

Pregnancy: Diagnosis of DVT and PE



Objective:

To provide a diagnostic approach to the evaluation of pregnant patients with a clinical suspicion of deep vein thrombosis (DVT) or pulmonary embolism (PE).

Background:

Pregnancy is a well-established risk factor for venous thromboembolism (VTE). DVT complicates approximately 1 per 1,000 pregnancies, while PE complicates 0.5 per 1,000 pregnancies. VTE occurs in all trimesters of pregnancy and the postpartum period. The daily risk of VTE is increased 5- to 10-fold during pregnancy and 15- to 35-fold early after delivery compared to non-pregnant women of similar age. Although most studies have reported that the elevated risk of VTE returns to baseline by the end of the sixth postpartum week, there is evidence that a small residual increase in risk may persist for 12 weeks after delivery.

Signs and Symptoms of DVT and PE in Pregnancy:

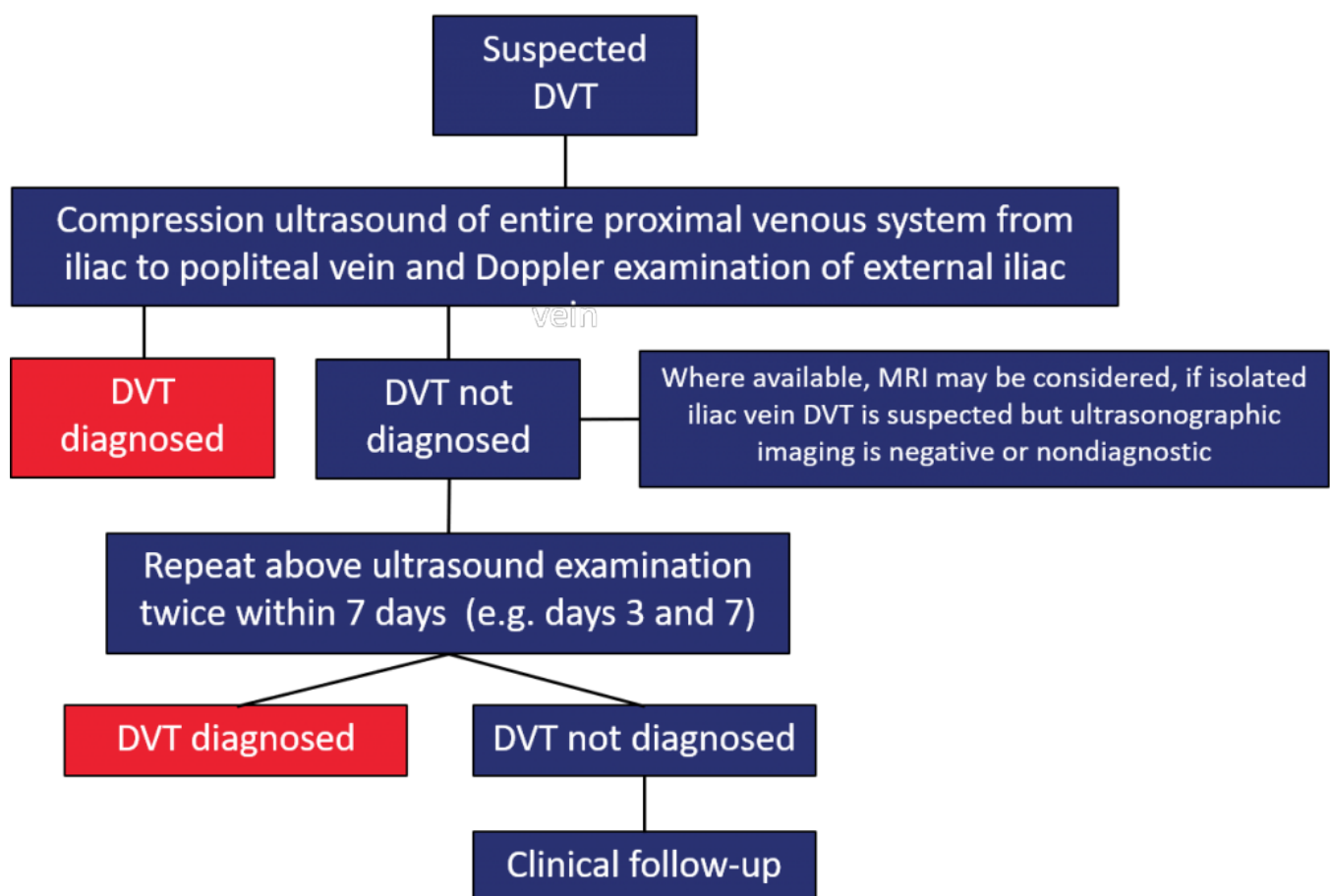
The presentation of DVT in pregnancy differs from that in non-pregnant patients. The left leg is affected in >80% of cases and pregnant patients are much more likely to present with isolated iliac and/or femoral vein thrombosis, i.e. not arising by contiguous extension of a thrombus in the calf. These isolated iliofemoral thrombi often present with swelling of the entire leg with flank, buttock, or back pain rather than symptoms lower in the leg and carry a greater risk of post-thrombotic syndrome.

Symptoms that mimic VTE, such as leg swelling, groin discomfort, and dyspnea are common in normal pregnancy. Therefore, the majority of pregnant women investigated for VTE (>90%) will not have VTE. However, the suspicion of VTE must be increased in patients with unilateral leg swelling (particularly of the left leg), previous history of VTE, family history of VTE, high risk thrombophilia, bedrest for 7 days (especially with increased body mass index) or medical illness. Since the consequences of failing to diagnose VTE in pregnancy are significant, the threshold for investigating pregnant women with suspected DVT or PE must be low. In addition, the consequences of assuming VTE is present when it is not are also significant because: 1) prolonged anticoagulation throughout pregnancy is costly, requires daily subcutaneous injection, and complicates delivery, 2) VTE prophylaxis with LMWH would be recommended in subsequent pregnancies, and 3) combined oral contraceptives would be subsequently contraindicated. Therefore, the investigation of DVT and PE in pregnancy should accurately diagnose (or exclude) clinically significant VTE.

Investigative Strategies:

Although it has been shown that physicians are able to risk stratify pregnant women with suspected DVT using the LEFt rule (in which 1 point is provided for each of left leg symptoms, edema of affected leg with more than a 2 cm difference (between legs), and presentation in the first trimester of pregnancy), there have been no published management studies demonstrating the safety of using this rule alone or with D-dimer testing to exclude DVT in this patient population. A prospective validation of a diagnostic strategy to diagnose DVT during pregnancy using the LEFt rule is ongoing (NCT01708239). As a result, compression ultrasound is the first choice for investigation of DVT, as it is safe for mother and fetus and is readily available. Compression ultrasound should visualize the entire proximal venous system, including the iliac veins, to rule out DVT. However, good visualization of the iliac veins with compression ultrasound can be limited in many pregnant women. A recent meta-analysis found the false-negative frequency of a single leg ultrasound with iliac imaging in pregnant women with suspected DVT to be low, at less than 2%. However, the safety of performing only a single test has not been well validated in patient management studies so additional testing (as outlined in Figure 1) is generally recommended if the initial ultrasound is negative.

Figure 1: Diagnosis of Suspected DVT in Pregnant Women



Adapted from Figure 1: Society of Obstetricians and Gynaecologists of Canada (SOGC) algorithm for investigation of suspected DVT in pregnant patients. Chan WS, et al. Venous thromboembolism and antithrombotic therapy in pregnancy: SOGC Clinical Practice Guideline. J Obstet Gynaecol Can 2014;36(6):527–553.

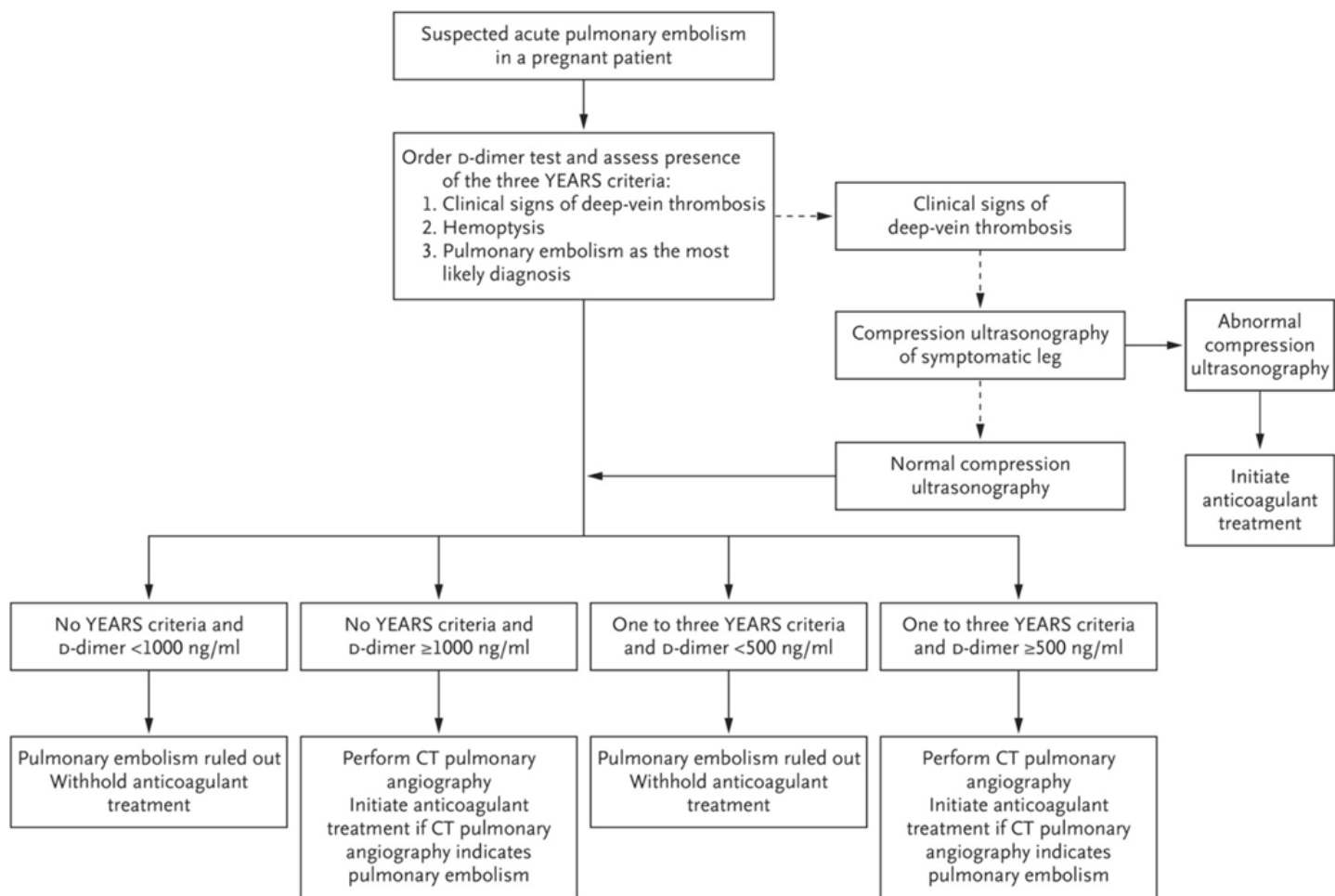
In patients in whom the iliac system cannot be visualized and in whom symptoms are suggestive of isolated iliac vein thrombosis - such as whole leg swelling, buttock, back, or flank pain - magnetic resonance imaging (MRI) should be considered, if available. Direct thrombus imaging (MRDTI), if available, eliminates the need for gadolinium. Alternatively, if MRI is not available, anticoagulation should be started and compression ultrasound repeated in 2 to 3 days; at that time, if the iliac veins are visualized and there is no evidence of DVT, anticoagulants can be stopped. MRI can be safely carried out in pregnant patients although the exact specificity and sensitivity of this technique is unclear.

Investigative Strategies for PE:

Two prospective diagnostic management outcome studies investigating diagnostic algorithms for diagnosis of PE during pregnancy have been published. Taken together, these studies suggest D-dimer measurement and pretest probability calculation can be used to safely direct investigation of pregnant patients with suspected PE. The most recent study, the pregnancy-adapted YEARS protocol (see Figure 2), which was evaluated in 498 pregnant women with suspected PE, is the best validated method for diagnosing and excluding PE in pregnancy. The algorithm starts with performance of a sensitive D-dimer test and calculation of the YEARS score (3 items with one point assigned for each: clinical signs of DVT, hemoptysis, PE as most likely diagnosis). All women with clinical signs of DVT (the first criterion on the YEARS score) should undergo a single leg ultrasound. If DVT is diagnosed, therapeutic anticoagulation is started and testing stopped. Patients with a negative ultrasound and those not requiring ultrasound are evaluated according to their YEARS criteria. The D-dimer threshold for excluding PE is dependent on the number of YEARS criteria satisfied. For patients with one or more positive criteria, the threshold for performance of radiologic testing is 500 ng/mL, while for those with no positive criteria, the threshold is 1000 ng/mL. In the validation study, the 3-month false negative rate for this protocol was 0.21% (95% confidence interval, 0.04 – 1.2%) and pulmonary diagnostic imaging was avoided in 39% of patients. The safety and effectiveness of this method has been externally validated in a retrospective cohort of 371 patients.

Use of D-dimers in pregnancy has been discouraged as D-dimers increase through normal pregnancy with highest levels in the 3rd trimester. However, a systematic review and meta-analysis found D-dimers are highly sensitive to rule out VTE with a very high negative predictive value of 100% (95% confidence interval, 99.1 – 100.0%). This further supports its use in diagnostic algorithm as described above.

Figure 2: Diagnosis of Suspected PE in Pregnant Patients using the YEARS Protocol



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Options for diagnostic imaging include ventilation/perfusion (V/Q) lung scan and computed tomographic pulmonary angiography (CTPA). The ranging average calculated radiation dose to the fetus with V/Q scan is 0.2-0.7 mGy and for CTPA is 0.002-0.51 mGy, well below the threshold of 50 mGy associated with increased risk of fetal health problems. However, the calculated minimum radiation dose to each breast for an average 60 kg woman is significantly higher for CTPA (10 to 70 mGy, although that number can be reduced by approximately 20% with the use of bismuth breast shields) than for V/Q scan (<1.5 mGy, depending on technique), raising theoretical concerns of increased breast cancer risk in pregnant women exposed to CTPA. As a result, some physicians prefer V/Q scanning (especially in women with normal chest radiography), if available. Nevertheless, in a large population-based cohort study, exposure to either CTPA or V/Q scan during pregnancy or the postpartum period did not lead to a detectable short-term excess risk of maternal breast cancer. In some centres, additional modifications of V/Q or CT techniques are available that can further reduce radiation exposure, so discussing with radiology and nuclear medicine can be helpful. Both CTPA and V/Q scan have a low false negative rate, and a similar non-diagnostic testing rate. The non-diagnostic CTPA testing rate, however, may be further reduced by using a specific protocol adapted to hemodynamic effects of pregnancy.

Investigation of suspected PE in pregnancy often creates anxiety in patients and physicians because of the radiation exposure to the mother and fetus. Clinical likelihood of PE, availability of timely imaging modalities, local expertise (ability to perform pregnancy-adapted CTPA) availability of V/Q, and patient preference should all be taken into consideration. It is essential that patients and physicians understand the risks and

consequences of not pursuing imaging and that patients and physicians are accurately informed of the potential radiation risks to mother and fetus before decisions are made.

Special Considerations:

If DVT or PE is suspected in the postpartum period, the patient should be investigated as in non-pregnant patients, remembering that the pretest probability will be higher as this is the highest risk time for VTE in pregnant patients. CT scan is safe in breastfeeding; however, radioisotopes used in V/Q scanning may contaminate breastmilk for 24-48 hrs.

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