

Community-wide Anticoagulation Workgroup Key points/Education Summary - May 2016

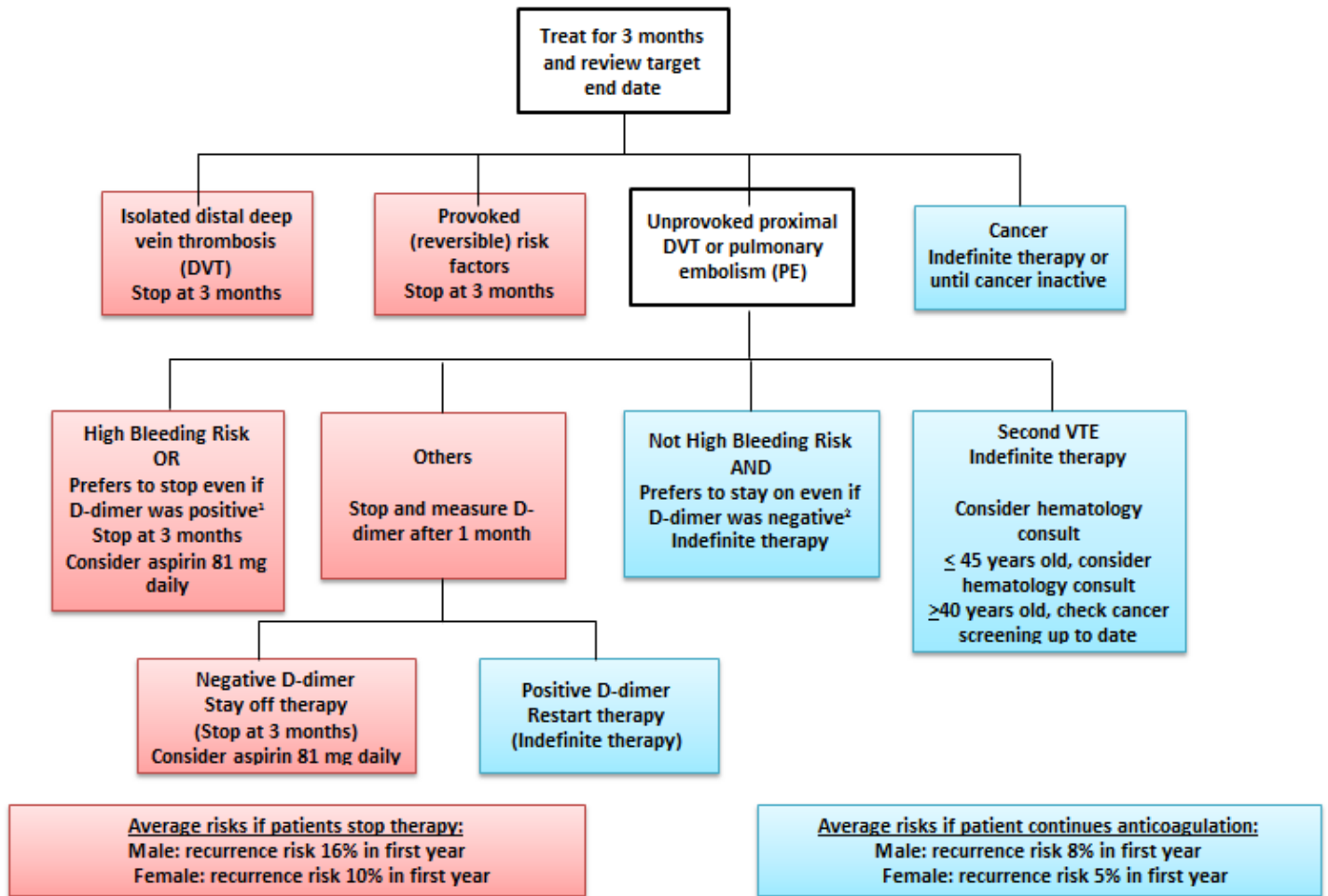
General:

- **Direct oral anticoagulants (DOACs) are becoming an important and attractive therapeutic option for patients with atrial fibrillation, DVT and PE. In certain patients DOACs may be preferred over warfarin. For venous thromboembolism (VTE) treatment, recent guidelines prefer DOACs over warfarin (non-cancer patients).¹**
 - **Cost for DOACs:** In the short term (i.e. VTE treatment), may be similar; however long term (i.e. atrial fibrillation) costs for DOACs may be 2-5 times higher for patients. Patients will need an individual cost assessment based on medications, labs and co-pays for visits.
 - **Pros for DOACs:** No INR monitoring (fewer clinic visits), fewer drug interactions, no vitamin K interactions, no injectable LMWH for deep vein thrombosis if rivaroxaban or apixaban are used, quick onset.
 - **Cons for DOACs:** Contraindicated for patients with mechanical heart valves, pregnancy, and breastfeeding. Limited data for using DOAC's in patients with active cancer, thrombophilia conditions and advanced age. Missed doses puts patients at high risk for embolic events, avoid in patients with in CrCl <30ml/min, and cost (Medicare patients with gaps, "the donut hole", in drug coverage). Edoxaban (Savaya) should NOT be used in A.fib patients with CrCl >95ml/min due to increased risk of stroke. Dabigatran (Pradaxa) should be avoided in patients >75 years old. If reversal of DOAC is needed, there are limited options.
- **Bridging peri-procedurally with low-molecular weight heparin (LMWH) will be used in fewer patients, based on recently published data.² Patients with high thromboembolic risks may still benefit from bridging.**
 - Individual patient thromboembolic risks and hemorrhagic risks need to be assessed before prescribing LMWH. Patients who LMWH in the past for procedures may no longer require it.
- **INR target ranges for warfarin < 2.0 have not been shown to provide adequate protection from embolic events and they still expose patients to the bleeding risk.**
 - With atrial fibrillation, lower INRs (< 2.0) vs. target INR ranges of 2.0-3.0 have been shown to have higher thromboembolic rates with similar bleeding risks.
- **After major bleeds, data has emerged regarding resuming anticoagulation - individual patient risk factor assessment will be needed in consultation with the specialist.**
 - Gastrointestinal (GI) bleed: Warfarin therapy resumption after GI bleed is associated with a lower risk for thrombosis and death without significantly increasing the risk for re-bleeding.^{3,4}
 - Intracranial hemorrhage: Mortality rates lower in those who restarted warfarin in-hospital and bleeding not increased.^{5,6}

DVT/PE :

- **We DO NOT recommend re-scanning the effected limb at the end of therapy since the blood flow will likely be abnormal.**
 - Re-scanning is only recommended if there are new or worsening symptoms.
- **Hypercoagulable panels are very expensive (\$1000-\$2,000) and limited by concurrent medications and infrequently changes panels the management plan.**
 - A hematology consult to the Cancer Partnership may be more cost-effective.
 - Certain patients who experience an unprovoked venous thromboembolic event may be referred to a hematology specialist for a hypercoaguable work-up, which include:
 - Strong family history of VTE (this is the key risk to consider)
 - VTE in an unusual location (i.e. mesenteric or upper extremity without a catheter)
 - Greater than one episode of VTE in a different area (i.e. left leg first clot, now has right leg clot)
 - Multiple VTE events (non-cancer patient)
 - Patients less than 40 years old
- **The Providence ACC and TEC anticoagulation clinics assess VTE patients usually daily to be able to adjust warfarin and transition them off LMWH as soon as possible. Receiving the consults and phone calls the same day as the patient is seen in the ED helps to facilitate getting them in as soon as possible.**
 - For patients on direct oral anticoagulants (DOACs), we also enroll them in clinic to ensure patients receive education, have appropriate doses based on renal function and indication, and have assistance for peri-procedure management.
- **The duration of treatment for most deep vein thrombosis (DVT) and pulmonary embolism (PE), has been shorted to 3 months for an initial provoked event (see diagram below) . Some considerations:**
 - For unprovoked events, the risk vs. benefit ratio for bleeding should be considered.
 - Patients with active cancer and a new venous thromboembolic event (VTE) should be considered for treatment with low-molecular weight heparin (LMWH), twice daily (BID) during the initial treatment phase.
 - Cancer patients should be considered for longer treatment, based on current stage and type of cancer – consult with their hematology/oncology provider for duration.

Duration of Venous Thromboembolism (VTE) Treatment⁷



Patients will need to understand the risks vs. benefits of stopping vs. continuing on anticoagulants, especially with unprovoked VTE. Considerations:

- Patient preferences
- Hemorrhagic risks (most prediction tools are based on atrial fibrillation patients):
 - Advanced age
 - Liver disease
 - Moderate to severe renal disease
 - Alcohol abuse
 - Concomitant anti-platelet therapy
 - Uncontrolled hypertension
 - History of bleeding, especially major bleed
 - Anemia
 - Excessive fall risk
- Embolitic risks:
 - Active cancer (or cancer treatment)
 - Location of clot (proximal DVT, PE)
 - Male gender
 - Elevated d-dimer one month after stopping oral anticoagulant therapy
 - Obesity
 - Chronic thrombotic pulmonary hypertension
 - Hereditary thrombophilias
 - Inflammatory bowel disease (persistent or intermittent)
 - Estrogens (may be reversible if stopped)

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References:

- 1) Kearon C, Akl EA, Ornelas J, et al. Antithrombotic Therapy for VTE Disease: CHEST Guideline and expert panel report. *CHEST* 2016;149(2):315-352.
- 2) Douketis JD, Spyropoulos AC, Kaatz S, et al for BRIDGE Investigators. Perioperative Bridging Anticoagulation in Patients with Atrial Fibrillation. *NEJM* 2015 DOI: 10.1056/NEJMoa1501035.
- 3) Qureshi W, Mittal C, Patsias I, et al. Restarting anticoagulation and outcomes after major gastrointestinal bleeding in atrial fibrillation. *Am J Cardiol* 2014;113:662-8.
- 4) Witt DM, Delate T, Garcia DA, et al. Risk of thromboembolism, recurrent hemorrhage, and death after warfarin therapy interruption for gastrointestinal tract bleeding. *Arch Intern Med* 2012;172:1484-91.
- 5) Yung D, Kapral MK, Asllani E, et al. Reinitiation of Anticoagulation After Warfarin-Associated Intracranial Hemorrhage and Mortality Risk: The Best Practice for Reinitiating Anticoagulation Therapy After Intracranial Bleeding (BRAIN) Study. *Can J Card* 2012;28:33–39.
- 6) Morgenstern LB, Hemphill JC, Anderson C, et al. Guidelines for the Management of Spontaneous Intracerebral Hemorrhage A Guideline for Healthcare Professionals from the American Heart Association/American Stroke Association. *Stroke*. 2010;41:2108-2129.
- 7) Kearon C, Akl EA. Duration of anticoagulant therapy for deep vein thrombosis and pulmonary embolism. *Blood* 2014;123(12):1794-1801.