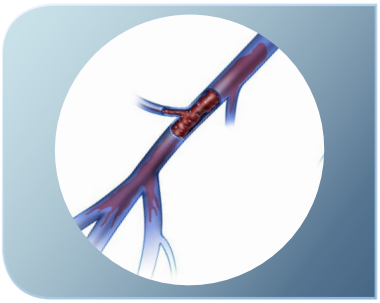

DIAGNOSIS AND MANAGEMENT OF

Venous Thromboembolism (VTE)

Minor update August 17, 2021

This care process model (CPM) was created by the Anticoagulation Task Force, Medical Specialties Clinical Program at Intermountain Healthcare. Groups represented on this team include Emergency Medicine, Thrombosis, Pulmonary/Critical Care, Pharmacy, Radiology, Women and Newborns, Medical Informatics, and others. This CPM provides expert advice for the management of venous thromboembolism (VTE) using current national practice guidelines, including those of the American College of Chest Physicians, the American College of Physicians, the American College of Emergency Physicians, the European Society of Cardiology, and the International Society on Thrombosis and Haemostasis.

Why Focus ON VTE?

- **Prevalence.** VTE is the third most common cause of cardiovascular death in the U.S., after heart attack and stroke. As many as two million people in the U.S. are diagnosed with deep vein thrombosis (DVT) each year, and half a million or more are affected by pulmonary embolism (PE). As many as one-fifth of PE cases are expected to be fatal, leading to 100,000 deaths each year.[GI0]
- **Difficulty of management.** VTE symptoms are often nonspecific and can range from mild to life-threatening. Medications for VTE carry a risk of bleeding, and there are a large number of medications to choose from.
- **Cost.** Patients with suspected VTE often undergo unneeded imaging tests. These tests drive up healthcare costs and expose patients to unnecessary medical risks.

Program Goals and Measures

- Increase the number of patients with suspected VTE who have a pre-test probability assessment and D-dimer test
- Reduce the number of CT pulmonary angiograms (CTPAs) for suspected PE
- Reduce the number of venous duplex ultrasounds for suspected DVT
- Reduce the rate of hospitalization of patients with low-risk PE
- Decrease the number of patients who receive an anticoagulant despite a contraindication

Throughout this CPM, this icon indicates an Intermountain measure.

WHAT'S INSIDE?

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SUBTYPES, SIGNS, AND SYMPTOMS OF VTE

PE is a blood clot in the lungs.

Signs / symptoms:

- Shortness of breath
- Pleuritic (most common) or dull pain anywhere in the chest
- Symptoms are usually of sudden onset and are persistent
- May be asymptomatic

DVT is a pathologic blood clot in larger veins in the body located deep to the skeletal muscles.

Signs / symptoms:

- Pain (usually aching)
- Swelling
- Edema worsening over course of a day
- Diffuse redness
- Visible enlargement of the superficial veins (usually unilateral)

SVT is a thrombosis in veins superficial to the muscle layer (previously called superficial thrombophlebitis).

Signs / symptoms:

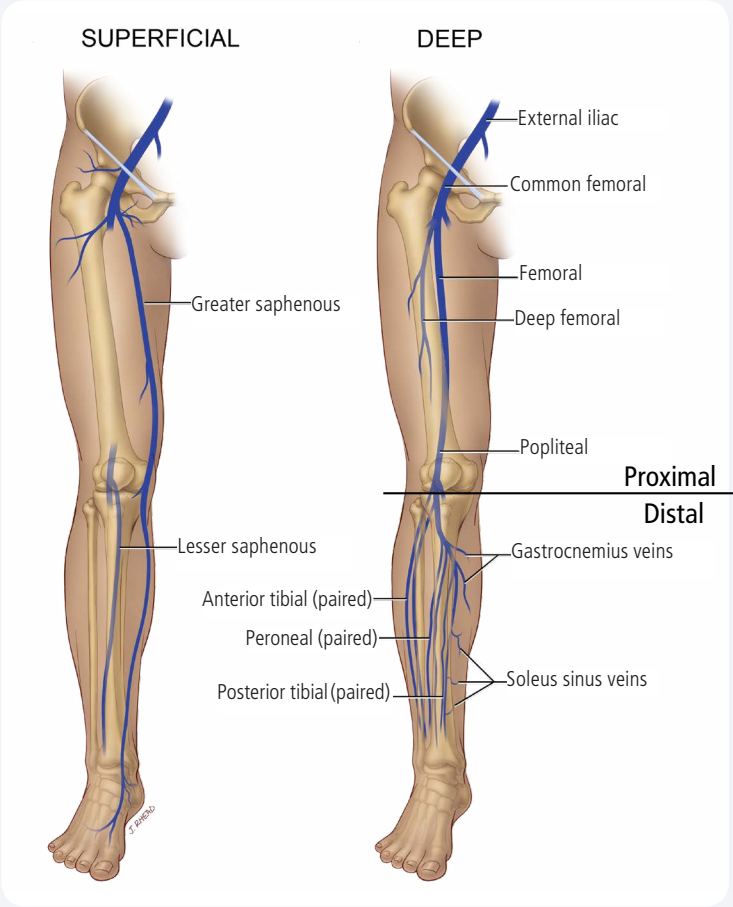
- Pain
- Tenderness
- Red, tender, swollen cord near the skin's surface
- Can occur with or without associated inflammation

OVERVIEW

Venous thromboembolism (VTE) comprises several conditions including pulmonary embolism (PE), deep vein thrombosis (DVT), and superficial vein thrombosis (SVT). See sidebar at left for definitions, signs, and symptoms of each condition.

The appropriate diagnosis and treatment of VTE depend crucially on the location of the thrombus. This CPM covers the diagnosis and treatment of each condition in descending order of clinical severity.

FIGURE 1. Leg vein anatomy



Deep veins are divided into proximal and distal (as thrombi in these locations have different management strategies) as follows:

- **Proximal:** Popliteal, femoral, deep femoral, common femoral, and iliac
- **Distal:** Anterior tibial, posterior tibial, peroneal, gastrocnemius, and soleus (soleus sinus)

KEY RECOMMENDATIONS FOR PE

- **Use pre-test probability testing combined with D-dimer testing** to rule out PE and avoid unnecessary imaging.
- **For those ≥ 50 years, age adjust D-dimer threshold** to age divided by 100..
- **CTPA is more specific** than V/Q scans but carries some significant risks.

Intermountain aims to reduce unnecessary imaging tests for VTE by increasing the number of patients who undergo appropriate pre-test probability screening and D-dimer testing when indicated.

Intermountain's *Proven Imaging: Suspected Pulmonary Embolism* CPM presents appropriate use criteria for imaging tests related to suspected PE in pregnant and non-pregnant patients.

PULMONARY EMBOLISM (PE)

Diagnosis

PE can be a life-threatening condition. Appropriate diagnostic management is critical to patient outcomes.

Pre-test risk assessment

If the patient's pre-test disease risk is low, there may not be a need to conduct imaging. The clinician should use the tools described below to determine whether or not the patient is at low risk (see PE diagnosis algorithm on page 4).

PERC. Pulmonary Embolism Rule-out Criteria (PERC) should always be considered before performing imaging tests. The number of criteria met is totaled. If the patient meets none of the criteria, PE is ruled out with no further testing needed.

RGS. If the patient meets any PERC criteria, the Revised Geneva Score (RGS) is calculated, and the number is used to direct further testing.

D-dimer. The D-dimer product forms during the breakdown of blood clots. If the D-dimer test has a normal value, VTE is unlikely. The D-dimer test has greater than 95 % sensitivity and can decrease the probability of PE to about 1 % in patients with RGS < 3 and less than 5 % in patients with RGS 4 – 10. However, elevated D-dimer is diagnostically nonspecific as small amounts of blood clot are formed and broken down in many disease states (e.g., recent major surgery and cancer). Skipping the test and proceeding as if the result were positive is recommended in these cases. In patients 50 years and older, age adjustment of the D-dimer threshold (to age x 10) preserves the negative predictive value but increases the number of patients who can avoid imaging.

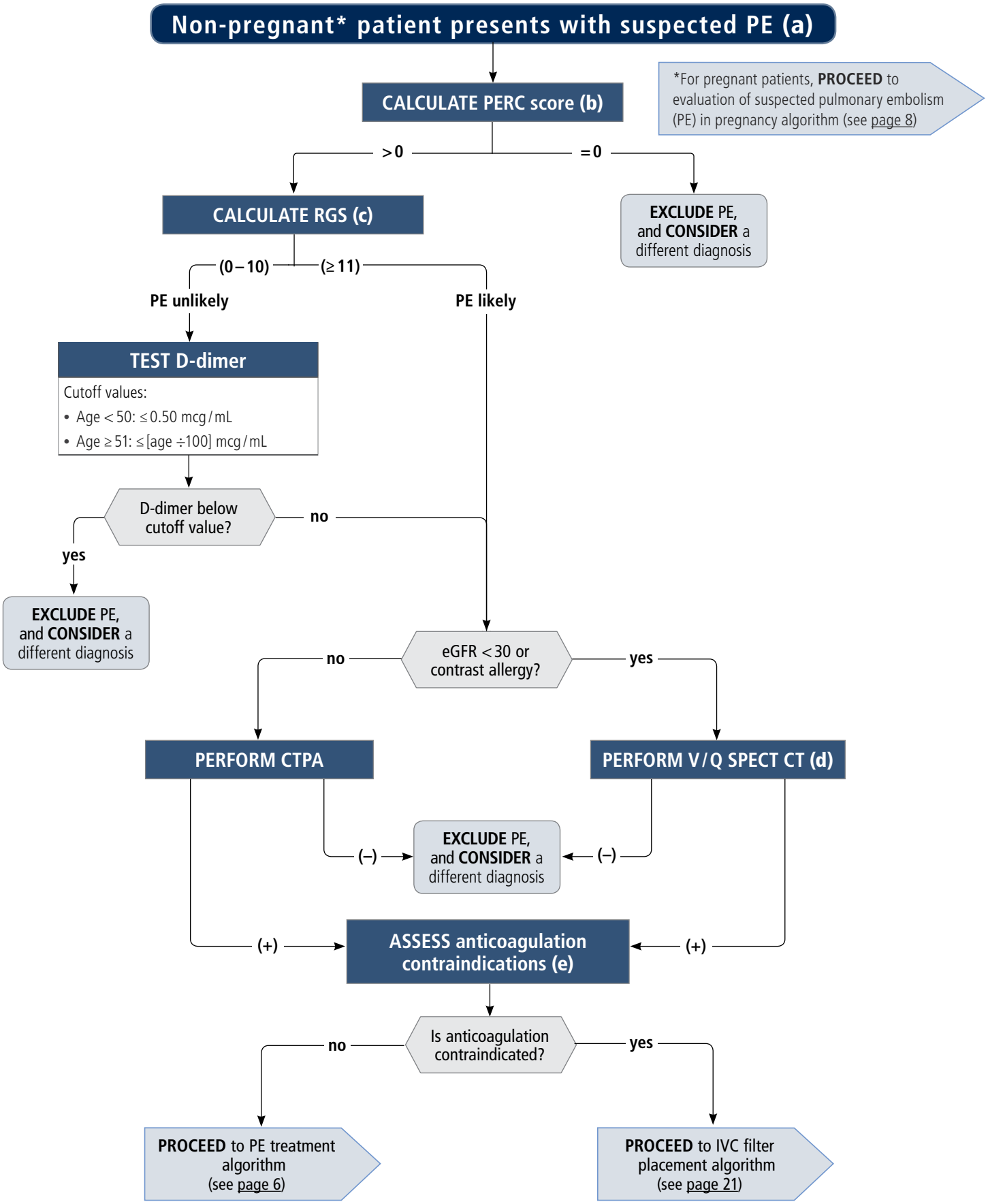
Imaging

- **CTPA (CT pulmonary angiography) is highly sensitive** and specific and can yield information about alternative diagnoses. However, CTPA carries some significant risks, including:
  - **Exposure to radiation.** The radiation dose for CTPA ranges from 10 – 15 mSv on average, the equivalent of up to 150 chest x-rays.
  - **Contrast-induced nephropathy** may occur, particularly in patients with chronic kidney disease, which in severe cases can result in the need for dialysis. Contrast is also associated with anaphylaxis and local tissue injury due to extravasation.
  - **Overdiagnosis of PE** occurs when CTPA identifies small filling defects in subsegmental pulmonary arteries that are either false-positive findings or clinically benign thrombi that require no treatment. Overdiagnosis increases the number of patients who suffer complications from anticoagulant therapy with no corresponding decrease in the number of PE-related deaths.
- **V/Q (ventilation/perfusion) scans have different methodologies:** Planar imaging has been available for many years and forms the basis of older management studies. Results are reported in probabilistic categories. V/Q SPECT CT and Q SPECT CT are newer methods which produce higher resolution images. Results are reported in a binary fashion (i.e., positive or negative). [BAJ]

Treatment

Most cases of PE are treated with anticoagulation. However, more severe cases may require an intervention to rapidly dissolve or remove existing clots to reduce the risk of death. The mildest form of PE is isolated subsegmental PE (ISSPE), which is isolated to the subsegmental branches (i.e., no segmental or more proximal PE present). ISSPE may not require any specific treatment.

ALGORITHM 1: PULMONARY EMBOLISM (PE) DIAGNOSIS



ALGORITHM NOTES

(a) PE signs / symptoms

Approximately half of patients with PE are asymptomatic. However, among patients with suspected PE, the most common signs and symptoms include:

- Difficulty breathing
- Chest pain that worsens with a deep breath or cough
- Hemoptysis
- Faster than normal or irregular heartbeat

(b) Pulmonary Embolism Rule-out Criteria (PERC)

Factor	Points
☐ Age > 50 years	1
☐ Hemoptysis	1
☐ Oxygen saturation < 93 %*	1
☐ Either surgery or trauma requiring treatment with general anesthesia in the previous 4 weeks	1
☐ Unilateral leg swelling	1
☐ Previous PE or DVT	1
☐ Estrogen use	1
☐ Heart rate ≥ 100 beats / minute	1
☐ Gestalt suspicion of PE ≥ 15 %	1
ADD total points	☐

* Value adjusted from the original 95 % based on Intermountain altitude adjustment tables.

(c) Revised Geneva Score (RGS)

Factor	Points
☐ Age > 65 years	1
☐ Hemoptysis	2
☐ Active malignant condition	2
☐ Surgery or fracture within 1 month	2
☐ Unilateral lower limb pain	3
☐ Previous PE or DVT	3
☐ Pain on lower-limb deep venous palpation and unilateral edema	4
☐ Heart rate 75 – 94 beats / minute	3
☐ Heart rate ≥ 95 beats / minute	5
ADD total points	☐

(d) Ventilation-perfusion (V / Q) scan

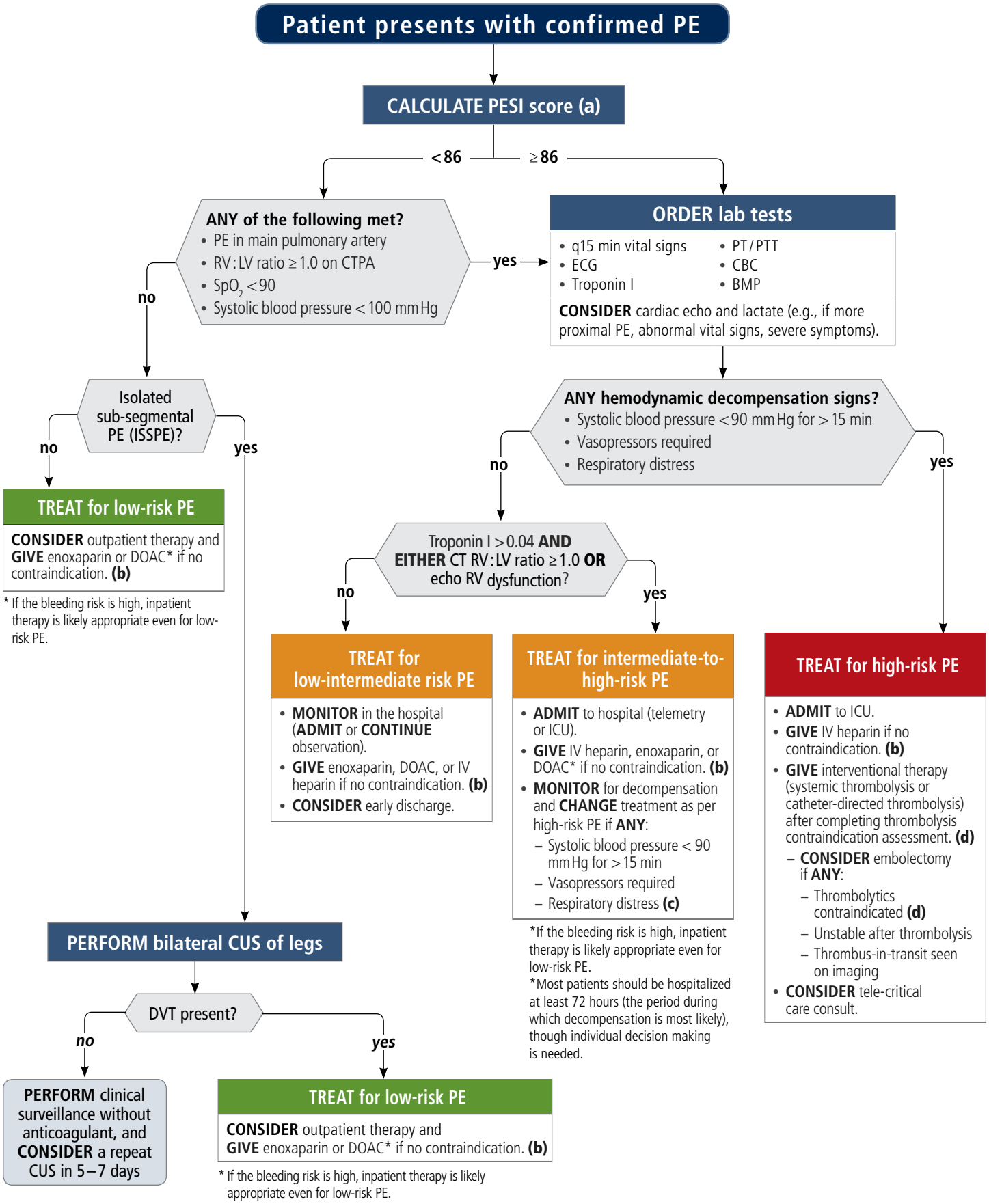
- **If CTPA is nondiagnostic** (e.g. poor visualization of segmental, lobar or main arteries), V/Q SPECT CT may yield a diagnostic result.
- **If CTPA is limited** (only subsegmental vessels poorly visualized) use clinical judgement regarding the need for additional imaging or consider thrombosis consult.
- **If both are non-diagnostic, or V/Q SPECT CT is not available PERFORM** a bilateral CUS and **TREAT** if DVT present.
- **If a CUS is negative**, **CONSIDER** additional testing or thrombosis consult. Thrombosis consultant can be contacted at 801-408-5060.

(e) Anticoagulation contraindication assessment*

Absolute contraindications	Relative contraindications
☐ Current active bleeding	☐ Intracranial or intraspinal tumor
☐ Major surgery in the last 7 days	☐ Aortic dissection
☐ Intracranial hemorrhage in the last 30 days	☐ GI bleeding in the last 7 days
☐ Platelet count < 25,000	☐ Platelet count < 50,000

* **Do NOT give anticoagulants** if a patient has **ANY** absolute contraindication(s). Anticoagulants are strongly discouraged in the presence of a relative contraindication, but the clinician must weigh the risks and benefits in each case.

ALGORITHM 2: RISK STRATIFICATION & TREATMENT OF PE



ALGORITHM NOTES

(a) PESI score calculator

Factor	Points
☐ Age	Age in years
☐ Male sex	10
☐ Cancer	30
☐ Heart failure	10
☐ Chronic lung disease	10
☐ Pulse ≥110 / min	20
☐ Systolic blood pressure <100 mmHg	30
☐ Respiratory rate ≥ 30 / min	20
☐ Temperature < 36 ° C	20
☐ Altered mental status	60
☐ Arterial oxygen saturation < 90 %	20
ADD total points	☐

(b) Anticoagulation contraindication assessment*

Absolute contraindications	Relative contraindications
☐ Current active bleeding	☐ Intracranial or intraspinal tumor
☐ Major surgery in the last 7 days	☐ Aortic dissection
☐ Intracranial hemorrhage in the last 30 days	☐ GI bleeding in the last 7 days
☐ Platelet count < 25,000	☐ Platelet count < 50,000

* **Do NOT give anticoagulants** if patient has **ANY** absolute contraindication(s). Anticoagulants are strongly discouraged in the presence of a relative contraindication, but the clinician must weigh the risks and benefits in each case.

(c) Respiratory Distress

Respiratory distress may include any of the following:

- Sustained tachypnea
- Marked work of breathing or requiring high-flow nasal canula
- Invasive or non-invasive ventilation support

(d) Thrombolytic contraindication assessment

Contraindications (risk of bleeding is greater than the potential benefit)

☐ Confirmed or suspected acute intracranial hemorrhage, subarachnoid hemorrhage, or major cerebral infarct
☐ Systolic blood pressure > 185 mm Hg or diastolic blood pressure > 110 mm Hg despite maximal treatment
☐ Platelet count < 100,000
☐ Known coagulopathy, including warfarin use with INR > 1.7
☐ Use of a thrombolytic agent in the last 4 days
☐ Pregnancy, lactation, or parturition within the last 30 days

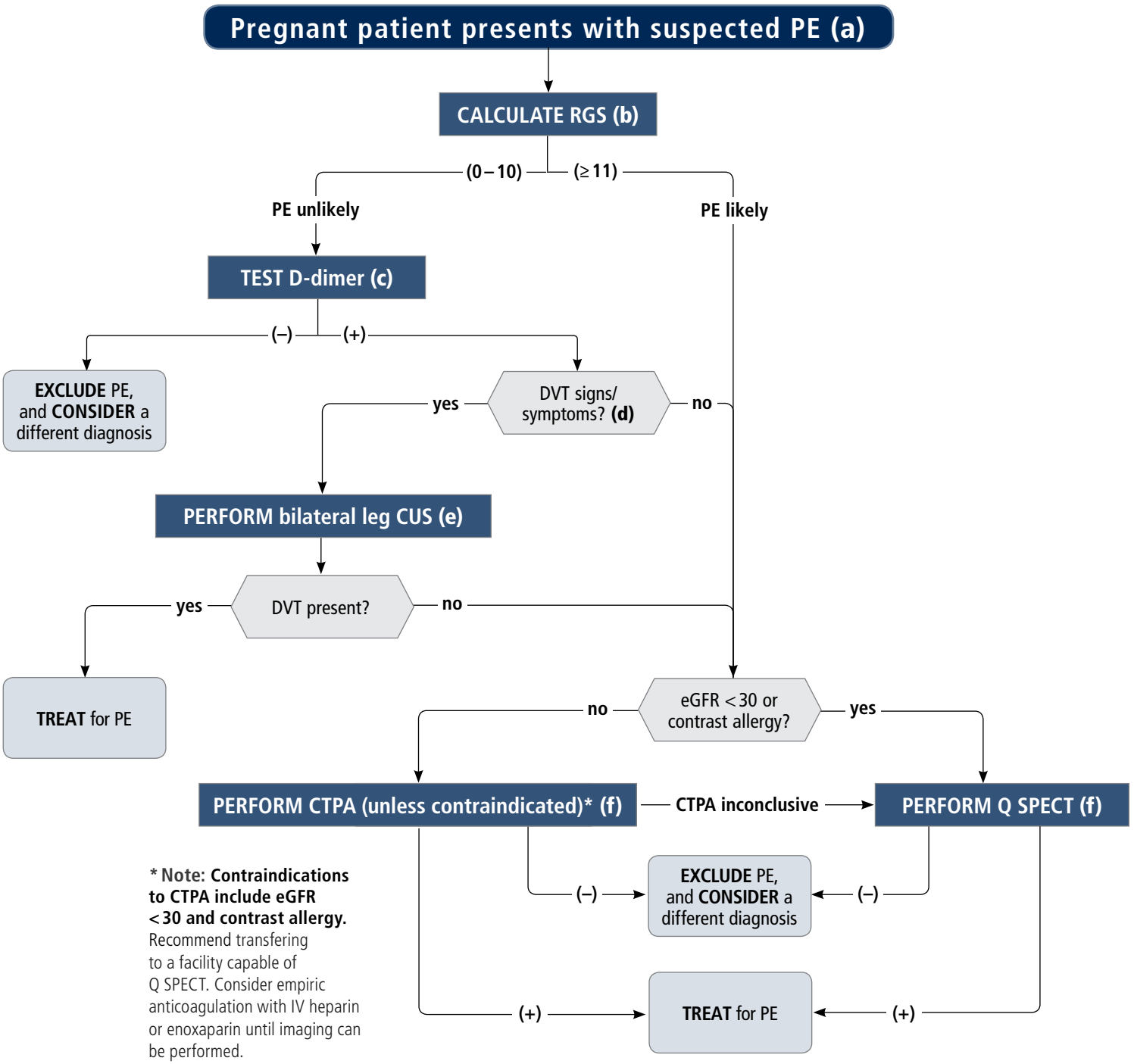
Warnings and precautions (use clinical judgment—benefits may merit the risk of thrombolysis*

☐ Recent surgery / major trauma (within prior 15 days)
☐ Recent active bleeding (within prior 22 days)
☐ Significant stroke or head trauma (within prior 3 months)
☐ Intracranial or spinal surgery (within prior 3 months)
☐ History of vascular malformation
☐ Any history of intracranial hemorrhage
☐ Any history of a brain aneurysm or tumor

* The clinician must make an assessment tailored to each patient based on the above criteria.

ALGORITHM 3: EVALUATION OF SUSPECTED PULMONARY EMBOLISM (PE) IN PREGNANCY

Pulmonary embolism (PE) in pregnancy, although infrequent, is nevertheless the leading cause of maternal deaths in the US.[CDC] Accurate and rapid diagnosis are critical to prevent mortality. Evaluating for PE in pregnancy is a challenge because the physiological changes of pregnancy can overlap with the signs and symptoms of PE or deep vein thrombosis (DVT). This section recommends an evidence-based protocol to evaluate suspected PE in pregnant patients (see the algorithm below). Based on recognized guidelines and expert consensus, it represents a collaborative effort including Intermountain's Medical Specialties, Cardiovascular, and Women and Newborn Clinical Programs; Intermountain's Imaging Service; and Intermountain Medical Center's Department of Emergency Medicine.



ALGORITHM NOTES

(a) PE signs / symptoms

Approximately half of patients with PE are asymptomatic. However, among patients with suspected PE, the most common signs and symptoms include:

- Difficulty breathing
- Chest pain that worsens with a deep breath or cough
- Hemoptysis
- Faster than normal or irregular heartbeat

(b) Revised Geneva Score (RGS)

Factor	Points
☐ Age > 65 years	1
☐ Hemoptysis	2
☐ Active malignant condition	2
☐ Surgery or fracture within 1 month	2
☐ Unilateral lower limb pain	3
☐ Previous PE or DVT	3
☐ Pain on lower-limb deep venous palpation and unilateral edema	4
☐ Heart rate 75–94 beats / minute	3
☐ Heart rate ≥ 95 beats / minute	5
ADD total points	☐

(c) D-dimer

Cutoff values:

- Age < 50: ≤ 0.50 mcg / mL
- Age ≥ 51: ≤ [age X 100] mcg / mL

(d) DVT signs / symptoms

DVT signs / symptoms include leg pain tenderness, edema, redness, and warmth. In pregnancy, thrombosis is more common on the left side in the first trimester and is restricted to the femoral or iliac veins in > 50 % of cases.[CHA]

(e) Bilateral CUS after a technically inadequate CTPA

Starting with bilateral CUS, if DVT signs are present, it allows you to treat without any workup involving radiation if the bilateral CUS results are positive. A negative CUS does not exclude PE, as PE can commonly be present without DVT.

A repeat CTPA should be performed only if a review of a prior study suggests a technical cause that can be remedied or improved. A positive CUS may preclude the need for further tests that involve radiation. **CONSIDER** repeating the CUS twice, on days 3 and 7. While serial ultrasound has not been directly studied in suspected PE, this strategy excludes suspected DVT (the most common etiology of PE) in pregnant patients.[BAT]

(f) Q SPECT vs CTPA

Clinicians must consider radiation exposure both to the fetus and to the mother. Radiation doses from CTPA and Q SPECT scans to the fetus are very similar and low (about 1 mSv) and nearly equivalent to the background radiation to the fetus during a typical pregnancy.[LEU, DOS] This is far below the 50 mSv threshold of concern for altered growth or abnormal brain development, but may still be associated with the slight excess risk of childhood cancer of 1 in 100,000.[LIN] The exposure to the developing maternal breast tissue from a typical CTPA at 10–60 mSv, however, is significantly higher than the typical (<1 mSv) dose from a Q SPECT scan.[BAJ] The higher-dose CTPA, therefore, puts the mother at higher risk for radiation-induced breast cancer. Q SPECT protocols in pregnancy are rapidlly evolving and a low-dose (2 mCi) protocol is an option for women who wish minimal radiation and can tolerate longer imaging times. If Q SPECT is negative, PE is excluded. If Q SPECT is positive, a ventilation scan is added to confirm mismatch.

CTPA results are more often indeterminate in pregnancy and, conversely, V / Q and Q SPECT scans are more often diagnostic. Approximately 17–36 % of CTPAs are nondiagnostic in pregnancy, largely because the physiologic changes related to pregnancy can lead to poor arterial enhancement on CTPA.[BAJ]

If a Q SPECT scan result is non-diagnostic, PERFORM bilateral CUS. If positive for DVT, treat. If negative, cosider CTPS or Thormbosis consult (available at 801-408-5060.)

KEY RECOMMENDATIONS FOR DVT

- **Use pre-test probability testing** combined with D-dimer to rule out DVT and avoid unnecessary imaging.
- **Monitor with serial CUS** when anticoagulation is not initiated for isolated distal DVT (IDDVT).
- **Carefully select** patients with femoral and iliac DVT who are candidates for management with catheter-directed thrombolysis.

DEEP VEIN THROMBOSIS (DVT)

DVT usually affects large veins in the thighs and / or lower legs but can also occur in the pelvis or arms. The anatomical division of deep veins into proximal and distal is relevant for DVT management as thrombi in proximal veins are at higher risk for traveling to the lungs.

Diagnosis

Imaging with venous duplex ultrasound has become the reference standard for DVT diagnosis. However, DVT is confirmed in only about 10 % of the patients in whom it is suspected. Therefore, an approach that combines pre-test probability assessment (see sidebar) and D-dimer, analogous to that used for PE, can be used both to rule out DVT in some cases and to reduce unnecessary ultrasound testing.

As a pre-test risk assessment, the two-level Wells score combines favorable diagnostic performance with relative simplicity. The simplified Wells score is not sensitive or specific enough to definitively diagnose or exclude suspected DVT, but a Wells score of "DVT unlikely" (< 2) can be combined with D-dimer testing to rule out DVT with a ~ 1 % chance of missed DVT.[BAT] This strategy avoids the need for imaging in more than one-third of suspected DVT cases.

Treatment

The prognosis and risk for complications from DVT vary widely depending upon the degree of thrombus burden and the proximal extent of thrombosis. Most DVT is treated with **therapeutic anticoagulation**, which prevents propagation and embolization of the existing thrombus and allows healing via the intrinsic thrombolytic system (see DVT treatment algorithm on page 14). Treatment considerations for specific types of DVT are as follows:

- **Isolated distal DVT (IDDVT)** confined to the calf veins (i.e., tibial, peroneal, gastrocnemius, or soleus) resolves without treatment in 80 – 90 % of cases. Monitoring patients via serial ultrasounds is an alternative to initial anticoagulation. However, 10 – 20 % of IDDVT propagate into proximal deep veins and require definitive treatment. Therefore, monitoring with serial CUS to exclude proximal propagation is necessary when therapeutic anticoagulation is not initiated.
- **Common femoral and iliac DVT,** in contrast, carry a high risk for the development of **post-thrombotic syndrome (PTS)**. Interventional therapy with catheter-based techniques can be considered to hasten symptom relief and possibly reduce the risk for PTS. Due to the increased bleeding risk and expense of these procedures, candidate patients should be carefully selected.

KEY RECOMMENDATIONS FOR SVT

- **SVT is common,** carries significant risks, and can lead to DVT.
- **Favor more conservative treatment measures** unless SVT is extensive and/or patient is highly symptomatic.
- **When using NSAIDs to treat SVT, monitor patient** for possible progressive disease.

SUPERFICIAL VEIN THROMBOSIS (SVT)

Superficial vein thrombosis (SVT) is nearly as common as DVT (see page 10). Although historically considered a minor illness, SVT carries significant risks. Most importantly, it may lead to DVT by propagating through the two vein systems, especially at the junction between the greater saphenous and femoral veins near the groin.

Diagnosis

The diagnosis of SVT follows the same procedures as DVT. When a patient presents with symptoms of SVT, DVT is also present 25% of the time.

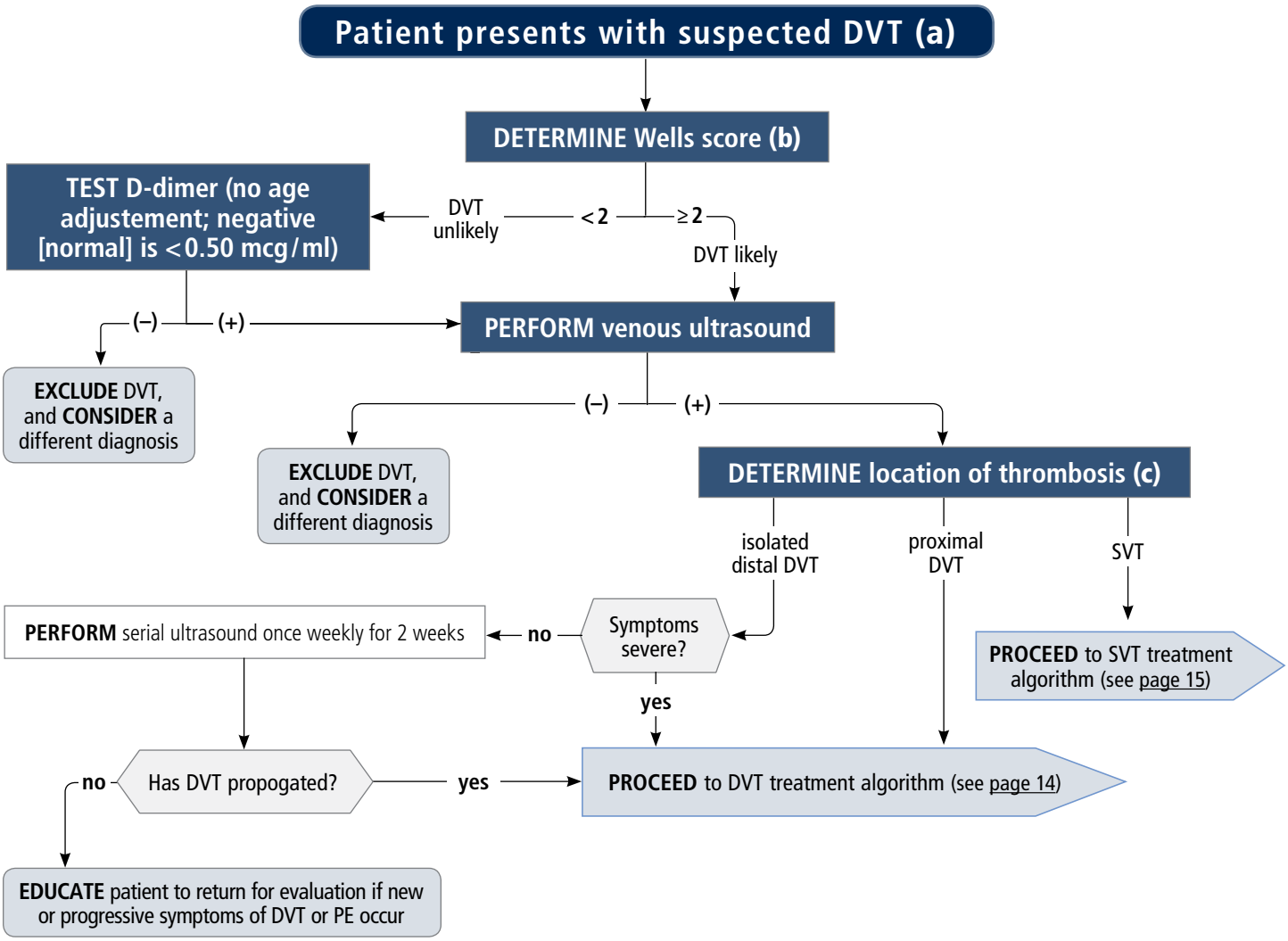
Treatment

Treatment of SVT differs from that for DVT, favoring more conservative measures in many cases, and requiring lower doses when anticoagulants are used. Treatment of SVT often includes:

- Local measures, such as warm compresses
- NSAIDs
- Low-dose anticoagulants in more severe cases

While anticoagulants are effective for the treatment of SVT, they are generally reserved for extensive and/or highly symptomatic cases of SVT due to their expense and potential complications. If NSAIDs are used, patients should be monitored for possible progressive disease.

ALGORITHM 4: DVT DIAGNOSIS



ALGORITHM NOTES

(a) DVT signs / symptoms

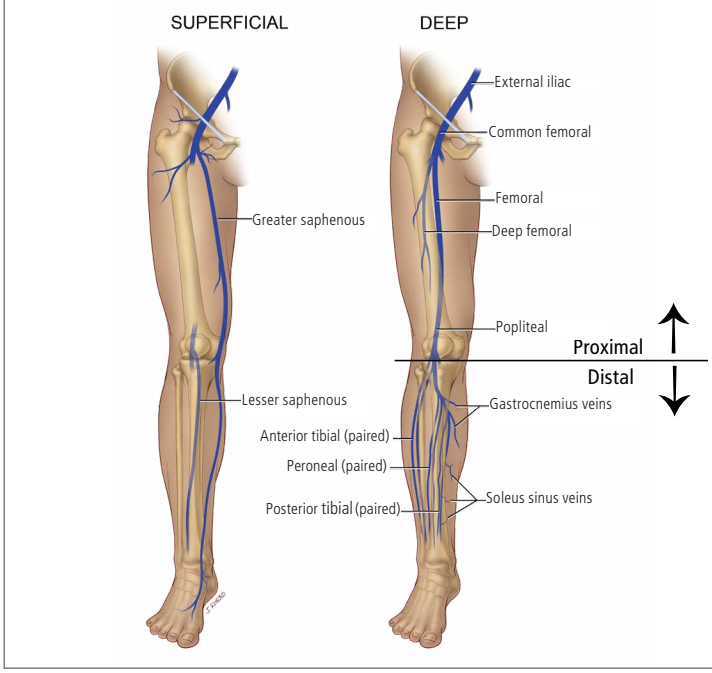
DVT signs / symptoms include leg pain tenderness, edema, redness, and warmth. In pregnancy, thrombosis is more common on the left side in the first trimester and is restricted to the femoral or iliac veins in > 50 % of cases.[CHA]

(b) Wells score

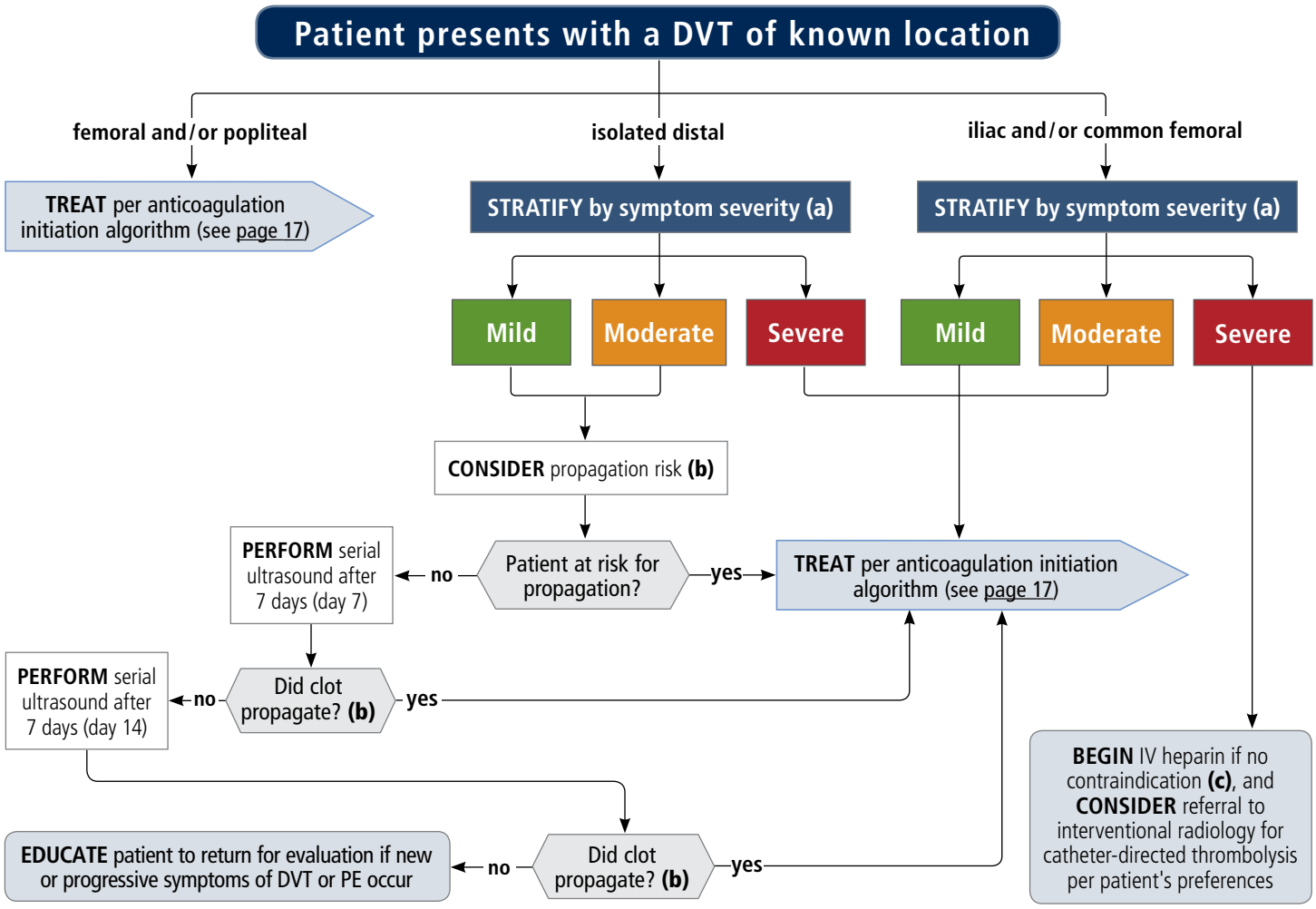
Risk factors	Points
☐ Active cancer	1
☐ Paralysis, paresis, or recent cast	1
☐ Bedridden or surgery in the past 12 weeks	1
☐ Localized tenderness	1
☐ Entire leg swollen	1
☐ ≥ 3 cm calf asymmetry	1
☐ Pitting edema in the affected leg	1
☐ Collateral (non-varicose) veins	1
☐ Previous DVT	1
Alternate diagnosis as likely	-2
ADD total points*	☐

* Total points < 2: DVT unlikely; ≥ 2: DVT likely.

(c) Leg vein anatomy



ALGORITHM 5: DVT TREATMENT



ALGORITHM NOTES

(a) Symptom severity stratification tool for DVT*

	Isolated distal DVT	Iliac and/or common femoral DVT
Mild	• Mild pain or discomfort • Mild swelling, trace or mild pitting edema • Distal erythema	
Moderate	• Moderate pain or discomfort • Moderate pitting edema • Diffuse erythema or hyperpigmentation	
Severe	• Severe pain • Severe edema • Difficulty bearing weight • Loss of sensation • Venous claudication	• Phlegmasia • Severe pain • Difficulty bearing weight • Severe edema • Loss of sensation • Loss of strength/paresis • Venous claudication • Venous gangrene

* The patient's preferences are an important component of management decisions. A given patient may prefer treatment or serial ultrasound for isolated distal DVT or may prefer anticoagulation or catheter-directed thrombolysis (CDT) for iliac or femoral DVT.

(b) Propagation risk factors for distal DVT

If a patient has any of these risk factors, **CONSIDER** proceeding with anticoagulation **(c)** rather than serial ultrasound, even if symptoms are mild or moderate. Risk factors are:

- D-dimer is positive (particularly when markedly so without an alternative reason)
- Thrombosis is extensive (e.g., >5 cm in length, involves multiple veins, >7 mm in maximum diameter)
- Thrombosis close to the proximal veins
- No reversible provoking factor for DVT
- Active cancer
- History of VTE
- Inpatient status or persistent immobility

(c) Anticoagulation contraindication assessment*

Absolute contraindications	Relative contraindications
☐ Current active bleeding	☐ Intracranial or intraspinal tumor
☐ Major surgery in the last 7 days	☐ Aortic dissection
☐ Intracranial hemorrhage in the last 30 days	☐ GI bleeding in the last 7 days
☐ Platelet count <25,000	☐ Platelet count <50,000

* **Do NOT give anticoagulants** if a patient has **ANY** absolute contraindication(s). Anticoagulants are strongly discouraged in the presence of a relative contraindication, but the clinician must weigh the risks and benefits in each case.

ALGORITHM 6: SVT TREATMENT

Patient with SVT diagnosed

DETERMINE location (a)

STRATIFY by severity

Mild	Moderate	Severe (Saphenofemoral SVT)
If **ANY** of the following: • Lesser saphenous vein or varicosity • Distal location • < 5 cm in length • Mild symptoms	If **ANY** of the following: • Greater saphenous vein • Proximal location • ≥ 5 cm in length • Severe symptoms	If proximal clot < 5 cm from the junction of the greater saphenous and common femoral vein
TREAT SVT • **INITIATE** NSAID therapy. • **INITIATE** local treatment measures. • **FOLLOW UP** after ~ 1 week.	**TREAT SVT** • **COMPLETE** anticoagulation contraindication assessment. **(b)** • **INITIATE** low-dose anticoagulant if no contraindication. **(b)** (See low-dose section of table 1 on page 17.) • **INITIATE** local treatment measures.	**MANAGE** as DVT (see DVT treatment algorithm on page 14)

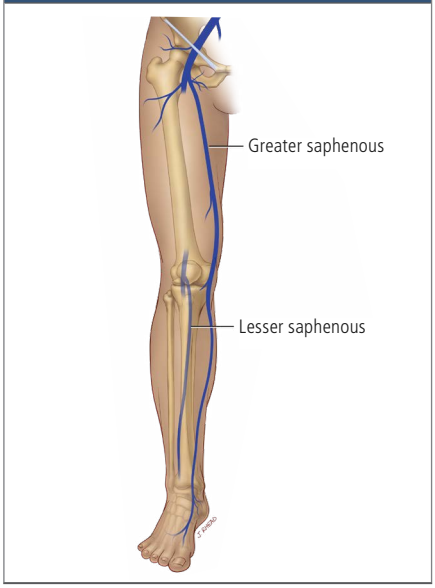
Did symptoms progress?

- yes → **PERFORM** serial ultrasound (day 7 & 14), and **CONSIDER** low-dose anticoagulation if thrombi have propagated
- no → **CONTINUE** management for ~ 6 weeks, and **FOLLOW UP** as needed after completion of therapy

FOLLOW UP as needed after completion of therapy

ALGORITHM NOTES

(a) Superficial vein anatomy



(b) Anticoagulation contraindication assessment*

Absolute contraindications	Relative contraindications
☐ Current active bleeding	☐ Intracranial or intraspinal tumor
☐ Major surgery in the last 7 days	☐ Aortic dissection
☐ Intracranial hemorrhage in the last 30 days	☐ GI bleeding in the last 7 days
☐ Platelet count < 25,000	☐ Platelet count < 50,000

* **Do NOT give anticoagulants** if a patient has **ANY** absolute contraindication(s). Anticoagulants are strongly discouraged in the presence of a relative contraindication, but the clinician must weigh the risks and benefits in each case.

ANTICOAGULATION

Progressive VTE occurs in fewer than 5% of patients after starting anticoagulant therapy, making anticoagulation an extremely effective treatment for VTE.[KEA] The major risk of all anticoagulants is bleeding, which can be estimated with the bleeding risk assessment tool on page 19 (see also the anticoagulation contraindication assessment on page 17). Because anticoagulants do not dissolve existing thrombi, an interventional therapy may be needed to more rapidly remove existing clots in very severe cases. See **Algorithm 5: DVT Treatment** (page 14) and **Algorithm 2: Risk Stratification & Treatment of PE** (page 6).

Initiation (first several days of therapy)

The clinical goal during this phase is to impair the activated state of the coagulation system and to arrest the active formation and embolization of new thrombi. This is achieved through the use of rapid-acting anticoagulant agents at high doses. Initiation uses different dosing strategies depending upon the anticoagulant regimen selected. The potential approaches are:

- **Overlapping:** A rapid-acting parenteral anticoagulant is started immediately, and overlapped with warfarin for the initiation period.
- **Switching:** Low-molecular-weight heparin is used for the initiation period and then changed to an oral anticoagulant.
- **Loading:** A direct oral anticoagulant (DOAC) is used at a higher dose for the initiation period, and the dose is then reduced.

See **Algorithm 7: Anticoagulation Initiation** (page 17) and **table 1** (page 18).

Indefinite anticoagulation vs. cessation

Anticoagulant use carries a risk of major bleeding, which can be fatal. Following three months of anticoagulation treatment after a VTE event, the goal of continued anticoagulation treatment is secondary prevention. Despite past guidelines, it is no longer recommended to continue anticoagulation for intermediate durations (i.e., 12–24 months).[KEA] Therefore, the treatment options are either time-limited therapy (i.e., at least 3 months), and indefinite/extended therapy (no planned stop date).

The decision to continue anticoagulation into the extended/indefinite phase is based on:

- An assessment of the risk for recurrent thrombosis if anticoagulation is stopped.
- The risk of major bleeding if anticoagulation is continued. (See the bleeding risk table on page 19.) This tool has not been validated in VTE populations but may inform shared decision making with the patient regarding comparative potential harms and benefits of anticoagulation therapy for VTE.
- Patient preference.

Bleeding risk and patient preferences may change over time. Patients continuing anticoagulation into the extended/indefinite phase should be reevaluated annually and/or when there is any major change to their clinical status.

ALGORITHM 7: ANTICOAGULATION INITIATION

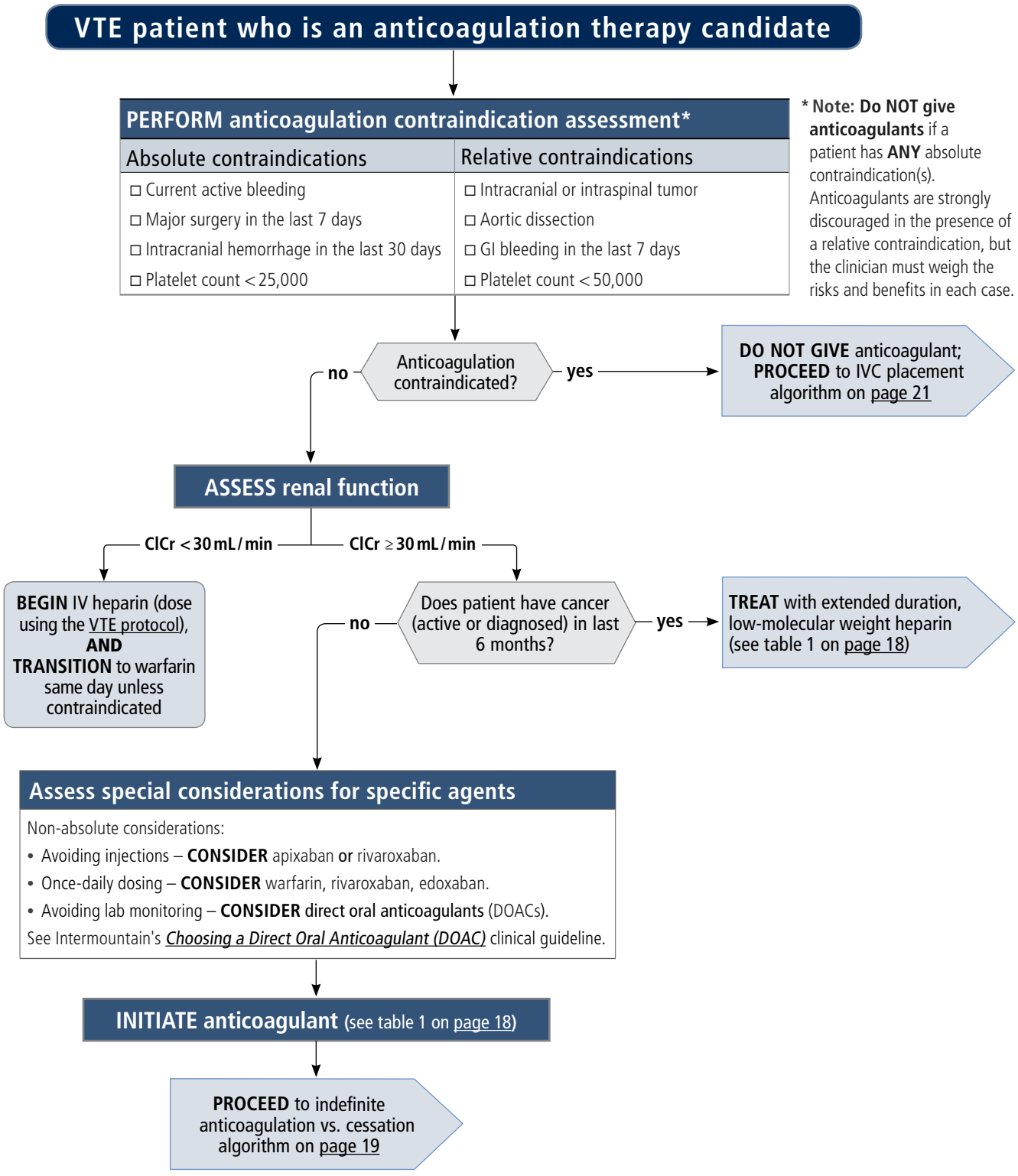


TABLE 1. Anticoagulant Dosing by Phase and Type of Therapy *

Medication	Standard anticoagulation therapy		
	Initiation (5–30 days)	Acute phase‡ (3 months)	Extended/indefinite§
IV unfractionated heparin (UFH) per Intermountain's VTE Power Plan	**OVERLAP** with warfarin†	**CONTINUE** warfarin, INR 2.0–3.0	**CONTINUE** warfarin, INR 2.0–3.0
enoxaparin (overlapped to warfarin)	**OVERLAP** with warfarin†	**CONTINUE** warfarin, INR 2.0–3.0	**CONTINUE** warfarin, INR 2.0–3.0
enoxaparin (switched to dabigatran)	1 mg/kg twice daily x 7 days	**STOP** enoxaparin and **CHANGE** to dabigatran, 150 mg twice daily	**CONTINUE** dabigatran, 150 mg twice daily
enoxaparin (switched to edoxaban)	1 mg/kg twice daily x 7 days	**STOP** enoxaparin and **CHANGE** to edoxaban, 60 mg daily	**CONTINUE** edoxaban, 60 mg daily
enoxaparin (extended therapy for cancer-associated thrombosis)	1 mg/kg twice daily x 30 days [no transition to oral agents in cancer patients]	**CONTINUE** enoxaparin, 1 mg/kg twice daily¶	**CONTINUE** enoxaparin, 1 mg/kg twice daily¶
dalteparin (extended therapy for cancer-associated thrombosis)	200 IU/kg daily x 30 days [no transition to oral agents in cancer patients]	**REDUCE** dalteparin dose to 150 IU/kg daily	**CONTINUE** dalteparin, 150 IU/kg daily
apixaban	10 mg twice daily x 7 days	**REDUCE** apixaban dose to 5 mg twice daily	**REDUCE** apixaban dose to 2.5 mg twice daily
rivaroxaban	15 mg twice daily x 21 days	**CHANGE** rivaroxaban dose to 20 mg daily	**REDUCE** rivaroxaban dose to 10 mg once daily
Medication	Low-dose anticoagulation therapy (for SVT)		
enoxaparin	40 mg SQ daily x 4–6 weeks	N/A	N/A
fondaparinux	2.5 mg daily x 45 days	N/A	N/A
rivaroxaban	10 mg daily x 45 days	N/A	N/A

* This figure reviews the dosing of various anticoagulants through the successive phases of therapy, including instances in which agents or doses are changed as the phases of therapy progress. Renal adjustment may be necessary. Please see relevant package inserts for details.

† IV unfractionated heparin (UFH) or enoxaparin should be overlapped with warfarin until 2 standards have been met—(1) at least 5 days of overlapping therapy have been given, AND (2) the INR has been ≥2.0 for at least 24 hours.

‡ The acute phase is defined as 3 months by most guidelines. Some practitioners prefer a 6-month acute phase of treatment.

§ For patients who will proceed with indefinite (no planned stop date) therapy. See indefinite anticoagulation vs. cessation algorithm on page 19.

¶ Enoxaparin can be changed to 1.5 mg/kg subcutaneous injection once daily if a patient prefers fewer injections.

Also, see Intermountain's ***Choosing a Direct Oral Anticoagulant (DOAC)*** clinical guideline.

ALGORITHM 8: INDEFINITE ANTICOAGULATION VS. CESSATION

Patient completed acute phase (≥ 3 months) of anticoagulation

ASSESS for clear transient provocation

Major transient risk factors (must have occurred within 3 months of VTE):
- Surgery with anesthesia > 30 minutes
- Hospitalization with bedrest (or bathroom privileges only) for ≥ 3 days
- Cesarean section

Minor transient risk factors (must have occurred within 2 months of VTE):
- Surgery of < 30 minutes duration
- Hospitalization < 3 days
- Estrogen use
- Pregnancy (non-cesarean) and post-partum
- Home bed rest for at least 3 days
- Leg injury with reduced mobility for at least 3 days

Does patient have clear transient provocation?

no →

ASSESS bleeding risk (a)

Low bleeding risk **AND** patient agreeable to anticoagulation	**Intermediate** bleeding risk **AND** patient agreeable to anticoagulation	**High** bleeding risk **OR** patient prefers no anticoagulation
• **INITIATE** indefinite anticoagulation • **REASSESS** annually	• **INITIATE** indefinite anticoagulation • **REASSESS** at least once annually	• **STOP** anticoagulation • **CONSIDER** aspirin therapy **(b)**

yes →

STOP anticoagulation

- **ADVISE** patient to seek care promptly if future signs or symptoms of thrombosis develop.
- **ENSURE** VTE prophylaxis is given in risk situations, such as surgery or hospitalization.
- **ADVISE** patient to ambulate frequently and / or wear compression stockings during long travel.
- **ADVISE** female patients to avoid using estrogens.
- **RECOMMEND** smoking cessation if applicable.

ALGORITHM NOTES AND ASSESSMENT TOOLS

(a) Bleeding risk factors (1 point each)

- ☐ Age > 65 years (2 points if age > 75 years)
- ☐ Previous bleeding
- ☐ Cancer
- ☐ Metastatic cancer
- ☐ Renal failure
- ☐ Liver failure
- ☐ Thrombocytopenia
- ☐ Previous stroke
- ☐ Diabetes
- ☐ Anemia
- ☐ Antiplatelet therapy
- ☐ Poor anticoagulant control
- ☐ Comorbidity and reduced functional capacity
- ☐ Recent surgery
- ☐ Frequent falls
- ☐ Alcohol abuse
- ☐ Nonsteroidal anti-inflammatory drug (NSAID) use

ADD total points: ☐

Based on the number of points at left, the following provides an estimate for the risk of major bleeding during the first 3 months of anticoagulation, and the annual risk if anticoagulation is continued beyond 3 months. High bleeding risk is not considered a contraindication to using anticoagulation for the acute phase of therapy, but these patients should be monitored carefully during treatment, and anticoagulation should be discontinued if possible after 3 months.[KEA]

	Low risk (0 risk factors)	Intermediate risk (1 risk factors)	High risk (≥ 2 risk factors)
0 – 3 months	1.6 %	3.2 %	12.8 %
> 3 months (annualized)	0.8 %	1.6 %	6.5 % +

(b) Aspirin therapy

Low-dose aspirin (100 mg was used in the relevant trials) was found to reduce the risk of recurrent VTE by about 35 % vs. placebo.[SIM] This is much less effective than the risk reduction from anticoagulants (85 – 90 %); therefore, aspirin should **NOT** be considered as a reasonable alternative for patients without a contraindication to continuing anticoagulants. Patients for whom anticoagulants are contraindicated may also have contraindications to aspirin.

INFERIOR VENA CAVA (IVC) FILTERS

Potential benefits

IVC filters are intended to capture a venous embolism from the lower extremity veins while allowing for blood flow through the vein. IVC filters are placed under fluoroscopic guidance in the infrarenal inferior vena cava. The primary potential benefit of an IVC filter is an approximate 50 % reduced risk for PE.[KAU] See the decision guide box below for situations in which IVC filters may be considered.

Risks

IVC filter placement is associated with the following risks:

- Increased risk for recurrent DVT
- IVC perforation
- Filter migration / embolization
- Filter fracture with embolization of components
- Infection
- Inferior vena cava syndrome

Given these risks, IVC filters should not be placed solely on the basis of SVT or for DVT isolated to the calf veins. Isolated distal DVT (i.e., DVT confined to the tibial, peroneal, soleus, or gastrocnemius veins) has a low risk of causing PE without first propagating to the proximal deep veins. IVC filters should not be used for a purely prophylactic indication.

Decision guide

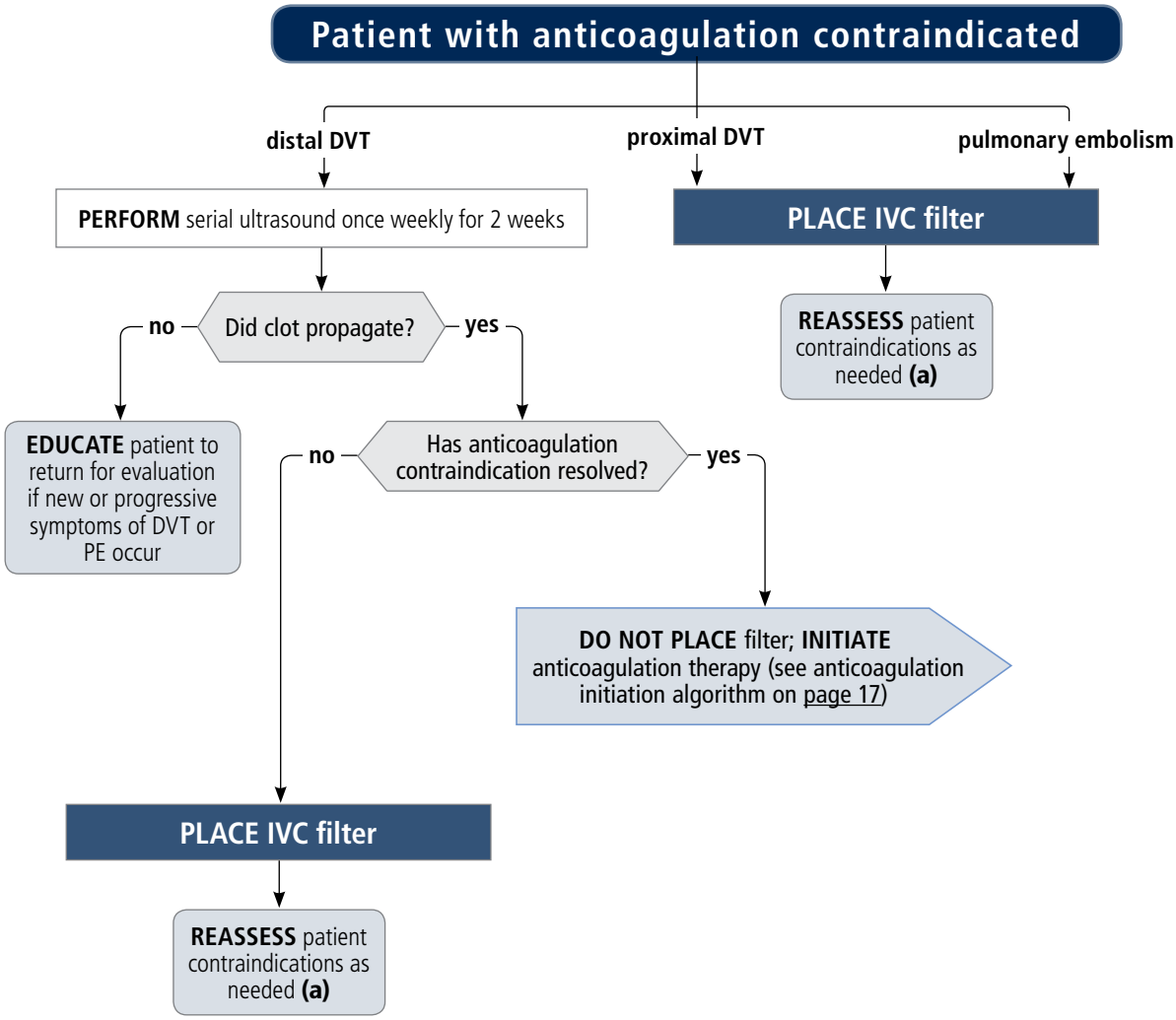
The only evidence-based indication for placing an IVC filter is the presence of an acute proximal DVT or PE and a contraindication to anticoagulation. Some guidelines suggest IVC filter placement in other situations, listed in the "consider" category below. While the benefit of an IVC filter is not proven in these situations, a clinician may choose to place an IVC filter after careful consideration.

IVC filter placement considerations	
PLACE filter if **BOTH:** (see page 20)	**CONSIDER** placing **IF ANY:**
• Confirmed acute PE or proximal DVT **AND** • Anticoagulation contraindication	• New proximal DVT or PE despite adequate anticoagulation • Anticoagulation therapy must be interrupted during acute phase of treatment after new proximal DVT or PE • Impaired cardiac reserve and significant proximal DVT • Undergoing interventional therapy for DVT (catheter-directed thrombolysis)

If an IVC filter is placed, anticoagulation contraindications should be monitored over time and anticoagulation should be reconsidered when resolved. If anticoagulants are resumed and are tolerated, the IVC filter should be removed. The chance of a successful retrieval remains high for at least the first two to three months that the filter is in place. Be sure to implement a follow-up plan with a reminder system to ensure that the IVC filter is retrieved when anticoagulation has been resumed and is being tolerated.

See the IVC filter placement algorithm on page 21 for further instructions.

ALGORITHM 9: INFERIOR VENA CAVA (IVC) FILTER PLACEMENT



ALGORITHM NOTE

(a) REASSESS patient contraindications

REASSESS patient weekly for up to ~3 months.

If contraindication resolves:

- **BEGIN** anticoagulant therapy (see table 1 on page 18)
- **RETRIEVE** IVC filter if patient tolerates anticoagulation therapy (1–2 weeks of therapy without bleeding)

If contraindication does not resolve and is not expected to resolve upon re-evaluation, consider leaving IVC filter in place permanently. Some clinicians consider retrieving IVC filter after 3–6 months if the original thrombosis resolved. There is no strong evidence to guide this decision, and individual clinical judgment is required.

RESOURCES

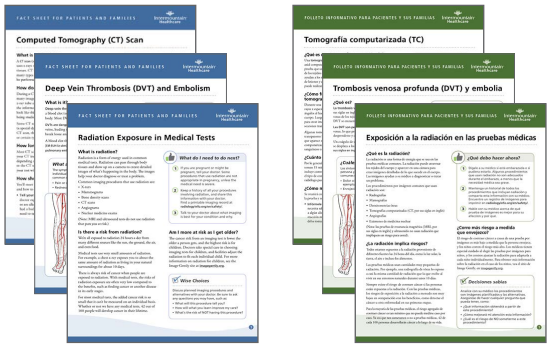
Intermountain-approved patient education

Intermountain education materials are designed to support educating and engaging patients and families. They complement and reinforce clinical team interventions by providing a means for patients to reflect and learn in another mode and at their own pace.

To access these materials (available in both English and Spanish), go to intermountainphysician.org, and search for the **Patient Education Library** under the **A–Z Index**. Then, search the title in the appropriate area. Clinicians can also order Intermountain patient education booklets and fact sheets for distribution to their patients from Intermountain's Design and Print Center.

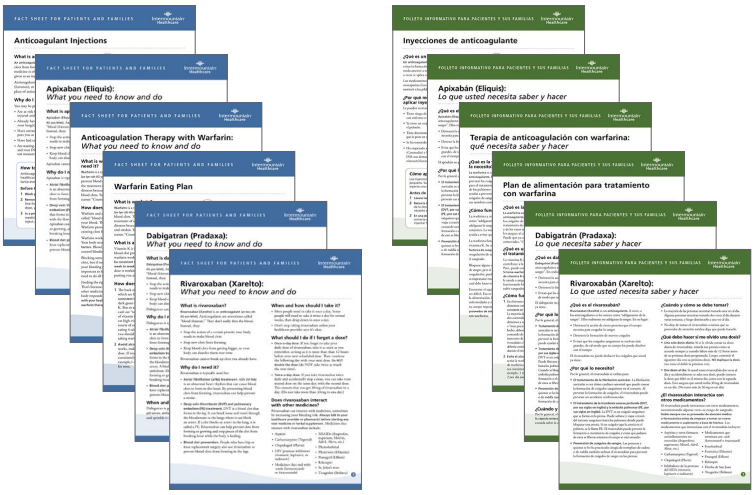
Fact sheets (non-medication related):

- *Computed Tomography (CT) Scan*
- *Deep Vein Thrombosis and Pulmonary Embolism*
- *Radiation Exposure in Medical Tests*



Fact sheets (medication-related):

- *Anticoagulant Injections*
- *Apixaban (Eliquis): What you need to know and do*
- *Anticoagulation Therapy with Warfarin: What you need to know and do*
- *Warfarin Eating Plan*
- *Dabigatran (Pradaxa): What you need to know and do*
- *Rivaroxaban (Xarelto): What you need to know and do*



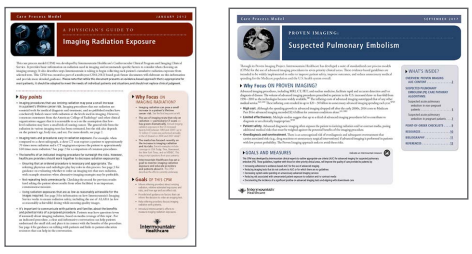
Provider resources

To find this CPM, clinicians can go to intermountainphysician.org/clinical/ and click on **Clinical Topics A–Z** on the left side of the screen. Then, select **Vascular Disease** under "V."

To find and print Intermountain anticoagulation guidelines, go to intermountain.net, and type "ATF" in the search bar. Select **Anticoagulation Task Force (ATF)** from the query results.

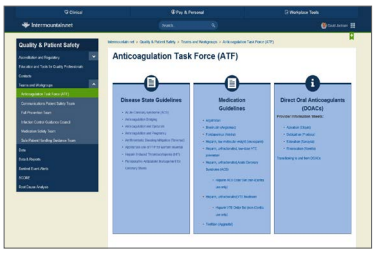
Care process models (CPMs):

- *Imaging Radiation Exposure*
- *Proven Imaging: Suspected Pulmonary Embolism*



Anticoagulation Task Force guidelines:

- Disease State Guidelines
- Medication Guidelines
- Direct Oral Anticoagulants



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CHA2 Chan WS, Lee A, Spencer FA, et al. Predicting deep venous thrombosis in pregnancy: Out in "LEFt" field? *Ann Intern Med.* 2009;151(2):85–92. Accessed Jan 18, 2013.

DOS Doshi SK, Negus IS, Oduko JM. Fetal radiation dose from CT pulmonary angiography in late pregnancy: A phantom study. *Br J Radiol.* 2008;81(968):653–658. Accessed Dec. 6, 2012.

GIO Giordano NJ, Jansson PS, Young MN, Hagan KA, Kabrhel C. Epidemiology, pathophysiology, stratification, and natural history of pulmonary embolism. *Tech Vasc Interv Radiol.* 2017;20(3):135-140.

KAU Kaufman JA, Kinney TB, Streiff MB, et al. Guidelines for the use of retrievable and convertible vena cava filters: Report from the Society of Interventional Radiology multidisciplinary consensus conference. *J Vasc Interv Radiol.* 2006;17(3):449-459.

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This CPM presents a model of best care based on the best available scientific evidence at the time of publication. It is not a prescription for every physician or every patient, nor does it replace clinical judgment. All statements, protocols, and recommendations herein are viewed as transitory and iterative. Although physicians are encouraged to follow the CPM to help focus on and measure quality, deviations are a means for discovering improvements in patient care and expanding the knowledge base. Send feedback to Scott Stevens, MD, Intermountain Healthcare, Co-director, Intermountain Medical Center Thrombosis Clinic (scott.stevensmd@imail.org).