Diagnosis and management of thrombotic disorders in intensive care patients

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Objectives

- Etiology
- Symptoms and Signs
- Diagnosis
- Treatment

- **Etiology**
- Balance between procoagulant and anticoagulant.
- Genetic, acquired and environmental factors can tip the balance.
- Thrombus in veins eg DVT
- Thrombus in arteries eg myocardial infarction or ischemic stroke.

Thrombus in cardiac chamber can be detached as embolus (pulmonary embolism or cerebral stroke).

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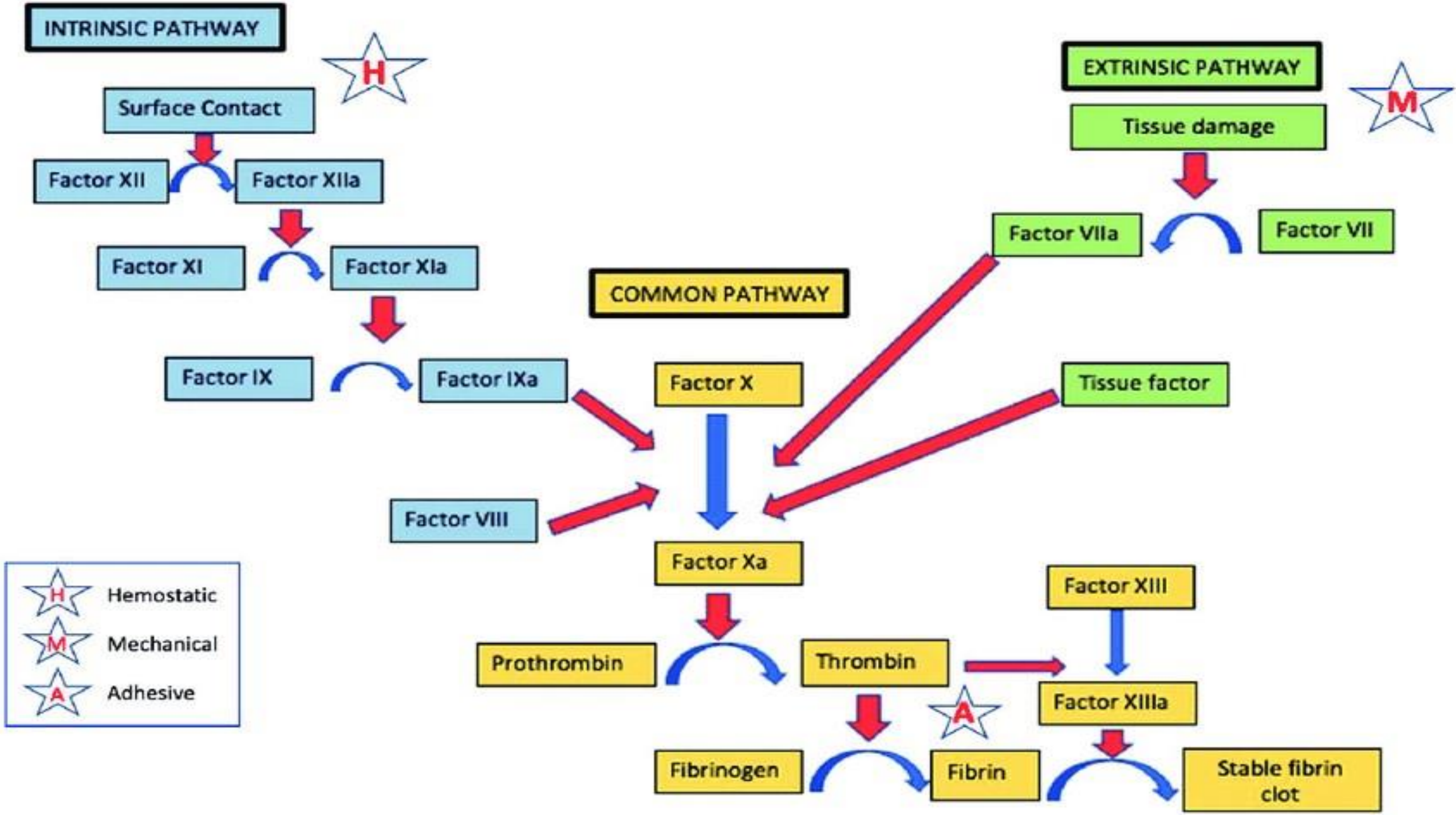
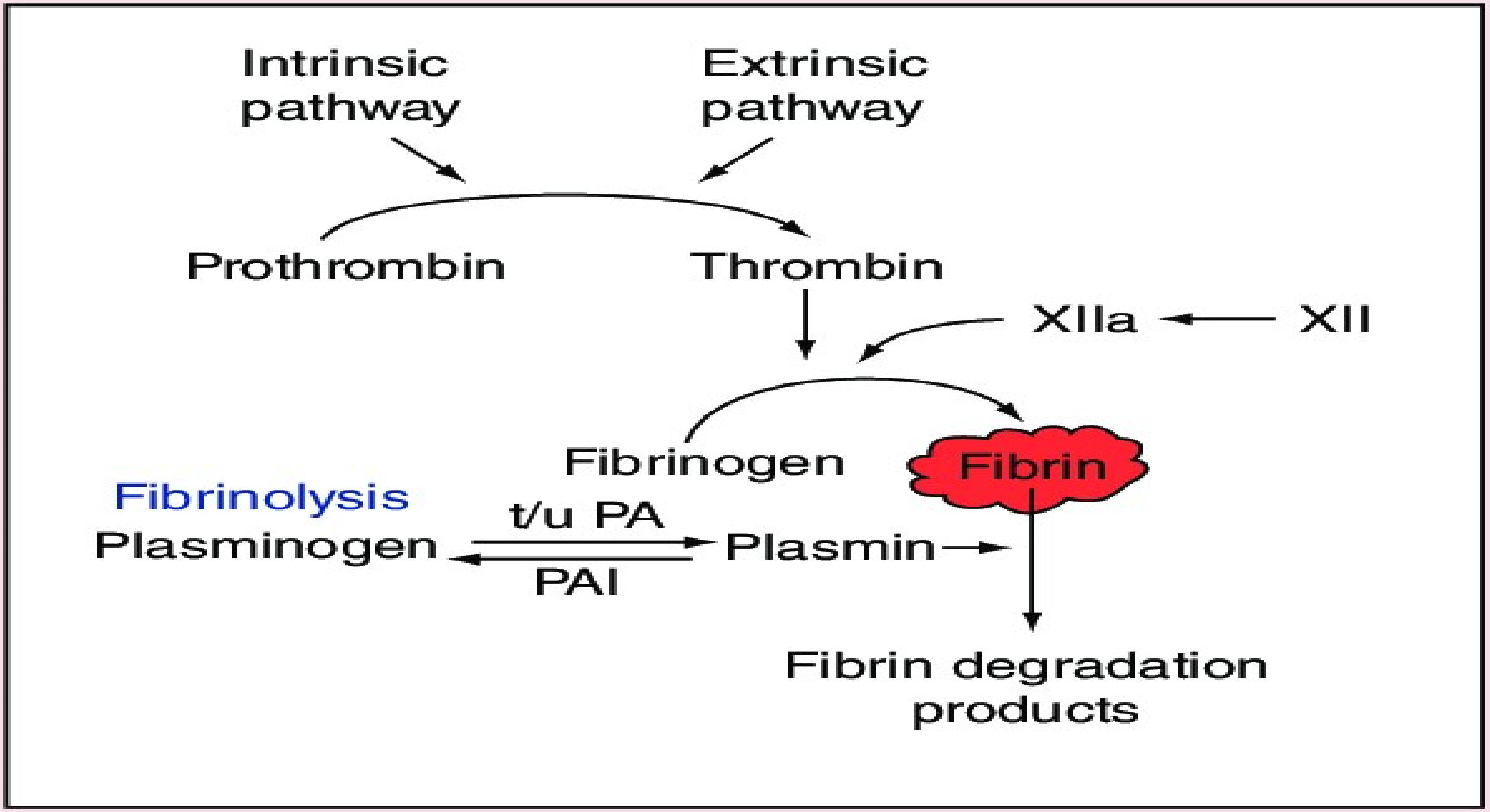

INTRINSIC PATHWAY
H
Surface Contact
Factor XII
Factor XIIa
Factor XI
Factor XIa
Factor IX
Factor IXa
EXTRINSIC PATHWAY
M
Tissue damage
Factor VIIa
Factor VII
COMMON PATHWAY
Factor X
Tissue factor
Factor VIII
Factor Xa
Factor XIII
Prothrombin
Thrombin
A
Factor XIIIa
Fibrinogen
Fibrin
Stable fibrin clot
H Hemostatic
M Mechanical
A Adhesive


Intrinsic pathway
Extrinsic pathway
Prothrombin
Thrombin
XIIa
XII
Fibrinogen
Fibrin
Fibrinolysis
t/u PA
Plasminogen
Plasmin
PAI
Fibrin degradation products

CONGENITAL FACTORS

Genetic defects that increase the propensity for venous thromboembolism include

- Factor V Leiden mutation, which causes resistance to activated protein C (APC)
- Prothrombin 20210 gene mutation
- Deficiency of protein C
- Deficiency of protein S
- Deficiency of protein Z
- Antithrombin deficiency

Elevated factor VIII, IX, and XI levels

- **Acquired Causes of Thromboembolism**

ANTIPHOSPHOLIPID SYNDROME

ATHEROSCLEROSIS

CANCER PATIENTS

HEPARIN INDUCED THROMBOCYTOPENIA

VITAMIN DEFICIENCY (FOLATE B6, B12)

SEPSIS

OCPS

TISSUE INJUIRY

VENOUS STASIS

SYMPTOMS AND SIGNS OF THROMBOTIC DISORDERS

SYMPTOMS

- Chest pain and shortness of breath: Possible PE or myocardial infarction
- Leg pain, warmth, redness, and swelling: DVT
- Weakness/numbness of one side of the body, problems speaking, and problems with balance and walking: Possible ischemic stroke
- Abdominal pain: Possible splanchnic arterial or venous thrombosis

DVT

Leg pain

Swelling

Tenderness

Discolouration

Pitting oedema

PE

Shortness of breath

Cough

Chest pain

Tachycardia

Hypotension

Low-grade fever

PREDISPOSING FACTORS

- IF the condition is clinically obvious (eg, recent surgery or trauma, prolonged immobilization, cancer, infection, medical illness, generalized atherosclerosis). If no predisposing factor is readily apparent, further evaluation should be considered in patients.

PREDISPOSING FACTORS (CONT)

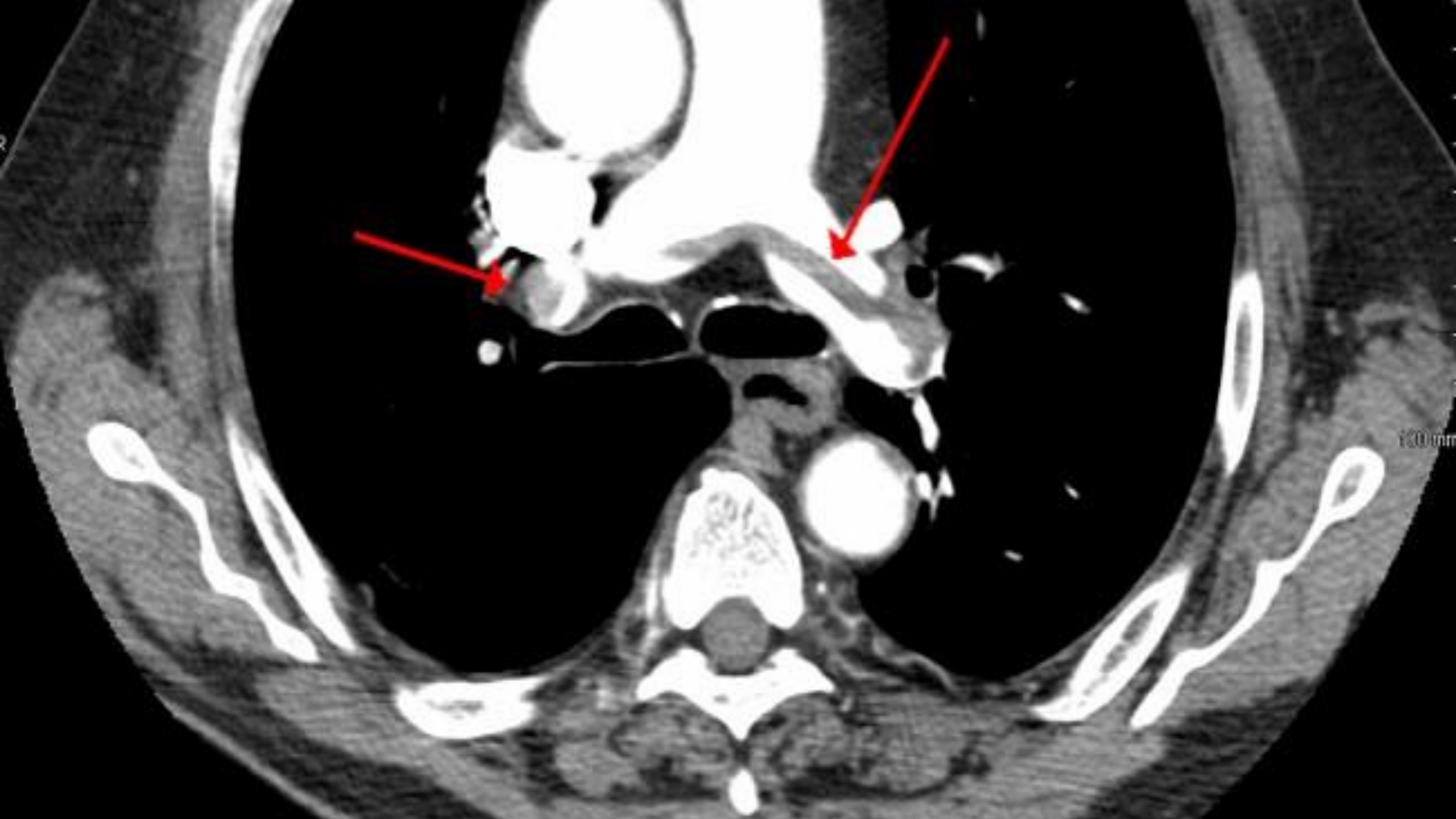
- A family history of venous thrombosis (first-degree relative with venous thromboembolism before age 50 years)
- More than one episode of venous thrombosis
- Venous or arterial thrombosis before age 50 years
- Unusual sites of venous thrombosis (eg, cavernous sinus, splanchnic veins)

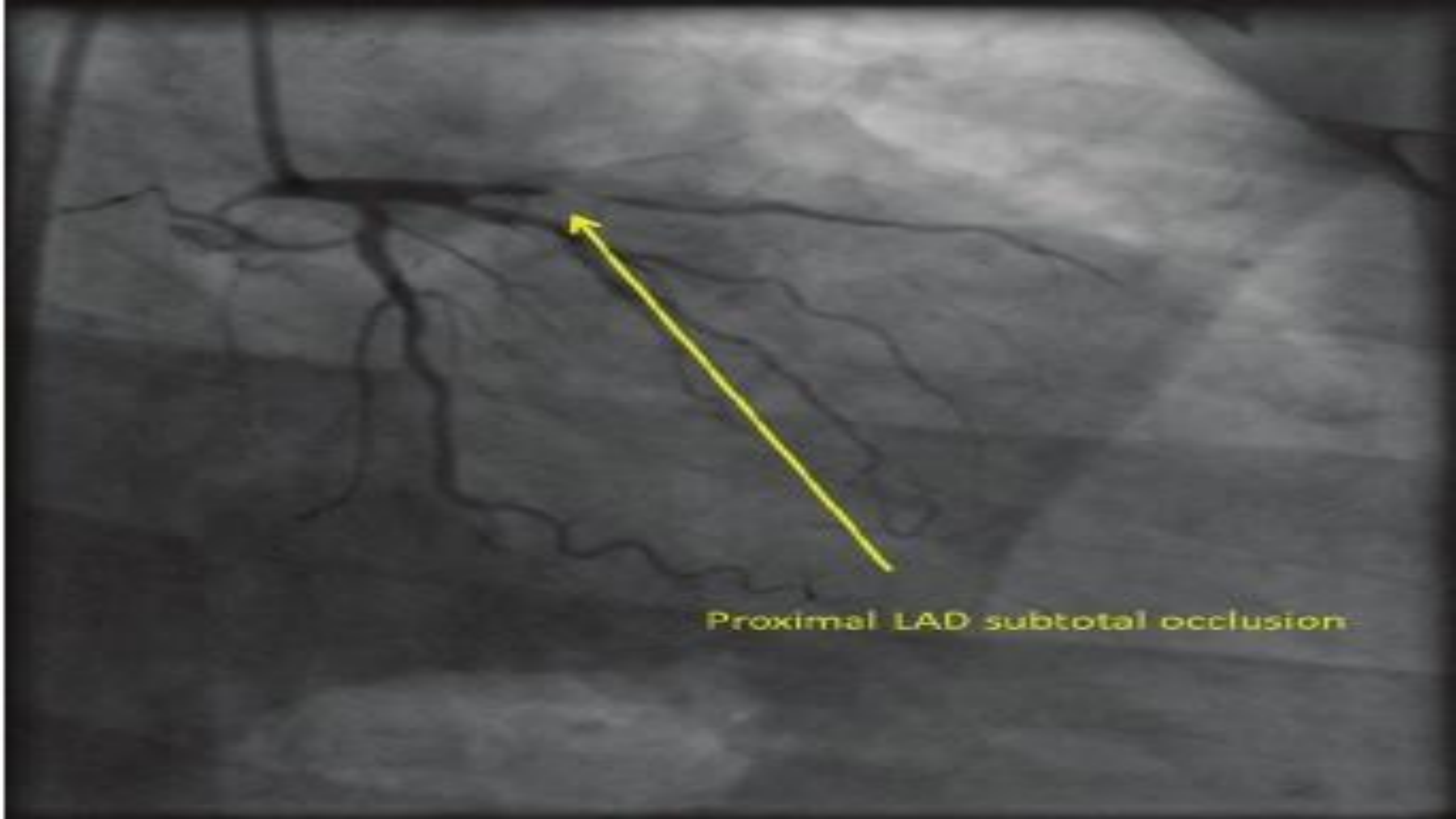
INVESTIGATIONS

- Clotting assay for lupus anticoagulant
- Clotting assay for resistance to
- activated protein C
- Genetic test for factor V Leiden
- Genetic test for prothrombin gene mutation (G20210A)
- Factors VIII, IX, and XI activity
- Functional assay of antithrombin

INVESTIGATIONS (CONT)

- Functional assay of protein C
- Functional assay of protein S
- Antigenic assays of total and free protein S.
- Measurement of plasma homocysteine levels
- Immunoassays for antiphospholipid antibodies
- National Institute on Health and Care Excellence (NICE): Venous thromboembolic diseases: diagnosis, management and thrombophilia testing. NICE guideline [NG 158]. March 26, 2020.




Proximal LAD subtotal occlusion

Features	Score (points)
Clinical signs and symptoms of DVT	3.0
No alternative diagnosis	3.0
Heart rate >100 beats/min	1.5
Immobilization ≥3 days or surgery in the previous 4 weeks	1.5
Previous DVT or PE	1.5
Hemoptysis	1.0
Malignancy with active treatment in the past 6 months or under palliative care	1.0
Pretest clinical probability	
PE unlikely	≤4.0
PE likely	>4.0

PE = Pulmonary embolism, DVT = Deep vein thrombosis

TREATMENT OF THROMBOTIC DISORDERS

TREATMENT PROTOCOL

- Anticoagulation is cornerstone.

THROMBOPROPHYLAXIS IN CRITICAL CARE

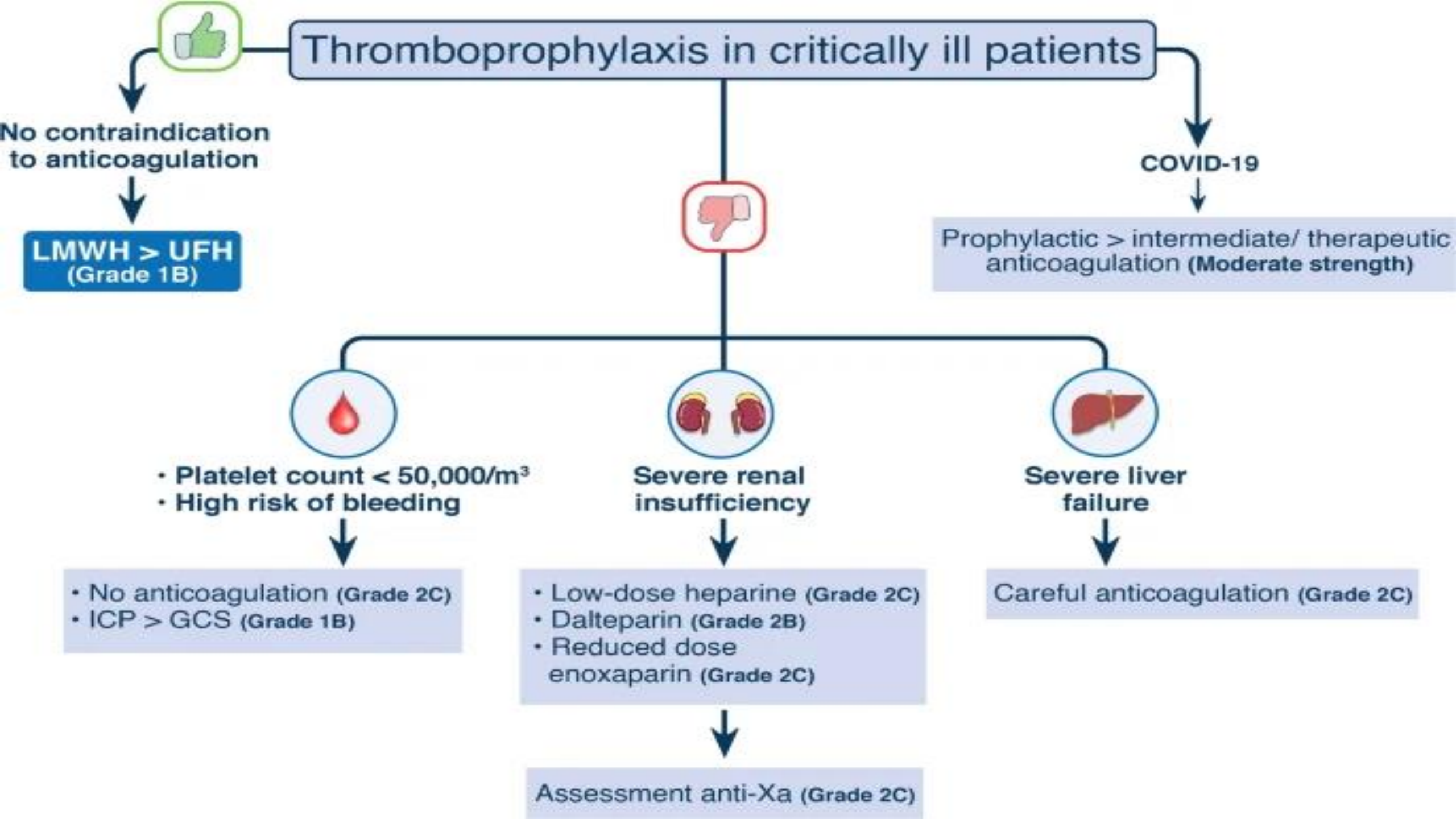
- Venous thromboembolism (VTE) in critically ill patients may be a life-threatening complication increasing duration of mechanical ventilation and stay in the intensive care unit
- Heparin was started as thromboprophylaxix 1960.
- Low-molecular-weight heparin (LMWH) was discovered in the 1980s mainly to reduce HIT

- Lasting Legacy in Intensive Care Medicine
- Published: 29 August 2022
- volume 49, pages75–78 (2023)

THROMBOPROPHYLAXIS (CONT)

- **Consistent with clinical studies which seem to provide a superior efficacy of LMWH compared to UFH, without an increase in bleeding complications, the European and American guidelines recommend pharmacological prophylaxis with LMWH over UFH in critically ill patients The guidelines also suggest no prophylaxis or the use of intermittent pneumatic compression in patients with a platelet count less than 50,000/mm^3 or a high risk of bleeding and the careful use of pharmacological prophylaxis in patients with severe liver failure.**

- **Duranteau J, Taccone FS, Verhamme P, Ageno W, Force EVGT (2018) European guidelines on perioperative venous thromboembolism prophylaxis: intensive care. Eur J Anaesthesiol 35:142–146**


Thromboprophylaxis in critically ill patients
No contraindication to anticoagulation
LMWH > UFH (Grade 1B)
COVID-19
Prophylactic > intermediate/ therapeutic anticoagulation (Moderate strength)
• Platelet count < 50,000/m³
• High risk of bleeding
• No anticoagulation (Grade 2C)
• ICP > GCS (Grade 1B)
Severe renal insufficiency
• Low-dose heparine (Grade 2C)
• Dalteparin (Grade 2B)
• Reduced dose enoxaparin (Grade 2C)
Assessment anti-Xa (Grade 2C)
Severe liver failure
Careful anticoagulation (Grade 2C)

TREATMENT PROTOCOL (CONT)

- **DOACs include factor Xa inhibitors (rivaroxaban, apixaban) and the direct thrombin inhibitor dabigatran. Unlike warfarin, DOACs do not require regular laboratory monitoring, and some of these medications (apixaban, rivaroxaban) can be used in acute treatment without initial parenteral anticoagulation.**
- **In contrast to warfarin, DOACs have fewer drug-drug interactions and their effectiveness is not influenced by diet.**

TREATMENT PROTOCOL (CONT)

- Patients with acute, massive pulmonary embolism (PE) causing hemodynamic instability may be treated initially with a thrombolytic agent (eg, tissue plasminogen activator [t-PA]). t-PA has increasingly been used as the first-choice thrombolytic agent.

RT-PA

- Indications
- Thrombolytic treatment administered in acute PE associated with hemodynamic instability in patients who do not seem prone to bleeding,. [36]
- Contraindications
- Absolute contraindications for thrombolysis include the following:
- Gastrointestinal (GI) bleeding within the past 6 months
- Active or recent internal bleeding
- History of hemorrhagic stroke
- Intracranial or intraspinal disease
- Pregnancy

CONTIN

- Relative contraindications include the following:
- Major surgery or trauma within the past 2 weeks
- Biopsy within 10 days
- Other invasive procedures

THROMBECTOMY, EMBOLECTOMY, IVC FILTER, AND LIGATION

THANK YOU