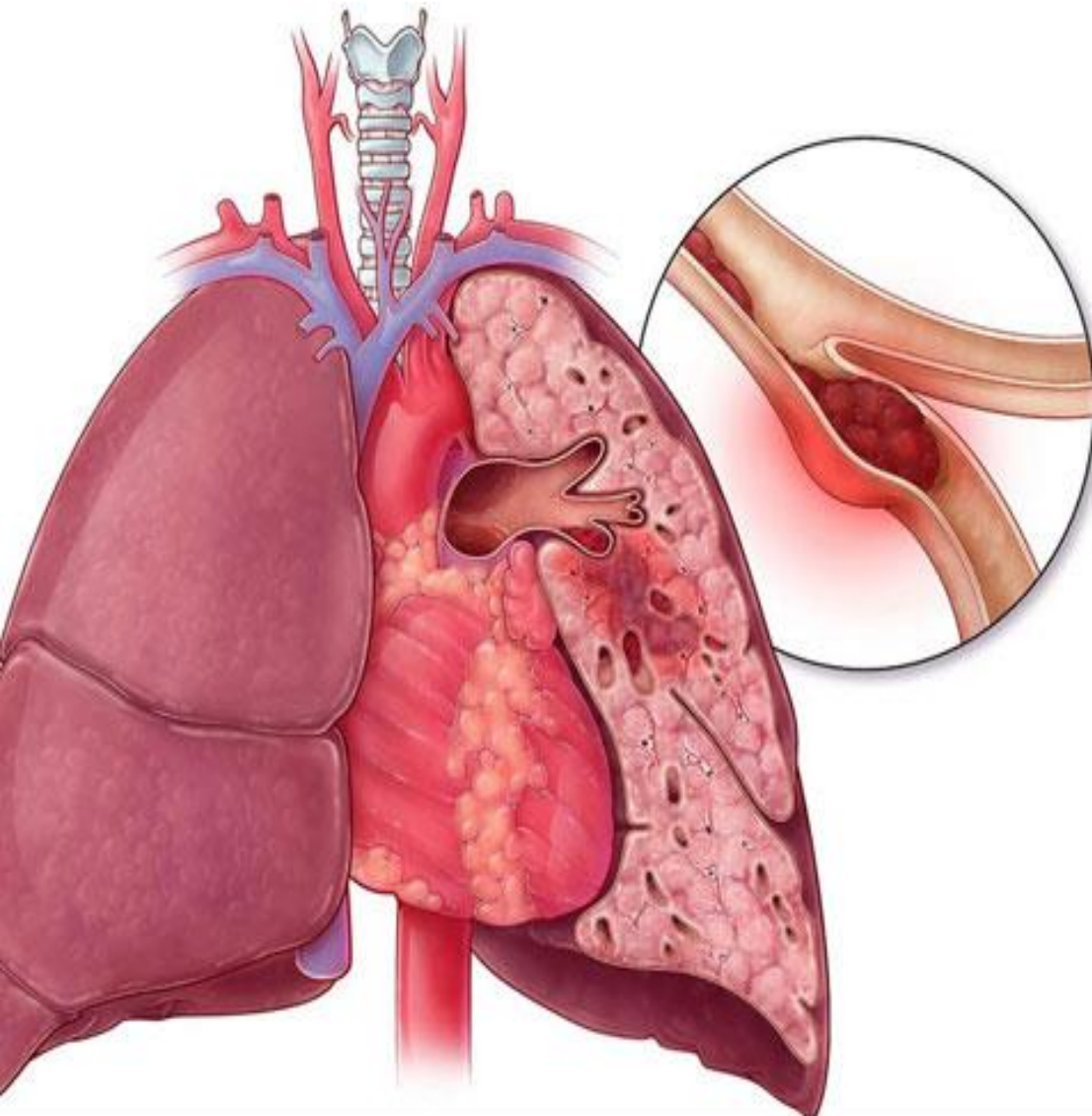


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VTE IN PREGNANCY AND POSTPARTUM

By:Dr.L.Namvar(pulmonologist)

VTE IN PREGNANCY

- Pregnancy and the puerperium (postpartum period) are well-established risk factors for venous thromboembolism (VTE)
- **1 in 1600** pregnancies
- In the United States, PE is the **sixth** leading cause of maternal mortality (9%)

VTE IN PREGNANCY

- The ideal approach to diagnosing PE in pregnancy requires a **high index of clinical suspicion** while **avoiding overtesting**.
- Such an approach ensures that **few cases of PE are missed** and minimizes the risk of radiation and contrast exposure.

RISK FACTORS

- **4 to 50 times** higher compared to nonpregnant women
- Increased risk for VTE is **highest** in the postpartum period
- Pregnancy and the postpartum period are marked by the presence of all three components of Virchow's triad: **venous stasis, endothelial injury, and a hypercoagulable state**

ANTEPARTUM RISK FACTORS

- Most studies report **equal distribution** of VTE across the **trimesters** of pregnancy

ANTEPARTUM RISK FACTORS

- Multiple births
- Varicose veins
- Inflammatory bowel disease
- Urinary tract infection
- Diabetes
- Hospitalization for non-delivery reasons (particularly those >3 days)
- BMI ≥ 30 kg/m²
- Increased maternal age ≥ 35 years

POSTPARTUM RF

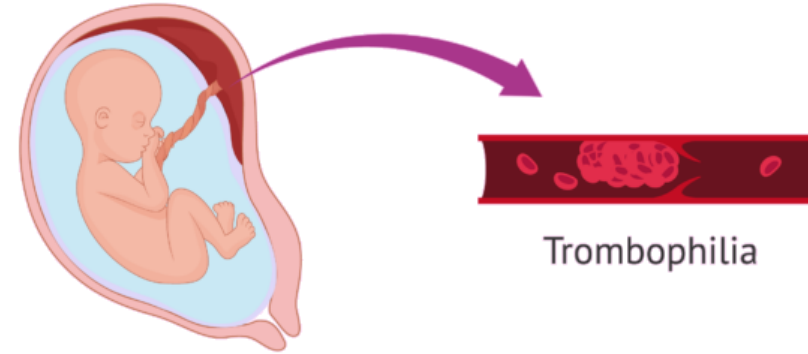
- ❑ Compared with the antepartum period, VTE is two to five times more common postpartum
- ❑ The risk is highest in the first six weeks postpartum and declines to rates that approximate that of the general population by about 13 to 18 weeks

POSTPARTUM RF

- **Cesarean section (especially emergent CS)**
- **Medical comorbidities (eg, varicose veins, cardiac disease, inflammatory bowel disease)**
- **BMI ≥ 25 kg/m²**
- **Young gestational age (preterm delivery <36 weeks)**
- **Obstetric hemorrhage**
- **Stillbirth**

POSTPARTUM RF

- **Increased maternal age ≥ 35 years**
- **Hypertension**
- **Smoking**
- **Eclampsia or preeclampsia**
- **Postpartum infection**
- **Transfusions**
- **Thrombophilia disorders**



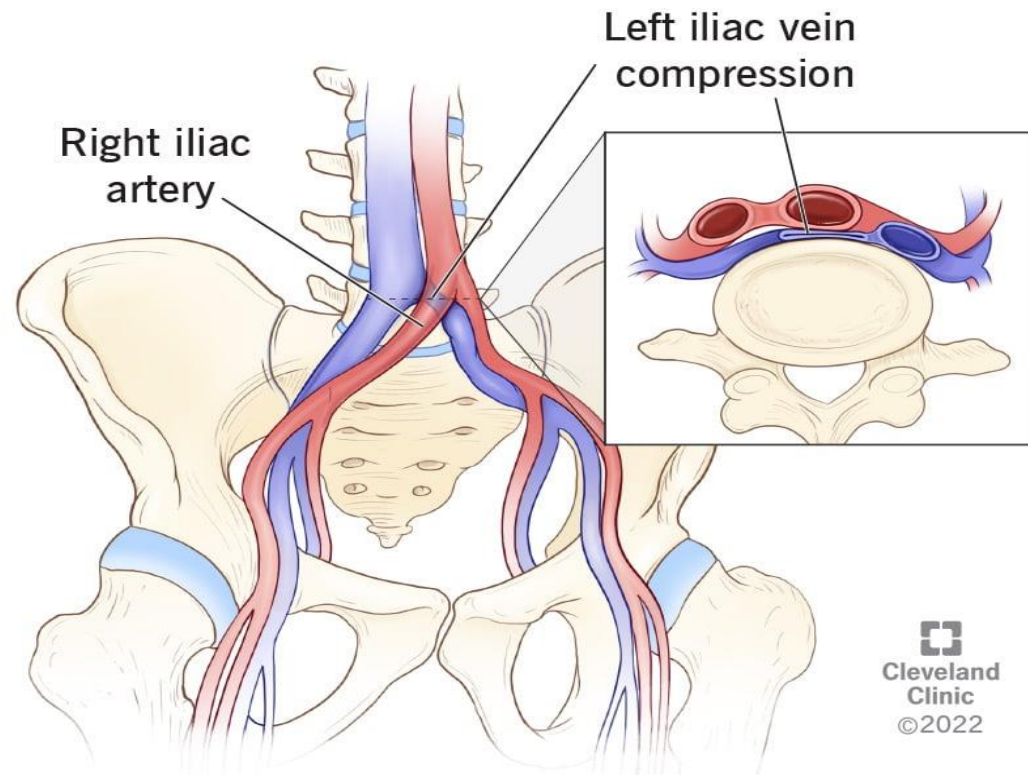
- The risk of VTE is further **magnified in pregnant women** who have inherited thrombophilia
 - factor V Leiden → **three times higher**
 - inheritable deficiency of antithrombin III, protein S, or protein C
→ **eight-fold increased**
- **Inherited thrombophilias**

CLINICAL PRESENTATION

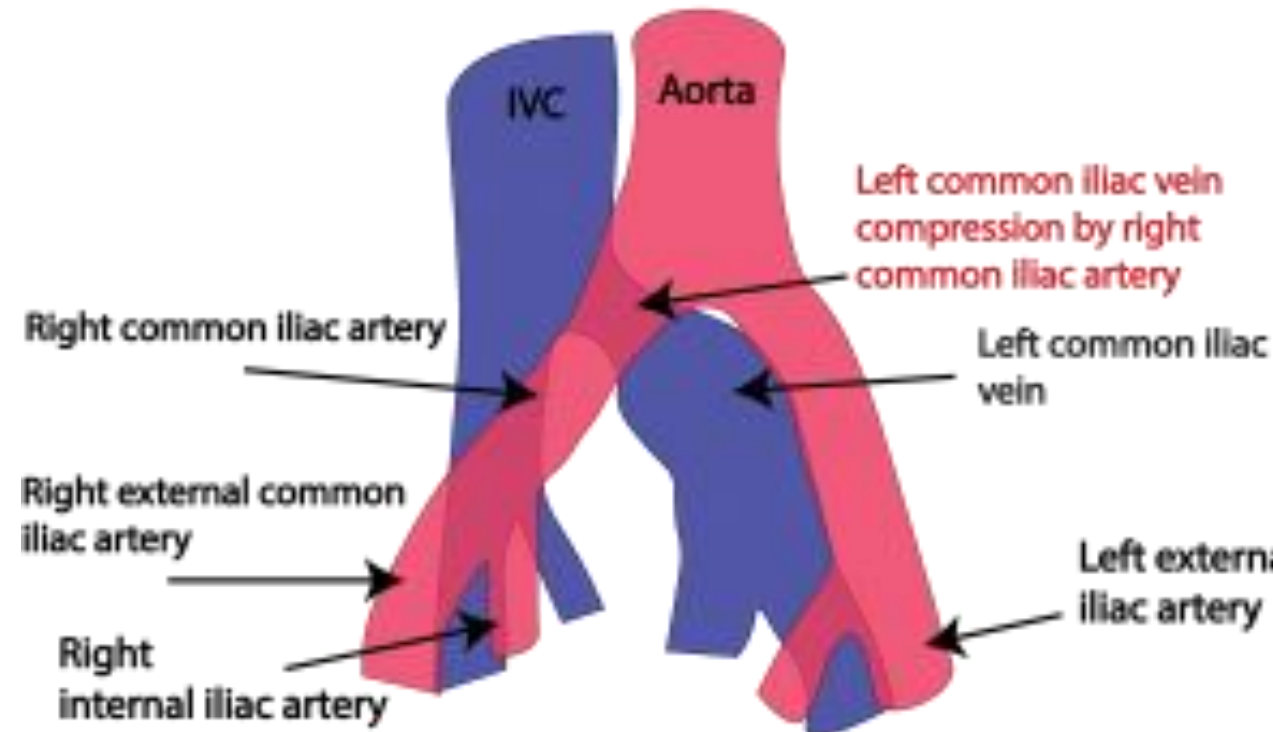
- Other than the **higher propensity** to develop **left-sided DVT** and **iliac vein thrombosis**, the clinical presentation of DVT during pregnancy is identical to that in nonpregnant females.
- The majority of lower extremity DVTs during pregnancy are **left-sided (70 to 90 percent)**.
- **Pelvic vein thrombosis is significantly higher during pregnancy and the puerperium**, although DVT remains most often found in the proximal veins (eg, femoral vein)

MAY-THURNER SYNDROME

May-Thurner Syndrome



Cleveland
Clinic
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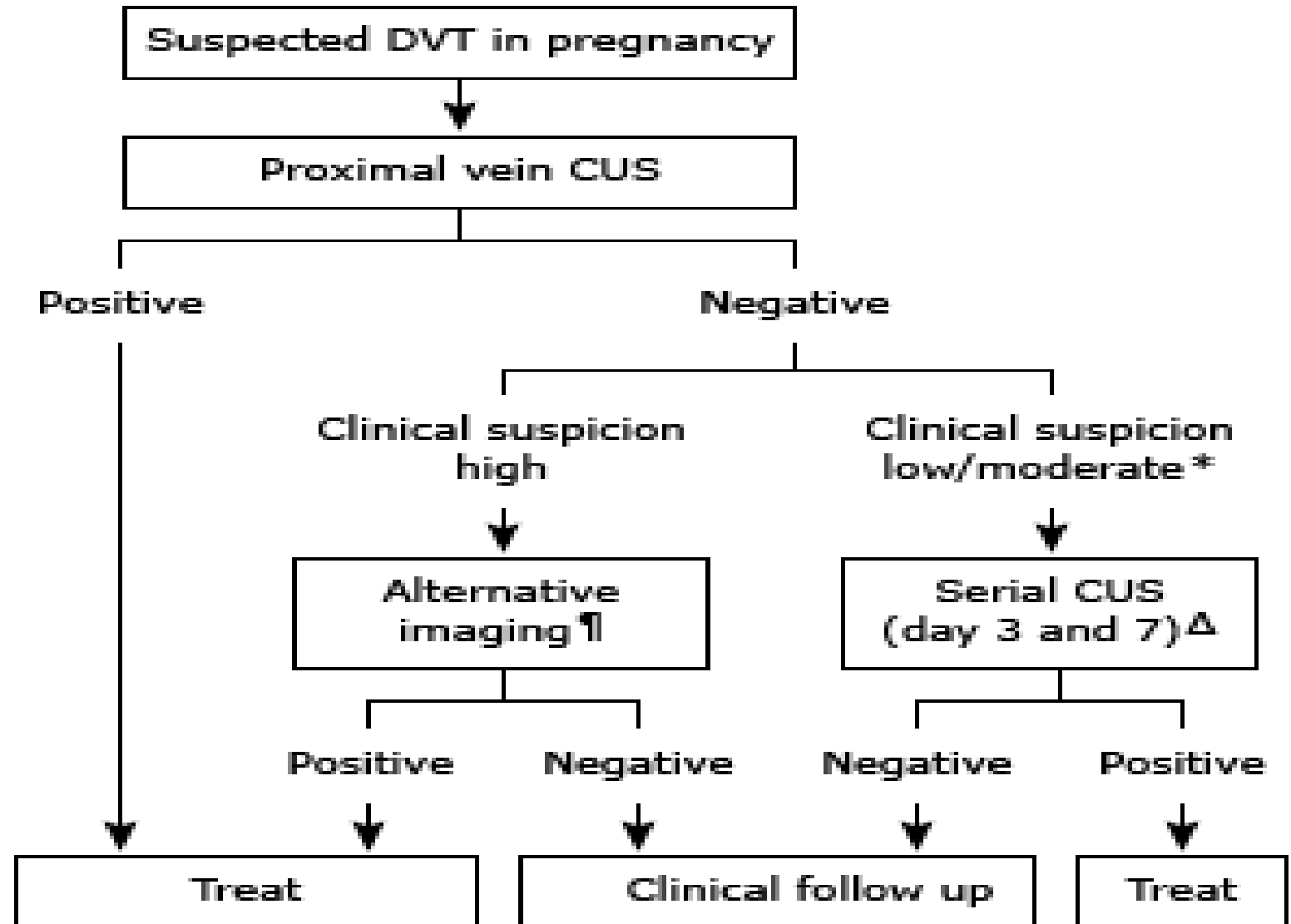


DIAGNOSTIC ALGORITHM IN PREGNANCY

A negative CUS **does not rule out** DVT in the pregnant patient.

Alternative imaging techniques include **doppler ultrasound of the iliac vein** and **contrast or magnetic resonance venography**.

D-dimer level **<500 ng/mL** is considered negative and no further testing is needed.



CLINICAL PRESENTATION (PE)

- Nonspecific and are **similar** to nonpregnant individuals.
- There are **no clinical signs or symptoms** that are specific for PE
- This nonspecific presentation is **magnified during pregnancy** due to an overlap between symptoms seen in patients with PE and those associated with the normal physiologic changes of pregnancy (eg, **dyspnea** occurs in **up to 70 percent** of normal pregnancies)

CLINICAL PRESENTATION (PE)

acute onset dyspnea

pleuritic pain

hemoptysis and

cough and sweating should always raise alarm and increase the clinical suspicion for a PE during pregnancy.

OXYGENATION MEASURES

- Importantly, **normal oxygenation** parameters do **not confidently exclude** the possibility of PE while abnormal oxygenation should raise the suspicion further for PE.



LABORATORY STUDIES

- **Arterial blood gases:**

- Neither sensitive nor specific diagnostically
- **Respiratory alkalosis** is a very common feature of both pregnancy and PE
- A normal PO_2 , PCO_2 , or alveolar-arterial difference is common with PE
- The presence of **hypoxemia with normal chest radiograph** should raise the clinical suspicion for PE in pregnancy and prompt further evaluation.

LABORATORY STUDIES

- **D-dimer**
- D-dimer levels increase during the course of a normal pregnancy and slowly decline postpartum

D-DIMER

For pregnant patients with a **negative D-dimer (eg, <500 ng/mL)** and **low suspicion** for PE, we do not typically proceed with further testing.

For patients with a positive **D-dimer (eg, ≥ 500 ng/mL)** and **low suspicion** for PE, we proceed with further testing as outlined for patients with a **moderate or high suspicion of PE**

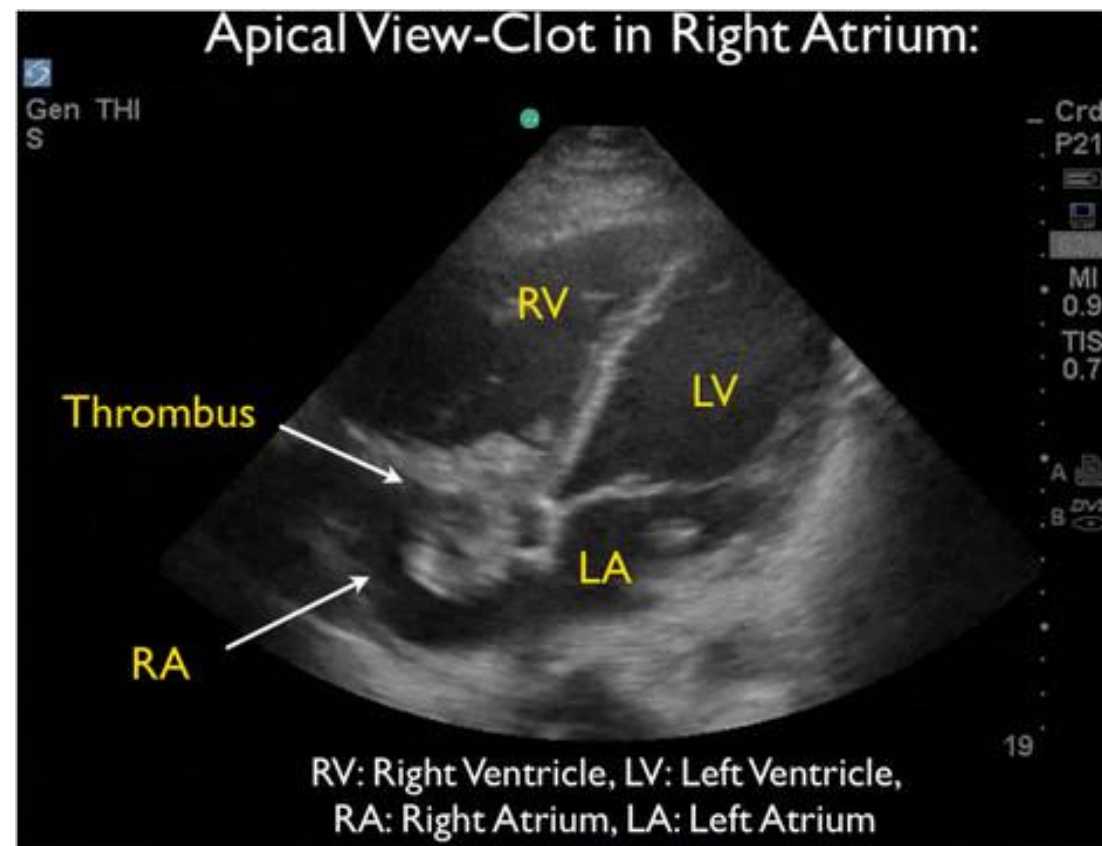
ECHOCARDIOGRAPHY

- **Electrocardiographic findings are similar to those in the nonpregnant population.**

ECHOCARDIOGRAPHY

- Echocardiography is **not routinely performed** in the diagnostic evaluation of a pregnant patient suspected of having a PE
- Rarely, **thrombus** may be visualized in the right atrium, right ventricle (RV), or pulmonary artery to definitively diagnose PE.
- An enlarged RV may support a diagnosis of PE when PE is hemodynamically significant unstable, but such a finding is **not definitively diagnostic of PE itself**.

ECHOCARDIOGRAPHY



DETERMINING PRETEST PROBABILITY

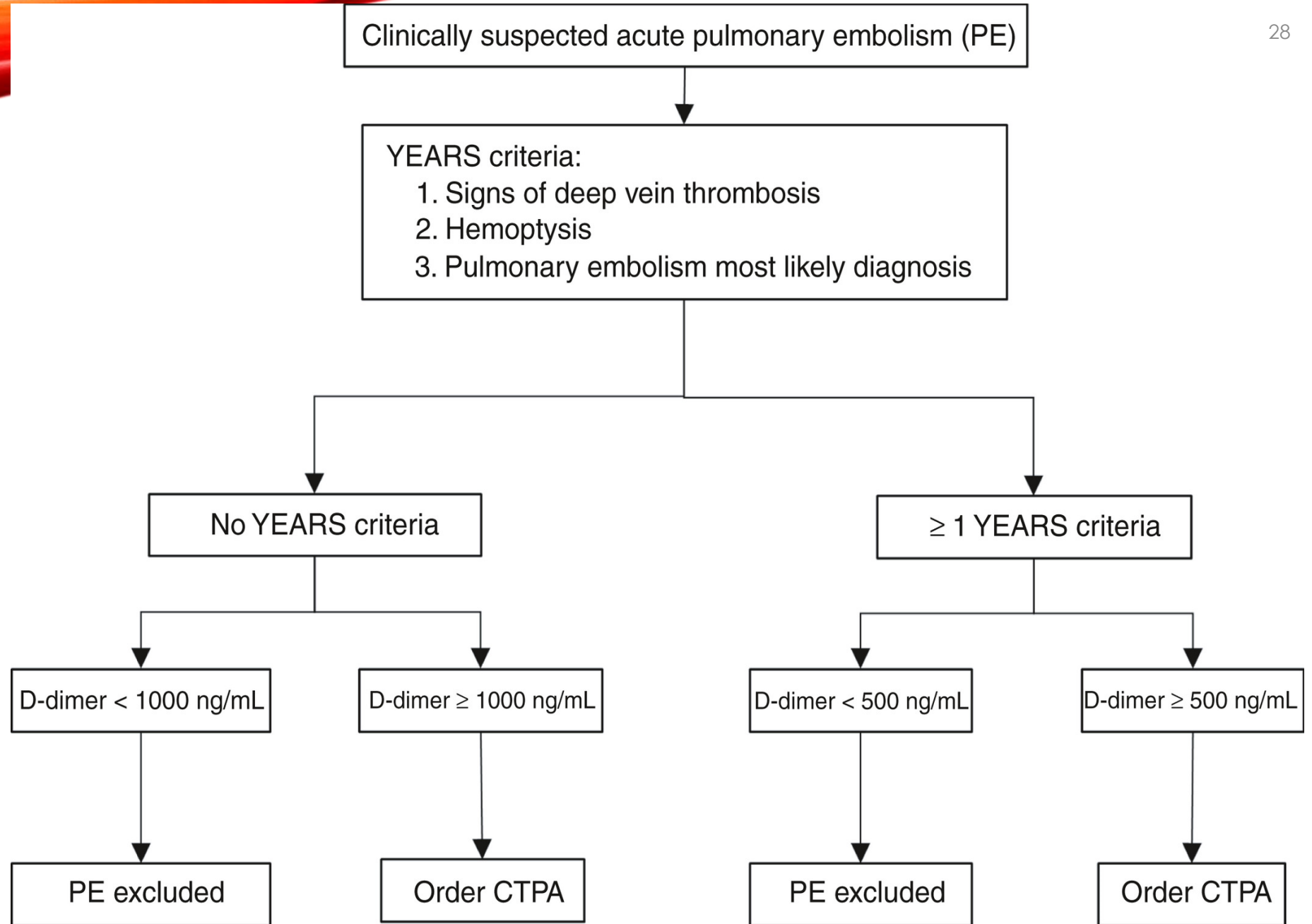
- Similar to nonpregnant patients, any one or combination of **acute-onset dyspnea, pleuritic pain, hemoptysis, syncope,** or **hypoxemia**, particularly in the setting of a **normal chest radiograph**, should raise the clinical suspicion for a PE during pregnancy

DETERMINING PRETEST PROBABILITY

- Traditionally, clinical decision rules such as the **Wells or revised Geneva scoring systems** have had **limited value during pregnancy**.
- Pregnancy → high prevalence of **baseline tachycardia**

DETERMINING PRETEST PROBABILITY

- revised Geneva score or **YEARS criteria** :
- **clinical signs of deep venous thrombosis [DVT]**
- **hemoptysis**
- **PE as the most likely diagnosis**) in conjunction with both **D-dimer** and **targeted PE imaging** has gained traction and may reduce the number of unnecessary scans performed for PE during pregnancy.



CHEST RADIOGRAPH

- Despite poor diagnostic accuracy → **perform chest radiography in every pregnant patient in whom a PE is suspected.**
- The chest radiograph primarily **evaluates alternative diagnoses** (eg, pneumonia, pneumothorax, pulmonary edema, cardiomegaly).
- The chest radiograph **helps decide what diagnostic test needs** to be performed.

CHEST RADIOGRAPH

- **Normal CXR** improves the diagnostic accuracy of **ventilation/perfusion (V/Q)** scanning when compared with nonpregnant individuals.
- In contrast, an **abnormal chest radiograph** decreases the diagnostic accuracy of V/Q scanning and should prompt the clinician to directly proceed to computed tomographic (CT) **pulmonary angiography (CTPA)**.

SELECTION OF IMAGING MODALITY

- PE cannot be **definitively diagnosed** without confirmatory imaging
- For those in whom the clinical evaluation suggests **coexistent lower extremity DVT** (eg, **leg pain, swelling, and/or erythema**), we perform **bilateral lower extremity proximal vein CUS**.

SELECTION OF IMAGING MODALITY

- The risks and benefits of each modality need to be weighed separately in the context of:
 - **patient preference**
 - **diagnostic accuracy**
 - **Availability**
 - **comorbidities** (eg, renal insufficiency or allergy to contrast)
 - **amounts of radiation and contrast exposure.**

CTPA IS ALSO THE PREFERRED MODALITY WHEN:

- ▶ **chest radiograph is abnormal**
- ▶ **doubt by ventilation perfusion (V/Q) scan (eg, indeterminate/moderate probability V/Q scan)**
- ▶ **V/Q scanning is not available**

CTPA

- In **contrast-allergic patients**:
- **premedicate for the allergy** and consider **empiric anticoagulation**
while waiting for the CTPA

ABNORMAL CHEST RADIOGRAPH: CTPA

- When the **chest radiograph is normal**, **V/Q scanning** or **CTPA** are appropriate.
- **In the past**, V/Q scanning was the preferred test in pregnant patients with suspected PE who had a normal chest radiograph
- Most clinicians, **now use CTPA as the primary modality** for evaluating pregnant patients for PE:

NORMAL CHEST RADIOGRAPH: CTPA OR V/Q

- **CTPA is more readily available than V/Q scanning**
- **may provide an alternate diagnosis** in 12 to 13 percent of cases,
- **associated with lower doses of radiation** than in the past
- has **better interobserver agreement for radiologists** than nuclear scans.
- In **contrast-allergic patients**, however, we perform **V/Q scanning** as a reasonable and equally diagnostic alternative to CTPA in the setting of a normal chest radiograph.

RADIATION AND CONTRAST EXPOSURE

- **CTPA** delivers slightly **lower fetal radiation** doses than V/Q scanning (0.003 to 0.131 mGy versus 0.32 to 0.74 mGy, in the first through third trimester)
- **CTPA** delivers **higher maternal doses** of radiation than V/Q scanning (7.3 versus 0.9 mSv)

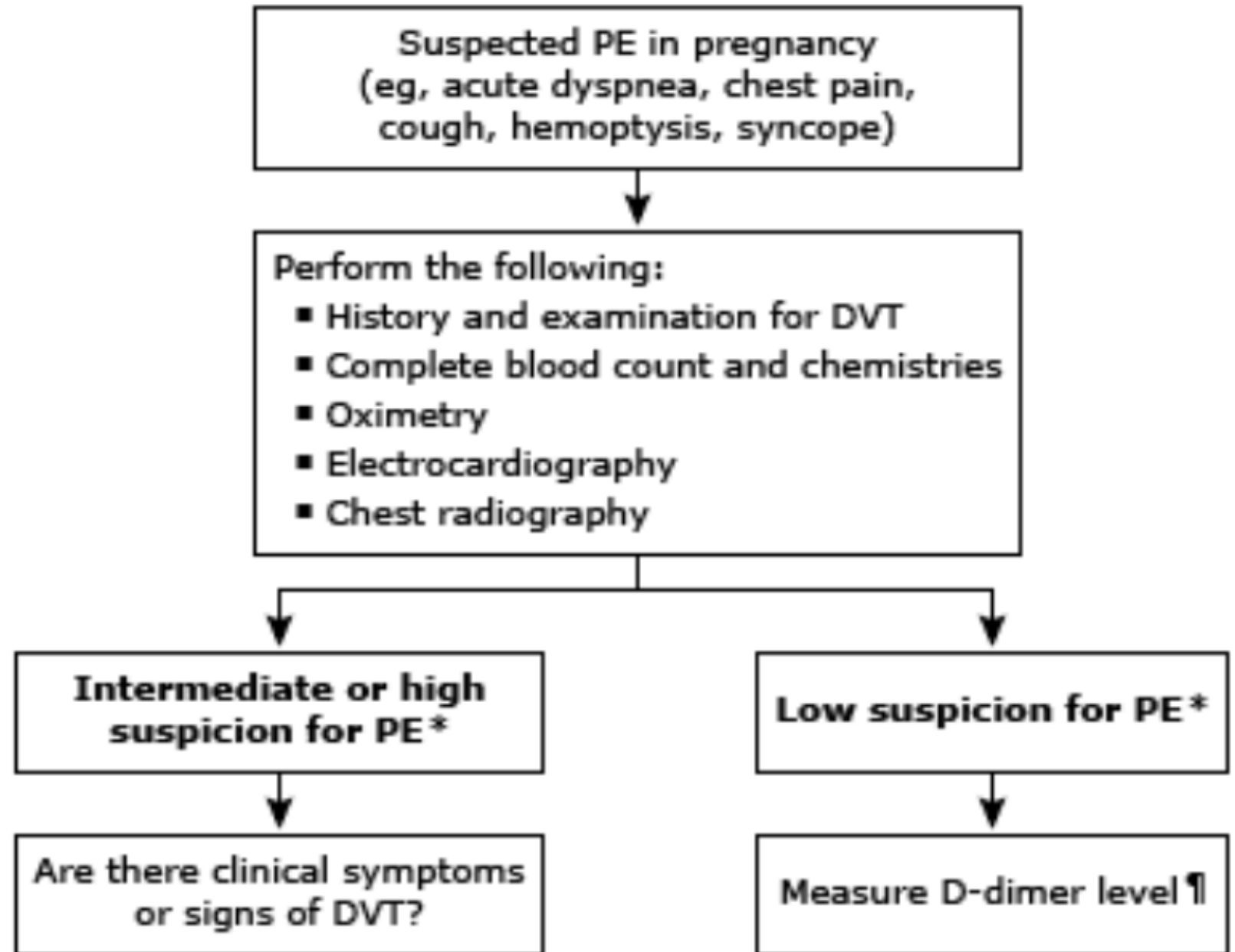
Table 12 Estimated amounts of radiation absorbed in procedures used to diagnose pulmonary embolism (based on various references^{385,392–398})

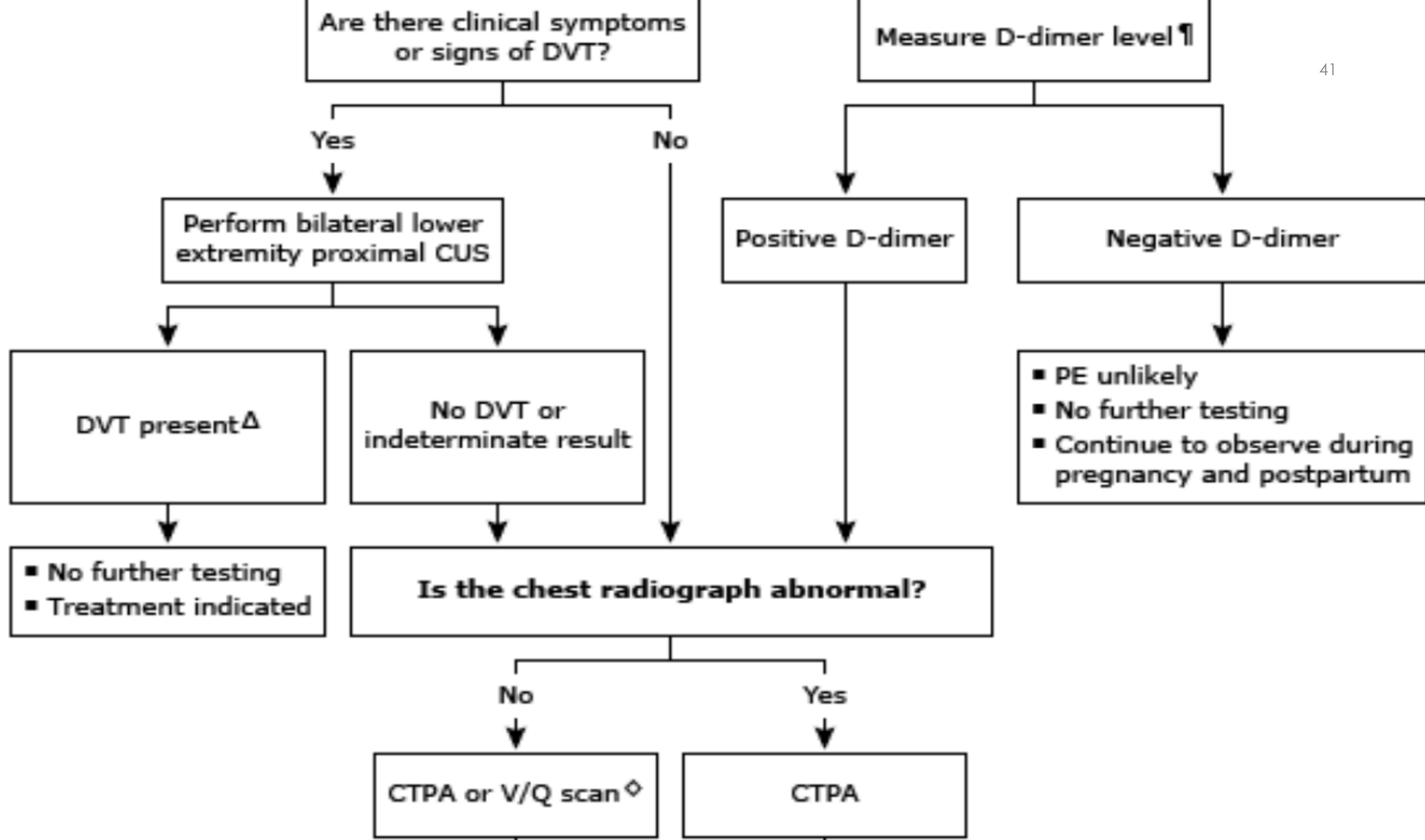
Test	Estimated foetal radiation exposure (mGy) ^a	Estimated maternal radiation exposure to breast tissue (mGy) ^a
Chest X-ray	<0.01	<0.1
Perfusion lung scan with technetium-99m-labelled albumin		
Low dose: ~40 MBq	0.02–0.20	0.16–0.5
High dose: ~200 MBq	0.20–0.60	1.2
Ventilation lung scan	0.10–0.30	<0.01
CTPA	0.05–0.5	3–10

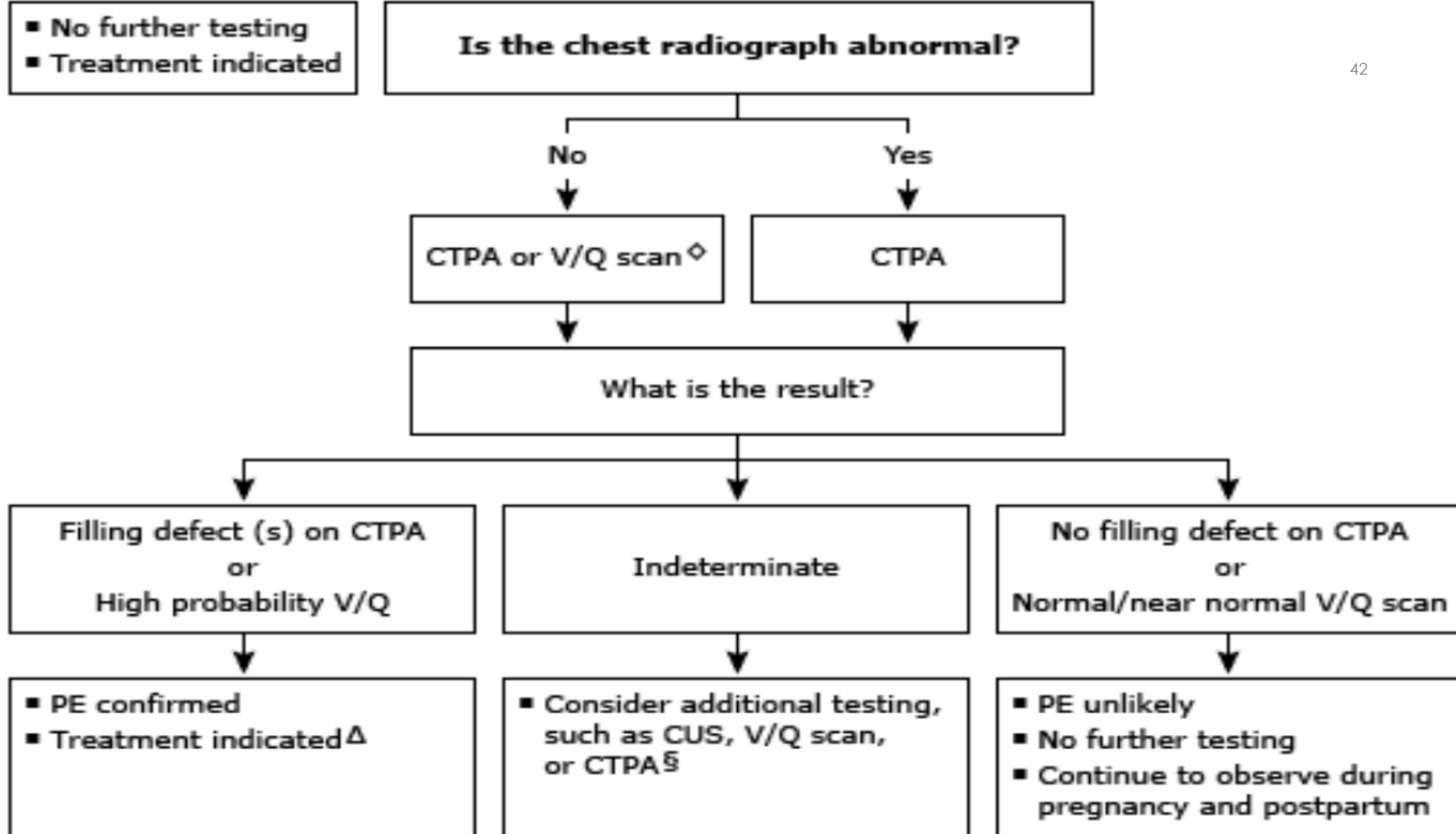
CTPA = computed tomography pulmonary angiography; mGy = milligray; MBq = megabecquerel; PE = pulmonary embolism

DIAGNOSTIC ALGORITHM

- Similar to nonpregnant patients, any one or combination of **acute-onset dyspnea, pleuritic pain, hemoptysis, syncope, or hypoxemia**, particularly in the setting of a normal chest radiograph, should raise the clinical suspicion for PE during pregnancy.







SUSPECTED PE DURING PREGNANCY

High pretest probability, or intermediate/low probability and positive D-dimer result

Anticoagulate with LMWH

- Chest X-ray^a
- Compression proximal duplex ultrasound, if symptoms or signs suggestive of DVT^b

Proximal DVT not present

SPECIFIC INVESTIGATION FOR PE

- If chest X-ray normal => CTPA or perfusion lung scan
- If chest X-ray abnormal^a => CTPA^c

Negative

PE ruled out

Negative

Review by radiologist or nuclear physician experienced in diagnosis of PE in pregnancy

Indeterminate or positive

Positive

Proximal DVT present



- Continue with LMWH at therapeutic dose^d
- Assess PE severity and the risk of early death^e
- Refer to multidisciplinary team with experience of PE management in pregnancy
- Provide plan to guide management of pregnancy, labour and delivery, postnatal and future care

- اگه قراره از زندگی لذت ببریم، الان وقتشه!
- نه فردا، نه ماه دیگه، نه سال دیگه.
- امروز باید زیباترین روز زندگیت باشه،
- از همین امروز لذت ببرید،
- زندگی همین لحظه ست.

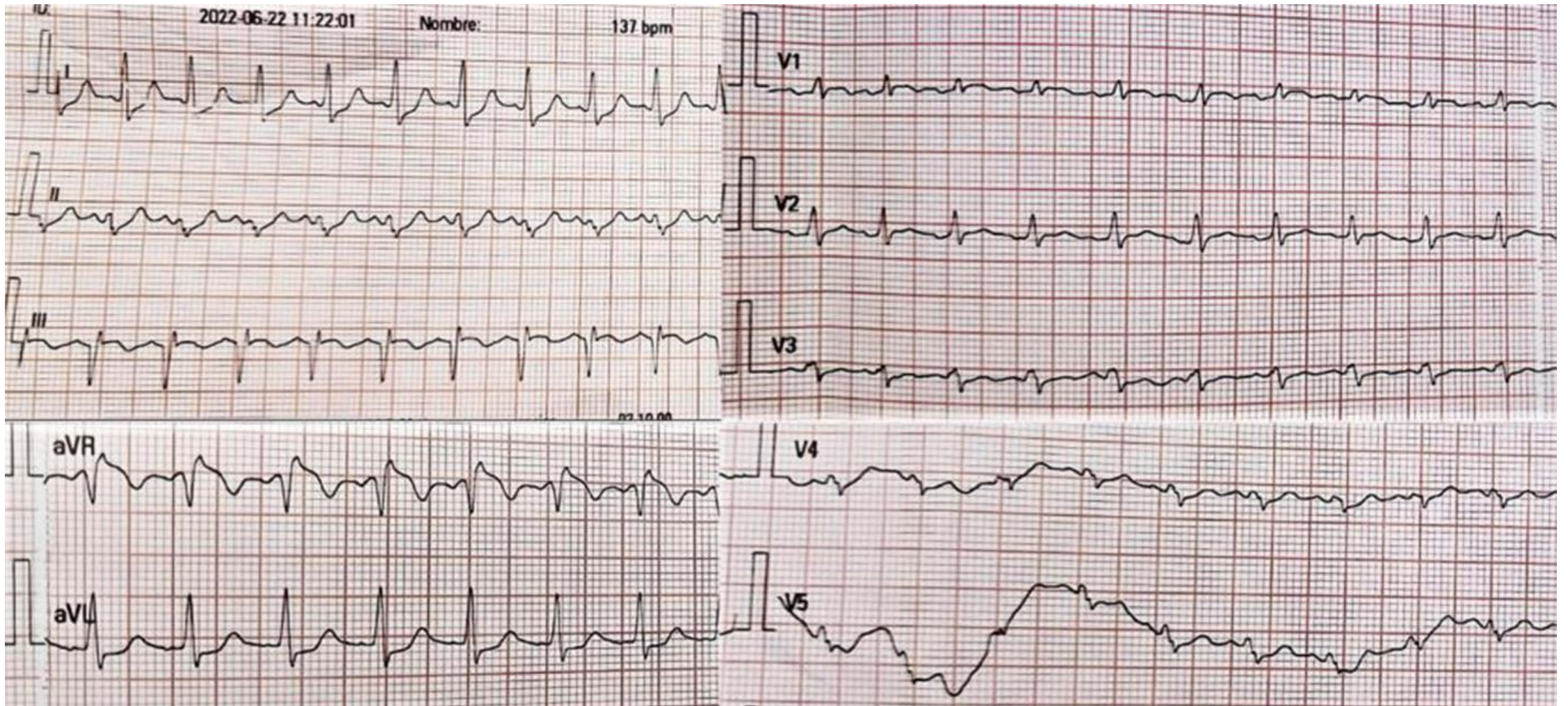


CASE

- **A 24-year-old female patient, gravidity 3 Parity 2, 26 weeks pregnant, was admitted to the emergency department after being found unconscious, diaphoretic, and cold, with subsequent partial recovery of consciousness, and after collapsing three times**

- the patient was **stuporous, diaphoretic, and cold**, with a blood pressure of **60/28 mmHg** and a heart rate of **155 bpm**.
Fluid replacement was started

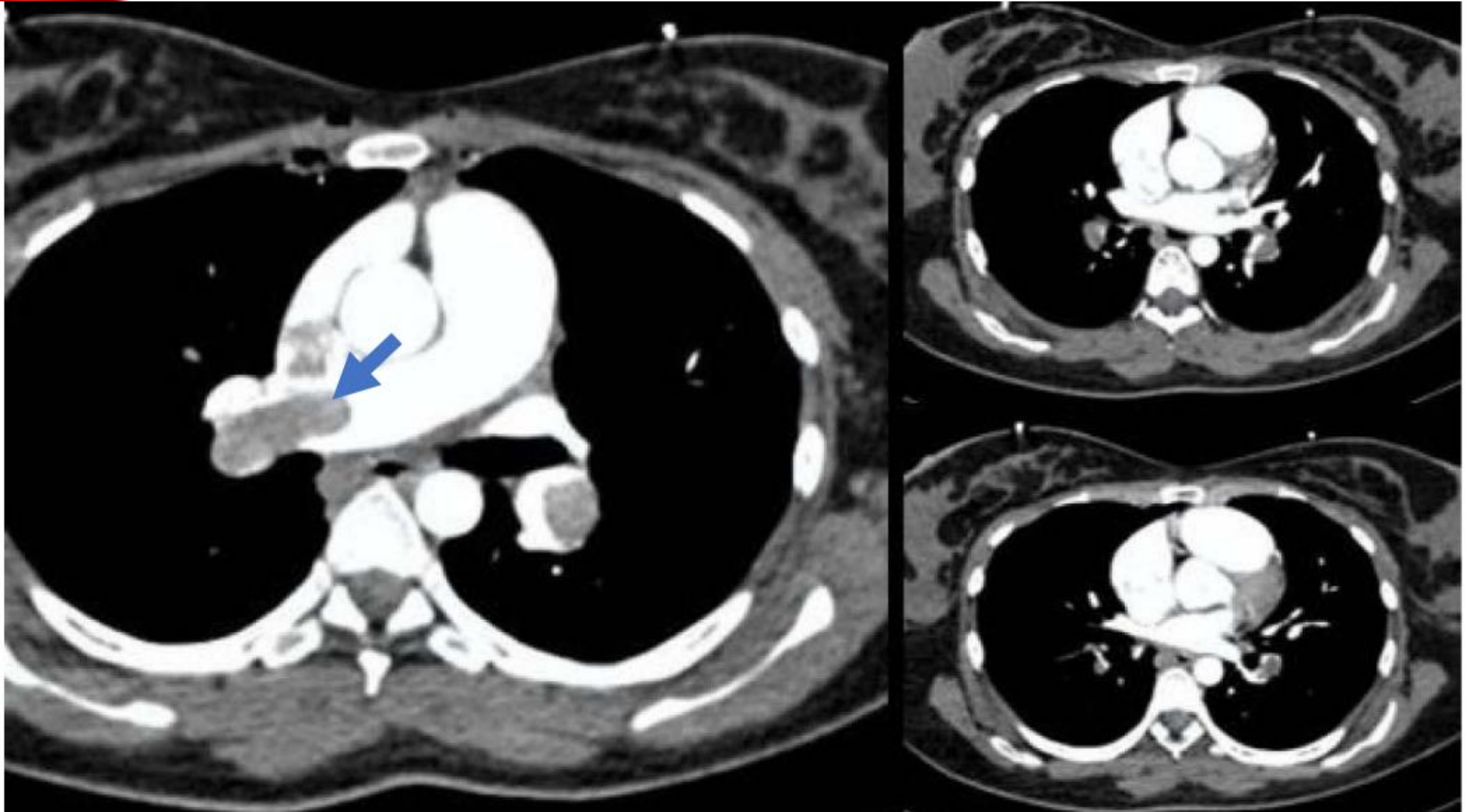
Q-WAVE IN DIII, AND AN INVERTED T-WAVE IN DERIVATIVE DII



- Point of care ultrasound (POCUS) was performed, which revealed right ventricular dilatation, and **PTE was suspected**



- **Enoxaparin 60 mg** subcutaneously every 12 hours
- initiating vasopressors centrally
- **ECHO:** signs of right ventricular dysfunction or pulmonary hypertension=**Thrombolysis with 100 mg of tissue plasminogen activator (Alteplase-Reteplase)**



TREATMENT

- multidisciplinary approach (eg, PE response team, **pulmonology, maternal-fetal medicine, obstetric anesthesia, hematology, neonatology**).

NON-LIFE-THREATENING THROMBOSIS

- **Assess bleeding risk**

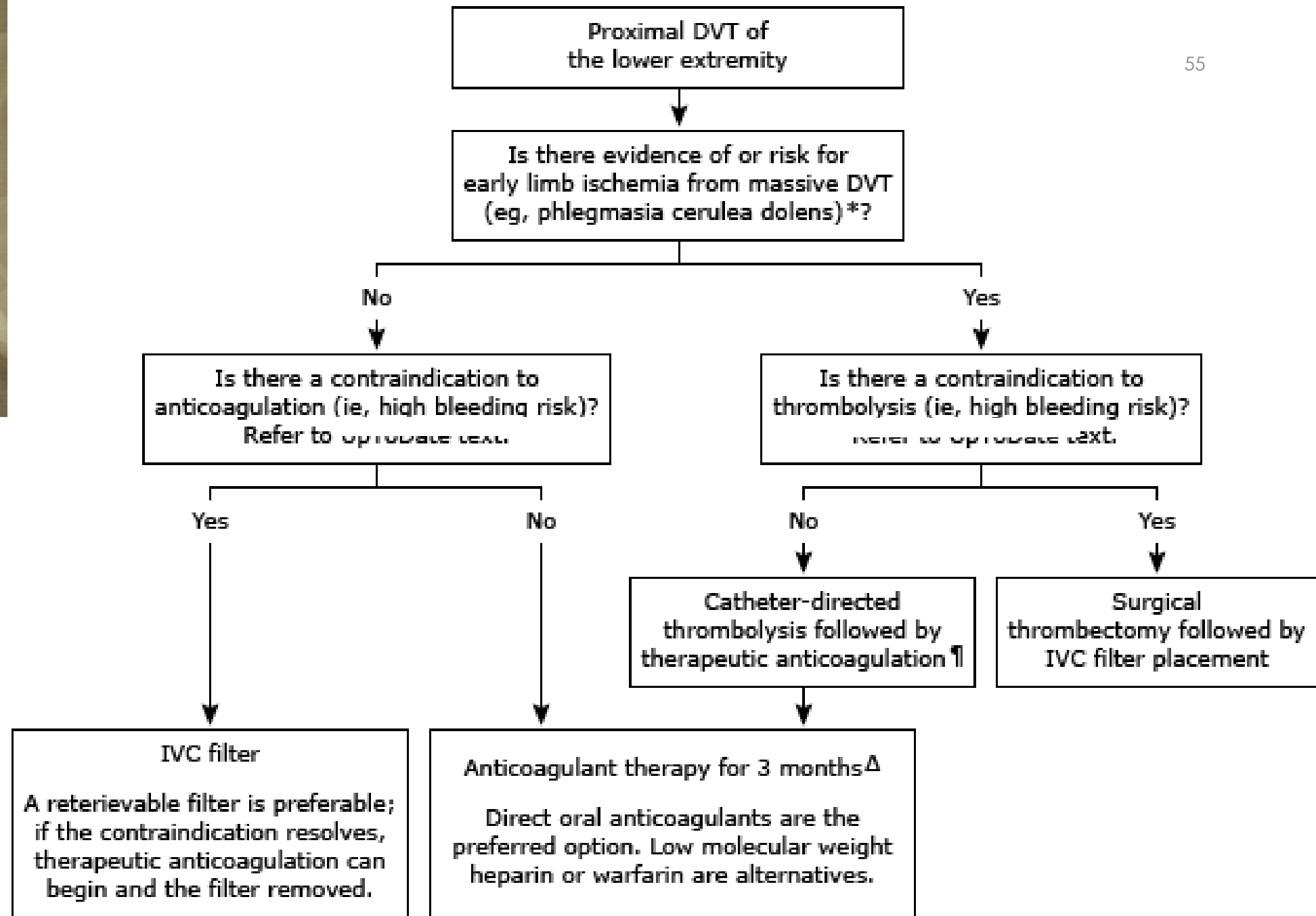
- **General bleeding risk**

- **Obstetric-specific risk**

- Unique to pregnancy are the risks of **antepartum placental abruption** (with both **consumptive and dilutional disseminated coagulopathy**) and **postpartum hemorrhage**

TREATMENT OF PROXIMAL DVTOF THE LOWER EXTREMITY

- Manifestations of DVT that are concerning for potential or actual limb-threatening ischemia include **sudden severe pain, swelling, cyanosis, edema, venous gangrene, compartment syndrome, and absent pulses.**
- Delay in treatment may result in circulatory collapse, shock, death, or loss of the patient's limb.



TREATMENT (PE)

- When there is a **high clinical suspicion** for acute PE, **empiric anticoagulant therapy** is indicated prior to the diagnostic evaluation.
- For those patients in whom PE is suspected but **anticoagulant therapy is contraindicated**, diagnostic evaluation should be **expedited**. Anticoagulation-independent therapy (eg, **inferior vena cava filter (suprarenal, temporary, retrievable IVC filter)**) is indicated if VTE is confirmed.
- When there is suspicion for **DVT alone** (no clinical evidence or suspicion of acute PE), **anticoagulant therapy is generally withheld until VTE is confirmed**.

DURING PREGNANCY

- For most pregnant patients, subcutaneous **low molecular weight (LMWH) heparin** is the agent of **choice**.
- LMW heparin may be switched to **unfractionated heparin (UFH)** in some patients **prior to labor**.

DURING PREGNANCY

- **Warfarin** and direct oral anticoagulants (**DOACs**) are typically **avoided** in pregnancy.∅
- **Fondaparinux**, a synthetic heparin pentasaccharide, is generally avoided due to a paucity of safety data during pregnancy, with the **only potential indication in the setting of heparin-induced thrombocytopenia (HIT)**.

DURING PREGNANCY

- **Subcutaneous LMWH** is preferred over IV UFH or subcutaneous UFH in most patients because it is easier to use and it appears to be more efficacious and has a better safety profile.
- In contrast, **IV UFH** is preferred in patients who have an **elevated risk of bleeding or persistent hypotension due to pulmonary embolism (PE)**.

DURING PREGNANCY

- The rationale is that its **short half-life** and near complete reversal with **protamine** are desirable if the anticoagulant effect needs to be stopped due to bleeding or to perform a procedure.
- **severe renal failure** → **UFH** (either IV or subcutaneous) is preferred

DOSING LMWH

dalteparin 200units/kg once daily,

tinzaparin 175 units/kg once daily

enoxaparin 1 mg/kg every 12 hours

DOSING UFH

- **IV UFH** : IV UFH bolus of **80 units/kg**, followed by a continuous infusion of **18 units/kg per hour**
- The infusion is titrated **every six** hours to achieve a therapeutic activated partial thromboplastin time (aPTT).
- IV UFH can be transitioned to **subcutaneous UFH** or **subcutaneous LMWH** if long-term or outpatient anticoagulant therapy is planned.

DOSING UFH

- **Subcutaneous UFH:**
- A reasonable initial dose of subcutaneous UFH is **17,500 units every 12 hours**.
- The dose is then titrated to achieve a therapeutic aPTT
- **The first aPTT** is generally measured **six hours after the second dose**. Most adjustments should be an increase or decrease of 10 to 30 percent.
- Once a stable dose is achieved, the aPTT may be measured after **three to four days** of treatment and then **every few weeks**.

LABOR AND DELIVERY

- Treatment with subcutaneous LMWH be converted to UFH **>36 h prior to delivery**. The UFH infusion should be stopped **4 - 6 h prior** anticipated delivery
 - Particularly important for patients who desire **neuraxial anesthesia** because **anticoagulation during insertion (or removal) of a neuraxial anesthesia catheter increases the risk for spinal hematoma.**

LABOR AND DELIVERY

- A period of 24 to 36 hours without anticoagulant therapy may be undesirable in pregnant women who are at high risk for recurrent VTE (eg, those with **an acute PE or proximal DVT that developed within the past month**).
 - Such patients may benefit from having their subcutaneous LMWH or subcutaneous UFH switched to **IV UFH**, which can be **discontinued 4 to 6 hours prior to delivery**.

LABOR AND DELIVERY

- Delivery despite full anticoagulation may also occur if **labor begins unexpectedly.**

Many patients who deliver while anticoagulated will not have excessive intrapartum bleeding .

Neuraxial anesthesia should **not be administered to an anticoagulated patient.**

POSTPARTUM AND LACTATION

- heparin regimen (subcutaneous LMWH, IV UFH, or subcutaneous UFH) should be restarted **12 hours after a cesarean** delivery or **six hours after a vaginal birth**, assuming that significant bleeding has not occurred.
- Options for long-term anticoagulant therapy include **subcutaneous LMWH, subcutaneous UFH, or an oral vitamin K antagonist (eg, warfarin)**.

POSTPARTUM AND LACTATION

- **If warfarin therapy is chosen, the patient should receive both warfarin and heparin for at least five days.**
- The heparin should not be stopped until the international normalized ratio (**INR**) has been within therapeutic range (**usually 2 to 3**) for two consecutive days.

LACTATION

- **LMWH** through the postpartum period or transition to **warfarin**
- For patients in whom a potential procedure is anticipated, intravenous **UFH** is the usual alternative.
- **DOACs** are avoided during breast feeding

DURATION OF THERAPY

- For those with VTE diagnosed during pregnancy, we treat with anticoagulant therapy for **at least three months**
 - this duration should include the **remainder of pregnancy and at least six weeks postpartum.**

DURATION OF THERAPY

- For those with VTE diagnosed postpartum, we treat with anticoagulation for a minimum of **three months**.
- Once the definite period of anticoagulant therapy is completed, we evaluate patients for possible continued or indefinite therapy (eg, persistent risk factors).

Indication	Type of heparin	Dosing information
VTE prevention	LMW heparin	<ul style="list-style-type: none"> •Low dose (also called prophylactic dose): Enoxaparin: <ul style="list-style-type: none"> • Weight <100 kg: 40 mg SUBQ once daily • Weight ≥100 kg: 60 mg SUBQ once daily •or •Dalteparin: <ul style="list-style-type: none"> • Weight <100 kg: 5000 units SUBQ once daily • Weight ≥100 kg: 7500 units SUBQ once daily
		<ul style="list-style-type: none"> •Intermediate dose*: Enoxaparin 40 mg SUBQ once daily, increase as pregnancy progresses and weight increases to 1 mg/kg once daily •or •Dalteparin 5000 units SUBQ once daily, increase as pregnancy progresses and weight increases to 100 units/kg once daily
	UFH	<ul style="list-style-type: none"> •According to trimester¹: First trimester: 5000 to 7500 units SUBQ every 12 hours •Second trimester: 7500 to 10,000 units SUBQ every 12 hours •Third trimester: 10,000 units SUBQ every 12 hours
VTE treatment (therapeutic dose)	LMW heparin	Enoxaparin 1 mg/kg SUBQ every 12 hours or Dalteparin 100 units/kg SUBQ every 12 hours
	UFH	Can be given as a continuous IV infusion or SUBQ dose every 12 hours. Titrated to keep the aPTT in the therapeutic range.

Indications and potential indications for thrombolytic therapy in venous thromboembolism

Indication

- High-risk (massive) PE (ie, presence of hypotension related to PE)*

Potential indication

- Patients with severe right ventricular dysfunction due to PE (ie, intermediate risk PE)
- Others:
 - Presence of severe hypoxemia (particularly in those with a contribution from concomitant cardiopulmonary disease)
 - Patients with acute PE who appear to be decompensating but are not yet hypotensive
 - Extensive clot burden

CHARACTERISTICS OF ANTICOAGULANTS

Anticoagulant	Crosses Placenta	Secreted by Breast Milk	Recommended During Pregnancy	Recommended During Breastfeeding
LMWH	No	Yes	Yes	Yes
UFH	No	Yes	Yes	Yes
Fondaparinux	Yes	Yes	No	Yes
VKA	Yes	Yes	No	Yes
DOAC	Yes	Yes	No	No

Abbreviations: LMWH, Low molecular weight heparin; UFH, Unfractionated heparin; VKA, Vitamin K antagonist; DOAC, Direct oral anticoagulant.

SUMMARY

- ✓ **highest rate VTE in the six weeks postpartum .**
- ✓ **Clinical suspicion DVT low or moderate 3&7 day DUS**
- ✓ **acute onset dyspnea pleuritic pain hemoptysis and cough**
- ✓ **normal oxygenation parameters do not confidently exclude**
- ✓ **YEARS criteria** :clinical signs [DVT] ,hemoptysis ,PE as the most likely diagnosis)

SUMMARY

- ✓ **CXR ,every pregnant patient in whom a PE is suspected.**
- ✓ **high clinical suspicion** for acute PE, **empiric anticoagulant therapy** is indicated But not for suspicion DVT
- ✓ **NL CXR,contrast allergy,renal failure=V/Q**
- ✓ **Ab NL CXR,V/Q Unavailable OR intermediat V/Q=CTAG**
- ✓ **Treatment choic:Enoxaparin,UFH,**
- ✓ **Warfarin and DOAC conterindicate**

SUMMERY

- ✓ **LMWH discontinued at least 24 hours prior to delivery**
- ✓ **UFH discontinued 4 to 6 hours prior to delivery**
- ✓ **if labor begins unexpectedly Nuroaxial anesthesia is conterindicat.**
- ✓ **restarted 12 hours after a cesarean delivery or six hours after a vaginal birth**
- ✓ **lactation: DOACs are avoided during breast feeding**
- ✓ **LMWH ,WARFARIN**

REFERENCES

- ❖ **2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS)**
- ❖ **Pulmonary Thromboembolism in Pregnancy: A Case Report and Literature Review**
- ❖ **UP TO DATE**

با سپاس از توجه شما

