>HBPM, HNF x 3 Fondaparinux, anti-vit.K AAS Anticoagulantes orales directos (AODs)</i>

# **Tromboembolismo Venoso (TEV) Diagnóstico**

**1- Probabilidad clínica pre-test**

**2- Dímero-D**

**3- Técnicas de imágenes**

# Modelo para Trombosis Venosa Profunda (TVP)

Condición clínica	Puntaje
- Trombosis venosa profunda previa	1
- Parálisis, paresia o yeso en MMII	1
- Inmovilización reciente > 3 días o cirugía mayor en las últimas 12 semanas	1
- Tumefacción / dolor a lo largo trayecto venoso	1
- Pierna entera edematizada	1
- Pantorrilla edematizada (> 3cm)	1
- Edema con godet en pierna comprometida	1
- Dilatación venosa no varicosa	1
- Diagnóstico alternativo	- 2

- 2 o > : TVP probable
- 0, 1 o 2 : TVP poco probable

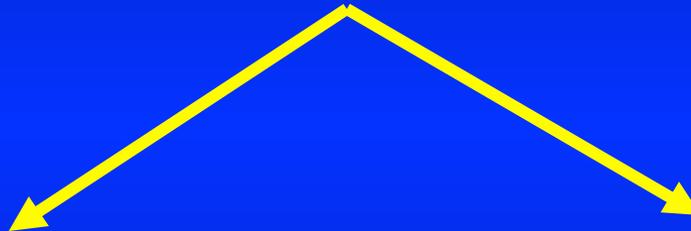
# Metodología Diagnóstica para TVP

**TVP Poco Probable**



- → *Dímero -D excluye TEP\**

**Ultrasonografía por compresión (USC)**



**Negativa**



**Excluye TVP**

**Positiva**



**Confirma TVP**

*\* Test de dímero-D ajustado a edad (Righini M, y col. JAMA 2014)*



# Tromboembolismo de Pulmón (TEP)

## Regla de decisión clínica dicotomizada

Variable	Puntaje
Signos clínicos y síntomas de TVP	3.0
Baja probabilidad de diagnóstico alternativo	3.0
Frecuencia cardíaca mayor de 100/min	1.5
Inmovilización > de 3 días o cirugía en las 4 semanas previas	1.5
TEV previo	1.5
Hemoptisis	1.0
Neoplasia en tratamiento	1.0

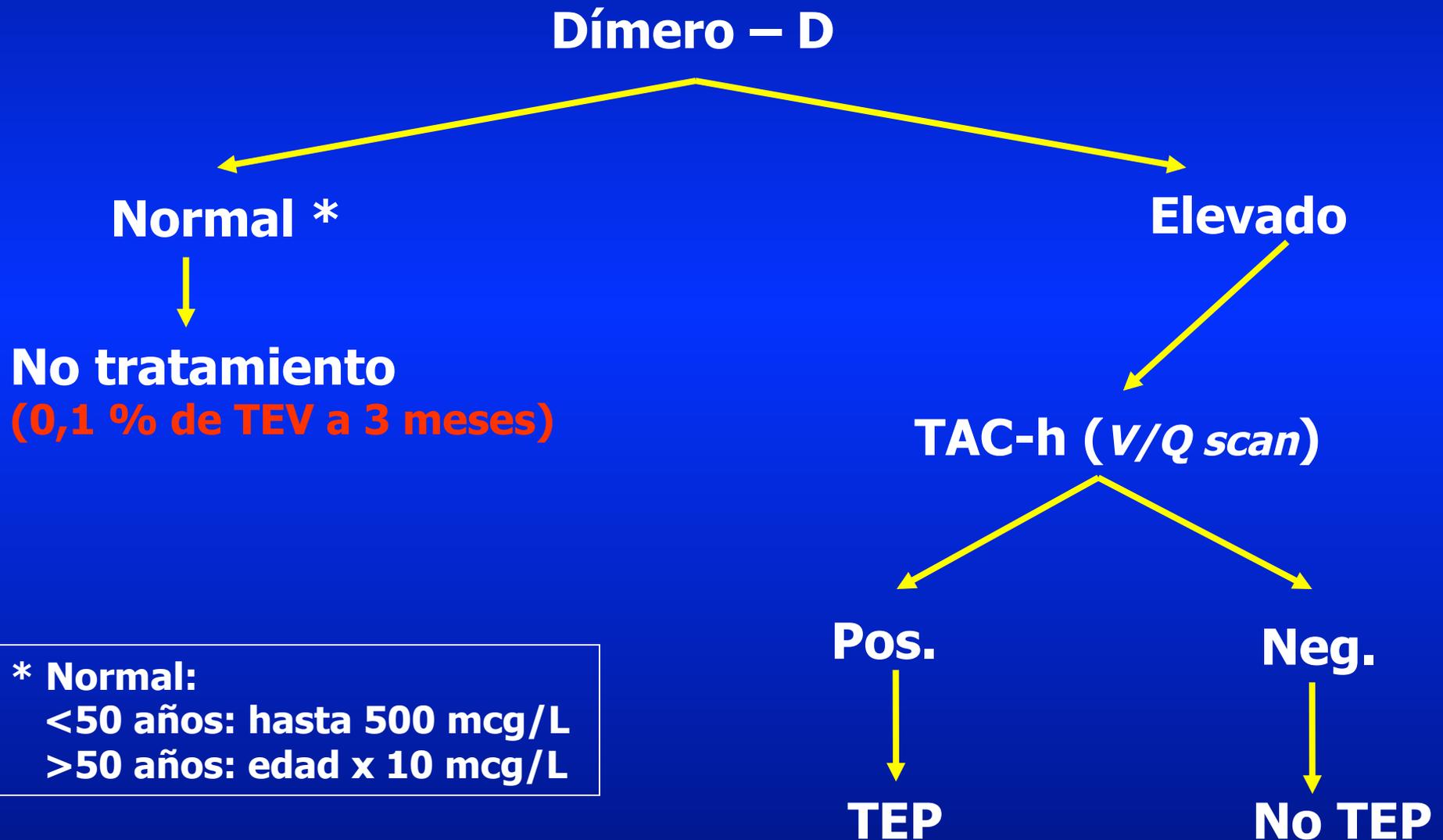
TEP poco probable:  $\leq 4$  puntos (10% de probabilidad)

TEP probable :  $\geq 5$  puntos (40-70%)

*Wells PS, y col. Thromb Haemost.*

# Enfermos sin Inestabilidad Hemodinámica

## TEP Poco Probable (Wells dicotomizado)



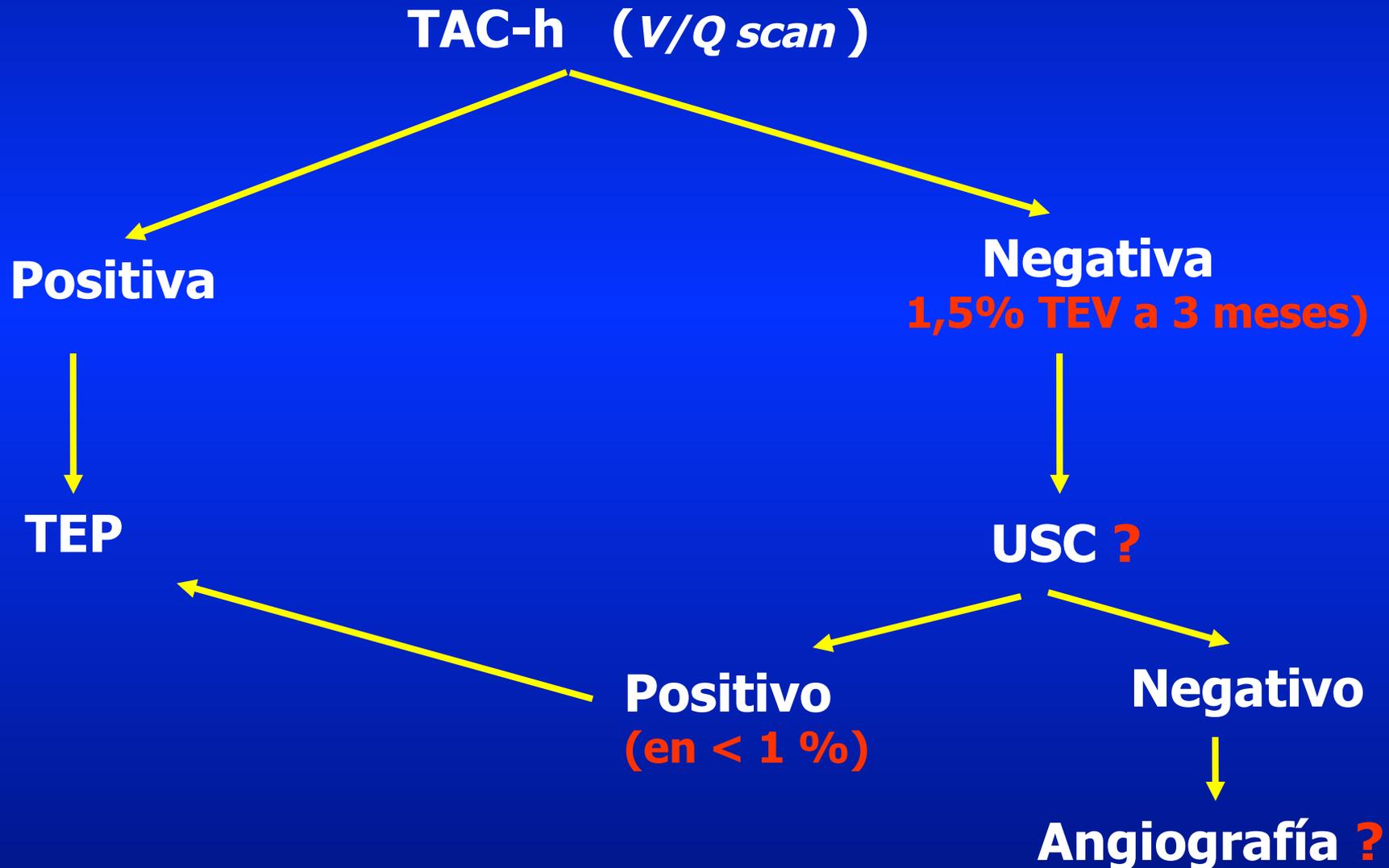
\* Normal:

<50 años: hasta 500 mcg/L

>50 años: edad x 10 mcg/L

# Enfermos sin Inestabilidad Hemodinámica

## TEP Probable ( Wells dicotomizado)



# Enfermos con Inestabilidad Hemodinámica

¿TAC-h disponible?

NO

SI

Ecocardiograma

Neg.

Pos.

Pos.

Neg.

Otra causa

TEP

Otra causa

American Society of Hematology 2018 guidelines for management of venous thromboembolism: venous thromboembolism in the context of pregnancy

## Diagnosis of VTE

**Recommendation 30.** For pregnant women with suspected pulmonary embolism, the ASH guideline panel *suggests* ventilation-perfusion (V/Q) lung scanning over computed tomography (CT) pulmonary angiography (conditional recommendation, low certainty in evidence about effects ⊕⊕○○).

**Recommendation 31.** For pregnant women with suspected DVT, the ASH guideline panel *suggests* additional investigations, including serial compression ultrasound or magnetic resonance venography compared with no further investigations after an initial negative ultrasound with imaging of the iliac veins (conditional recommendation, low certainty in evidence about effects ⊕⊕○○).

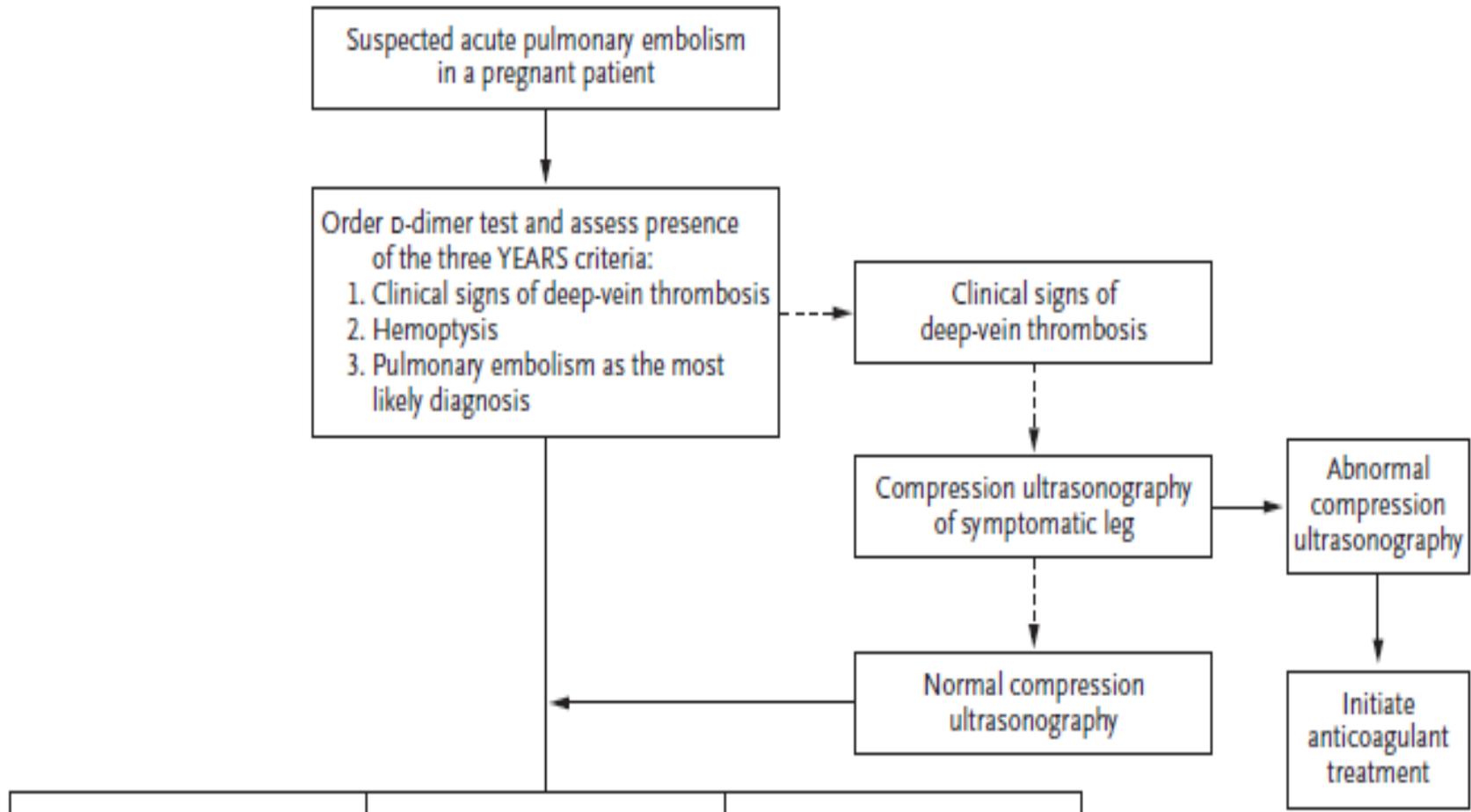


## Imaging of Pregnant and Lactating Patients: Part I, Evidence-Based Review and Recommendations

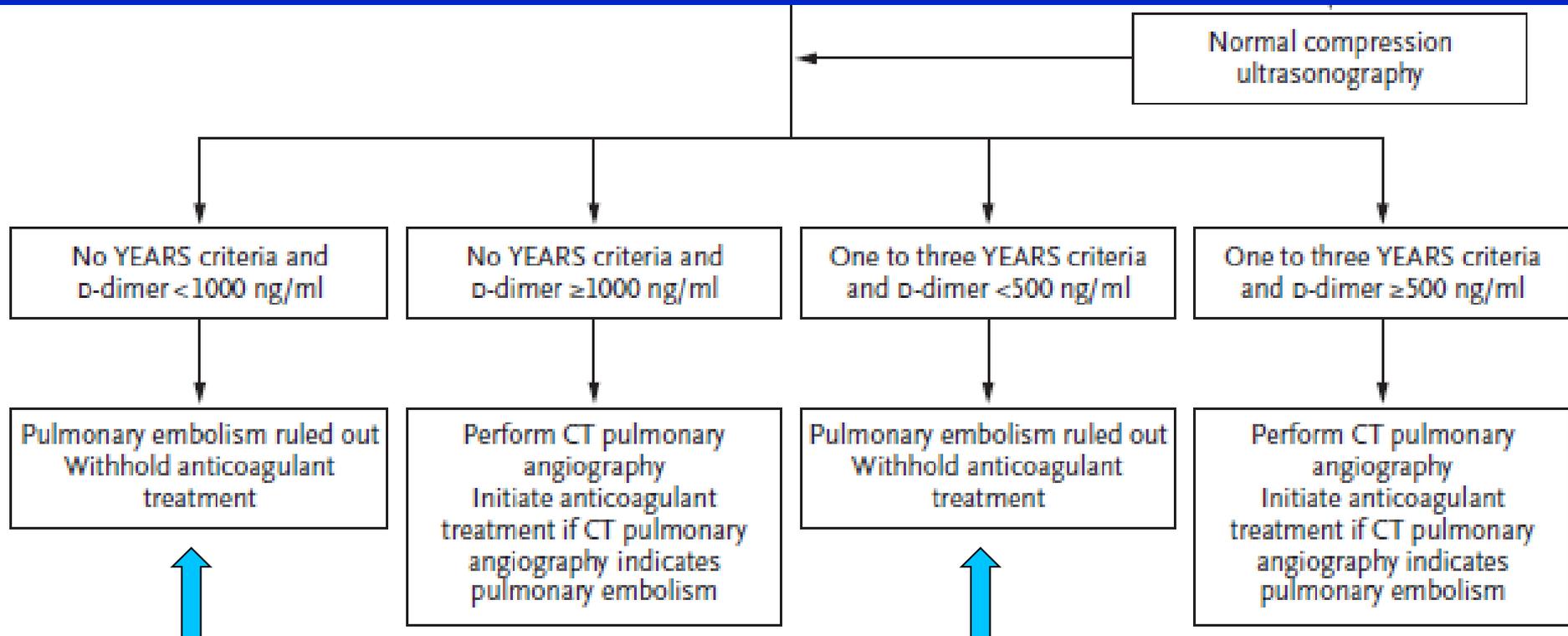
### Conclusiones para exposición fetal

- Toxicidad determinística con  $> 100$  mSv (10 rads=0,1 Gy)
- Los métodos diagnósticos habituales están debajo de ese nivel (TAC tórax = 0,2 mSv. Es algo  $>$  con scan V/Q). El problema radicaría en la acumulación o repetición
- Toxicidad estocástica : sin umbral de exposición fetal, pero 10-50 mSv (p.ej. TAC tórax +abdomen+pelvis con contraste) duplica el riesgo de leucemia

## Pregnancy-Adapted YEARS Algorithm for Diagnosis of Suspected Pulmonary Embolism



## Pregnancy-Adapted YEARS Algorithm for Diagnosis of Suspected Pulmonary Embolism



**TC evitada : 65% en primer trimestre y 32% en el tercero**

# Metodología Diagnóstica para TEP en Embarazo

**Rx tórax (*iniciar HBPM*)**

***Anormal***

***Normal***

**TAC**

**Doppler**

***Neg.***

***Pos.***

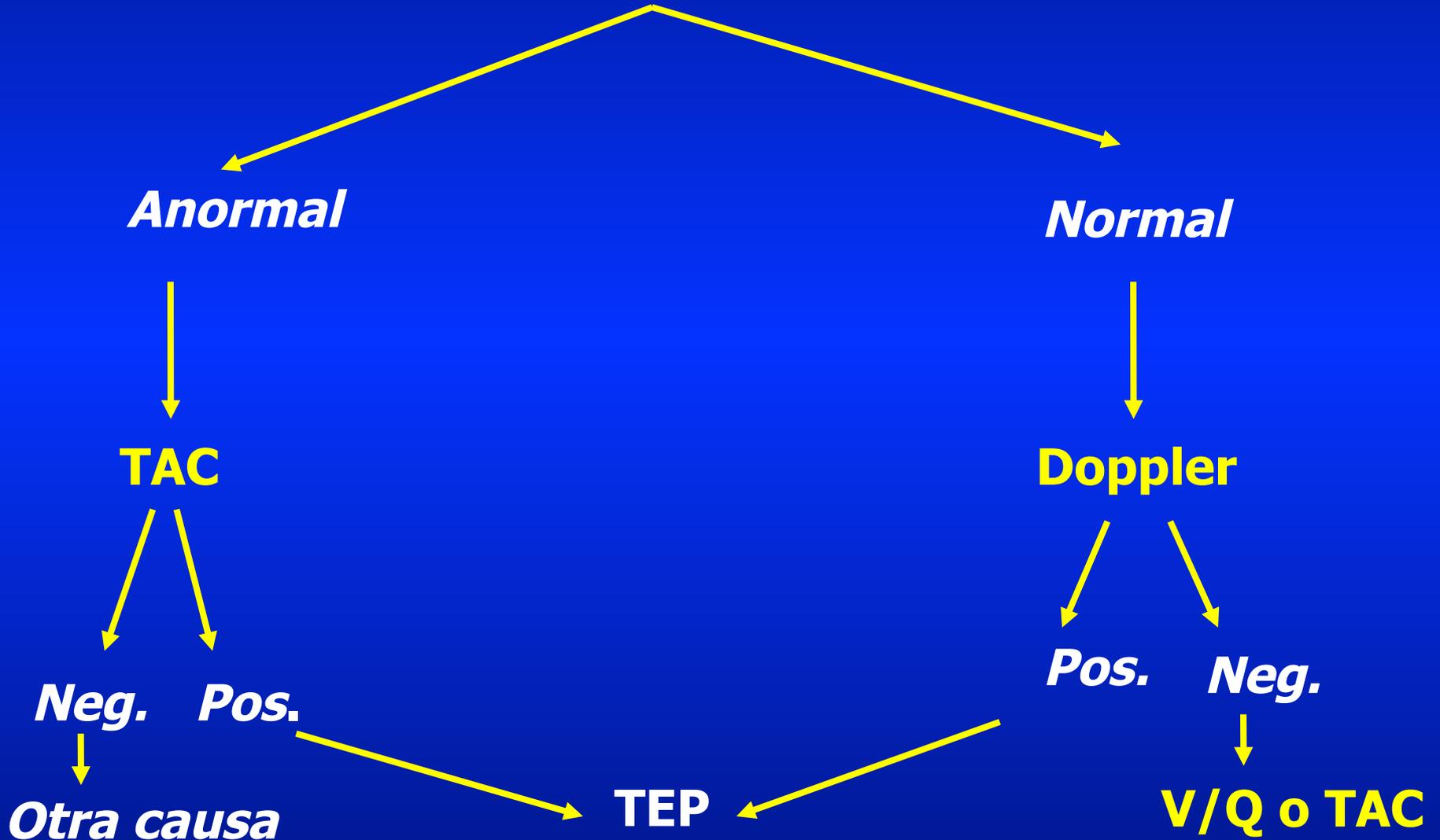
***Pos.***

***Neg.***

***Otra causa***

**TEP**

**V/Q o TAC**



# Tratamiento del TEV

- **Fases del tratamiento**
  - Aguda: hasta días 5- 10**
  - Prolongada: primeros 3 meses**
  - Extendida con tope: 6-12-24 meses**
  - Extendida sin tope: "indefinida"**
- **¿Internado o en su casa?**
- **¿Anticoagulación, trombolisis o filtro?**
- **Elección del agente y duración del tratamiento**
- **Prevención del síndrome postrombótico**

# Tratamiento del TEV

- *Fases del tratamiento*
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- **Prevención del síndrome postrombótico**

# **PESI Simplificado (PESIs)**

**Edad > de 80 años**

**Neoplasia ( antecedente o activa)**

**Cardiopatía o EPOC o nefropatía o enf. cerebrovascular**

**Frecuencia cardíaca >110/min**

**Presión arterial sistólica <100 mm Hg**

**Saturación de oxígeno arterial <90%**

*Cada factor = 1 punto*

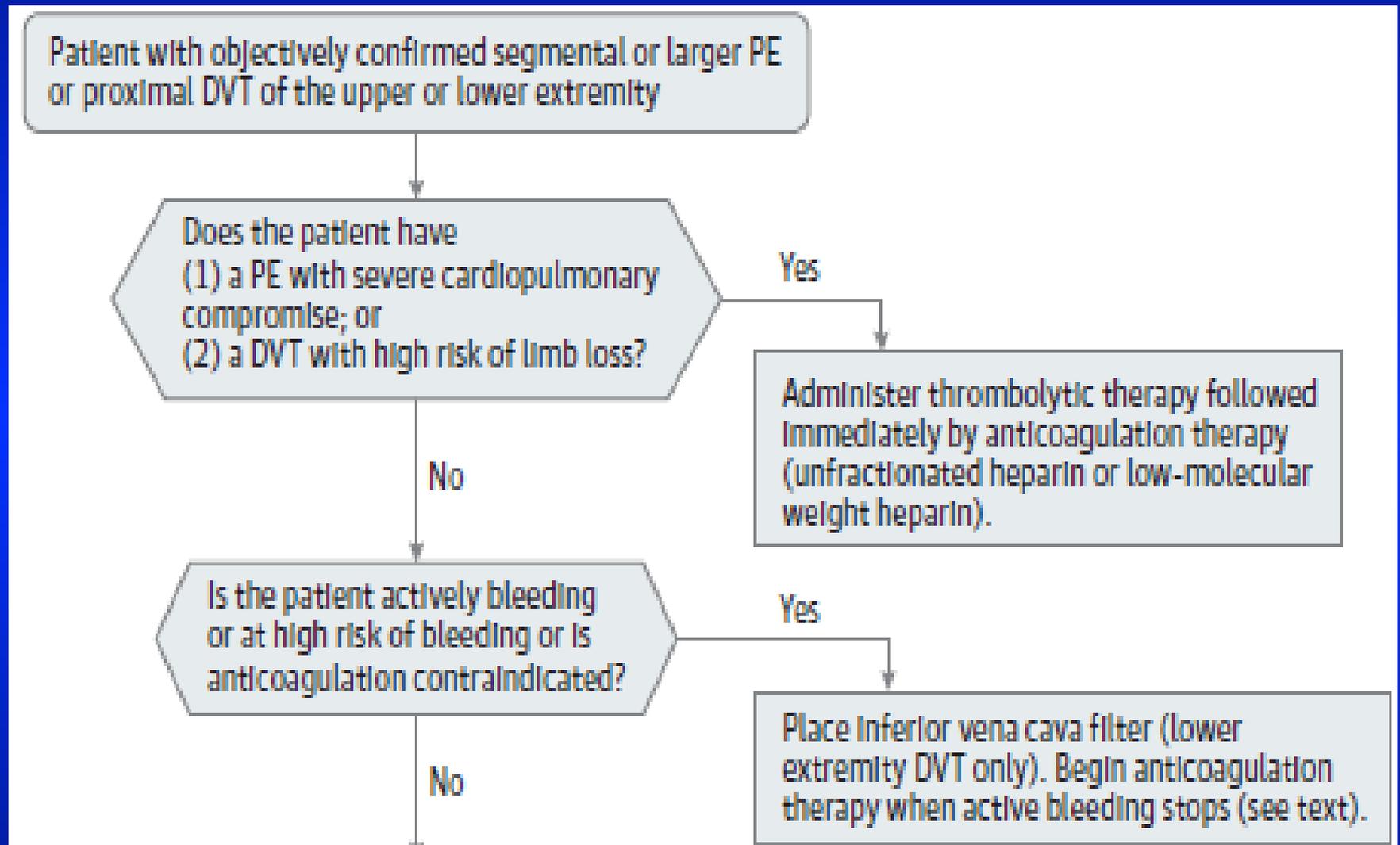
*Score 0 puede ser tratado en forma ambulatoria*

***Jimenez D, y col. Arch Intern Med 2010***

# Tratamiento del TEV

- *Fases del tratamiento*
  - Aguda: hasta días 5- 10*
  - Prolongada: primeros 3 meses*
  - Extendida con tope: 6-12-24 meses*
  - Extendida sin tope: "indefinida"*
- *¿Internado o en su casa?*
- **¿Anticoagulación, trombolisis o filtro?**
- **Elección del agente y duración del tratamiento**
- **Prevención del síndrome postrombótico**

# Tratamiento Inicial sin Anticoagulación



**Wells PS, y col. JAMA 2014;311(7):717-728**

# Trombolisis vs HNF en TEP

- Un meta-análisis demostró que la trombolisis endovenosa redujo la mortalidad y el TEP recurrente entre los enfermos hemodinámicamente inestables cuando se la comparó con la HNF (9,4% vs 19%)

**Contraindicaciones:** HTA no controlada, hemorragia cerebral y trauma o cirugía mayor en las 3 semanas previas.

***Wan S, y col. Circulation 2004***

# Trombolisis en Tratamiento Inicial del TEP

**TEP masivo o sub- masivo con falla hemodinámica**

## **Fármacos**

- Estreptoquinasa: 250.000U EV en 30 min y luego  
100.000 U / hora por 24 hs**
- Uroquinasa: 4.400 U / kg EV en 10 min y luego  
4.400 U / Kg / hora por 12 horas**
- Alteplase:
  - 10 mg en bolo EV y 90 mg en  
infusión de 2 horas**
  - 50 mg EV en 15 minutos en casos con  
de falla cardiorrespiratoria****

# Trombolisis en Tratamiento Inicial de la TVP

- Puede mejorar el síndrome postrombótico a costa de mayor sangrado
- No reduce riesgo de recurrencia, TEP ni muerte
- Se recomienda en casos con compromiso arterial
- La modalidad guiada por catéter puede ser mejor en casos de localización iliofemoral, antes de los 14 días, con bajo riesgo de sangrado y expectativa vida > 1 año

## How I use catheter-directed interventional therapy to treat patients with venous thromboembolism

Suresh Vedantham<sup>1</sup> and Akhilesh K. Sista<sup>2</sup>

### Patient 1

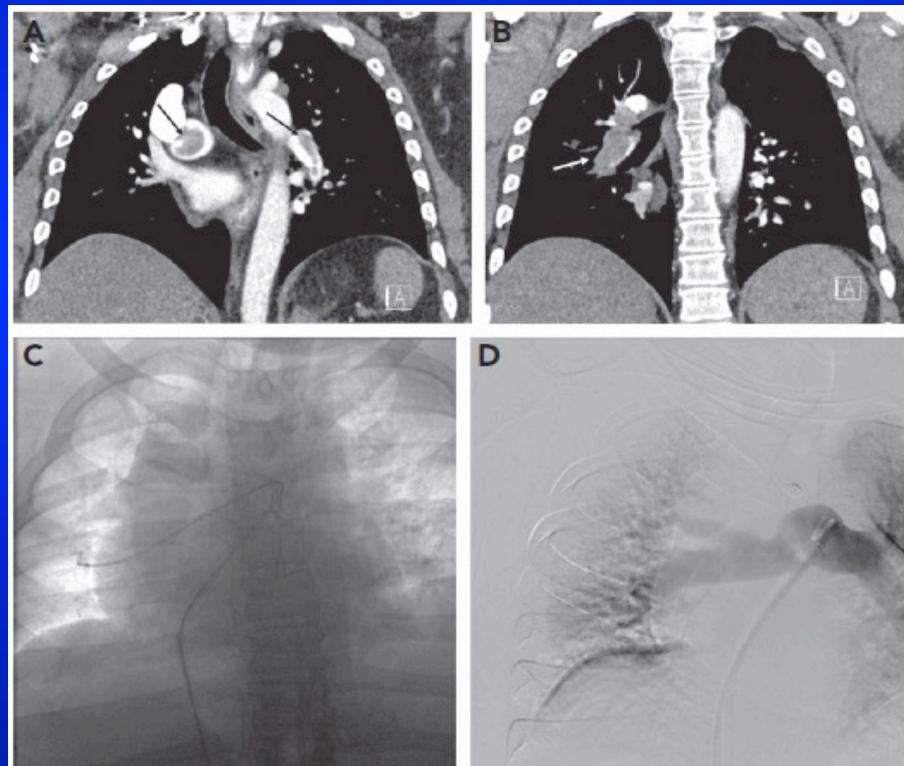
Proximal DVT and PTS

### Patient 2

Submassive PE

### Patient 3

Massive PE



# Filtro en Vena Cava Inferior

- **Falla de tratamiento bajo heparinización**
- **Contraindicación absoluta de anticoagulación**

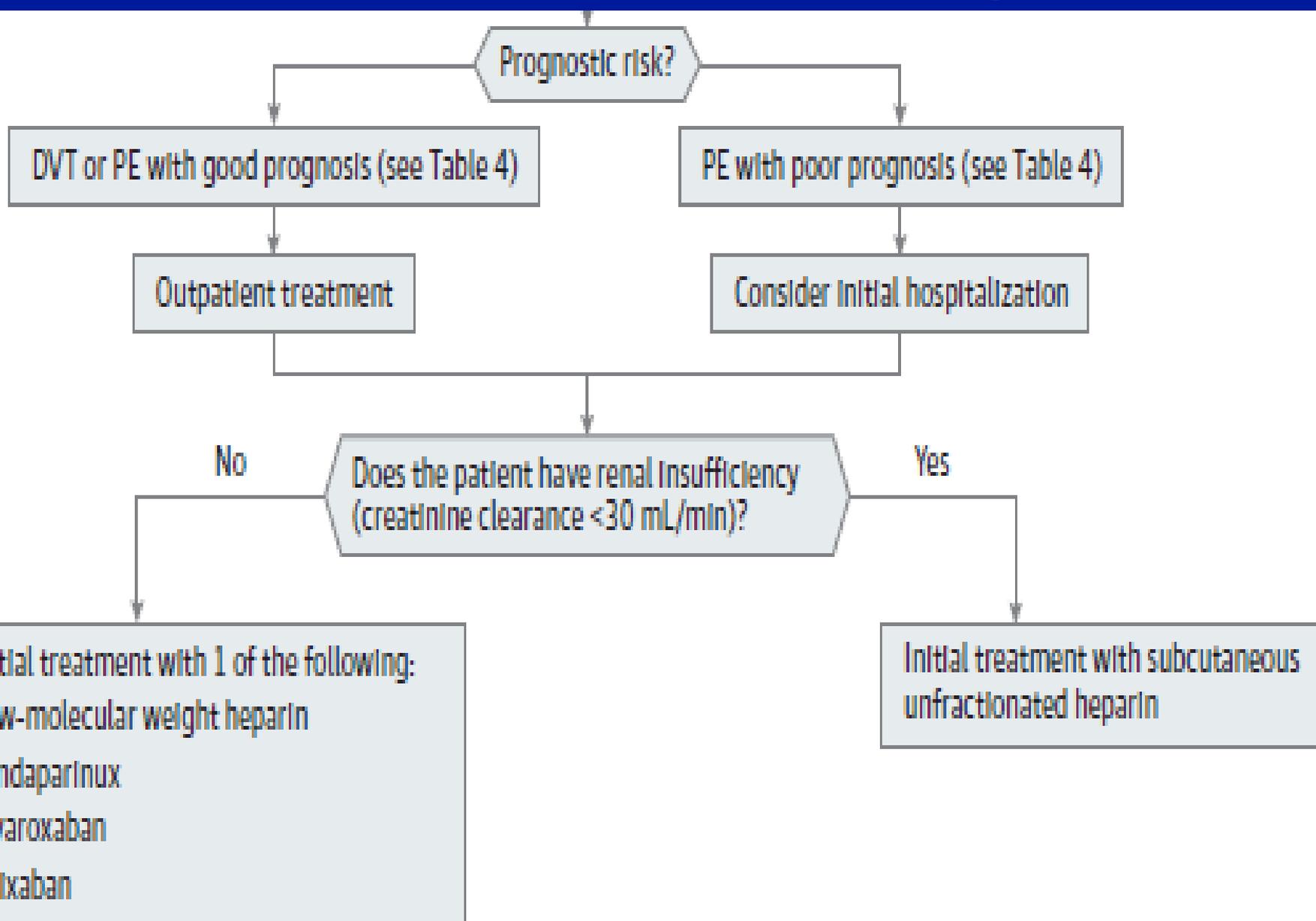
**Observaciones: incrementa el riesgo de TVP recurrente y no es seguro que disminuya el riesgo de TEP y mortalidad.**

***Wells PS. JAMA 2014***

# Tratamiento del TEV

- *Fases del tratamiento*
  - Aguda: hasta días 5- 10*
  - Prolongada: primeros 3 meses*
  - Extendida con tope: 6-12-24 meses*
  - Extendida sin tope: "indefinida"*
- *¿Internado o en su casa?*
- *¿Anticoagulación, trombolisis o filtro?*
- **Elección del agente y duración del tratamiento**
- **Prevención del síndrome postrombótico**

# Tratamiento Inicial con Anticoagulación



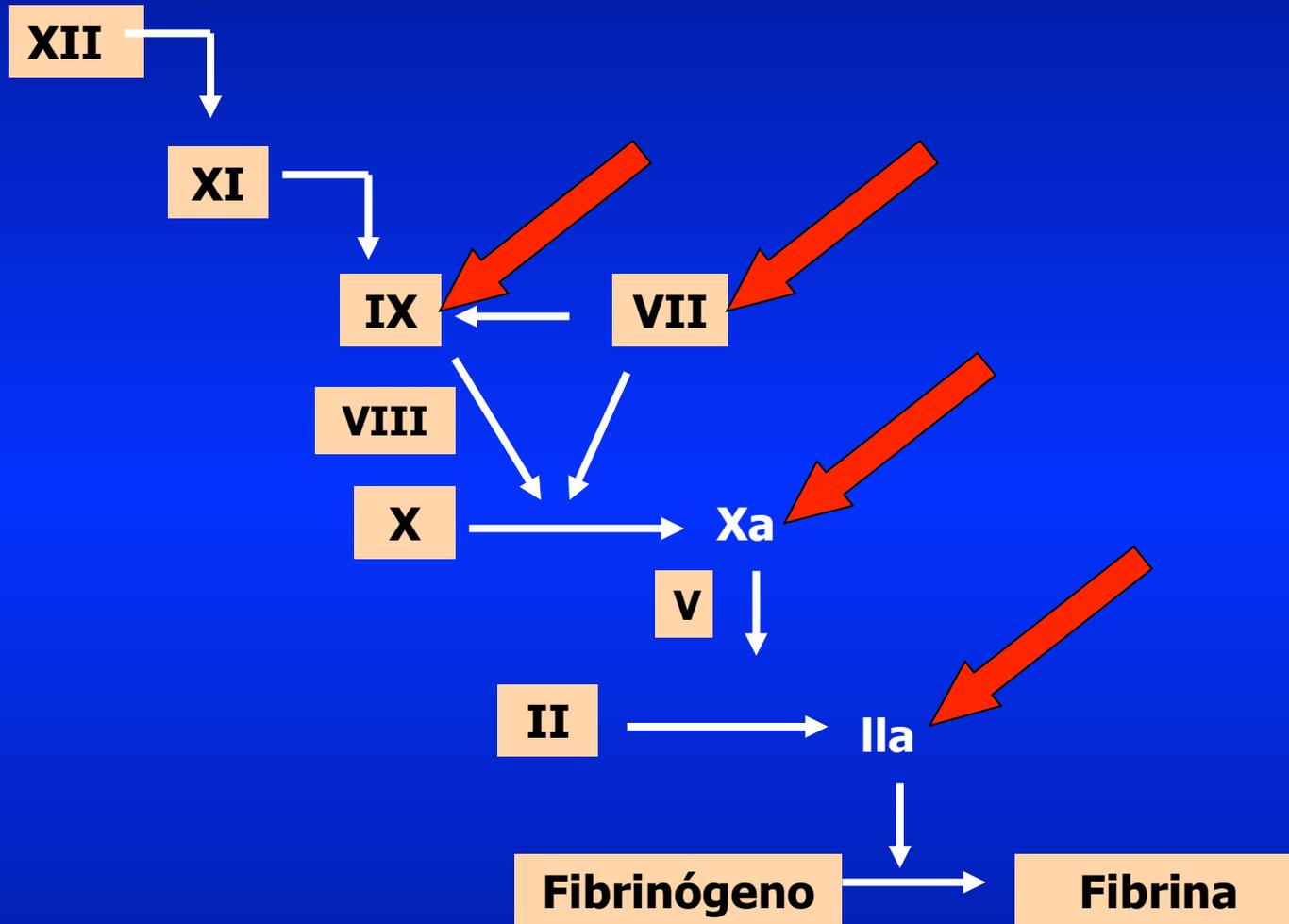
# **HBPM . Características que las Diferencian de HNF**

- **Farmacocinética más predecible**
- **> anti Xa que anti IIa**
- **> vida media**
- **< riesgo de efectos adversos no hemorrágicos**

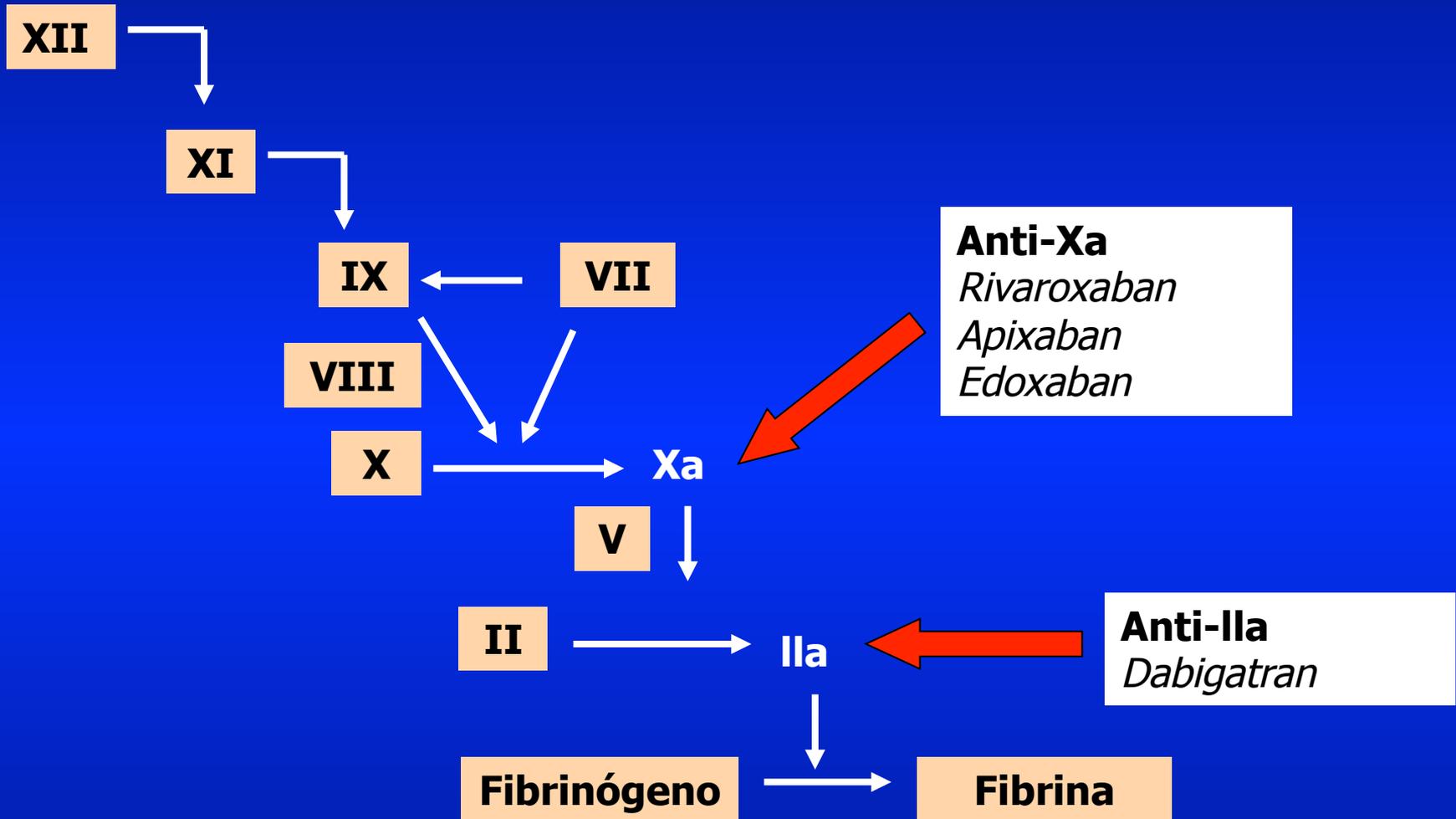
**1- Aplicación subcutánea (1 a 2 veces x día)**

**2- Sin necesidad de monitoreo**

# Dicumarínicos



# Anticoagulantes Orales Directos (AODs)



# Drogas para el Tratamiento del TEV

Agente	Dosis	Vida media (horas)	Eliminación renal (%)
Heparina	<ul style="list-style-type: none"> <li>• Bolo EV: 80 U/kg</li> <li>Luego : 18 U/kg/hora (KPTT/ antiXa) *</li> <li>• SC: 333 U/kg</li> <li>Luego: 250 U/kg c/12 hs</li> </ul>	1,5	30
Enoxaparina	<ul style="list-style-type: none"> <li>• SC: 1 mg/kg c/12 hs</li> <li>• SC: 1,5 mg/kg c/24 hs</li> </ul>	3-4	80
Nadroparina	<ul style="list-style-type: none"> <li>• SC: 86 UI/kg c/12 hs</li> <li>• SC: 171 UI/kg c/24 hs</li> </ul>	3-4	80

\* Heparinemia: HNF = 0,3-0,7 UI/ml  
 HBPM = 0,5-1,2 UI/ml

# Drogas Orales para el Tratamiento del TEV

<b>Agente</b>	<b>Dosis</b>	<b>Vida media (horas)</b>	<b>Eliminación renal (%)</b>
<b>Anti-Vit.K</b>	<ul style="list-style-type: none"><li>• Warfarina: 0,5-6 mg/día</li><li>• Acenocumarol: 1-3 mg/día VO (RIN 2-3)</li></ul>	<b>36-48 hs</b>	<b>2</b>
<b>Rivaroxaban</b>	<ul style="list-style-type: none"><li>• 15 mg c/12 hs x 3 sem. Luego 20mg c/24 hs</li></ul>	<b>7-11</b>	<b>33</b>
<b>Apixaban</b>	<ul style="list-style-type: none"><li>• 10 mg c/12 hs x 10 días Luego 5 mg c/24 hs</li></ul>	<b>8-12</b>	<b>25</b>
<b>Dabigatran</b>	<ul style="list-style-type: none"><li>• 150 mg c/12 hs luego de 7-10 días con HBPM</li></ul>	<b>14-17</b>	<b>80</b>

# Diferencias Farmacológicas

<b>Variable</b>	<b>Dicumarínicos</b>	<b>AODs</b>
<b>Interacción con alimentos</b>	>	
<b>Interacción con medicamentos</b>	>	
<b>Eliminación renal</b>		>
<b>Vida media</b>	> (40 horas)	(7-14 horas)
<b>Velocidad de acción</b>	(4-5 días)	> (2-4 horas)
<b>Medición de efecto y ajuste de dosis</b>	Sí	No

# AODs y Función Renal

<b>Agente</b>	<b>ClCr &gt; 50 ml/min</b>	<b>ClCr 30-49 ml/ min</b>	<b>ClCr 15-29 ml/ min</b>
<b>Rivaroxaban</b>	<b>20mg c/24 hs</b>	<b>15 mg c/24 hs</b>	<b>Evitar uso</b>
<b>Apixaban</b>	<b>5mg c/12 hs</b>	<b>5mg c/12 hs</b>	<b>5mg c/12 hs</b>
<b>Dabigatran</b>	<b>150 mg c/12 hs</b>	<b>150 mg c/12 hs</b>	<b>Evitar uso</b>

# AODs

- **Problemas generales**

**1- Ausencia de monitoreo (adherencia y control)**

**2- Falta de antídoto**

**3- Bioacumulación por deterioro renal**

**4- Traslado de los costos al paciente**

# AODs

## No candidatos para su uso en TEV

- 1- Preferencia del paciente (costo económico)
- 2- Acceso a buen control del RIN
- 3- Insuficiencia renal ( $<30$  ml/min)
- 4- Uso concomitante de inductores o inhibidores de P-gp o CYP3A4
- 5- Antecedentes de patología digestiva y/o  $> 80$  años
- 6- Posibilidad de mala adherencia al tratamiento

## AODs vs Warfarina en TEV

<b>Variable</b>	<b>Apixaban</b>	<b>Rivaroxaban</b>	<b>Dabigatran</b>
<b>Recurrencia del TEV</b>	<b>- 1,8%</b>	<b>- 1,2%</b>	<b>+ 1,0%</b>
<b>Hemorragia mayor</b>	<b>- 7,5%</b>	<b>- 5.0%</b>	<b>- 2,6%</b>
<b>Costos/ pac./año</b>	<b>- U\$S 4.440</b>	<b>- U\$S 2.971</b>	<b>- U\$S 572</b>

***Amin A, y col. Clin Appl Thromb/Hemost. 2016***

\*2. In patients with DVT of the leg or PE and no cancer, as long-term (first 3 months) anticoagulant therapy, we suggest dabigatran, rivaroxaban, apixaban, or edoxaban over vitamin K antagonist (VKA) therapy (all Grade 2B).

For patients with DVT of the leg or PE and no cancer who are not treated with dabigatran, rivaroxaban, apixaban, or edoxaban, we suggest VKA therapy over low-molecular weight heparin (LMWH) (Grade 2C).

# Tratamiento Inicial del TEV ( días 1-10)

- TEV sospechado: -HNF 5.000 U (EV)  
o HBPM 1 mg /kg (SC)
- TEV confirmado:
  - HNF (EV)\* /HBPM\*\* /HNF (SC)\*\*\* + dicumarínicos  
o  
-AODs (rivaroxaban / apixaban)

*\* Preferible en: disfunción VD, phlegmasia caerulea/alba dolens, riesgo alto para sangrado ,incertidumbre sobre la necesidad de trombolisis, insuficiencia renal*

*\*\* Puede aplicarse 1 vez por día*

*\*\*\* Con clearance de creatinina <30ml/min. Dosis inicial 250 U/kg y luego 200 U/kg c/12 hs.*

# TEP. Tratamiento Inicial Según Riesgo de Muerte

## Riesgo alto

*(shock-hipotensión + disfunción VD)*

- Trombolisis + heparina no fraccionada (HNF) o heparina de bajo peso molecular (HBPM)

## Riesgo int.

*(normotensión, con/sin disfunción VD con/sin injuria miocárdica)*

- HBPM o HNF

## Riesgo bajo

*(normotensión, sin disfunción VD sin injuria miocárdica)*

- HBPM o rivaroxaban o apixaban (en domicilio)

## Antithrombotic Therapy for VTE Disease CHEST Guideline and Expert Panel Report



*Clive Kearon, MD, PhD; Elie A. Akl, MD, MPH, PhD; Joseph Ornelas, PhD; Allen Blaivas, DO, FCCP; David Jimenez, MD, PhD, FCCP; Henri Bounameaux, MD; Menno Huisman, MD, PhD; Christopher S. King, MD, FCCP; Timothy A. Morris, MD, FCCP; Namita Sood, MD, FCCP; Scott M. Stevens, MD; Janine R. E. Vintch, MD, FCCP; Philip Wells, MD; Scott C. Woller, MD; and COL Lisa Moores, MD, FCCP*



**13. In patients with acute isolated distal DVT of the leg and (i) without severe symptoms or risk factors for extension (see text), we suggest serial imaging of the deep veins for 2 weeks over anticoagulation (Grade 2C) or (ii) with severe symptoms or risk factors for extension (see text), we suggest anticoagulation over serial imaging of the deep veins (Grade 2C).**

14. In patients with acute isolated distal DVT of the leg who are managed with anticoagulation, we recommend using the same anticoagulation as for patients with acute proximal DVT (Grade 1B).

15. In patients with acute isolated distal DVT of the leg who are managed with serial imaging, we (i) recommend no anticoagulation if the thrombus does not extend (Grade 1B), (ii) suggest anticoagulation if the thrombus extends but remains confined to the distal veins (Grade 2C), and (iii) recommend anticoagulation if the thrombus extends into the proximal veins (Grade 1B).

# TEV . Extensión del Tratamiento

- **Considerar**

- 1- Tipo y etiología**

**TVP, TVD, TEP**

**Provocado o no provocado**

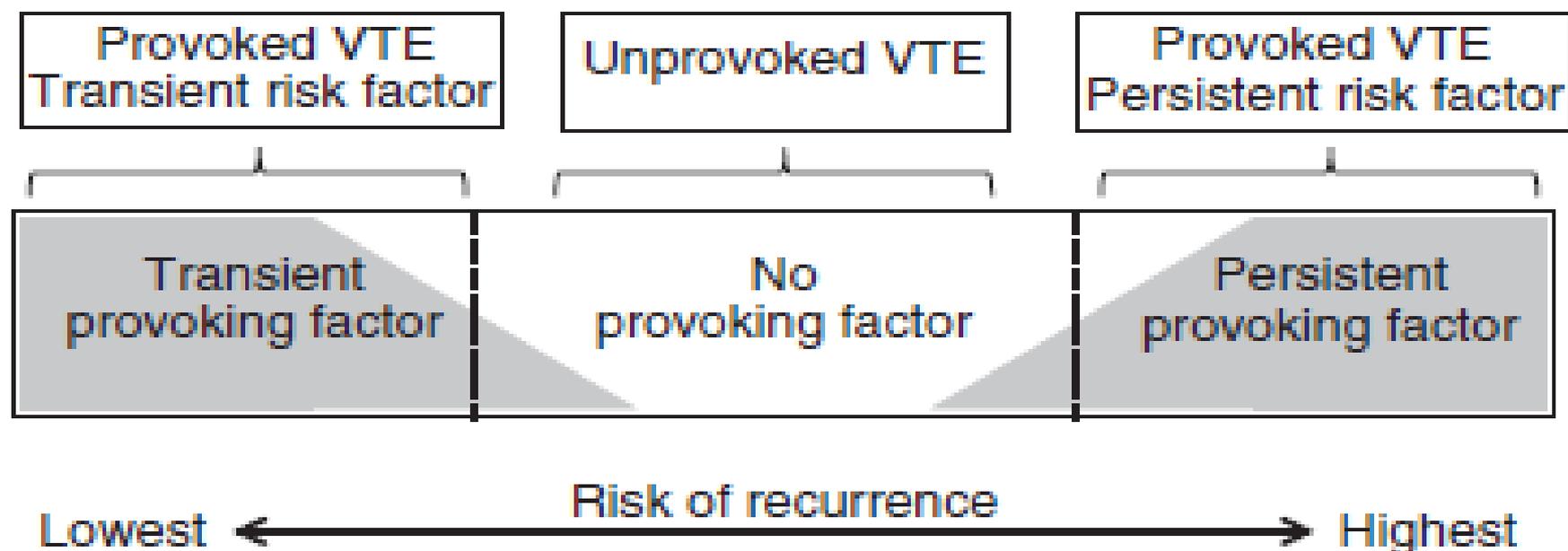
- 2-Riesgo de recurrencia**

- 3-Riesgo de hemorragia**

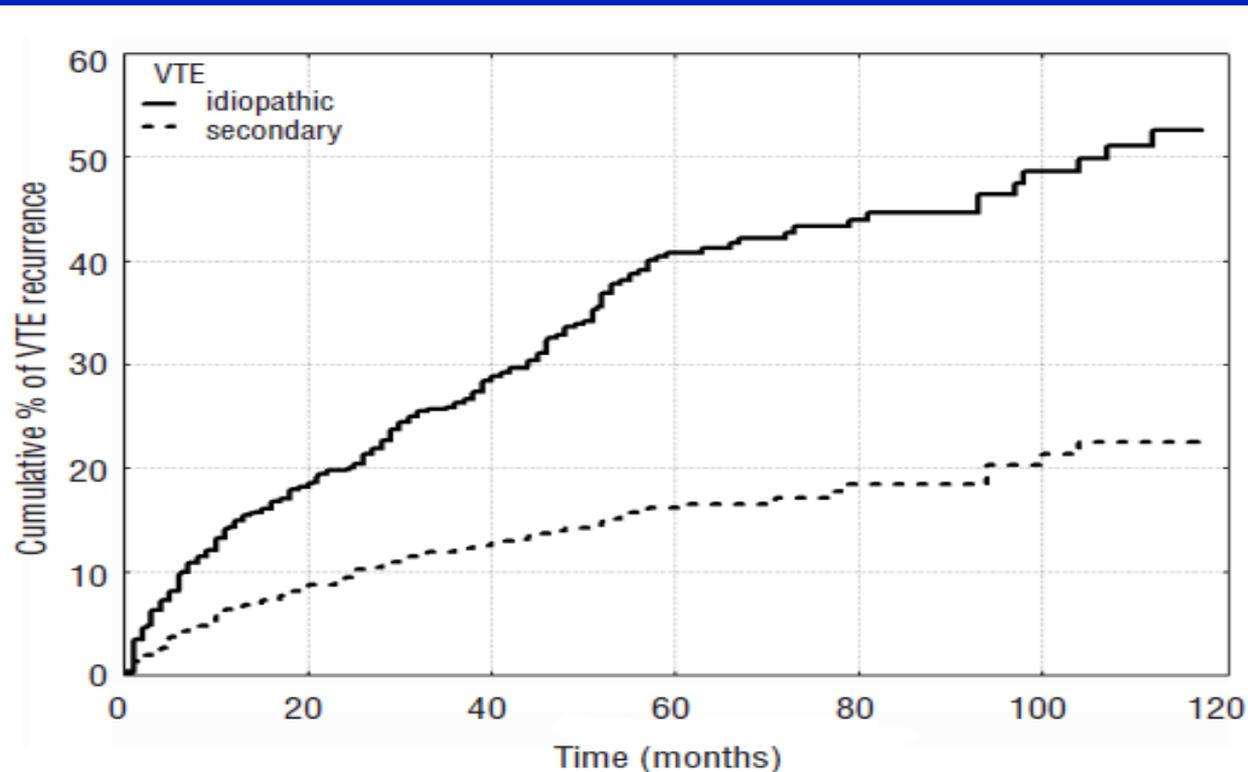
## Categorization of patients as having provoked or unprovoked venous thromboembolism: guidance from the SSC of ISTH

C. KEARON,\* W. AGENO,† S. C. CANNEGHIETER,‡ B. COSMI,§ G.-J. GEERSING¶ and P. A. KYRLE,\*\*  
FOR THE SUBCOMMITTEES ON CONTROL OF ANTICOAGULATION, AND PREDICTIVE AND  
DIAGNOSTIC VARIABLES IN THROMBOTIC DISEASE

\*McMaster University, Hamilton, ON, Canada; †University of Insubria, Varese, Italy; ‡Leiden University, Leiden, the Netherlands; §University of Bologna, Bologna, Italy; ¶Utrecht University, Utrecht, the Netherlands; and \*\*Medical University of Vienna, Vienna, Austria



# The risk of recurrent venous thromboembolism after discontinuing anticoagulation in patients with acute proximal deep vein thrombosis or pulmonary embolism. A prospective cohort study in 1,626 patients



## Interpretation and Conclusions

Besides unprovoked presentation, other factors independently associated with a statistically significant increased risk of recurrent VTE are thrombophilia, clinical presentation with primary DVT, shorter duration of anticoagulation, and increasing age.

**Prandoni P, y col. Haematologica 2007**



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## Long-term risk of venous thrombosis after stopping anticoagulants for a first unprovoked event: A multi-national cohort

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**H**yperpigmentation

**E**dema

**R**edness

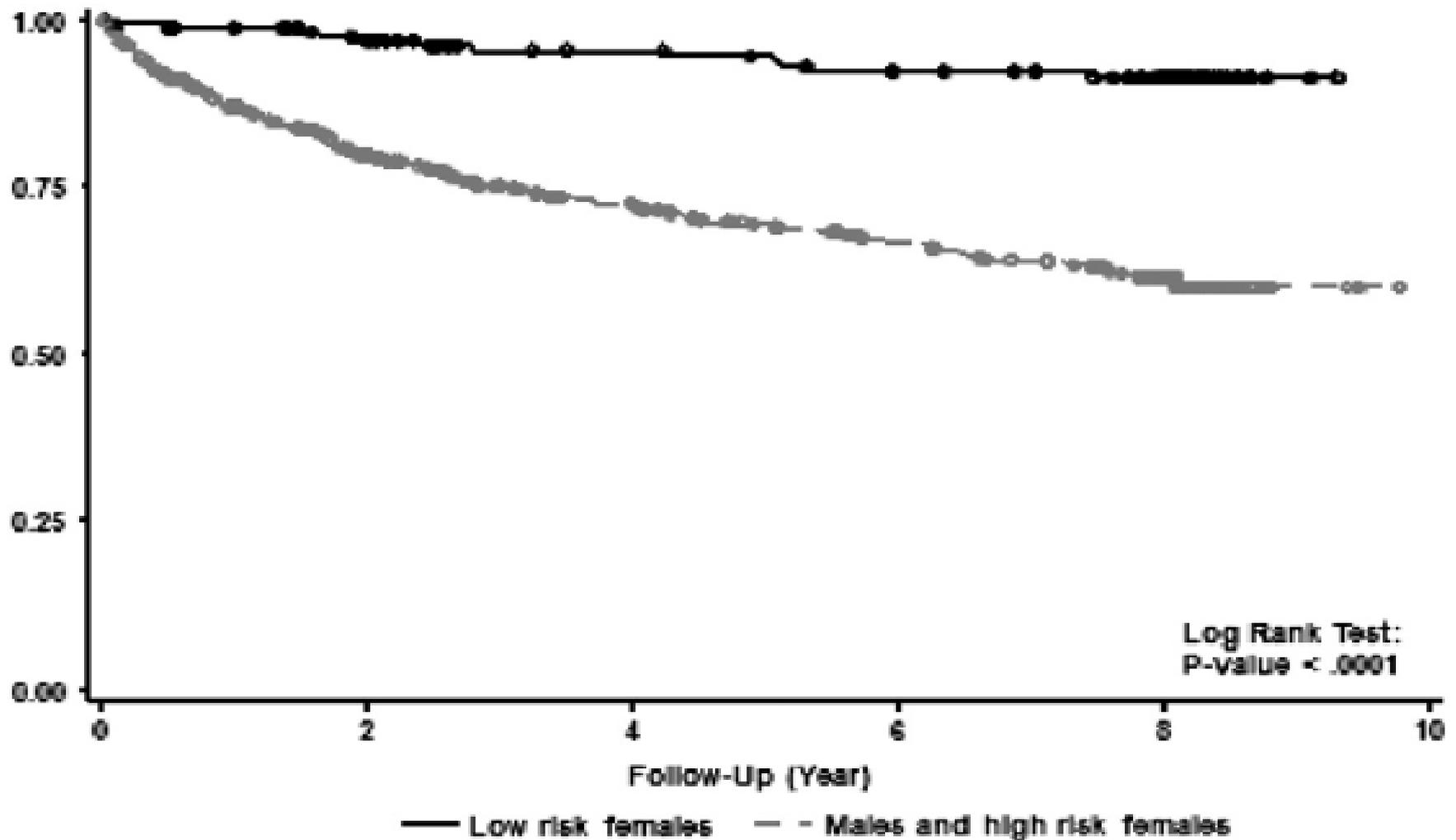
**D**-dimer (Vidas > 250 mcg/ml)

**O**besity (BMI > 30 kg/m<sup>2</sup>)

**O**lder (> 60 años)

***Rodger MA, y col. Thrombosis Research 2016***

## Recurrence free survival



**Bajo riesgo: mujeres HERDOO  $\leq 1$**

**Alto riesgo: Hombres/mujeres HERDOO  $\geq 2$**

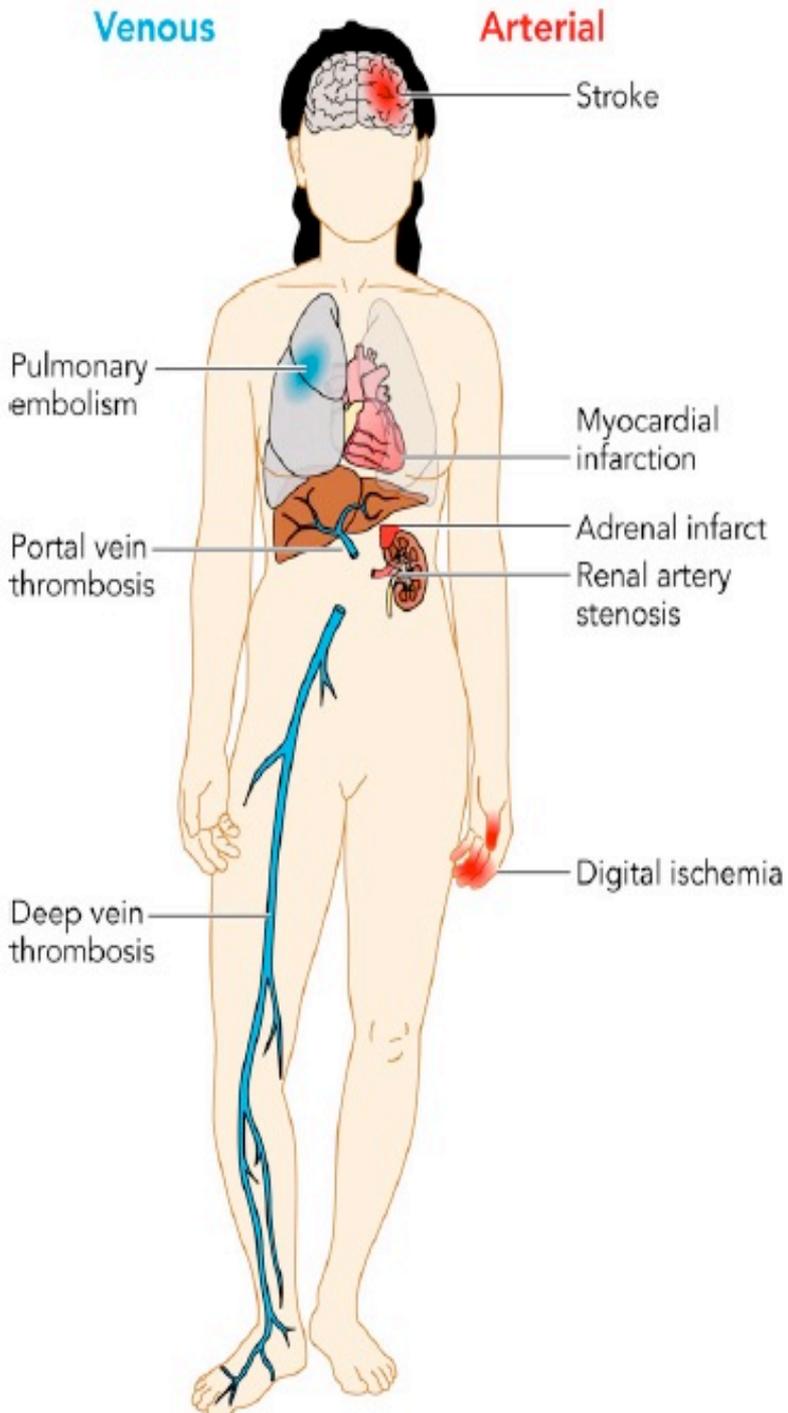
## 2014 ESC Guidelines on the diagnosis and management of acute pulmonary embolism

The Task Force for the Diagnosis and Management of Acute Pulmonary Embolism of the European Society of Cardiology (ESC)

Endorsed by the European Respiratory Society (ERS)

The assessment of the risk of recurrence in patients with unprovoked PE is more complex.<sup>54–56</sup> The following risk factors may help to identify patients at higher long-term relative risk of recurrence (1.5–2.0): (i) one or more previous episodes of VTE, (ii) antiphospholipid antibody syndrome, (iii) hereditary thrombophilia and (iv) residual thrombosis in the proximal veins. An additional risk factor for recurrence after PE was reported to be the persistence of RV dysfunction at hospital discharge as assessed by echocardiography.<sup>366</sup> On the other hand, a negative D-dimer test one month after withdrawal of VKA seems to be a protective factor for recurrence of VTE (RR 0.4).<sup>367</sup>

**Konstantinides SV, y col. European Chest Journal 2014**



# Trombofilia de alto riesgo

- Anticuerpos antifosfolípidos
- Déficit de Prot C-S, o de AT
- Factor V Leiden homocigota
- P20210 homocigota
- Síndromes mieloproliferativos Ph negativos
- Hemoglobinuria paroxística nocturna

*Laureano M. y Crowter MA. Blood 2018*  
*Pengo V. y col. Blood 2018*  
*Connors JM. N Engl J Med 2107*

**Table 1. Clinical Characteristics Suggestive of Inherited Thrombophilia in Patients with Venous Thromboembolism (VTE).**

Thrombosis at a young age (<50 yr), especially in association with weak provoking factors (minor surgery, combination oral anticoagulants, or immobility) or unprovoked VTE

Strong family history of VTE (first-degree family members affected at a young age)

Recurrent VTE events, especially at a young age\*

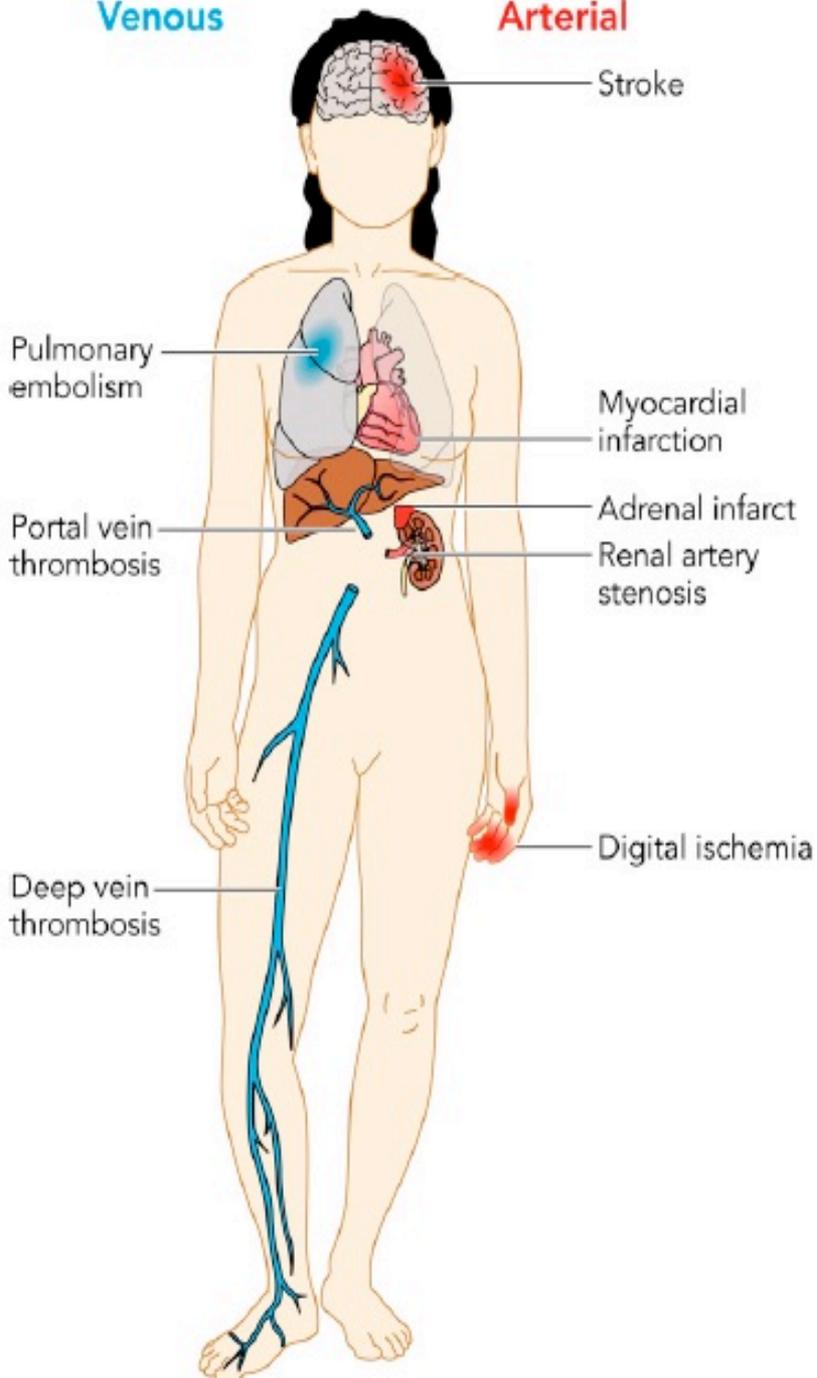
VTE in unusual sites such as splanchnic or cerebral veins†

\* The antiphospholipid syndrome must also be considered, but it is not inherited.

† Patients with splanchnic-vein VTE should be assessed for myeloproliferative neoplasms and paroxysmal nocturnal hemoglobinuria.

Venous

Arterial



CLINICAL TRIALS AND OBSERVATIONS

Comment on Pengo et al, page 1365

## Higher-risk APS: do we dare to DOAC?

Marissa Laureano and Mark A. Crowther | McMaster University

In this issue of *Blood*, Pengo et al present a randomized control trial comparing the use of rivaroxaban and warfarin in high-risk patients with anti-phospholipid antibody syndrome (APS). The trial was stopped early because of an increased number of events in the rivaroxaban arm.<sup>1</sup>

***Warfarina (RIN 2-3) sigue siendo el tratamiento estándar. Rivaroxaban produjo más hemorragias.***

***Laureano M. y Crowther MA. Blood 2018  
Pengo V. y col. Blood 2018***

# Long term risk of symptomatic recurrent venous thromboembolism after discontinuation of anticoagulant treatment for first unprovoked venous thromboembolism event: systematic review and meta-analysis

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by a major transient risk factor.<sup>3-5</sup> Consequently, anticoagulant treatment is discontinued after three to six months in patients with VTE due to a major transient provoking factor, whereas current guidelines suggest extended (ie, indefinite) anticoagulation in patients with unprovoked proximal deep vein thrombosis or pulmonary embolism who have a non-high bleeding risk.<sup>6-8</sup> This is, however, a weak (grade 2B) recommendation, in large part as a result of

**TABLE 11 ] Risk Factors for Bleeding with Anticoagulant Therapy and Estimated Risk of Major Bleeding in Low-, Moderate-, and High-Risk categories<sup>a</sup>**

Risk Factors <sup>b</sup>
Age >65 y <sup>184-193</sup>
Age >75 y <sup>184-188,190,192,194-202</sup>
Previous bleeding <sup>185,191-193,198,201-204</sup>
Cancer <sup>187,191,195,198,205</sup>
Metastatic cancer <sup>181,204</sup>
Renal failure <sup>185,191-193,196,199,201,206</sup>
Liver failure <sup>186,189,195,196</sup>
Thrombocytopenia <sup>195,204</sup>
Previous stroke <sup>185,192,195,207</sup>
Diabetes <sup>185,186,196,200,202</sup>
Anaemia <sup>185,189,195,198,202</sup>
Antiplatelet therapy <sup>186,195,196,202,208</sup>
Poor anticoagulant control <sup>189,196,203</sup>
Comorbidity and reduced functional capacity <sup>191,196,204</sup>
Recent surgery <sup>189,209,c</sup>
Frequent falls <sup>195</sup>
Alcohol abuse <sup>191,192,195,202</sup>
Nonsteroidal anti-inflammatory drug <sup>210</sup>

# Riesgo de Hemorragia

<b>Tiempo de anticoagulación</b>	<b>Sin factores de riesgo</b>	<b>Un factor de riesgo</b>	<b>Más de 1 factor de riesgo</b>
<b>Hasta 3 meses</b>	<b>1,6 %</b>	<b>3,2%</b>	<b>12,8%</b>
<b>Después de los 3 meses</b>	<b>0,8%/año</b>	<b>1,6%/año</b>	<b>&gt; 6,5%/año</b>

# Fase Prolongada y de Extensión

Patient with PE or proximal upper or lower extremity DVT stable on acute phase treatment (see Figure 1)

Etiology of VTE?

Transient risk factor

Unprovoked VTE

Treatment with  
1 of following:  
Vitamin K antagonist  
Rivaroxaban  
Apixaban  
Edoxaban  
Dabigatran

Treatment with  
1 of following:  
Vitamin K antagonist  
Rivaroxaban  
Apixaban  
Edoxaban  
Dabigatran

Discontinue treatment after 3 mo.

Consider extended treatment (> 6 mo.)

Low to moderate

Bleeding risk?

High

Continue treatment indefinitely  
with 1 of following:  
Vitamin K antagonist  
Rivaroxaban  
Apixaban  
Edoxaban  
Dabigatran

Discontinue treatment  
after 3 to 6 mo.

# Recomendaciones ACCP

<b>Tipo</b>	<b>Duración de anticoagulación</b>	<b>Agente</b>
<b>TVD*, TVP, TEP. (Provocados)</b>	<b>3 meses</b>	<b>AODs &gt; anti-K (heparina antes de dabi o edox y superpuesta a anti-K)</b>
<b>TVD*, TVP, TEP. ("Idiopáticos")</b>	<b>3 meses y luego evaluar riesgo de extensión</b>	<b>AODs &gt; anti-K (si se suspenden a 3 meses se puede continuar con AAS)</b>
<b>TEV asociado a cáncer</b>	<b>"Indefinido"</b>	<b>Primeros 3 meses HBPM &gt; AODs/anti-K</b>

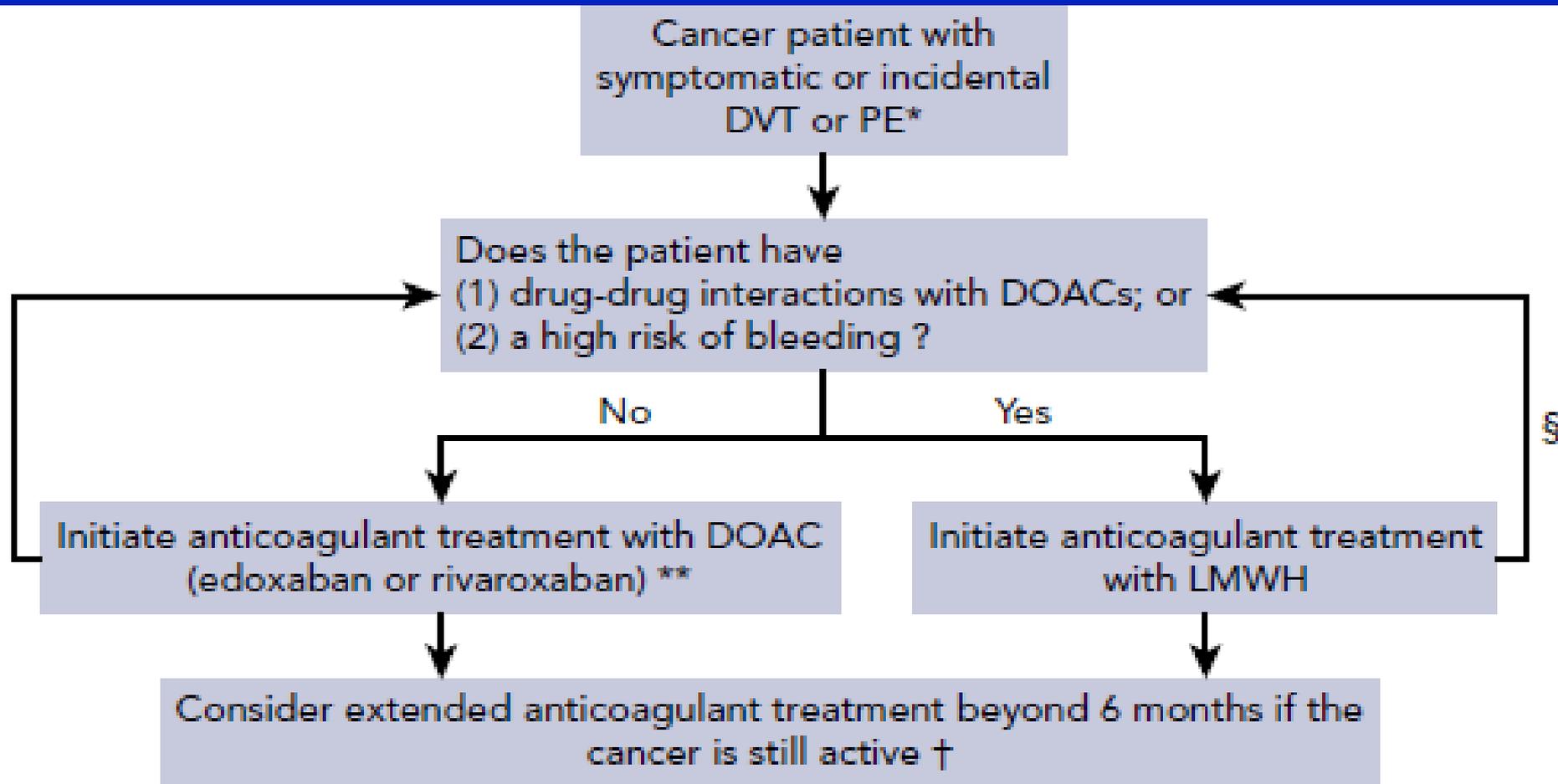
**\* En TVD puede decidirse no anticoagular y hacer seguimiento con ultrasonografía (dependiendo esta instancia de la existencia o no de factores de riesgo)**

***Kearon C, y col. Chest 2016***

# How I treat cancer-associated venous thromboembolism

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***Kraaijpoel N. y Carrier M. Blood 2019***

## **Anticoagulating patients with high risk acquired thrombophilias: APS, HIT and PNH**

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<sup>1</sup>Division of Hematology and Hematological Malignancies, Department of Medicine, University of Calgary, Canada; <sup>2</sup>Department of Community Health Sciences, University of Calgary, Calgary, Canada; <sup>3</sup>Clinical Epidemiology Program, Ottawa Hospital Research Institute, Ottawa, Canada

Randomized trials evaluating DOACs in patients with APS are reviewed. Further research is needed prior to widely adopting DOACs for use in these high-risk acquired thrombophilias; however, there may be selected low-risk subgroups where DOAC use is possible after careful consideration and patient discussion.

***Skeith L, y col. Blood 2018***

# Tratamiento del TEV

- *Fases del tratamiento*
  - Aguda: hasta días 5- 10*
  - Prolongada: primeros 3 meses*
  - Extendida con tope: 6-12-24 meses*
  - Extendida sin tope: "indefinida"*
- *¿Internado o en su casa?*
- *¿Anticoagulación, trombolisis o filtro?*
- *Elección del agente y duración del tratamiento*
- **Prevención del síndrome postrombótico**

# How I treat the postthrombotic syndrome

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<sup>1</sup>Thrombosis and Hemostasis Unit, Hematology Institute, Soroka University Medical Center, Faculty of Health Sciences, Ben Gurion University of the Negev, Beer Sheva, Israel; <sup>2</sup>Center for Clinical Epidemiology, Jewish General Hospital/Lady Davis Institute, and <sup>3</sup>Division of Internal Medicine, Department of Medicine, McGill University, Montreal, QC, Canada

**The postthrombotic syndrome (PTS) is a chronic complication of deep vein thrombosis (DVT) that imposes significant morbidity, reduces quality of life, and is costly. After DVT, 20% to 50% of patients will develop PTS, and up to 5% will develop severe PTS. The principal risk factors for PTS are anatomically extensive DVT, recurrent ipsilateral DVT, obesity, and older age. By preventing the initial DVT and DVT recurrence, primary and secondary prophylaxis of DVT will reduce occurrence of PTS. The effectiveness of elastic compression stockings (ECSs) for PTS prevention is controversial. Catheter-directed thrombolysis is not effective to prevent PTS overall but may prevent more severe forms of PTS and should be reserved for select patients with extensive thrombosis, recent symptoms onset, and low bleeding risk. For patients with established PTS, the cornerstone of management is ECS, exercise, and lifestyle modifications. Surgical or endovascular interventions may be considered in refractory cases. Because of a lack of effective therapies, new approaches to preventing and treating PTS are needed. This article uses a case-based approach to discuss risk factors for PTS after DVT, how to diagnose PTS, and available means to prevent and treat PTS, with a focus on new information in the field. (*Blood*. 2018;131(20):2215-2222)**

*Comment on Amin et al, page 2298*

# Postthrombotic syndrome: simple prevention

Susan Solymoss | The McGill University Health Center

In this issue of *Blood*, Amin et al provide data showing early compression therapy post-venous thromboembolism (VTE) to be effective in reducing the incidence of postthrombotic syndrome (PTS) by achieving reduced residual vein obstruction (RVO) on follow-up ultrasound.<sup>1</sup>

***Solymoss S. Blood 2018***

# **Algunos Problemas en el Manejo del Tromboembolismo Venoso Conclusiones**

- 1- Diagnóstico centrado en score clínico, dímero-D y TAC**
- 2- Varias opciones terapéuticas ( HNF, HBPM, dicumarínicos, AODs) que deben seleccionarse en forma personalizada**
- 3- No se recomiendan AODs en trombofilia severa ni en cáncer con alto riesgo hemorrágico**
- 4- La utilización de AODs requiere necesariamente del control y asesoramiento hematológico**