
In The Name Of
GOD

Diagnosis and Treatment of Pulmonary Embolism

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DVT & PE

Hypercoagulable state is characteristic of pregnancy, and DVT occurs in about 1 in 500 pregnancies.
In pregnant most unilateral DVTs occur in the left leg because the left ilaic vein is compressed by the right iliac artery and the uterus compresses the IVC.

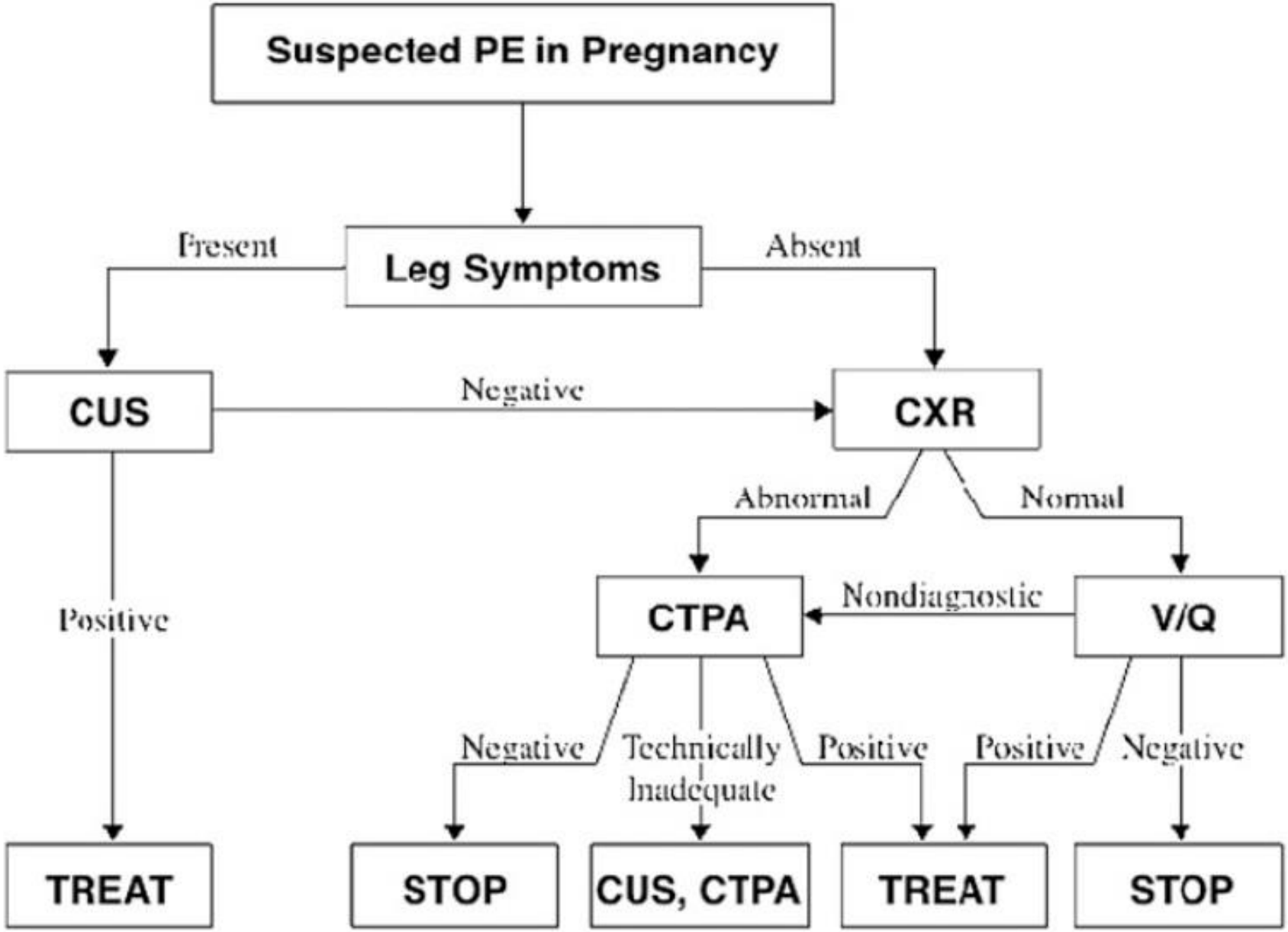


Figure 1. Diagnostic algorithm for suspected PE in pregnancy.

VTE: A strong relationship between DVT and PE

About 50% of patients with proximal DVT of the leg have asymptomatic PE[1]

DVT (mainly asymptomatic) is found in around 80% of patients with PE[2]

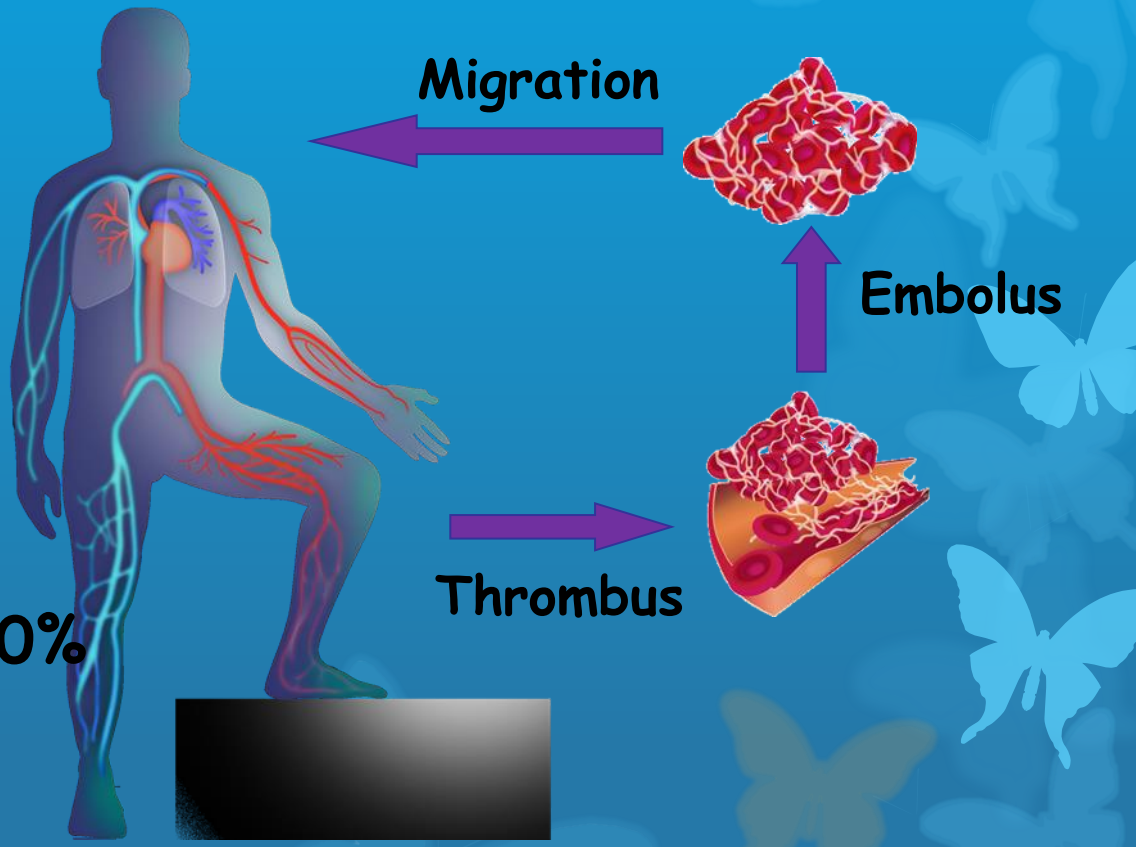


Table 57-1 Thromboembolic Risk Factors

HEREDITARY THROMBOPHILIAS

Protein C deficiency
Protein S deficiency
Antithrombin III deficiency
Factor V Leiden mutation
Prothrombin 20210 G → A variation
Hyperhomocysteinemia
Dysfibrinogenemia
Familial plasminogen deficiency

ACQUIRED SURGICAL PREDISPOSITIONS

Major thoracic, abdominal, or neurosurgical procedures requiring general anesthesia and lasting >30 min
Hip arthroplasty
Knee arthroplasty
Knee arthroscopy
Hip fracture
Major trauma
Open prostatectomy
Spinal cord injury

ACQUIRED MEDICAL PREDISPOSITIONS

ACQUIRED MEDICAL PREDISPOSITIONS

Prior venous thromboembolism
Advanced age (>60 yr)
Malignancy
Congestive heart failure
Cerebrovascular accident
Nephrotic syndrome
Estrogen therapy
Pregnancy and the postpartum period
Obesity
Prolonged immobilization
Antiphospholipid antibody syndrome
Lupus anticoagulant
Inflammatory bowel disease
Paroxysmal nocturnal hemoglobinuria
Behçet syndrome

VENOUS THROMBOEMBOLISM

Deep vein thrombosis and pulmonary embolism

- Identical pathophysiology
- Similar risk factors
- Identical therapeutic goals
- Similar treatment strategies

DX of PE

Clinical history and physical exam.

- PE cannot be diagnosed or excluded on clinical grounds as symptoms and signs are often nonspecific
- CXR
- ECG
- ABG
- Perfusion scan
- D-Dimer
- Spiral CT scan
- MRI angiography
- Echocardiography
- Pulmonary angiography
- Cardiac troponin and brain natriuretic peptide.
  - Cardiac enzymes troponin I and T (right ventricular dysfunction).
  - BNP (left ventricular dysfunction, and acute right ventricular overload)

Diagnosis of Pulmonary Embolism

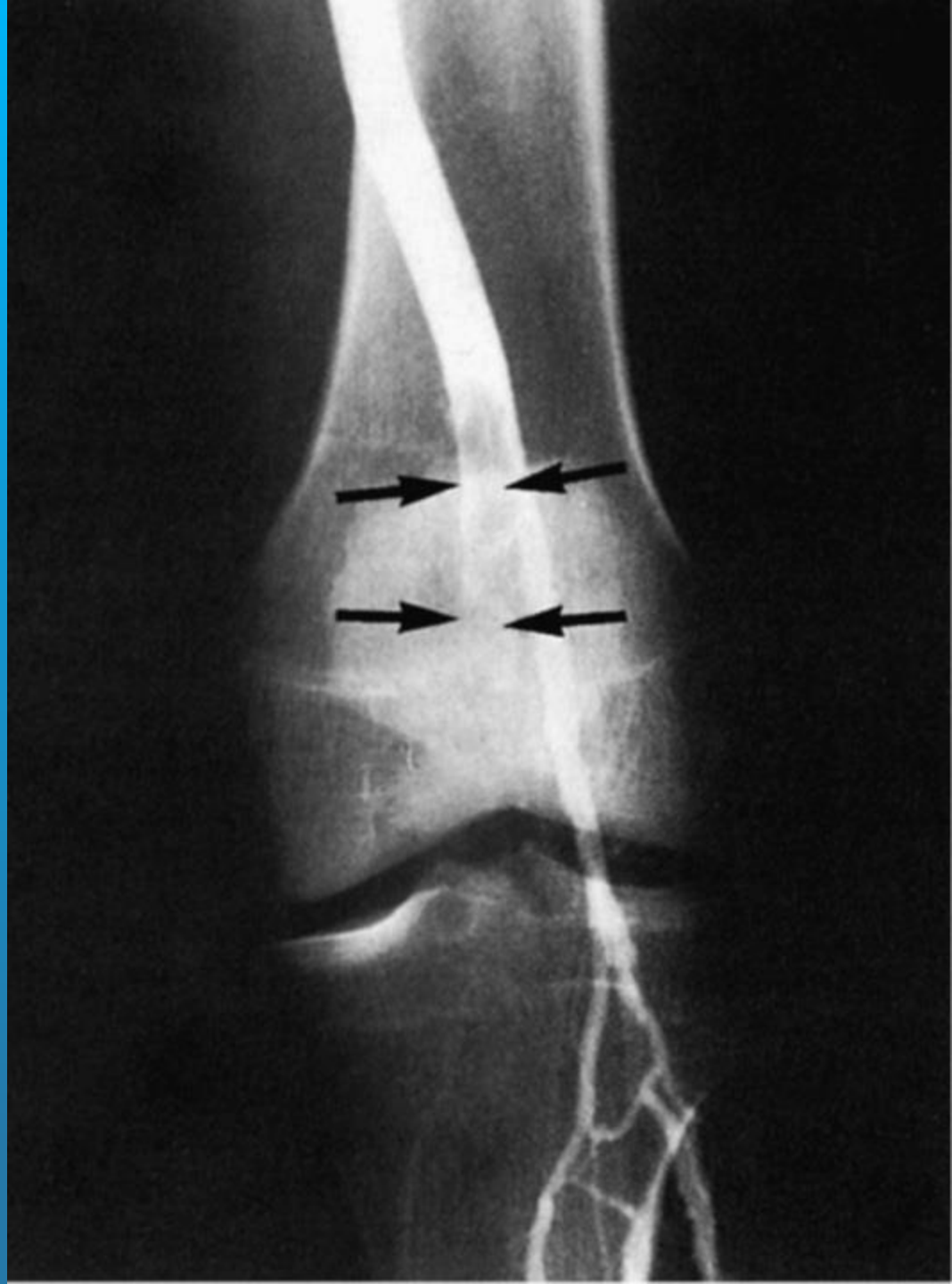
PE should always be considered whenever

unexplained dyspnea is present.

Dyspnea, pleuritic chest pain, and hemoptysis are common in PE but, again, are nonspecific.

Tachypnea and tachycardia are the most common signs of PE but are also nonspecific.

Figure 57-1
Venography for DVT.
Contrast venogram shows a large filling defect (arrows) due to thrombus in the popliteal and distal superficial femoral veins. Such thrombi pose substantial embolic risk.



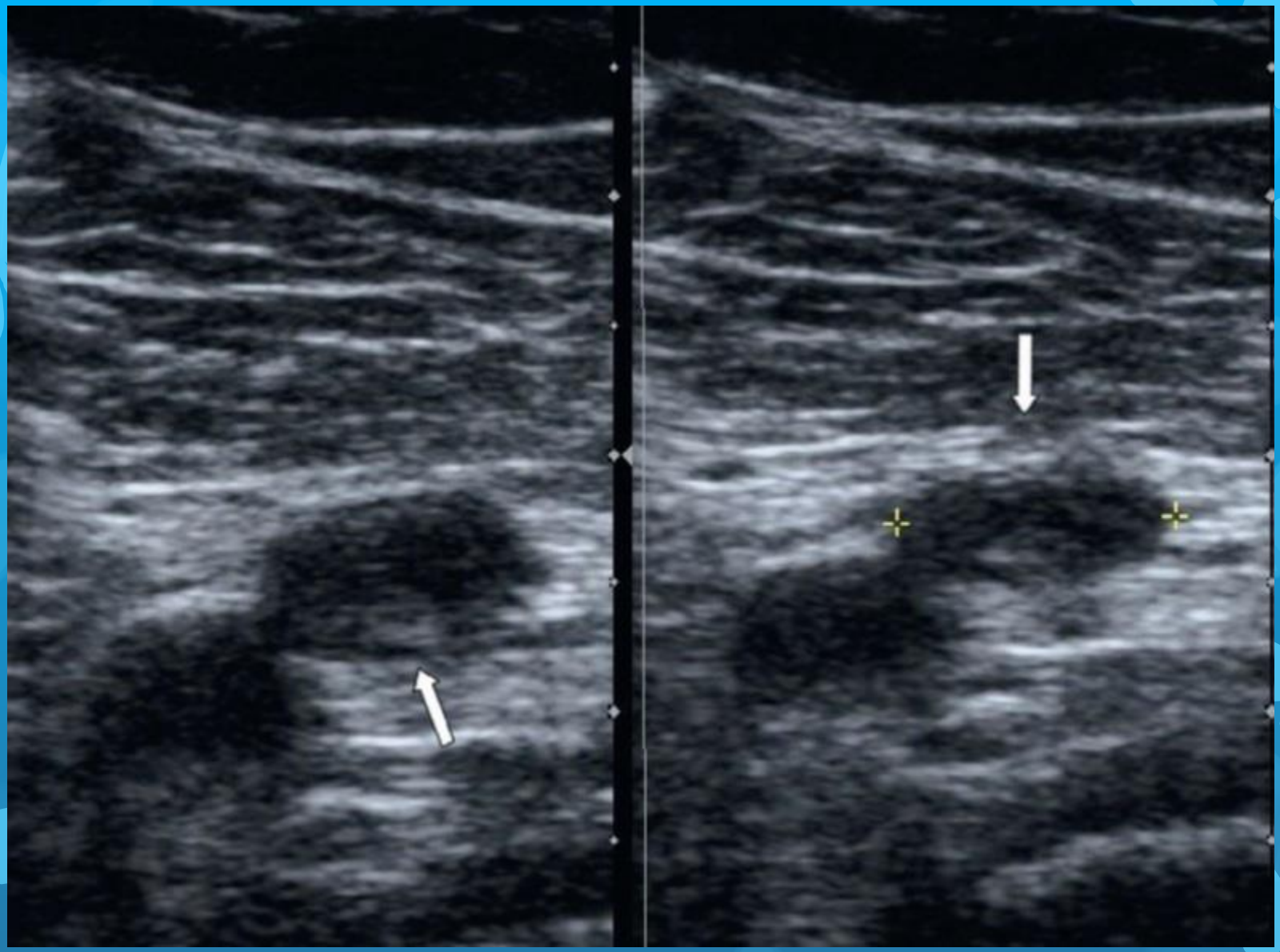


Figure 57-2 Compression ultrasonography for DVT. A, Rest and **B,** compression duplex ultrasonography demonstrates a noncompressible distal superficial femoral vein containing an echogenic mass (arrows), consistent with venous thrombosis.

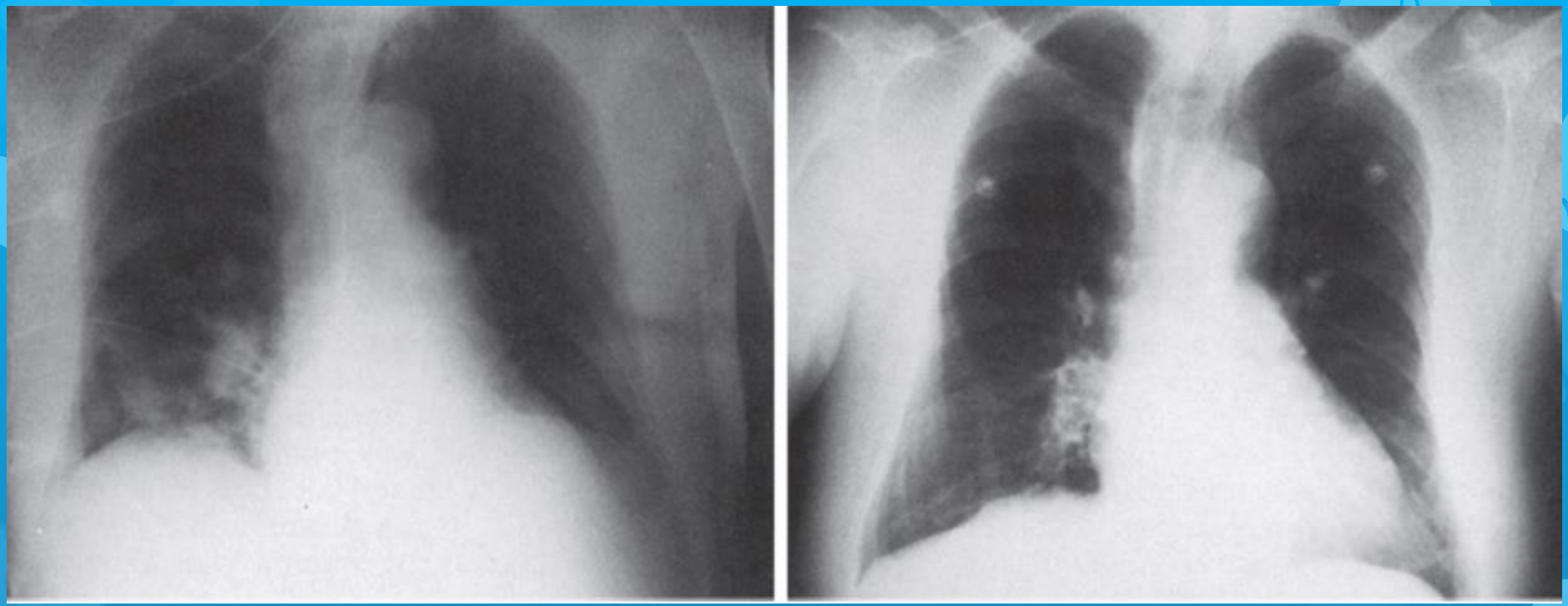


Figure 57-3 Chest radiographs in a patient with pulmonary embolism. A, Opacities caused by atelectasis with edema in the right lower lobe and in the retrocardiac area in a patient with angiographically confirmed pulmonary embolus. **B,** Two weeks later, the opacities have cleared. (Courtesy Michael Gotway, MD.)

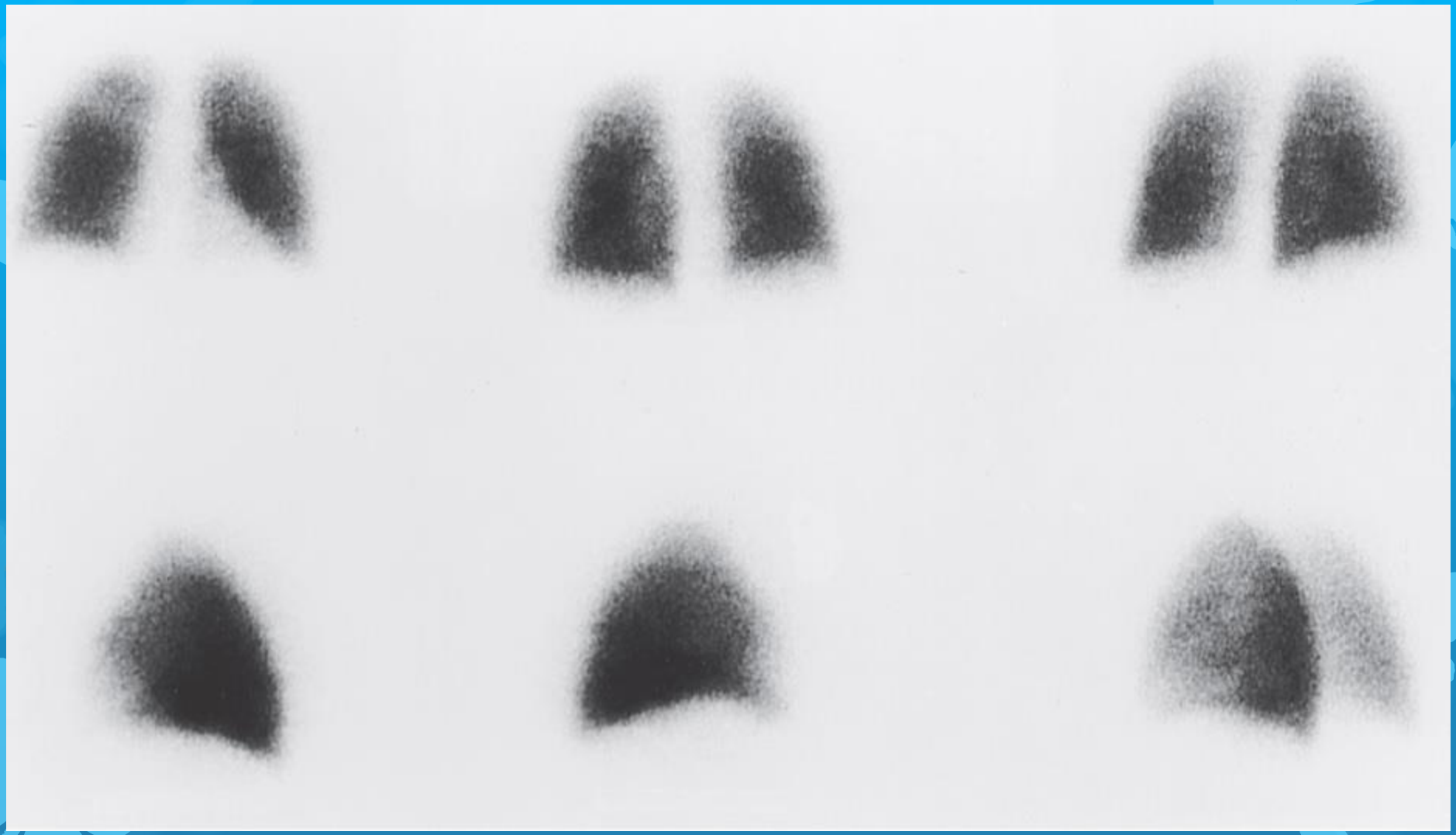


Figure 57-4 Normal six-view lung perfusion scan. This finding is capable of excluding the diagnosis of embolism.

Figure 57-5 Lung perfusion (Q) scan shows major segmental and lobar defects bilaterally. The ventilation scan (not shown) and chest radiograph were normal. This pattern is strongly associated with the presence of embolism.

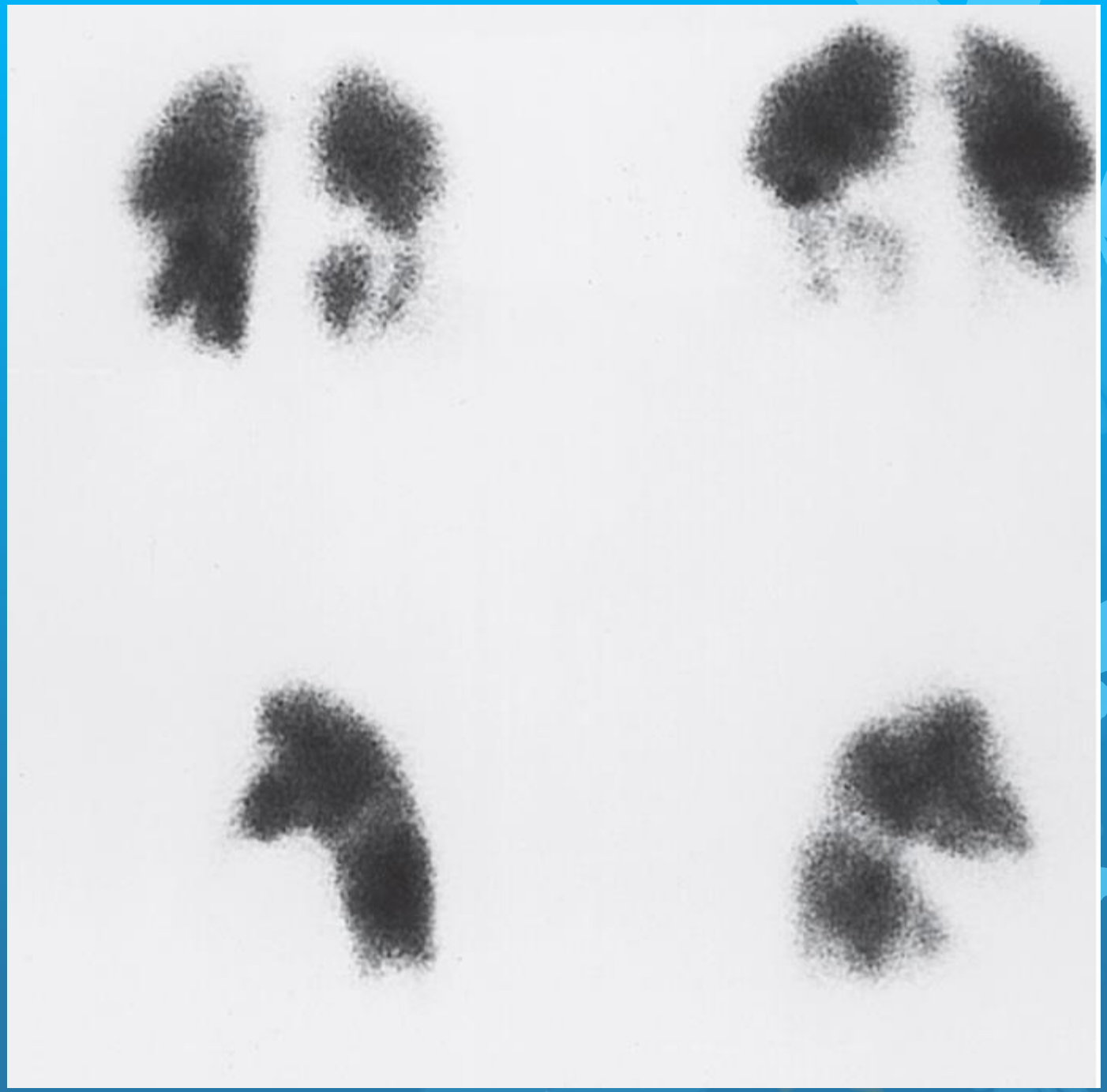


Figure 57-6 CT pulmonary angiography of pulmonary embolism. A–D, Chest CT pulmonary angiography shows bilateral pulmonary emboli, including a "saddle" embolism (black arrowheads, **B** and **C**); right upper lobe emboli (white arrowheads, **A** and **C**), and interlobar emboli (arrows, **B–D**). For a video clip of the full CT study, see Video 57-3.

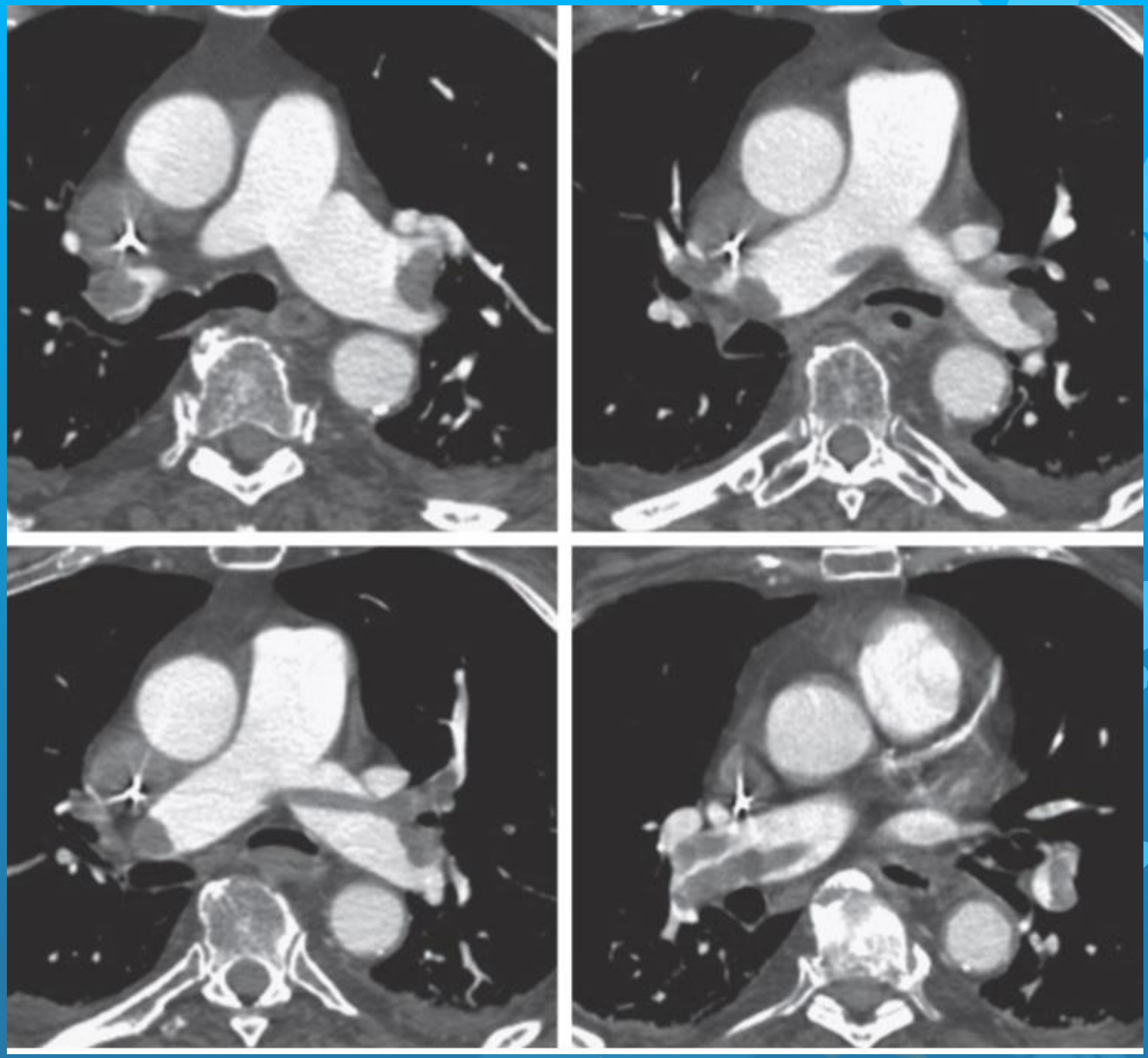


Figure 57-7 Pulmonary angiography for pulmonary embolism. Left-sided pulmonary angiogram shows extensive filling defects within the left pulmonary artery (arrow) and the upper lobe, lingula, and lower lobe arteries, consistent with the diagnosis of pulmonary embolism.

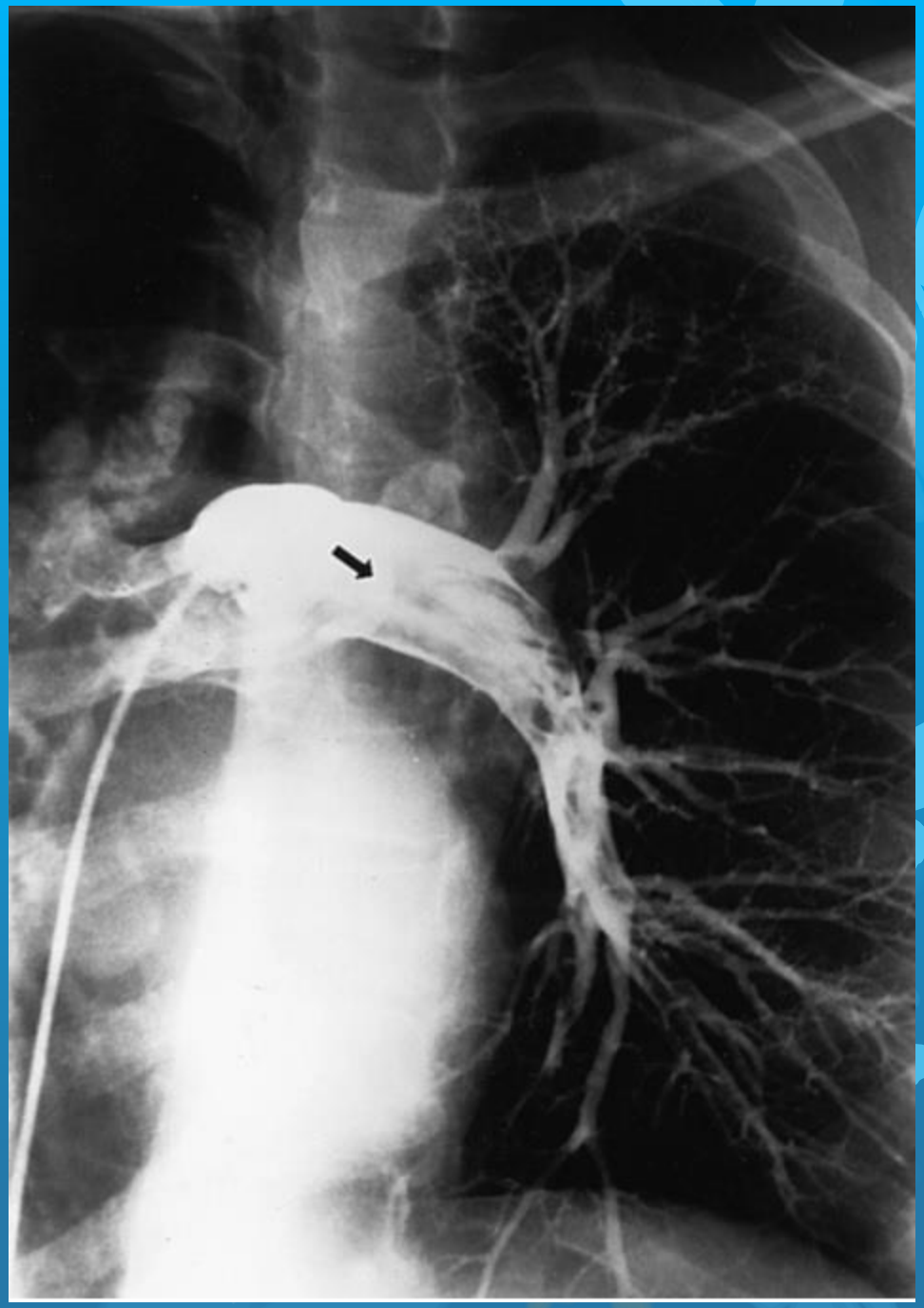
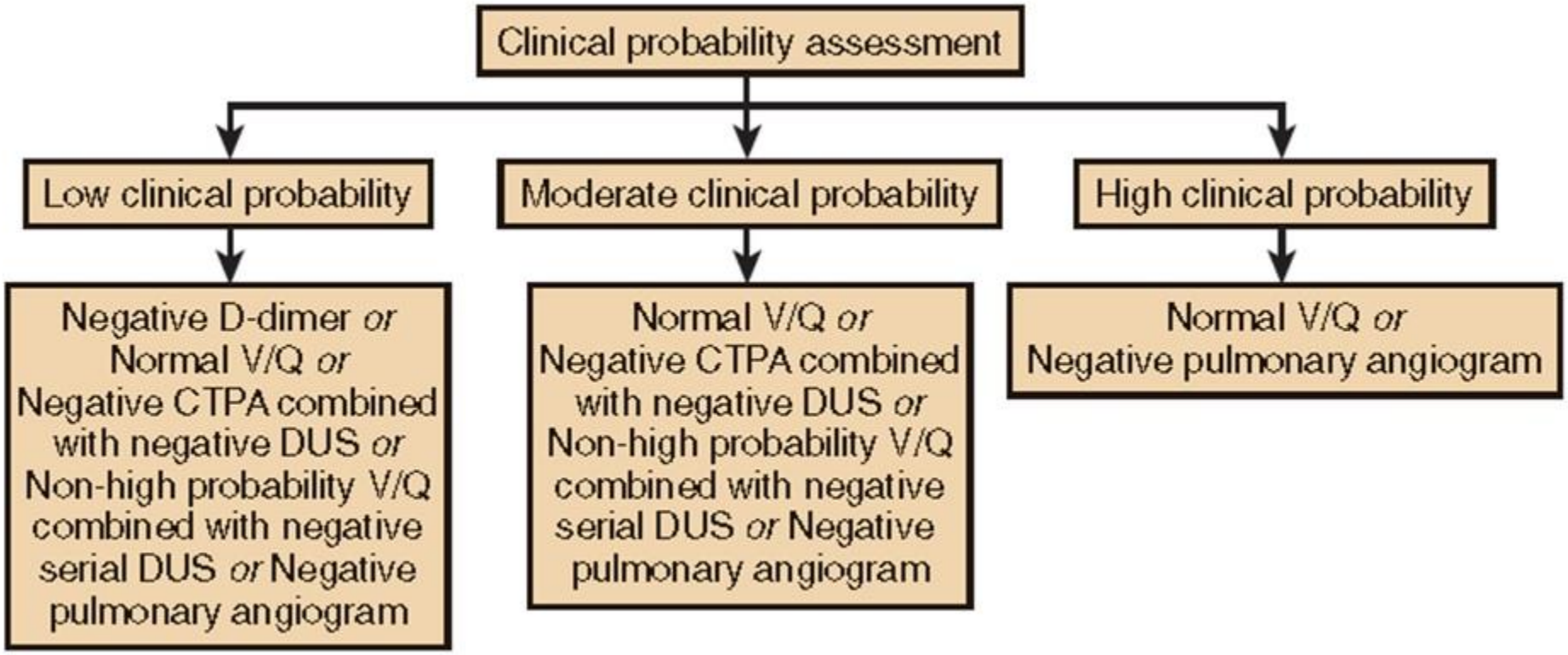


Table 57-3 Wells Clinical Model for Predicting the Pretest Probability of Pulmonary Embolism

Variable	Points Assigned
Clinical signs and symptoms of deep venous thrombosis	3.0
An alternative diagnosis is less likely than pulmonary embolism	3.0
Heart rate >100 beats/min	1.5
Immobilization or surgery in the previous 4 wk	1.5
Previous deep venous thrombosis or pulmonary embolism	1.5
Hemoptysis	1.0
Malignancy (on treatment, treated in the past 6 mo, or palliative)	1.0

Score	Clinical Assessment Probability
<2 points	Low probability
2–6 points	Intermediate probability
>6 points	High probability

From Kearon C: Diagnosis of pulmonary embolism. *CMAJ* 168:183–194, 2003.


Clinical probability assessment
Low clinical probability
Moderate clinical probability
High clinical probability
Negative D-dimer or Normal V/Q or Negative CTPA combined with negative DUS or Non-high probability V/Q combined with negative serial DUS or Negative pulmonary angiogram
Normal V/Q or Negative CTPA combined with negative DUS or Non-high probability V/Q combined with negative serial DUS or Negative pulmonary angiogram
Normal V/Q or Negative pulmonary angiogram

A

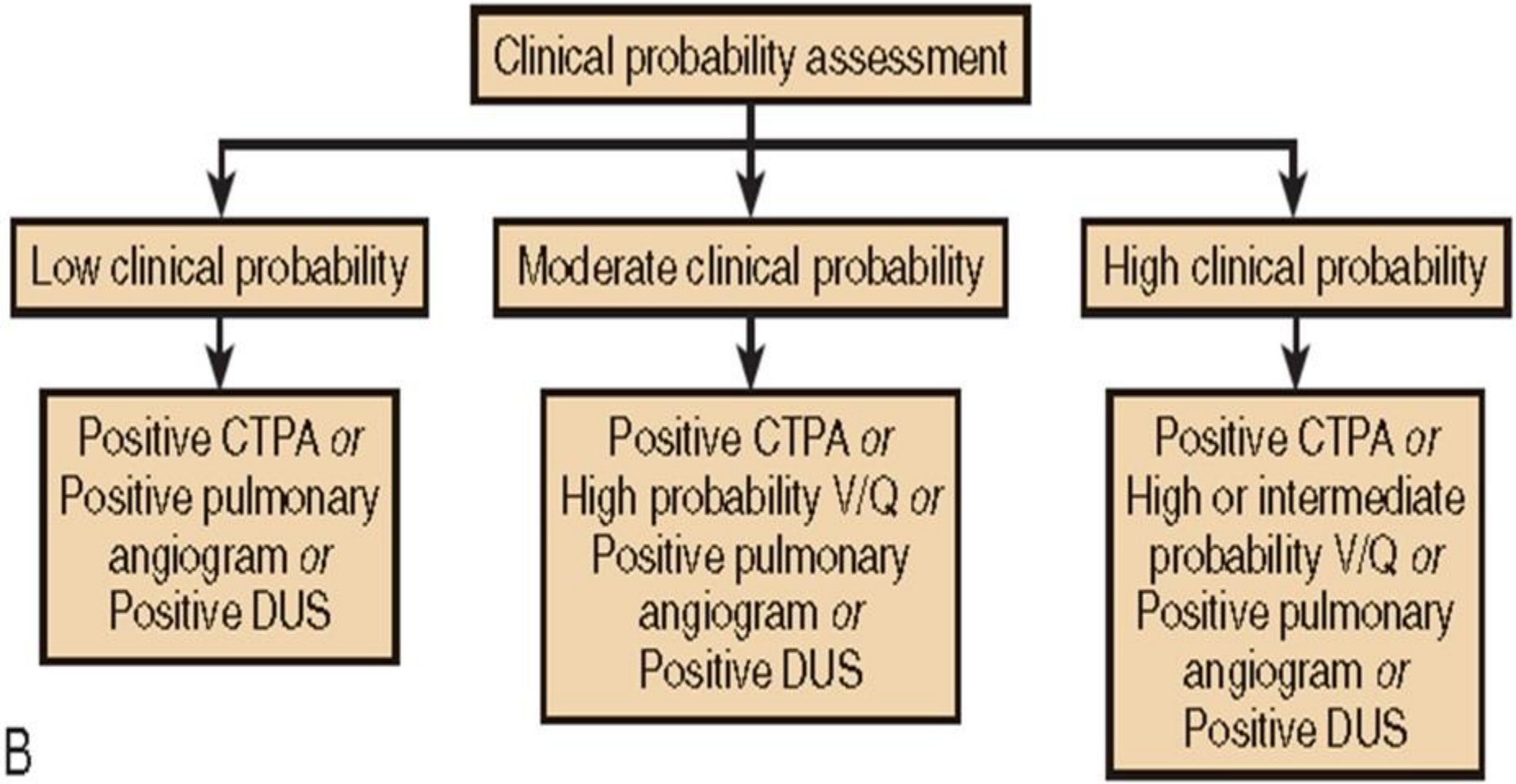


Figure 57-8 Diagnostic strategies capable of excluding (A) and confirming (B) the diagnosis of pulmonary embolism. CTPA, computed tomographic pulmonary angiography; DUS, Doppler ultrasound; serial DUS, serial Doppler ultrasound (1-2 additional tests over the subsequent week); V/Q, ventilation-perfusion scan.

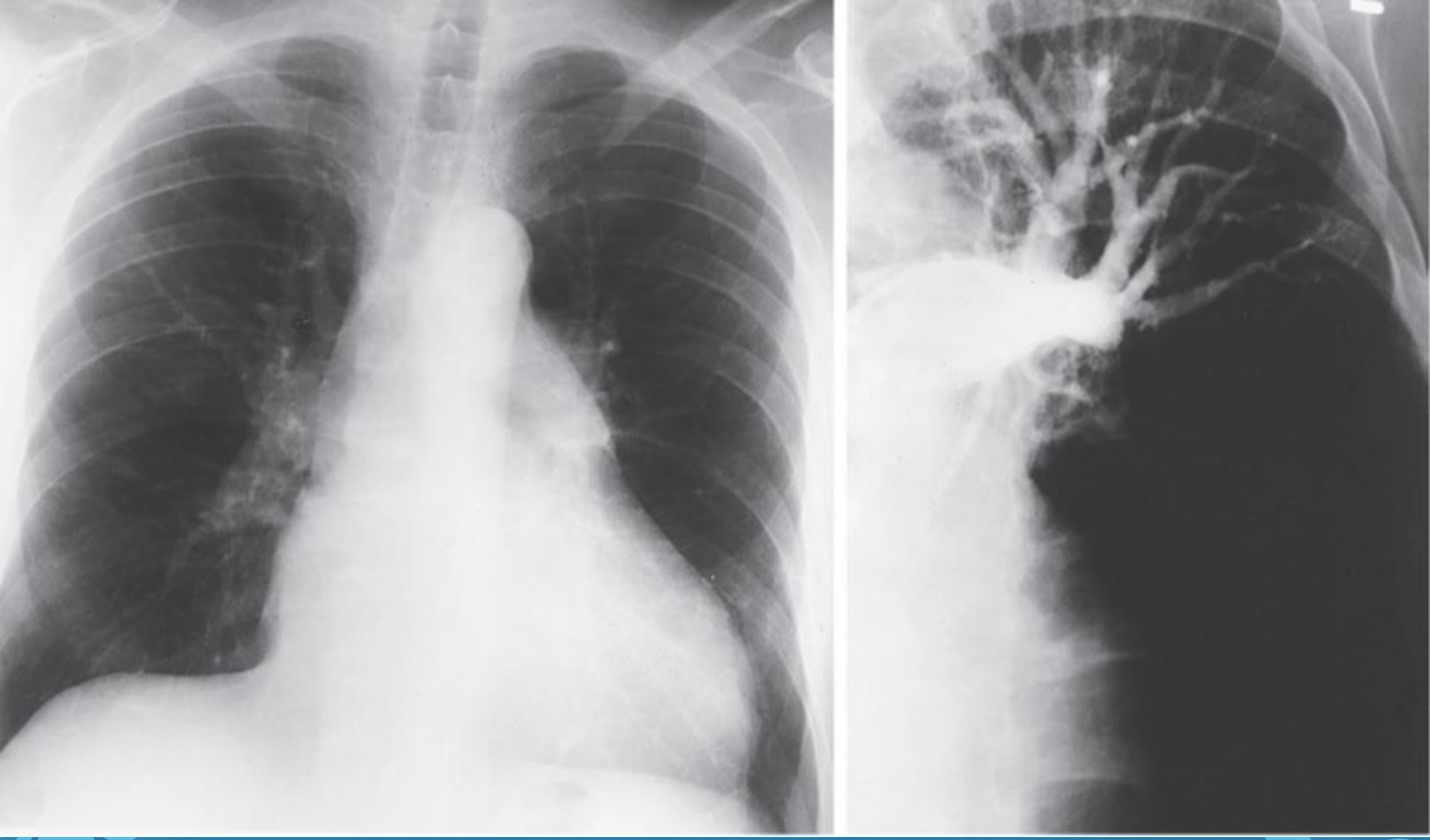


Figure 57-10 Chest radiograph in a patient with chronic thromboembolic pulmonary hypertension. A, Note asymmetry of central pulmonary arteries, absence of descending left pulmonary artery, left lower lobe oligemia, and peripheral opacity representing prior infarct. **B,** Angiogram in the same patient demonstrates complete proximal occlusion of the descending left pulmonary artery.

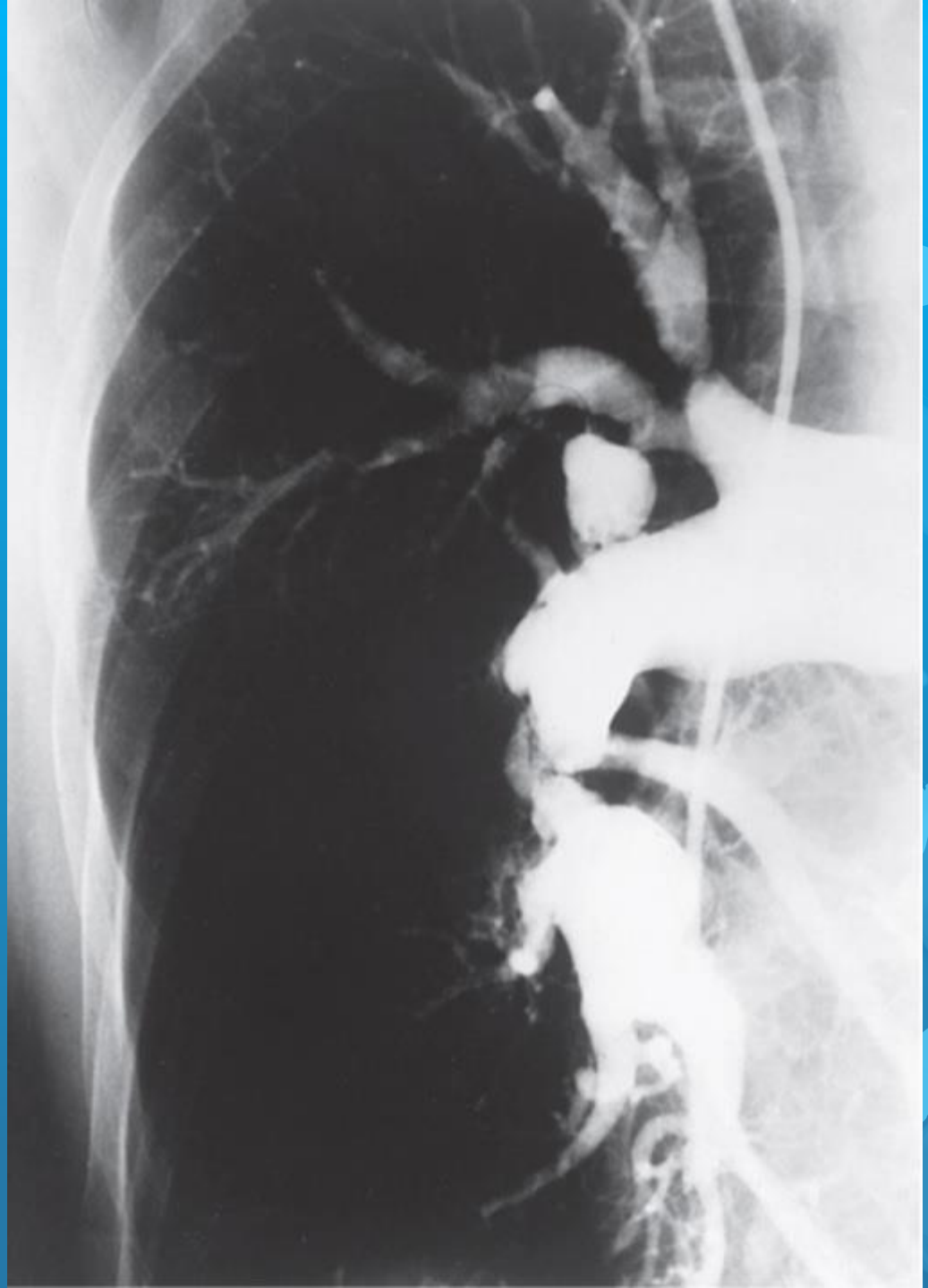
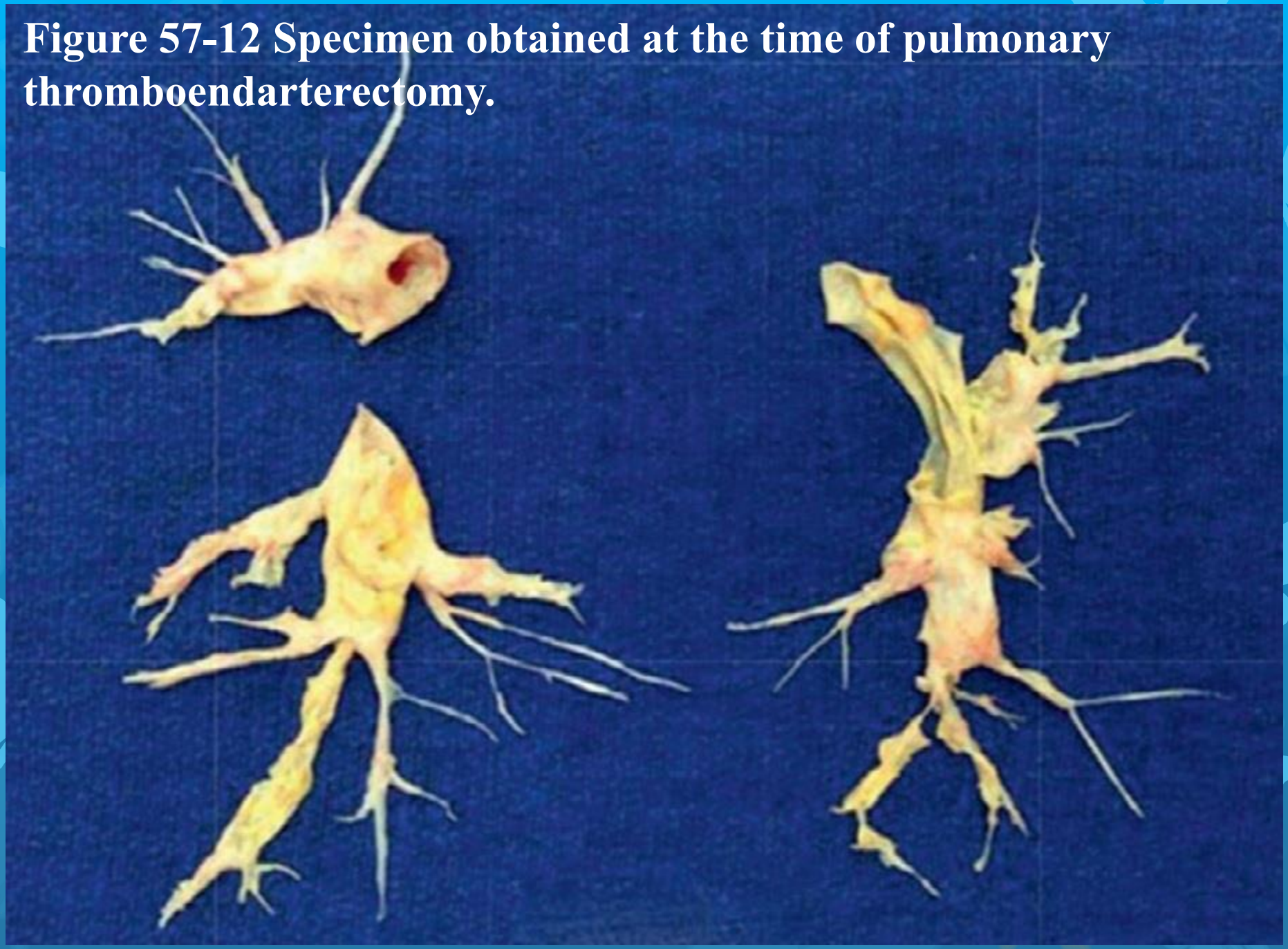


Figure 57-11 Right-sided pulmonary angiogram in a patient with chronic thromboembolic pulmonary hypertension.

Figure 57-12 Specimen obtained at the time of pulmonary thromboendarterectomy.



Before Thromboendarterectomy **Soon After Thromboendarterectomy**

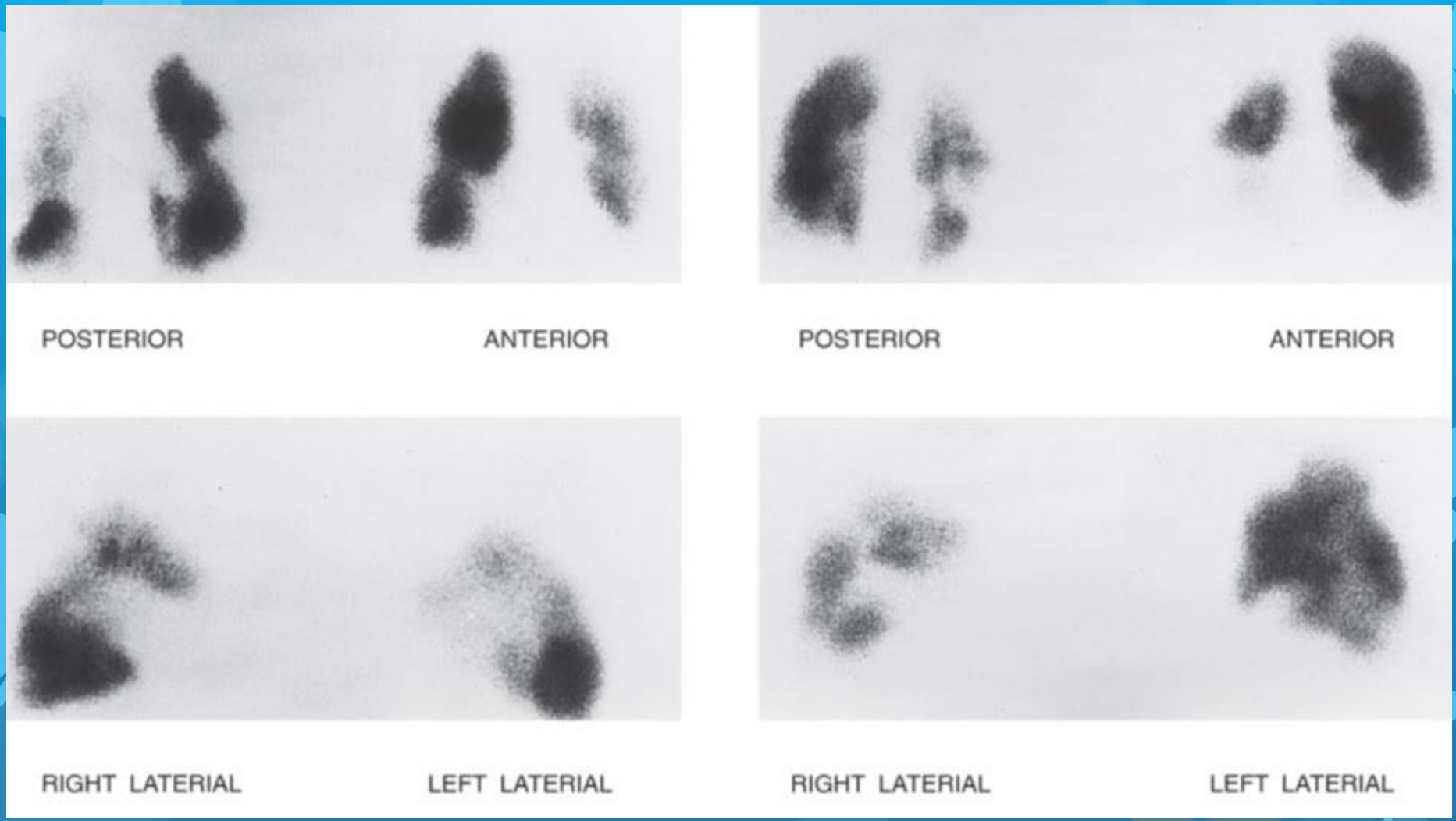


Figure 57-13 Perfusion scans show pulmonary artery steal.

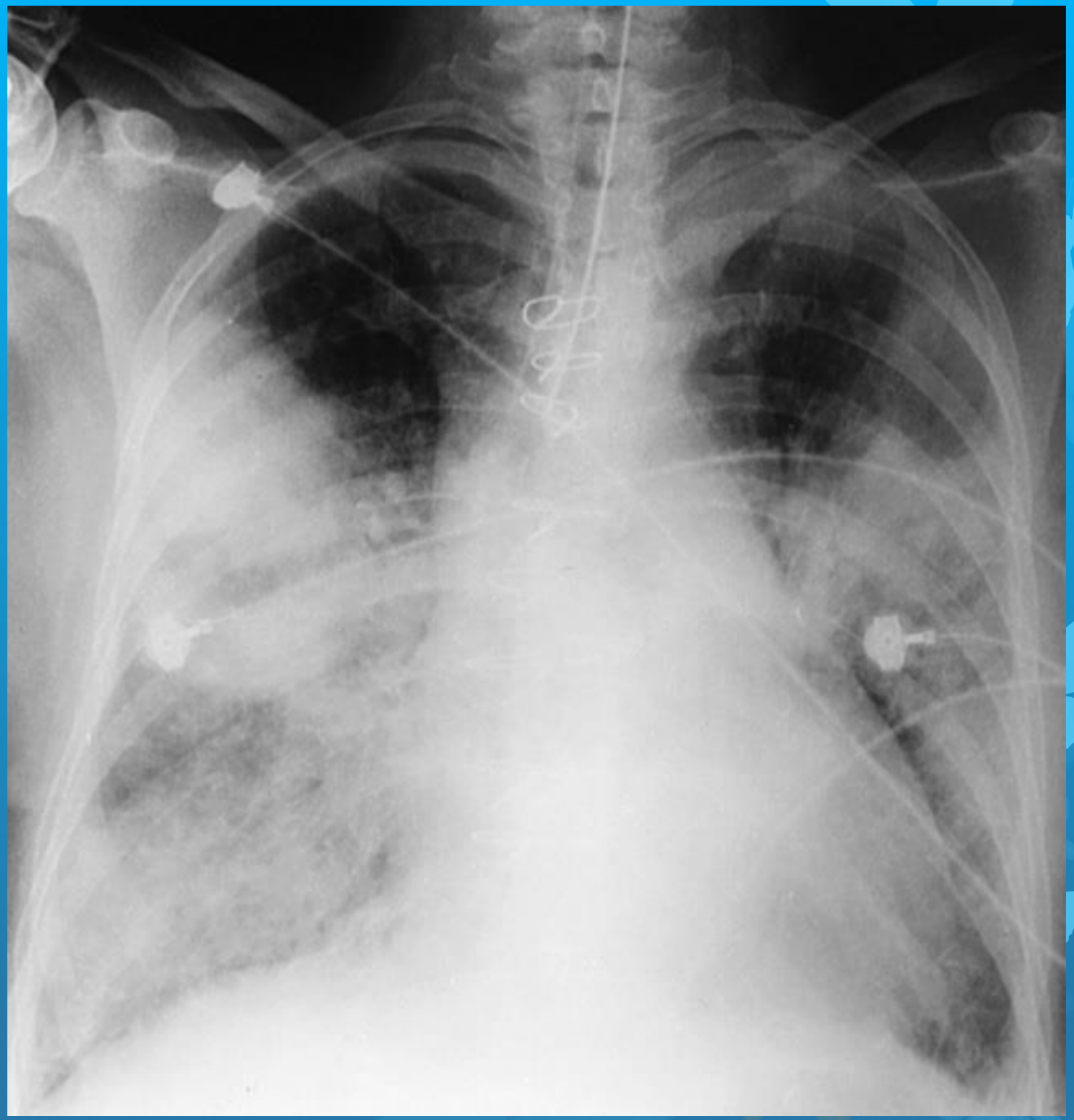


Figure 57-14 Chest radiograph shows postoperative reperfusion pulmonary edema.

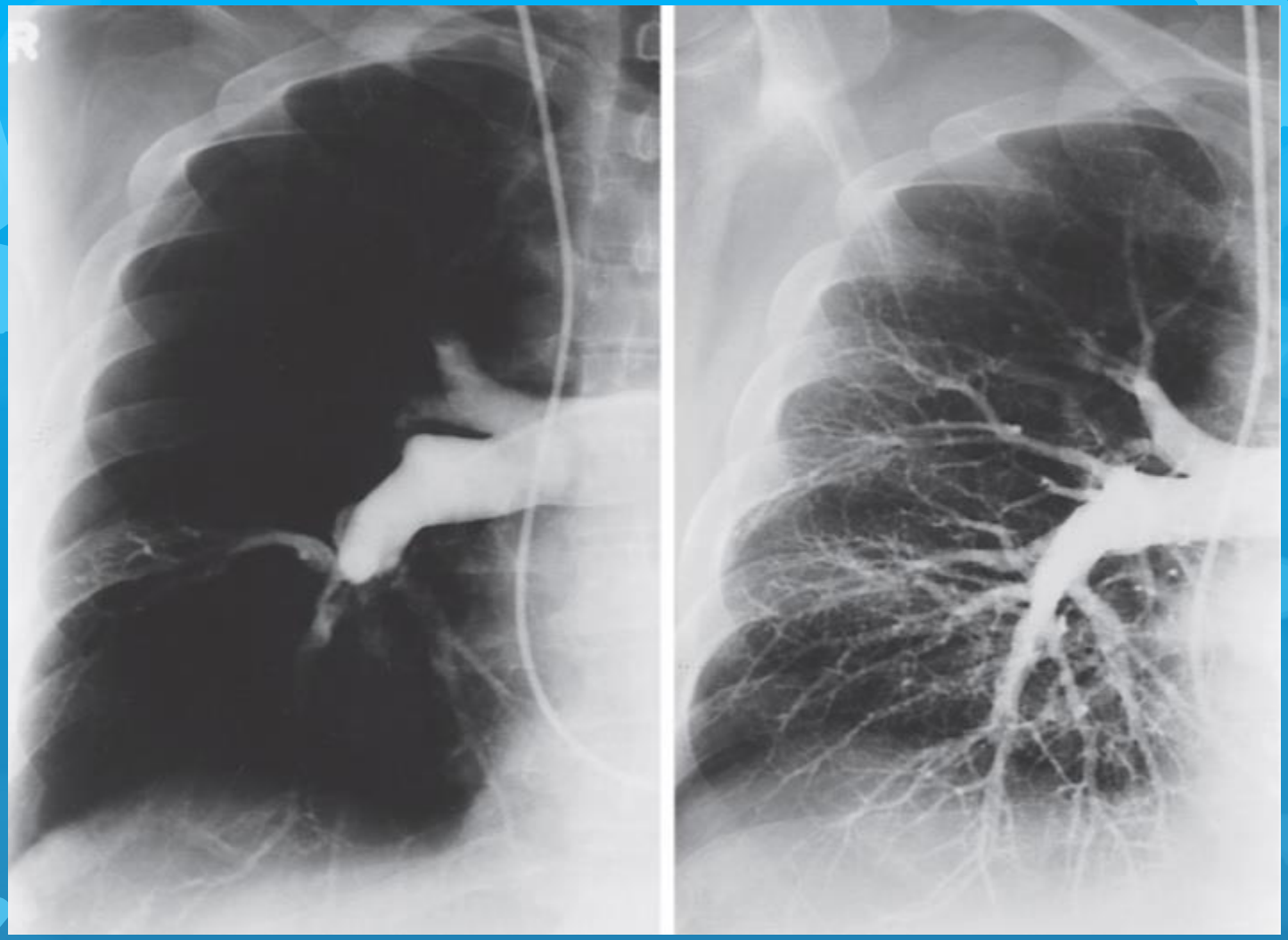
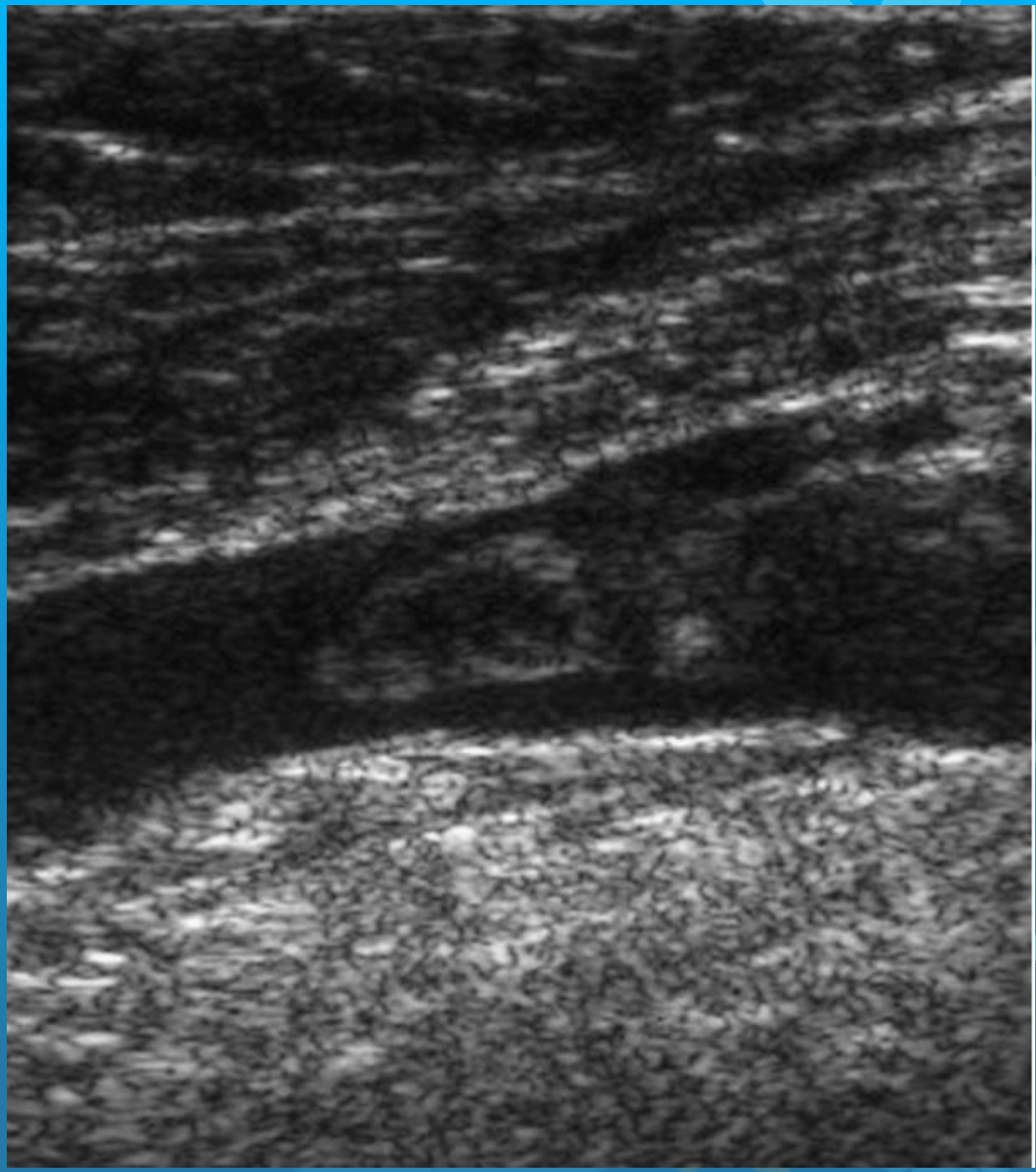
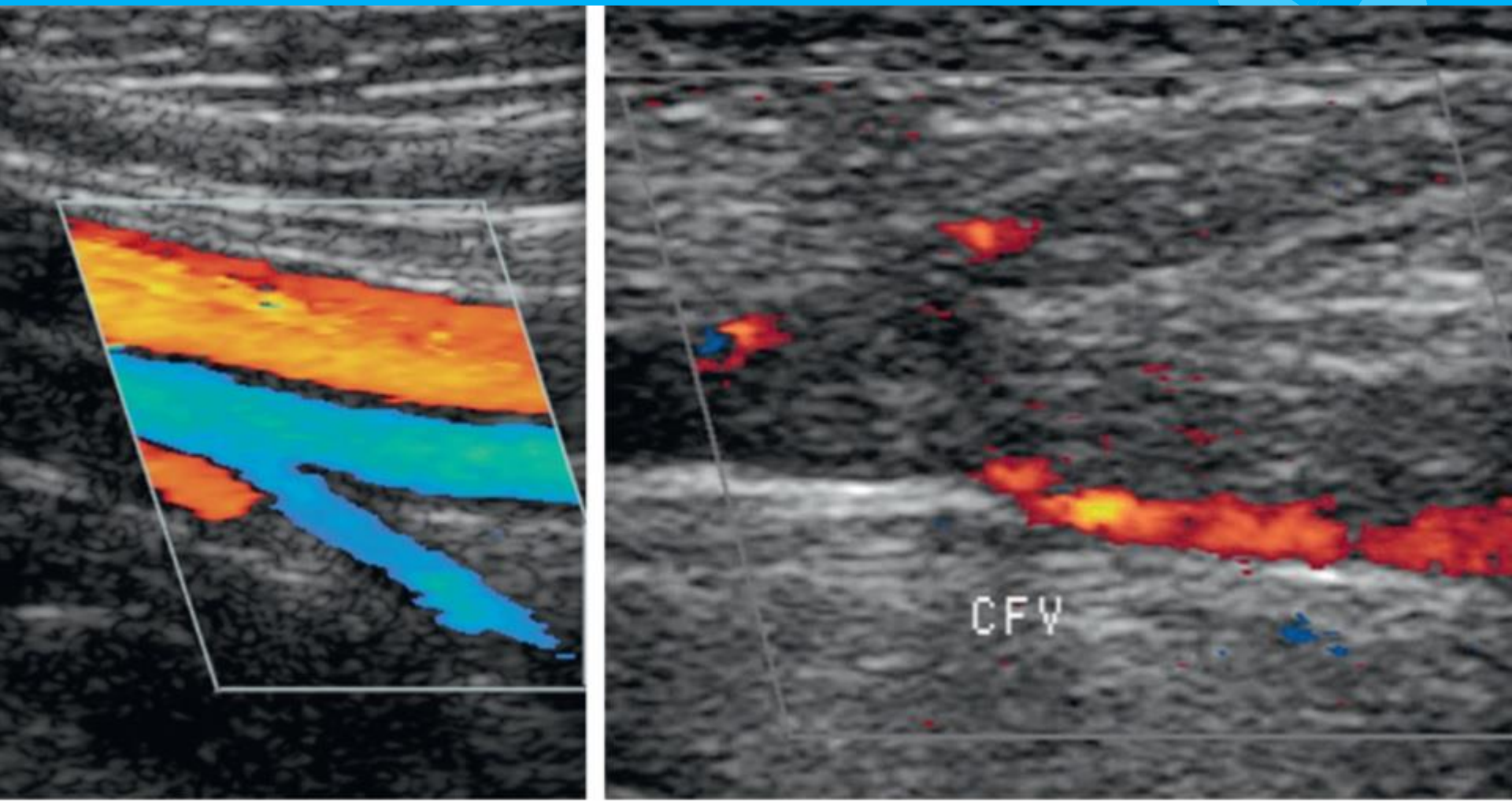


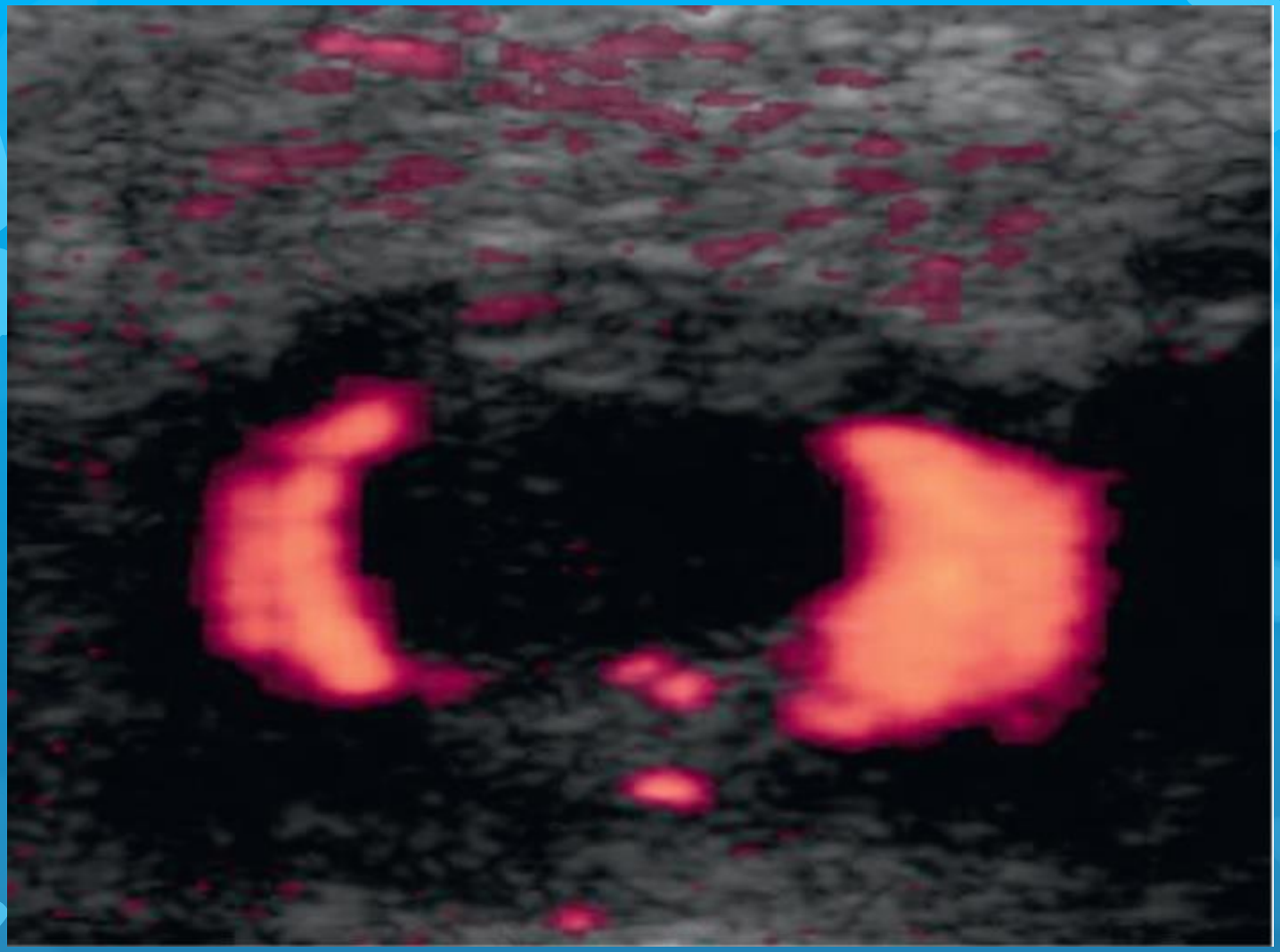
Figure 57-15 Pulmonary angiography before and after thromboendarterectomy. A, Preoperative pulmonary angiogram shows thromboembolic obstruction involving the right upper, middle, and lower lobe arteries. **B,** Postoperative angiogram shows near-normalization of flow. This angiographic improvement was accompanied by a corresponding hemodynamic improvement.



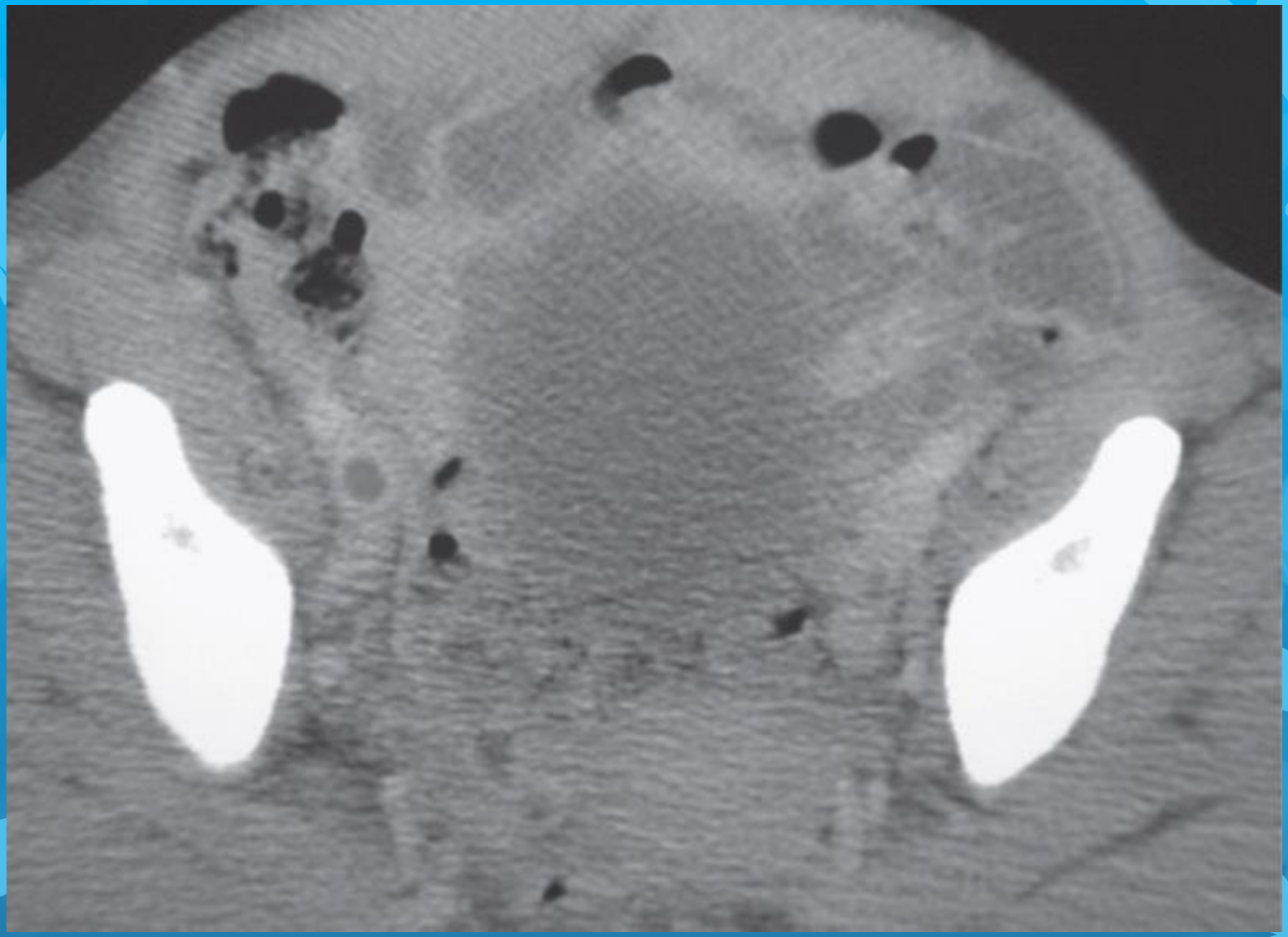
eFigure 57-1 Ultrasound image of DVT. Longitudinal ultrasound image shows mixed echogenicity material within the popliteal vein, consistent with acute deep venous thrombosis.



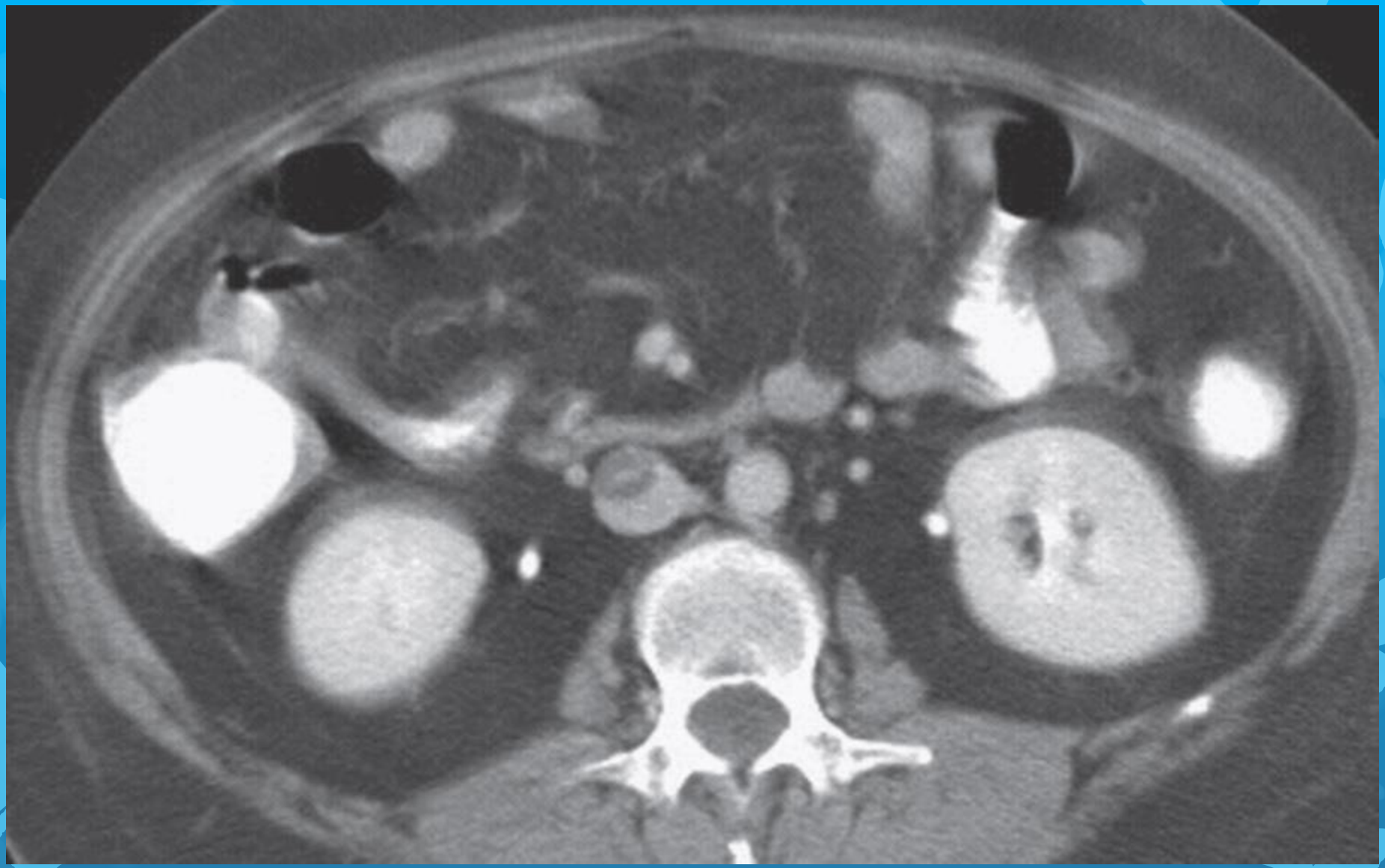
eFigure 57-2 Color Doppler ultrasound of the lower extremity. A, Normal color Doppler examination of the lower extremity venous and arterial systems. **B,** Echogenic material representing deep venous thrombosis (arrowheads) is present with the superficial femoral vein, entering the common femoral vein; thrombus can be seen filling the saphenous vein anteriorly at the junction of the superficial and common femoral veins. Note the displacement of color Doppler flow to the periphery of the thrombosed superficial femoral vein.



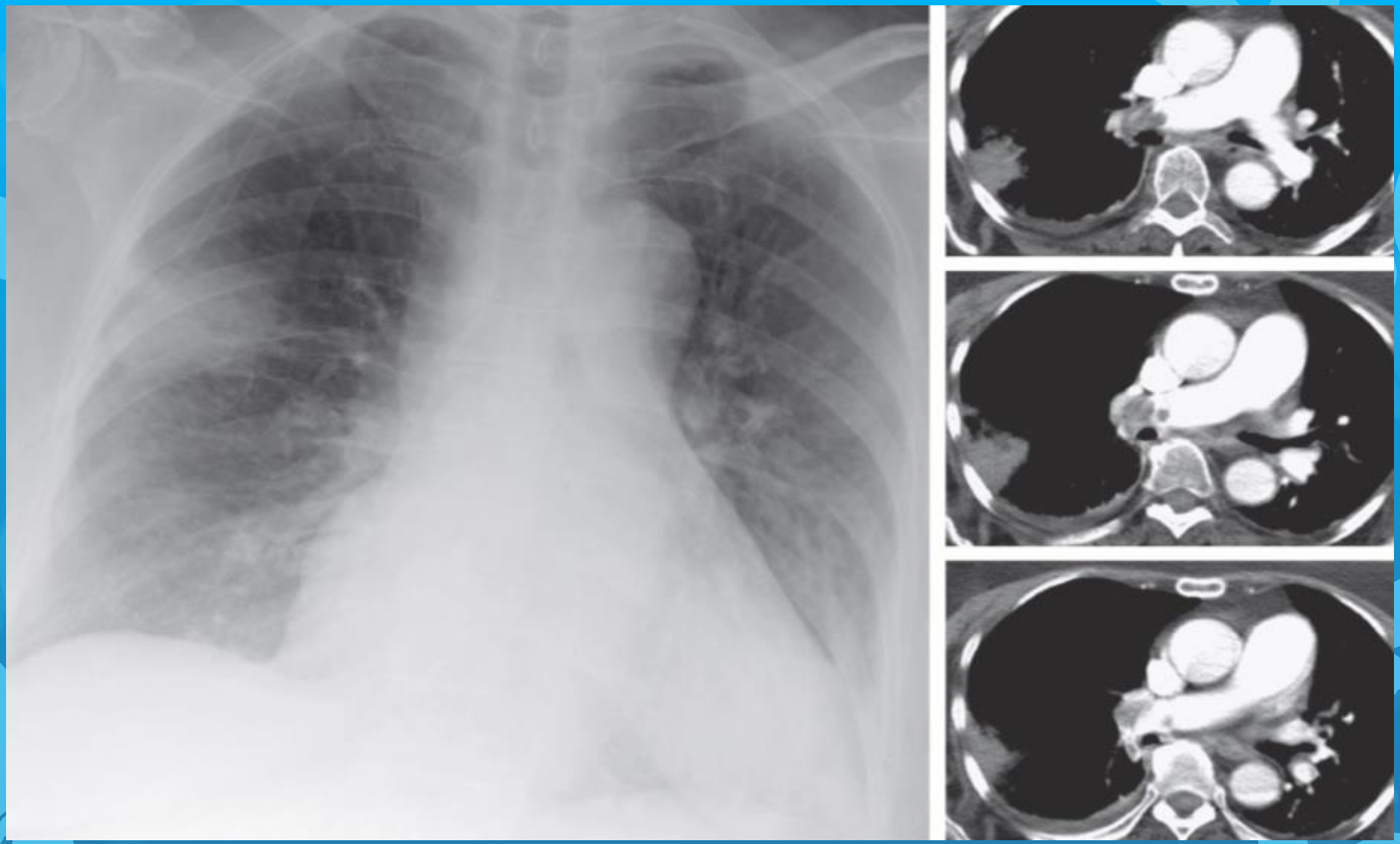
eFigure 57-3 Acute deep venous thrombosis presenting as nearly completely anechoic material filling the venous lumen. Note peripheral displacement of color Doppler signal, marking the remaining patent lateral portions of the common femoral vein. Some echogenic thrombus is seen peripherally both anteriorly and posteriorly as well.



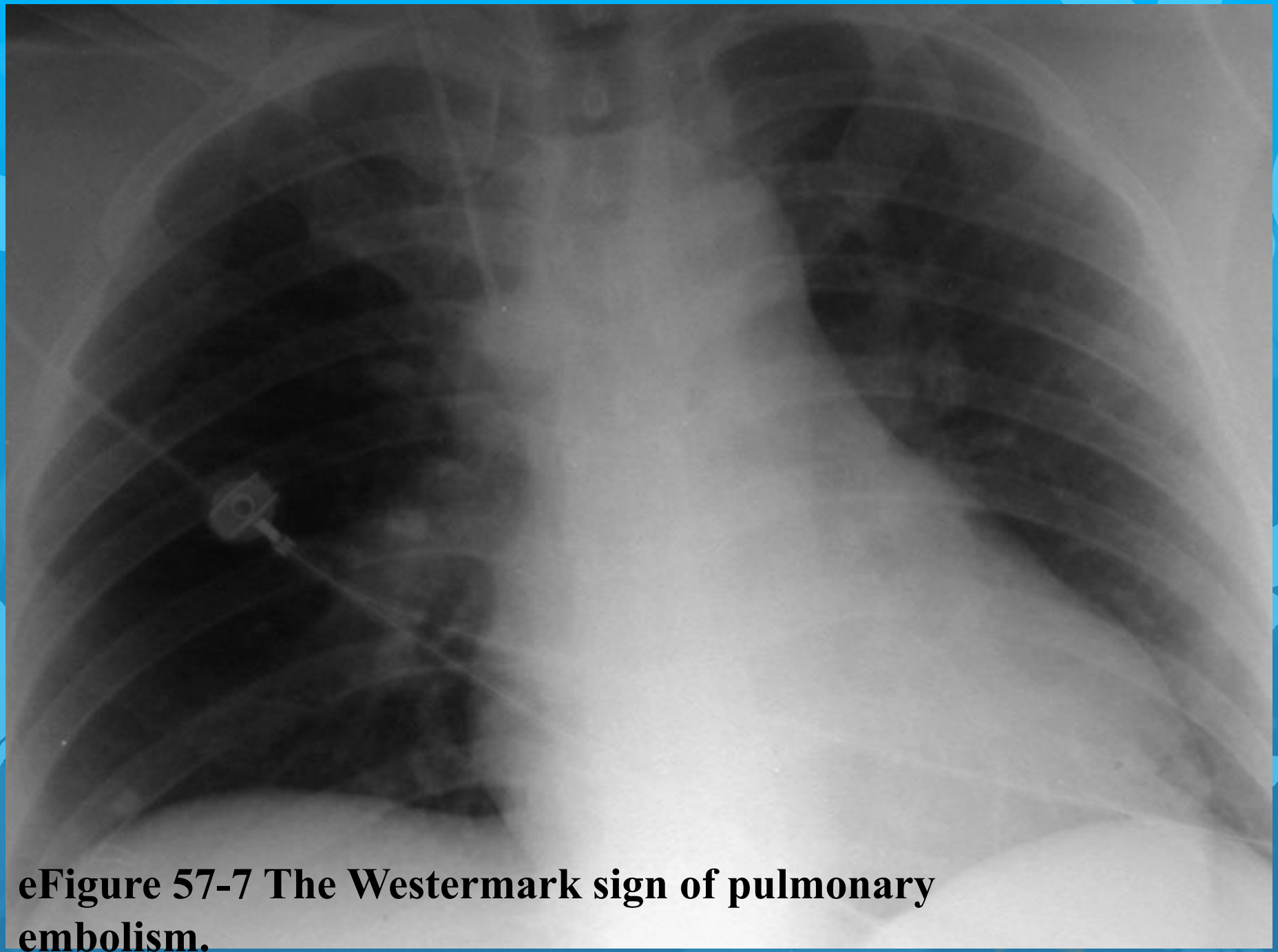
eFigure 57-4 Indirect contrast venography. Axial contrast-enhanced image through the pelvis performed in the course of indirect contrast venography shows a low-attenuation filling defect within the right external iliac vein (arrow), consistent with deep venous thrombosis.



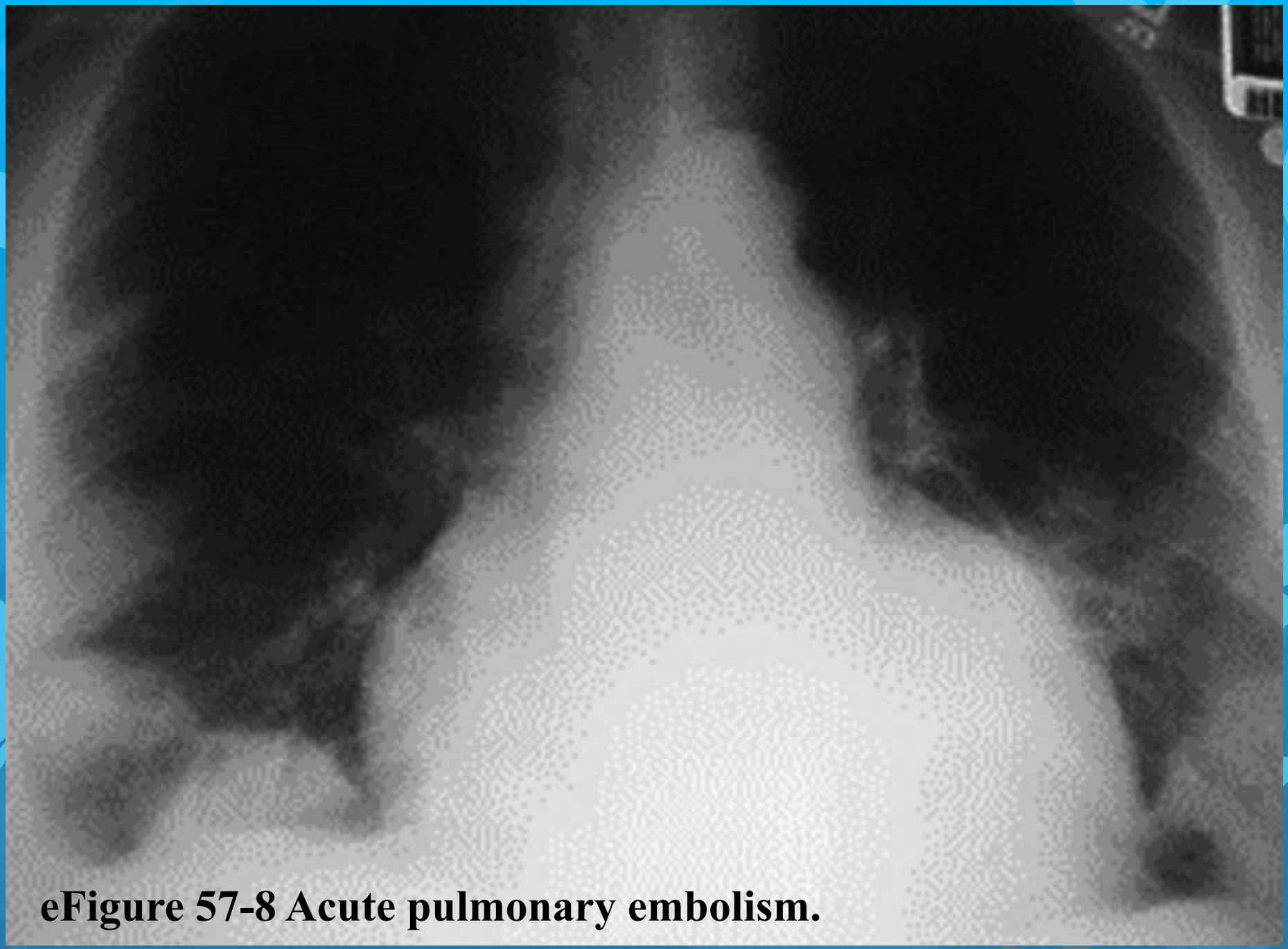
eFigure 57-5 Indirect contrast venography. Axial contrast-enhanced image through the lower abdomen performed in the course of indirect contrast venography shows a low-attenuation filling defect within the inferior vena cava (arrow), consistent with deep venous thrombosis.



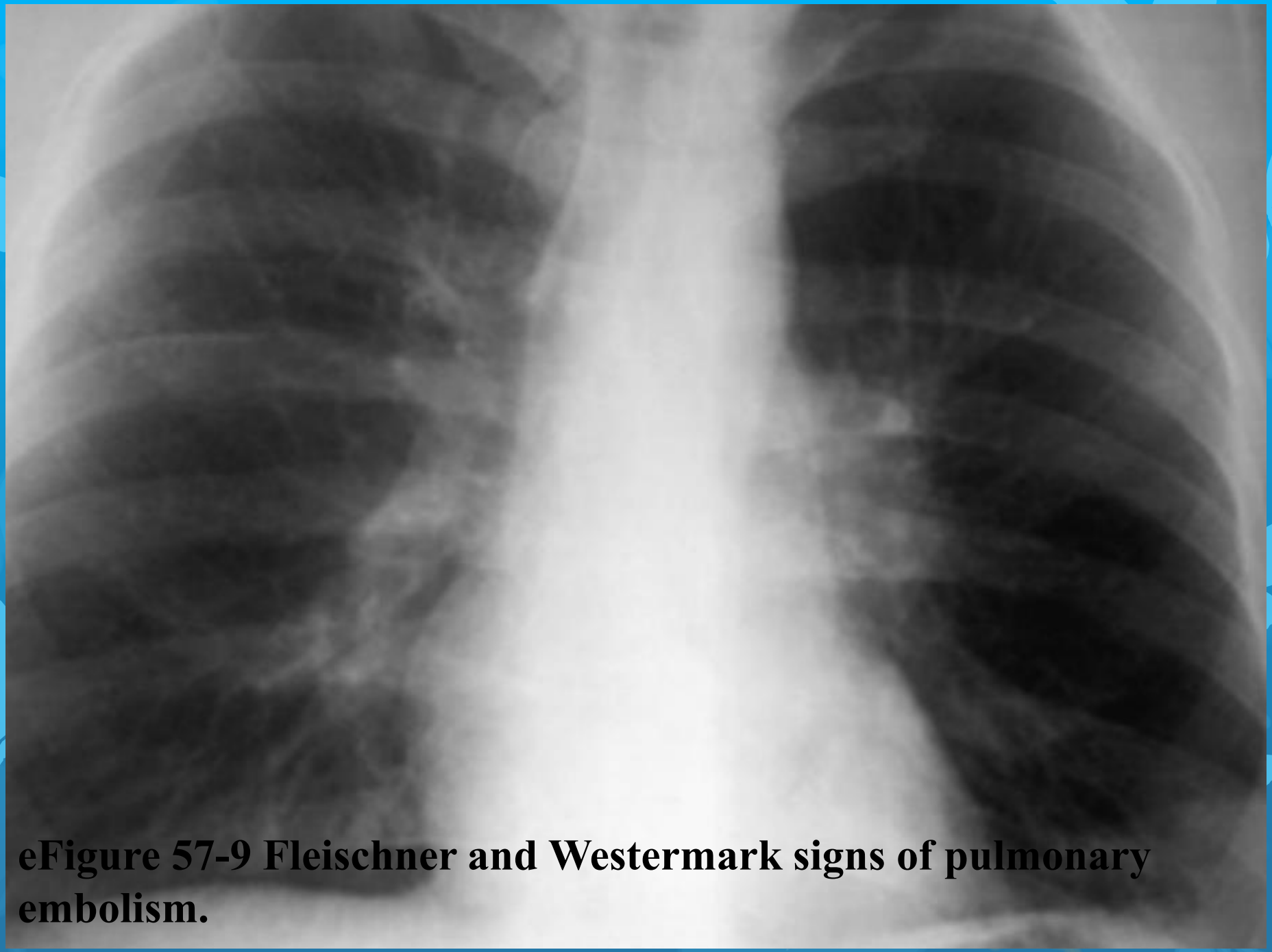
eFigure 57-6 Acute pulmonary embolism. A, Frontal chest radiograph in a patient with acute pulmonary embolism shows a rounded opacity in the peripheral right upper lung (arrow) shown to represent pulmonary infarction. **B–D,** Chest CT pulmonary angiography shows pulmonary emboli in the right upper and interlobar arteries (arrowheads) as well as subpleural, wedge-shaped opacity representing pulmonary infarction (arrows).



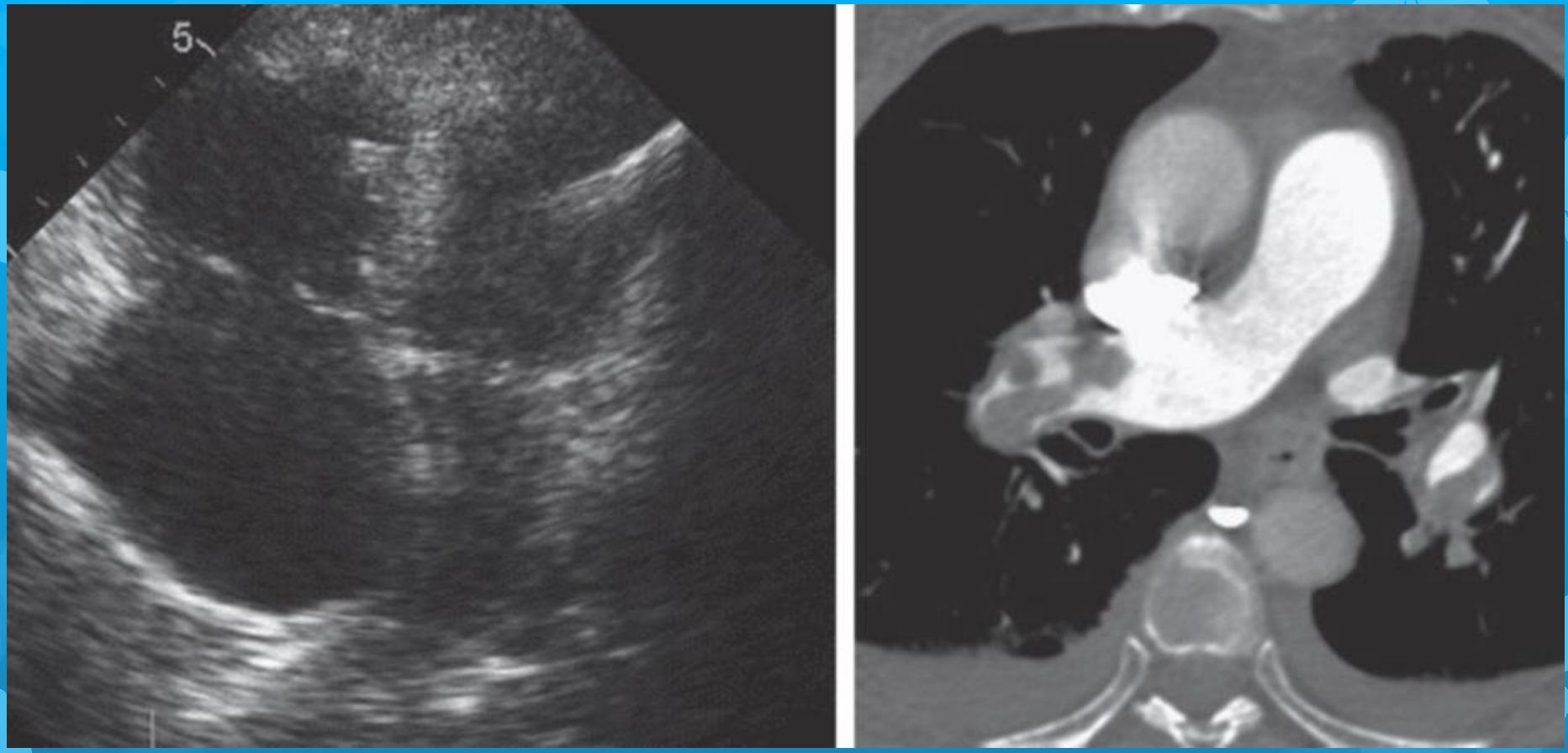
eFigure 57-7 The Westermark sign of pulmonary embolism.



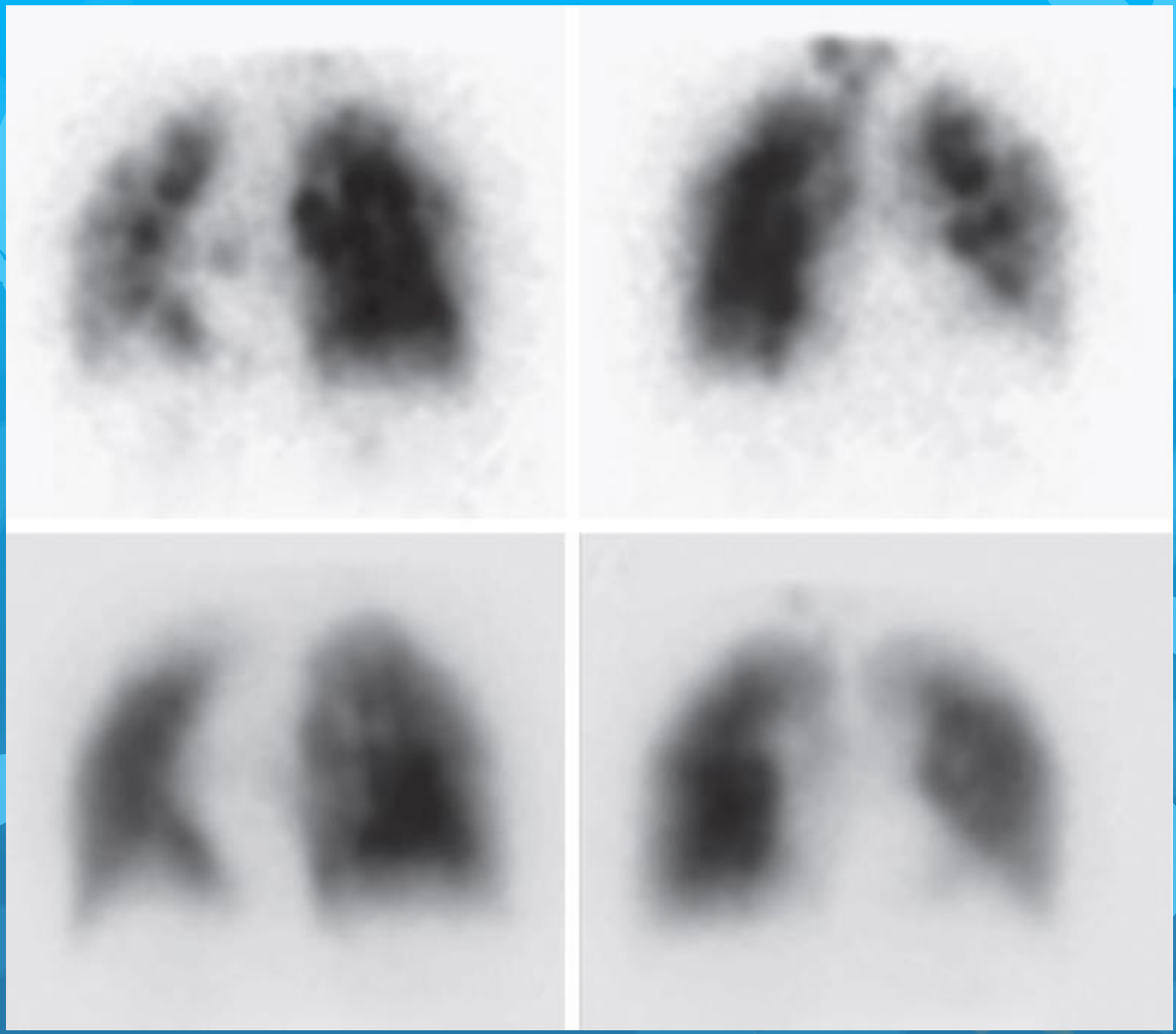
eFigure 57-8 Acute pulmonary embolism.

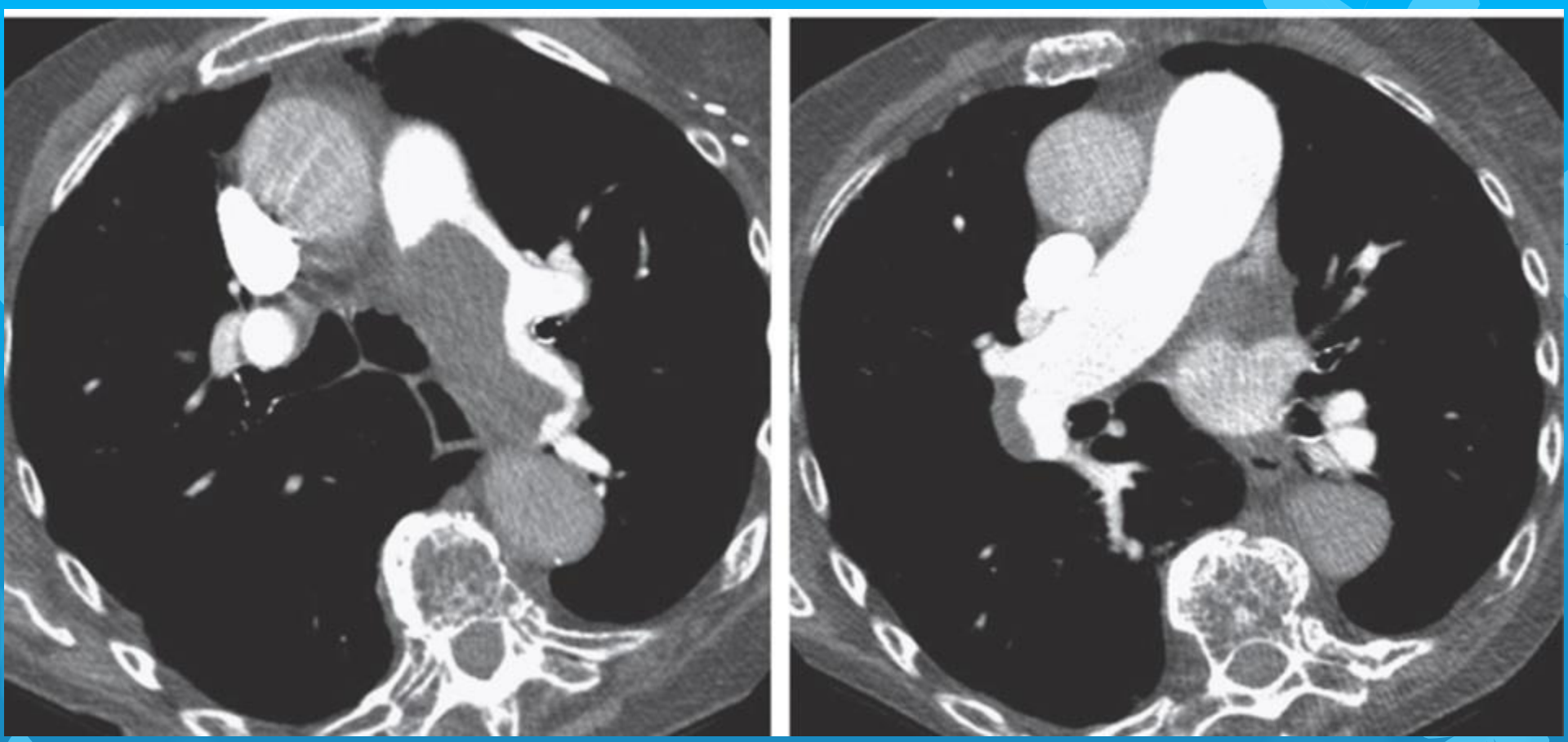


eFigure 57-9 Fleischner and Westermark signs of pulmonary embolism.

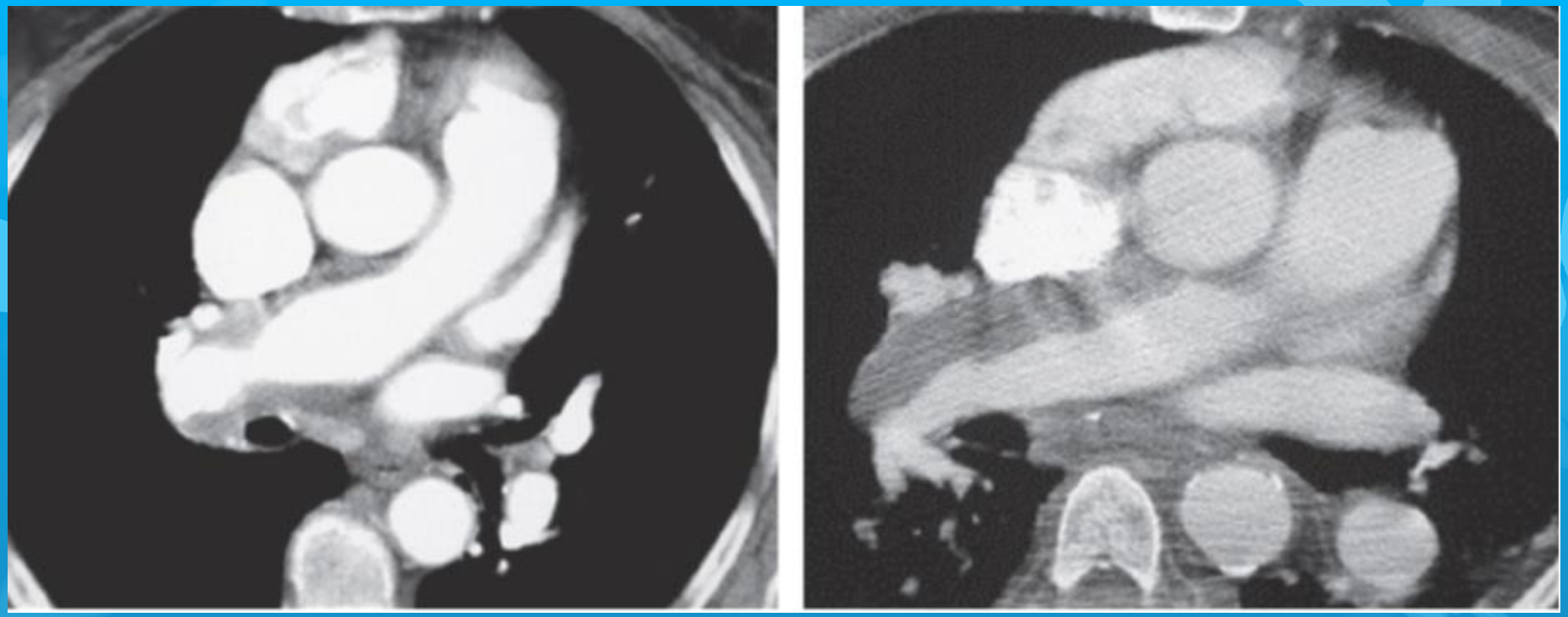


eFigure 57-10 Right ventricular enlargement with pulmonary embolism. A, Four-chamber echocardiographic image shows enlargement of the right atrium (RA) and right ventricle (RV). **B,** Chest CT pulmonary angiography shows bilateral pulmonary emboli (arrows), indicating the cause of the right heart chamber enlargement.

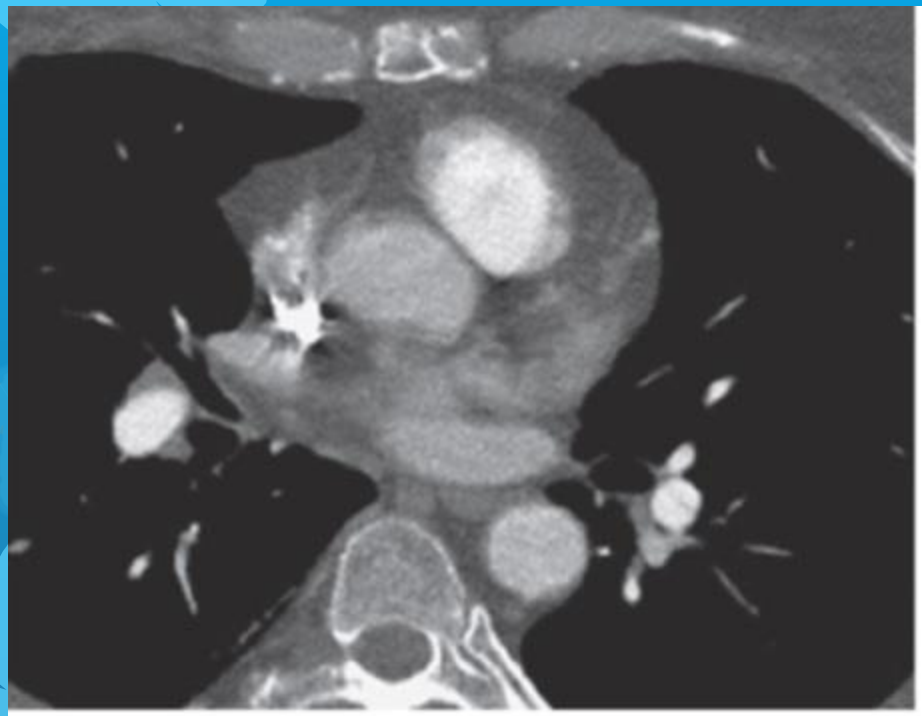


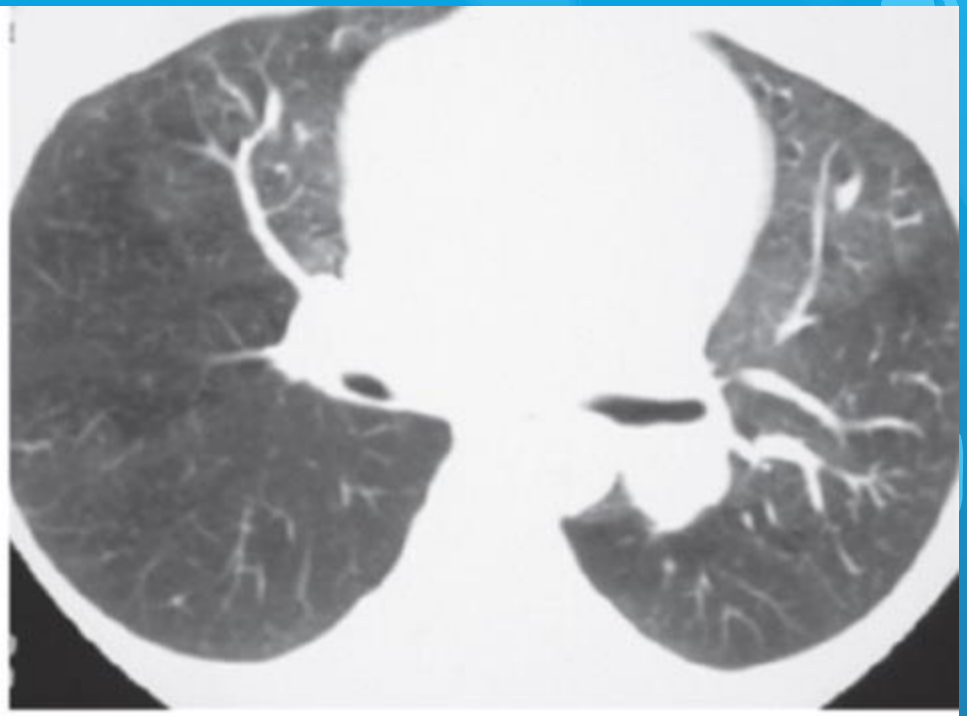


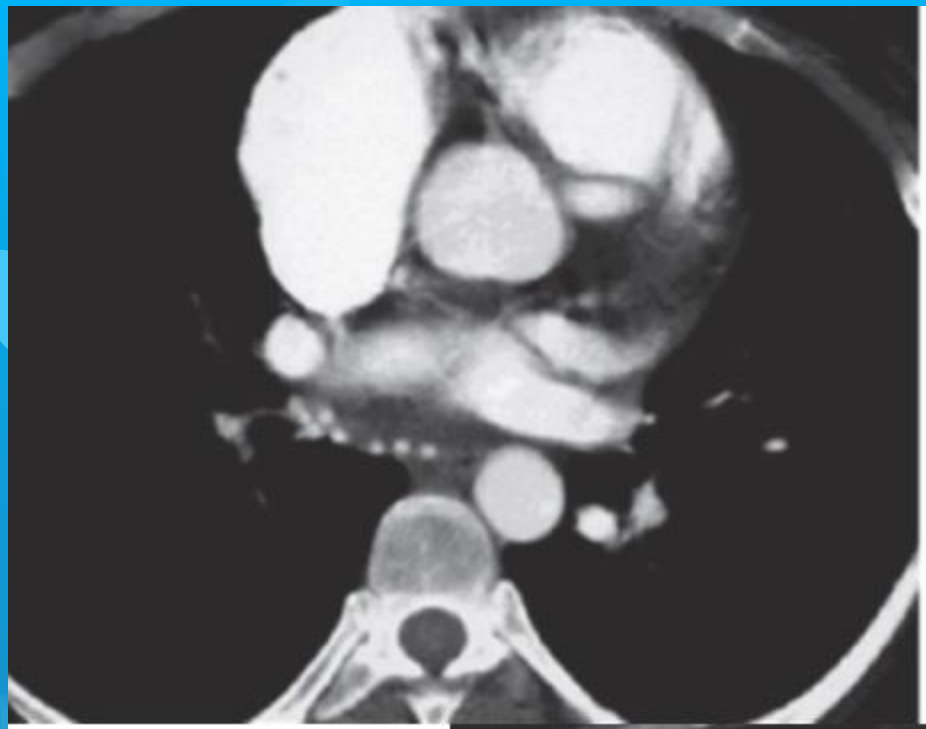
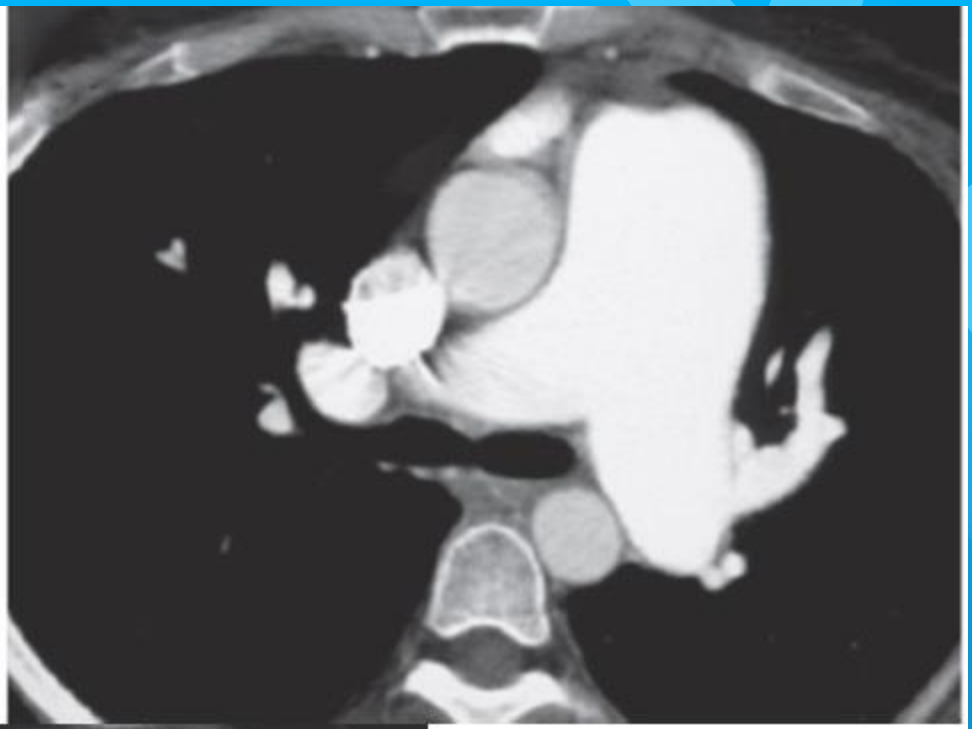
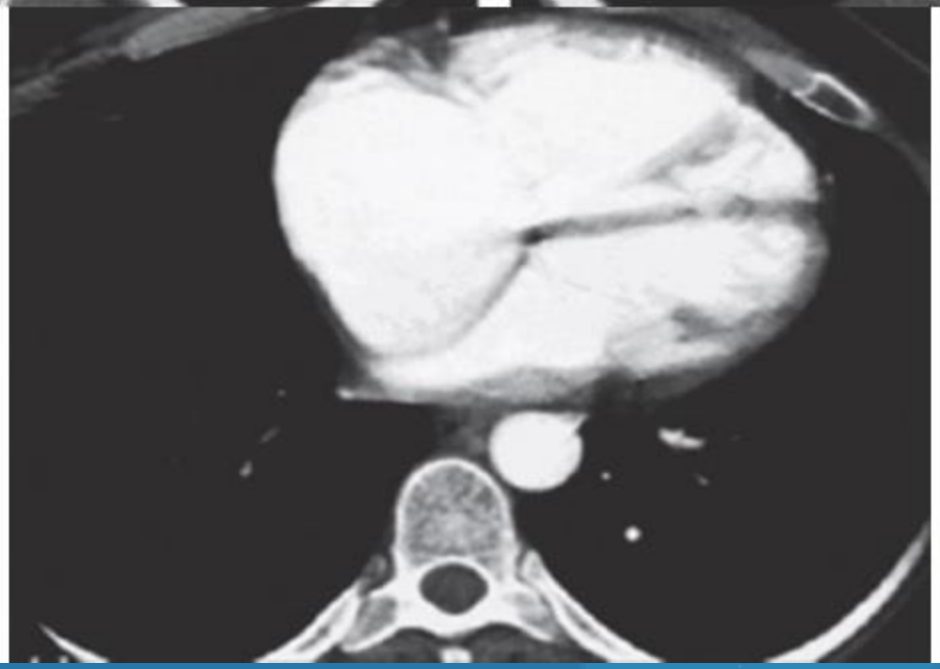
eFigure 57-11 Chronic thromboembolic disease. A–D, Ventilation-perfusion scintigraphy (**A** and **B**, ventilation images performed with 133Xenon; **C** and **D**, perfusion images performed with 99Tc-macroaggregated albumin) show inhomogeneous ventilation bilaterally, but perfusion images show relatively uniform tracer distribution. The study is consistent with a low probability for pulmonary embolism. **E** and **F**, Chest CT pulmonary angiography shows eccentric low-attenuation material (arrows) within the central pulmonary arteries consistent with chronic thromboembolic disease.

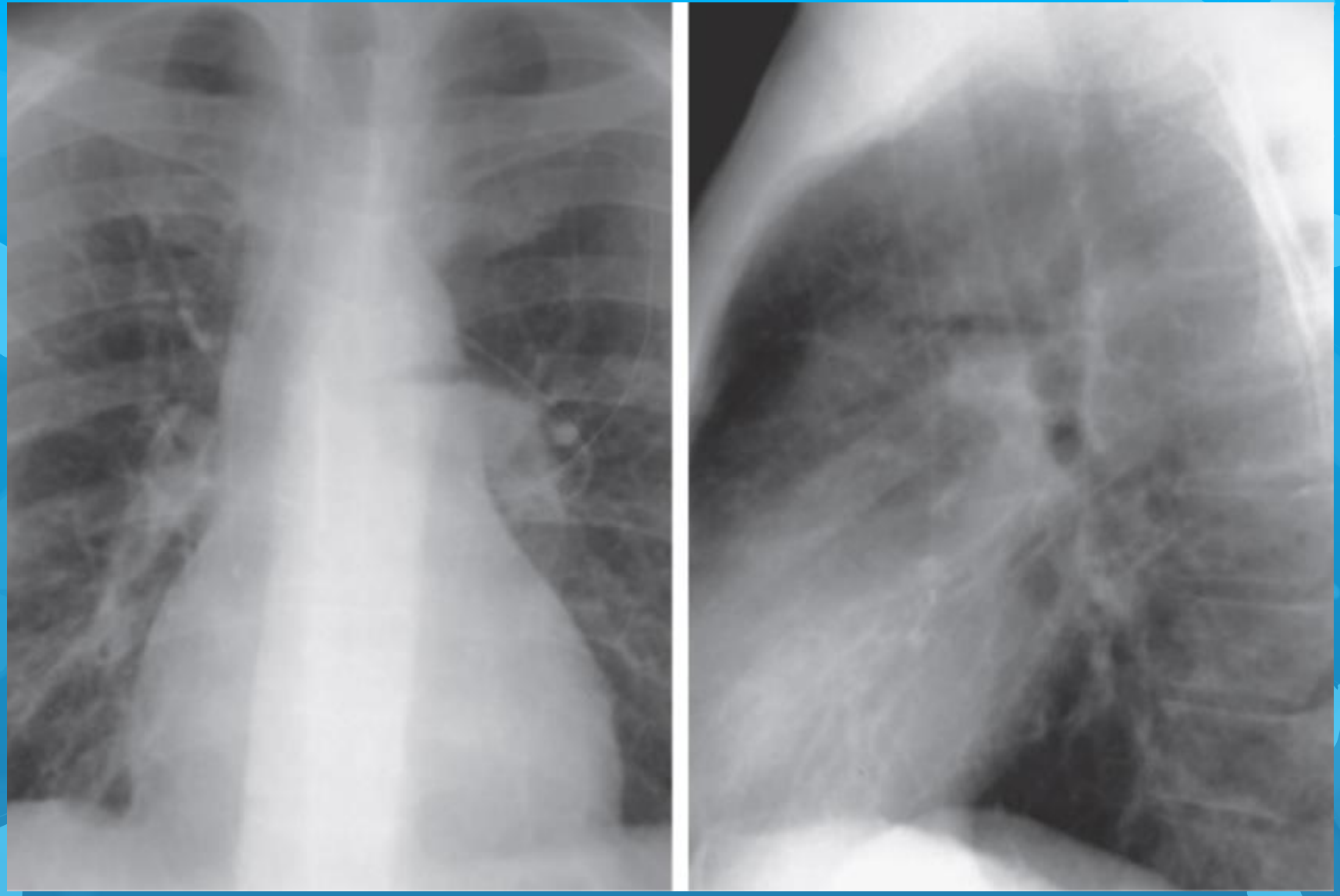


eFigure 57-12 Chronic thromboembolic disease. Chest CT pulmonary angiographic findings of chronic thromboembolic disease. **A,** Recanalized arterial lumen, showing peripheral hypoattenuating material (arrows); **B,** Eccentric low-attenuation material along the wall of the affected vessel (arrow); **C,** Intravascular web (arrowhead); **D,** Inhomogeneous lung opacity representing areas of oligemia (the areas of decreased attenuation); **E,** Bronchial artery collateral vessels (arrowheads); **F,** Main pulmonary artery (MPA) enlargement, consistent with pulmonary hypertension; and **G,** Enlargement of the right atrium (RA) and right ventricle (RV), consistent with pulmonary hypertension. Note straightening of the interventricular septum, also consistent with elevated right heart pressures.

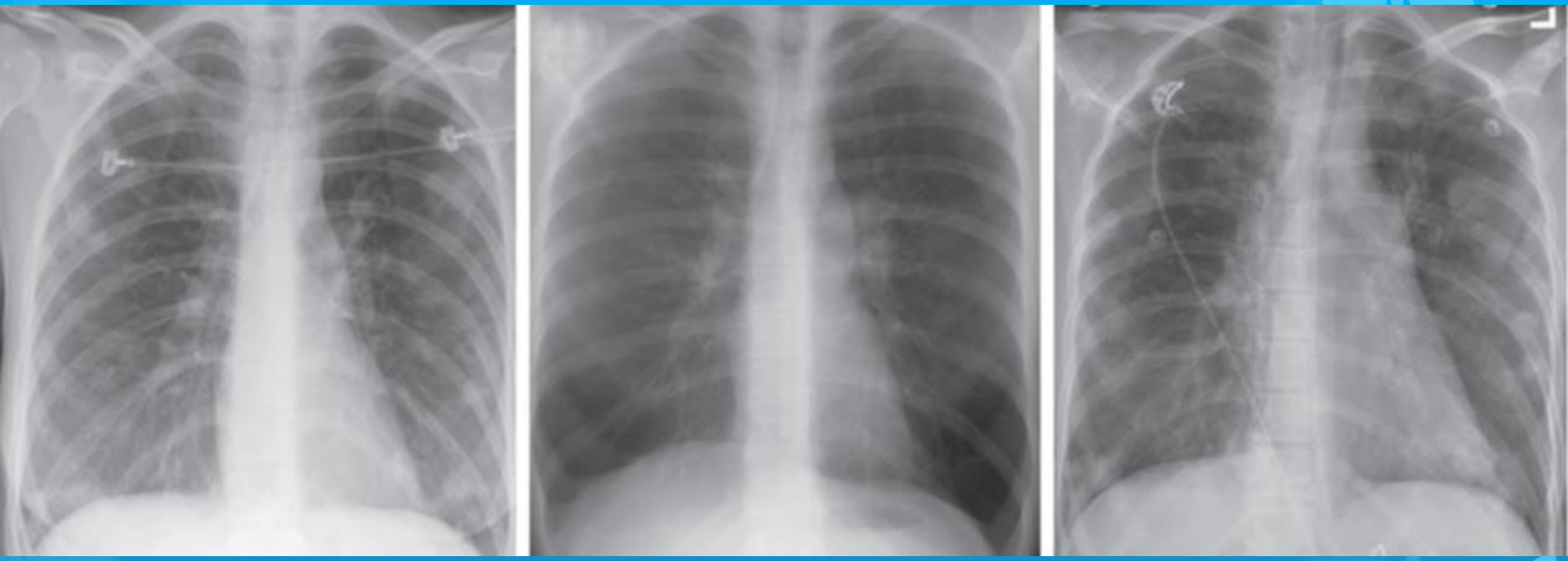




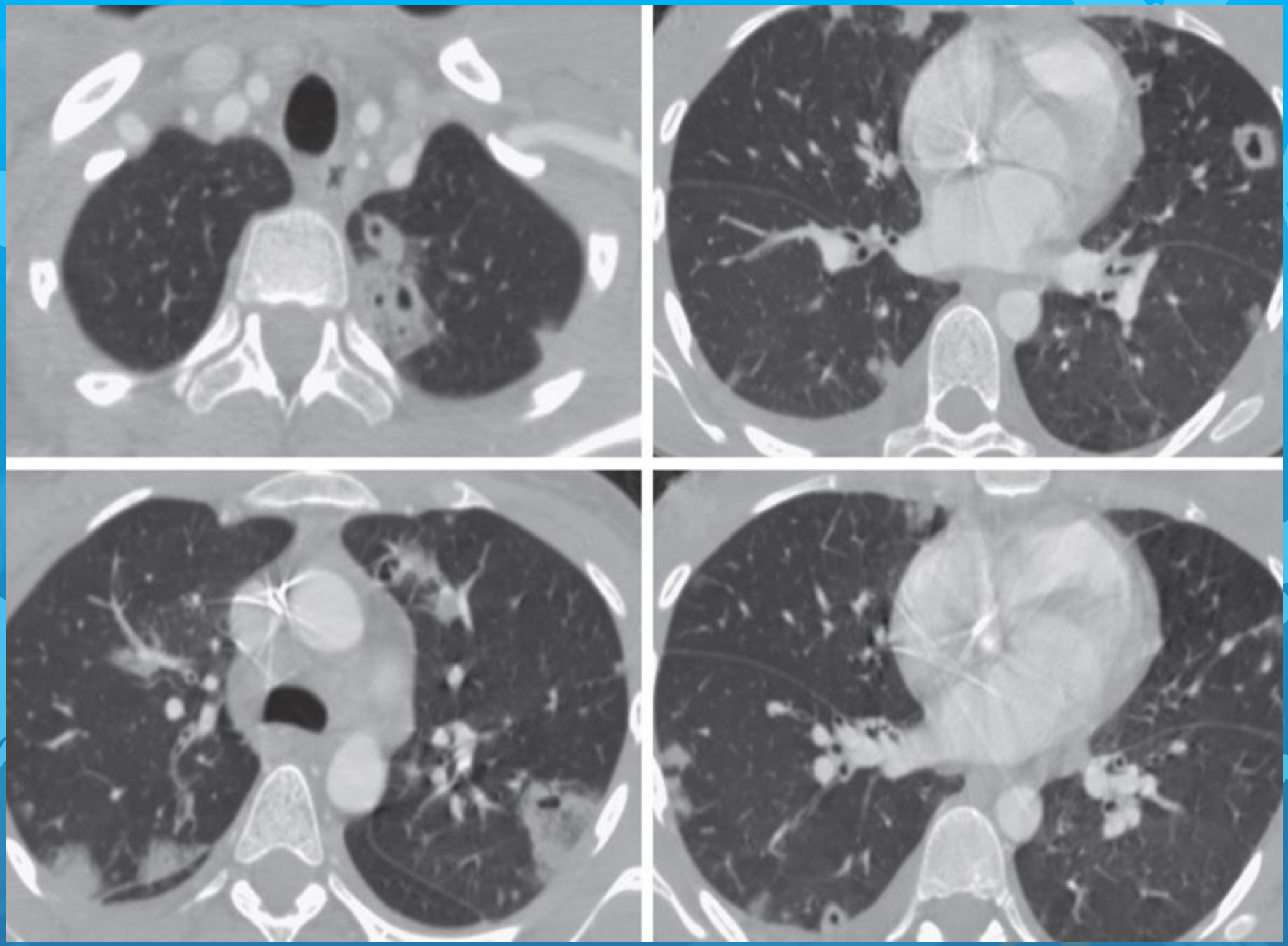




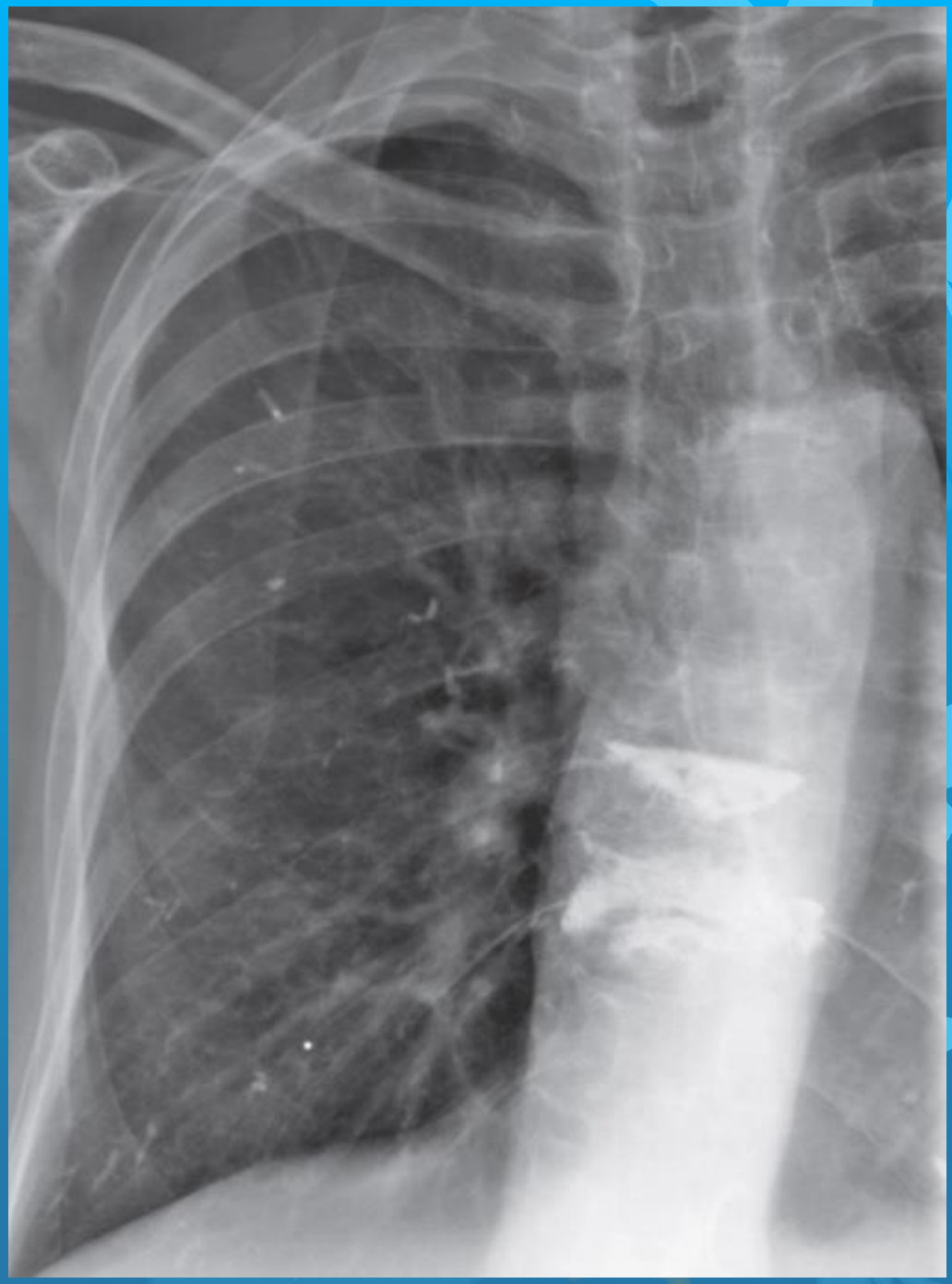


eFigure 57-13 Pulmonary artery air embolism. A, Frontal and B, lateral chest radiography performed for acute-onset chest pain following manipulation of a central venous catheter shows a gas and fluid level (arrowheads) in the main pulmonary artery. This finding resolved without sequelae.

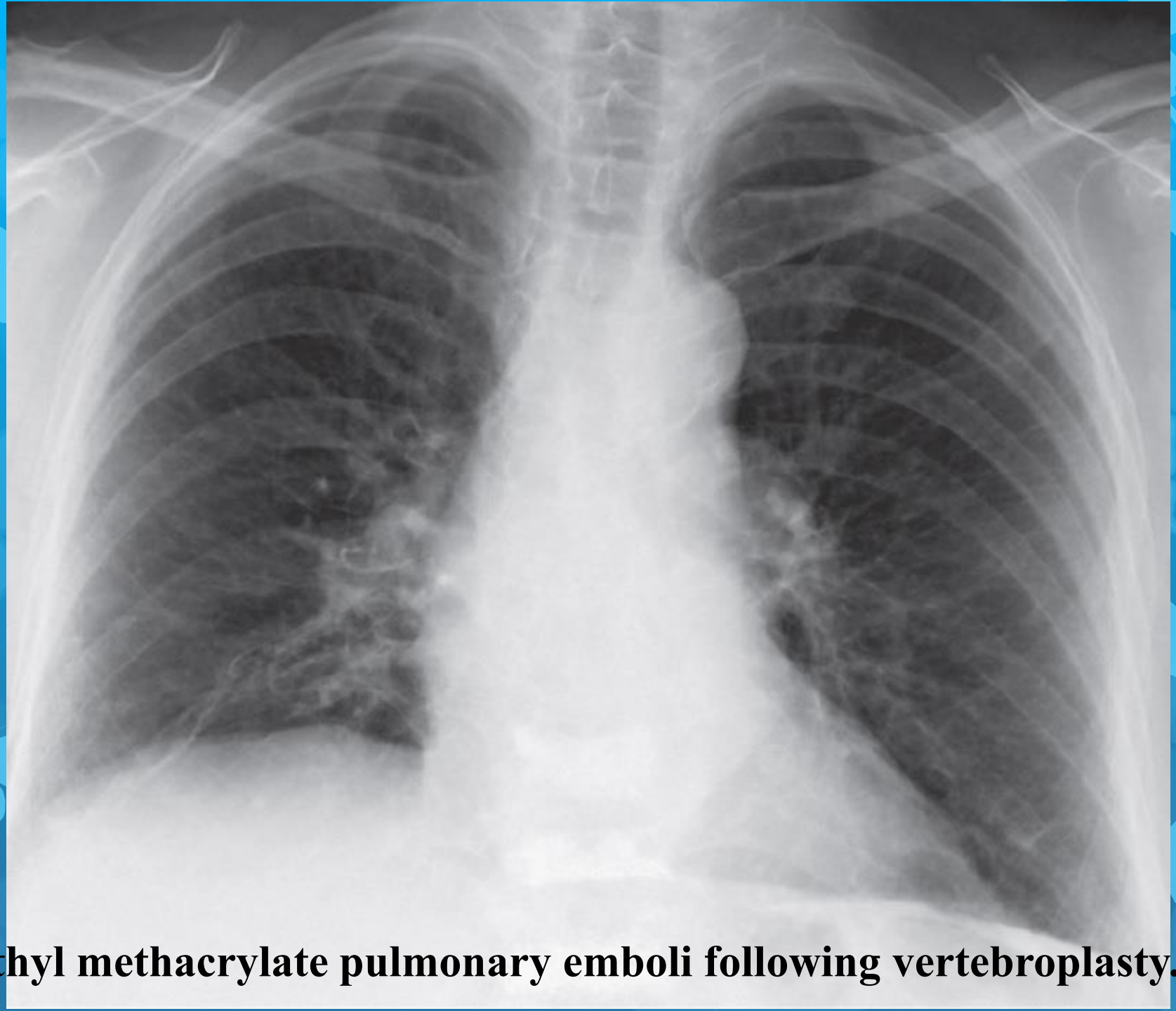


eFigure 57-14 Septic embolization. A, Frontal chest radiography performed in an intravenous drug user with fever shows multiple, bilateral, poorly defined nodular opacities (arrows), one of which is cavitary (arrowhead). **B,** Frontal chest radiography performed 2 years earlier, for comparison, appears normal. **C,** Frontal chest radiography performed one day following **(A)** shows progression in size of the nodular opacities (arrows). **D-G,** Axial-enhanced chest CT confirms the presence of multiple, bilateral, peripherally distributed nodules (arrows), many of which are cavitary (arrowheads).



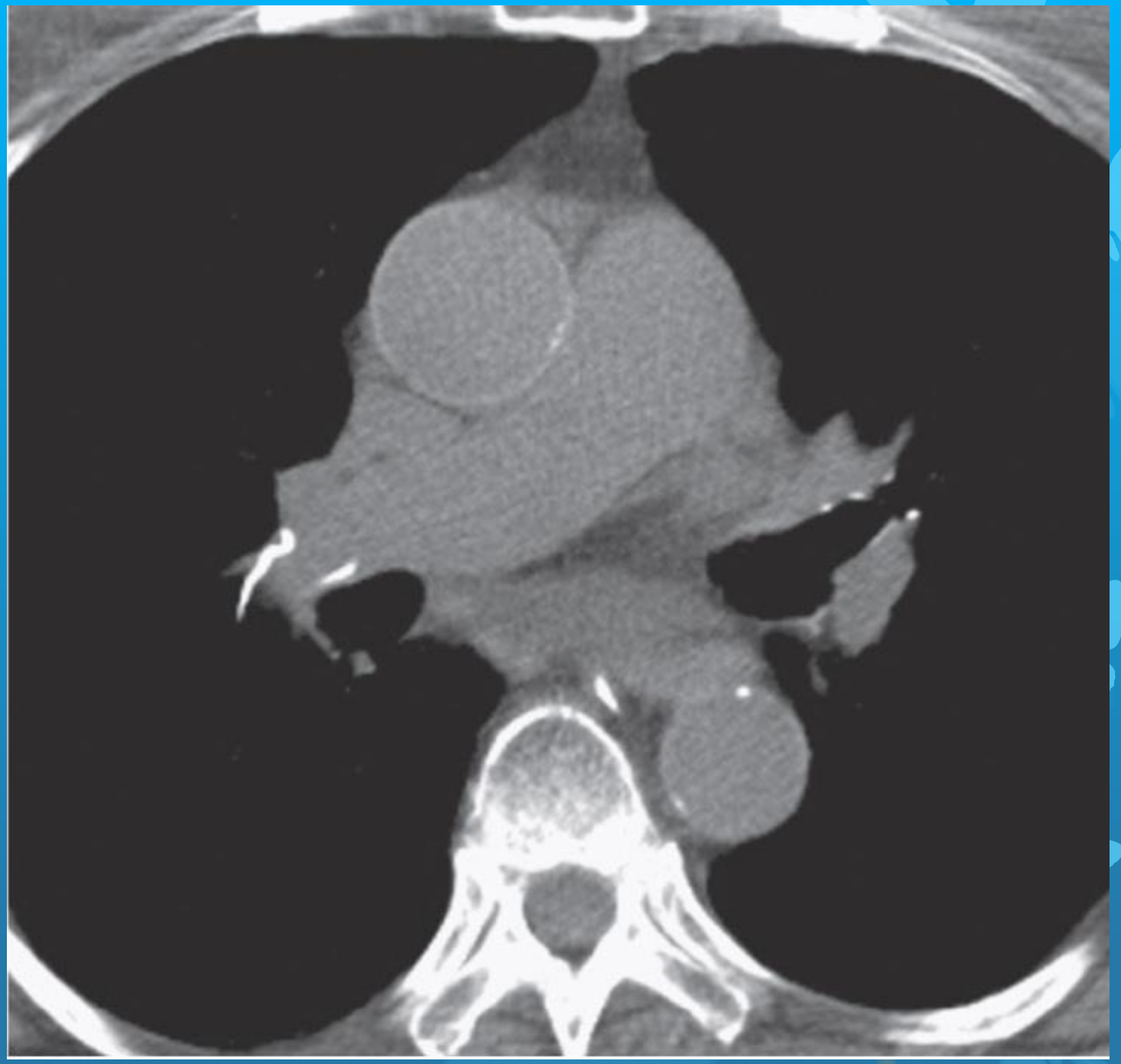


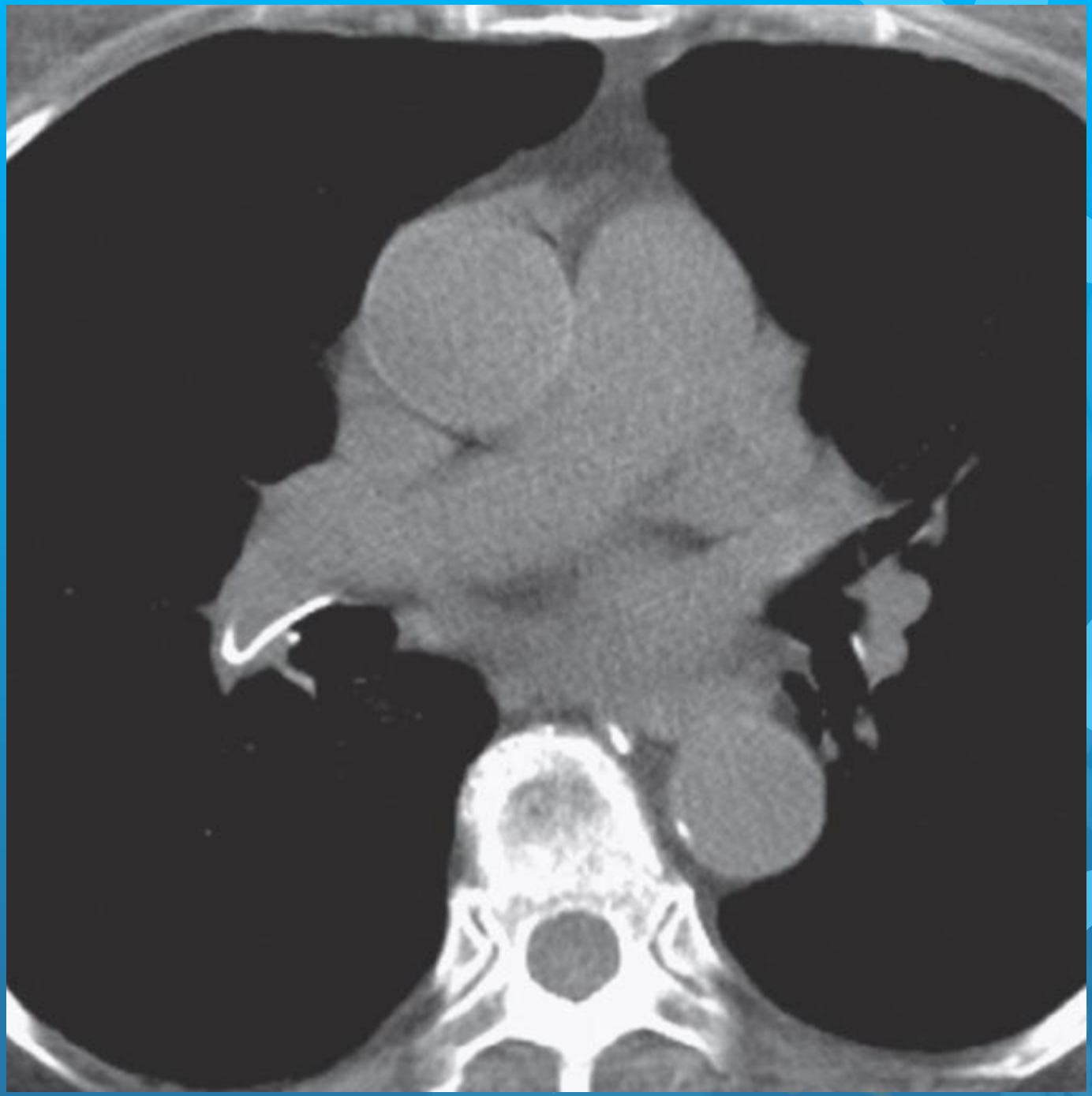
eFigure 57-15 Methyl methacrylate pulmonary emboli following vertebroplasty. Oblique frontal image of the chest shows thoracic spine vertebroplasty material (arrows) with small foci of methyl methacrylate emboli in the right upper lobe (arrowheads).



Methyl methacrylate pulmonary emboli following vertebroplasty.

A, Frontal chest radiograph shows thoracic spine vertebroplasty material (arrows) with a small curvilinear focus of methyl methacrylate in the right interlobar pulmonary artery (arrowhead).





C, Axial unenhanced chest CT confirms high attenuation in the right interlobar pulmonary artery (arrows), representing a methyl methacrylate embolism. Methyl methacrylate is also present in the azygos vein (arrowheads).

TABLE 300-2 DIFFERENTIAL DIAGNOSIS

DVT
Ruptured Baker's cyst
Cellulitis
Postphlebitic syndrome/venous insufficiency
PE
Pneumonia, asthma, chronic obstructive pulmonary disease
Congestive heart failure
Pericarditis
Pleurisy: "viral syndrome," costochondritis, musculoskeletal discomfort
Rib fracture, pneumothorax
Acute coronary syndrome
Anxiety

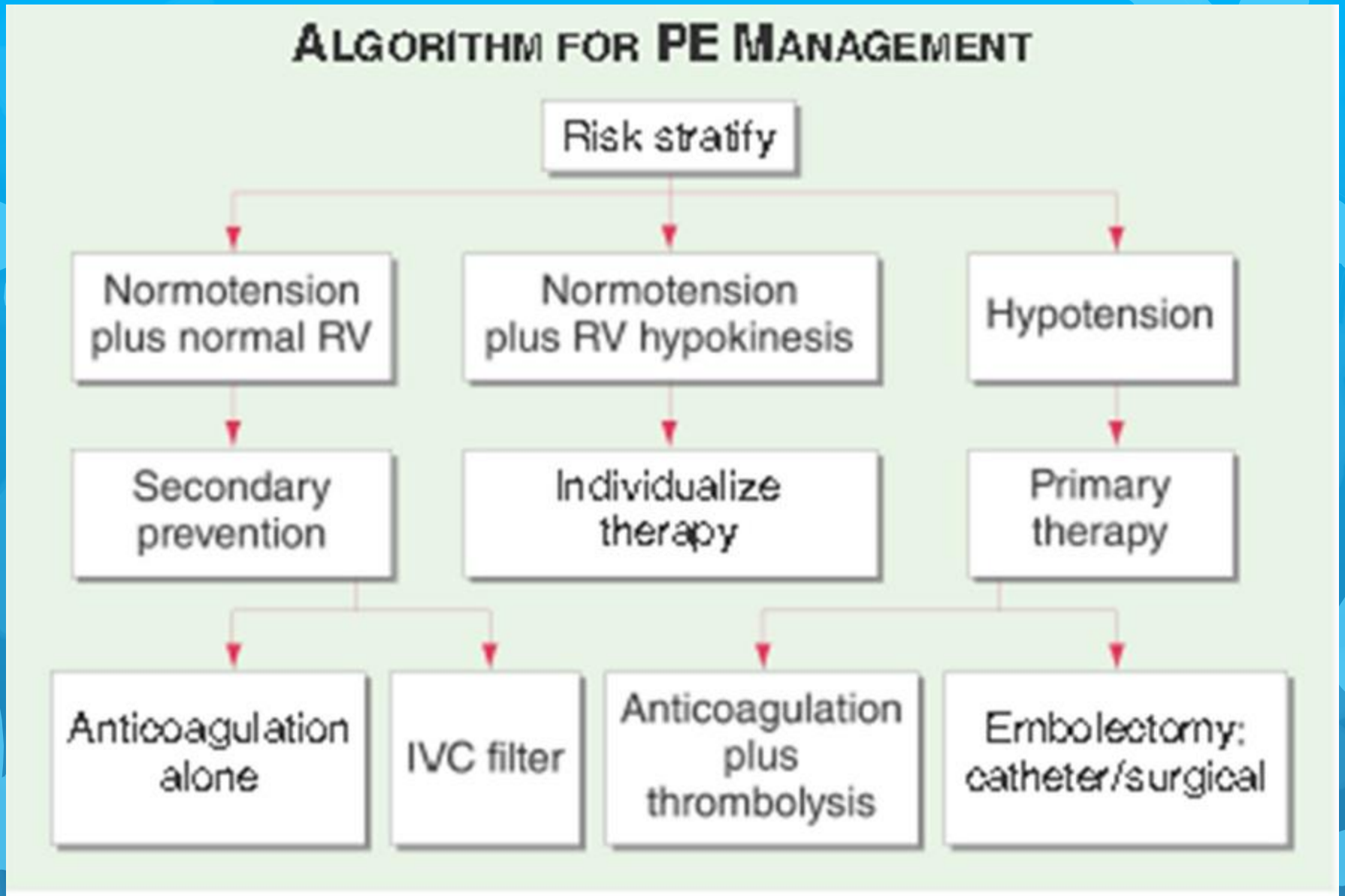


FIGURE 300-7 **Acute management of pulmonary thromboembolism.** RV, right ventricular; IVC, inferior vena cava.

TABLE 300-3 ANTICOAGULATION OF VTE

Immediate Anticoagulation
Unfractionated heparin, bolus and continuous infusion, to achieve aPTT 2 3 times the upper limit of the laboratory normal, *or*
Enoxaparin 1 mg/kg twice daily with normal renal function, *or*
Dalteparin 200 U/kg once daily or 100 U/kg twice daily, with normal renal function, *or*
Tinzaparin 175 U/kg once daily with normal renal function, *or*
Fondaparinux weight based once daily; adjust for impaired renal function
Direct thrombin inhibitors: argatroban or bivalirudin
Rivaroxaban 15 mg twice daily for 3 weeks, followed by 20 mg once daily with the dinner meal thereafter
Apixaban (not yet licensed)
Warfarin Anticoagulation
Requires 5 10 days of administration to achieve effectiveness as monotherapy
(Unfractionated heparin, low-molecular-weight heparin, and fondaparinux are the usual immediately effective "bridging agents" used when initiating warfarin)
Usual start dose is 5 mg
Titrate to INR, target 2.0 3.0
Continue parenteral anticoagulation for a minimum of 5 days and until two sequential INR values, at least 1 day apart, achieve the target INR range
Novel Oral Anticoagulants for Extended-Duration Anticoagulation following Initial Parenteral Anticoagulation
Edoxaban (not yet licensed)
Dabigatran (not yet licensed)

TABLE 300-4 PREVENTION OF VENOUS THROMBOEMBOLISM AMONG HOSPITALIZED PATIENTS

Condition	Prophylaxis Strategy
High-risk nonorthopedic surgery	Unfractionated heparin 5000 units SC bid or tid
	Enoxaparin 40 mg daily
	Dalteparin 2500 or 5000 units daily
Cancer surgery, including gynecologic cancer surgery	Enoxaparin 40 mg daily, consider 1 month of prophylaxis
Major orthopedic surgery	Warfarin (target INR 2.0–3.0)
	Enoxaparin 40 mg daily
	Enoxaparin 30 mg bid
	Dalteparin 2500 or 5000 units daily
	Fondaparinux 2.5 mg daily
	Rivaroxaban 10 mg daily
	Aspirin 81–325 mg daily
	Dabigatran 220 mg daily (not in the United States)
	Apixaban 2.5 mg bid (not in the United States)
	Intermittent pneumatic compression (with or without pharmacologic prophylaxis)
Medically ill patients, especially if immobilized, with a history of prior VTE, with an indwelling central venous catheter, or with cancer (but without active gastroduodenal ulcer, major bleeding within 3 months, or platelet count <50,000)	Unfractionated heparin 5000 units bid or tid
	Enoxaparin 40 mg daily
	Dalteparin 2500 or 5000 units daily
	Fondaparinux 2.5 mg daily
Anticoagulation contraindicated	Intermittent pneumatic compression devices (but whether graduated compression stockings are effective in medical patients is controversial)

MANAGEMENT OF VENOUS THROMBOEMBOLISM

UNFRACTIONATED HEPARIN AND LOWMOLECULAR-WEIGHT HEPARIN

- Heparin, both unfractionated and LMWH, remains the mainstay of therapy for venous thrombosis and for PE not associated with hemodynamic compromise.
- With a strong suspicion of embolism based on clinical findings and laboratory tests, heparin therapy should be instituted immediately, without awaiting diagnostic confirmation unless anticoagulation places the patient at significant risk.

- Data suggest that physician practices in the administration of unfractionated heparin often result in levels of anticoagulation that fall below those currently recommended in the literature.
- To overcome these problems, standardized protocols for heparin administration and monitoring have been recommended.

- A number of different intravenous heparin dosing schemes have been published, all of which have demonstrated the potential to reach a therapeutic threshold more rapidly than a nonstandardized approach.
- The most widely utilized of these is a weightbased system that includes an 80 unit/kg intravenous bolus of heparin followed by an 18 unit/kg/hr infusion.

- Whatever regimen is used, an activated partial thromboplastin time (a PTT) is generally obtained 6 hours after the bolus dose, 6 hours after each prescribed dose adjustment, and then on a daily basis for the duration of therapy.

- Because maintenance of the a PTT within a rigidly defined range does not appear to increase the efficacy or safety of the drug, frequent dosage adjustments are not necessary once the dose has been stabilized within a therapeutic range. This therapeutic range of a PTT, which corresponds to heparin levels of 0.2 to 0.4 unit/mL by protamine sulfate titration or 0.3 to 0.7 unit/mL by anti-factor Xa assay, may vary substantially depending on the sensitivity of the reagent utilized and among coagulation analyzers.

- Given the variance in a PTT values possible with different reagents and analyzers, individual institutional validation should be performed to define a therapeutic a PTT value. It also should be recognized that heparin requirements tend to decrease during the course of therapy, resulting in an increase in the level of the a PTT.

- For patients with heparin resistance (defined as the need for >40,000 units/day), monitoring heparin with an anti-factor Xa assay appears safe and effective and results in less escalation of the heparin dose than monitoring with the a PTT.

- Interestingly, supratherapeutic a PTT values are not associated with an increased risk of clinically important bleeding complications.
- There is no direct evidence that the absolute dose of heparin or the level of the a PTT can predict the likelihood of bleeding. Instead, bleeding during heparin therapy appears to be related to the presence of concurrent illness such as renal disease, a history of heavy alcohol consumption, aspirin use, and prior surgical procedures or peptic ulcer disease.

- Thus these data encourage adequate use of heparin doses. In fact, failure to treat patients early with sufficient heparin doses appears to have long-term and short-term implications for thromboembolic recurrence. It is somewhat controversial, however, whether the a PTT level itself, independent of the heparin dose, is associated with higher recurrence rates or whether it is strictly a matter of insufficient dosing itself.

- Subcutaneous LMWHs are widely used for the treatment of VTE because of their high bioavailability and longer halflife, which allows the strategy of dosing once or twice daily, with adjustment for weight but without the need for adjustment by a PTT monitoring.
- Indeed, the same strategy is appropriate for subcutaneous (unfractionated) heparin as well, administered in high doses.

- An approach utilizing a fixed dose of subcutaneous unfractionated heparin, administered as an initial dose of 333 U/kg followed by a dose of 250 U/kg every 12 hours, has been demonstrated to be as safe and effective as LMWH in patients presenting with venous thrombosis and PE. Clinicians must recognize that the administration of LMWH may not be preferable under certain clinical circumstances.

- Standardized dosing can be a problem in patients at the extremes of body weight;
- Because the drug is renally cleared, dose adjustments and monitoring with anti-factor Xa levels are necessary in patients with renal insufficiency;
- The anticoagulant effect of the drug cannot be monitored easily; populations exist (e.g., patients at high bleeding risk) in which a longer drug halflife is not a desirable effect;
- The ability of protamine sulfate to reverse the anticoagulant effect remains uncertain;
- Drug costs are substantially higher than with unfractionated heparin.

- Clinical trials have demonstrated that the safety and efficacy of LMWH preparations are comparable with those of unfractionated heparin in patients with venous thrombosis.
- In selected patients, fixed-dose subcutaneous LMWH appears to be safer and more effective than intravenous adjusted-dose unfractionated heparin.
- However, fixeddose subcutaneous LMWH appears to be comparable with subcutaneous unfractionated heparin, either in adjusted doses or fixed doses.

- Trials have also demonstrated that most patients with acute venous thrombosis can be treated safely on an outpatient basis with LMWH and that outpatient therapy can reduce total medical expenditure.
- However, not all patients with venous thrombosis can or should be treated in an outpatient setting. Approximately 50% of patients are ineligible for outpatient therapy owing to such factors as major bleeding risk, compliance problems, renal failure, significant comorbid disease, inadequate cardiopulmonary reserve, and inaccessibility for follow-up.

- Furthermore, embolism can happen during the early aspects of therapy in patients treated with both unfractionated and LMWH preparations.
- Although this circumstance would not be diminished in an inpatient setting, the potential consequences of recurrence, especially in patients with preexisting cardiopulmonary disease, might be more promptly detected and managed in this setting.

- The Hestia Study demonstrated the feasibility of outpatient therapy for acute PE patients who are hemodynamically stable (without perceived need for thrombolysis or embolectomy),
- At low risk for bleeding,
- Not hypoxemic,
- Free of severe liver or kidney dysfunction,
- Without severe pain or other reason for hospital admission
- Who did not develop PE while on anticoagulants or while pregnant.

- About one quarter of the patients who met these criteria were briefly admitted for evaluation and discharged in less than 24 hours.
- The Hestia criteria for outpatient therapy appear to be useful even in patients with CTPA evidence of enlarged right ventricular dimensions, provided they are otherwise hemodynamically stable.
- Even in patients who require initial inpatient management, the duration of hospitalization can be decreased considerably by a quick transition to outpatient therapy as their conditions stabilize.

- In terms of duration of heparin/LMWH therapy, studies have shown that utilizing a 5-day course of therapy in patients with proximal venous thrombosis is associated with a recurrence rate identical to that of a 10-day course.
- This assumes, of course, that warfarin is started early and is in a therapeutic range for 2 consecutive days before heparin is discontinued, a target often difficult to achieve.
- It is likely that a short course of heparin therapy would be similarly effective in patients with uncomplicated PE.

- However, a longer course of therapy is advisable in patients with major PE or extensive iliofemoral venous thrombosis.
- The major complications of unfractionated heparin and LMWH are bleeding and the development of thrombocytopenia.

- There are no predisposing factors to heparin associated thrombocytopenia other than a history of a previous exposure, and it develops at the same frequency with either (unfractionated) heparin or LMWH.

- Two types of thrombocytopenia are associated with heparin administration:
- An early-onset (1-5 days), non–immunemediated reduction in platelet count (type I) believed to be secondary to a direct agglutinating effect of heparin on platelets
- A late-onset (≥4 days), immune-mediated thrombocytopenia (type II) that may be associated with venous and arterial thrombosis.

- Immune-mediated thrombocytopenia can also arise within a day of initiating therapy in patients who have been exposed to the drug within the prior 100 days.
- The incidence of thrombosis with heparin-associated thrombocytopenia appears to be low, but when it happens, it is associated with considerable morbidity and mortality.

- Therefore heparin should be immediately withdrawn if this diagnosis is suspected.
- If heparin-associated thrombocytopenia type II is confirmed by either a functional assay or an immunoassay, withdrawal of heparin alone may be associated with an adverse outcome.
- A number of therapeutic alternatives exist, including direct thrombin inhibitors (lepirudin or argatroban), which do not react with heparin antibodies, or danaparoid, which appears to have a low rate of in vivo cross reactivity with heparin.
- Cross reactivity between unfractionated heparin and LMWH is relatively common, and these drugs should be avoided.

FONDAPARINUX

- Fondaparinux is effective and safe for the initial treatment of PE and of DVT.
- The dosing regimen used in these trials was straightforward: 7.5 mg subcutaneously once daily in patients who weighed from 50 to 100 kg (85% of cases).
- The dose was decreased to 5 mg in patients weighing less than 50 kg and increased to 10 mg in those weighing more than 100 kg.
- As is the case for unfractionated heparin and LMWH, the treatment was continued for at least 5 days, during which time warfarin was administered.

- After 5 days and once warfarin was therapeutic, treatment with fondaparinux was stopped. In a double-blinded randomized trial for the treatment of acute proximal lower extremity DVT, this regimen was as effective in preventing recurrent symptomatic VTE as enoxaparin, 1 mg/kg body weight twice per day. A randomized, open-label clinical trial compared the same fondaparinux treatment regimen with intravenous unfractionated heparin (using standard a PTTdriven dosage adjustments) for the treatment of pulmonary embolism.

- The outcomes of the two treatments appeared identical: the fondaparinux and standard therapy groups did not significantly differ with respect to the incidence of recurrent VTE, bleeding, overall mortality, or mortality due to PE.
- It is noteworthy that fondaparinux may accumulate to dangerous levels in patients with renal insufficiency because of its near total renal clearance.

DIRECT INHIBITORS OF FACTOR Xa AND OF THROMBIN

- Rivaroxaban is a synthetic inhibitor of Xa that can be used in the acute phase of VTE treatment.
- It differs from the parenteral agents (unfractionated, LMWH, and fondaparinux) in that it is a direct inhibitor. For this reason, it does not depend on the body's antithrombin in order to inactivate thrombosis.

- Another important difference is that it is well absorbed when given orally.
- Rivaroxaban is safe and effective for the treatment of the acute phase, as well as the 3-month follow-up phase of treatment for PE and for DVT.
- However, the acute phase of VTE treatment with rivaroxaban lasts for 3 weeks, as opposed to the shorter acute phase used with parenteral agents.

- The high bioavailability and pharmacokinetic predictability of once- or twice-daily oral rivaroxaban, as well as the safety of using it without the need for adjustment by INR values, is advantageous.
- Rivaroxaban is cleared by both renal and hepatic routes, including cytochrome P450-mediated metabolism.
- In the trials listed earlier, patients with severe renal or hepatic dysfunction were excluded.
- There are also potential drug interactions with agents that inhibit cytochrome P4503A4, such as azole compounds or HIV-protease inhibitors.

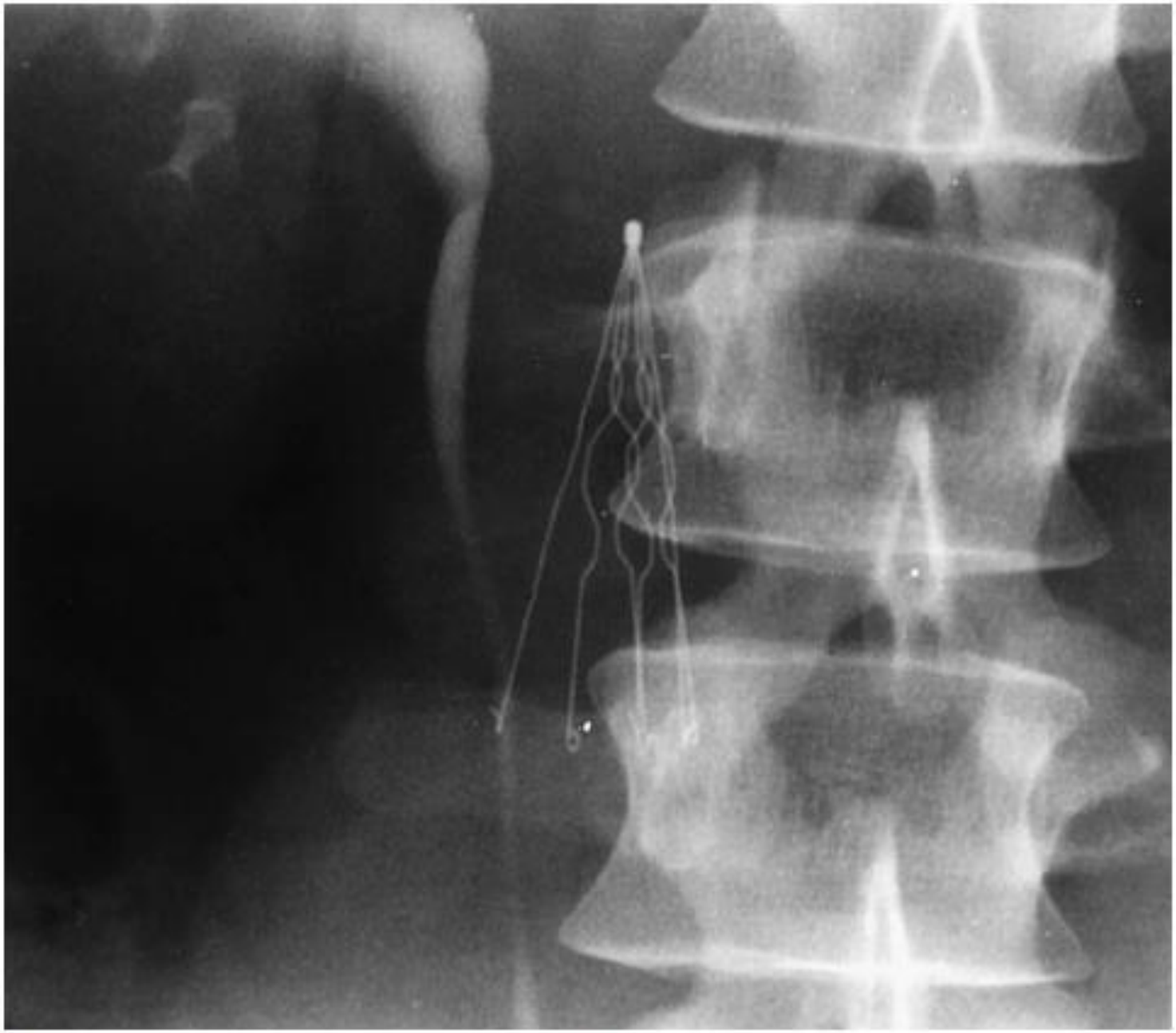


Figure 57-9 Inferior vena cava filter in place below the renal veins.

INFERIOR VENA CAVA FILTERS

- Scientific evidence supporting the use of inferior vena cava filters is limited.
- Established indications for filter placement in the therapy of VTE include
- 1) protection against PE in patients with acute VTE in whom conventional anticoagulation is contraindicated (recent surgery, hemorrhagic cerebrovascular accident, active bleeding, heparin-associated thrombocytopenia, etc.);
- 2) protection against PE in patients with acute VTE in whom conventional anticoagulation has proved ineffective;

- 3) protection of an already compromised pulmonary vascular bed from further thromboembolic risk (massive PE, chronic thromboembolic pulmonary hypertension).
- In support of the third indication is the recent review of a national inpatient database that disclosed that unstable PE patients who received inferior vena cava (IVC) filters had higher survival rates than those who did not receive them.

- Mortality from filter placement appears to be quite low regardless of what filter is used.
- Nonfatal complications of IVCs include
- 1) complications relating to the insertion process,
- 2) venous thrombosis at the site of insertion,
- 3) filter migration,
- 4) filter erosion through the inferior vena cava wall,
- 5) inferior vena cava obstruction.
- The majority of clinically important complications appear to involve venous thrombosis at the insertion site and inferior vena cava obstruction.

- Filter placement should not be considered as the sole therapy for VTE unless an absolute contraindication to anticoagulation exists.
- Although protecting the pulmonary vascular bed, filter placement does not inhibit the extension of existing venous thrombi or diminish the systemic prothrombotic state.

- Small thrombi can pass through patent filters or through collaterals around obstructed filters; furthermore, thrombus can extend through the filter itself.
- One study demonstrated that placement of a vena cava filter was capable of diminishing the incidence of early PE.
- The benefit was somewhat offset by an increased risk of recurrent DVT within 2 years, although an 8-year follow-up did not disclose an increased risk of recurrence or postthrombotic syndrome.

- The development of retrievable filters suggests that the intervention will no longer be irreversible, although extensive randomized clinical trials have not yet been performed to establish the safety and efficacy of this strategy.
- Given these considerations, long-term anticoagulation should be placement if no contraindications exist or as soon as any utilized following filter existing bleeding risk resolves.


THANK
YOU