# DVT and PE Anticoagulation Management Recommendations

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| July 1, 2019 | DVT AND PE ANTICOAGULATION MANAGEMENT RECOMMENDATIONS |
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**Introduction:**
Over the past six decades, warfarin has proven effective in reducing the risk of recurrent venous thromboembolism (VTE) in patients with acute deep vein thrombosis (DVT) and/or pulmonary embolism (PE). However, there have been multiple challenges with using warfarin including delayed onset of action, need for bridging and monitoring as well as many drug-drug and drug-food interactions. Hence, long years of research have led to the development of direct oral anticoagulants (DOACs). Of the four currently FDA-approved DOACs, one is a direct thrombin inhibitor (dabigatran) and the other three are direct factor Xa inhibitors (apixaban, edoxaban and rivaroxaban). DOACs have been found to be at least as effective as warfarin with fewer bleeding complications. This document provides evidence based recommendations for the anticoagulation management of VTE.

**Evidence:**
DOACs provide more convenient treatment of VTE in the outpatient setting compared to heparin + warfarin due to less monitoring, and drug-drug and drug-food interactions. The 2016 CHEST guidelines suggest treatment of DVT of the leg and PE, in the absence of cancer, with a DOAC over warfarin therapy (Grade 2B) based on the potential for less bleeding and greater convenience with similar efficacy.[1] There is growing evidence to support the use of apixaban and rivaroxaban in cancer related VTE management. Dabigatran and edoxaban require 5-10 days of parenteral anticoagulation prior to their use whereas rivaroxaban and apixaban can be started immediately for the management of acute VTE. The clinical trials with rivaroxaban and apixaban demonstrated similar efficacy outcomes compared to heparin + warfarin with less major bleeding.[2,3,4] Insurance coverage of the DOACs is variable but improving. There are manufacturer provided copay discounts available for patients with private insurance but not for those with state funded insurance. Most patients, regardless of insurance status, are able to get 1 month of medication free of charge through manufacturer provided discount cards. Patient selection is important to maximize efficacy, safety, and compliance with therapy. Exclusion criteria based on criteria used in the clinical trials and other theoretical contraindications are necessary to assess candidacy for DOAC treatment (Table 1, see appendix). Warfarin might be considered in case of severe allergies to the DOACs or in patients with end stage renal disease (ESRD).

The 2016 CHEST Guidelines for Antithrombotic Therapy for VTE Disease support home treatment of low-risk PE (Grade 2B) and DVT (Grade 1B) in clinically stable patients with good cardiopulmonary reserve, good social support with ready access to medical care, and who are expected to be compliant with follow-up.[1] For PE, the CHEST guidelines support the use of the PE severity index (PESI) to identify patients with a low mortality risk (~1% at 30 days) who may be suitable for home management acknowledging that the risk score is only one of many considerations when determining the need for hospital admission after PE (Table 2, see appendix).[1,5,6] The PESI has been simplified (Table 2, see appendix) for usability with retention of its prognostic accuracy.[7] A score of 0 (i.e. the patient has no variables of the score) is deemed low risk. Please refer to "Massive and Submassive Pulmonary Embolism Algorithm" document for further recommendations regarding thrombolytic therapy in patients with PE.

**Recommendations:**

1- We suggest using a DOAC over heparin/warfarin for the management of lower or upper extremity DVT and or PE not associated with cancer.
2- We particularly suggest using apixaban or rivaroxaban without parenteral anticoagulation, to help simplify transitions of care. Consider out of pocket cost.
3- We suggest using apixaban, rivaroxaban or low molecular weight heparin (LMWH) over warfarin in cancer associated lower extremity DVT and or PE. The choice should be based on convenience and cost.
4- Warfarin might be considered in case of severe allergy to DOACs or in case of ESRD.
5- In patients with lower or upper extremity DVT and or PE who receive extended therapy, we suggest that there is no need to change the choice of anticoagulant after the first 3 months.
6- Suggest treatment at home or early discharge over standard discharge in low-risk patients with adequate home circumstances:
   A. Clinically stable with good cardiopulmonary reserve
   B. No recent bleeding, severe renal or liver disease, or severe thrombocytopenia (i.e., <70,000/mm3)
   C. Expected to be compliant with treatment and
   D. Patient feels well enough to be treated at home
7- Consider using the simplified PESI (Table 2) to help identify low risk patients with PE who may be eligible for outpatient treatment. This should not replace clinical judgement.
8- In patients with acute proximal DVT of the leg, we suggest anticoagulation therapy alone over catheter directed thrombolysis (CDT).
9- Consider CDT in patients with severe lower extremity DVT (e.g., phlegmasia), high risk of post-thrombotic syndrome, and low risk of bleeding.
10- In patients with acute upper extremity DVT involving the axillary or more proximal veins, we suggest anticoagulation therapy alone over thrombolysis.
11- Consider using CDT for severe upper extremity DVT with high risk for post-thrombotic syndrome and low risk for bleeding, especially in cases with underlying thoracic outlet syndrome (TOS). First rib resection can follow CDT in patients with TOS.
12- In catheter-induced upper extremity DVT involving the axillary or more proximal veins, we suggest anticoagulation therapy. We favor anticoagulation for up to three months if the thrombosis is symptomatic, associated with cancer, or the catheter remains in place. A longer duration of anticoagulation may be warranted if the catheter remains in place, particularly for patients with cancer. It is reasonable to continue using the catheter as long as it is functional. If the catheter is not functioning, the catheter can be removed as long as the patient is on therapeutic anticoagulation.
13- We recommend against the use IVC filter in patients with acute DVT or PE who are treated with anticoagulants.
14- We recommend three months of anticoagulation for provoked proximal DVT and or PE.
15- In patients with unprovoked VTE, we suggest (for first event) or recommend (for recurrent event) extended anticoagulation therapy over three months period in patients with low or moderate bleeding risk. We recommend (for first event) or suggest (recurrent event) three months of anticoagulation in patients with high risk of bleeding.
16- In all patients who receive extended anticoagulant therapy, the continuing use of treatment should be reassessed at periodic intervals (e.g., annually).

17- We suggest aspirin over no aspirin in patients with unprovoked proximal DVT or PE who are stopping anticoagulation therapy and have no contraindication to aspirin.
18- In Patients with isolated sub-segmental PE without proximal DVT, we suggest clinical surveillance over anticoagulation in patients with low, and suggest anticoagulation over surveillance in patients with high, risk for VTE recurrence.
19- In high risk symptomatic patients with provoked or unprovoked distal (below the popliteal vein) DVT, we recommend three months of anticoagulation over shorter or longer periods. Asymptomatic lower risk patients with high risk of bleeding can be followed by ultrasound periodically (e.g., every 2 weeks).
20- In patients with acute DVT of the leg, we suggest not using compression stockings routinely to prevent PTS. However, we recommend using them in patients with symptomatic edema.
21- Please refer to "Massive and Submassive Pulmonary Embolism Algorithm" document for further recommendations regarding thrombolytic therapy in patients with PE.
22- Please refer to the DOAC related protocols for dosing, management of bleeding and peri-procedural anticoagulation recommendations.
23- Please refer to the warfarin and heparin protocols for dosing and monitoring.

**References**


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**APPENDIX**

**Table 1:** Proposed Exclusion Criteria for the use of a DOAC[#]

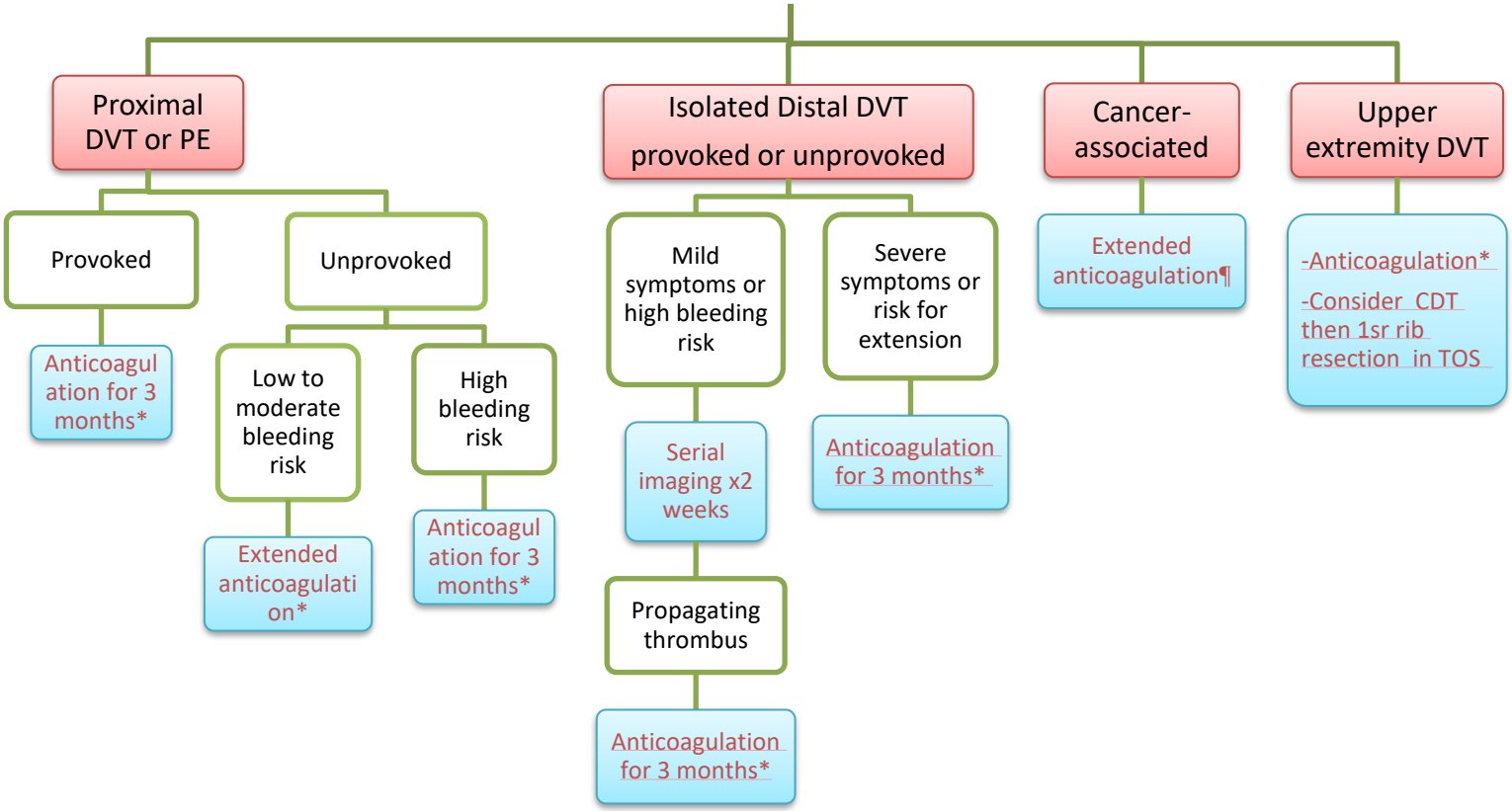
| Patient History | Lab Values/Vitals | Medications | Social History |
|---|---|---|---|
| **Active cancer treatment** | **Hgb < 10 g/dL with evidence of bleeding** | **Dual Antiplatelet Therapy** | **No prescription insurance coverage** |
| **Mechanical Heart Valve** | **Platelets < 70 K** | **Major Drug Interactions with Rivaroxaban/ Apixaban** (Strong dual inducers of P-gp and CYP3A4 eg, rifampin, phenytoin, carbamazepine, St. John's wort) | **Homeless** |
| **Concern for active bleeding** | **CrCl < 30ml/min for rivaroxaban* CrCl < 25ml/min for apixaban*** | | **Known history of poor compliance with medications and/or follow up** |
| **Bleeding risk outweighs risk of thromboembolic event** | **ALT >3 times ULN or T Bili >1.5 time ULN** | | **EtOH or IV drug abuse** |
| **Bacterial endocarditis** | **Blood Pressure >180/110 mmHg** | **Major Drug Interactions with Rivaroxaban** (strong dual inhibitors of P-gp and CYP3A4 eg, ketoconazole, itraconazole, ritonavir, clarithromycin) | |
| **HIT ≤ 3 months** | | Severe allergy to the DOAC* | |
| **Pulmonary arterial hypertension** | | | |
| **Child-Pugh Class B/C Cirrhosis or elevated INR related to liver disease** | | | |
| **Pregnancy** | | | |

*Warfarin might be considered in case of severe allergies to the DOACs or in case of end stage renal disease (ESRD).
CrCl: creatinine clearance; DOAC: direct oral anticoagulant, EtOH: ethanol, Hgb: hemoglobin, HIT: heparin induced thrombocytopenia ULN: upper limit of normal, P-gp: permeability glycoprotein.

**Table 2:** Original and Simplified PESI Score [5,6,7]

| Parameter | Original version[214] | Simplified version[218] |
|---|---|---|
| Age | Age in years | 1 point (if age >80 years) |
| Male sex | +10 points | – |
| Cancer | +30 points | 1 point |
| Chronic heart failure | +10 points | 1 point |
| Chronic pulmonary disease | +10 points | |
| Pulse rate ≥110 b.p.m. | +20 points | 1 point |
| Systolic blood pressure <100 mm Hg | +30 points | 1 point |
| Respiratory rate >30 breaths per minute | +20 points | – |
| Temperature <36 °C | +20 points | – |
| Altered mental status | +60 points | – |
| Arterial oxyhaemoglobin saturation <90% | +20 points | 1 point |
| | Risk strata[a] | |
| | **Class I:≤65 points**<br>very low 30-day mortality risk (0–1.6%)<br>**Class II: 66–85 points**<br>low mortality risk (1.7–3.5%)<br><br>**Class III: 86–105 points**<br>moderate mortality risk (3.2–7.1%)<br>**Class IV: 106–125 points**<br>high mortality risk (4.0–11.4%)<br>**Class V: >125 points**<br>very high mortality risk (10.0–24.5%) | **0 points**= 30-day mortality risk 1.0%<br>(95% CI 0.0%–2.1%)<br><br>**≥1 point(s)**= 30-day mortality risk 10.9%<br>(95% CI 8.5%–13.2%) |

# Figure 1: Anticoagulation Therapy Algorithm for VTE




CDT: catheter directed thrombolysis, DOAC: direct oral anticoagulant, DVT: deep vein thrombosis, LMWH: low molecular weight heparin, PE: pulmonary embolism, TOS: thoracic outlet syndrome.

***** We favor using a DOAC over enoxaparin + warfarin.
¶ We favor apixaban, rivaroxaban, or low molecular weight heparin over warfarin.