

# PULMONARY EMBOLISM PHARMACOLOGIC TREATMENT

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6/25/2023

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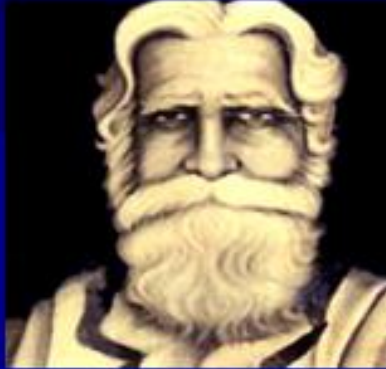
متخصص بیهوشی و فوق تخصص مراقبت‌های ویژه

دانشگاه علوم پزشکی گیلان

تابستان 1402

## History

- Susruta (Ayurveda physician and surgeon, 600-1000 B.C.) – patient with a “swollen and painful leg that was difficult to treat”
- Giovanni Battista Morgagni, 1761 – recognized clots in pulmonary arteries after sudden death, but didn’t make the connection to DVT



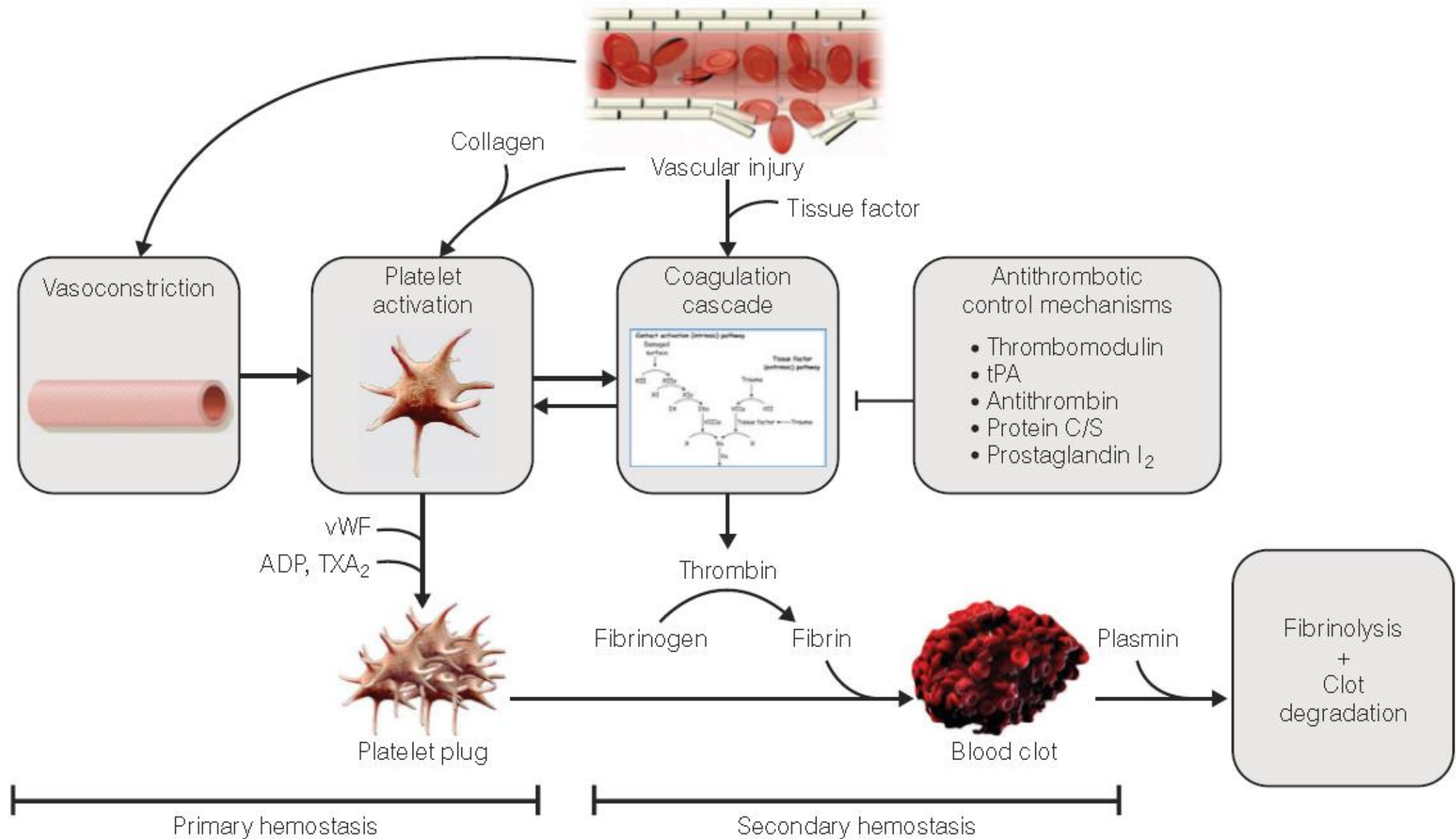
## Virchow Strikes Again

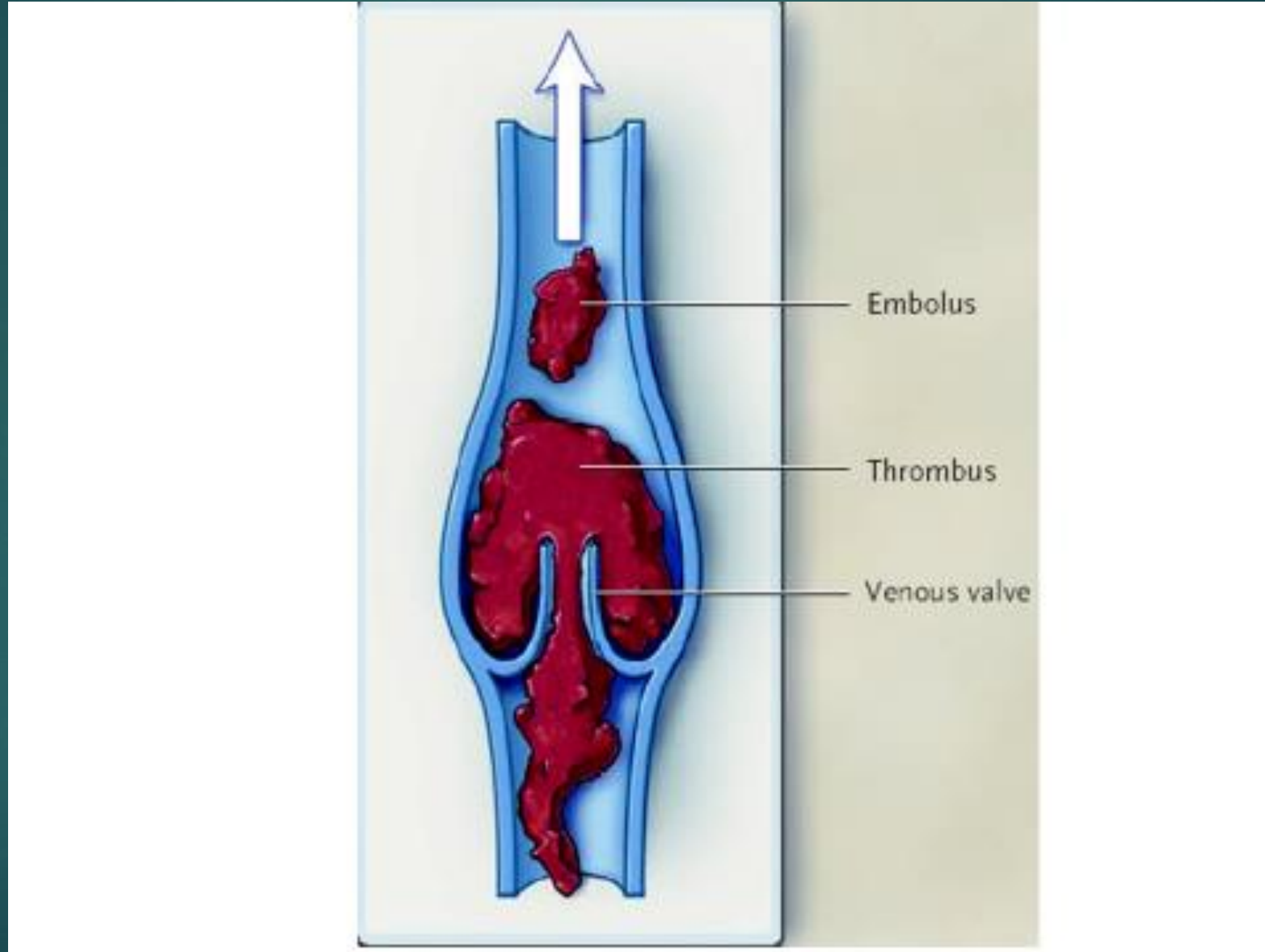
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- “Discovered” PE in 1846 – “the detachment of larger or smaller fragments from the end of a softening thrombus which are carried along the current of blood and driven into remote vessels. This gives rise to the very frequent process on which I have bestowed the name Embolia”

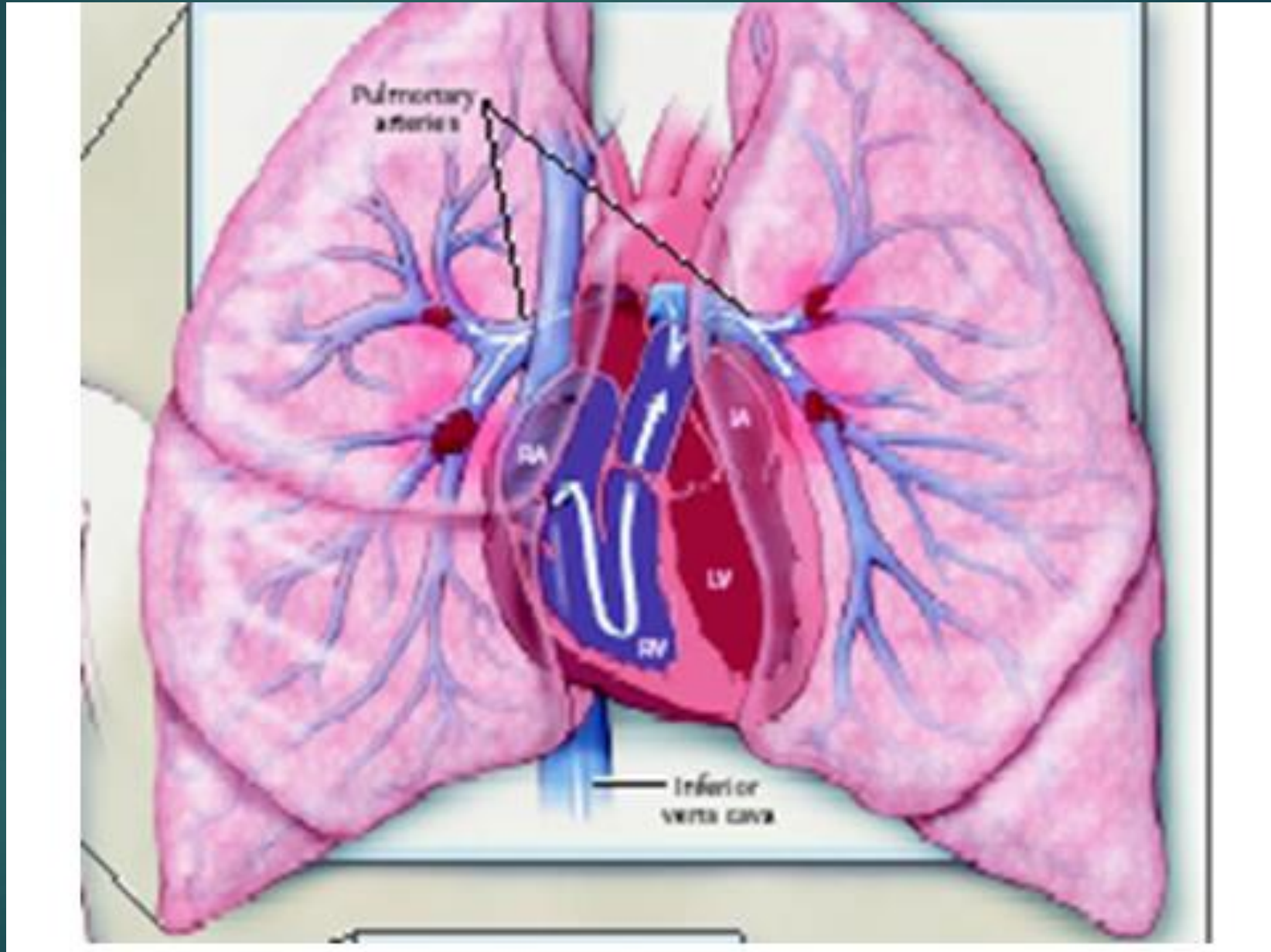


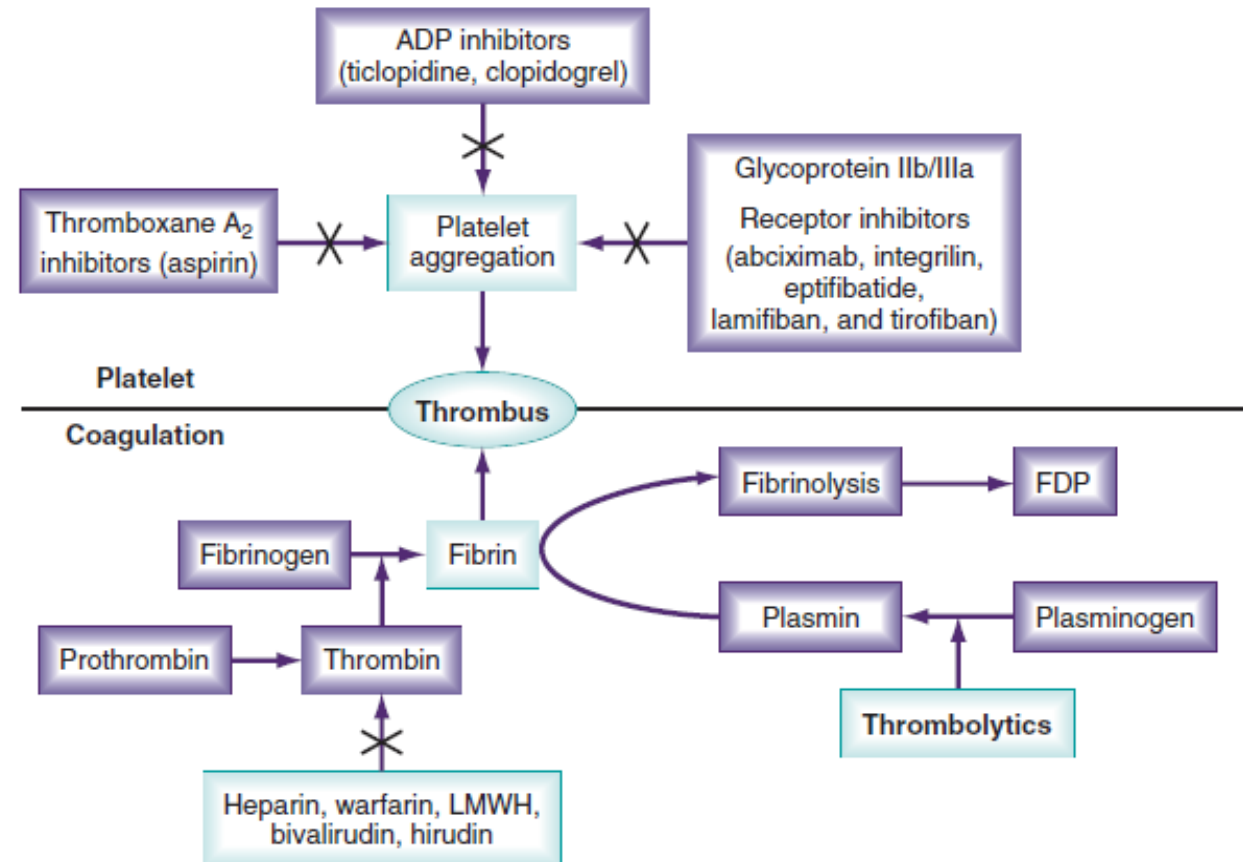
## Major Components of Hemostasis



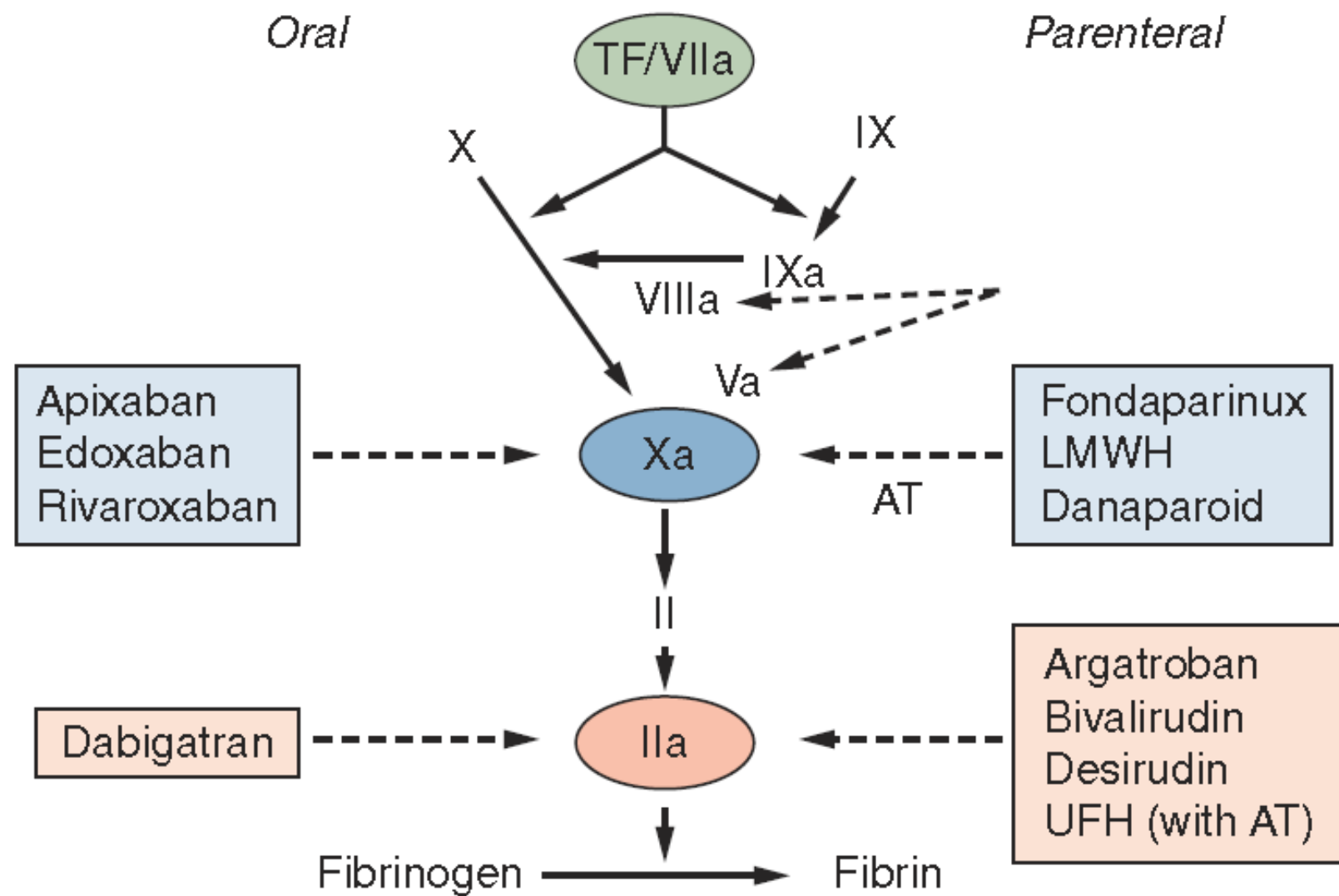








**Fig. 152.1** Components of thrombus formation and effects of various antithrombotic and thrombolytic agents. *FDP*, Fibrin degradation products; *LMWH*, low-molecular-weight heparin.



**Fig. 128.1** The Sites of Action of Oral and Parenteral Anticoagulation Agents. The non-vitamin K oral anticoagulants, also called direct

# Fig. 128.1 The Sites of Action of Oral and Parenteral Anticoagulation Agents.

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The non-vitamin K oral anticoagulants, also called direct oral anticoagulants, include apixaban, edoxaban, and rivaroxaban.

These drugs directly inhibit factor Xa, whereas

dabigatran directly inhibits factor IIa (thrombin).

The parenteral/intravenous anticoagulants that inhibit factor Xa include fondaparinux and low-molecular-weight heparin (*LMWH*) by antithrombin (*AT*)-cofactor dependent binding.

Parenteral direct thrombin inhibitors include argatroban, bivalirudin, and desirudin that also directly inhibit thrombin, and unfractionated heparin (*UFH*) by antithrombin (*AT*)-cofactor dependent binding.

Not shown in the figure is the mechanism of action of vitamin K antagonists (e.g., warfarin) that inhibit the posttranslational modification of coagulation factors II, VII, IX, and X to the active forms.

Warfarin and its cogenders are anticoagulants because they decrease the circulating levels of critical hemostatic factors involved in coagulation.

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# TREATMENT OF ACUTE PE

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## ▶ Initial Resuscitation

- ▶ Volume Administration
- ▶ Vasopressors
- ▶ Vasodilator Therapies
- ▶ Supplemental Oxygen
- ▶ Intubation and Mechanical Ventilation

# Treatment

- ▶ For hypotensive patients, a cautious fluid challenge with administration of IV crystalloid in small-volume boluses (such as 250–500 mL) may improve cardiac output.
- ▶ A volume status examination should occur before and after administration of fluid and should be tailored to the hemodynamics of the patient.
- ▶ Aggressive administration of IV fluids should be avoided, as this may result in RV overdistention, compression of the LV by the septum, decreased cardiac output, and myocardial ischemia.

# Vasopressors

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- ▶ If the administration of an initial bolus of IV fluids does not improve the patient's hypotension, vasopressors should be administered.
- ▶ There are limited experimental data on the appropriate initial vasopressor, but expert consensus suggests **that norepinephrine** should be the initial agent in blood pressure support.
- ▶ **Dobutamine** has been used in selected cases but may worsen hypotension via peripheral beta-2 agonism unless coadministered with norepinephrine.
- ▶ **Vasopressin** may play an accessory role as a vasopressor that does not raise pulmonary vascular resistance.

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# Supplemental Oxygen

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- ▶ Hypoxemia occurs commonly in hemodynamically significant acute PE, and hypoxemic vasoconstriction may worsen acute pulmonary hypertension.
- ▶ Expert consensus recommends the administration of supplemental oxygen to target a pulse oximetry saturation of 90% or greater.

# Vasodilator Therapies

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- ▶ Pulmonary arterial vasodilators may decrease pulmonary vascular resistance and pulmonary arterial pressure, thereby decreasing RV afterload.
- ▶ The successful use of inhaled nitric oxide and epoprostenol have been reported in several case series.
- ▶ However, a recent clinical trial failed to show benefit of inhaled nitric oxide in hemody-namically stable patients with PE and RV dysfunction.

# Intubation and Mechanical Ventilation

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- ▶ Great caution should be exercised in the intubation and ventilation of a patient with acute PE, as these procedures may precipitate
- ▶ hemodynamic collapse and cardiac arrest.
- ▶ Because the increased intra-thoracic pressure brought by mechanical ventilation can further lower preload and worsen RV failure, preintubation hemodynamics should be optimized and an infusion of vasopressors should be considered for those patients needing intubation.
- ▶ Therefore intubation should be rapidly accomplished by a skilled operator, using induction medications that preserve cardiovascular stability.
- ▶ Careful attention should also be paid to postintubation ventilator management to optimize RV function

# Supportive Care

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- ▶ Inhaled Nitric Oxide
- ▶ Extracorporeal Membrane Oxygenation
- ▶ Future Directions

# Massive PE

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- ▶ The American Heart Association (AHA) defines massive PE as an acute PE with sustained hypotension, pulselessness, or persistent profound bradycardia (heart rate <40 beats per minute with evidence of shock).
- ▶ Sustained hypotension is defined as a systolic blood pressure <90 mm Hg or the need for inotropic support and cannot be the result of a cause other than PE, such as an arrhythmia, hypovolemia, sepsis, or LV dysfunction.
- ▶ Based on the ICOPER study, the mortality rate for patients with massive PE was 58.3% compared with 15.3% in those with PE without cardiovascular collapse.
- ▶ In patients requiring cardiopulmonary resuscitation, the mortality rate may be as high as 65%.
- ▶ As hemodynamic instability portends such a poor prognosis, more aggressive interventions must be considered in this patient population.

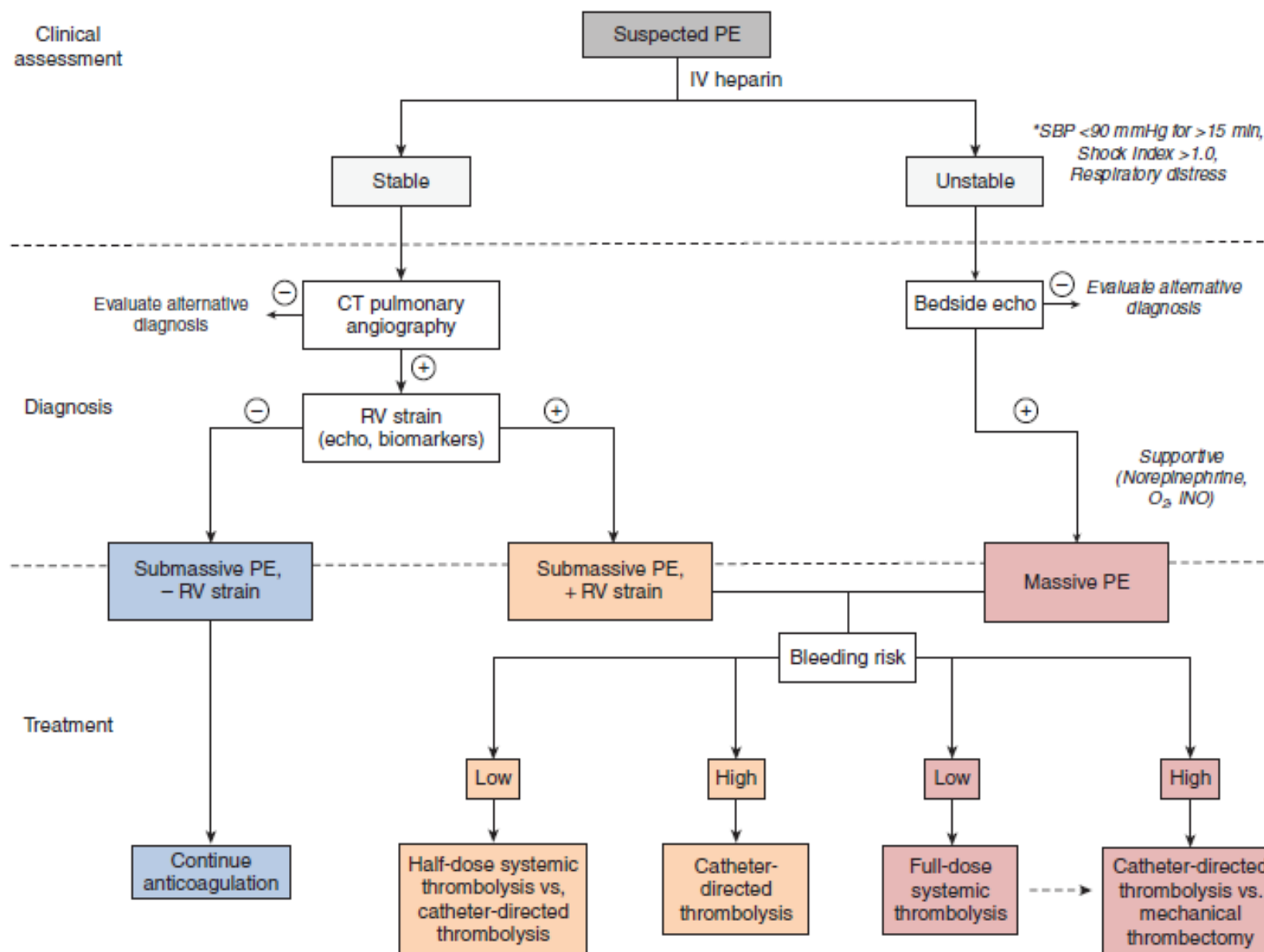
# Submassive Pulmonary Embolism with Right Ventricular Strain

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- ▶ Submassive PE with RV strain describes patients with acute PE who are normotensive but have some evidence of RV dysfunction or myocardial ischemia on ECG, echocardiogram, CTPA, or laboratory work such as elevated troponin or brain natriuretic peptide.
- ▶ This heterogeneous group spans the entire spectrum with respect to risk associated with their PE.
- ▶ Some patients with mild evidence of RV strain are likely to recover well with anticoagulation alone.
- ▶ However, others within this -efit from more aggressive and higher-risk interventions.

# Submassive PE without RV Strain (Low-Risk PE)

- ▶ Patients with acute PE who are hemodynamically stable and have no evidence of RV dysfunction or myocardial injury fall within the submassive PE without RV strain category and have the lowest risk of adverse outcome.
- ▶ In-hospital mortality for these patients is estimated at 8.1%.



**Fig. 127.3** Treatment Algorithm for Suspected Pulmonary Embolism (PE) in Critically Ill Patients.

# Anticoagulation

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Unfractionated Heparin

Low-Molecular-Weight Heparin

Fondaparinux

Vitamin K Antagonists

Direct Oral Anticoagulants

Thrombolytic Therapy

- ▶ features such as metabolism and excretion,
  - ▶ bleeding risk, drug interactions, and reversibility.
  - ▶ Upcoming procedures or anticipated thrombolysis may favor a medication with a shorter half-life,
  - ▶ whereas patients at high risk of bleeding may benefit from an anticoagulant with a readily available reversal agent.
- 
- ▶ The choice of anticoagulant in the ICU should focus on short-term management, whereas long-term treatment choices can be deferred until after the patient leaves the ICU
  - ▶ Initial anticoagulation after the diagnosis of PE is usually accomplished with a parenteral agent in the immediate management period before transitioning to an oral agent.

# Unfractionated Heparin

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- ▶ Despite the development of new anticoagulant medications, unfractionated heparin (UFH) remains the initial parenteral medication of choice for many patients with acute PE in the ICU.

Though endogenously produced, commercial UFH is isolated from porcine or bovine intestines as a mix of different-length polysaccharides.

These long chains bind to antithrombin III (AT), potentiating the inactivation of factors Xa and IIa (thrombin).

After an initial bolus, the infusion rate of UFH is commonly titrated using a nomogram based on the activated partial thromboplastin time (aPTT) or the anti-Xa level and monitored every 6 hours until a steady state is reached.

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# Unfractionated Heparin

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- ▶ The efficacy of UFH depends partly on achieving a therapeutic level of UFH within the first 24 hours of treatment.
- ▶ Unfortunately, the anticoagulant response to a standard dose of UFH varies widely among patients, and numerous studies have demonstrated difficulties in clinical practice with reliably administering therapeutic doses of IV UFH, even despite the use of a dosing protocol and nomogram.
- ▶ Because of its short half-life,
- ▶ utility with renal dysfunction,
- ▶ and availability of a reversal agent,
- ▶ UFH is often the first medication used for treatment of acute high-risk PE in the ICU.

# Heparin-induced thrombocytopenia (HIT)

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- ▶ occurs within 5–10 days of the initiation of heparin in about 5% of patients.
- ▶ HIT type I (HIT-I), characterized by a transient decrease in platelet count, occurs within the first 2 days of therapy because of a direct effect of heparin that causes platelet aggregation.
- ▶ HIT-I is not clinically significant and does not require a change in therapy.
- ▶ HIT type II (HIT-II) is much more concerning and is an immune-mediated disorder caused by antibodies targeting the platelet–heparin complex (specifically, platelet factor 4 [PF4]).
- ▶ Recognition of the PF4–heparin complex by immunoglobulin G (IgG) leads to both thrombocytopenia and an activation of the clotting cascade, leading to arterial and venous thrombosis, which can be life-threatening.
- ▶ Patients with HIT-II have a 30-fold increased thrombotic risk

# Heparin-induced thrombocytopenia (HIT)

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- ▶ The diagnosis of HIT-II is made clinically using the 4T score while awaiting laboratory confirmation (e Table 65.5).
- ▶ Laboratory diagnosis is typically accomplished using the highly sensitive immunoassay for the PF4–heparin complex and confirmed using the highly specific serotonin release functional assay.
- ▶ For patients in whom there is a high suspicion for HIT-II, heparin therapy should be discontinued immediately and the patient transitioned to an alternative form of anticoagulation, typically a parenteral direct thrombin inhibitor.

# Low-Molecular-Weight Heparin

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- ▶ Low-molecular-weight heparin (LMWH) is obtained by the chemical or enzymatic degradation of UFH from approximately 45 saccharides to 15 saccharides.
- ▶ Similarly to UFH, LMWH binds to AT to inactivate factors Xa and II (thrombin).
- ▶ The decreased length of the LMWH chains decreases the ability of AT to bind thrombin compared with UFH, and therefore its major mechanism of action is from the inactivation of Xa.
- ▶ Several different formulations of LMWH are commercially available with similar characteristics.

# Low-Molecular-Weight Heparin

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- ▶ LMWH is given subcutaneously and has excellent bioavailability (.90%) and a longer half-life when compared with UFH.
- ▶ LMWH is renally cleared and thus is contraindicated in renal failure.
- ▶ It is administered once or twice a day in weight-based dosing and does not require laboratory monitoring.
- ▶ Nonetheless, anti-Xa levels can be used to measure its efficacy, if needed.
- ▶ When compared with UFH, LMWH has a more predictable anticoagulant response.

## Low-Molecular-Weight Heparin

- ▶ Overall, LMWH appears to have fewer serious complications,
- ▶ more reliable anticoagulation,
- ▶ lower rates of recurrent thrombus,
- ▶ a lower risk of bleeding,
- ▶ and requires less monitoring than UFH.
- ▶ LMWH also appears to have a lower rate of heparin-induced thrombocytopenia.
- ▶ Protamine can be used to reverse LMWH, but its efficacy in reversing Xa blockade is limited.

**Absolute contraindications to anticoagulation are rare but include**

(1) active intracranial hemorrhage uncontrolled bleeding related to conditions such as trauma, recent surgery, gastrointestinal or genitourinary pathology, or preexisting coagulopathy.

**Temporary contraindications** should be regularly reassessed, and anticoagulation should be reconsidered as the initial contraindication abates.

# Major contraindications to anticoagulant treatment

- ▶ intra-cranial bleeding, severe active bleeding, or recent neurologic or spi-nal surgery.
- ▶ **Relative contraindications include**  
recent major surgery, ischemic stroke, nonsevere active bleeding, thrombocytopenia, or bleeding diathesis

## Factors that influence agent selection for anticoagulation in patients with acute venous thromboembolism

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Factor	Preferred anticoagulant	Qualifying remarks
Cancer	LMWH, factor Xa inhibitors	More so if: Just diagnosed, extensive VTE, metastatic cancer, very symptomatic; vomiting; on cancer chemotherapy.
Initial parenteral therapy to be avoided	Rivaroxaban; apixaban	VKA, dabigatran, and edoxaban require initial parenteral therapy.
Once daily oral therapy preferred	Rivaroxaban; edoxaban; VKA	
Liver disease and coagulopathy	LMWH	DOACs contraindicated if INR raised because of liver disease; VKA difficult to control and INR may not reflect antithrombotic effect.
Renal disease and creatinine clearance <30 mL/min	VKA	DOACs and LMWH contraindicated with severe renal impairment. However, dosing of some DOACs can be renally adjusted, although adjustment varies with different levels of renal impairment depending on the DOAC.
Coronary artery disease	VKA, rivaroxaban, apixaban, edoxaban	Coronary artery events appear to occur more often with dabigatran than with VKA. This has not been seen with the other DOACs, and they have demonstrated efficacy for coronary artery disease. Antiplatelet therapy should be avoided if possible in patients on anticoagulants because of increased bleeding.

Dyspepsia or history of GI bleeding	VKA, apixaban	Dabigatran increased dyspepsia. Dabigatran, rivaroxaban, and edoxaban may be associated with more GI bleeding than VKA.
Poor compliance	VKA	INR monitoring can help to detect problems. However, some patients may be more compliant with a DOAC because it is less complex.
Thrombolytic therapy use	UFH infusion	Greater experience with its use in patients treated with thrombolytic therapy.
Reversal agent needed	VKA, UFH, DOACs	Reversal agents for DOACs may not be universally readily available.
Pregnancy or pregnancy risk	LMWH	Potential for other agents to cross the placenta.
Cost, coverage, licensing	Varies among regions and with individual circumstances	

e TABLE 65.1 DASH Prediction Score for Recurrent VTE

Criterion	Points
D-dimer abnormal 1 month after stopping anticoagulation	+2
Age ≤50 years	+1
Male patient	+1
Hormone use at VTE onset (if female)	−2
<b>Interpretation:</b>	
Cumulative Points	Annual Recurrence Risk
≤1	
Consider discontinuing anticoagulation	3.1%
≥2	
Consider continuing anticoagulation	9.3%

TABLE 65.1 Risk Factors for PE

<b>Inherited Risk Factors</b>	34
Factor V Leiden	
Prothrombin mutation	
Antithrombin deficiency	
Protein C deficiency	
Protein S deficiency	6/25/2023
<b>Acquired Risk Factors</b>	
<b>Vascular Damage</b>	
Surgery	
Trauma/burns	
Previous VTE	
<b>Inflammatory or Procoagulant States</b>	
Active cancer	
Antiphospholipid syndrome	
Chronic inflammatory diseases	
Pregnancy	
Obesity	
Nephrotic syndrome	
Heparin-induced thrombocytopenia	
<b>Venous Stasis</b>	
Hospitalization or immobility	
Paralysis	
Prolonged travel	
<b>Factors Common in the ICU</b>	
Sepsis	
Central venous catheter	
Pharmacologic paralysis	
Acute renal failure, dialysis	
Mechanical ventilation	
Blood products	
Vasopressors	

# Direct Oral Anticoagulants

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- ▶ the DOACs have a more rapid onset,
- ▶ shorter half-life,
- ▶ wider therapeutic window,
- ▶ and more predictable pharmacokinetics without the need for therapeutic monitoring.
- ▶ The DOACs are categorized into two major categories,
- ▶ the direct factor Xa inhibitors and the direct thrombin inhibitors.

# Direct Oral Anticoagulants

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- ▶ Orally administered, the factor Xa inhibitors directly bind factor Xa to prevent the cleavage of prothrombin to thrombin.
- ▶ Unlike heparin, they do not require the presence of antithrombin.
- ▶ The two DOACs approved for the initial treatment of VTE, rivaroxaban and apixaban, both require a higher dosage in the first week(s) of therapy before de-creasing to a maintenance dose .
- ▶ **Edoxaban**, a third approved DOAC, requires at least 5 days of overlapping parenteral therapy before being used as monotherapy, whereas the fourth medication, **betrixaban**, is approved only for VTE prophylaxis.

# Direct Oral Anticoagulants

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- ▶ When compared with **LMWH and VKAs** in large clinical trials, the factor Xa antagonists have shown equivalent efficacy for the treatment of VTE, while offering a more favorable safety profile.
- ▶ Although these medications have become the first-line treatment for most patients in the outpatient setting
- ▶ Because of their reliable anticoagulant effect with-out the need for routine monitoring, a number of factors limit
- ▶ their use in the ICU, including oral dosing, limitations of use in renal dysfunction, and until recently, limited options for anticoagulation reversal.

e TABLE 65.4 Initial Anticoagulant Therapy for VTE

Medication	Route	Initial Dosing*	Monitoring	Maintenance Dosing
Unfractionated heparin	IV	80 units/kg bolus, then 18 units/kg/hr infusion	aPTT 1.5–2.5 normal or anti-Xa 0.3–0.7	–
Low-molecular-weight heparin	SQ	Enoxaparin 1 mg/kg BID Dalteparin 200 units/kg daily Tinzaparin 175 IU/kg daily	None	Same as initial
Fondaparinux	SQ	5–10 mg daily (based on patient weight)	None	Same as initial
Warfarin	PO	5 mg daily (generally) with heparin bridge	INR 2.0–3.0	Adjusted by INR
Apixaban	PO	10 mg BID × 1 week	None	5 mg BID
Rivaroxaban	PO	15 mg BID × 3 weeks	None	20 mg daily

\*Initial dosing for patients with normal renal function. Dose adjustments or discontinuation may need to be made for patients with reduced renal function. *aPTT*, Activated partial thromboplastin time; *INR*, international normalized ratio; *VTE*, venous thromboembolism.

# Thrombolytic Therapy

- ▶ In contrast to anticoagulant medications, which prevent clot propagation,
- ▶ thrombolytic (or fibrinolytic) drugs lead to rapid clot lysis by converting plasminogen to plasmin.
- ▶ Earlier thrombolytic drugs such as streptokinase and urokinase have largely been replaced by more fibrin-specific agents modeled on the naturally occurring enzyme tissue plasminogen activator (tPA).
- ▶ Recombinant genetic engineering has led to the development of three major thrombolytic medications: alteplase (recombinant tissue-type plasminogen activator or r-tPA),
- ▶ reteplase (recombinant plasminogen activator, rPA),
- ▶ and tenecteplase (TNK-tPA).
- ▶ Alteplase is given as a 100-mg IV bolus over 2 hours,
- ▶ reteplase is given as 10 units IV over 2 minutes
- ▶ and then repeated 30 minutes later, and tenecteplase is given as a single weight-based bolus dose.

# Thrombolytic Therapy

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- ▶ Thrombolysis can be performed via systemic administration or using a catheter-based approach. Recent studies have found lower rates of bleeding complications with improved outcomes using catheter-based thrombolysis as opposed to systemic thrombolysis.
- ▶ The utility of thrombolysis in the treatment of severe PE, approximately one-third of patients with massive PE have significant contra-indications to thrombolysis.
- ▶ The prevalence of absolute contraindication is likely even higher in an ICU population.
- ▶ Mechanical thrombectomy and additional supportive interventions play an important role in patients who may benefit from thrombolysis but are not candidates for the therapy.

# Thrombolytic Therapy

- ▶ Thrombolytic therapy provides more rapid lysis of PE than anticoagulation.
- ▶ This clot resolution can restore pulmonary perfusion and promptly lower pulmonary artery pressure and resistance, thereby improving RV function.
- ▶ The benefit-to-risk ratio of thrombolysis therefore seems to be highest in those patients with hemodynamic instability in the setting of acute PE (e.g., high-risk or “massive” PE) and intermediate and high-risk patients **who are showing signs of hemodynamic worsening despite appropriate anticoagulation**
- ▶ Expert consensus recommends that UFH be stopped during the administration of r-tPA and TNK-tPA, though it can be continued if rPA is used.
- ▶ When fibrinolytics are given in cardiac arrest, consensus recommendations suggest cardiopulmonary resuscitation (CPR) should be continued for at least 60–90 minutes before terminating resuscitation attempts.

# Thrombolytic Therapy

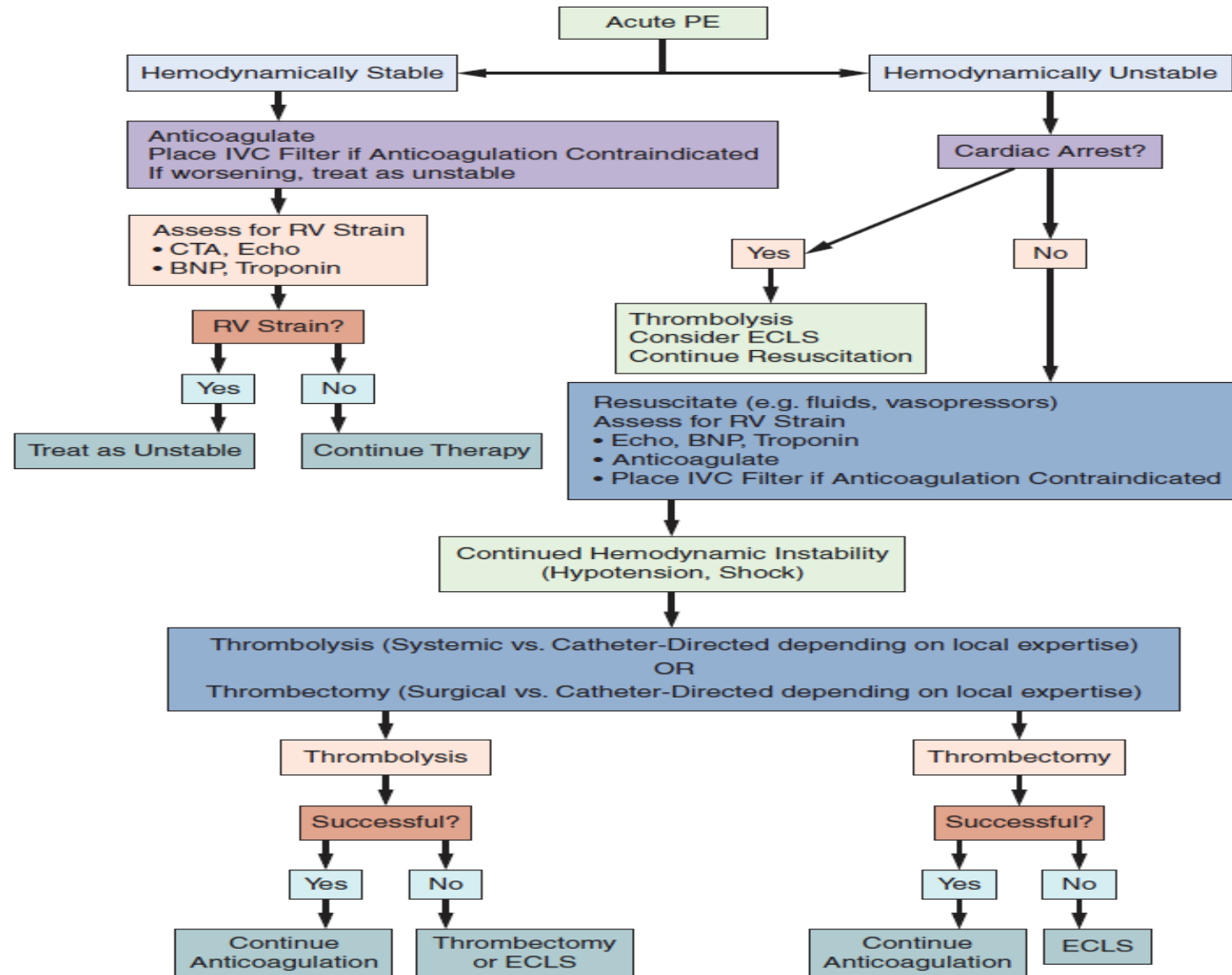
- ▶ Although no mortality benefit has been demonstrated with empiric thrombolysis in undifferentiated cardiac arrest, fibrinolysis is generally recommended in cardiac arrest resulting from presumed or known PE.
- ▶ **Alteplase** may be given as a 50-mg bolus and
- ▶ **tenecteplase**, although technically weight-based, is typically given as a 50-mg bolus for ease of administration.
- ▶ When fibrinolytics are given in cardiac arrest, consensus recommendations suggest cardiopulmonary resuscitation (CPR) should be continued for at least 60–90 minutes before terminating resuscitation attempts.

**TABLE 65.4 Contraindications to Fibrinolytic Therapy****Major Contraindications**

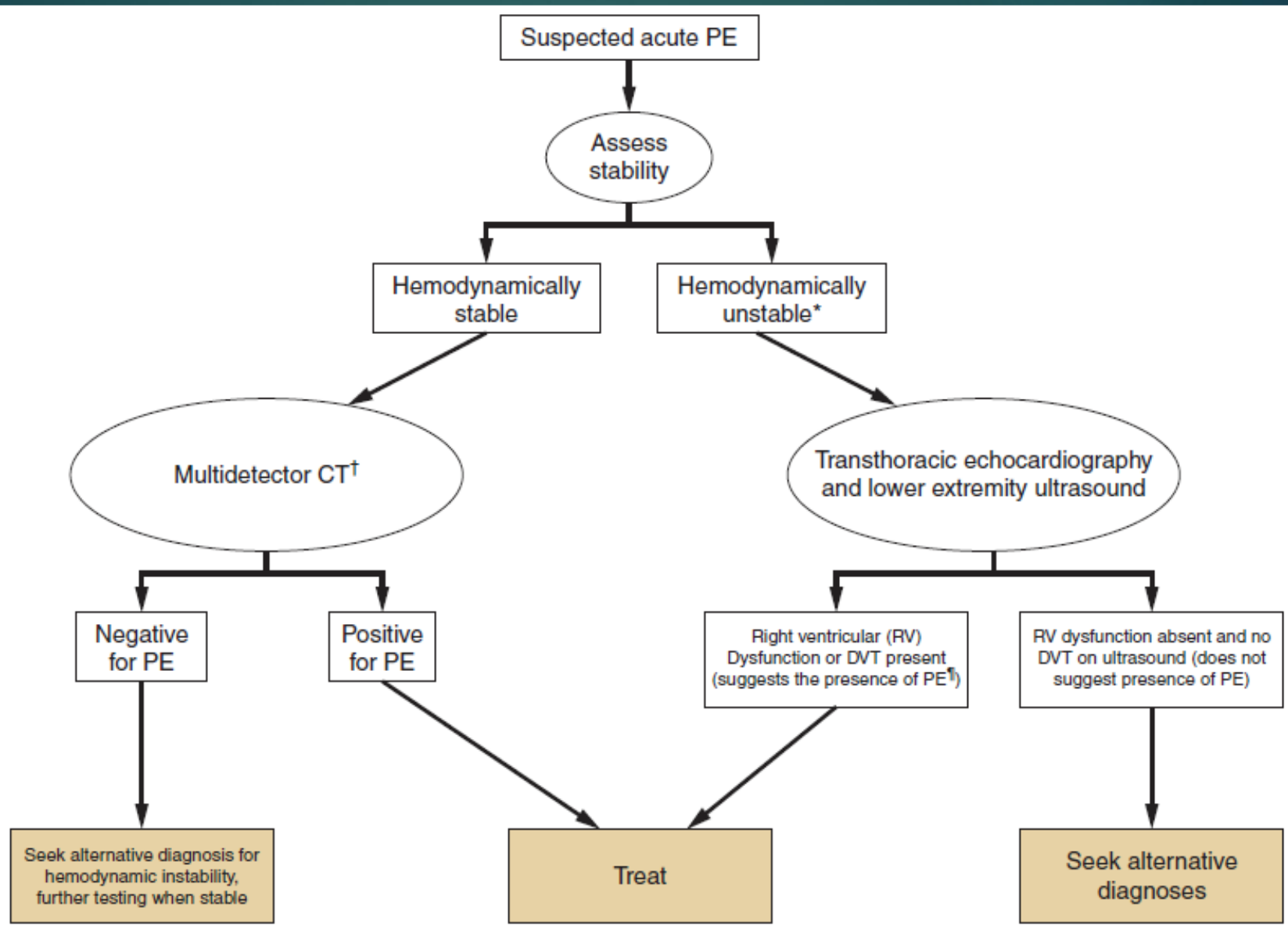
Structural intracranial disease  
Previous intracranial hemorrhage  
Recent ischemic stroke (3 months)  
Active bleeding  
Recent brain or spinal surgery  
Recent head trauma with fracture or brain injury  
Bleeding diathesis

**Relative Contraindications\***

Systolic blood pressure >180 mm Hg  
Diastolic blood pressure >110 mm Hg  
Recent (nonintracranial) bleeding  
Recent surgery  
Recent invasive procedure  
Noncompressible vascular puncture  
Remote ischemic stroke (>3 months)  
Therapeutic anticoagulation  
Traumatic cardiopulmonary resuscitation  
Pericarditis or pericardial fluid  
Diabetic retinopathy  
Pregnancy  
Age >75 years  
Low body weight (<60 kg)  
Female  
Black race



**Fig. 65.4** BNP, Brain natriuretic peptide; CTA, computed tomography angiography; ECLS, extracorporeal life support; IVC, inferior vena cava; PE, pulmonary embolism; RV, right ventricle.



# Interventional Techniques Inferior Vena Cava Filter

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- ▶ Insertion of an IVC filter is indicated for patients with acute PE with an absolute contraindication to anticoagulant therapy or for patients with recurrent PE despite adequate anticoagulation.
- ▶ Many clinicians also favor insertion of an IVC filter for patients with large PE and residual iliofemoral DVT that could result in sudden cardiac arrest if it were to embolize.
- ▶ IVC filters prevent the embolization of thrombus to the heart and pulmonary vasculature but do not aid in resolution of the thrombus; therefore the patient should receive anticoagulation if the contraindication to anticoagulation resolves.
- ▶ The routine placement of IVC filters for patients with proximal DVT without PE is not supported, as it does not reduce mortality and increases the risk of subsequent DVT.

# Catheter-Directed Treatment

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- ▶ Catheter-directed treatment includes a variety of endovascular treatments for acute PE, including thrombolysis and thrombectomy.
- ▶ Catheter-directed thrombolysis involves the insertion of a catheter into affected pulmonary arteries to directly deliver fibrinolytic into the thrombus, theoretically avoiding the shunting of blood away from the occluded artery and into nonoccluded vessels.
- ▶ Some catheters include ultrasound to facilitate the entry of thrombolytics into the thrombus, though the clinical benefit of this functionality is unknown.
- ▶ Catheter-based techniques allow the delivery of much lower doses of thrombolytic medications over a longer period, theoretically reducing the risk of major bleeding.

# Catheter-directed thrombolysis

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- ▶ Catheter-directed thrombolysis appears to be as effective as systemic thrombolysis in high-risk PE with a lower risk of bleeding and may be superior to anticoagulation alone in intermediate- and high-risk PE, though large clinical trials comparing catheter-directed thrombolysis with either anticoagulation alone or with systemic thrombolysis have not yet been performed.
- ▶ Other percutaneous catheter-based techniques include fragmentation, aspiration thrombectomy, and mechanical thrombectomy.
- ▶ These procedures are only available at specialized centers, and data supporting these techniques are limited to case series

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# Supportive Care

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- ▶ **Inhaled Nitric Oxide** Inhaled nitric oxide (iNO) acts as a selective pulmonary artery vasodilator,
- ▶ thus partially offloading RV pressure without negatively affecting systemic blood pressure.
- ▶ mean pulmonary artery pressure in the acute setting, few studies exist evaluating its use in patients with PE, and none of them are adequately powered to assess whether its use confers a mortality benefit.

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# Extracorporeal Membrane Oxygenation

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- ▶ Extracorporeal membrane oxygenation (ECMO) represents a potentially beneficial characteristics that lend to its possibilities as an adjunctive treatment.
- ▶ ECMO allows for offloading of the RV and can provide a bridge to other therapeutic interventions (i.e., surgical embolectomy or catheter-directed therapy).
- ▶ An additional advantage of ECMO is that cannulation can be performed at the bedside.
- ▶ Evidence for the utility of ECMO for massive PE is primarily composed of case series, and most guidelines consider ECMO as an adjunct to thrombolysis or embolectomy.

# Future Directions

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- ▶ CLOTT investigators are also examining thromboelastography data that suggest that certain critically injured patients are incapable of lysing clots after injury.
- ▶ This syndrome is referred to as *fibrinolytic shutdown*,
- ▶ and the risk factors for and the incidence of this new diagnosis are the central goals of the CLOTT Study Part 2.
- ▶ Of particular importance is the association of fibrinolytic shutdown with the development of VTE events.
- ▶ A better understanding of this pathology could change the focus of VTE prevention in at-risk trauma patients from preventing clots from forming to assisting in clot dissolution.

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