Anticoagulation in Venous Thromboembolism

**Determining Need for Anticoag.**

- Anticoagulation is recommended for most cases of VTE unless there is a strong contraindication.
- Two types of VTE may not require anticoagulation if certain conditions are met (see table below).

<table>
<thead>
<tr>
<th>Type/Location</th>
<th>Risk factors*</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute isolated distal DVT of leg without severe symptoms or risk factors for extension</td>
<td>Risk factors for extension: positive D-dimer, thrombosis is extensive, thrombosis is close to proximal veins, no reversible/provoking risk factor, active cancer, no VTE, or inpatient status</td>
<td>- No anticoagulation&lt;br&gt;- Serial imaging for 2 weeks</td>
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<tr>
<td>Subsegmental PE without proximal DVT or risk factors for recurrence</td>
<td>Risk factors for VTE recurrence: hospitalized/immobile patients, active cancer, no reversible/provoking risk factor</td>
<td>- No anticoagulation&lt;br&gt;- Clinical surveillance</td>
</tr>
</tbody>
</table>

**Length of Treatment**

- DOACs (dabigatran, rivaroxaban, apixaban, and edoxaban) are recommended over warfarin for DVT of the leg or PE. However, DOACs are contraindicated in pts with severe renal insufficiency (CrCl<30 mL/min), mechanical heart valves, mod/sev hepatic dysfunction, and pregnancy.
- LMWH is recommended for DVT of the leg or PE in pregnancy. Edox. or riva. are now suggested over LMWH in CA-associated VTE pts with low bleed risk.*

**Anticoagulant**

- **Apixaban (Eliquis®)**
  - 10 mg BID X 7 days then 5 mg BID
  - Reduced dose by 50% if co-administered with strong dual inhibitors of cytochrome CYP3A4 and P-gp (eg. ketoconazole and clarithromycin)
  - Avoid use with strong dual inducers of CYP3A4 and P-gp (eg. rifampin)
  - Avoid in patients with mechanical heart valves
- **Dabigatran (Pradaxa®)**
  - 150 mg BID (if CrCl>50 mL/min) after 5-10 days of parenteral tx
  - Avoid use with P-gp inducers (eg. rifampin)
  - Avoid use with P-gp inhibitors if CrCl<50 mL/min
  - Avoid in patients with mechanical heart valves
- **Edoxaban (Savaysa®)**
  - 60 mg daily after 5-10 days of parenteral tx
  - 30 mg daily if CrCl 15-50 mL/min**; wt 50 kg, or if taking verapamil, quinidine, azithromycin, clarithromycin, oral iraconazole or ketokonazole
  - Avoid use with rifampin
  - Avoid in patients with mechanical heart valves
- **Rivaroxaban (Xarelto®)**
  - 15 mg BID X 21 days then 20 mg daily
  - Avoid use with combined P-gp and strong CYP3A4 inducers or inhibitors (eg. ketoconazole and ritonavir)
  - Avoid in patients with mechanical heart valves
- **Warfarin (Coumadin®)**
  - Initial dose: 5mg is a typical starting dose, but a lower dose may be considered in certain patients (eg. elderly, malnourished, liver disease)
  - Subsequent dosing based on INR with target range 2-3.
  - Parenteral tx should be given for at least 5 days and until INR is in range
  - Avoid in pregnancy
- **LMWH**
  - Enoxaparin: 1 mg/kg SC 12h (if CrCl>30), 1mg/kg SQ daily (if CrCl<30)
  - Dalteparin (only FDA approved for VTE treatment in CA): 200 IU/kg SC daily
  - (if CrCl<50 mL/min*), 150 IU/kg SC daily (month 1-2) (do not exceed 150,000 IU/24 h)
  - Drug of choice in pregnancy
  - Baseline: CBC, creatinine

**Setting of Treatment**

- Guidelines support home initial treatment for some types of VTE as long as certain criteria are met.

<table>
<thead>
<tr>
<th>Type/Location</th>
<th>Clinical criteria for initial treatment in home</th>
<th>Home environment criteria for initial treatment in home</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low-risk PE</td>
<td>Clinically stable with good cardiopulmonary reserve, including age ≤50, no hx of CA or chronic cardiopulmonary disease, HR &lt;110, SBP ≥100 mm Hg, and CrCl ≥90%</td>
<td>Well-maintained living conditions&lt;br&gt;- Strong support network&lt;br&gt;- Ready access to medical care&lt;br&gt;- Expected to be compliant&lt;br&gt;- Access to phone</td>
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**Choice of Anticoagulant**

- For DVT of leg or PE provoked by surgery or transient/reversible risk factor, 3 months is the recommended length of treatment.
- For an unprovoked DVT of leg or PE, treat for 3 months and then evaluate the benefit/risk ratio for extended treatment. (see table below)
- If active CA, extended treatment is recommended.

**Length of Treatment**

- Initial treatment in home criteria: for initial treatment in home setting.
- Home environment criteria: for initial treatment in home setting.
- For additional info about anticoagulation in VTE, visit www.anticoagulationtoolkit.org

**Long-term surveillance after 6-12 months of anticoagulation:** In patients with continued need for anticoagulation due to risk of VTE recurrence, options include: reduced dose rivaroxaban (10 mg daily), reduced dose apixaban (2.5 mg BID), continued full dose dabigatran (150 mg BID), or continued warfarin or LMWH. Aspirin should not be first choice for long-term secondary prevention of VTE.

**Patient Education**

- For patient handouts, visit www.anticoagulationtoolkit.org

**Long-term management**

- Follow-up: at each flu, assess for compliance, s/sx of bleeding or thromb., interacting meds, and reinforce ed.
- DOACs: assess liver function, and renal function (more often if renal insufficiency)
- Warfarin: INRs 3-5 days after re-starting or any changes that can effect INR. (ex. med, diet change, or illness) and approx. 7 days after any dose changes. INRs can gradually be spaced out to monthly, if stable
- Bridging: Bridging with DOACs is not generally necessary. For warfarin, bridging is not necessary unless patient has high thromboembolic risk (eg. VTE <3 months ago, severe thrombophilia). If bridging, start LMWH approx. 3 days before (when INR gets below range) and stop it 24 hrs before proc. Restart LMWH 24 hrs following low risk proc or after 48-72 hrs after high risk proc. Stop LMWH when INR in range.
References


Drug package inserts

- Apixaban: https://packageinserts.bms.com/pi/pi_eliquis.pdf
- Dabigatran: http://docs.boehringer-ingelheim.com/Prescribing%20Information/PIs/Pradaxa/Pradaxa.pdf
- Edoxaban: http://dsi.com/prescribing-information-portlet/getPIContent?productName=Savaysa&inline=true
- Enoxaparin: http://products.sanofi.us/lovenox/lovenox.html

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