Overview of the treatment of lower extremity deep vein thrombosis (DVT)

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INTRODUCTION — Deep vein thrombosis (DVT) and acute pulmonary embolism (PE) are two manifestations of venous thromboembolism (VTE). VTE contributes to significant morbidity and mortality both in the community and in hospital. The mainstay of therapy for DVT is anticoagulation, provided there is no contraindication. Following initial anticoagulation, patients with DVT are anticoagulated further to prevent future recurrences, embolism, and thrombosis-related death.

An overview of the treatment of lower extremity DVT (distal and proximal), including indications for anticoagulation, alternate therapies, and treatment of special populations of patients with DVT, are discussed in this topic. Initial, long-term, and extended (indefinite) anticoagulation for DVT, as well as the treatment of PE, upper extremity DVT, and the diagnosis and prevention of DVT, are discussed in detail separately. (See "Venous thromboembolism: Initiation of anticoagulation (first 10 days)" and "Venous thromboembolism: Anticoagulation after initial management" and "Rationale and indications for indefinite anticoagulation in patients with venous thromboembolism" and "Treatment, prognosis, and follow-up of acute pulmonary embolism in adults" and "Clinical presentation and diagnosis of the nonpregnant adult with suspected deep vein thrombosis of the lower extremity" and "Prevention of venous thromboembolic disease in acutely ill hospitalized medical adults" and "Prevention of venous thromboembolic disease in surgical patients").

NOMENCLATURE — For the purposes of discussion in this topic, the following terms apply:

● The term unprovoked deep vein thrombosis (DVT) implies that no identifiable provoking environmental event for DVT is evident [1]. In contrast, a provoked DVT is one that is usually caused by a known event (eg, surgery, hospital admission). VTE events can be provoked by transient major risk factors (ie, major surgery >30 minutes, hospitalization or immobility ≥3 days, Cesarean section), transient minor risk factors (minor surgery <30 minutes, hospitalization <3 days, pregnancy, estrogen therapy, reduced mobility ≥3 days) or persistent risk factors. Persistent risk factors include reversible conditions (eg, curable malignancy, inflammatory bowel disease that resolves) and irreversible conditions such as inheritable thrombophilias, chronic heart failure, and metastatic end-stage malignancy. (See "Overview of the causes of venous thrombosis".)

● Proximal DVT is one that is located in the popliteal, femoral, or iliac veins. Isolated distal DVT has no proximal component, is located below the knee, and is confined to the calf veins (peroneal, posterior, anterior tibial, and muscular veins) (table 1).

● Symptomatic DVT refers to the presence of symptoms that usually leads to the radiologic confirmation of DVT, whereas asymptomatic DVT refers to the incidental finding of DVT on imaging in a patient without symptoms (eg, computed tomography). (See "Clinical presentation and diagnosis of the nonpregnant adult with suspected deep vein thrombosis of the lower extremity").
Initial anticoagulation refers to anticoagulant therapy that is administered during the first few days (up to 10 days) following a diagnosis of DVT. Long-term anticoagulant therapy is typically administered for a finite time beyond the initial period, usually three to six months, and occasionally up to 12 months. Extended anticoagulation refers to therapy that is administered indefinitely. (See "Venous thromboembolism: Initiation of anticoagulation (first 10 days)" and "Venous thromboembolism: Anticoagulation after initial management" and "Rationale and indications for indefinite anticoagulation in patients with venous thromboembolism").

Direct factor Xa and thrombin inhibitors have been referred to using a variety of names including newer/novel oral anticoagulants, non-vitamin K antagonist oral anticoagulants (NOAs, NOACs), direct oral anticoagulants (DOACs), and target-specific oral anticoagulants (TOACs, TSOACs) [2,3]. Throughout this topic, we refer to these agents by their pharmacologic class, direct factor Xa and thrombin inhibitors. (See "Direct oral anticoagulants and parenteral direct thrombin inhibitors: Dosing and adverse effects").

INDICATIONS — Anticoagulation is the mainstay of therapy for patients with deep vein thrombosis (DVT) (algorithm 1). Anticoagulation is indicated for all patients with proximal DVT and select cases of distal DVT. The decision to anticoagulate must weigh the benefits of anticoagulation against the risk of bleeding for an individual. The primary objective of anticoagulation is the prevention of further thrombosis and of early and late complications. Major early complications of DVT include further clot extension, acute pulmonary embolus (PE), major bleeding (from anticoagulation), and death. Late complications include recurrent clot, post-thrombotic (post phlebitic) syndrome, and chronic thromboembolic pulmonary hypertension. (See "Treatment, prognosis, and follow-up of acute pulmonary embolism in adults" and "Post-thrombotic (postphlebitic) syndrome" and "Clinical manifestations and diagnosis of chronic thromboembolic pulmonary hypertension").

The indication to anticoagulate is stronger for patients with proximal DVT (popliteal, femoral, iliac vein) than with distal DVT (calf vein) because the risk of complications is higher, especially embolization and death. As an example, older studies reported that over 90 percent of acute PE arise from the proximal veins [4,5]. Another prospective analysis of 1643 patients anticoagulated for acute DVT (OPTIMEV) reported that the mortality rate of proximal DVT is higher than that of distal DVT (8 versus 4 percent) [6].

The indications to anticoagulate are based upon a definitive diagnosis of DVT, usually made on compressive ultrasound (CUS) of the lower extremities. In patients with asymptomatic proximal or distal DVT found incidentally by another imaging modality, usually computed tomography (CT), the diagnosis should be sought using CUS before anticoagulation due to the poorer sensitivity and specificity of CT. (See "Clinical presentation and diagnosis of the nonpregnant adult with suspected deep vein thrombosis of the lower extremity", section on 'Diagnostic ultrasonography suspected first DVT'.)

Proximal DVT — Proximal lower extremity DVT is thrombus that is located in the popliteal, femoral, or iliac veins (table 1). Anticoagulant therapy is indicated for all patients with proximal DVT, regardless of the presence of symptoms and provided there is no contraindication to anticoagulation (algorithm 1). This approach is supported by a seminal randomized trial that demonstrated a survival benefit with anticoagulation as well as randomized trials and meta-analyses of patients treated with variable durations of anticoagulant therapy.

Accurate estimates of recurrent thrombosis and death in patients with proximal DVT who are not treated with anticoagulant therapy are unknown. In the seminal trial, performed in 1960, that compared anticoagulation with observation in patients with acute DVT, anticoagulation resulted in a dramatic reduction in recurrence, which translated into a mortality benefit [7]. Since then, most other
trials have compared various doses and durations of anticoagulant therapy for DVT to provide an estimate of the risk of recurrence [8]. Nonetheless, these data all support low rates of recurrent venous thromboembolism (VTE) and death in patients treated with anticoagulant therapy for proximal DVT, with the greatest benefit occurring within the first few days or weeks of the initial event. As an example, one 2010 meta-analysis of 13 prospective cohort studies and 56 randomized clinical trials reported rates of recurrent VTE and fatal VTE during the first three months of anticoagulant therapy as 3.4 and 0.4 percent, respectively [8].

For patients with proximal DVT, the absence of symptoms (ie, incidental proximal DVT) does not alter the indication for anticoagulation. Although the safety and efficacy of anticoagulant therapy in patients with asymptomatic proximal vein DVT compared with symptomatic DVT is unknown, we and others prefer that this population of patients be managed in the same manner as symptomatic patients [9]. This preference is based upon the rationale that proximal DVT has a high risk of embolization and upon indirect evidence from patients with symptomatic proximal DVT that report a reduction in the risk of recurrence with anticoagulation.

Distal DVT — Isolated distal DVT encompasses thromboses located below the knee in the calf veins (ie, the popliteal vein is not involved). Most calf vein DVTs are located in the posterior tibial and peroneal veins while anterior tibial and muscular vein DVTs are uncommon (table 1). Notably, isolated distal DVT cannot be detected by routine proximal vein compression ultrasonography (proximal CUS) and although it can be detected by whole leg ultrasonography, the latter is difficult to perform and interpret and its use is institution-dependent; thus, to overcome this disadvantage serial proximal CUS can be used to detect thrombus that extends into the proximal veins. (See "Clinical presentation and diagnosis of the nonpregnant adult with suspected deep vein thrombosis of the lower extremity".)

The treatment of isolated distal DVT varies among centers and clinicians and represents a major challenge therapeutically. While some experts prefer that all patients with isolated distal DVT be anticoagulated, we and other experts agree that a select minority can avoid anticoagulation. This preference is based upon the rationale that patients with isolated distal DVT are at lower risk of embolization (approximately half the risk) than those with proximal DVT and that in some patients, the distal DVTs resolve spontaneously without therapy [9-21]. When the decision is made to anticoagulate patients with isolated distal DVT, full therapeutic anticoagulation should be administered similar to those with proximal DVT.

Anticoagulation — While in the past whole leg ultrasound frequently identified asymptomatic patients with isolated distal DVT, a shift towards presentation with symptomatic DVT has occurred such that we and others use symptoms as well as other clinical features to help us decide who to treat. In general, the following indications for anticoagulation apply:

● **Symptomatic** – In general, most clinicians agree that anticoagulation is indicated in most patients with symptomatic isolated distal DVT, provided the risk of bleeding is low [9,22-24]. However, some experts choose not to treat select patients who are considered a very low risk of embolization and are suitable candidates for surveillance; such patients include those with minor thrombosis in the muscular veins, those with a negative D-dimer level, those with nondiagnostic ultrasonography results, those with minor symptoms who are without risk factors for extension (see list in "Asymptomatic" bullet, below), and those at high risk of bleeding. (See 'Surveillance with serial ultrasound' below.)

● **Asymptomatic** – Additional indications for anticoagulation in asymptomatic patients or in patients with symptomatic DVT who opt for surveillance include (see 'Surveillance with serial ultrasound' below):
Patients with documented DVT extension into or toward the proximal veins during surveillance

Patients considered by their clinician to be at risk of extension to the proximal veins. This includes patients with:

- Unprovoked DVT
- D-dimer >500 mg/mL
- Extensive thrombosis involving multiple veins (eg, >5 cm in length, >7 mm in diameter)
- Thrombosis close to the proximal veins
- Persistent/irreversible risk factors such as active cancer [25]
- Prior DVT or PE
- Prolonged immobility
- Inpatient status

Support for this approach is based upon the risk of extension into the proximal veins (ie, the popliteal vein or higher) where the indication to anticoagulate is stronger due to the higher risk of embolization and the proven efficacy in this population of anticoagulation in reducing clot extension [9]. As examples:

- Natural history studies suggest that when left untreated, approximately one-third of patients with symptomatic isolated distal DVT will develop extension into the proximal veins, most often within the first two weeks after diagnosis [10-19].

- One meta-analysis that included two randomized and six nonrandomized cohort studies of patients with isolated distal DVT reported that, compared with those who were followed with serial ultrasound, proximal thrombus propagation was less likely to occur in those receiving anticoagulation (odds ratio [OR] 0.29, 95% CI 0.14-0.62) [20]. However, the methodologic quality of most studies was poor and the number of outcome events that occurred (ie, deaths, PE, proximal DVT extension, bleeding) was small, which limited the analysis. A similar meta-analysis reported a reduction in the risk of recurrent VTE (OR 0.5) in those who were anticoagulated without an increased risk in the rate of bleeding (OR 0.64) compared with those who did not receive anticoagulation [26].

Surveillance with serial ultrasound — Select patients with isolated distal DVT may be subjected to surveillance with serial ultrasound to look for extension of lower extremity clot into the proximal veins. Candidates that may be suitable for this approach are discussed above. (See 'Distal DVT' above.)

Support for this approach is derived from studies that suggest that the risk of embolization in patients with isolated distal DVT is low and approximately half that of proximal DVT [27]. As an example, several retrospective and prospective observational studies reported that limited thrombosis confined to the muscular veins, compared with extensive thrombosis of multiple calf veins, appears to have a low risk of extension without therapy (about 3 versus 15 percent) [9-12,14,17,18,23]. In addition, if extension does not occur within two weeks, it is unlikely to occur.
The optimal frequency, duration, and method of surveillance are unknown. We generally survey patients every week for two weeks with proximal compressive ultrasound (CUS) for clot extension or resolution.

- If thrombus resolves, no anticoagulation is required.
- If thrombus extension is observed into the proximal veins, patients should be anticoagulated or treated with an inferior vena cava filter if a contraindication to anticoagulation exists.
- If thrombus extends toward the proximal veins but remains confined to the calf, we suggest anticoagulation rather than continued surveillance with CUS.
- For patients in whom clot does not resolve but remains stable, longer periods of surveillance may be required.

For surveillance, we prefer proximal rather than whole leg CUS because it is sufficient for the detection of proximal DVT, where the indication for anticoagulation is strong.

**ASSESSING BLEEDING RISK** — All patients should be assessed before and during anticoagulant therapy for bleeding risk (table 2 and table 3). Patients, especially those on direct factor Xa and thrombin inhibitors and those >75 years, should also be assessed for the signs and symptoms of conditions that may affect the half-life of the administered anticoagulant (eg, renal failure, weight loss, pregnancy). In all patients, the decision to anticoagulate should be individualized and the benefits of venous thromboembolism (VTE) prevention carefully weighed against the risk of bleeding. Absolute and relative contraindications to anticoagulation are discussed separately. (See 'Patients with contraindications to anticoagulation' below.)

The administration of anticoagulation is always associated with an increased risk of bleeding, which is in turn dependent upon the degree of anticoagulation and the presence of pre-existing factors for bleeding. Tools are available for estimating the risk of bleeding in anticoagulated individuals (eg, HAS-BLED score) (calculator 1). However, none of these tools has been validated in patients anticoagulated for VTE and no one index can reliably predict bleeding risk in a particular patient such that for practical purposes, many clinicians use a gestalt estimate for assessing bleeding risk. A VTE-specific bleeding score has been generated (VTE-Bleed) using data derived from randomized trials that studied the direct oral thrombin inhibitor, dabigatran, as an anticoagulant for VTE [28]; however, VTE-bleed requires external validation before it can be recommended for routine use. Details regarding the use of scoring systems that estimate the risk of bleeding are discussed separately. (See "Rationale and indications for indefinite anticoagulation in patients with venous thromboembolism", section on 'Assessing the risk of bleeding' and "Management of warfarin-associated bleeding or supratherapeutic INR", section on 'Bleeding risk'.)

Most clinicians agree that patients with a three-month bleeding risk of less than 2 percent (low risk) should be anticoagulated. In addition, most clinicians agree that patients with a three-month bleeding risk of more than 13 percent (high risk) should not be anticoagulated [9]. For patients with an estimated bleeding risk between these values, there is no agreement regarding the preferred approach such that the decision to anticoagulate in this population must be individualized according to the values and preferences of the patient as well as the risk-benefit ratio, which may change over time. As an example, the benefits of anticoagulation are greater during the initial period of anticoagulation than at the end of a finite period of three months. Patients who wish to avoid the risk of bleeding on anticoagulation should be considered for an inferior vena cava filter. (See "Rationale and indications for indefinite anticoagulation in patients with venous thromboembolism", section on
'Our approach' and "Placement of vena cava filters and their complications" and 'Inferior vena cava filter' below.)

ANTICOAGULATION

Initial anticoagulation (first 10 days) — Initial anticoagulation refers to systemic anticoagulation administered for the first few days (up to 10 days) following a diagnosis of deep vein thrombosis (DVT) [9,24,29]. In most patients, anticoagulation should be started immediately as a delay in therapy may increase the risk of potentially life threatening embolization [30,31].

Selection of agent — Options include subcutaneous low molecular weight (LMW) heparin, subcutaneous fondaparinux, the oral factor Xa inhibitors rivaroxaban or apixaban, or unfractionated heparin (UFH). A decision between these agents is usually made based upon clinician experience as well as the risks of bleeding, patient comorbidities, preferences, cost, and convenience (table 4). Warfarin cannot be administered alone as an initial anticoagulant for DVT because of the delay in depletion of the vitamin K-dependent coagulation factors. Selecting an initial anticoagulant, dosing for parenteral and oral anticoagulants, and empiric anticoagulation in the general population as well as in patients with malignancy and pregnancy, are discussed in detail, separately. (See "Venous thromboembolism: Initiation of anticoagulation (first 10 days)" and "Treatment of venous thromboembolism in patients with malignancy" and "Deep vein thrombosis and pulmonary embolism in pregnancy: Treatment".)

Outpatient therapy — Not all patients who have acute DVT need to be admitted to the hospital for systemic anticoagulation. The decision to treat DVT in the outpatient setting should be made in the context of the patient's understanding of the risk-benefit ratio, preferences, and clinical condition. Factors determining who may be considered for outpatient therapy are not well defined. However, several randomized trials and meta-analyses that have compared outpatient therapy with LMW heparin to inpatient therapy with IV UFH suggest that treatment at home with LMW heparin is safe and effective in select patients [9,32-45]. Anticoagulant therapy should not be delayed while the decision is being made to treat the patient at home.

When considering outpatient administration of LMW heparin, patient selection is critical:

● Outpatient therapy can be considered when patients have all of the following features (table 5):

  • Hemodynamically stable

  • A low risk of bleeding

  • No renal insufficiency

  • A practical system in place at home for the administration and surveillance of anticoagulant therapy (eg, good living conditions, caregiver support, phone access, understanding and ability to return to the hospital should deterioration occur)

● Outpatient therapy is not appropriate in patients with [46]:

  • Massive DVT (eg, iliofemoral DVT, phlegmasia cerulea dolens)

  • Concurrent symptomatic pulmonary embolism (PE)
High risk of bleeding on anticoagulant therapy

Comorbid conditions or other factors that warrant in-hospital care

For patients in whom outpatient therapy is selected, we suggest the use of LMW heparin overlapped with warfarin (dual therapy), pre-treatment with LMW heparin followed by the administration of either dabigatran or edoxaban (dual therapy), or anticoagulation with either rivaroxaban or apixaban (monotherapy; ie, no need for heparin pre-treatment). Selecting an agent should be individualized and is dependent upon the risk of bleeding, patient comorbidities, preferences, cost, and convenience. Data that support these approaches are discussed below:

**LMW heparin plus warfarin** – Evidence to support this combination is derived from randomized trials and meta-analyses that have compared LMW heparin delivered at home following immediate discharge from the emergency or outpatient department or following a brief inpatient stay (eg, one day). However, these trials have been intrinsically flawed because of differences in the LMW heparin used, follow-up therapy (warfarin and LMW heparin), and differences in randomization to home therapy, which was not explicitly performed in many studies. (See "Venous thromboembolism: Anticoagulation after initial management", section on 'Low molecular weight heparin'.)

As examples:

- One 2012 meta-analysis of six randomized trials totaling 1708 patients with acute DVT compared outpatient use of LMW heparin with inpatient IV UFH [9]. Outpatient therapy with LMW heparin was associated with reductions in the rate of recurrent venous thromboembolism (VTE; risk reduction [RR] 0.61, 95% CI 0.42-0.9), major bleeding (RR 0.67, 95% CI 0.33-1.36), and mortality (RR 0.72, 95% CI 0.45-1.15). Another 2007 meta-analysis of six older studies reported similar results [43].

- A 2003 meta-analysis of eight trials that also included patients with brief inpatient stays (24 hours or less) for acute DVT reported that compared with inpatients treated with heparin, those treated as an outpatient had similar rates of recurrent DVT (4 versus 6 percent) and major bleeding (0.5 versus 1 percent) [39].

**LMW heparin followed by dabigatran or edoxaban** – Randomized trials that support efficacy of this combination only studied efficacy for dabigatran (direct thrombin inhibitor) and edoxaban (factor Xa inhibitor) when patients were treated with these agents following a 5 to 10 day course of heparin (usually LMW heparin; ie, dual therapy). Consequently, we suggest that dabigatran and edoxaban not be routinely used as a monotherapy for initial anticoagulation in outpatients but can be used in this setting provided that an initial course of heparin has been administered, similar to the original study protocols that proved their efficacy [47,48]. These studies and how to transition from heparin to these agents are discussed in detail separately. (See "Venous thromboembolism: Anticoagulation after initial management", section on 'Direct thrombin and factor Xa inhibitors'.)

**Rivaroxaban or apixaban monotherapy** – Randomized trials of rivaroxaban and apixaban reported efficacy of both of these factor Xa inhibitors as the sole initial anticoagulant (monotherapy) [49,50]. Although short periods (<48 hours) of heparin were allowed prior to randomization, our experience with these agents is in keeping with the data that suggest monotherapy with these agents is safe and effective when administered to the outpatient population (ie, without heparin pre-treatment). These studies are discussed in detail separately. (See "Venous thromboembolism: Anticoagulation after initial management", section on 'Direct thrombin and factor Xa inhibitors'.)
Subcutaneous unfractionated heparin (UFH) has not been adequately studied in this population and as such cannot be routinely recommended. (See "Heparin and LMW heparin: Dosing and adverse effects").

Cost savings due to the avoidance of an inpatient stay is a frequently cited advantage of outpatient anticoagulation, and is estimated to range from $500 to $2500 per patient [39,51-57]. Randomized trials and meta-analyses of nonrandomized trials have suggested that the cost of outpatient therapy with LMW heparin is similar to, or lower than, the cost of strategies that utilize unfractionated heparin, regardless of the treatment setting (eg, inpatient versus outpatient) [51,52,58-60]. These data should be interpreted with caution as many studies were biased and were limited in their sensitivity analysis.

The outpatient treatment of PE is discussed separately. (See "Treatment, prognosis, and follow-up of acute pulmonary embolism in adults", section on 'Outpatient anticoagulation'.)

Long-term anticoagulation (10 days to 3 months) — Long-term anticoagulant therapy is administered beyond the initial few days of anticoagulation for a finite period of typically three to six months, and up to 12 months in some cases (eg, phlegmasia cerulea dolens, a persisting but reversible risk factor). In some patients this is the same agent that was selected for initial anticoagulation (eg, LMW heparin, rivaroxaban and apixaban), but in others, the initial agent and the selected long term agent belong to different classes, such that transitioning from one agent to another is necessary (eg, heparin to warfarin, heparin to edoxaban or dabigatran). Full anticoagulation should be ensured during transition periods and interruptions should be minimized during the first three months of long-term anticoagulation because this is the period that has the highest risk of recurrent thrombosis. (See "Venous thromboembolism: Anticoagulation after initial management").

Selection of agent — Options for long-term anticoagulation are either oral or subcutaneous. Oral anticoagulants include direct factor Xa inhibitors (rivaroxaban, apixaban, or edoxaban), thrombin inhibitors (dabigatran), and vitamin K antagonists (warfarin); subcutaneous anticoagulants include LMW heparin, and fondaparinux. While the factor Xa and thrombin inhibitors are preferred, a decision between these agents is usually made based upon clinician experience as well as the risks of bleeding, patient comorbidities, preferences, cost, and convenience (table 4). Because individual patients perceive burdens differently, patient’s values and preferences are particularly critical in selecting a long-term agent for anticoagulation in acute DVT. Selecting an agent and dosing in the general population as well as in patients with malignancy and pregnancy, are discussed in detail separately. (See "Venous thromboembolism: Anticoagulation after initial management", section on 'Selection of agent' and "Deep vein thrombosis and pulmonary embolism in pregnancy: Treatment" and "Treatment of venous thromboembolism in patients with malignancy").

Duration of therapy — A decision regarding the optimal duration of anticoagulation must take into account the presence or absence of provoking events, risk factors for recurrence and bleeding, and the individual patient's preferences and values. Although there is agreement on the minimum length of time a patient with a first episode of DVT should be treated (ie, three months), the optimal length of time is not known. For most patients with a first episode of DVT (provoked and unprovoked, proximal and distal), anticoagulants should be administered for three months rather than for shorter periods (eg, four or six weeks) (algorithm 1). Most experts also agree that extending anticoagulation beyond three months is considered in select populations. Duration of therapy and indications for indefinite anticoagulation are discussed in detail separately. (See "Venous thromboembolism: Anticoagulation after initial management", section on 'Duration of treatment' and "Rationale and indications for indefinite anticoagulation in patients with venous thromboembolism", section on 'Our approach').
Indefinite anticoagulation — The decision to anticoagulate patients with DVT indefinitely should be based upon an estimate of the risk of recurrence and bleeding in the context of the clinical nature of the episode of the DVT (eg, provoked or unprovoked DVT, reversible or irreversible risk factors) as well as the patient's values and preferences (eg, occupation, life expectancy, burden of therapy). While there is consensus regarding the need to anticoagulate select patients with acute DVT indefinitely, there is no agreed-upon best approach [9,24,61,62]. Patients in whom indefinite anticoagulation should be considered and agent selection for this population are discussed separately. (See "Rationale and indications for indefinite anticoagulation in patients with venous thromboembolism" and "Venous thromboembolism: Anticoagulation after initial management", section on 'Duration of treatment'.)

SPECIAL POPULATIONS — Special populations of patients with acute deep vein thrombosis (DVT) require specific consideration including those listed in this section (table 4).

Patients with contraindications to anticoagulation — For patients with acute proximal DVT in whom anticoagulation is contraindicated or in whom the risk of bleeding is estimated by the clinician to outweigh the risk of venous thromboembolism (VTE), an inferior vena cava (IVC) filter should be placed promptly. Patients with acute distal DVT in whom anticoagulation is contraindicated may be managed with surveillance ultrasonography. The indications and details of IVC filter placement are discussed separately. (See 'Inferior vena cava filter' below.)

Absolute contraindications to anticoagulation include:

- Active bleeding
- Severe bleeding diathesis
- Platelet count <50,000/microL (sometimes lower depending upon the strength of the indication)
- Recent, planned, or emergent high bleeding-risk surgery/procedure
- Major trauma
- History of intracranial hemorrhage (ICH) particularly recent ICH

Relative contraindications to anticoagulation include:

- Recurrent bleeding from multiple gastrointestinal telangiectasias
- Intracranial or spinal tumors
- Platelet count <100,000/microL
- Large abdominal aortic aneurysm with concurrent severe hypertension
- Stable aortic dissection
- Recent, planned, or emergent low bleeding-risk surgery/procedure

Patients with a remote history of ICH (eg, due to aneurysm successfully ablated), may be candidates for anticoagulation.
Special consideration should also be given to avoiding anticoagulation, when feasible, in older patients (eg, >65 years) with a history of multiple falls and the presence of more than one factor that elevates the bleeding risk. Such patients are at high risk of bleeding or have a high risk of a catastrophic result should a bleed occur. Consequently, the decision to anticoagulate in these populations should be even more cautious to allow the benefits of VTE prevention to be carefully weighed against the risk of bleeding.

Patients with a recent episode of minor bleeding such as epistaxis or heavy menstrual bleeding are not generally considered high risk for bleeding and anticoagulation can usually be administered safely in this population.

The management of anticoagulation perioperatively and assessing the risk of bleeding are discussed separately. (See 'Assessing bleeding risk' above and "Rationale and indications for indefinite anticoagulation in patients with venous thromboembolism", section on 'Assessing the risk of bleeding' and "Perioperative management of patients receiving anticoagulants").

Patients with malignancy — In patients with cancer, treatment of DVT is associated with higher morbidity, due to higher than usual rates of both recurrent thrombosis and anticoagulant-associated bleeding. For patients with malignancy and DVT who have a reasonable life expectancy and who do not have severe renal insufficiency (creatinine clearance <30 mL/minute), or a contraindication to anticoagulation, low molecular weight (LMW) heparin is preferred for both initial and long-term anticoagulation rather than other agents. Further discussion of the treatment of venous thromboembolism in patients with malignancy is discussed in detail, separately. (See "Treatment of venous thromboembolism in patients with malignancy").

Pregnancy — Pregnancy is a risk factor for the development of DVT. Adjusted-dose subcutaneous LMW heparin is the preferred agent for initial and long-term anticoagulation in pregnant women with acute DVT. This agent is preferred, because it has a more favorable safety profile, especially when compared with warfarin. Warfarin freely crosses the placental barrier and can produce an embryopathy when given between the sixth and ninth weeks of pregnancy. Intravenous and subcutaneous forms of unfractionated heparin (UFH) are alternatives to LMW heparin. Fondaparinux and oral factor Xa and direct thrombin inhibitors have not been adequately tested in pregnant women with acute DVT and as such should not be administered. The treatment of DVT and use of anticoagulants in pregnancy are discussed in detail separately. (See "Deep vein thrombosis and pulmonary embolism in pregnancy: Treatment" and "Use of anticoagulants during pregnancy and postpartum").

Phlegmasia cerulea dolens — Although uncommon, it is important to identify patients with phlegmasia cerulea dolens (PCD; massive iliofemoral DVT) because they should be considered for more aggressive management, usually thrombolysis and/or thrombectomy. Intravenous (IV) UFH is usually the anticoagulant of choice while a decision to pursue more aggressive therapy is being considered. Patients with extensive DVT but without signs of PCD do not routinely receive thrombolysis but should be anticoagulated and monitored closely for the development of PCD.

Clinical presentation — PCD is part of a clinical spectrum that ranges from phlegmasia alba dolens to venous gangrene [63-66]. PCD results from acute massive venous thrombosis that causes an obstruction of the venous drainage of an extremity (upper or lower) and is associated with a high degree of morbidity. Patients usually present with sudden severe pain, swelling, cyanosis, edema, venous gangrene, and compartment syndrome that together impair arterial supply, such that circulatory collapse and shock frequently ensue. Delay in treatment may result in death or loss of the patient's limb.
PCD occurs at any age but is more common during the fifth and sixth decades [63,64,67]. The incidence is higher in females than in males. Malignancy is the most common triggering factor and is present in approximately 20 to 40 percent of patients. Other associated risk factors include the typical risk factors for thrombosis (eg, inherited thrombophilias, surgery, trauma, vena caval filter insertion, pregnancy). Approximately 10 percent of patients have idiopathic PCD.

In the lower extremities, left-sided involvement is three to four times more common than right-sided involvement [64]. Upper extremity PCD is unusual and occurs in less than 5 percent of patients.

Manifestations may be gradual or fulminant. Most cases are preceded by phlegmasia alba dolens, with symptoms of edema, pain, and blanching (alba) without cyanosis. As it progresses, massive fluid sequestration may lead to bleb and bullae formation and eventually cyanosis (cerulea) and venous gangrene ensue. The pain is constant, severe, and usually starts at the femoral triangle and progresses to the entire extremity. Cyanosis is the pathognomonic finding of PCD, progressing from distal to proximal areas.

Management — PCD is the only accepted indication for thrombolysis and/or thrombectomy in patients with DVT, especially in those with signs of ischemia or gangrene. Accordingly, catheter-directed thrombolysis or rapid removal of the occluding thrombus using manual techniques (eg, surgical or catheter-directed thrombectomy) should be seriously considered in this population of patients [68-74]. Thus, it is prudent to obtain an interventional radiology and/or vascular surgery consultation for patients with PCD, especially those with impending gangrene. The selected intervention(s) will depend upon available expertise. Detailed discussion of thrombolytic therapy and thrombectomy for this population are discussed separately. (See "Fibrinolytic (thrombolytic) therapy in acute pulmonary embolism and lower extremity deep vein thrombosis", section on 'Lower extremity deep vein thrombosis' and 'Thrombolytic therapy and thrombectomy' below.)

Importantly, delayed implementation of these procedures should not prohibit the administration of initial systemic anticoagulation with IV UFH. Our preference for IV UFH as the initial anticoagulant is based upon clinical experience and lack of data to support low molecular weight heparin or direct oral anticoagulants in this population, as well as the potential need to acutely discontinue anticoagulation when/if the decision is made to proceed with thrombolysis or thrombectomy. Once the threat of ischemia is resolved, most experts similar to the general population treat with anticoagulants for minimum of three months, similar to the general population; however, the selection of agent for long term therapy and total duration of therapy should be individualized [9]. (See "Venous thromboembolism: Anticoagulation after initial management" and "Rationale and indications for indefinite anticoagulation in patients with venous thromboembolism".)

Heparin-induced thrombocytopenia — For patients with a DVT and a diagnosis of heparin-induced thrombocytopenia (HIT), all forms of heparin should be discontinued. This includes UFH, LMW heparin, heparin flushes, heparin-bonded catheters, and heparin-containing medications. Immediate anticoagulation with a non-heparin anticoagulant (eg, argatroban, danaparoid, fondaparinux) is indicated, unless there is a strong contraindication to anticoagulation. The diagnosis and management of patients with HIT are discussed in detail, separately. (See "Clinical presentation and diagnosis of heparin-induced thrombocytopenia" and "Management of heparin-induced thrombocytopenia".)

ADDITIONAL THERAPIES — Additional considerations for patients diagnosed with acute deep vein thrombosis (DVT) include ambulation and graduated compression stockings for the prevention of post-thrombotic syndrome (postphlebitic) (PTS) as well as thrombolytic therapy and inferior vena cava filter placement, which are discussed in the sections below.
Ambulation — Despite prior concerns regarding the potential for embolization, early ambulation is safe in patients with acute DVT and should be encouraged as soon as is feasible.

Several small randomized studies and meta-analyses have shown that early ambulation does not increase the risk of recurrent or fatal pulmonary embolism (PE) [32,33,75-83]. The risk of PE during more aggressive forms of exercise, physical therapy, or rehabilitation is unknown. However, in this setting we typically gradually increase exercise training as tolerated by the patient. Symptoms such as pain or leg edema may limit ambulation. Compression stockings may be useful for symptomatic relief and the promotion of ambulation.

Compression stockings for the prevention of PTS — In general, we prefer to avoid the routine use of elastic graduated compression stockings (GCS) that provide 30 to 40 mmHg of ankle pressure for the prevention of PTS. This preference is based upon randomized studies that have not shown clear consistent benefit. However, if the decision is made to use compression stockings, they should be started after anticoagulant therapy, within two weeks of the diagnosis, and continued for two years.

Evidence evaluating elastic GCS for the prevention of PTS is conflicting with smaller trials suggesting benefit and one large randomized trial reporting no benefit [9,58,84-94]. Most trials were hampered by methodologic flaws including imprecise estimation of recurrence and differing criteria for the assessment of PTS (Ginsberg or Villalta criteria). In addition, many trials were not blinded and had variable initial randomization periods (zero to two weeks) and control groups (no stockings, stockings with 5 mmHg pressure at the ankles, GCS one to two sizes too big).

● Small randomized trials of patients with acute DVT (first or recurrent) that used the Villalta criteria for PTS, suggested that GCS that apply an ankle pressure of 30 to 40 mmHg started within two weeks and continued for two years to reduce the occurrence of PTS by 50 percent without increasing the frequency of recurrent VTE [85,86]. Patients most likely to benefit included those with a proximal DVT, prior DVT, and those with symptoms.

● In contrast, a randomized placebo-controlled trial of 806 patients with first proximal DVT reported no difference in the rate of PTS with GCS as measured by the less stringent Ginsberg criteria (leg pain and swelling one month or more; 14 versus 13 percent) [92]. A similar lack of benefit was reported when the more rigorous Villalta criteria were applied. Based upon this study, we and other experts do not routinely apply GCS for the prevention of PTS.

Although GCS are not harmful, many patients also decline their use because they are uncomfortable, costly, inconvenient, and often require a healthcare giver for their application. However, a subset of patients with recurrent DVT or moderate to severe symptoms may consider the potential benefits of GCS to outweigh these inconveniences. In such patients, the purpose of GCS is often focused on symptom reduction rather than prevention of PTS.

When the decision is made to wear GCS, they should be started after anticoagulant therapy. This is to avoid the theoretical risk of promoting embolism to the lung from fresh clot in the lower extremity. GCS should be continued for two years, replaced every six months, and may require refitting once local swelling is reduced. Alternative approaches of compressive bandages, application of GCS for limited periods (eg, for the duration of anticoagulation) or following thrombolytic therapy have not been adequately evaluated.

Contraindications to GCS include skin ulceration, severe arterial insufficiency, allergy to the stocking material, and inability to apply stockings.
The use of compression stockings as a therapy for PTS is discussed separately. (See "Post-thrombotic (postphlebitic) syndrome").

Thrombolytic therapy and thrombectomy — For most patients with acute lower extremity DVT, anticoagulant therapy alone is sufficient such that the routine use of thrombolytic therapy (systemic and catheter-directed) and/or thrombectomy (surgical or catheter-directed) is not indicated. Thrombolysis and/or thrombectomy are usually reserved for patients with phlegmasia cerulea dolens or massive iliofemoral DVT or for patients who fail therapeutic anticoagulation. Additionally, suitable candidates for thrombolysis should have symptoms for <14 days (ie, fresh clot; organized clot will not undergo lysis), good functional status, and low bleeding risk [9].

Thrombolytic therapy is not routinely administered for most patients with DVT. When compared with parenteral anticoagulation, although thrombolysis is associated with more rapid and complete lysis, reduced rates of PTS, and higher rates of preserved venous valve function, rates of recurrent venous thromboembolism and mortality are unchanged. In addition, the risk of major bleeding associated with systemic thrombolysis is considered by most experts to be unacceptably high when weighed against the benefits of decreased PTS.

Thrombolytic agents can be administered systemically or via a catheter inserted into the affected lower extremity vein (catheter-directed thrombolysis). It is generally considered that compared with systemic thrombolysis, catheter-directed thrombolysis can achieve clot lysis more rapidly and with lower doses, thereby reducing the risk of bleeding. One theoretical advantage of thrombolysis is a more complete removal of clot from smaller venules that cannot be removed surgically, a feature that may be important for patients with PCD who have severe venous gangrene [95,96]. (See 'Phlegmasia cerulea dolens' above.)

Mechanical thrombectomy (using catheter extraction or fragmentation) or surgical thrombectomy may also be considered as an alternative or adjunctive therapy to thrombolysis. It is thought that combined catheter-directed procedures (eg, thrombolysis plus fragmentation) may further minimize the risk of bleeding [9].

Thrombolytic therapy and the regimens used for acute PE and DVT are discussed in detail, separately. (See "Fibrinolytic (thrombolytic) therapy in acute pulmonary embolism and lower extremity deep vein thrombosis", section on 'Lower extremity deep vein thrombosis' and "Treatment, prognosis, and follow-up of acute pulmonary embolism in adults", section on 'Embolectomy'.)

Inferior vena cava filter — Inferior vena cava (IVC) filters, as stand-alone or adjunctive therapy, are not routinely inserted in patients with acute DVT. Typically, IVC filters (table 6) are used in patients with acute proximal DVT and PE who have an absolute contraindication to anticoagulant therapy (eg, recent surgery, hemorrhagic stroke, active bleeding) [97]. Although not considered absolute indications, placement of an IVC filter is also often considered as an adjunctive therapy in patients with recurrent embolism despite adequate anticoagulation, as well as in patients in whom an additional embolic event would be poorly tolerated (eg, those with poor cardiopulmonary reserve from massive PE or underlying cardiopulmonary disease, hemodynamically unstable patients), although this approach is unproven. The efficacy of IVC filter placement in patients with symptomatic isolated distal DVT is unknown and not generally performed. Filters are typically placed in the infrarenal portion of the IVC; as such, their major purpose is the prevention of embolization of lower extremity clot to the lung. In general, we prefer retrievable filters but the compliance with retrieval tends to be low. (See "Placement of vena cava filters and their complications").
For patients in whom an IVC filter is placed, we and others agree that once the risk of bleeding is assessed as low that a conventional course of anticoagulation therapy should be administered and the filter removed, when feasible [9]. (See 'Initial anticoagulation (first 10 days)' above.)

The many types of filters that are available, some of which are approved by regulatory agencies, are listed in the table (table 6). However, there are no data to suggest that one type of filter is superior to another.

In patients with acute DVT who have a contraindication to anticoagulation, retrospective and observational case series report that rates of recurrent PE following filter insertion are low (2 to 4 percent in most series) [97-100]. Although some cohort studies of patients with contraindications to anticoagulation report lower short-term fatality rates in patients with IVC filters, there is no evidence that IVC filters prevent PE-related death [97,101,102].

When IVC filters are used as an adjunctive therapy to anticoagulation, reports suggest no convincing efficacy. As examples:

● In one of the largest trials to date (PREPIC1) that examined the effectiveness of IVC filters, 400 patients with proximal DVT were randomly assigned to either standard anticoagulation alone or anticoagulation plus insertion of an IVC filter [103]. During the first 12 days after randomization, significantly fewer patients in the IVC filter group developed a PE (1 versus 5 percent). However, after a two-year follow-up period, there were no significant differences in survival or symptomatic PE between the two groups, and a significantly higher rate of DVT was observed among patients who had received an IVC filter (21 versus 12 percent). An eight-year follow-up of the same population of patients confirmed these findings that filter placement was associated with a successful reduction in the rate of PE (15 versus 6 percent) but an increase in the rate of DVT (35 versus 28 percent) [104]. No difference in mortality was reported.

● A similarly designed randomized trial (PREPIC2) reported outcomes in 399 patients with severe PE (eg, older patients >75 years, active cancer, signs of right ventricle dysfunction, chronic respiratory insufficiency) who received either standard anticoagulation alone or anticoagulation plus an IVC filter that was retrieved at three months [105]. The addition of an IVC filter to anticoagulation did not alter the rate of PE recurrence (1.5 versus 3 percent), DVT recurrence (0.5 percent), or mortality (7.5 versus 6 percent) at three months. The lack of benefit associated with IVC filter placement persisted by six months. The rate of filter complications (eg, thrombosis) was low (<2 percent).

● Data derived from the National Inpatient Sample reported that compared with thrombolytic therapy alone, the insertion of a vena cava filter was associated with a lower in-hospital case fatality rate among unstable patients who received thrombolytic therapy (8 versus 18 percent) as well as unstable patients who did not receive thrombolytic therapy (33 versus 51 percent) [102,106]. Filters did not improve in-hospital case fatality rate if DVT was diagnosed in hemodynamically stable patients. Although a database analysis of over 13,000 patients with PE who were treated with either thrombolytic or anticoagulant therapy demonstrated a reduction in hospital mortality in those who were adjunctively treated with an IVC filter compared with those who did not receive a filter (3 versus 5 percent), this study was limited by methodologic flaws [107].

Several studies report higher rates of DVT with IVC filter insertion, particularly in those in whom anticoagulation is contraindicated and those with known DVT [98,105,108-110]. As examples:

● A comprehensive review of retrospective case series reported that venous thrombosis at the site of insertion occurs in 10 percent of patients when an IVC filter was placed when anticoagulation was contraindicated [98].
An additional prospective observational study of patients in whom permanent filters were placed reported that filter thrombosis occurred in 30 percent, DVT in 20 percent, and PE in 5 percent [108].

A systematic review of 11 studies in patients in whom a permanent filter was placed for primary or secondary prevention reported high rates of the signs and symptoms of PTS (50 and 20 percent, respectively) [108,109].

In PREPIC1, which was comprised of patients with DVT who were fully anticoagulated, the rate of DVT associated with adjunctive IVC filter insertion was 21 and 35 percent, at two and eight years, respectively. In contrast, in PREPIC2, which was comprised of patients with PE who were fully anticoagulated, rates of DVT in association with a retrievable filter were less than 1 percent [105].

Although retrievable filters have the theoretical potential to eliminate the risk of DVT, there is no direct evidence to support this hypothesis and data from observational case series suggest low compliance with their insertion as well as low retrieval rates in practice [111-114].

Several practical factors that may influence the decision to place a filter should be considered in every patient:

- The site of origin of the embolic event must be such that the filter will provide a beneficial effect. For example, infrarenal caval filter placement will not be of prophylactic value if the emboli originated in the renal veins, a cardiac chamber, or the upper extremity veins.

- IVC filter placement is associated with its own set of complications (eg, guidewire entrapment, local hemorrhage, fracture, embolization) and mortality (0.12 to 0.3 percent) such that weighing these risks against those of recurrence is prudent. (See "Placement of vena cava filters and their complications", section on 'Complications' and "Placement of vena cava filters and their complications", section on 'Mortality'.)

For patients with PE who do not have proven clot in the lower extremities who also have a contraindication to anticoagulation, vena cava filters are often placed. This is because clot can quickly reform in the leg veins after embolization and may also remain undetected in the pelvis or calf veins with the potential to embolize. (See "Treatment, prognosis, and follow-up of acute pulmonary embolism in adults", section on 'Inferior vena cava filters'.)

The placement and complications of IVC filters are discussed separately. (See "Placement of vena cava filters and their complications".)

MONITORING AND FOLLOW-UP — Patients should be monitored for the complications of deep vein thrombosis (DVT) as well as those of anticoagulation. These include further clot extension, recurrence, embolization, post-thrombotic (postphlebitic) syndrome, chronic thromboembolic pulmonary hypertension, bleeding, thrombocytopenia, and thrombosis-related or bleeding-related death.

During anticoagulation patients should also be monitored for the development of conditions that affect the half-life of the anticoagulant used (eg, renal failure, pregnancy, weight gain/loss).

The most common laboratory test used to monitor warfarin is the prothrombin time (PT) ratio usually expressed as the international normalized ratio (INR). The goal INR is 2 to 3 (target 2.5). Low molecular weight heparin, fondaparinux, and the factor Xa and direct thrombin inhibitors do not require routine laboratory monitoring, although in rare circumstances this may be used to increase the probability of therapeutic anticoagulation with a specific agent. (See "Heparin and LMW heparin:"
Dosing and adverse effects”, section on ‘Laboratory monitoring/measurement’ and "Direct oral anticoagulants and parenteral direct thrombin inhibitors: Dosing and adverse effects” and "Clinical use of coagulation tests”, section on ‘Tests used for therapeutic drug monitoring’.

Monitoring patients for therapeutic efficacy and bleeding is discussed separately. (See "Venous thromboembolism: Anticoagulation after initial management", section on 'Monitoring' and "Rationale and indications for indefinite anticoagulation in patients with venous thromboembolism", section on 'Making the decision to indefinitely anticoagulate'.)

INFORMATION FOR PATIENTS — UpToDate offers two types of patient education materials, “The Basics” and “Beyond the Basics.” The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on “patient info” and the keyword(s) of interest.)

● Basics topics (see "Patient education: Deep vein thrombosis (blood clots in the legs) (The Basics)"

● Beyond the Basics topics (see "Patient education: Deep vein thrombosis (DVT) (Beyond the Basics)" and "Patient education: Warfarin (Coumadin) (Beyond the Basics)"

SUMMARY AND RECOMMENDATIONS

● Anticoagulation is the mainstay of therapy for patients with acute lower extremity deep vein thrombosis (DVT). Initial anticoagulation refers to anticoagulant therapy that is administered immediately and for up to 10 days following a diagnosis of DVT to provide protection from recurrent thrombosis in this period of highest risk. Long-term (finite) anticoagulation is administered for a minimum of three months and extended for 6 to 12 months in some cases. A small population of patients will require indefinite anticoagulation. (See ‘Nomenclature’ above.)

● For most patients with acute symptomatic proximal DVT, we recommend anticoagulation rather than no anticoagulation (Grade 1B), provided the risk of bleeding is not high. In patients with asymptomatic proximal DVT, we suggest anticoagulation identical to that for patients with symptomatic DVT. For most patients with symptomatic isolated distal DVT, we suggest anticoagulation rather than serial compression ultrasonography (Grade 2C). For select patients with isolated distal DVT (eg, those at high risk of bleeding, negative D-dimer level, asymptomatic or minor symptoms, without risk factors for extension, and/or minor thrombosis of the muscular veins), we suggest surveillance with serial ultrasound over a two-week period rather than anticoagulation (Grade 2C). Those who exhibit signs of thrombus extension should be anticoagulated. (See 'Indications' above.)

● In most patients, anticoagulation should be started immediately (initial anticoagulation) as a delay in therapy increases the risk of potentially life-threatening embolization. Options include subcutaneous low molecular weight (LMW) heparin, subcutaneous fondaparinux, the oral factor Xa inhibitors rivaroxaban or apixaban, or unfractionated heparin (UFH). A decision between these agents is usually made based upon clinician experience as well as the risks of bleeding, patient comorbidities,
preferences, cost, and convenience. (See "Venous thromboembolism: Initiation of anticoagulation (first 10 days)" and 'Initial anticoagulation (first 10 days)' above.)

● Outpatient anticoagulation rather than inpatient therapy can be considered when patients are hemodynamically stable, have a low risk of bleeding, do not have renal insufficiency, and have a practical system in place at home for the administration and surveillance of anticoagulant therapy (table 5). It is not appropriate in patients with massive DVT (eg, iliofemoral DVT, phlegmasia cerulea dolens), concurrent pulmonary embolism, a high risk of bleeding on anticoagulant therapy, comorbid conditions, or other factors that warrant in-hospital care. (See 'Outpatient therapy' above.)

● Therapeutic anticoagulation should be ensured during the transition from initial to long-term (maintenance) therapy. Options for long-term agents are oral anticoagulants (direct factor Xa inhibitors, [rivaroxaban, apixaban, edoxaban], thrombin inhibitors [dabigatran], and vitamin K antagonists [warfarin]), as well as subcutaneous agents (LMW heparin and fondaparinux). While the factor Xa and thrombin inhibitors are preferred, a decision between these agents is usually made based upon clinician experience as well as the risks of bleeding, patient comorbidities, preferences, cost, and convenience (table 4). Interruptions should be minimized during the first three months of anticoagulation due to the high risk of recurrent thrombosis. (See "Venous thromboembolism: Anticoagulation after initial management" and 'Long-term anticoagulation (10 days to 3 months)’ above.)

● For patients with acute DVT, the duration of anticoagulation should be individualized according to the presence or absence of provoking events, risk factors for recurrence and bleeding, and the individual patient's preferences and values (algorithm 1). Although there is agreement on the minimum length of time a patient with a first episode of DVT should be treated (ie, three months), the optimal length of time is not known. For most patients with a first episode of DVT (provoked and unprovoked, proximal and distal), anticoagulants should be administered for three months rather than for shorter periods (eg, four or six weeks). Most experts also agree that extending anticoagulation beyond three months is considered in select populations. (See "Venous thromboembolism: Anticoagulation after initial management", section on 'Duration of treatment' and "Rationale and indications for indefinite anticoagulation in patients with venous thromboembolism").

● Special populations of patients with acute DVT require specific consideration:

  ● For patients in whom anticoagulation is contraindicated or in whom the risk of bleeding is estimated to outweigh the risk of recurrent thromboembolism, we suggest the insertion of an IVC filter rather than no therapy (Grade 2C). We also suggest that an IVC filter be placed for patients with acute proximal DVT who have recurrent embolism despite adequate anticoagulation and for patients who have poor cardiopulmonary reserve who may not tolerate additional embolism. We prefer retrievable filters for the avoidance of long term complications of filter placement. Additionally, we prefer that patients with DVT receive a conventional course of anticoagulation once the contraindication resolves. (See 'Patients with contraindications to anticoagulation' above and 'Inferior vena cava filter' above.)

  ● For patients with active malignancy and pregnant women, we suggest that LMW heparin be selected as the initial and long-term anticoagulant of choice rather than other agents (Grade 2C). In patients with active malignancy, warfarin and direct oral anticoagulants are alternatives when LMW heparin cannot be administered. Factor Xa and direct thrombin inhibitors have not been adequately tested in pregnant women with acute DVT and as such should not be administered. (See 'Special populations’ above and "Treatment of venous thromboembolism in patients with malignancy" and "Deep vein thrombosis and pulmonary embolism in pregnancy: Treatment".)
For patients with massive iliofemoral DVT or phlegmasia cerulea dolens with symptoms for <14 days and good functional status, we suggest systemic or catheter-directed thrombolytic therapy, and/or clot removal (eg, catheter extraction, catheter fragmentation, surgical thrombectomy) rather than anticoagulation alone (Grade 2C). The most appropriate intervention depends upon the institution's expertise. (See ‘Phlegmasia cerulea dolens’ above and "Fibrinolytic (thrombolytic) therapy in acute pulmonary embolism and lower extremity deep vein thrombosis", section on 'Lower extremity deep vein thrombosis'.)

For patients with a DVT and a diagnosis of heparin-induced thrombocytopenia (HIT), all forms of heparin should be discontinued and immediate anticoagulation with a non-heparin anticoagulant started. (See "Management of heparin-induced thrombocytopenia".)

For patients with acute DVT who are fully anticoagulated, hemodynamically stable, and whose symptoms (eg, pain, swelling) are under control, we suggest early ambulation in preference to bed rest (Grade 2C). We also suggest that elastic graduated compression stockings (GCS) not be routinely administered in patients for the prevention of post thrombotic (postphlebitic) syndrome (Grade 2B). (See 'Ambulation' above and 'Compression stockings for the prevention of PTS' above.)

Patients should be monitored for the complications of DVT as well as those of anticoagulation. These include further clot extension, recurrence, embolization, post-thrombotic (postphlebitic) syndrome, chronic thromboembolic pulmonary hypertension, bleeding, thrombocytopenia, and thrombosis-related or bleeding-related death. (See 'Monitoring and follow-up' above.)

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