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Venous Thromboembolism – Diagnosis and Management

Effective Date: February 29, 2024

Scope

This guideline provides recommendations for the diagnosis and management of venous thromboembolism (VTE) in adults aged ≥ 19 years with hemodynamic stability. It includes lower limb deep vein thrombosis (DVT) and pulmonary embolism (PE) diagnosis in the outpatient setting and management of acute VTE.

Superficial thrombophlebitis and thrombosis in unusual sites (e.g., cerebral venous thrombosis, splanchnic vein thrombosis, upper extremity thrombosis) are outside the scope of this guideline. For information refer to the Thrombosis Canada Guidelines.

Key Recommendations[1,2]

- When DVT/PE is suspected, first calculate the Wells Score to determine the likelihood of DVT/PE as "likely" or "unlikely" before ordering any testing.
- For outpatients with suspected DVT/PE:
  - Do not order D-dimer if DVT/PE is deemed "likely" per Wells Score. Proceed directly to imaging.
  - Order D-dimer when deemed 'unlikely' per Wells Score because a negative test indicates imaging is not necessary and DVT/PE is excluded.
- For inpatients, proceed directly to imaging because risk stratification using D-dimer has not been validated.
- While awaiting objective imaging to diagnose VTE, start empiric anticoagulant therapy in patients with higher likelihood ("likely") of DVT/PE.
- Most patients with hemodynamically stable VTE can be treated on an outpatient basis.
- Direct Oral Anticoagulants (DOACs) are considered as first line therapies for most outpatients. They are contraindicated in pregnancy, breastfeeding, liver failure (Child-Pugh class C), dialysis, or triple-positive antiphospholipid syndrome (i.e., has lupus anticoagulant, anticardiolipin and antibeta-2-glycoprotein-1 antibodies).
- Ensure appropriate anticoagulant dosage is used for the specific treatment phase (initial therapy, primary treatment, secondary prevention).
- Minimum duration of anticoagulation is 3-6 months for all patients with an acute DVT/PE.
- Referral to a thrombosis specialist is recommended to help determine optimal duration of anticoagulation. Continue anticoagulation therapy while awaiting referral.
- Avoid elective surgeries during the first 3-6 months of treatment.
- Hereditary thrombophilia testing and occult cancer screening are not indicated in most patients with thrombosis because results rarely influence management.

Background and Epidemiology

VTE affects at least one in 1000 individuals each year[3] and is the third most common cause of vascular death worldwide.[4] VTE most commonly manifests as DVT in the legs and/or PE.

Up to 10% of symptomatic PEs are fatal within the first hour of symptom onset.[5] Independent predictors of mortality within the first few days after PE diagnosis include hypotension (systolic blood pressure < 90 mmHg), clinical right heart failure, right ventricular dilatation on computer tomography pulmonary angiogram (CTPA) or echocardiography, elevated troponin, and elevated brain natriuretic peptide.

Early diagnosis and treatment reduce VTE morbidity and mortality.

Risk Factors

The most common VTE risk factors include recent surgery, hospitalization, active cancer, and high estrogen states such as oral contraception (OCP) and pregnancy.[3,6,7] See Table 1: Common Clinical Risk Factors for Venous Thromboembolism for examples of major and minor VTE risk factors.

Table 1: Common Clinical Risk Factors for Venous Thromboembolism[2,8,9]

Major risk factors, examples include:
• Age >70 years • Active cancer (e.g., ongoing chemotherapy; recurrent, metastatic, or progressive disease) • Major trauma • Surgery with general anesthesia for ≥30 min • Confined to bed for ≥3 days (“bathroom privileges” only) • Emergency caesarean section
Minor risk factors, examples include:
• Surgery with local or regional anesthesia • Admission to hospital for <3 days • Estrogen or selective estrogen receptor modulator therapy (e.g., OCP, hormone replacement therapy, tamoxifen) • Pregnancy or puerperium • Obesity • Long distance travel >6 hr • First degree relative with VTE

Assessment and Diagnosis

- Objective imaging and/or blood testing are required to confirm or exclude DVT/PE because signs and symptoms are nonspecific.
- Clinical pretest probability models (e.g., Wells scores) are recommended to help guide necessary investigations.
- Combined use of clinical pretest probability and D-dimer testing can help exclude VTE, but imaging tests are required to confirm a diagnosis.
- Patients with PE might have silent DVT, and some patients with DVT might have silent PE.
- Clinicians should always apply their clinical judgement and discretion in following the diagnostic algorithms, especially in cases where history or symptoms are not reliable and there are no alternative diagnoses to explain patient’s presentation.

Diagnosis of DVT

Classic signs and symptoms of DVT include limb swelling, pain or muscle ache, warmth, and erythema. Cyanotic discolouration or skin mottling might indicate extensive venous congestion from limb-threatening thrombosis. However, these findings are nonspecific for DVT.

When a DVT is suspected, first calculate the Wells Score for DVT. See Table 2: Wells Score for Diagnosis of DVT in Outpatients. Total score indicates the probability of DVT as "unlikely" or "likely". Follow the algorithm in Figure 1: Algorithm for Diagnosis of DVT in Outpatients to determine further investigations. For inpatients, proceed directly to imaging because risk stratification using D-dimer has not been validated.

While awaiting objective imaging to diagnose DVT, start empiric anticoagulant therapy in patients with higher likelihood ("likely") of DVT.

Investigations used for diagnosis of DVT:

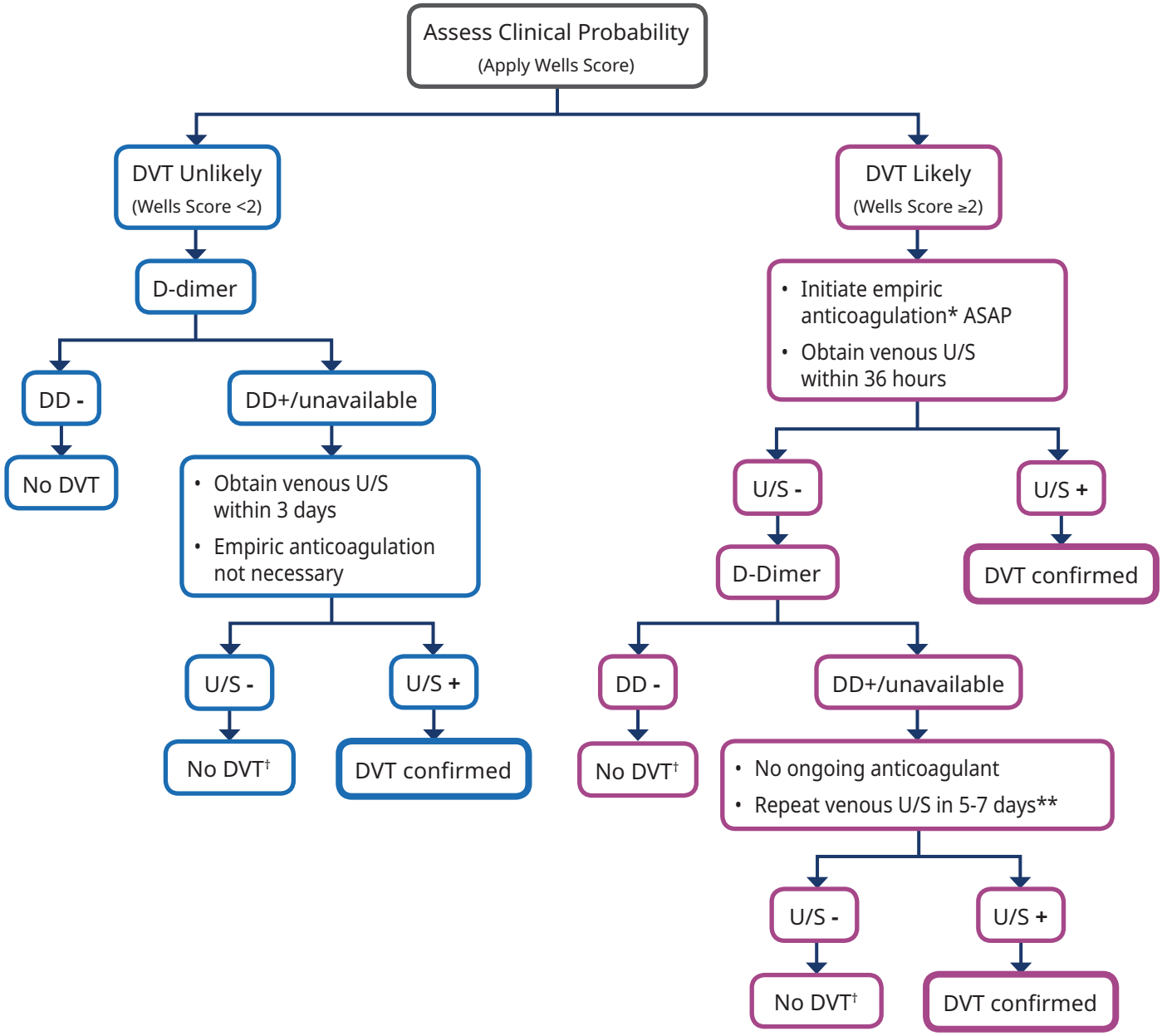
- Venous ultrasound – Various techniques, including compression and/or Doppler, are used. Order venous ultrasound of the affected limb(s) and specify that it is for possible DVT to ensure correct technique is used. See Appendix A: Proximal and Distal DVT for location of thrombus.
- D-dimer – This biomarker is elevated when there is active clot formation and breakdown. It can be elevated in acute DVT/PE, but also with infection, infarction, inflammation, surgery/trauma, cancer, and pregnancy. Consequently, an elevated result does not confirm DVT/PE, but a negative result can safely rule out an acute DVT in patients with "unlikely DVT" (See Figure 1: Algorithm for Diagnosis of DVT). See Appendix B: D-dimer Cut-off Values.

Table 2: Wells Score for Diagnosis of DVT in Outpatients

Two-Level Wells Score for DVT Diagnosis	
Clinical Findings	**Points**
Paralysis, paresis or recent orthopedic casting of lower extremity	1
Bedridden >3 days recently or major surgery within past 12 weeks	1
Localized tenderness of deep veins	1
Swelling of entire leg	1
Calf swelling 3 cm greater than other leg (measured 10cm below the tibial tuberosity)	1
Pitting edema in the symptomatic leg	1
Non-varicose collateral superficial veins	1
Active cancer or cancer treated within 6 months	1
Previously documented DVT	1
Alternative diagnosis at least as likely as DVT (Baker's cyst, cellulitis, muscle damage, superficial vein thrombosis, post-thrombotic syndrome, inguinal lymphadenopathy, extrinsic venous compression)	-2

Total Score: DVT unlikely <2; DVT likely ≥2

Figure 1: Algorithm for Diagnosis of DVT in Outpatients



* When a significant delay in diagnostic testing is expected for those with "DVT likely" pretest probability, low molecular weight heparin, rivaroxaban or apixaban should be initiated while awaiting testing.

** Not required if initial U/S report indicates calf DVT is excluded OR if leg symptoms have resolved.

† By following this algorithm the likelihood of DVT is 2% or less.

Abbreviations: DVT – Deep Vein Thrombosis, DD – D-dimer, U/S – Ultrasound

Diagnosis of Pulmonary Embolism

Classic signs and symptoms of PE include unexplained dyspnea, tachypnea, and tachycardia (common), pleuritic chest pain and hemoptysis (uncommon). Syncope, hypoxemia, hypotension, or other features of right ventricular dysfunction (e.g., distended jugular veins) suggest life-threatening thrombotic burden. However, all these findings are non-specific for PE.

When a PE is suspected, first calculate the Wells Score for PE. See Table 3: Wells Score and PERC Rule for Diagnosis of PE in Outpatients. Total score indicates the probability of PE as "unlikely" or "likely". Follow the algorithm in Figure 2: Algorithm for Diagnosis of PE in Outpatients to determine further investigations. For inpatients, proceed directly to imaging because risk stratification using D–dimer has not been validated.

While awaiting objective imaging to diagnose PE, start empiric anticoagulant therapy in patients with higher likelihood ("likely") of PE.

Note that in patients categorized as "PE unlikely", further testing may not be necessary if NONE of the Pulmonary Embolism Rule-out Criteria (PERC) clinical features are true because the likelihood of PE is <2%. See Table 3: Wells Score and PERC Rule for Diagnosis of PE in Outpatients. This is useful for patients presenting in the outpatient office setting. The PERC rule should not be applied in patients in the "PE likely" category.

Investigations used for diagnosis of PE:

- Computer tomography pulmonary angiogram (CTPA) or CT PE protocol – This is a specialized, timed contrast CT dedicated for detection of PE. It is not the same as a CT chest for other investigations (e.g., cancer staging). It is the test of choice because of its high accuracy, wide availability, and ability to detect other pathologies.
- Ventilation-Perfusion (V/Q) lung scan – This test requires radioactive material and hence is only available at major clinical centres. It is the alternative to CTPA in patients with renal failure or contrast dye allergy.
- D-dimer – This biomarker is elevated when there is active clot formation and breakdown. It can be elevated in acute DVT/PE, but also with infection, infarction, inflammation, surgery/trauma, cancer, and pregnancy. Consequently, an elevated result does not confirm DVT/PE, but a negative result can safely rule out an acute DVT/PE in patients with low or unlikely clinical suspicion. See Appendix B: D-dimer Cut-off Values.

Table 3: Wells Score and PERC Rule for Diagnosis of PE in Outpatients

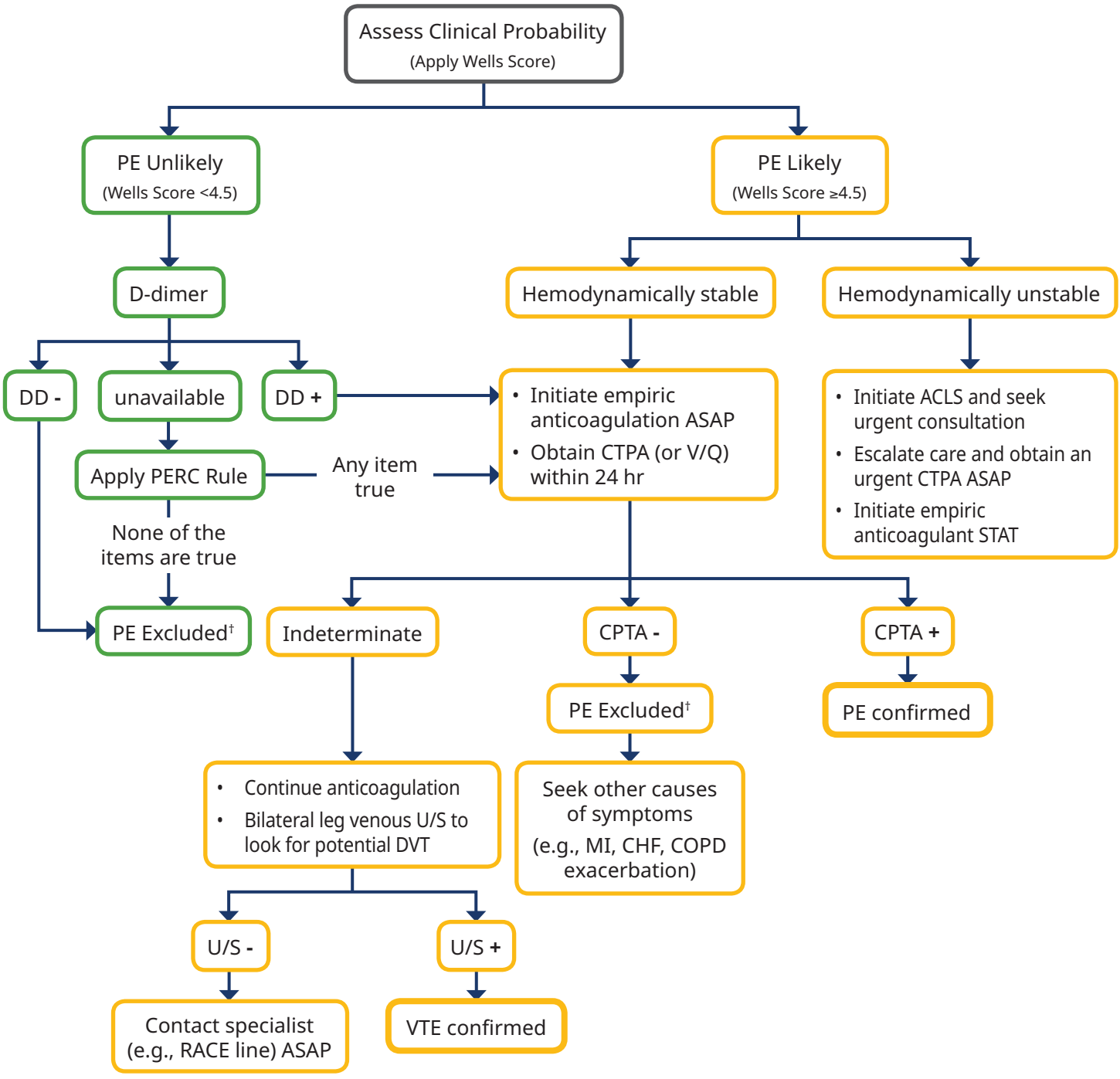
Wells Score for PE	
Variable	**Points**
Clinical symptoms and signs of DVT	3
Previous DVT or PE	1.5
Immobilization for >3 days or surgery within 4 weeks	1.5
Heart rate >100 beats/minute	1.5
Hemoptysis	1
Malignancy	1
No alternative diagnosis more likely than PE	3

Total Score: PE unlikely <4.5; PE likely ≥4.5

Clinical Features in PERC Rule
Clinical Features
Age >50
Initial heart rate >100 beats/min
Initial O_2 saturation <94% on room air
Unilateral leg swelling
Hemoptysis
Surgery or trauma ≤4 weeks
History of VTE
Estrogen use

If NONE of the clinical features in PERC Rule are true AND Wells Score is <4.5, likelihood of PE is <2%.

Figure 2: Algorithm for Diagnosis of PE in Outpatients



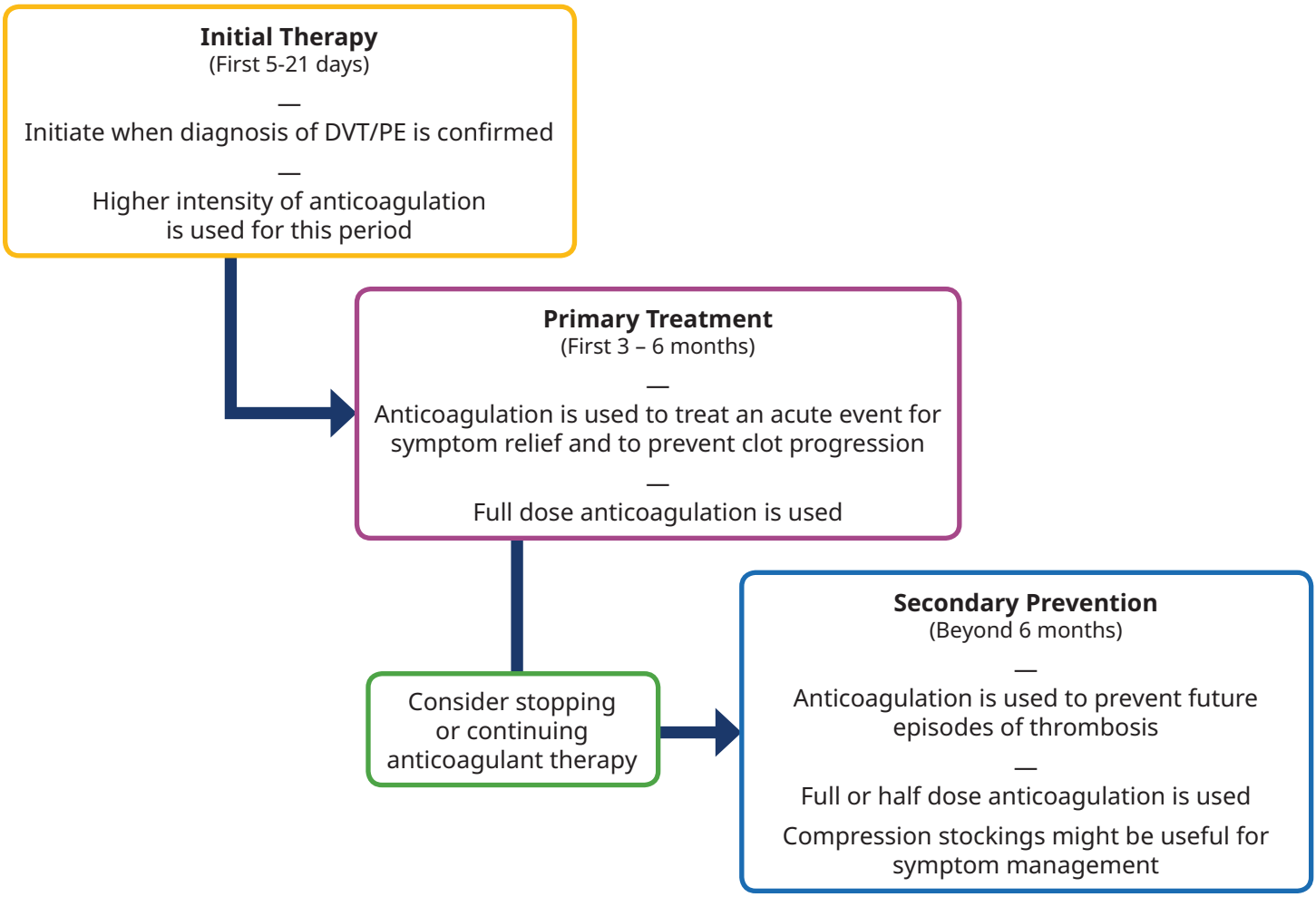
† By following this algorithm the likelihood of PE is 2% or less.

Abbreviations: ACLS – Advanced Cardiovascular Life Support, CHF – Chronic Heart Failure, COPD – Chronic Obstructive Pulmonary Disease, CPTA – CT Pulmonary Angiography Scan, DD – D-dimer, DVT – Deep Vein Thrombosis, MI – Myocardial Infarction, PE – Pulmonary Embolism, PERC – Pulmonary Embolism Rule-out Criteria, U/S – Ultrasound, VTE – Venous Thromboembolism, V/Q – Ventilation-Perfusion Lung Scan.

Management of Acute DVT/PE[2,10]

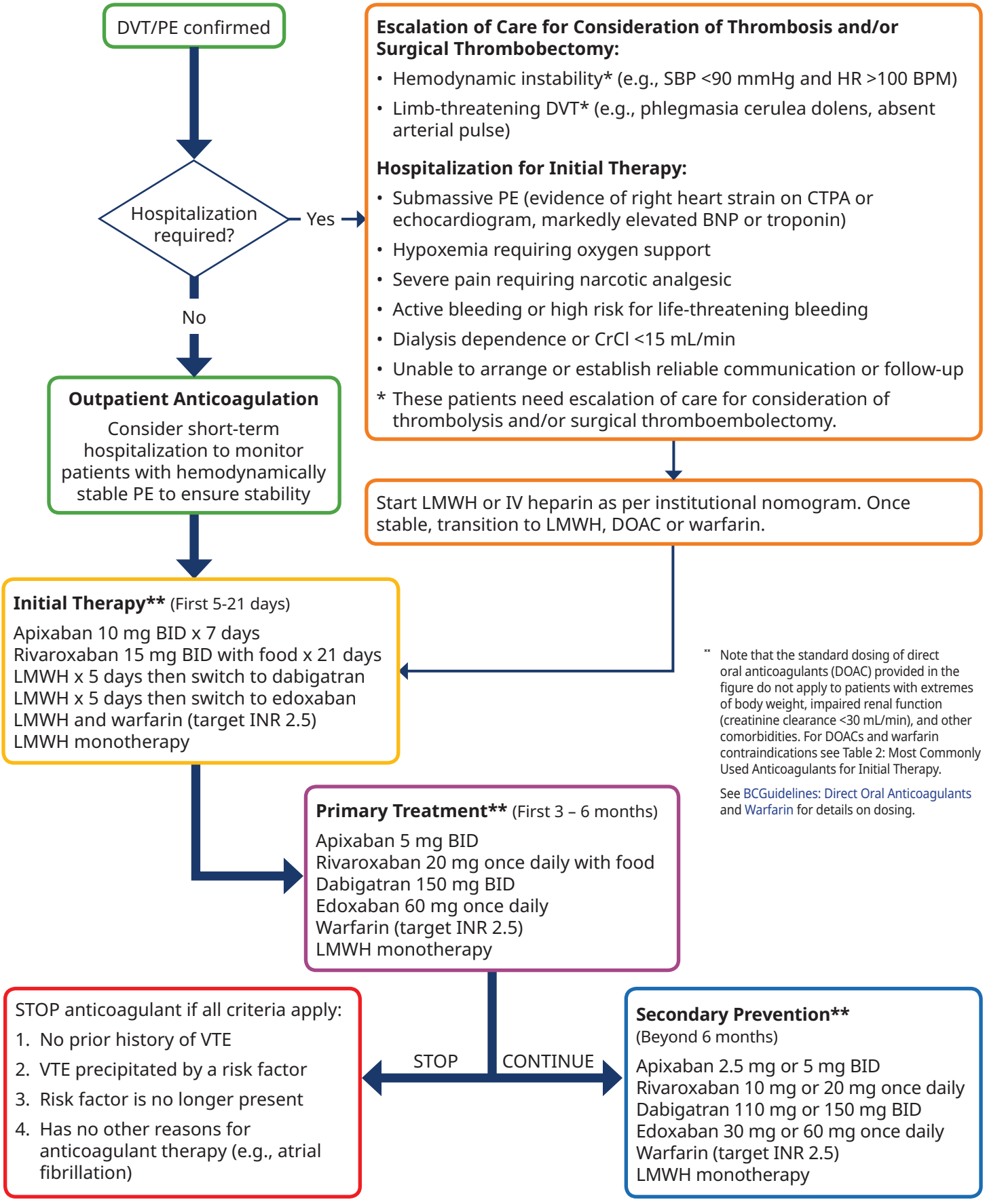
Treatment of DVT/PE is typically considered in different phases that correspond to the likelihood of thrombosis recurrence and intensity (i.e., dosing) of anticoagulation needed. The terminology for these phases varies. The guideline uses terminology outlined in Figure 3: Time Frame of Treatment Phases.

Figure 3: Time Frame of Treatment Phases*



Abbreviations: DVT – Deep Vein Thrombosis, PE – Pulmonary Embolism

Figure 4: Treatment Algorithm for DVT/PE



Abbreviations: BPM – Beats Per Minute, BID – Twice Daily, BNP – B -Type Natriuretic Peptide, CPTA – CT Pulmonary Angiography, CrCl – Creatinine Clearance, DOACs – Direct Oral Anticoagulants, DVT – Deep Vein Thrombosis, HR – Heart Rate, INR – International Normalized Ratio, IV – Intravenous, LMWH – Low Molecular Weight Heparin, PE – Pulmonary Embolism, SBP – Systolic Blood Pressure.

The cornerstone of DVT/PE treatment is anticoagulant therapy. Currently, the most frequently used options include DOACs (mainly apixaban or rivaroxaban), warfarin, LMWH, and intravenous unfractionated (IV) heparin. Each have strengths and limitations, and the most appropriate anticoagulant depends on the clinical scenario, patient factors, and resources available. Refer to BC Guidelines: Direct Oral Anticoagulants and BC Guidelines: Warfarin.

Initial Therapy (first 5-21 days after diagnosis)

- Most patients with DVT and many patients with hemodynamically stable PE can be managed on an outpatient basis. This includes patients with subsegmental or incidental PE.[11] However, most patients with PE will benefit from short period of observation in the emergency department or hospital admission to allow risk stratification and monitor for hemodynamic stability.
- Initial treatment should be with an immediate acting anticoagulant (onset of action within 2-3 hr), such as apixaban, rivaroxaban, LMWH or IV heparin. See Table 4: Most Commonly Used Anticoagulants for Initial Therapy.
- Apixaban or rivaroxaban are the first-line anticoagulants for most non-pregnant patients because they are effective, safe, and convenient. Indirect evidence suggests patients treated with apixaban experienced a lower rate of recurrent VTE and lower rate of bleeding as compared to rivaroxaban.[12] The choice between apixaban and rivaroxaban depends on practical and pharmacological considerations. See Table 5: Most Commonly Used Anticoagulants for Initial Therapy.
- For patients who cannot be therapeutically anticoagulated due to active bleeding or very high bleeding risks, urgent consultation should be initiated with a hematologist or thrombosis specialist through the RACE line. Management may include placement of a retrievable inferior vena cava filter (i.e., IVC filter) if therapeutic anticoagulation cannot be safely provided in the acute setting.

Table 4: Most Commonly Used Anticoagulants for Initial Therapy

Apixaban

Refer to BC Guidelines: Direct Oral Anticoagulants

- Available in generic form and is a PharmaCare regular benefit medication.
- Must be taken twice a day (every 12 hours), with or without food.
- Use with caution in patients with small or large bowel diarrhea, short gut syndrome, or active inflammatory bowel disease as it is absorbed throughout the GI tract, including ascending colon.
- Contraindications: pregnancy, breastfeeding, liver failure (Child-Pugh class C), dialysis, or triple-positive antiphospholipid syndrome (has lupus anticoagulant, anticardiolipin and antibeta-2-glycoprotein-1 antibodies).

Rivaroxaban

Refer to BC Guidelines: Direct Oral Anticoagulants

- Available in generic form and is a PharmaCare regular benefit medication.
- Twice daily for the first 3 weeks then once-daily thereafter. Must be taken with food.
- Avoid use in patients with upper GI surgery, such as gastrectomy, Whipple procedure, or bariatric surgery as it is absorbed primarily in the stomach and proximal small bowel, hence suboptimal absorption might occur.
- Contraindications: pregnancy, breastfeeding, liver failure (Child-Pugh class B or C), dialysis, or triple-positive antiphospholipid syndrome (has lupus anticoagulant, anticardiolipin and antibeta-2-glycoprotein-1 antibodies).

LMWH

Appendix C: Medications for the Treatment and Prevention of Venous Thromboembolism and Thrombosis Program: Heparin (LMWH)

- Often preferred when the clot burden is large, is associated with cancer (particularly gastrointestinal or genitourinary tumours) and during initial hospitalization period while investigations or care plans are being organized.
- Mainstay of treatment for pregnancy-associated VTE. Also safe in breastfeeding.
- Adjust dose based on actual body weight and round up to the next prefilled syringe size. There is no capping of maximum dose. Divide into 2 injections if the total dose exceeds the largest syringe dose available (e.g., if total dose is 25,000 units, prescribe 12,500 units every 12 hours).
- LMWH and warfarin are started concomitantly and must overlap for a minimum of 5 days and until 2 consecutive therapeutic INRs are achieved, after which time LMWH is discontinued. See BC Guidelines: Warfarin for details.

Intravenous Heparin

- Preferred anticoagulant in hemodynamically unstable patients, patients with very high risk of bleeding or require imminent surgery, and end stage renal disease (CrCl < 15 mL/min or dialysis dependent).
- Requires meticulous and frequent monitoring of the PTT and dose adjustment to achieve a therapeutic level within the first 24 - 48 hours of therapy. Use an institution-approved nomogram.
- Subtherapeutic IV heparin dosing has been shown to increase the risk of recurrent thrombosis. Once patient is stable, can transition to LMWH, DOACs or warfarin if there are no contraindications.

Primary Treatment (first 3 – 6 months)

- All patients with an acute VTE episode require at least 3 months of therapeutic anticoagulation. See Table 5: Most Commonly Used Anticoagulants for Primary Treatment and Secondary Prevention.
- Some experts recommend extending treatment up to 6 months (or longer) in patients who presented with a large clot burden (e.g., submassive PE, iliofemoral DVT), who remain symptomatic at 3 months, or whose risk factor is still present at 3 months (e.g., cancer).
- Patients are at high risk of recurrent thrombosis during the first 3 months. Elective surgery or procedures that require interruption of anticoagulation should be avoided during this period.

Secondary Prevention (after the first 6 months)

- In general, patients with a first episode of thrombosis that was triggered by a risk factor (e.g., surgery) can stop anticoagulant therapy after 3-6 months, if the risk factor is no longer present after completing primary treatment. The risk of recurrence is typically < 3-5% in these patients.
- Patients without any clear precipitating factor (i.e., unprovoked VTE) are more likely to develop VTE recurrence and may benefit from continuing anticoagulation beyond 6 months. Risk of recurrence in patients with unprovoked VTE is approximately 10% in the first year, 25% in the first 5 years, and up to 40% in the first 10 years after stopping anticoagulant therapy.
- Referral to a hematologist or thrombosis specialist (see BC Thrombosis Network for thrombosis clinics in BC and referral information), especially for those with unprovoked VTE, is recommended to determine if anticoagulation beyond 6 months is indicated, considering the risks of recurrence versus bleeding. While awaiting referral, continuing anticoagulation is recommended.
  - Risk of recurrence depends on the precipitating factor(s), the persistence of risk factors (e.g., cancer), physiological predisposition (e.g., age, sex, hereditary thrombophilia), and how strongly each factor promotes clotting (see Table 1: Common Clinical Risk Factors for Venous Thromboembolism).
  - Risk of bleeding is multifactorial and increases with the number of risk factors present. Important factors to consider include age >70, active cancer, anemia, concomitant antiplatelet therapy, chronic kidney disease (CKD), chronic liver disease, prior history of bleeding, and thrombocytopenia (platelet count < 50 x 109/L).
- Work-up for occult cancer in patients with unprovoked VTE is not indicated beyond the usual age appropriate malignancy screening.[13]
- Hereditary thrombophilia testing is not indicated for most patients with thrombosis because it does not often influence choice or duration of anticoagulant therapy and is costly.

Table 5: Most Commonly Used Anticoagulants for Primary Treatment and Secondary Prevention

Apixaban/Rivaroxaban Refer to BC Guidelines: Direct Oral Anticoagulants

- Preferred anticoagulants for primary therapy and secondary prevention. See Table 2: Most Commonly Used Anticoagulants for Initial Therapy for details.
- Different doses are used in different phases of therapy (initial therapy vs primary treatment vs secondary prevention). **NOTE:** DOAC dosing for VTE is also **not** the same as for stroke prevention in non-valvular atrial fibrillation.
- After the first 6 months of therapy, a lower dose of apixaban or rivaroxaban has been shown to be similarly effective and safe compared with a full dose in patients with an unprovoked thrombosis.[14,15]
- Only the approved regimens should be used, and these agents are not considered 'interchangeable'.

Warfarin Refer to BC Guidelines: Warfarin

- Drug of choice for patients with antiphospholipid syndrome because it is superior to DOACs in preventing recurrent thrombosis, particularly stroke or arterial thromboembolism.
- Also used in patients on hemodialysis.
- Target INR is 2.5 for treatment of VTE.
- In those with recurrent thrombosis, a higher INR target 3.0 has been used. Consultation with a specialist recommended.
- Safe in those who are breastfeeding.

LMWH

- Used in pregnancy-associated VTE and select patients with cancer-associated thrombosis who have a high risk of GI or GU bleeding.
- Often used in patients with recurrent thrombosis, particularly those who 'broke through' with recurrence while taking another anticoagulant. Consultation with a specialist is recommended to manage patients with recurrent thrombosis.
- Safe in those who are breastfeeding.

Supportive Measures

Compression stockings

- Graduated compression stockings are useful for reducing venous congestion symptoms such as edema and muscle tightness or aching. They **do not** reduce the risk of recurrent thrombosis.
- Over the counter knee-high options (i.e., less than 20 mm Hg pressure) are easy to use and often helpful, particularly for some patients with varicose veins. Prescription grade stockings (i.e., 30-40 mmHg pressure) are often necessary for patients with post thrombotic syndrome (PTS).
- Poorly fitted stockings can cause discomfort and skin breakdown. Tourniquet effect below the knee might cause even more venous stasis and promote thrombosis.

IVC filters

- Filters are sometimes placed in patients with high-risk thrombosis who are unable to receive anticoagulant therapy due to active or high risk of bleeding.
- They should be removed as soon as anticoagulant therapy is safely initiated. Prolonged placement reduces the likelihood of successful retrieval.
- Although evidence is limited, anticoagulation is typically continued if a filter remains in-situ because it is a known cause of recurrent thrombosis.

Health Behaviours

- Foods and supplements cannot be used as an alternative to anticoagulants.
- While taking anticoagulants, patients should avoid herbal supplements due to drug-drug interactions (e.g., St. John's Wort) and others that can increase the bleeding risk (e.g., ginkgo, garlic, and turmeric).[16,17]
- Regular exercise and maintaining a healthy body weight are important behaviours overall and might mitigate the risk of recurrent thrombosis because sedentary lifestyle and obesity contribute to thrombosis formation.

Special populations

Pregnancy

- Thrombosis risk is higher during pregnancy and the first 6-12 weeks postpartum.
- LMWH is the mainstay of treatment for pregnancy associated VTE. Management requires coordination of multiple specialists including hematology/thrombosis, obstetrics, and anesthesia.
- Either LMWH or warfarin can be used in the postpartum period, as neither crosses over into breastmilk.
- DOACs are contraindicated in pregnancy and breastfeeding.

Cancer

- Clinical practice guidelines recommend using LMWH, apixaban, or rivaroxaban for the treatment of cancer-associated thrombosis.
- Some DOACs are associated with an increased risk of bleeding in certain malignancies (i.e., intraluminal GI or urothelial tumour site) when compared to LMWH.
- Subspecialist consultation is advised to guide management of cancer-associated thrombosis.

Chronic Kidney Disease

- Patients with CKD are at increased risks of thrombosis and bleeding.
- Patients with stage 4 CKD (i.e., CrCl < 30 mL/min) were excluded from many clinical drug trials so are typically treated with warfarin. Low-dose DOAC is being evaluated in this setting and LMWH (dose adjusted based on anti-Xa level) has also been used.
- Subspecialist consultation (including nephrologist) is advised to guide management.

Antiphospholipid Antibody Syndrome

- APS is an acquired thrombophilia that increases the risk of venous and/or arterial thrombosis events, as well as pregnancy-associated morbidity. Those with triple positivity (has lupus anticoagulant, IgG or IgM anticardiolipin antibodies and IgG or IgM antibeta-2-glycoprotein-1 antibodies) are at highest risk.
- The diagnosis of APS should be made by a specialist due to complex and changing laboratory and clinical diagnostic criteria.
- Treatment of APS-related thrombosis should also be in consultation with a specialist. In general, LMWH and warfarin are the mainstay of therapy in APS. DOACs should be avoided in APS due to weak evidence of efficacy in preventing recurrent (particularly arterial) thrombosis.

Heparin-Induced Thrombocytopenia (HIT)

- HIT is a very rare complication from unfractionated heparin (UFH) or LMWH use that can result in fatal thromboembolism. The onset of thrombocytopenia occurs day 5-14 after first exposure to heparin.
- Consult a specialist immediately if HIT is suspected or confirmed. Heparin should be discontinued immediately and alternate anticoagulation (e.g., fondaparinux or argatroban or DOACs) should be initiated.

Unusual site (splanchnic vein, cerebral vein, upper extremity DVT)

Thrombosis in these sites accounts for approximately 10% of VTE. The optimal therapeutic approach is uncertain due to lack of high-quality evidence. Certain sites of thrombosis may be associated with specific disease states (i.e., splanchnic vein thrombosis in cirrhosis, upper extremity DVT associated with central venous catheters or in thoracic outlet syndrome, cerebral vein thrombosis from OCP use or pregnancy). The management of unusual site thrombosis should be guided by subspecialty expertise.

Follow Up

Most patients will experience improvement in leg and respiratory symptoms within 48-72 hours. Pleuritic chest pain from pulmonary infarction typically lasts a week or longer. By one month, many patients will feel much better and by 3-6 months, most patients will be almost back to baseline. Approximately 1/3 of patients experience residual swelling and/or discomfort in the affected limb (See Thrombosis Canada: Post-thrombotic Syndrome)

There is no risk to exercising or returning to usual activities while on anticoagulation. Exercise is encouraged and patients should be as active as their symptoms allow. The only activities to avoid are contact sports and other activities that put the patient at a higher risk for serious injuries, especially intracranial hemorrhage.

Patients on long-term anticoagulation (i.e., >6 months) should be reviewed annually to determine if continuing anticoagulation remains beneficial. This requires assessing the risks of recurrent thrombosis vs the risk of serious bleeding. See BC Guidelines: Direct Oral Anticoagulants and BC Guidelines: Warfarin for long-term monitoring requirements.

After completion of primary treatment (3-6 months), repeating imaging may be considered on a case-by-case basis per thrombosis specialist recommendation. Note that 1/3 patients will have residual clot on imaging and the presence of residual clot does not determine the duration of anticoagulation.

Resources

Abbreviations:

ACLS	Advanced Cardiovascular Life Support
APS	Antiphospholipid Antibody Syndrome
BID	Twice Daily
BNP	B -Type Natriuretic Peptide
BPM	Beats Per Minute
CHF	Chronic Heart Failure
CKD	Chronic Kidney Disease
COPD	Chronic Obstructive Pulmonary Disease
CPTA	CT Pulmonary Angiography Scan
CrCl	Creatinine Clearance
CTPA	Computer Tomography Pulmonary Angiogram
DOACs	Direct Oral Anticoagulants
DVT	Deep Vein Thrombosis
HIT	Heparin-Induced Thrombocytopenia
HR	Heart Rate
INR	International Normalized Ratio
IV	Intravenous
IVC Filter	Inferior Vena Cava Filter
LMWH	Low Molecular Weight Heparin
PE	Pulmonary Embolism
SBP	Systolic Blood Pressure
UFH	Unfractionated Heparin
V/Q	Ventilation-Perfusion
VTE	Venous Thromboembolism

Practitioner Resources

- BC Thrombosis Network: comprises a community of Thrombosis Specialists dedicated to the care of patients with venous thromboembolic disorders. See www.bcthrombosisnetwork.ca/
- **RACE Line:** Rapid Access to Consultative Expertise Program: raceconnect.ca/. A phone consultation line for physicians, nurse practitioners and medical residents. **If the relevant specialty area is available through your local RACE line, please contact them first.**
- **Pathways:** An online resource that allows GPs and nurse practitioners and their office staff to quickly access current and accurate referral information, including wait times and areas of expertise, for specialists and specialty clinics. See: https://pathwaysbc.ca/login
- **Health Data Coalition:** An online, physician-led data sharing platform that can assist you in assessing your own practice in areas such as chronic disease management or medication prescribing. HDC data can graphically represent patients in your practice with chronic diseases in a clear and simple fashion, allowing for reflection on practice and tracking improvements over time. See: Health Data Coalition – Better Information. Better Care. Better Patient Outcomes. (hdcbc.ca)

Patient, Family and Caregiver Resources

- HealthLinkBC: You may call HealthLinkBC at 8-1-1 toll-free in B.C., or for the deaf and the hard of hearing, call 7-1-1. You will be connected with an English-speaking health-service navigator, who can provide health and health-service information and connect you with a registered dietitian, exercise physiologist, nurse, or pharmacist. See: healthlinkbc.ca/
  - HealthLinkBC: Deep Vein Thrombosis
  - HealthLinkBC: Pulmonary Embolism
- Thrombosis Canada: Patient Resources

Diagnostic Codes

I26 - I28 Pulmonary Embolism

I82 Deep Vein Thrombosis

Billing Codes

415.1 Pulmonary Embolism

453 Other Venous Embolism And Thrombosis

451 Deep Vein Thrombosis

452 Portal Vein Thrombosis

Appendices

- Appendix A: Proximal and Distal DVT
- Appendix B: D-dimer Cut-off values
- Appendix C: Medications for the Treatment and Prevention of Venous Thromboembolism

Associated Documents

- List of Contributors

References

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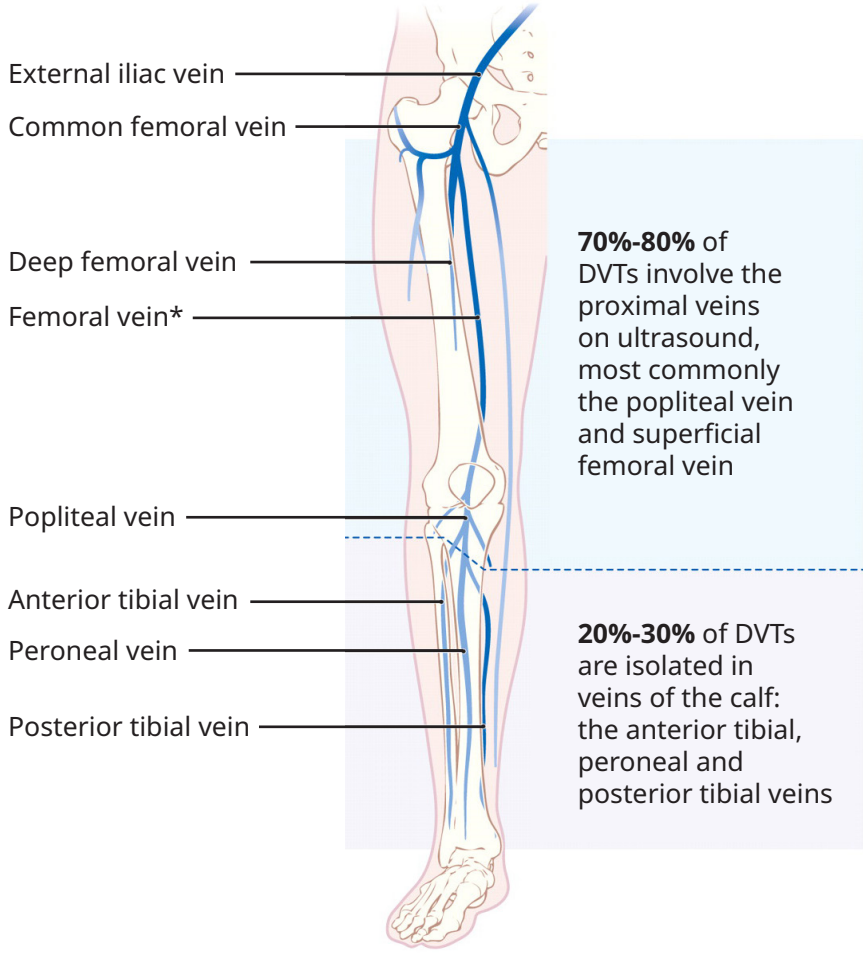
BC Guidelines are developed for the Medical Services Commission by the Guidelines and Protocols Advisory Committee, a joint committee of Government and the Doctors of BC. BC Guidelines are adopted under the *Medicare Protection Act* and, where relevant, the *Laboratory Services Act*.

Disclaimer: This guideline is based on best available scientific evidence and clinical expertise as of February 29, 2024. It is not intended as a substitute for the clinical or professional judgment of a health care practitioner.

Appendix A: Proximal and Distal DVT



* often referred to as "superficial femoral vein" however it is a deep vein of the leg.

Figure adapted from Diagnosis and treatment of deep-vein thrombosis, CMAJ October 24, 2006 175 (9) 1087-1092; DOI: https://doi.org/10.1503/cmaj.060366

Appendix B: D-dimer Cut-off Values

No standard validated D-dimer cut offs exist. Different cut-offs for D-dimer have been suggested based on age and clinical probability, however they have not been extensively studied or validated using different D-dimer assays. We recommend using your local D-dimer cut-off values. The proposed cut-off values referenced in the Point-Of-Care Emergency Clinical Summary, Provincial Health Services Authority in British Columbia, are summarized in the tables below.

Age Adjusted Cut-off

Age	D-dimer cut-off (µg/L FEU*)
>50 years	Value is considered normal if less than patient age multiplied by 10 (e.g., if someone is aged 68, the cut-off value is 680 µg/L FEU)
<50 years	Value is considered normal if <500 µg/L FEU

Clinical Probability Cut-off

	Clinical Probability (Wells Score)	D-dimer cut-off (µg/L FEU*)	
PE	Low (0 to 4)	<1000	**PE ruled out** (i.e.., likelihood less than 2%)
	Moderate (4.5 to 6)	<500	
DVT	Low (-2 to 0)	<1000	**DVT ruled out** (i.e., likelihood less than 2%)
	Moderate (1 to 2)	<500	

*FEU - Fibrinogen Equivalent Units

Appendix C: Parenteral Medications for the Treatment and Prevention of Venous Thromboembolism

For DOAC medication table, see BC Guidelines: Direct Oral Anticoagulants and BC Guidelines: Warfarin for dosing and therapeutic considerations.

Name/Dosage forms	Adult Dosage[A]	Cost per month[B]	PharmaCare Coverage[C]	Therapeutic Considerations[D]
Low molecular weight heparin (LMWH)				

Dalteparin
FRAGMIN
Prefilled syringes: 2500, 3500, 5000, 7500, 10,000, 12,500, 15,000, 16,500, 18,000 units
 	
Ampoule: 10,000 units/mL
Multi-dose vial: 25,000 units/mL
	200 units/kg subcut daily[1,2]
	OR
	100 units/kg subcut BID[1,2]
		$1120	Limited Coverage	• Contraindicated/avoid use[1,2]:
				  • CrCl < 30 mL/min
				  • History of heparin-induced thrombocytopenia (HIT)
				  • Septic endocarditis, severe uncontrolled hypertension
				  • Bleeding/major clotting disorders, diabetic or hemorrhagic retinopathy
				  • Spinal/epidural anesthesia with treatment dosing
				• Multi-dose vial contains benzyl alcohol - avoid use in pregnancy[2]
				• Cannot be used interchangeably unit for unit with unfractionated heparin or other LMWHs[2]
				• Consider BID dosing if > 100 kg1 or increased risk of bleeding[2]
				• May increase risk of hyperkalemia in DM, CKD, use with K+ sparing medications[2]
				• Drug interactions: caution with anticoagulants, platelet inhibitors, NSAIDs, thrombolytic agents[2]

Enoxaparin *LOVENOX*, biosimilars Prefilled syringes: 30, 40, 60, 80, 100, 120, 150 mg Multi-dose vial: 100 mg/mL	1.5 mg/kg subcut daily[1] **OR** 1 mg/kg subcut BID[1]	$540 (daily) $755 (BID)	Limited Coverage	• Contraindicated/avoid use: same as dalteparin • 1.5 mg/kg is equivalent to 150 units/kg[3] • 1 mg/kg BID is recommended for complicated thromboembolic disorders, e.g., cancer, increased risk of recurrent VTE or symptomatic PE [3]
Nadroparin *FRAXIPARINE* Prefilled syringes: 1900, 2850, 3800, 5700, 9500, 11,400, 15,200, 19,000 units	171 units/kg subcut daily[1,4] **OR** 86 units/kg subcut BID[1,4]	$355 (daily) $590 (BID)	Limited Coverage	• Contraindicated/avoid use: same as dalteparin • 11,400, 15,200 and 19,000 unit prefilled syringes are graduated, which allows for administration of adjusted dosages

Name/Dosage forms	Adult Dosage[A]	Cost per month[B]	PharmaCare Coverage[C]	Therapeutic Considerations[D]
Tinzaparin *INNOHEP* Prefilled syringes: 2500, 3500, 4500, 8000, 10,000, 12,000, 14,000, 16,000, 18,000 units Multi-dose vials: 10,000, 20,000 units/mL	175 units/kg subcut daily[1]	$1190	Limited Coverage	• Contraindicated/avoid use: same as dalteparin, except: • May use if CrCl ≥ 20 mL/min, limited data for CrCl < 20 mL/min[1] • Multi-dose vials contain benzyl alcohol - avoid use in pregnancy[5] • All syringes and vials are latex-free[5] • 8000 to 18,000 unit prefilled syringes are graduated, which allows for administration of adjusted dosages
Unfractionated heparin				

Heparin
generics
Vial: 10,000 units/mL
	333 units/kg subcut, then 250 units/kg subcut q12h[1]
	OR
	5000 units iv (or 80 units/kg) then infusion 18 to 20 units/kg/hr to achieve target PTT[1]
		$525 (subcut)	Regular Benefit	• Contraindicated/avoid use[6]:
				  • Severe thrombocytopenia, history of HIT
				  • If PTT monitoring cannot be performed (iv route), e.g., elevated baseline PTT
				• Narrow therapeutic range, inter-individual variation in anticoagulant effect, need for laboratory monitoring, increased risk of HIT[1]
				• Reserve heparin for the following[1]:
				  • CrCl < 30 mL/min in whom LMWH should be avoided
				  • Increased risk of bleeding where rapid reversal may be needed
				  • Considered for thrombolytic therapy
				• No PTT monitoring required for subcutaneous regimen[1]

Factor Xa inhibitor				

Fondaparinux
ARIXTRA, generics
Prefilled syringes: 2.5, 5, 7.5, 10 mg
	5 mg subcut daily (weight < 50 kg)[7]
	7.5 mg subcut daily (weight 50 to 100 kg)[7]
	10 mg subcut daily (weight > 100 kg)[7]
		$590	Non-benefit	• Contraindicated/avoid use[7]:
				  • CrCl < 30 mL/min
				  • Thrombocytopenia associated with a positive anti-platelet antibody in presence of fondaparinux
				• Reserve for patients with history of HIT
				• Rare reports of HIT in fondaparinux-treated patients have been reported[7]
				• Concomitant VKA should be initiated as soon as possible, within 72 h, if platelet count is >150 x 109/L. Continue treatment for at least 5 days until INR 2 to 3.[7]
				• Latex-free stopper and needle shield[7]

Direct thrombin inhibitor				
Argatroban generics Vial: 100 mg/mL Must be diluted prior to infusion	Starting dose: 1 to 2 mcg/kg per min[8] by continuous iv infusion. Adjust to achieve target PTT.	NA	Non-benefit	• Contraindicated/avoid use[9]: • Hereditary fructose intolerance • Reserve for patients with history of HIT[9]

Abbreviations: PTT partial thromboplastin time; **CrCl** creatinine clearance; **CKD** chronic kidney disease; **DM** diabetes mellitus; **subcut** subcutaneous; **K+** potassium; **NA** pricing information Not Available; **VKA** vitamin K antagonist.

A For normal renal and hepatic function. Consult product monograph for detailed dosing instructions and dose adjustments for unique patient populations.
B Drug costs are BC retail cost of the generic for a 70 kg patient (where applicable), rounded up to nearest $5. Current as of April 2023 and excludes retail markups and pharmacy fees.
C PharmaCare coverage as of April 2023 (subject to revision). Regular Benefit: Eligible for full reimbursement. Limited Coverage: Requires Special Authority to be eligible for reimbursement. Non-benefit: Not eligible for reimbursement. Reimbursement is subject to the rules of a patient's PharmaCare plan, including any deductibles. In all cases, coverage is subject to drug price limits set by PharmaCare. See: www.health.gov.bc.ca/pharmacare/plans/index.html and www.health.gov.bc.ca/pharmacare/policy.html for further information.
D Not an exhaustive list of all therapeutic considerations. Please consult product monographs and drug-interaction checker(s) for comprehensive information.

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