Venous Thromboembolism
Blood Clots in Veins and Lungs

FACULTY
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This educational material was developed by the
American Association of Nurse Practitioners, www.aanp.org,
in cooperation with
Upside Communications, Los Angeles, CA
and
Design by Kat&Dog Communications, Austin, TX

This counseling tool was developed by the American Association of Nurse Practitioners.
Supported by Bristol-Myers Squibb and Pfizer Alliance.
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**Points to Emphasize:**
- Emphasize that VTE is common and affects men and women of all ages
- The incidence of VTE rises with age, so VTE is likely to be seen more frequently in clinical practice based on demographics alone
- Convey that patients may be asymptomatic or only realize, in retrospect, that they have experienced symptoms
- Reassure that VTE is treatable
  - Explain that there are newer medications, direct acting oral anticoagulants (DOACs), that are easy to use and work well
  - Relate that most patients, even those with pulmonary embolism (PE), can be treated on an outpatient basis

**Additional Information for Healthcare Provider:**
- VTE is a multifactorial disease that can result from a variety of conditions or scenarios
- VTE typically reflects the complex interplay of a patient’s risk for thrombosis based on inherited and acquired factors
  - Examples of acquired factors include: age, obesity, use of contraceptive hormones, etc.
- A complete medical history, including recent surgeries or procedures, is vital
- As VTE can arise from inherited conditions, it’s also important to obtain a complete family history
- Patients should be asked about lifestyle, including daily activities and recent travel
- Guidelines recommend DOACs over vitamin K antagonists or low molecular weight heparin (LMWH) for most patients

Tipos de TEV

- Hay 2 tipos principales de TEV
  - **Trombosis venosa profunda (TVP):** Cuando un coágulo se forma en una vena profunda grande de la pierna, la pelvis y, a veces, el brazo
  - **Embolia pulmonar (EP):** Cuando un coágulo de sangre se desprende y se desplaza en la sangre hasta los pulmones y causa una obstrucción

¿A quiénes afecta el TEV?

- Un 30% muere dentro del primer mes de ser diagnosticado
- El TEV es más común en las mujeres en edad de procrear que en los hombres
- El riesgo de una TEV aumenta con la edad tanto para los hombres como para las mujeres
- Teniendo una TEV aumenta el riesgo de que se repita una TEV
  - El recibir tratamiento (y seguir las instrucciones del tratamiento) para TEV reduce el riesgo de que suceda otra vez


Points to Emphasize:

- Explain that VTE is common: 1 out of 1,000 Americans have VTE
- Point out that VTE, particularly DVT, is often undiagnosed
  - DVT accounts for ~2/3 of VTE
- Explain that, untreated, VTE has serious consequences, including pulmonary hypertension and death
  - 10%-30% of people die within the first month of diagnosis
  - Sudden death happens in about 25% of patients with PE
  - Half of patients with DVT develop post-thrombotic syndrome
- Emphasize that it’s critical that patients take VTE treatment as directed to reduce the risk of VTE recurrence
  - Half of patients with DVT with get PE
  - About one-third of patients with VTE will have recurrence within 10 years

Additional Information for Healthcare Provider:

- People of all races and ages can get VTE:
  - However, African-Americans and Caucasians are more likely to get VTE than Asian-Americans and Native Americans
  - Women are more likely to have VTE than men until age 45
  - After the age of 45, both men and women are more likely to have PE versus DVT
¿Qué es la trombosis venosa profunda (TVP)?
- La TVP ocurre cuando un coágulo (trombo) se forma en una vena grande y profunda
- Generalmente, la TVP sucede en la pierna o el muslo, pero puede aparecer en otros lugares como la pelvis o un brazo

¿Por qué se forman los coágulos?
- Los coágulos se pueden formar por distintas razones:
  — Una lesión en el interior de una vena como resultado de una cirugía o de un accidente grave
  — Flujo sanguíneo lento debido a falta de movimiento (estar sentado o acostado por largo tiempo)
  — Como respuesta del cuerpo a la inflamación
  — Una enfermedad sanguínea hereditaria

¿Cuáles son los síntomas de TVP?
Estos síntomas pueden aparecer en la parte afectada del cuerpo:
- Inflamación.
- El área hinchada se pone caliente
- Dolor o sensibilidad al tacto
- Enrojecimiento o decoloración en la piel (morada, azulada)

Points to Emphasize:
- Review the most common reasons for a blood clot to form:
  — Recent surgery, bone fracture, or serious accident often leads to DVT because of:
    — Injury to a deep vein’s inner lining
- Explain that lack of movement is a common cause of DVT for patients who:
  — Have had a surgery
  — Are medically ill or hospitalized
  — Have had a knee or hip replacement
  — Have had long flights or travel
- Relate that 5%-8% of Americans have hereditary factors that heighten their risk for thrombosis
  — Inform that testing for genetic factors is not recommended during the first 3 months of DVT treatment

Additional Information for Healthcare Provider:
- 50% of patients with symptomatic proximal DVT will develop PE
- Approximately half of patients with DVT are asymptomatic
- Often patients don’t realize that they have experienced lower extremity symptoms
- Symptoms should be correlated with potential precipitating factors, such as a long car ride, to assess the likelihood of DVT
- Inflammatory pathways are indicated in DVT, however, the precise interplay remains unclear
  — Symptoms of DVT are also classic symptoms of inflammation

¿Hay factores de riesgo para la TVP?
A casi cualquier persona le puede ocurrir, pero hay factores de riesgo que aumentan las probabilidades:

- Una lesión grave en una vena
  - Por una quebradura o una lesión muscular
- Circulación sanguínea lenta
  - Poco movimiento durante un viaje
  - Reposo en cama por mucho tiempo
- Aumento de hormonas en la sangre
  - Terapia hormonal
  - Durante el embarazo o después de un parto
- Algunas condiciones médicas
  - Cardiopatías o enfermedades pulmonares
  - Cáncer, actual o en el pasado
  - Enfermedad inflamatoria intestinal
- Otras cosas relacionadas con la persona
  - TVP anteriores
  - Edad avanzada
  - Exceso peso corporal
  - Fumar
  - Un catéter venoso central en una vena grande
  - Antecedentes familiares con problemas de coagulación

Points to Emphasize:
- Review the most common risk factors for provoked DVT: Surgery, broken bone, long travel, and hormone therapy
- Explain that some DVTs are considered unprovoked because there is no clear cause
- Discuss that the duration of travel can affect VTE risk:
  - Flights lasting 4-8 hours double the incidence of VTE
  - Flights lasting 12-16+ hours have a VTE incidence of 5.3%-5.7%
  - VTE risk remains elevated for ~4 weeks after travel
- If applicable, advise that hormone therapy increases the relative risk of VTE by 2x-4x depending on estrogen dose, progestin type, and other factors
- Be mindful that active cancer increases VTE risk by 4x-6x
  - 10% of patients with unprovoked DVT have an undiagnosed malignancy

Additional Information for Healthcare Provider:
- In rare cases, pregnancy can lead to DVT
  - DVT risk is higher early in post-partum and continues through 12 weeks
- Inflammatory bowel disease raises the relative risk for recurrent VTE by 2.5x
- Obesity increases the relative risk for recurrent VTE by 1.6x
  - Where appropriate, weight loss should be included in overall treatment plans
- Factor V Leiden gene mutation is the most common inherited thrombophilia, accounting for 40% to 50% of cases

Diagnóstico de la TVP

Los proveedores de atención médica usan una combinación de estudios para determinar si una persona tiene TVP:
- Examen físico
- Análisis de sangre (Dímero D)
- Ultrasonido
  - El ultrasonido usa ondas acústicas para crear imágenes de la circulación en las venas
  - El ultrasonido es un estudio no invasivo; los dispositivos para crear las imágenes se usan por afuera del cuerpo
- Otros exámenes de imagen con o sin contraste
  - También se puede usar tomografía computarizada y resonancia magnética para ver las venas y los coágulos
  - La venografía, que utiliza rayos X para tomar imágenes de las venas, es más invasivo ya que requiere de inyección continua de contraste

Points to Emphasize:
- Complete a medical history and exam
- Perform a pre-test probability for DVT:
  - The Wells clinical prediction algorithm is the best known pre-test probability model
- Explain that a test for D-dimer in blood may be used in DVT diagnosis:
  - A low pre-test probability of DVT and a negative D-dimer test reliably excludes DVT
- Discuss that compression ultrasound is the first-line imaging test for intermediate or high pre-test probability for DVT
  - High sensitivity (89%-96%) and specificity (94%-99%)

Additional Information for Healthcare Provider:
- CT also has high sensitivity and specificity for DVT but is not typically used because of radiation exposure to patient
- Magnetic resonance imaging (MRI) is used infrequently because of the expense
- Venography is reserved for cases with high suspicion of DVT but other tests have not confirmed DVT or presented discordant results

<table>
<thead>
<tr>
<th>Wells Prediction Rule for DVT</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active cancer (or within 6 months of treatment)</td>
<td>1</td>
</tr>
<tr>
<td>Paralysis, paresis, or recent cast of lower limb</td>
<td>1</td>
</tr>
<tr>
<td>Recently bedridden for ≥ 3 days or major surgery within previous 12 weeks</td>
<td>1</td>
</tr>
<tr>
<td>Localized tenderness along deep venous system</td>
<td>1</td>
</tr>
<tr>
<td>Swollen leg</td>
<td>1</td>
</tr>
<tr>
<td>Calf swelling at least 3 cm larger than asymptomatic Side (measured 10 cm below tibial tuberosity)</td>
<td>1</td>
</tr>
<tr>
<td>Pitting edema confined to symptomatic leg</td>
<td>1</td>
</tr>
<tr>
<td>Collateral superficial veins (non-varicose)</td>
<td>1</td>
</tr>
<tr>
<td>Previously documented DVT</td>
<td>1</td>
</tr>
<tr>
<td>Alternative diagnosis as least as likely as DVT</td>
<td>-2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pre-Test Probability of DVT</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>≤0</td>
</tr>
<tr>
<td>Intermediate</td>
<td>1-2</td>
</tr>
<tr>
<td>High</td>
<td>≥3</td>
</tr>
</tbody>
</table>

Points to Emphasize:

- Discuss that most patients with DVT can be treated on an outpatient basis with an oral anticoagulant (OAC)
- Patients may ask why they need to take medication for their DVT; reiterate that 50% of patients with symptomatic proximal DVT will develop PE
  - If applicable, explain that acute extensive proximal DVT sometimes needs to be treated with inpatient parenteral anticoagulation
  - If parenteral anticoagulation is the initial treatment, inform that an overlap with OAC is needed for some OACs
- Emphasize that treatment duration depends on whether DVT is provoked or unprovoked

<table>
<thead>
<tr>
<th>DVT Type</th>
<th>Bleeding Risk</th>
<th>OAC Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Provoked</td>
<td></td>
<td>3 Months</td>
</tr>
<tr>
<td>Unprovoked</td>
<td>High</td>
<td>3 Months</td>
</tr>
<tr>
<td>Unprovoked</td>
<td>Low/Moderation</td>
<td>Unscheduled</td>
</tr>
</tbody>
</table>

Additional Information for Healthcare Provider:

- For cancer-associated DVT, low molecular weight heparin is recommended
- If OAC is stopped in unprovoked DVT, aspirin is recommended

Anticoagulantes orales para el tratamiento de la TVP

- Hay varios tipos de anticoagulantes para diferentes partes del proceso de formación de coágulos (vitamina K, factor Xa o inhibidores directos de trombina).
- Los medicamentos inhibidores de la vitamina K se han utilizado por muchos años como tratamiento de la TVP.
- Son necesarios los análisis de sangre rutinarios para asegurarse de que la persona tiene la cantidad correcta de medicamento en la sangre.
- La comida puede afectar su funcionamiento.
- Los medicamentos que inhiben el factor Xa o la trombina directamente, son tratamientos más nuevos para la TVP.
- Estos anticoagulantes nuevos funcionan tan bien como los tratamientos basados en la vitamina K.
- Generalmente, se necesitan pocos análisis de sangre con estos anticoagulantes nuevos en comparación con los inhibidores de la vitamina K.
- Su capacidad no depende de restricciones dietéticas.
- La guía médica recomienda que, cuando posible, los pacientes tomen los nuevos anticoagulantes en lugar de los medicamentos que tratan la TVP usando la vitamina K.

Points to Emphasize:

- Explain that medical guidelines recommend a direct-acting oral anticoagulant (DOAC) over warfarin for most patients.
- DOACs have been studied for VTE in many clinical trials:
  - They are just as effective as warfarin but have a lower risk of bleeding in the brain.
  - Kidney function must be assessed prior to starting a DOAC.
- Inform that dose adjustments are needed for some DOACs based on kidney function or other medications.
- If applicable, explain that patients with certain conditions cannot take DOACs: Severe kidney disease, pregnancy, breastfeeding, and mechanical heart valve.
- Ability to pay for, or insurance that permits, a DOAC is a consideration in treatment planning.

Additional Information for Healthcare Provider:

<table>
<thead>
<tr>
<th>DOAC Dosing for VTE Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dabigatran</strong></td>
</tr>
<tr>
<td>Dosing</td>
</tr>
<tr>
<td>DVT prevention after hip replacement surgery: 110 mg QD first day, 220 mg QD thereafter (May be taken with or without food)</td>
</tr>
<tr>
<td>Kidney Function</td>
</tr>
<tr>
<td>Drug-Drug Interactions and Dose Adjustments</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Other</td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>

Points to Emphasize:

• Explain that procedures are rarely performed to treat DVT
• Discuss that procedures are reserved for patients with acute DVT who cannot have anticoagulant therapy or for whom anticoagulants aren’t sufficient
• Review the rationale for a procedure:
  — Prevent development of PE
  — Stop clot extension
  — Reduce risk of late complications (e.g., post-thrombotic syndrome, chronic venous insufficiency, chronic thromboembolic pulmonary hypertension)

Additional Information for Healthcare Provider:

• If patients can take anticoagulants, inferior vena cava (IVC) filters are not recommended
  — If IVC filters are indicated, retrievable filters are preferred over permanent IVC filters
• Catheter-directed or intravenous (IV) thrombolysis, with or without mechanical clot removal, is typically reserved for acute DVT and imminent venous gangrene
Points to Emphasize:
- Reinforce that if they experience an adverse reaction to contact their healthcare provider before stopping OAC:
  —To address the adverse reaction or make changes to medication(s)
- Reinforce that not taking medication increases the risk DVT will recur
- Remind them that minor bleeding is normal and suggest ways to minimize minor bleeding:
  — Use a soft bristle toothbrush and gently “massage” gums
  — Use an electric razor
  — Avoid activities that could result in injury
- Reinforce that it’s OK to exercise and suggest:
  — Walking, swimming, and bike riding are safe (preferred)

Additional Information for Healthcare Provider:
- Patients who are taking aspirin or an antiplatelet in addition to an OAC should take a proton pump inhibitor (PPI) for prevention of GI bleeding

### Potential Adverse Reactions*

<table>
<thead>
<tr>
<th>Dabigatran</th>
<th>Rivaroxaban</th>
<th>Apixaban</th>
<th>Edoxaban</th>
</tr>
</thead>
<tbody>
<tr>
<td>GI bleeding</td>
<td>GI bleeding</td>
<td>Hematuria</td>
<td>GI bleeding</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>Dyspepsia</td>
<td>Subconjunctival hemorrhage</td>
<td>Rash</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>Back pain</td>
<td>Urinary tract infection</td>
<td>Abnormal liver tests</td>
</tr>
<tr>
<td>Epidural or spinal hematomas for patients undergoing neuraxial anesthesia or spinal puncture</td>
<td>Epidural or spinal hematomas for patients undergoing neuraxial anesthesia or spinal puncture</td>
<td>Epidural or spinal hematomas for patients undergoing neuraxial anesthesia or spinal puncture</td>
<td>Anemia</td>
</tr>
</tbody>
</table>

*Non-major bleeding.
Sources: Prescribing information package inserts.
Points to Emphasize:
- Reiterate that minor bleeding is common
  — 1 out of 4 patients will have a minor bleed
  — In most cases, not a cause for alarm
- Distinguish between “nuisance” bleeding and serious bleeding
- Patients can manage minor bleeding at home:
  — Demonstrate applying pressure to a wound
  — Demonstrate how to stop a nose bleed

Additional Information for Healthcare Providers:
- Most patients benefit from being given, or directed to, resources for managing minor bleeding
- Additional resources can be found at:
  — http://www.anticoagulationtoolkit.org/patients
  — http://www.clotconnect.org/patients/resources/brochures

Questions to ask if the patient reports bleeding:
- Which OAC are you taking?
- When was the last dose of anticoagulant?
- Are you or did you take any other medications such as aspirin or an NSAID?
- How long have you been bleeding? Has it stopped?
- What were you doing when you started bleeding?
- How severe is the bleeding?
Points to Emphasize:

- Discuss that not taking the prescribed medication increases the risk of VTE recurrence
  - Ease and convenience of DOACs may improve adherence
  - Explain that DOACs have rapid onset and offset, which increases the importance of adherence

- Assist patients with suggestions to improve adherence:
  - Take medication at the same time(s) every day
  - Set a calendar reminder on computer or alarm on mobile phone

- Reinforce that aspirin, ibuprofen, and other OTC pain relief medication can make the blood “more thin” and lead to bleeding
  - Acetaminophen can be taken for pain relief as long as there is no known liver disease

- Advise patients taking warfarin:
  - Avoid fluctuations in the amount of food high in vitamin K
  - Consistency is important to maintaining appropriate medication level

- Inform patients taking a DOAC
  - Apixaban and rivaroxaban require dose adjustments at 7 and 21 days, respectively
  - Avoid taking OTC medications and supplements, including vitamins, as they may make the anticoagulant less effective or may increase the risk of bleeding

Additional Information for Healthcare Provider:

- Many DOACs require dose adjustment for change in kidney function
  - Check baseline kidney function and every 6 months thereafter

Points to Emphasize:

- Emphasize that bleeding in the brain is rare with DOACs
  - Clinical trials have demonstrated that DOACs have significantly less intracranial hemorrhage (ICH) compared to warfarin
  - Since there are no head-to-head trials for DOACs in VTE, it’s unknown if 1 DOAC is superior to others on overall incidence of ICH
- Mention that when going to the ED, it’s important to tell medical staff which OAC they are taking
  - They should keep a card in their wallet that indicates which OAC
- Suggest they wear medical alert jewelry/tag with the name of their OAC in case of an emergency and they are unable to communicate
- Emphasize that symptoms of PE are a medical emergency and they should call 9-1-1

Additional Information for Healthcare Provider:

- ICH occurs in ~0.1% of cases with DOACs
- There is an approved reversal agent for dabigatran (idarucizumab) for use in emergency major bleeding
  - Other reversal agents for DOACs are in development
  - Fresh frozen plasma and prothrombin complex concentrate also can be used to treat major bleeds associated with DOACs

Points to Emphasize:

- Emphasize that the risk for recurrent DVT is highest in the first 3 months
- Obesity, combined with other risk factors, significantly increases DVT risk
  - Eating more fish and vegetables, and less red meat, can reduce VTE incidence by 30%-45%
- Reinforce that sluggish blood flow is a DVT risk factor, so frequent movement helps prevent DVT
  - Avoid sitting for long periods of time (>4 hours)
  - Stand and walk around every hour or so if possible
  - Flex muscles, do toe-to-heel exercises, and circle ankles if seated for long periods (travel)
- Regular exercise may reduce the risk of DVT
  - Take a brisk walk every day
- Compression stockings can reduce symptoms and improve blood flow although not recommended in acute DVT patients
  - Explain that it may reduce the risk of post-thrombotic syndrome
  - Offer tips to help the patient be compliant (compliance is often suboptimal)
  - Some patients don’t tolerate graduated compression

Additional Information for Healthcare Provider:

- DVT is high following hospitalization and surgery (particularly orthopedic and pelvic)
  - Up to 40% of general surgery patients, 40%-60% of orthopedic surgery patients

Sources:

Points to Emphasize:
- Reiterate that PE can be life-threatening so it’s important to get treatment as soon as possible
  — 10%-30% of people die within the first month of diagnosis
- Perform risk assessment for acute massive PE
  — Criteria = Hypotension or heart rate <40 bpm
- If applicable, explain that low risk patients can be treated on outpatient basis

Additional Information for Healthcare Provider:
- Up to 25% of patients do not have sudden onset of symptoms
  — Symptoms may precede diagnosis by ≥2 weeks and get progressively worse (e.g., increasing fatigue)

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### PE Severity Index (PESI) Score

<table>
<thead>
<tr>
<th>Predictors</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, in years</td>
<td></td>
</tr>
<tr>
<td>Altered mental status</td>
<td>+60</td>
</tr>
<tr>
<td>Systolic BP &lt;100 mmHg</td>
<td>+30</td>
</tr>
<tr>
<td>History of cancer</td>
<td>+30</td>
</tr>
<tr>
<td>Arterial oxygen sat. &lt;90%</td>
<td>+20</td>
</tr>
<tr>
<td>Temp &lt; 36°C</td>
<td>+20</td>
</tr>
<tr>
<td>Respiratory rate ≥ 30/min</td>
<td>+20</td>
</tr>
<tr>
<td>Pulse ≥ 110/min</td>
<td>+20</td>
</tr>
<tr>
<td>Male sex</td>
<td>+10</td>
</tr>
<tr>
<td>Heart failure</td>
<td>+10</td>
</tr>
<tr>
<td>COPD</td>
<td>+10</td>
</tr>
</tbody>
</table>

**HOW TO ARRIVE AT PESI SCORE:**

Add points for each predictor that the patient has to the patient’s age

<table>
<thead>
<tr>
<th>Risk</th>
<th>PESI Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very low</td>
<td>≤65</td>
</tr>
<tr>
<td>Low</td>
<td>65-85</td>
</tr>
<tr>
<td>Intermediate</td>
<td>86-105</td>
</tr>
<tr>
<td>High</td>
<td>106-125</td>
</tr>
<tr>
<td>Very high</td>
<td>&gt;125</td>
</tr>
</tbody>
</table>

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Points to Emphasize:
- Explain that ~95% of PE is from proximal DVT
- Ask about recent events that should raise suspicion of PE in symptomatic patients:
  - Surgery
  - Broken bone
  - Hip/knee replacement
  - Serious accident
  - Hospitalization
  - Myocardial infarction (MI)
  - Onset of heart failure (HF)
  - Air travel of ≥ 12 hours
- If applicable, discuss that cancer type, stage, and treatment affect PE risk
  - More aggressive cancers typically hold greater risk for PE
  - VTE likely in first 3 months of cancer diagnosis
  - VTE also more likely with Stage 3 and 4 cancers
  - Surgery and some chemotherapies increase the risk of PE

Additional Information for Healthcare Provider:
- Age increases the risk of PE for both men and women
- Inherited thrombophilia should be considered for patients with unprovoked PE
  - Factor V Leiden accounts for 40%-50% of inherited thrombophilia
  - Others include deficiencies in protein C or S or antithrombin
  - Testing for genetic factors is not recommended during the first 3 months of treatment

Diagnóstico de la EP
Los proveedores de atención médica usan una combinación de estudios para determinar si una persona tiene PE:
• Examen físico
• Análisis de sangre
• Pulsioximetría para medir el porcentaje de oxígeno en la sangre con un monitor en el dedo
• Su proveedor de atención médica puede pedir exámenes de imagen especiales no invasivos:
  — Radiografía de pecho
  — Tomografía computarizada
  — Resonancia magnética del pecho
• Algunos exámenes de imagen invasivos se pueden ordenar para determinar si hay EP:
  — Una examen especial llamada angiografía, que toma imágenes de las arterias pulmonares
  — Un estudio avanzado, llamado gammagrafía de ventilación-perfusión (V/Q), que con inyección de materiales especiales para evaluar la respiración y la circulación en los pulmones

<table>
<thead>
<tr>
<th>Wells Prediction Rule for PE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Characteristic</td>
</tr>
<tr>
<td>Active cancer (or within 6 months of treatment)</td>
</tr>
<tr>
<td>Recently bedridden for ≥ 3 days or major surgery within previous 12 weeks</td>
</tr>
<tr>
<td>Prior DVT or PE</td>
</tr>
<tr>
<td>Hemoptysis</td>
</tr>
<tr>
<td>Heart rate ≥ 100 beats/min</td>
</tr>
<tr>
<td>PE assessed to be most likely diagnosis</td>
</tr>
<tr>
<td>Signs &amp; symptoms of DVT</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pre-Test Probability of PE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk</td>
</tr>
<tr>
<td>Low:</td>
</tr>
<tr>
<td>Intermediate:</td>
</tr>
<tr>
<td>High:</td>
</tr>
</tbody>
</table>

Additional Information for Healthcare Provider:
• If patient has a high pre-test probability for PE, it’s appropriate to skip D-dimer testing and proceed to imaging tests
• Pulmonary angiography is rarely used because of expense and right heart catheterization
• Use of magnetic resonance angiography (MRA) depends on facility protocols

Points to Emphasize:
• Perform a pre-test probability for PE
  — The Wells clinical prediction algorithm is frequently used
• Review the most commonly used imaging tests used in PE diagnosis
  — A CT scan is usually the first-line imaging tool used when PE is suspected
  — CT angiography uses a CT scanner to take pictures of the arteries in the lungs to detect PE
  — A ventilation-perfusion (V/Q) scan uses radioactive material to take images of blood flow in the lungs and measure breathing capacity
• Explain that a chest x-ray may be used to rule out other causes of symptoms, such as pneumonia

Points to Emphasize:

- Discuss that treatment type depends on PE severity and the patient’s hemodynamic stability
- Explain that those with high PESI scores are typically treated in the hospital
  — If parenteral/IV therapy is used initially, there may be overlap with OAC treatment
- Reiterate that most patients can be treated on an outpatient basis with an anticoagulant, either an injectable or OAC
  — If applicable, explain that low molecular weight heparin is recommended for cancer-associated PE
- Inform that treatment duration depends on whether PE is provoked or unprovoked
  — For most patients with provoked PE, treatment duration is 3 months

Additional Information for Healthcare Provider:

**Treatment should be personalized**

Review these with your patient as you work together to develop a treatment plan

- Is treatment for acute PE or prevention of recurrent PE?
- Is PE provoked or unprovoked?
- How is the patient’s kidney function?
- What other medications is the patient taking?
- Is cost an issue?
- Would diet changes be an issue?
- Can patient manage frequent blood draws?
- Once daily or twice daily dosing?

Points to Emphasize:

- Discuss that medical guidelines recommend a direct-acting oral anticoagulant (DOAC) over warfarin for most patients
  — DOACs are just as effective as warfarin but have a lower risk of bleeding in the brain
- Explain that kidney function must be tested prior to starting a DOAC
  — Dose adjustments of a DOAC may be needed based on kidney function or other medications
- If applicable, advise that patients with certain conditions can’t take DOACs: Severe kidney disease, pregnancy, breastfeeding, and mechanical heart valve
- Ability to pay for, or insurance that permits, a DOAC is a consideration in treatment planning


**Anticoagulantes orales para tratamiento de la EP**

- Hay varios tipos de anticoagulantes orales, para diferentes partes del proceso de formación de coágulos (vitamina K, factor Xa o inhibidores directos de trombina)
- Se han utilizado antagonistas de la vitamina K para tratar el EP por muchos años
  — La comida puede afectar su funcionamiento
  — Son necesarios los análisis de sangre rutinarios para asegurarse de que la persona está tomando la cantidad correcta de medicamento
- Los anticoagulantes que inhiben el factor Xa o la trombina directa son nuevos tratamientos para el EP
- Estos anticoagulantes nuevos son tan eficaces como los tratamientos que usan la vitamina K
  — Su efectividad no depende de restricciones dietéticas
  — Generalmente, se necesitan pocos análisis de sangre con estos anticoagulantes nuevos en comparación con los inhibidores de la vitamina K
- La guía médica recomienda que, cuando posible, los pacientes tomen los nuevos anticoagulantes en lugar del medicamento antagonista, vitamina K, como tratamiento para la EP

**DOAC Dosing for VTE Treatment**

<table>
<thead>
<tr>
<th>DOAC</th>
<th>Dosing</th>
<th>Kidney Function</th>
<th>Drug-Drug Interactions and Dose Adjustments</th>
<th>Other</th>
</tr>
</thead>
</table>
| Dabigatran | 150 mg BID after ≥5 days parenteral anticoagulation  
DVT prevention after hip replacement surgery: 110 mg QD first day, 220 mg QD thereafter  
(May be taken with or without food) | Do not use if CrCl <30 mL/min | • Do not use with any P-gp inducer  
• Do not use with any P-gp inhibitor when CrCl<50 mL/min | Must be kept in original container  
(can’t use pill box)  
Take with full glass of water  
Swallow whole, do not cut or crush |
| Rivaroxaban | 15 mg BID with food x 3 weeks  
then 20 mg QD with food  
DVT prevention after hip or knee replacement surgery: 10 mg QD with or without food | Do not use if CrCl <30 mL/min | • Do not use with combined P-gp and strong CYP3A4 inhibitors or inducers  
• Do not use with dual strong CYP3A4 and P-gp inducers  
• Do not use with dual strong CYP3A4 and P-gp inhibitors, decrease dose by 50% if dose ≥2.5mg BID  
• If dose is 2.5mg BID, avoid use with dual strong CYP3A4 and P-gp inhibitors | 15 mg & 20 mg must be taken with food (largest meal of day – typically the evening meal) |
| Apixaban | 10 mg BID for 7 days, then 5 mg BID (with or without food)  
For secondary prevention, reduce dose to 2.5 mg BID after 6 months  
DVT prevention after hip or knee replacement surgery: 2.5 mg BID | No dose adjustment/restriction | • Use 30 mg QD with use of certain P-gp inhibitors | Use 30 mg QD if weight < 60 kg |
| Edoxaban | 60 mg QD after 5-10 days parenteral anticoagulation | Use 30 mg QD for CrCl 15-50 mL/min  
Do not use if CrCl <15 mL/min | • Use 30 mg QD with use of certain P-gp inhibitors | Use 30 mg QD if weight < 60 kg |

Additional Information for Healthcare Provider:

Points to Emphasize:
- Explain that procedures are usually reserved for massive PE
- Thrombolytics ("clot busters") quickly dissolve blood clots
  - Usually administered via IV in the emergency department
  - Some facilities perform catheter-directed thrombolytics
  - Excessive bleeding is a risk with thrombolytics
- Embolectomy (removal of clot) can be performed surgically or with a catheter

Additional Information for Healthcare Provider:
- ACCP guidelines suggest IV administration of thrombolytics be reserved for:
  - High-risk PE: Systemic hypotension and RV impairment
  - Some intermediate-risk PE: Normotensive, RV impairment
- Patients with intermediate-risk PE that are initially placed on OAC, not IV thrombolytics, should be monitored for deterioration
  - IV thrombolytics may be indicated

Reacciones adversas al tratamiento del EP

- Todos los medicamentos tienen posibles reacciones adversas:
  - Si tiene una reacción adversa póngase en contacto con su proveedor de atención médica
  - Su proveedor de atención médica le dirá si debe hacer algún cambio en el anticoagulante
- El tipo de reacción adversa más común de cualquier anticoagulante es el sangrado
- Puede reducir al mínimo ciertos tipos de sangrados:
  - Usando un cepillo de dientes blando
  - Rasurándose con máquina eléctrica en lugar de usar un rastrillo de afeitar
  - Evite las actividades y los deportes que pueden causar lesiones (caminar, nadar y montar en bicicleta son seguras)
- Entre las reacciones adversas menos comunes están las náuseas, diarrea o estreñimiento, dolor de cabeza, mareos y reacciones en la piel como sarrojillo o comezón

Points to Emphasize:
- Reinforce that if they experience any adverse reaction to contact their healthcare provider before stopping OAC:
  - To address the adverse reaction or make changes to medication(s)
- Reinforce that not taking medication increases the risk that PE will recur
- Remind them that minor bleeding is normal and suggest ways to minimize minor bleeding:
  - Use a soft bristle toothbrush and gently “massage” gums
  - Avoid activities that could result in falls, bumps, or bangs
- Reinforce that it’s OK to exercise and suggest:
  - Walking, swimming, and bike riding are safe (preferred)

Additional Information for Healthcare Provider:
- Patients who are taking aspirin or an antiplatelet in addition to an OAC should take a proton pump inhibitor (PPI) for prevention of GI bleeding

### Potential Adverse Reactions*

<table>
<thead>
<tr>
<th>Dabigatran</th>
<th>Rivaroxaban</th>
<th>Apixaban</th>
<th>Edoxaban</th>
</tr>
</thead>
<tbody>
<tr>
<td>GI bleeding</td>
<td>GI bleeding</td>
<td>Hematuria</td>
<td>GI bleeding</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>Dyspepsia</td>
<td>Subconjunctival hemorrhage</td>
<td>Rash</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>Back pain</td>
<td></td>
<td>Abnormal liver tests</td>
</tr>
<tr>
<td></td>
<td>Urinary tract infection</td>
<td></td>
<td>Anemia</td>
</tr>
<tr>
<td>Epidural or spinal hematomas for patients undergoing neuraxial anesthesia or spinal puncture</td>
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<td></td>
</tr>
</tbody>
</table>

*Non-major bleeding.
Sources: Prescribing information package inserts.
**Points to Emphasize:**
- Reiterate that minor bleeding is common
  - 1 out of 4 patients will have a minor bleed
  - In most cases, not a cause for alarm
- Distinguish between “nuisance” bleeding and serious bleeding
- Patients can manage minor bleeding at home:
  - Demonstrate applying pressure to a wound
  - Demonstrate how to stop a nose bleed

**Additional Information for Healthcare Provider:**
- Most patients benefit from being given, or directed to, resources for managing minor bleeding
- Additional resources can be found at:
  - http://www.anticoagulationtoolkit.org/patients
  - http://www.clotconnect.org/patients/resources/brochures

**Questions to ask if the patient reports bleeding**
- Which OAC are you taking?
- When was the last dose of anticoagulant?
- Are you or did you take any other medications such as aspirin or an NSAID?
- How long have you been bleeding? Has it stopped?
- What were you doing when you started bleeding?
- How severe is the bleeding?
Points to Emphasize:

- Discuss that not taking the prescribed medication increases the risk of VTE recurrence
  - Ease and convenience of DOACs may improve adherence
  - Explain that DOACs have rapid onset and offset, which increases the importance of adherence

- Assist patients with suggestions to improve adherence:
  - Take medication at the same time(s) every day
  - Set a calendar reminder on computer or alarm on mobile phone

- Reinforce that aspirin, ibuprofen, and other OTC pain relief medication can make the blood “more thin” and lead to bleeding
  - Acetaminophen can be taken for pain relief as long as there is no known liver disease

- Advise patients taking warfarin:
  - Avoid fluctuations in the amount of food high in vitamin K
  - Consistency is important to maintaining appropriate medication level

- Inform patients taking a DOAC
  - Apixaban and rivaroxaban require dose adjustments at 7 and 21 days, respectively
  - Avoid taking OTC medications and supplements, including vitamins, as they may make the anticoagulant less effective or may increase the risk of bleeding

Additional Information for Healthcare Provider:

- Many DOACs require dose adjustment for change in kidney function
  - Check baseline kidney function and every 6 months thereafter
Points to Emphasize:

- Emphasize that bleeding in the brain is rare with DOACs
  — Clinical trials have demonstrated that DOACs have significantly less intracranial hemorrhage (ICH) compared to warfarin

- Mention that when going to the ED, it’s important to tell medical staff which OAC they are taking
  — They should keep a card in their wallet that indicates which OAC

- Suggest they wear medical alert jewelry/tag with the name of their OAC in case of an emergency and they are unable to communicate

- Emphasize that symptoms of PE are a medical emergency and they should call 9-1-1

Additional Information for Healthcare Provider:

- ICH occurs in ~0.1% of cases with DOACs
  — Since there are no head-to-head trials for DOACs in VTE, it’s unknown if one DOAC is superior to another with regard to ICH incidence

- There is an approved reversal agent for dabigatran (idarucizumab) for use in emergency major bleeding
  — Other reversal agents for DOACs are in development
  — Fresh frozen plasma and prothrombin complex concentrate also can be used to treat major bleeds associated with DOACs for major bleeding in patients taking DOACS

Provider Resources

- Anticoagulationtoolkit.org (http://www.anticoagulationtoolkit.org/providers)
  — Provider resource on anticoagulation

  — Guidelines for pulmonary vascular

- Clot Connect (http://www.clotconnect.org/healthcare-professionals/hospital-associated-venous-thromboembolism-vte)
  — Resources and clinical care guidelines for VTE

Recursos para el paciente

- American Heart Association (www.heart.org)
  — Información y videos para pacientes

- National Blood Clot Alliance (www.stoptheclot.org)
  — Información, relatos y foros comunitarios

- Centers for Disease Control and Prevention (www.cdc.gov)
  — Tromboembolia venosa: conozca los riesgos, las señales y los síntomas de los coágulos

- North American Thrombosis Forum (www.natfonline.org)
  — Información para pacientes, grupos de apoyo y defensa del paciente