Emergency Department Anticoagulation Guidelines

Anticoagulation Work Flow for Deep Vein Thrombosis (DVT) or Pulmonary Embolism (PE)

Does the patient have any of the following exclusion criteria?

- ☐ Active bleeding
- ☐ Coexisting conditions requiring inpatient admission
- ☐ Hemodynamic instability
- ☐ Platelet count < 100, 000
- ☐ Recurrent thrombosis, patient already on anticoagulation

Consider **admission** for inpatient workup

NO

Confirmed DVT or PE

DVT

Does the patient have any of the following exclusion criteria?

- ☐ Massive DVT
  - Swelling of entire lower limb, acrocyanosis, venous limb ischemia, extension of DVT into iliofemoral veins or inferior vena cava
- ☐ Concomitant symptomatic PE
- ☐ High-risk of bleeding with anticoagulant therapy
  - Active bleeding, bleeding within 4 weeks, surgery or trauma within 1 week, platelets < 100 x10^6/L, INR > 1.4 or aPTT > 40, advanced cancer with intracerebral or intrahepatic metastases

NO

Consider **outpatient management** or admission to **ED observation**

- *Consider admission to observation unit in the setting of malignancy (suspected or confirmed), obesity weight ≥ 120 kg or BMI ≥ 35 kg/m2, pregnancy, or cost prohibiting factor*

YES

Consider **admission** for inpatient workup

PE

Calculate the Simplified PE Severity Index Score (PESI)

sPESI	
Criteria	**Points**
Age ≥ 80 years	1
History of cancer	1
Chronic cardiopulmonary disease	1
sBP < 100 mmHg	1
HR ≥ 110 bpm	1
O_2 saturation < 90%	1

sPESI ≥ 1

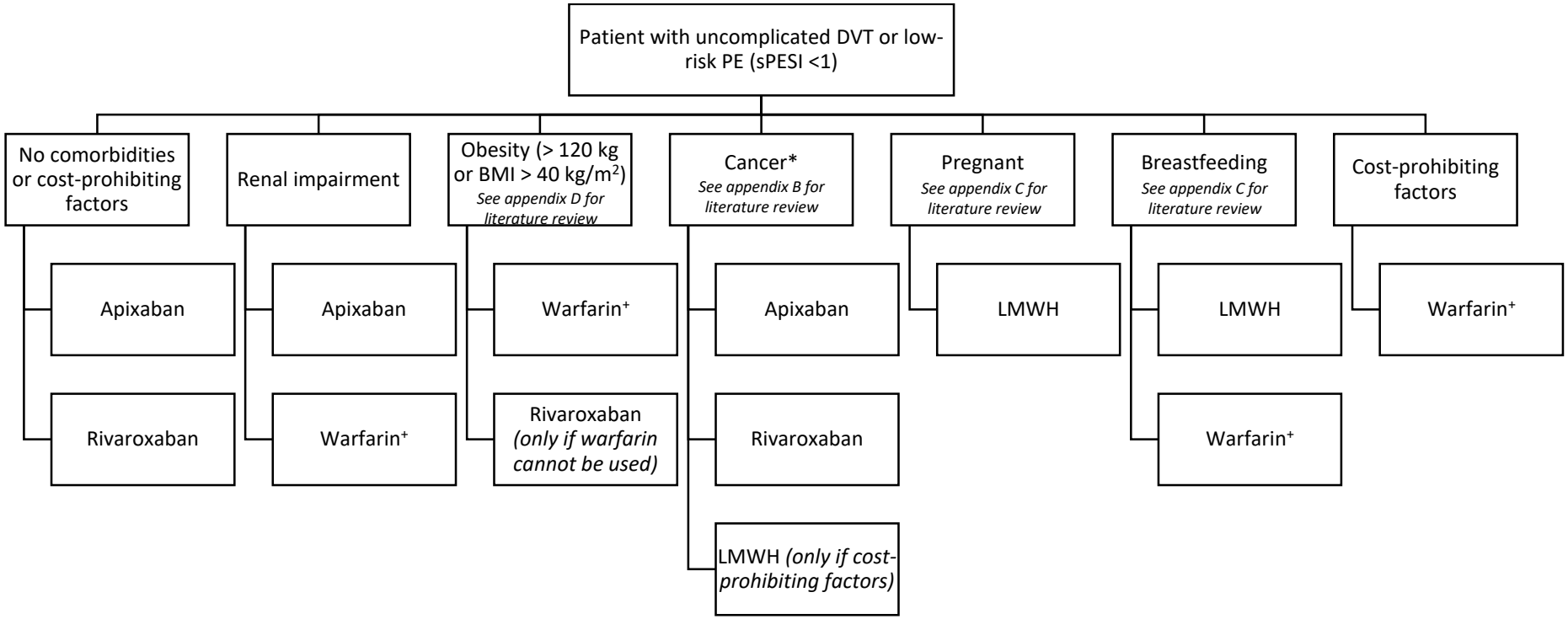
NO

Consider **outpatient management** or admission to **ED observation**

YES

Consider **admission** for inpatient workup

Algorithm for Early Discharge of a Patient with VTE



+requires bridging with LMWH or UFH
*does not qualify for discharge per the sPESI criteria if treating a PE

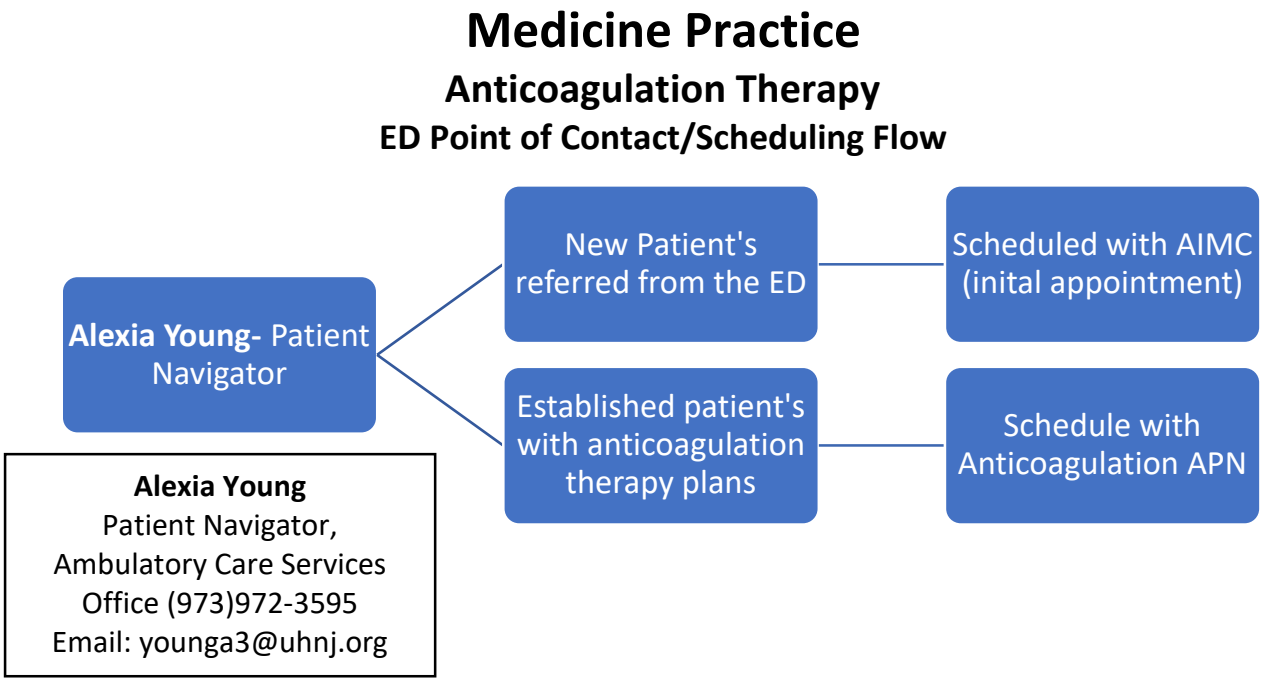
Discharge Instructions:

- **Schedule follow up appointment**: Patient to follow up in ACC by (page 4)
- **Discharge patient with a prescription** for 30 days of therapy based on the below dosing recommendations
  - Provide coupon card to patient with prescription (hard-copy or print via link on page 3)
- **Educate** patient on anticoagulation using the education material in the chart on page 3

Review of Anticoagulants for Treatment of VTE

Medication	Mechanism	Dose (for VTE treatment only)	Special Considerations	Access
Apixaban (Eliquis®)[25]	Anti-Xa inhibitor	10 mg PO BID x7 days, then 5 mg PO BID *Renal dose adjustment:* - No dose adjustment required when treating VTE, even if on dialysis	- Preferred DOAC in patients with renal impairment (even if on dialysis) - Twice daily dosing may be difficult for some patients - Limited data in obese patients (avoid use in patients > 120 kg or BMI > 40 kg/m^2)[23, 24] - Consider in patients with cancer [10, 11]	Virtual coupon card Education
Rivaroxaban (Xarelto®)[26]	Anti-Xa inhibitor	15 mg PO BID x21 days, then 20 mg PO daily *Renal dose adjustment:* - CrCl < 30 mL/min: avoid use - ESRD on dialysis: avoid use	- Must be taken with food - Preferred DOAC for obese patients but data is still limited, consider alternative[23, 24] - Safe in patients with cancer[10, 11]	Coupon: Have patient text "VOUCHER" to 29479 or call 888-XARELTO (888-927-3586) Education
Warfarin (Coumadin®)[27]	Vitamin K antagonist	Variable, titrate to achieve INR 2-3 *Renal dose adjustment:* - No dose adjustment required	- Patients with VTE must be bridged with LMWH or UFH - Requires INR monitoring in the outpatient setting (every 1-4 weeks) - Preferred oral anticoagulant for obese patients - Safe in breastfeeding patients but not during pregnancy	Education
Enoxaparin [LMWH] (Lovenox®)[28]	Antithrombin	1 mg/kg SC BID *Obesity dose adjustments:* - BMI > 50 kg/m^2: 0.7 mg/kg SC BID *Renal dose adjustment:* - CrCl < 30 mL/min: 1 mg/kg SC daily - ESRD on dialysis: avoid use	- Subcutaneous administration makes outpatient treatment challenging - No longer the only preferred agent in patients with cancer - Preferred in pregnant patients - Safe in breastfeeding patients - Consider aPTT monitoring in obese patients	
UFH[29]	Antithrombin	80 units/kg IV bolus, then continuous infusion at 18 units/kg/hr IV titrated to achieve target aPTT *Renal dose adjustment:* - No dose adjustment required	- Not feasible for outpatient treatment due to IV administration - Preferred agent for inpatient with renal impairment	

ED Point of Contact/Scheduling Flow



- Patient Navigator will be the initial contact for all scheduling needs.
- Patient Navigator will conduct appointment confirmation/reminder calls.
- Patient Navigator will follow-up *NO SHOW* patients for rescheduling.
- In the event that the assigned Patient Navigator is unavailable, please contact Cecilia Santos at (973)972-3528 or santoscg@uhnj.org

Supporting Literature

Guideline Recommendations for At-Home Treatment of VTE

Guideline	DVT	PE
CHEST (2016)[1]	No recommendation	Home treatment or early discharge is recommended in patients with low-risk PE* and whose home circumstances are adequate
European Society of Cardiology (2018 and 2020)	Most patients with DVT may be treated at home[2]	Early discharge of a patient with acute PE should be considered if the risk of early PE-related death or serious complications is low*, there is no serious comorbidity or aggravating condition, and proper outpatient care and anticoagulant treatment can be provided[3]
American Society of Hematology (2020)[4]	Patients with uncomplicated DVT should be treated at home	Patients with PE with low risk of complications should be offered home treatment*

*see below for PE criteria for discharge

The HOME-PE trial compared the sPESI and HESTIA rule and determined that the HESTIA rule is noninferior to sPESI in terms of risk stratification.[9]

Design	Intervention	Results
Randomized, parallel, open-label n = 1,970 patients diagnosed with PE	sPESI (n = 986) - 64% hospitalized, 36% discharged HESTIA (n = 984) - 62% hospitalized, 38% discharged	All-cause death, recurrent VTE, or major bleeding at 30 days (P = 0.005, noninferiority) - sPESI: 3.6% - HESTIA: 3.8%

Guideline Recommendations for VTE Treatment in Patients with Active Malignancy

Guideline	Recommendation
American Society of Clinical Oncology (2019)[10]	Rivaroxaban may be utilized for initial and long-term treatment; apixaban may be considered for treatment beyond 6 months (*note: this recommendation was made prior to the CARAVAGGIO study; with this study, there is literature to support both rivaroxaban and apixaban for initial treatment*)
National Comprehensive Cancer Network (2020)[11]	Apixaban and rivaroxaban are preferred for patients without gastric or gastroesophageal lesions

DOAC	Trial	Comparator
Apixaban	ADOPT (2011)[12] CARAVAGGIO (2020)[13]	LMWH
	AMPLIFY (2013)[14]	Warfarin
	AVERT (2019)[15]*	Placebo
Rivaroxaban	MAGELLAN (2013)[16] SELECT-D (2018)[17]	LMWH
	EINSTEIN-DVT (2010)[18] EINSTEIN-PE (2012)[19]	Warfarin
	CASSINI (2019)[20]*	Placebo

*studied for VTE prophylaxis

The above recommendations are based on a number of clinical trials that utilized direct oral anticoagulants (DOACs) in patients with malignancy. Based on the available data, DOACs appear to be as safe and effective for VTE treatment as compared to low-molecular-weight heparin (LMWH) and warfarin.

Guideline Recommendations for VTE Treatment in Pregnant and Breastfeeding Patients

Guidelines	Anticoagulant	Pregnancy	Breastfeeding
American College of Obstetrics and Gynecologists (2018)[21] and American Society of Hematology (2018)[22]	DOACs	Avoid use (insufficient data, may cross the placenta)	Avoid use (insufficient data)
	LMWH	Safe	Safe (detectable, not orally absorbed)
	Warfarin	Avoid use (associated with fetal harm)	Safe (undetectable)

VTE Treatment in Obese Patients

Obese patients are a challenging patient population in which to treat DVT and PE. This is due to variability in therapeutic drug concentrations related to the less predictable volume of distribution. The anticoagulant effect of warfarin, can be monitored using INR, that of LMWH and unfractionated heparin (UFH) using aPTT or anti-Xa. There is currently no validated laboratory monitoring available for DOACs. Additionally, when DOACs were studied, < 15% of patients had a BMI > 35 kg/m^2. Because of the lack of monitoring and limited data in obese patients, DOACs should be avoided in patients with a BMI > 40 mg/m^2 or weight > 120 kg.[23] However, if a DOAC must be used, rivaroxaban does have data to suggest it may be used in obese patients < 300 kg.[24]

References

1. Kearon C, et al. *Chest.* 2016; 149(2):315-352.
2. Mazzolai L, et al. *Eur Heart J.* 2018; 39(47):4208-4218.
3. Konstantinides SV, et al. *Eur Heart J.* 2020; 41(4):543-603.
4. Ortel TL, et al. *Blood Adv.* 2020; 4(19):4693-4738.
5. Douketis JD. *Can Fam Physician.* 2005; 51(2):217-223.
6. Khatib R, et al. *Blood Adv.* 2020; 4(3):500-513.
7. Jimenez D, et al. *Arch Intern Med.* 2010; 170(15):1383-1389.
8. Zondag W, et al. *J Thromb Haemost.* 2011; 9(8):1500-1507.
9. Bavry AA. *Am Coll Cardiol.* 2020.
10. Key NS, et al. *J Clin Oncol.* 2020; 38(5):496-520.
11. Streiff MB, et al. *J Natl Compr Canc Netw.* 2020.
12. Goldhaber SZ, et al. *N Engl J Med.* 2011; 365:2167-2177.
13. Agnelli G, et al. *N Engl J Med.* 2020; 382:1599-1607.
14. Agnelli G, et al. *N Engl J Med.* 2013; 369:799-808.
15. Carrier M, et al. *N Engl J Med.* 2019; 380:711-719.
16. Cohen AT, et al. *N Engl J Med.* 2013; 368:513-523.
17. Young AM, et al. *J Clin Oncol.* 2018; 36(20):2017-2023.
18. EINSTEIN Investigators. *N Engl J Med.* 2010; 363:2499-2510.
19. EINSTEIN-PE Investigators. *N Engl J Med.* 2012; 366:1287-1297.
20. Khorana AA, et al. *N Engl J Med.* 2019; 380:720-728.
21. ACOG Committee on Practice Bulletins. *Obstet Gynecol.* 2018; 132(1):e1-e17.
22. Bates SM, et al. *Blood Adv.* 2018; 2(22):3317-3359.
23. Martin K, et al. *J Thromb Haemost.* 2016; 14(6):1308-1313.
24. Coons JC, et al. *Pharmacotherapy.* 2020; 40(3):204-210.
25. Eliquis (apixaban) [prescribing information]. Princeton, NJ: Bristol-Myers Squibb Company; 2019.
26. Xarelto (rivaroxaban) [prescribing information]. Titusville, NJ: Janssen Pharmaceuticals Inc; 2020.
27. Coumadin (warfarin) [prescribing information]. Princeton, NJ: Bristol-Meyers Squibb Company; 2019.
28. Lovenox (enoxaparin) [prescribing information]. Bridgewater, NJ: Sanofi-Aventis US LLC; 2020.
29. Heparin sodium injection [prescribing information]. Lake Zurich, IL: Fesenius Kabi; 2020.