Practice Essentials

Pregnancy increases the risk of venous thromboembolism (VTE) 4- to 5-fold over that in the nonpregnant state.\[1, 2\] The 2 manifestations of VTE are deep venous thrombosis (DVT) and pulmonary embolus (PE). Although most reports suggest that VTE can occur at any trimester in pregnancy, some studies suggest that VTE is more common during the first half of pregnancy (see the image below). Sequelae of DVT and PE include complications such as pulmonary hypertension, post-thrombotic syndrome, and venous insufficiency.

Signs and symptoms

The signs and symptoms of VTE are nonspecific and common in pregnancy. Diagnosis of VTE by physical examination is frequently inaccurate, even though one study found that 80% of pregnant women with DVT experience pain and swelling of the lower extremity.

Clinical signs and symptoms of PE are rarely encountered together; the classic symptoms are as follows:\[3\]:

- Dyspnea - 82%
- Abrupt onset of chest pain - 49%
- Cough - 20%

The most common presenting signs of PE are as follows:

- Tachypnea
- Crackles
- Tachycardia

Patients with massive PE may present with the following:

- Syncope
- Hypotension
- Pulseless cardiac electrical activity
- Death

See Clinical Presentation for more detail.

Diagnosis

Laboratory studies

D-dimer testing is often used in the diagnosis of DVT in nonpregnant patients due to its high negative predictive value. Pregnancy decreases the specificity of d-dimer testing, but the study still retains good negative predictive value. D-dimer is
also used for its negative predictive value in the diagnosis of PE.

**Imaging studies**

Imaging for DVT and/or PE is the best means of screening and evaluation for these conditions. The current initial test of choice in the evaluation of VTE is compression ultrasonography (CUS) of the lower extremity veins. CUS has been shown to be more than 95% sensitive and specific for proximal lower extremity DVT.\(^6\) CUS is less accurate for the diagnosis of pelvic DVT.\(^5\) In pregnancy, CUS should be performed with the patient in the left lateral decubitus position and with Doppler analysis of flow variation during respiration to maximize the study's ability to diagnose pelvic DVT.\(^6\)

However, if the CUS study is equivocal, if Doppler testing is abnormal, or if suspicion of pelvic DVT is high, further evaluation with magnetic resonance imaging (MRI) is recommended.\(^7, 8, 9\) MRI has been shown to have 97% sensitivity and 95% specificity for pelvic DVT in nonpregnant patients.\(^10\)

Imaging studies used in the diagnosis of PE include the following:

- Chest radiography: Recommended prior to the evaluation for PE to determine whether other etiologies may explain the patient's symptoms (eg, pneumonia, atelectasis) and to identify the next appropriate imaging test.
- Ventilation/perfusion (V/Q) scanning: In a pregnant patient with no known pulmonary disease and a normal chest radiograph, V/Q scanning is the recommended study to evaluate for PE.
- Spiral computed tomography pulmonary angiography (CT-PA): If the patient has an abnormal chest radiograph or known pulmonary disease, spiral CT-PA is recommended.\(^11\)

See Workup for more detail.

**Management**

Once the diagnosis of VTE is made, therapeutic anticoagulation should be initiated in the absence of contraindications. The common classes of anticoagulation drugs are as follows:

- Indirect thrombin inhibitors: Include unfractionated heparin and low-molecular-weight heparin (LMWH), as well as synthetic heparin pentasaccharides and orally administered Factor Xa inhibitors.
- Direct thrombin inhibitors: Include argatroban, lepirudin, and bivalirudin.
- Vitamin K antagonist: Warfarin is included in this class.

Heparin (unfractionated and low molecular weight) is the preferred drug for managing VTE in pregnancy.

See Treatment and Medication for more detail.

**Background**

Venous thromboembolism (VTE) may occur at any time during gestation. Studies report conflicting data as to the timing in pregnancy. Although most reports suggest that VTE can occur at any trimester in pregnancy, some studies suggest that VTE is more common during the first half of pregnancy. One study of 165 episodes of VTE in pregnancy documented a higher incidence in the first trimester (see the image below).\(^12\) Other studies have not confirmed an association between gestational age and frequency of VTE.\(^13, 14\)

![Graph showing estimated gestational age at time of diagnosis of antepartum deep venous thrombosis (n=94).](image)

Estimated gestational age at time of diagnosis of antepartum deep venous thrombosis (n=94).

Note that most evidence suggests that VTE is more common in the postpartum period.\(^11, 15, 16\) In a 30-year population-based study, Heit et al documented that the risk of VTE and pulmonary embolism (PE) was 5-fold and 15-fold, respectively, in the postpartum period compared to during pregnancy.\(^6\)
In pregnancy, deep venous thrombosis (DVT) is much more likely to occur in the left leg compared with the right leg. One study examined 60 cases of DVT in pregnancy: 58 occurred in the left leg, 2 were bilateral, and none occurred in the right leg.\(^1\) The predilection for left lower extremity DVT is postulated to be the consequence of May-Thurner syndrome, in which the left iliac vein is compressed by the right iliac artery (see the image below).

Another special consideration relevant to accurate diagnosis in pregnancy is that 12% of DVTs in pregnancy are in pelvic veins, whereas only 1% of DVTs in the general population are in pelvic veins.\(^2\) This predilection for pelvic site DVTs in pregnancy warrants special consideration when Doppler ultrasound studies of the lower extremities do not demonstrate noncompressible regions of lower extremity veins, yet suspicion for VTE is high or Doppler flow analysis of venous flow is abnormal.

**Pathophysiology**

Pregnancy is a state characterized by Virchow's triad (1: hypercoagulability, 2: venous stasis and turbulence, 3: endothelial injury and dysfunction). Pregnancy is a state of hypercoagulability due to alterations of coagulation proteins. Factors I, II, VII, VIII, IX, and X increase in pregnancy. Pregnancy increases resistance to the anti-thrombotic factors such as protein C and protein S.\(^3\) Thrombophilias can exacerbate these changes in coagulation proteins, further increasing the patient’s risk for VTE (see the image below).

Venous stasis also increases as dilation of lower extremity veins occurs followed by venous compression by the gravid uterus and enlarging iliac arteries. Situations of decreased mobility (eg, surgery, cesarean delivery, bed rest, prolonged travel or air travel) may exacerbate these factors. Endothelial injury may transpire at time of delivery.\(^4\) These factors work together to increase risk of VTE in the pregnant and postpartum patient.

**Sequelae of VTE**

Sequelae of DVT and PE include complications such as pulmonary hypertension, post-thrombotic syndrome, and venous insufficiency. Post-thrombotic syndrome is not well defined; however, most definitions consist of a constellation of symptoms
(pain, cramps, heaviness, pruritus, and paresthesia) and signs (edema, skin induration, hyperpigmentation, venous ectasia, redness, pain during calf compression, and in more severe forms, venous stasis ulcer) in the extremity affected by DVT. Mild post-thrombotic syndrome occurs in 20-40% of patients after VTE, and severe post-thrombotic syndrome occurs in 5% of patients after VTE.\[20\]

**Epidemiology**

According to the Center for Disease Control’s National Pregnancy Registry Surveillance System, between 1991 and 1999, pulmonary embolism (PE) was the leading cause of maternal mortality. Of the 4,200 pregnancy related deaths reported in the United States during those years, 20% of maternal death was attributed to PE, surpassing pregnancy-related hypertensive disorders, postpartum hemorrhage, and infection.\[21\] In a retrospective study of 1,461,270 deliveries, PE accounted for 9% (9 of 95) of pregnancy-related deaths.\[22\]

Pregnancy increases the risk of VTE 4-fold to 5-fold over the nonpregnant state.\[2,1\] Overall, the prevalence of VTE in pregnancy is 0.5-2.0 per 1,000 pregnancies and accounts for 1.1 deaths per 100,000 pregnancies.\[23,12,24,25,13,26,27\] Approximately 75-80% of embolic events in pregnancy are venous.\[27\]

The 2 manifestations of VTE are deep venous thrombosis (DVT) and pulmonary embolus (PE). DVT is approximately 3 times more common that PE in pregnancy.\[2\]

**Clinical Presentation**

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**References**


