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Doctor in Medicine

Venous thromboembolism disease in internal medicine: epidemiological trends, etiological factors, and management patterns. A five-year retrospective observational study at Laghouat Mixed Hospital.

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*BABAOUAMER Meriem
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Dedication

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The man whose sacrifices paved the path on which I proudly walk today. You bore your responsibilities in silence and worked tirelessly. Every lesson you taught me became a light guiding my steps. This achievement is a reflection of your efforts before it is mine.

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ABSTRACT

Introduction:

Venous thromboembolic disease (VTE), including deep vein thrombosis (DVT) and pulmonary embolism (PE), is a frequent and potentially life-threatening condition associated with substantial morbidity, mortality, and healthcare burden. In Algeria, particularly in southern regions, epidemiological and management data remain limited.

Objective:

To assess the hospital prevalence of VTE in the Internal Medicine Department of Laghouat Mixed Hospital and to describe its epidemiological profile, etiological factors, clinical characteristics, therapeutic management, and in-hospital outcomes over a five-year period (January 1, 2021 to December 31, 2025).

Materials and Methods:

This was a retrospective descriptive study conducted over five years. Among 5,968 hospitalizations recorded in the Internal Medicine Department, all patients with clinically, biologically, and imaging-confirmed VTE were included. Demographic, risk factor, localization, clinical, etiological, therapeutic, and outcome data were collected from medical records and analyzed descriptively.

Results:

A total of 267 confirmed VTE cases were identified, corresponding to a hospital prevalence of 4.47%. Cases increased progressively over the study period, with the highest number recorded in 2025 (22.8%). The mean age was 50.8 ± 19.9 years (range: 16–92), with a female predominance (64.8%; sex ratio: 0.54). Regarding anatomical distribution, lower-limb DVT was the most frequent localization (45.5%), followed by pulmonary embolism (17.9%) and cerebral venous thrombosis (14.1%). Isolated DVT accounted for 69.6% of cases, isolated PE for 21.5%, and combined DVT with PE for 8.8%. Less frequent sites included upper-limb, splanchnic, and unusual venous thromboses. Clinically, the most common manifestations were limb edema, warmth, and redness (33.1%), limb pain (17.7%), and dyspnea (9.6%). Etiologically, the main causes were idiopathic or unprovoked VTE (31%), active cancer (17.2%), immobilization, surgery, or trauma (16.7%), and thrombophilia (14.3%). Women were more frequently exposed to hormonal and pregnancy-related factors, whereas men more often presented with cancer-associated or idiopathic events, COVID-19 was found (8.6%) as prothrombotic risk factor. Younger patients were more commonly affected by thrombophilia, cerebral venous thrombosis, and hormonal causes, while older patients predominantly presented with cancer-related VTE and transient acquired risk factors. Therapeutically, initial treatment was mainly based on low-molecular-weight heparin (85.8%). Maintenance therapy was dominated by vitamin K antagonists (53.5%), followed by direct oral anticoagulants (21.4%). Clinical evolution was favorable in 88.8% of patients. The in-hospital complication rate was 9.7%, while mortality reached 7.1%, with the highest rates observed in cancer-associated VTE.

Conclusion:

VTE is a frequent and heterogeneous condition in internal medicine practice at Laghouat Mixed Hospital, predominantly affecting women and middle-aged adults. Lower-limb DVT remains the most common presentation, while cerebral venous thrombosis and thrombophilia were notable in younger patients. Idiopathic cases remain frequent, whereas cancer represents the main predictor of poor prognosis. LMWH and VKA remain the cornerstone of treatment, while DOAC use is increasing but still limited. Strengthening prevention, early diagnosis, thrombophilia screening in selected patients, and broader access to modern anticoagulation strategies may improve outcomes.

Keywords: Venous thromboembolism; deep vein thrombosis; pulmonary embolism; cerebral venous thrombosis; thrombophilia; epidemiology; risk factors; anticoagulation; Algeria.

RÉSUMÉ

Introduction :

La maladie thromboembolique veineuse (MTEV), comprenant la thrombose veineuse profonde (TVP) et l'embolie pulmonaire (EP), est une affection fréquente et potentiellement grave, associée à une morbidité, une mortalité et un coût de santé publique importants. En Algérie, particulièrement dans les régions du Sud, les données épidémiologiques et thérapeutiques restent limitées.

Objectif :

Évaluer la prévalence hospitalière de la MTEV dans le service de médecine interne de l'hôpital mixte de Laghouat et décrire son profil épidémiologique, ses facteurs étiologiques, ses caractéristiques cliniques, sa prise en charge thérapeutique et son évolution intrahospitalière sur une période de cinq ans (du 1er janvier 2021 au 31 décembre 2025).

Matériels et Méthodes :

Il s'agit d'une étude descriptive rétrospective menée sur cinq ans. Parmi 5 968 hospitalisations enregistrées dans le service de médecine interne, tous les patients présentant une MTEV confirmée cliniquement, biologiquement et par l'imagerie ont été inclus. Les données démographiques, facteurs de risque, localisations, caractéristiques cliniques, étiologies, traitements et évolution ont été recueillies à partir des dossiers médicaux et analysées de manière descriptive.

Résultats :

Au total, 267 cas confirmés de MTEV ont été identifiés, correspondant à une prévalence hospitalière de 4,47 %. Le nombre de cas a augmenté progressivement au cours de la période d'étude, avec un pic en 2025 (22,8 %). L'âge moyen était de $50,8 \pm 19,9$ ans (extrêmes : 16–92), avec une prédominance féminine (64,8 % ; sex-ratio : 0,54). Concernant la répartition anatomique, la TVP des membres inférieurs était la localisation la plus fréquente (45,5 %), suivie de l'EP (17,9 %) et de la thrombose veineuse cérébrale (14,1 %). La TVP isolée représentait 69,6 % des cas, l'EP isolée 21,5 % et l'association TVP + EP 8,8 %. Des localisations plus rares comprenaient les thromboses des membres supérieurs, splanchniques et autres sites inhabituels. Cliniquement, les manifestations les plus fréquentes étaient l'œdème, la chaleur et la rougeur d'un membre (33,1 %), la douleur d'un membre (17,7 %) et la dyspnée (9,6 %). Sur le plan étiologique, les principales causes étaient les MTEV idiopathiques (31 %), le cancer actif (17,2 %), l'immobilisation, la chirurgie ou le traumatisme (16,7 %), et la thrombophilie (14,3 %). Les femmes étaient plus exposées aux facteurs hormonaux et gravidopuerpéraux, tandis que les hommes présentaient plus souvent des formes liées au cancer ou idiopathiques. Une infection antérieure par la COVID-19 a été retrouvée dans 8,6 % des cas valides comme facteur prothrombotique. Les sujets jeunes étaient plus fréquemment concernés par la thrombophilie, la thrombose veineuse cérébrale et les causes hormonales, alors que les sujets âgés présentaient surtout des MTEV liées au cancer et aux facteurs acquis transitoires. Sur le plan thérapeutique, le traitement initial reposait principalement sur les héparines de bas poids moléculaire (85,8 %). Le traitement d'entretien était dominé par les antivitamines K (53,5 %), suivis des anticoagulants oraux directs (21,4 %). L'évolution clinique était favorable chez 88,8 % des patients. Le taux de complications intrahospitalières était de 9,7 %, tandis que la mortalité atteignait 7,1 %, avec les taux les plus élevés observés dans les MTEV associées au cancer.

Conclusion :

La MTEV est une affection fréquente et hétérogène en pratique de médecine interne à l'hôpital mixte de Laghouat, touchant principalement les femmes et les adultes d'âge moyen. La TVP des membres inférieurs demeure la présentation la plus fréquente, tandis que TVC et la thrombophilie étaient particulièrement notables chez les sujets jeunes. Les formes idiopathiques restent fréquentes, alors que le cancer constitue le principal facteur de mauvais pronostic. Les HBPM et les AVK demeurent la base du traitement, tandis que

l'utilisation des AOD progresse mais reste limitée. Le renforcement de la prévention, du diagnostic précoce, du dépistage ciblé de la thrombophilie et un meilleur accès aux anticoagulants modernes pourraient améliorer le pronostic.

Mots-clés : Maladie thromboembolique veineuse; thrombose veineuse profonde; embolie pulmonaire; thrombose veineuse cérébrale; thrombophilie; épidémiologie; facteurs de risque; anticoagulation; Algérie.

ملخص

المقدمة:

يعد مرض الانصمام الخثاري الوريدي، والذي يشمل خثار الأوردة العميقة والانصمام الرئوي، حالة طبية شائعة ومهددة للحياة، ترتبط بمعدلات اعتلال ووفيات مرتفعة، وتُشكل عبئاً كبيراً على نظام الرعاية الصحية. وفي الجزائر، ولا سيما في المناطق الجنوبية، لا تزال البيانات الوبائية والمتعلقة بكيفية التعامل مع هذا المرض محدودة.

الهدف:

تقييم معدل الانتشار الاستشفائي للانصمام الخثاري الوريدي في قسم الطب الباطني بالمستشفى المختلط بالأغواط، ووصف خصائصه الوبائية، العوامل المسببة، المظاهر السريرية، الإدارة العلاجية، والنتائج الاستشفائية على مدى فترة خمس سنوات (من 1 جانفي 2021 إلى 31 ديسمبر 2025).

المنهجية والأدوات:

أُجريت هذه الدراسة الوصفية الاستيعادية على مدار خمس سنوات. من بين 5,968 حالة استشفاء مسجلة في قسم الطب الباطني، شملت الدراسة جميع المرضى الذين تأكدت إصابتهم بالانصمام الخثاري الوريدي سريرياً، وبيولوجياً، وعبر التصوير الطبي. جُمعت البيانات الديموغرافية، عوامل الخطر، موقع الإصابة، والبيانات السريرية، المسببة، العلاجية، والنتائج من السجلات الطبية وتم تحليلها وصفيًا.

النتائج:

تم تحديد 267 حالة مؤكدة من الانصمام الخثاري الوريدي، وهو ما يعادل انتشاراً استشفائياً بنسبة 4.47%. وقد تزايدت الحالات تدريجياً خلال فترة الدراسة، حيث سُجل أعلى عدد في عام 2025 (22.8%). بلغ متوسط العمر 50.8 ± 19.9 سنة (يتراوح بين 16 و92 سنة)، مع غلبة واضحة للإناث (64.8%؛ نسبة الجنس: 0.54). من حيث التوزيع التشريحي، كان خثار الأوردة العميقة في الأطراف السفلية هو الموقع الأكثر شيوعاً (45.5%)، يليه الانصمام الرئوي (17.9%) ثم خثار الجيوب الوريدية الدماغية (14.1%). مثل خثار الأوردة العميقة المنعزل نسبة 69.6%، والانصمام الرئوي المنعزل 21.5%، بينما اجتمع كلاهما في 8.8% من الحالات. ومن بين المسببات الرئيسية: الحالات مجهولة السبب (31%)، السرطانات النشطة (17.2%)، العجز عن الحركة أو الجراحة أو الصدمات (16.7%)، واعتلالات التخثر بنسبة 14.3%. كما تم رصد كوفيد-19 كعامل خطر محفز للتخثر في 8.6% من الحالات. علاجياً، اعتمد العلاج الأولي بشكل أساسي على الهيبارين منخفض الوزن الجزيئي بنسبة 85.8%. أما العلاج الوقائي المستمر، فقد سادت فيه مضادات فيتامين ك بنسبة 53.5%، تليها مضادات التخثر الفموية المباشرة بنسبة 21.4%. كانت التطورات السريرية مواتية لـ 88.8% من المرضى، بينما بلغ معدل الوفيات 7.1%، وكانت أعلى المعدلات مرتبطة بالمرضى المصابين بالسرطان.

الخلاصة:

يعتبر الانصمام الخثاري الوريدي حالة متكررة وغير متجانسة في ممارسة الطب الباطني بالمستشفى المختلط بالأغواط، حيث تؤثر بشكل رئيسي على النساء والبالغين في منتصف العمر. لا يزال خثار الأوردة العميقة في الأطراف السفلية هو العرض الأكثر شيوعاً، مع ملاحظة بروز خثار الجيوب الوريدية الدماغية واعتلالات التخثر لدى الفئات الشابة. إن تعزيز الوقاية، والتشخيص المبكر، وتوسيع نطاق الوصول إلى استراتيجيات التخثر الحديثة أمر ضروري لتحسين النتائج العلاجية.

الكلمات المفتاحية: الانصمام الخثاري الوريدي؛ خثار الأوردة العميقة؛ الانصمام الرئوي؛ خثار الأوردة الدماغية؛ اعتلال التخثر؛ الوبائيات؛ عوامل الخطر؛ مضادات التخثر؛ الجزائر.

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Abbreviations List

ACS: Acute Coronary Syndrome
ADP: Adenosine Diphosphate
aPL: Antiphospholipid antibodies
aPLS: Antiphospholipid Syndrome
aPTT: Activated Partial Thromboplastin Time
AT: Antithrombin
BCS: Budd–Chiari Syndrome
BMI: Body Mass Index
BNP: B-type Natriuretic Peptide
BRVO: Branch Retinal Vein Occlusion
CBC: Complete Blood Count
CHU: Centre Hospitalier Universitaire (University Hospital Center)
CNAMTS: French National Health Insurance Fund for Salaried Workers
COPD: Chronic Obstructive Pulmonary Disease
CRVO: Central Retinal Vein Occlusion
CTEPH: Chronic Thromboembolic Pulmonary Hypertension
CTPA: Computed Tomography Pulmonary Angiography
CTV: CT Venography
CVI: Chronic Venous Insufficiency
CVS: Cerebral Venous System
CVT: Cerebral Venous Thrombosis
DOACs: Direct Oral Anticoagulants
DVS: Deep Venous System
DVT: Deep Vein Thrombosis
ECG: Electrocardiogram
EJV: External Jugular Vein
ENT / ORL: Ear, Nose and Throat (Otorhinolaryngology)
FiO₂: Fraction of Inspired Oxygen
GP IIb/IIIa: Glycoprotein IIb/IIIa
HCC: Hepatocellular Carcinoma
HRT: Hormone Replacement Therapy
ICH: Intracranial Hypertension
IJV: Internal Jugular Vein
INR: International Normalized Ratio
IVC: Inferior Vena Cava
JAK2: Janus Kinase 2 mutation
JVT: Jugular Vein Thrombosis
LMWH: Low Molecular Weight Heparin
MI: Myocardial Infarction
MRI: Magnetic Resonance Imaging
MRV: MR Venography
mmHg: Millimeters of Mercury
NETs: Neutrophil Extracellular Traps
NO: Nitric Oxide
NT-proBNP: N-terminal pro-B-type Natriuretic Peptide

PaO₂: Partial Pressure of Arterial Oxygen
PAI-1: Plasminogen Activator Inhibitor-1
PE: Pulmonary Embolism
PERC: Pulmonary Embolism Rule-out Criteria
PESI: Pulmonary Embolism Severity Index
PLTs: Platelets
PNH: Paroxysmal Nocturnal Hemoglobinuria
PoVT / PVT: Portal Vein Thrombosis
PTS: Post-thrombotic Syndrome
PT: Prothrombin Time
PVR: Pulmonary Vascular Resistance
RV: Right Ventricle
SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus 2
SCVC: Superficial Collateral Venous Circulation
SOS: Sinusoidal Obstruction Syndrome
sPESI: Simplified Pulmonary Embolism Severity Index
SpVT: Splanchnic Vein Thrombosis
SVS: Superficial Venous System
SVC: Superior Vena Cava
SVT: Superficial Vein Thrombosis
t-PA: Tissue Plasminogen Activator
TF: Tissue Factor
TFPI: Tissue Factor Pathway Inhibitor
TIPS: Transjugular Intrahepatic Portosystemic Shunt
TXA₂: Thromboxane A₂
UEDVT: Upper Extremity Deep Vein Thrombosis
UFH: Unfractionated Heparin
ULL: Unilateral Lower Limb
US-VTE: Unusual-Site Venous Thromboembolism
u-PA: Urokinase-type Plasminogen Activator
VA/Q: Ventilation/Perfusion Ratio
VDU: Venous Duplex Ultrasonography
VITT: Vaccine-induced Immune Thrombocytopenia and Thrombosis
VKAs: Vitamin K Antagonists
VTE: Venous Thromboembolism
vWF: von Willebrand Factor

I . INTRODUCTION

Venous thromboembolic disease (VTE) currently represents a major public health challenge because of its high incidence, substantial morbidity and mortality, and the wide spectrum of its clinical presentations. It primarily encompasses deep vein thrombosis (DVT) and pulmonary embolism (PE), and constitutes the third most common cardiovascular disease after myocardial infarction and stroke. Its annual incidence is estimated at 1 to 2 cases per 1,000 inhabitants in the general population, with a progressive increase according to age and associated comorbidities (1). Among hospitalized patients, VTE remains one of the leading preventable causes of in-hospital mortality, mainly due to diagnostic challenges and delays in therapeutic management.

The pathophysiology of this condition is classically based on Virchow's triad, which combines venous stasis, endothelial injury, and hypercoagulability (2). Numerous acquired and inherited risk factors are involved in the occurrence of thromboembolic events, including prolonged immobilization, surgery, malignancies, inflammatory diseases, pregnancy, hormonal contraceptives, and inherited or acquired thrombophilia. Certain systemic diseases, such as Behçet's disease and antiphospholipid syndrome, are particularly associated with recurrent or atypical thrombotic forms frequently encountered in internal medicine practice.

The clinical presentation of thromboembolic events is highly heterogeneous, ranging from asymptomatic forms to severe life-threatening conditions. Lower-limb DVT represents the most common localization, whereas PE remains its most feared manifestation owing to the risk of acute hemodynamic failure and sudden death. However, VTE disease is not limited to these classical forms. Unusual-site venous thromboses including cerebral venous thrombosis, portal vein thrombosis, Budd–Chiari syndrome, jugular vein thrombosis, and upper-extremity venous thrombosis represent rarer but increasingly recognized entities in clinical practice (3). Their diagnosis often remains challenging because of their polymorphic clinical manifestations and the absence of specific symptoms.

The diagnosis of VTE currently relies on an approach combining clinical probability assessment, laboratory investigations, and medical imaging. Venous Doppler ultrasonography remains the investigation of choice for the diagnosis of peripheral venous thrombosis, while computed tomography pulmonary angiography plays a central role in confirming PE. Other techniques, such as magnetic resonance venography and thrombophilia workup, may be required in atypical localizations or complex clinical situations (4). Early management is essential to prevent both short- and long-term complications, particularly post-thrombotic syndrome, chronic thromboembolic pulmonary hypertension, neurological sequelae, and thromboembolic recurrence.

From a therapeutic perspective, major advances have been achieved through the development of anticoagulant therapies, leading to significant improvement in the prognosis of patients with VTE. Low-molecular-weight heparins and vitamin K antagonists long represented the cornerstone of treatment before the advent of direct oral anticoagulants, which have profoundly modified therapeutic strategies by simplifying patient management and follow-up (5). Nevertheless, therapeutic management remains complex in particular situations, especially unusual-site thrombosis, recurrent thromboembolic events, cancer-associated thrombosis, and patients at high bleeding risk.

Despite the major clinical burden associated with VTE disease, epidemiological data on VTE in Algeria remain scarce, particularly in the southern regions of the country (6). The currently available studies have predominantly focused on the conventional presentations of DVT and PE, while thromboses occurring at unusual venous sites remain insufficiently explored. To the best of our knowledge, no previous study conducted in the wilaya of Laghouat has comprehensively assessed the entire spectrum of VTE disease within an internal medicine department. This paucity of regional data underscores the need for local epidemiological investigations in order to better define the epidemiological, clinical, and etiological characteristics of VTE in our population and to improve understanding of its specific features in our clinical setting.

This dissertation aims to investigate VTE disease within the Internal Medicine Department of the Mixed Hospital of Laghouat through the analysis of clinical, biological, radiological, and therapeutic data collected over a five-year period extending from January 1st, 2021 to December 31st, 2025. The objectives of this study are to determine the hospital prevalence of VTE, identify the principal associated risk factors, characterize the various thrombotic localizations and their underlying etiologies, and evaluate therapeutic management, clinical outcomes, and complications encountered in our practice.

II . LITERATURE REVIEW

Chapter 1:
**General Considerations on Venous
Thromboembolism (VTE)**

1. General Considerations on Venous Thromboembolism (VTE):

1.1. Definition and Fundamentals of VTE:

1.1.1. Definition of Venous Thromboembolism:

Venous thromboembolism (VTE) is a common condition that primarily includes deep vein thrombosis (DVT) and pulmonary embolism (PE) (4,7). It is characterized by the formation of a thrombus within the venous system (8). From a histological perspective, the venous thrombus is mainly composed of fibrin, in which formed blood elements «particularly red blood cells» are trapped, forming what is referred to as a “red” or fibrin-rich thrombus (10).

VTE can involve various anatomical sites. The most frequent are deep vein thromboses of the lower limbs (1). However, other locations may also be affected, including upper limb thromboses and thromboses in unusual sites such as the vena cava, subclavian or axillary veins, hepatic veins (Budd–Chiari syndrome), the portal vein, mesenteric or splenic veins, as well as cerebral, retinal, renal, adrenal, or ovarian veins (8,9).

PE is a diagnostic and therapeutic emergency, defined as the sudden partial or complete obstruction of a pulmonary artery or one of its branches by a thrombus, most often originating from deep veins (4,7). This thrombus typically migrates from the veins of the lower limbs, and less frequently from the upper limbs or the right heart chambers (7). PE may lead to obstruction of the pulmonary circulation, resulting in potentially severe hemodynamic and respiratory consequences, which can progress to pulmonary infarction (4,9).

1.1.2. Historical Background and Evolution of the Concept of VTE:

The concept of VTE was primarily established in the 19th century through the work of Rudolf Virchow. In 1856, he described the three main mechanisms involved in thrombus formation « venous stasis, endothelial injury, and hypercoagulability » thus defining the “Virchow’s triad,” which remains the cornerstone of the pathophysiological understanding of venous thrombosis (11).

Subsequently, Armand Trousseau highlighted the association between thrombosis and cancer, describing migratory thrombophlebitis that may reveal an underlying malignancy, now known as Trousseau syndrome (12).

These major contributions laid the foundations for the pathophysiological and clinical understanding of VTE, which have since been further developed through advances in modern diagnostic and therapeutic approaches.

1.1.3. Place of Venous Thromboembolism (VTE) Among Cardiovascular Diseases:

At the global level, VTE is the third most common acute cardiovascular syndrome, after myocardial infarction (MI) and stroke (4). Its annual incidence is approximately 1 per 1,000 individuals in the general middle-aged population, rising to nearly 1% per year in individuals over 90 years of age.

Approximately 50% of all VTE cases occur following a current or recent hospitalization for surgery or an acute medical illness (13), making it the leading preventable cause of death in hospitalized patients (14). The 30-day mortality rate is estimated at 4.6% for DVT and 9.7% for PE (15).

1.2. Epidemiology of Venous Thromboembolism (VTE):

1.2.1. Incidence and Prevalence:

- **Global annual incidence:**

VTE represents a major public health issue worldwide. The annual incidence in Western countries is estimated at 104 to 183 cases per 100,000 individuals, comparable to that of stroke. In the general population, the overall incidence is approximately 1 to 2 cases per 1,000 inhabitants per year, with about two-thirds corresponding to DVT and one-third to PE.

The specific incidence ranges from 29 to 78 cases per 100,000 individuals for PE (with or without DVT) and from 45 to 117 cases per 100,000 individuals for DVT alone. According to estimates, VTE accounts for more than 500,000 deaths annually in the United States and the European Union combined (total population ≈ 800 million) (16).

- **Recurrence rate of VTE:**

The risk of recurrence depends on the time elapsed since the first episode. It is highest between 6 and 12 months, then gradually decreases: approximately 20 cases per 1,000 individuals at 1 year, 10 at 2 years, 6 at 5 years, and 5 at 10 years.

Extended anticoagulant therapy after the acute phase of an unprovoked VTE significantly reduces this risk. Direct oral anticoagulants (DOACs) at reduced doses have demonstrated efficacy with a favorable benefit–risk profile (16).

A retrospective study based on data from the French National Health Insurance Fund for Salaried Workers (CNAMTS), covering 77% of the French population, reported a VTE recurrence rate of 5.5% within one year of follow-up (17).

- **Mortality associated with VTE:**

PE is the third leading cause of death, after cardiovascular diseases and cancer (18,19), with fewer than 300,000 deaths per year in the United States.

In six European countries totaling 454.4 million inhabitants, more than 370,000 VTE-related deaths were estimated in 2004. Among these patients, 34% died suddenly or within hours of the acute event, before treatment could be initiated. In 59% of cases, death was attributed to an acute PE diagnosed post-mortem, while only 7% of patients had received a correct diagnosis before death (4).

1.2.2. Geographic Distribution:

The incidence of VTE varies across populations and geographic regions. It is higher among Black populations and lower among Asian, Asian American, and Native American populations (20).

- **Europe and North America:**

In the United States, the annual incidence is estimated at 300,000 to 600,000 cases per year and increases with age, ranging from 0.1 per 1,000 in men aged 20–39 years to 8.9 per 1,000 after the age of 75 (21,22).

In France, the incidence of VTE is approximately 1.83 per 1,000 per year, including 1.24 per 1,000 per year for DVT and 0.60 per 1,000 per year for PE, with an associated mortality rate of 5–10% (16). Each year, nearly 35,000 patients are hospitalized for PE, with an overall in-hospital mortality rate of 5% (23,24).

- **Asia:**

In Korea, Taiwan, and Hong Kong, the annual incidence rates of VTE are 13.8, 15.9, and 19.9 per 100,000 inhabitants, respectively, representing 15–20% of the rates observed in Western countries (≈100 per 100,000). Reported incidence has increased over time, highlighting the need for greater awareness of this condition.

Hospital-based studies from China, Hong Kong, India, Japan, Korea, and Singapore report incidence rates as

follows: **DVT:** 11 to 65 per 10,000 hospitalized patients, **PE:** 2.5 to 23 per 10,000, **Overall VTE:** 11 to 88 per 10,000. In Singapore, the hospital prevalence of DVT increased from 16 cases per 10,000 admissions (1996–1997) to 65 per 10,000 (2006). (25)

- **Sub-Saharan Africa:**

VTE represents a significant public health concern, with hospital prevalence rates ranging from 2.7% to 9.12%, depending on the country: Senegal: 2.78%, Cameroon: 1.6% (for DVT), Mali (Bamako University Hospital, cardiology, 2015): 4.02%, and (internal medicine, 2017–2018): 4.76% for VTE.

Pulmonary embolism accounted for 8% of hospitalizations at CHU Luxembourg (2017–2022). (26)

- **Maghreb countries and Algeria:**

In Algeria, VTE appears to be increasing steadily. However, its true incidence remains poorly defined due to the lack of published epidemiological studies assessing its frequency and associated thrombotic risk factors (23). Available data are mainly derived from academic theses, providing indirect estimates:

8% of hospital admissions in the internal medicine department of the Central Military Hospital (Sadouki study) (27). 6% of hospital admissions in internal medicine departments in the Algiers region (Ayoub study) (28). In Maghreb countries, VTE tends to affect relatively young patients (20–30 years), with a female predominance (29).

1.2.3. Incidence According to Anatomical Location:

- **Deep Vein Thrombosis (DVT):**

The incidence of DVT is estimated at 53 to 162 cases per 100,000 inhabitants, increasing with age (4). For symptomatic lower-limb DVT, the incidence ranges from 45 to 117 cases per 100,000 persons per year. One study reported a median age at diagnosis of 62 years, a sex ratio close to 1, and a left-sided predominance in 57% of cases (30).

- **Pulmonary Embolism (PE):**

The annual incidence of PE ranges from 39 to 115 cases per 100,000 inhabitants (4), with a high mortality estimated at 60,000–100,000 deaths per year in the United States (31). In France, approximately 48,000 patients are hospitalized each year for PE, corresponding to more than 60 cases per 100,000 inhabitants, with a continuously increasing trend. This rise in incidence is explained by population aging and improvements in diagnostic techniques, particularly computed tomography pulmonary angiography (CTPA), which allows the detection of previously unrecognized distal emboli (32).

- **Other venous locations:**

The epidemiology of unusual-site venous thromboembolism (US-VTE) is characterized by its rarity and specific patient profiles. These account for only 5–10% of all VTE cases.

- ◆ **Cerebral venous thrombosis (CVT):**

The incidence is estimated at 1–2 cases per 100,000 inhabitants per year. It can occur at any age, with a peak incidence during the third decade of life. A female predominance is currently observed, with a female-to-male ratio ranging from 1.5 to 5 (33).

- ◆ **Upper extremity deep vein thrombosis (UEDVT):**

Represents 4–10% of all DVT cases, with an annual incidence of 0.4 to 1 case per 10,000 persons. Its incidence is increasing due to the growing use of central venous catheters and implantable devices (34,35).

- ◆ **Jugular vein thrombosis (JVT):**

JVT is a rare form of VTE, often secondary to central venous catheterization (with an incidence of 7.5% to 16.9% in such patients) or cancer. It mainly occurs in intensive care settings, and its frequency is increasing with the use of intravascular devices (36).

- ◆ **Splanchnic vein thrombosis (SVT):**

These are among the most frequent unusual-site VTEs (portal vein, mesenteric veins, splenic veins, Budd–

Chiari syndrome). Their incidence is estimated at 4–15 per 100,000 inhabitants per year, approximately 25 times lower than that of usual-site VTE. Portal vein thrombosis is the most common, often incidental, followed by mesenteric vein thrombosis, while Budd–Chiari syndrome remains rare but with improved prognosis. These conditions are associated with significant morbidity and mortality, with an in-hospital mortality of approximately 13% (37,38).

- ◆ **Superficial vein thrombosis (SVT):**

Located in superficial veins of the limbs, its incidence ranges from 64 to 131 per 100,000 per year, with a risk of progression to DVT or PE of about 10% (40).

- ◆ **Other rare and specific localizations.**

1.2.4. Distribution by Age and Sex:

The incidence of VTE increases significantly with age. It is approximately eight times higher in individuals over 80 years old compared to those aged 50–59 years (4). In the United States, it rises from 143 cases per 100,000 inhabitants among individuals aged 40–49 years to 1,134 cases per 100,000 among those aged 80 years and older (20).

In children, VTE remains rare, with an estimated incidence of 1.4 to 4.9 cases per 100,000 inhabitants, but it is higher in hospitalized settings (53 to 57 cases per 100,000) (4).

The relationship between VTE and sex varies with age. Before the age of 55, the incidence is higher in women, particularly due to hormonal factors. After 60 years, it becomes more frequent in men, and then increases again in women after the age of 80, likely due to their longer life expectancy (20).

1.2.5. Medical and Economic Impact:

VTE represents a major public health issue due to its significant impact on morbidity, mortality, and healthcare costs (23). The incidence of pulmonary embolism has increased over time, with an estimated multiplication factor ranging from 4 to 7 (30). In Europe, VTE is responsible for approximately 370,000 deaths per year across six major countries, and up to more than 500,000 deaths annually across the European Union (40).

From an economic perspective, the total annual cost of VTE is estimated between €1.5 and €13.2 billion in Europe (4,30). In the United States, VTE-related medical costs are estimated between \$6.7 and \$9.8 billion, with an average cost of approximately \$15,000 per case (33).

These costs include expenses related to hospitalization, treatment, and follow-up, as well as those associated with long-term complications, particularly recurrences, post-thrombotic syndrome, and chronic thromboembolic pulmonary hypertension. Thus, VTE represents a growing burden on healthcare systems, especially in the context of an aging population, highlighting the importance of prevention strategies and early management (4,30).

1.3. Anatomical Overview of the Venous Vascular System:

(APPENDIX 01)(APPENDIX 02)

1.3.1. General Organization of the Venous System:

The vascular system comprises three main components: the arterial, venous, and lymphatic systems, which are responsible for blood circulation, venous return, and the maintenance of fluid homeostasis, respectively.

The venous system is a capacitance network containing approximately two-thirds of the total blood volume and ensuring the return of blood to the heart. It includes systemic components (peripheral and central veins), the portal system (hepatic portal circulation), and cerebral components (dural venous sinuses).

It is a low-pressure system in which venous return is facilitated by the presence of venous valves that prevent backflow, as well as by the action of the muscle pump, particularly in the lower limbs. Veins are also characterized by thinner walls than arteries, composed of three layers: the intima, media, and adventitia (41) (Figure 1).

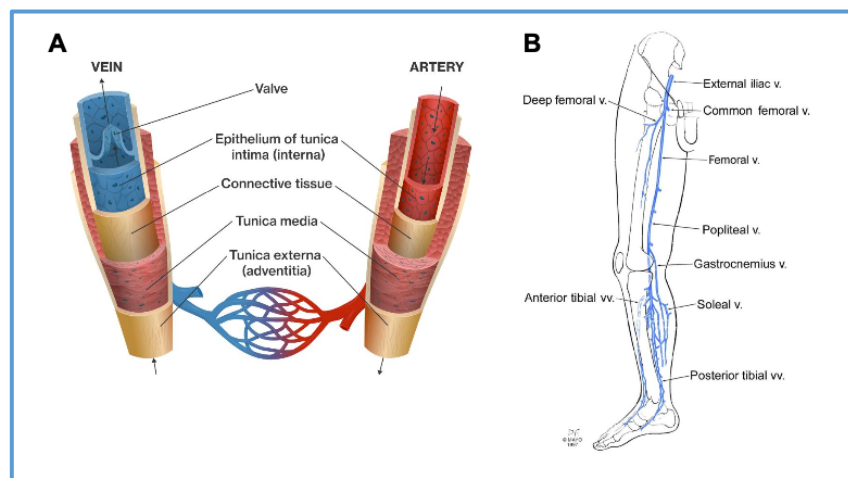


Figure n°1 : General organization of the venous system.

1.3.2. Structure of the Venous Wall:

Blood vessels ensure the transport of blood between the heart and organs. Their wall is composed of three layers: the intima, media, and adventitia, whose organization determines their mechanical and functional properties.

Veins have a structure similar to that of arteries but with a thinner wall and less smooth muscle tissue, which gives them high compliance and allows them to function as a blood reservoir.

- **The intima**, the inner layer, consists of a monolayer of endothelial cells resting on a basement membrane. It plays a key role in vascular homeostasis and the regulation of coagulation.
- **The media** is composed of smooth muscle cells associated with elastic fibers and collagen, contributing to the elastic properties and strength of the vessel wall.
- **The adventitia**, the outer layer, is made of connective tissue rich in collagen and fibroblasts, providing structural support and protection to the vessel (30).

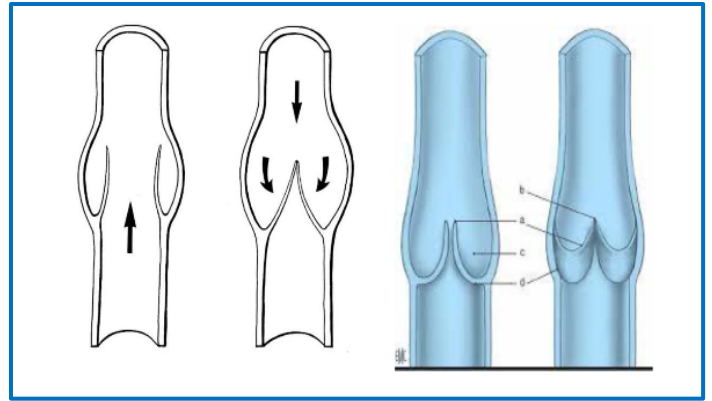
1.3.3. Venous Valves:

Venous valves are bicuspid, unidirectional structures that prevent blood reflux and ensure venous return toward the heart. They are formed by folds of the intima creating two cusps that delimit a valvular sinus.

Their function is passive and depends on pressure variations: they open during forward (antegrade) flow and close in case of reflux, with an activity of approximately 20 cycles per minute in the standing position. Valve dysfunction promotes venous stasis and contributes to thrombus formation, as part of Virchow's triad (26).

Figure n°2 : Venous valve anatomy.

- (a) free edge of the valve (cusp)
- (b) valvular commissure
- (c) valvular sinus
- (d) insertion of the valve into the venous wall



1.3.4. Differences Between Veins and Arteries:

Although veins and arteries share a similar histological structure composed of three layers, they differ in their functional and mechanical properties.

Veins are low-pressure vessels (3–20 mmHg) with thinner and more distensible walls, a less developed media, and a predominant adventitia. They have a larger lumen and contain approximately two-thirds of the total blood volume. In contrast, arteries are exposed to high, pulsatile pressure (80–130 mmHg) and have thicker walls rich in smooth muscle and elastic fibers (30).

These differences explain the susceptibility of the venous system to blood stasis and thrombosis. (APPENDIX 03)

1.4. Physiological Aspects of Hemostasis:

1.4.1. Hemostatic Balance Under Physiological Conditions:

Hemostasis is a physiological process that maintains blood in a fluid state while ensuring the cessation of bleeding in the event of vascular injury. It relies on a dynamic balance between coagulation mechanisms and the fibrinolytic system. Following vascular damage, a sequence of cellular and biochemical events is triggered to ensure sealing of the lesion and control of hemorrhage.

Classically, hemostasis consists of three overlapping stages:

- **Primary hemostasis**, leading to the formation of a platelet plug (3 to 5 minutes);
- **Secondary hemostasis (coagulation)**, ensuring stabilization of the thrombus through fibrin formation (5 to 10 minutes);
- **Fibrinolysis**, allowing clot degradation after vascular repair (48 to 72 hours).

All these mechanisms are tightly regulated by systems of activators and inhibitors, ensuring that the process remains localized to the site of injury and preventing inappropriate activation of coagulation (42).

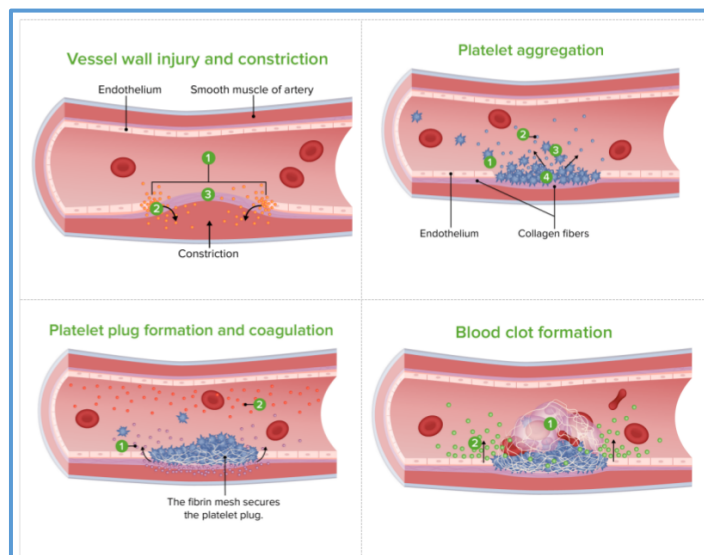


Figure n°3 : Stages of Hemostasis (From Vessel Injury to Blood Clot Formation).

1.4.2. Primary Hemostasis:

Primary hemostasis refers to the set of mechanisms that ensure the initial sealing of a vascular injury through the formation of a platelet thrombus, known as the “platelet plug.” It consists of two phases: a vascular phase and a platelet phase (42).

1. Key Components of Primary Hemostasis:

This phase involves four main elements: the vascular wall, platelets, von Willebrand factor, and fibrinogen.

1.1. The Vascular Wall:

The endothelium, located at the level of the intima, plays a crucial role in the regulation of hemostasis. Under normal conditions, it exhibits anticoagulant and anti-aggregatory properties.

In the event of injury, exposure of the subendothelium, rich in collagen, promotes platelet adhesion and initiates the hemostatic process.

1.2. Platelets (PLTs):

Platelets are anucleate blood elements derived from megakaryocytes, circulating at a concentration of 150 to $400 \times 10^9/L$. Their role is essential in primary hemostasis, where they ensure platelet adhesion, activation, and aggregation.

1.3. von Willebrand Factor (vWF):

von Willebrand factor is a glycoprotein synthesized by endothelial cells and megakaryocytes. It plays a key role in platelet adhesion to subendothelial collagen and facilitates platelet aggregation. It also serves as a carrier for factor VIII.

1.4. Fibrinogen:

Fibrinogen is a plasma protein synthesized by the liver. It contributes to platelet aggregation by forming bridges between activated platelets, thereby participating in the formation of the platelet plug.

2. Mechanism of Primary Hemostasis:

Following vascular injury, primary hemostasis relies on interactions between the vascular wall, platelets, and various mediators. It comprises two main stages:

2.1. Vascular Phase:

In the event of vascular injury, an immediate reflex vasoconstriction occurs, reducing local blood flow. This vasoconstriction is reinforced by the release of platelet mediators, notably serotonin and thromboxane A_2 (TXA₂).

In contrast, the intact endothelium secretes vasodilatory and anti-aggregatory substances such as nitric oxide (NO) and prostacyclin, contributing to the regulation of hemostasis.

2.2. Platelet Phase:

The platelet phase includes three successive steps:

a. Platelet adhesion:

Following endothelial injury, platelets adhere to the exposed subendothelium, rich in collagen, via von Willebrand factor and platelet receptors.

b. Platelet activation:

Activated platelets undergo a shape change and release the contents of their granules (ADP, serotonin, fibrinogen), promoting amplification of the platelet response. They also express procoagulant phospholipids on their surface, facilitating coagulation.

c. Platelet aggregation:

Aggregation corresponds to the adhesion between activated platelets, mediated by fibrinogen linking platelet receptors (GP IIb/IIIa), leading to the formation of the platelet plug.

These steps occur simultaneously in vivo and allow the rapid formation of a platelet thrombus at the site of injury.

3. Assessment of Primary Hemostasis:

The evaluation of primary hemostasis mainly relies on platelet count, with normal values ranging between 150 and $400 \times 10^9/L$.

1.4.3. Secondary Hemostasis (Coagulation):

Coagulation refers to the set of biological reactions leading to the formation of fibrin, which stabilizes the platelet clot.

Fibrin results from the cleavage of fibrinogen by thrombin, the key enzyme in coagulation. (42)

1. Key Components of Coagulation:

1.1. Cellular Components:

Tissue factor (TF) is a membrane protein expressed by subendothelial cells. It is the main initiator of coagulation in the event of vascular injury, by coming into contact with circulating factor VII.

Under certain pathological conditions, its expression may be increased in endothelial cells, leukocytes, and platelets.

1.2. Non-cellular Components: (APPENDIX 04)

Coagulation involves a cascade of factors numbered in Roman numerals, circulating in an inactive form (zymogens) and activated sequentially.

Most of these factors are synthesized by the liver. Some are vitamin K-dependent, notably factors II, VII, IX, and X.

Activation of this cascade leads to thrombin generation, followed by the conversion of fibrinogen into fibrin, ensuring clot stabilization.

2. Mechanism of Coagulation:

Coagulation is based on an enzymatic cascade resulting in fibrin formation. It involves two activation pathways, intrinsic and extrinsic, which converge into a common pathway (Fig. 04).

- **Extrinsic pathway:** also called the exogenous pathway, it is triggered by exposure of tissue factor (TF) following vascular injury. TF binds to factor VII to form the TF–VIIa complex, which activates factor X.
- **Intrinsic pathway:** also called the endogenous pathway, it is initiated by activation of factor XII upon contact with subendothelial surfaces. It involves sequential activation of factors XII, XI, and IX. Activated factor IX, together with activated factor VIII, forms the tenase complex, which activates factor X.
- **Common pathway:** both pathways converge on the activation of factor X. Activated factor X, together with activated factor V, forms the prothrombinase complex, which converts prothrombin into thrombin. Thrombin plays a central role by converting fibrinogen into fibrin, thereby ensuring stabilization of the clot.

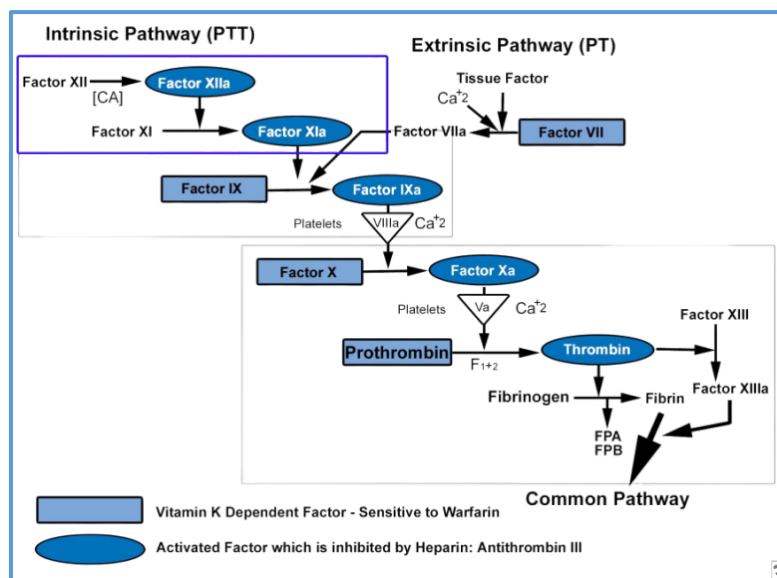


Figure n°4 : Coagulation Cascade: Intrinsic, Extrinsic, and Common Pathways.

3. Regulation of Coagulation (Inhibitors):

Coagulation is tightly regulated by several natural anticoagulant systems that limit clot extension and prevent excessive activation.

The main inhibitors are:

- ◆ **Antithrombin (AT):** the principal inhibitor of thrombin; it also neutralizes factors IXa, Xa, XIa, and XIIa. Its activity is markedly enhanced by heparin.
- ◆ **Tissue factor pathway inhibitor (TFPI):** produced by endothelial cells, it inhibits the tissue factor–factor VIIa complex, thereby regulating the extrinsic pathway.
- ◆ **Protein C–Protein S system:** activated protein C, in the presence of its cofactor protein S, inactivates factors Va and VIIIa. These proteins are vitamin K–dependent.
- ◆ **Other inhibitors:** such as alpha-2 macroglobulin and alpha-1 antitrypsin, which play a complementary role in coagulation regulation.

4. Assessment of Coagulation:

Biological evaluation of coagulation relies on standard tests:

- **Prothrombin time (PT) / INR:** assesses the extrinsic and common pathways (factors II, V, VII, X, and fibrinogen). It is mainly used for monitoring vitamin K antagonist therapy.
- **Activated partial thromboplastin time (aPTT):** evaluates the intrinsic pathway (factors VIII, IX, XI, XII) as well as the common pathway. Prolongation may indicate a deficiency in coagulation factors.

1.4.4. Physiological Fibrinolysis:

Fibrinolysis is an enzymatic process that allows the degradation of the fibrin clot, thereby restoring vascular patency after repair. It relies on the action of plasmin, an enzyme generated from plasminogen activation. This system is essential for maintaining balance by limiting thrombus extension and preventing vascular occlusion.

1. Key Components of Fibrinolysis

1.1. Cellular Components:

Endothelial cells play a central role by producing both activators and inhibitors of fibrinolysis, particularly tissue plasminogen activator (t-PA) and plasminogen activator inhibitor-1 (PAI-1).

1.2. Plasma Components:

Plasmin is the key enzyme of fibrinolysis. It is derived from plasminogen, mainly synthesized by the liver, and is responsible for fibrin degradation.

2. Regulation of Fibrinolysis:

Fibrinolysis is regulated by a balance between activators and inhibitors:

2.1. Activators of Fibrinolysis:

t-PA (tissue plasminogen activator): the main activator, produced by the endothelium.

u-PA (urokinase): plays a secondary role in physiological fibrinolysis.

2.2. Inhibitors of Fibrinolysis:

PAI-1: inhibits t-PA and is the principal regulator of fibrinolysis.

α 2-antiplasmin: directly inhibits plasmin. (42)

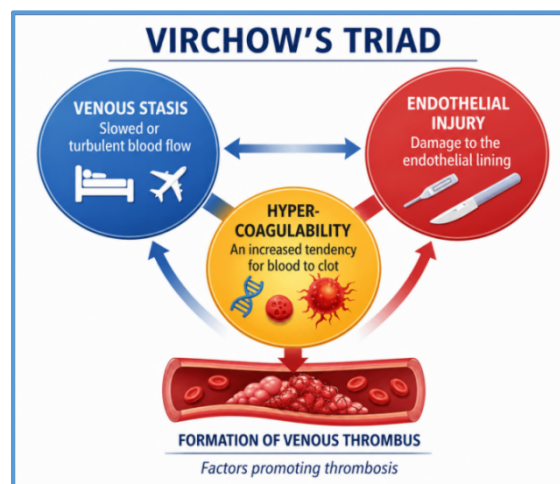


Figure n°5 : Virchow's Triad and the Pathogenesis of Venous Thrombosis.

1.5. Pathophysiology of Venous Thromboembolism (VTE):

1.5.1. Virchow's Triad:

VTE results from a disruption of the physiological balance between coagulation and fibrinolysis. Its pathophysiology is classically based on Virchow's triad, which includes venous stasis, hypercoagulability, and endothelial injury. Although Virchow greatly contributed to the study of thrombosis, this triad was formalized later and is now considered a fundamental model of venous thrombogenesis (4).

1. Venous Stasis:

Venous stasis refers to the slowing or cessation of blood flow within the veins, promoting the local accumulation of coagulation factors and reducing the activity of natural anticoagulants such as antithrombin and protein C. It mainly occurs during prolonged immobilization (bed rest, orthopedic surgery, fractures, long-distance travel), but also in patients with paralysis or chronic venous insufficiency (44).

Stasis leads to a reduction in laminar flow, facilitating interactions between blood cells and the vascular wall, thereby promoting thrombus formation. Venous thrombi preferentially develop in valve pockets of large veins, areas particularly prone to stasis, especially during prolonged immobilization (43).

2. Endothelial Injury:

Endothelial damage is a key component of Virchow's triad. Under physiological conditions, the endothelium has antithrombotic properties due to the production of mediators such as nitric oxide (NO) and prostacyclin. In response to injury, it becomes prothrombotic, with exposure of collagen and tissue factor, reduction of anticoagulant mechanisms, and activation of inflammation (22).

This activation is associated with increased expression of adhesion molecules (P-selectin, von Willebrand factor), promoting the recruitment of leukocytes and platelets, as well as the assembly of coagulation complexes on the endothelial surface. Stasis and associated hypoxia may further aggravate endothelial dysfunction by reducing natural anticoagulant properties (43).

The main causes include trauma, surgical procedures, venous catheters, infections, inflammatory states, and cancer. These alterations favor local thrombus formation at sites of injury.

3. Hypercoagulability:

Hypercoagulability refers to an increased tendency of the blood to clot, related to abnormalities in plasma proteins and circulating cells. It results from an imbalance between procoagulant factors and natural anticoagulant mechanisms, leading to excessive activation of coagulation and thrombus formation.

It may be congenital, as in hereditary thrombophilias such as factor V Leiden mutation, prothrombin gene mutation (G20210A), or deficiencies in antithrombin, protein C, or protein S. It may also be acquired, particularly in cancer, pregnancy or postpartum, hormonal contraception, antiphospholipid syndrome, inflammatory states, or in conditions such as polycythemia, thrombocythemia, or dehydration (45,46).

Elevated levels of coagulation factors (factor V, VIII, fibrinogen) or increased thrombin generation contribute to this prothrombotic state. Hypercoagulability promotes VTE recurrence and explains thrombosis in unusual locations such as cerebral, splanchnic, or retinal territories (43).

In clinical practice, Virchow's triad highlights the often multifactorial nature of VTE. For example, a patient immobilized after a fracture may combine venous stasis and endothelial injury related to surgery, significantly increasing thrombotic risk. Understanding these mechanisms is essential for VTE prevention and management, which relies on early mobilization, anticoagulant prophylaxis, and correction of associated risk factors.

1.5.2. Formation and Evolution of the Thrombus:

Venous thrombi may evolve along several pathways: lysis, extension, embolic migration, or organization. Spontaneous lysis occurs mainly in distal, small, and recent thrombi, especially if the triggering factor resolves rapidly. It is uncommon in proximal thrombosis, even under anticoagulant therapy.

The thrombus may also progress, worsening the obstruction or extending to adjacent segments, a process

favored by thrombogenic factors and inadequate treatment. Extension may be proximal or distal, the latter being more frequently observed in severe occlusive forms and detectable by Doppler ultrasound.

Finally, embolic migration to the right heart and pulmonary arteries mainly complicates proximal thromboses. Its frequency remains low in distal thrombosis (40).

1.6. Classification of Venous Thromboembolic Disease:

1.6.1. According to Anatomical Location:

Type of thrombosis	Main location
Lower limb DVT	Iliofemoral veins (proximal), tibial and fibular veins (distal)
Pulmonary embolism (PE)	Pulmonary trunk, main, lobar, segmental, and subsegmental pulmonary arteries
Cerebral venous thrombosis (CVT)	Cerebral venous sinuses (superior sagittal, transverse, cavernous)
Superficial venous thrombosis (SVT)	Lower limbs (great and small saphenous veins)
Upper Limb DVT (UEDVT)	Axillary, subclavian, brachial, and digital veins
Cava thrombosis	Superior vena cava (SVC), inferior vena cava (IVC)
Splanchnic veins (SpVT)	Portal vein, hepatic veins (Budd–Chiari syndrome), mesenteric veins, splenic vein
Renal vein	Renal vein
Genital veins	Ovarian vein, uterine vein (often postpartum)
Penile vein	Mondor’s disease
Retinal vein occlusion	Central (CRVO), branch (BRVO)
Jugular vein	Often related to catheterization or infection (Lemierre syndrome)
Adrenal vein	Adrenal vein

Table n° 1: Classification of VTE according to Anatomical Location

1.6.2. According to Etiological Context

1. Provoked VTE:

These are thrombotic events associated with an identifiable triggering factor.

Examples include: Prolonged immobilization (bed rest, long-distance travel), recent surgery (orthopedic, abdominal), major trauma, central venous catheter, pregnancy or postpartum period, oral contraceptives or hormone replacement therapy.

2. Unprovoked VTE:

These are thrombotic events occurring without an obvious triggering factor. They are often associated with genetic or acquired predispositions such as: Hereditary thrombophilias (factor V Leiden, prothrombin gene mutation, etc.), Antithrombin, protein C, or protein S deficiency, Antiphospholipid syndrome.

They are associated with a higher risk of recurrence compared with provoked VTE.

3. Cancer-associated VTE:

This occurs in patients with active cancer or recent cancer (within the past 6 months). It is often multifactorial and related to: Tumor-derived procoagulant factors, Chemotherapy or hormonal therapy, Central venous catheters, Immobilization or concomitant infection.

This category requires high clinical vigilance due to a significantly increased risk of recurrence and complications.

Chapter 2:

Deep Vein Thrombosis (DVT)

2. Deep Vein Thrombosis (DVT):

2.1. Definitions:

Deep vein thrombosis (DVT) is defined as the formation of a thrombus within a deep vein, most commonly occurring in the lower limbs. It is one of the two major clinical manifestations of VTE, along with pulmonary embolism. Diagnosis is based on the objective demonstration of a thrombus using venous imaging techniques (8,47).

◆ Temporal classification:

Based on symptom duration, DVT can be classified as follows:

- Acute DVT: symptoms lasting less than 14 days;
- Subacute DVT: symptoms lasting 15 to 28 days;
- Chronic DVT: symptoms persisting for more than 28 days.

Recurrent DVT refers to the occurrence of a new thrombotic event after a prior episode, whether affecting a different venous territory or the same site following a period of clinical or radiological resolution.

◆ Anatomical classification:

From an anatomical perspective, DVT is classified according to the location of the thrombus:

- Distal DVT: confined to the deep veins of the calf (tibial, peroneal, and muscular veins);
- Femoro-popliteal DVT: involving the popliteal and femoral veins;
- Iliofemoral DVT: involving the iliac veins and/or the common femoral vein, and often associated with a higher risk of complications (48).

2.2. Risk Factors for DVT:

Risk factors for DVT can be broadly categorised as inherited or acquired. Inherited thrombophilic conditions include non-O blood group, factor V Leiden mutation, and deficiencies of antithrombin, protein C, or protein S.

Acquired risk factors are more prevalent and include malignancy, prolonged immobilisation, recent surgery, trauma, acute medical illness, infection, inflammatory disorders, pregnancy, long-distance travel, hormone therapy, and aPL syndrome.

In the absence of an identifiable provoking factor, DVT is classified as unprovoked.

2.3. Diagnosis of DVT:

2.3.1. Clinical Diagnosis:

Clinical examination should be thorough and systematic, with particular attention to the lower limbs, and should include assessment for signs suggestive of associated PE or alternative diagnoses.

Clinical presentation does not reliably reflect the anatomical location of the thrombus. Furthermore, the presence of SVT does not exclude concomitant deep venous involvement.

In most cases, lower limb DVT presents with recent-onset unilateral symptoms and signs. The clinical presentation typically combines functional symptoms and objective physical findings, with variable severity (49,50,51).

Functional Symptoms	Physical Signs
Spontaneous calf or thigh pain (52,53)	ULL oedema (52,53)
Sensation of limb heaviness or tightness	Increased calf or thigh circumference
Pain on walking or functional limitation (50)	Tenderness along the course of the affected vein
Recent onset of symptoms	Localised unilateral warmth (53)
Occasional general malaise	Skin erythema or cyanosis (53)
	Superficial collateral venous circulation (54,53)
	Reduced calf compressibility (50)

Table n°2: Main clinical features of DVT.

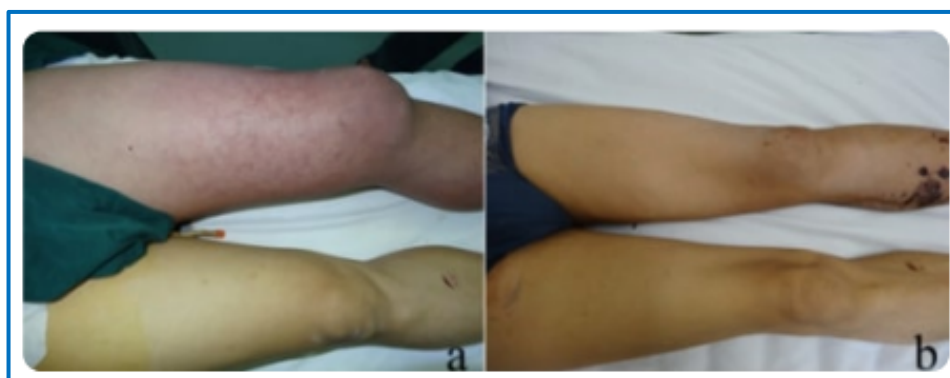


Figure n°6: Clinical comparison of unilateral lower limb swelling suggestive of DVT.

2.3.2. Clinical Probability Assessment:

The Wells score is the most widely used and validated clinical tool for estimating the pre-test probability of DVT. It is based on a set of clinical criteria that allow patients to be stratified into two categories:

Clinical Criteria	Points
Active cancer (ongoing treatment or within the last 6 months)	+1
Paralysis, immobilisation, or lower limb cast	+1
Bed rest $\geq$ 3 days or recent major surgery (< 12 weeks)	+1
Localised tenderness along the deep venous system	+1
Entire lower limb swelling	+1
Calf circumference increase > 3 cm compared to the asymptomatic side	+1
Unilateral pitting oedema	+1
Presence of superficial collateral venous circulation	+1
Previous documented DVT	+1
Alternative diagnosis at least as likely as DVT	-2

Table n°3 : Wells Score for Deep Vein Thrombosis (DVT).

- Low probability (score ≤ 2).
- High probability (score ≥ 3).

It is important to note that even with the lowest Wells score (-2), the prevalence of DVT remains approximately 5%, highlighting that the score alone cannot exclude the diagnosis.

2.3.3. Paraclinical Investigations:

The diagnosis of deep vein thrombosis (DVT) relies on objective diagnostic methods. First-line investigations combine plasma D-dimer testing with venous duplex ultrasonography, both of which play a central role in the diagnostic strategy (55).

1) D-dimer Testing:

D-dimers are fibrin degradation products that indicate ongoing thrombosis and fibrinolysis. They are highly sensitive (approximately 95–99%), making them particularly useful for ruling out DVT (56,57).

A level below 500 $\mu\text{g/L}$ excludes DVT in patients with low or intermediate clinical probability, whereas a positive result requires confirmation by venous ultrasonography. Their specificity remains limited, as levels may be elevated in various conditions such as ageing, inflammation, cancer, or pregnancy (56,47,58,59,60).

In patients over 50 years of age, an age-adjusted threshold ($\text{age} \times 10 \mu\text{g/L}$) improves diagnostic accuracy. D-dimer testing is not recommended in cases of high clinical probability, where imaging should be performed immediately (61).

◆ In clinical practice:

- Negative D-dimer: exclusion of DVT (if clinical probability is low or intermediate).
- Positive D-dimer: indication for venous duplex ultrasonography.
- Not indicated in cases of high clinical probability (immediate imaging required).

2) VDU of the Lower Limbs:

Venous duplex ultrasonography is the first-line reference imaging modality for the diagnosis of DVT, with sensitivity and specificity exceeding 95%. It provides both morphological and haemodynamic assessment of the venous system, primarily based on the evaluation of venous compressibility (56,61).

◆ Normal criteria (62):

- Compressible vein.
- Absence of intraluminal material.
- Doppler flow modulated by respiration.

◆ VDU signs of DVT:

- Major sign: venous incompressibility (56,61).
- Direct signs: visualisation of an intraluminal thrombus, often echogenic (61,60,63).
- Indirect signs: venous dilatation, venous stasis, Doppler flow abnormalities, decreased wall or valvular mobility (47,61).

The examination may also help guide the differential diagnosis (popliteal cyst, haematoma, muscle lesion (64)).

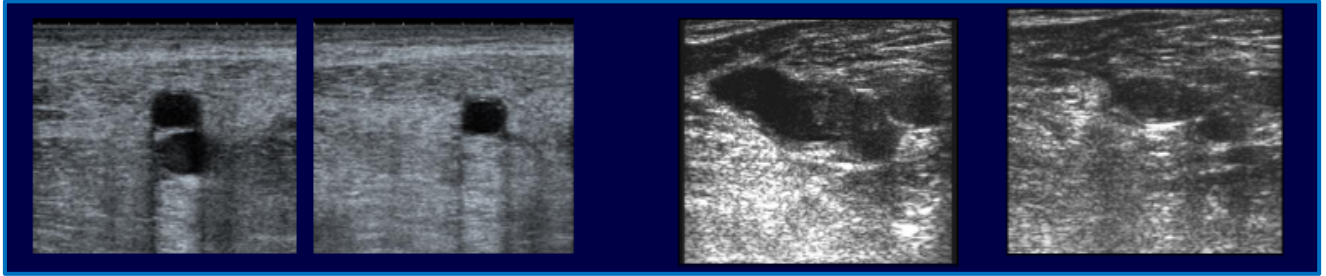


Figure n°7: Venous duplex ultrasonography of the lower limb demonstrating DVT, characterised by venous incompressibility and the presence of an intraluminal thrombus.

◆ **Exploration Strategies:**

- Proximal (limited) ultrasound: examines the common femoral and popliteal veins. If negative and clinical probability is low, DVT is excluded. If negative and clinical probability is high, repeat ultrasound after one week is required (65).
- Complete lower limb ultrasound: evaluates the entire venous system, including distal veins. A normal examination allows exclusion of DVT. Recommended in patients with likely clinical probability and positive D-dimers (65,66).

◆ **Limitations:**

Technical difficulties (oedema, body habitus, equipment), operator dependence, and difficulty in distinguishing recent from chronic thrombosis (61).

◆ **Alternative investigations:**

In cases where ultrasound is not feasible or non-diagnostic (e.g., cast, significant subcutaneous oedema):

- CT venography (66).
- MR venography (66,67).
- Direct MRI of the thrombus, particularly useful in ipsilateral recurrent DVT cases (65,66,68).

3) Other Complementary Investigations

Before initiating anticoagulant therapy, it is essential to evaluate:

- Renal function.
- Hepatic function.
- Haemostasis parameters (PT, aPTT).
- Platelet count.

2.4. Diagnostic Strategy:

The diagnostic approach to DVT is based on a sequential strategy integrating clinical probability assessment, D-dimer testing, and compression ultrasonography. This strategy helps avoid imaging in approximately one third of outpatients while maintaining high diagnostic safety.

1. Clinical probability

Clinical probability is estimated using the Wells score, which classifies patients into:

- DVT unlikely (≤ 2)
- DVT likely (> 2)

This score guides the diagnostic pathway but is not sufficient on its own to rule out DVT.

2. D-dimers

D-dimer testing is indicated in patients with low or intermediate clinical probability:

- Negative ($< 500 \mu\text{g/L}$): DVT excluded
- Positive: proceed to compression ultrasound
- In patients > 50 years, an age-adjusted threshold is used ($\text{age} \times 10$)
- D-dimer testing is not recommended in cases of high clinical probability

3. Compression ultrasonography

Compression ultrasound is the reference imaging test:

- Positive: DVT confirmed
- Negative + low probability: DVT excluded
- Negative + high probability: repeat ultrasound at day 5–7
- A complete whole-leg ultrasound can exclude DVT in all cases when normal

4. Special situations

- Cancer or hospitalised patients: direct imaging approach
- Elderly patients: age-adjusted D-dimer threshold

The entire diagnostic workup should ideally be completed within 24 hours of clinical presentation (65).

A schematic representation of the diagnostic and therapeutic algorithm for DVT is provided in APPENDIX 06.

2.5. Evolution and Complications:

2.5.1. Thrombus Resolution:

The resolution of deep vein thrombosis is a progressive and variable process, assessable during follow-up by Doppler ultrasonography. It is estimated at approximately 25% at one month, 50% at six months, and 60% at twenty-four months (69).

Resolution is generally slower in cases of proximal thrombosis, with thrombus persistence frequently observed at one year. Furthermore, resolution is less likely in the presence of an extensive thrombus or active malignancy (70).

2.5.2. Complications of DVT:

The complications of deep vein thrombosis may be acute or chronic and determine both short- and long-term prognosis (64,65)

◆ Pulmonary embolism (PE):

PE is the most serious acute complication of DVT. It results from the migration of a thrombus to the pulmonary circulation and may be life-threatening. DVT and PE represent two clinical manifestations of the same entity: VTE (64,65).

◆ Thrombus extension:

DVT most often originates in the distal veins of the calf. The thrombus may subsequently extend to the proximal veins, thereby increasing the risk of pulmonary embolism. This extension is favoured by the intensity of the prothrombotic state (70).

◆ Phlegmasia cerulea dolens:

This is a rare but severe form of DVT, usually involving massive iliofemoral thrombosis. It is characterised by

major venous obstruction leading to a marked increase in venous pressure, resulting in secondary ischaemia. Progression may lead to venous gangrene, potentially requiring amputation in the absence of urgent management.

◆ **Recurrent venous thromboembolism:**

Recurrence is a frequent complication. The risk is estimated at approximately 10% within two years after a first treated episode of DVT. It is higher in cases of unprovoked events and proximal thrombosis.

◆ **Post-thrombotic syndrome:**

PTS is the most common chronic complication. It occurs in approximately 20% of patients in the years following the acute episode. It is characterised by chronic pain, persistent oedema, a sensation of limb heaviness, and skin trophic changes that may progress to venous ulcers (65,70).

◆ **Chronic thromboembolic pulmonary hypertension:**

CTEPH is a rare but serious complication secondary to unresolved PE. It is related to persistent obstruction of the pulmonary arteries by organised thrombotic material, leading to progressive pulmonary hypertension and right heart failure (64,70).

2.6. Differential Diagnosis:

The differential diagnoses of DVT can be classified according to anatomical location, pathophysiological mechanism, or diagnostic urgency.

◆ **Venous disorders:**

- SVT: indurated and painful venous cord with localised erythema; an associated DVT is found in approximately 25% of cases (72).
- Chronic venous insufficiency: chronic oedema, varicose veins, and skin trophic changes (71).
- Post-thrombotic syndrome: sequelae of a previous DVT with signs of venous insufficiency (71).

◆ **Infectious and inflammatory disorders:**

- Cellulitis / erysipelas: diffuse erythema, local warmth, often associated with fever and a cutaneous entry site (73).

◆ **Musculoskeletal disorders:**

- Ruptured Baker's cyst: acute calf pain with oedema, sometimes associated with ecchymosis(74,75).
- Muscle injury (tear, haematoma): history of trauma with localised pain (76).
- Compartment syndrome: severe pain with muscle tension; a surgical emergency.

◆ **Lymphatic disorders:**

- Lymphoedema: chronic oedema involving the dorsum of the foot, with a positive Stemmer sign (71).

◆ **Arterial disorders:**

- Acute limb ischaemia: sudden pain, cold and pale limb, with absent peripheral pulses (vascular emergency).

◆ **Other causes:**

- Extrinsic venous compression (e.g., May–Thurner syndrome, tumour, pregnancy) (71).
- Lipoedema: bilateral, symmetrical involvement of the lower limbs with sparing of the feet.

Chapter 3:

Pulmonary Embolism (PE)

2. Pulmonary Embolism (PE):

2.1. Definition:

Pulmonary embolism (PE) is defined as the partial or complete obstruction of a pulmonary artery or one of its branches by a thrombus, most often fibrin-rich, originating from the deep venous circulation, particularly from the lower limbs or the pelvic venous system. Non-thrombotic embolisms (gaseous, fat, amniotic) are not included in this definition (77).

PE constitutes a major medical emergency and represents the third leading cause of cardiovascular mortality after myocardial infarction and stroke. Its diagnosis remains challenging due to the variability of its clinical presentation and the often non-specific nature of its signs (77).

2.2. Anatomical reminders:

The lungs are respiratory organs located within the thoracic cavity, on either side of the mediastinum. Each lung is connected to the mediastinum by a pulmonary pedicle comprising the bronchi, pulmonary vessels, and neural structures. Functionally, pulmonary vascularization consists of two systems: (78,79)

- **Pulmonary circulation (functional):**

It ensures the transport of venous blood from the right ventricle to the alveolar capillaries via the right and left pulmonary arteries. These arteries branch into lobar, segmental, and then subsegmental branches, following the bronchial tree. PE most commonly occur at the level of these branches. After gas exchange, oxygenated blood is drained by the pulmonary veins into the left atrium.

- **Bronchial circulation (nutritive):**

Arising from the aorta, it supplies the bronchial structures and the supporting pulmonary tissue (78,79). Knowledge of this dual vascular supply is essential for understanding the variable tolerance of PE particularly the risk of pulmonary infarction.

3.1. Physiological reminders:

3.3.1. Pulmonary physiology and hemodynamics:

The right ventricle (RV) and the pulmonary circulation form a finely coupled low-pressure system, in which any increase in vascular resistance is poorly tolerated by the thin-walled and highly compliant RV (77,78,79,80,81). In the setting of PE, the abrupt increase in afterload leads to RV dilatation, a reduction in cardiac output, and impaired left ventricular filling, resulting in hypotension (89,90,91). This overload also promotes RV ischemia due to impaired coronary perfusion, thereby establishing a vicious cycle that may progress to acute right heart failure, potentially evolving into shock and death (89,90,91,92).

3.3.2. Alveolar–capillary diffusion:

Pulmonary gas exchange occurs across the alveolar–capillary membrane, which is thin and extensive, allowing efficient diffusion of gases according to the pressure gradient and the properties of the membrane (92,93,94,95). Its efficiency also depends on the ventilation/perfusion (VA/Q) balance, which is normally well matched (97,98). In PE, vascular obstruction creates ventilated but non-perfused areas (dead space effect), increasing the VA/Q ratio and leading to hypoxemia, the main pathophysiological disturbance observed (89,90,99,100).

3.4. Pathophysiology of pulmonary embolism:

3.4.1. Origin of the thrombus:

In more than 90% of cases, PE results from the migration of a thrombus originating in the deep veins of the lower limbs. The formation of this thrombus is based on **Virchow's triad**, which includes venous stasis, hypercoagulability, and endothelial injury (31).

When fibrinolytic mechanisms are overwhelmed, the thrombus may become unstable and migrate to the pulmonary circulation via the inferior vena cava and the right heart. More rarely, the origin may be pelvic or

from the superior vena cava (31).

3.4.2. Hemodynamic consequences:

Obstruction of the pulmonary arterial bed leads to an abrupt increase in pulmonary vascular resistance (PVR), resulting from both mechanical obstruction and vasoconstriction mediated by vasoactive substances (thromboxane A₂, serotonin) (89,90). This increase in RV afterload results in:

- RV dilation.
- Decreased right ventricular contractility.
- Reduced cardiac output (90).

When obstruction exceeds 30–50% of the pulmonary vascular bed, acute pulmonary hypertension may develop and can progress to shock (89,90). Ventricular interdependence leads to a shift of the interventricular septum toward the left ventricle, reducing left ventricular filling and further worsening the decline in cardiac output (90).

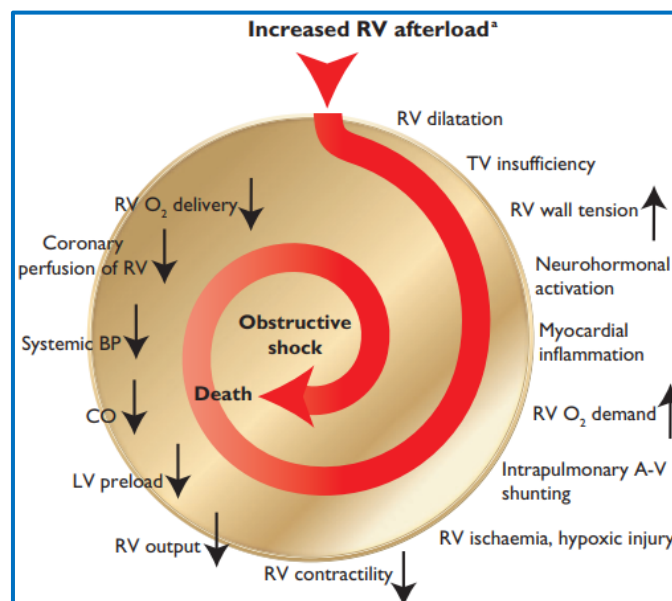


Figure n°8: Pathophysiologic Mechanisms of Obstructive Shock in Acute Pulmonary Embolism.

3.4.3. Respiratory consequences:

PE causes a ventilation/perfusion (V/Q) mismatch. Embolized regions are ventilated but not perfused, creating a dead space effect, while non-affected areas may exhibit a relative shunt effect (90). This imbalance constitutes the main mechanism of hypoxemia (89,92). Other contributing mechanisms include:

- Atelectasis.
- Decreased cardiac output.
- Right-to-left shunt in the presence of a patent foramen ovale (89,92).

Hypocapnia is frequently observed and is related to reflex hyperventilation (90).

3.4.4. Severity factors and prognosis:

The severity of PE mainly depends on:

- The extent of vascular obstruction.
- The adaptive capacity of the RV.
- The underlying cardiopulmonary status (90,101).

RV failure is the main determinant of prognosis and the leading cause of mortality in severe forms (89,90).

3.5. Diagnosis of Pulmonary Embolism:

3.5.1. Clinical Diagnosis:

The clinical manifestations of PE are variable and non-specific, depending on the size of the embolus, its location, and the patient's underlying condition. A small PE may be asymptomatic, whereas even a moderate PE can lead to hemodynamic instability in patients with comorbidities (102).

1) Functional signs:

The classic triad of dyspnea, chest pain, and hemoptysis is suggestive but rarely complete (102):

- **Dyspnea:** The most frequent symptom (≈ 70 – 80% of cases), typically of sudden onset and representing the main presenting complaint (103). It may occur in isolation, particularly in elderly or comorbid patients (4).
- **Chest pain:** Most often pleuritic in nature, observed in approximately 50 – 70% of cases, and frequently reflects peripheral involvement (103).
- **Hemoptysis:** Uncommon ($<20\%$), usually associated with pulmonary infarction; its absence does not exclude the diagnosis (104).
- **Syncope:** A sign of severity reflecting a reduction in cardiac output, reported in 13 – 19% of cases (103).
- **Other symptoms:** Cough, palpitations, anxiety, or a feeling of impending doom may occur, contributing to the non-specific presentation (102).

2) General signs:

- **Fever:** Possible (4 – 13%), with multifactorial origin (103).
- **Tachypnea:** Frequent but inconsistent; its presence increases diagnostic sensitivity when associated with dyspnea (104).
- **Tachycardia :** Found in approximately 50% of cases, non-specific (104).
- **Shock:** Present in 4 – 10% of cases and associated with high mortality ($\approx 50\%$) (103).

3) Physical signs:

Clinical examination is often unremarkable or normal.

- **Signs of deep vein thrombosis (DVT):** Lower limb edema or pain in 15 – 25% of cases (102).
- **Cardiovascular signs:**
 - ✓ Tachycardia.
 - ✓ Accentuated pulmonary component of the second heart sound (P2).
 - ✓ Signs of right ventricular overload (105).
- **Respiratory signs:**
 - ✓ Crackles, decreased vesicular breath sounds.
 - ✓ Occasionally wheezing.
 - ✓ However, auscultation is often normal (106).

4) Atypical presentations:

Atypical presentations are common, particularly in elderly or comorbid patients, and may mimic other conditions such as pneumonia, COPD, or ACS (102). PE may also be asymptomatic or incidentally discovered (4).

5) Importance of clinical assessment:

No single clinical sign can confirm or exclude PE. The combination of multiple findings improves diagnostic sensitivity. Estimation of clinical probability relies on validated scoring systems such as the Wells or Geneva scores (107).

3.5.2. Pre-test Probability Scores:

The assessment of the clinical pre-test probability of (PE) is based on the analysis of symptoms, clinical signs, and risk factors for VTE. It allows patients to be stratified into probability categories that are directly correlated with the actual frequency of confirmed PE (4).

This step is essential, as the diagnostic value of complementary investigations depends on the initial level of clinical probability (4). Clinical judgment can be standardized using validated scoring systems, mainly the Wells score and the Revised Geneva score, whose simplified versions have been widely validated (4).

The appropriate use of these scores helps guide the diagnostic strategy (D-dimer testing, imaging) and avoid unnecessary investigations (4,102). The prevalence of confirmed PE is estimated at approximately:

- 10% in low probability.
- 30% in intermediate probability.
- 65% in high probability (4).

1. Clinical probability scores:

a. Wells score:

The Wells score is the most widely used tool in clinical practice to estimate the probability of PE (77).

In patients with low clinical probability “PE unlikely”, a negative D-dimer test allows exclusion of PE without the need for imaging (77). (APPENDIX 07)

b. Revised Geneva score:

The Revised Geneva score is entirely objective and relies solely on standardized clinical parameters (77). (APPENDIX 08)

2. Pulmonary embolism exclusion criteria:

The PERC (Pulmonary Embolism Rule-out Criteria) (APPENDIX 09) allow the exclusion of PE without additional testing in patients with a low clinical probability (108). If all criteria are positive, PE is ruled out without the need for D-dimer testing. Summary algorithm in (APPENDIX 10)

3.5.3. Paraclinical investigations:

1) Biological tests:

A. B-type natriuretic peptide (BNP)):

BNP and NT-proBNP have limited diagnostic value in (PE), but they are useful for assessing the severity of right ventricular dysfunction induced by pressure overload [36]. Elevated levels are associated with increased mortality and complications, giving them important prognostic value. A normal level has a high negative predictive value but does not formally exclude PE (105).

B. Troponin:

Troponin is a marker of myocardial injury with low diagnostic value in PE (105). Its elevation, observed in 30–50% of moderate to severe PE cases, is associated with an increased risk of mortality, making it a useful tool for prognostic stratification (105).

C. Arterial blood gases:

Arterial blood gas analysis has limited diagnostic value in pulmonary embolism, as a normal PaO₂ does not exclude the diagnosis despite the frequent presence of hypoxemia (109). Hypoxemia is mainly due to ventilation/perfusion mismatch with increased dead space, blood flow redistribution, and more rarely shunt formation (110). Gas exchange findings most commonly include hypoxemia with hypocapnia and respiratory alkalosis, while severe cases may progress to metabolic acidosis (110). However, hypoxemia may be absent in approximately 26% of cases, limiting its diagnostic utility (110).

D. D-dimers:

D-dimers, fibrin degradation products, have a high negative predictive value allowing exclusion of PE or DVT when normal, but their specificity remains low as they may be elevated in many non-thromboembolic conditions. Age-adjusted thresholds (>50 years: age × 10) improve diagnostic accuracy without increasing false-negative results (4).

2) Electrocardiogram (ECG):

The ECG abnormalities in PE are non-specific and most often reflect acute right heart strain. Their absence does not exclude the diagnosis.

Sinus tachycardia is the most common abnormality. The classic S1Q3T3 pattern (S wave in lead I, Q wave and inverted T wave in lead III) may be observed, although it is inconsistent (11). Other possible findings include:

- Right axis deviation.
- Right bundle branch block.

- Atrial fibrillation (11).

ECG is mainly useful for differential diagnosis and severity assessment.

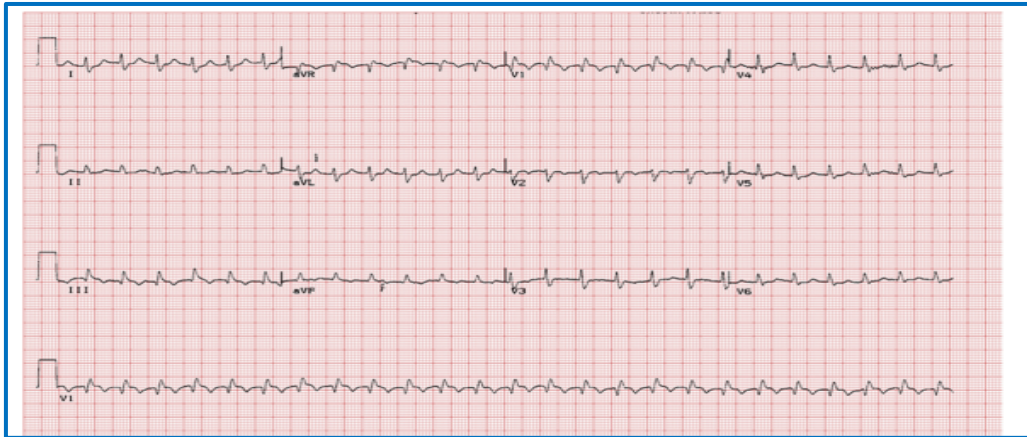


Figure n°9: Electrocardiographic Signs of Acute Pulmonary Embolism.

3) Chest radiography:

Chest radiography is most often normal or shows non-specific abnormalities (atelectasis, pleural effusion). Its main role is to exclude alternative diagnoses.

Some suggestive but insensitive signs may be observed:

- Hampton's hump (peripheral wedge-shaped opacity).
- Westermark sign (localized oligemia).
- Fleischner sign (pulmonary artery enlargement) (105).

These signs have relatively high specificity but low sensitivity, limiting their diagnostic value (105).

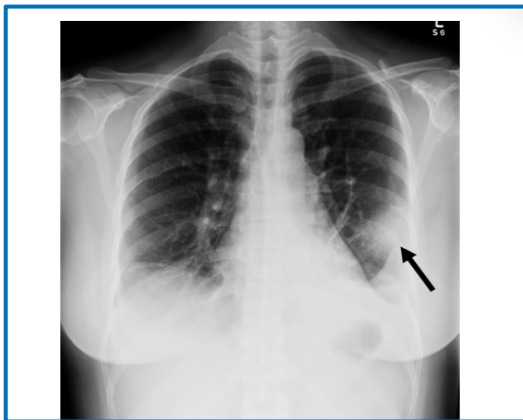


Figure n°10: Chest Radiograph Demonstrating Hampton's Hump.

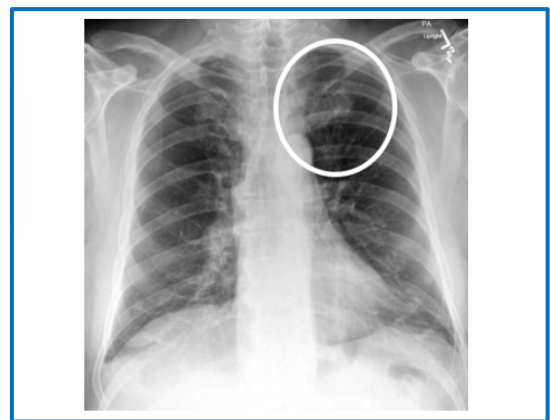


Figure n°11: Chest Radiograph Showing Westermark Sign.

4) Echocardiography (Cardiac Doppler ultrasound):

Echocardiography allows assessment of the hemodynamic consequences of pulmonary embolism on the RV. It is particularly useful in cases of hemodynamic instability (105).

It may reveal:

- **Direct signs:** right intracardiac thrombi (rare but highly specific).
- **Indirect signs:** right ventricular dilatation, increased pulmonary artery pressures, interventricular septal abnormalities.
- **Signs of severity:** RV systolic dysfunction, McConnell's sign, and the 60/60 sign (4).

The presence of these abnormalities is associated with a poor prognosis. However, a normal echocardiographic examination does not exclude PE due to its limited sensitivity (4). (APPENDIX 15)

- **5) Venous Doppler ultrasound of the lower limbs:**

Compression ultrasonography can detect deep vein thrombosis (DVT) in approximately 70% of patients with confirmed pulmonary embolism and is highly effective for proximal DVT detection. The identification of proximal DVT is sufficient to initiate anticoagulation therapy; however, its overall limited sensitivity makes it a complementary examination, particularly when thoracic imaging is contraindicated (4).

6) Chest computed tomography: CT pulmonary angiography (CTPA)

CT pulmonary angiography (CTPA) is the reference standard for the diagnosis of pulmonary embolism. It allows direct visualization of thrombi as intraluminal filling defects (4,11). Its diagnostic performance is high, especially for proximal emboli, but decreases for distal involvement (111). Interpretation must consider the pre-test clinical probability. Any discrepancy between clinical findings and imaging results requires further investigation (111). This examination may be contraindicated in cases of severe renal failure or iodinated contrast allergy (105).

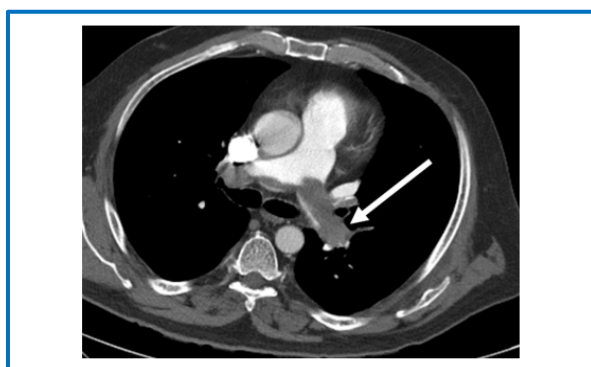


Figure n°12: CT Pulmonary Angiography Showing Saddle Pulmonary Embolism.

7) Ventilation–perfusion (V/Q) lung scintigraphy:

V/Q scintigraphy allows identification of ventilation–perfusion mismatches characteristic of PE. It is particularly indicated in:

- Young patients.
- Pregnant women.
- Patients with contraindications to iodinated contrast media.

A normal examination excludes PE, whereas an inconclusive result requires further diagnostic evaluation (4).

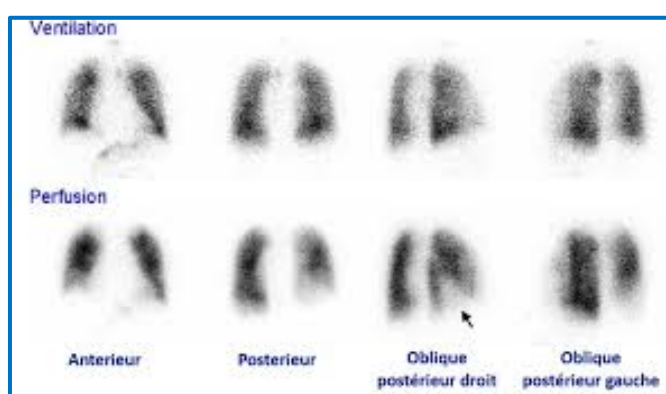


Figure n°13: Ventilation–Perfusion (V/Q) Lung Scintigraphy Revealing Ventilation–Perfusion Mismatch Suggestive of Pulmonary Embolism.

8) Magnetic resonance imaging (MRI):

MRI is not a first-line examination due to its limited sensitivity and reduced availability. It may be used as an alternative in cases where standard imaging modalities are contraindicated. When technically adequate, it demonstrates excellent diagnostic specificity (105).

9) Pulmonary angiography:

Pulmonary angiography is an invasive technique allowing direct visualization of thrombi. It is currently rarely used and reserved for specific situations (105). It may be combined with therapeutic procedures. However, it carries a risk of complications, with an estimated mortality rate of approximately 0.5% (4).

3.6. Diagnostic strategy:

In patients with suspected (PE), the diagnostic strategy is based on a sequential approach integrating pre-test clinical probability, D-dimer testing, and confirmatory imaging, particularly in hemodynamically stable patients (105). (APPENDIX 11) (APPENDIX 12)

3.7. Clinical course and clinical forms:

3.7.1. Prognosis:

The prognosis of pulmonary embolism (PE) mainly depends on hemodynamic status and right ventricular function. The presence of shock or right ventricular dysfunction is a major adverse prognostic factor, strongly associated with increased mortality. The association with (DVT) further increases this risk (105). In contrast to older data, the prognosis of pulmonary infarction is now considered favorable, with an in-hospital survival rate of approximately 97% (105).

• Prognostic scores: PESI and sPESI:

Several prognostic models have been developed to assess the severity of PE. Among them, the Pulmonary Embolism Severity Index (PESI) and its simplified version (sPESI) are the most widely used in clinical practice. The PESI score allows estimation of the 30-day mortality risk in patients with confirmed pulmonary embolism. Its main utility, similar to that of the sPESI, lies in identifying patients at low risk of mortality (PESI classes I and II) (105). (APPENDIX 13)

3.7.2. Severity classification:

The management of (PE) is based on stratification into three levels of severity (105). (APPENDIX 14)

3.8. Differential Diagnosis:

PE presents with a polymorphic clinical presentation, making its differential diagnosis broad. The main conditions to consider include:(105,111)

Dominant symptom	Possible diagnoses
Chest pain	Acute coronary syndrome, pneumothorax, pericarditis
Dyspnea	Chronic obstructive pulmonary disease, heart failure, pneumonia
Syncope	Arrhythmia, vasovagal syncope
Cough / fever	Pneumonia, bronchitis

Table n°4: Differential Diagnoses According to the Dominant Clinical Symptom.

3.9. Complications of pulmonary embolism:

The natural course of the thrombus is progressive resolution. However, PE remains a serious condition, associated with a mortality rate that may reach up to 30% in the absence of treatment or despite initial management. Complications may be acute or chronic and contribute significantly to morbidity and mortality. (77,104,108)

3.9.1. Acute complications:

- **Thromboembolic recurrence:** may occur early, often related to insufficient anticoagulation (104).
- **Right heart failure:** secondary to increased PVR, leading to RV dilatation and dysfunction.
- **Cardiogenic shock:** the most severe form, related to acute RV failure with systemic hypoperfusion (112).

3.9.2. Chronic complications :

- **Chronic thromboembolic disease:** persistence of thrombotic material without pulmonary hypertension.
- **Chronic thromboembolic pulmonary hypertension (CTEPH):** a late complication (2–4%), related to persistent obstruction and vascular remodeling, responsible for chronic dyspnea.

Persistent dyspnea following PE should raise suspicion of a chronic complication, particularly CTEPH, requiring further investigations. (104,112)

Chapter 4:

Unusual-Site Venous Thrombosis (USVT)

4. Unusual-Site Venous Thrombosis (USVT):

4.1. Cerebral Venous Thrombosis (CVT):

4.1.1. Definition:

CVT is defined as a partial or complete obstruction of the cerebral venous system by a thrombus, involving the dural venous sinuses, cortical veins, or deep cerebral veins. It is characterised by marked clinical and radiological variability, ranging from isolated headache to severe neurological presentations that may be life-threatening.

4.1.2. Cerebral Venous Anatomy and Drainage:

The CVS is classically divided into two main anatomical networks: the SVS and the DVS (5). The SVS drains the cerebral cortex and the subcortical white matter. It primarily drains into the superior sagittal sinus, transverse sinuses, and sigmoid sinuses through cortical veins, including the veins of Trolard and Labbé (8). The DVS drains deep cerebral structures, including the thalamus, striatum, and periventricular white matter. It mainly consists of the internal cerebral veins, the vein of Galen, and the straight sinus.

Both systems converge toward the confluence of sinuses (torcular Herophili), whose anatomy shows significant inter-individual variability, with the classical configuration observed in only 20–53% of cases.

The most frequently involved sites of thrombosis include the transverse sinuses (the most common location), followed by the superior sagittal sinus, the straight sinus, and isolated cortical veins, which are less frequently affected. From a pathophysiological perspective, thrombosis most often begins in a dural sinus and may subsequently extend to cortical veins (6).

The anatomical organisation of the CVS, including superficial and deep drainage pathways, is illustrated in APPENDIX 16.

4.1.3. Pathogenesis and Pathophysiology:

- **Mechanisms of thrombosis:**

The occurrence of CVT is classically explained by Virchow's triad: venous stasis, endothelial (vascular wall) injury, and a hypercoagulable state. These mechanisms may occur alone or in combination and account for the wide variety of aetiological settings of CVT.

- **Structure and evolution of the thrombus:**

From a histological perspective, cerebral venous thrombi do not differ significantly from other venous thrombi. In the early stage, they are mainly composed of fibrin and red blood cells, with a relatively lower proportion of platelets (113,114).

- **Pathophysiological consequences of venous occlusion:**

Occlusion of a venous sinus or cerebral vein leads to an increase in upstream venous and capillary pressure. This venous hypertension results in several major pathophysiological consequences (115,116,117), which are summarised in APPENDIX 17.

- **Parenchymal involvement:**

Cerebral lesions observed in CVT are variable and may include isolated cerebral oedema, venous infarction, intracerebral haemorrhage, and bilateral or non-territorial lesions. Unlike arterial infarctions, these lesions do not necessarily conform to a specific arterial vascular territory, which represents an important diagnostic clue (12,13).

A global schematic overview summarising the pathophysiology and cerebral parenchymal consequences of CVT is presented in APPENDIX 18.

4.1.4. Clinical Presentation and Diagnosis:

CVT is characterised by a highly polymorphic and often non-specific clinical presentation, which explains the frequent delay in diagnosis. Clinical manifestations depend on the site and extent of thrombosis, the speed of onset, and the degree of parenchymal involvement and intracranial hypertension (1).

The clinical predictive score for CVT is presented in APPENDIX 19.

Category	Description	Diagnostic Orientation / Features
Isolated intracranial hypertension syndrome	Progressive headache, nausea / vomiting, diplopia, papilloedema, transient visual disturbances	May mimic idiopathic intracranial hypertension
Focal or encephalopathic neurological syndrome	Motor or sensory deficit, aphasia, visual disturbances, seizures, confusion, altered consciousness	Often related to parenchymal involvement
Severe acute presentation	Rapid deterioration of consciousness, status epilepticus, coma, signs of brain herniation	Suggests deep, extensive, or haemorrhagic involvement
Headache	Recent, unusual, progressive, diffuse or localised	Most frequent symptom; sometimes isolated
Seizures	Focal or generalised, at onset or secondary	More frequent than in arterial stroke
Focal neurological deficits	Hemiparesis, aphasia, sensory, visual or coordination disorders	Often fluctuating or progressive
Altered consciousness	From drowsiness to coma	Mainly observed in severe forms
Warning signs	Unusual headache in a young patient, seizures, papilloedema, prothrombotic context	High diagnostic suspicion value

Table n°5 : Main clinical manifestations of CVT.

4.1.5. Paraclinical Diagnosis:

a) Cerebral Imaging

The definitive diagnosis of CVT relies primarily on imaging. In clinical practice, the reference examinations are CTV and MRV.

● Non-contrast brain CT scan:

A non-contrast brain CT is often the first-line emergency imaging study. It may be normal in up to 30% of cases, particularly early in the disease course, but may also demonstrate direct or indirect signs of CVT, which are described in detail in APPENDIX 20.

Note: A normal brain CT scan does not exclude the diagnosis of CVT if clinical suspicion remains high (119).

● CT Venography:

CTV is a widely available, rapid, and highly useful imaging modality in emergency settings. It can demonstrate a dural sinus filling defect, absence of venous opacification, or the classic “empty delta sign.” It has excellent

diagnostic performance for both superficial and deep venous sinuses, but is less sensitive for isolated cortical vein thrombosis.

- **Magnetic Resonance Imaging with Venography:**

MRI combined with MRV is the most comprehensive imaging technique, allowing evaluation of the thrombus itself, assessment of the venous system, and analysis of associated parenchymal lesions. The main suggestive signs include loss of the normal flow void, signal changes of the thrombus depending on its age, and the detection of venous infarction or atypical hemorrhages.

Remark: In clinical practice, CTV is often preferred in emergency settings due to its rapid acquisition and wide availability. MRI/MRV is particularly useful in cases of diagnostic uncertainty, non-contributory CT scan, or when a more detailed assessment of venous anatomy and parenchymal involvement is required (118,120,121).

b) Biological Investigations:

- **D-dimer testing:**

D-dimers may be elevated in CVT and can support the diagnosis; however, normal levels do not reliably exclude the condition, particularly in cases with isolated cortical vein thrombosis or chronic presentations.

- **Complementary biological workup:**

Depending on the clinical context, this may include: CBC, coagulation profile, thrombophilia workup, aPL antibodies, inflammatory markers, and, in specific situations, anti-PF4 antibodies in cases of suspected VITT.

4.1.6. Differential Diagnosis:

Category	Examples / Distinguishing Features
Arterial ischaemic stroke	Headache less common, lesions located within an arterial vascular territory
Idiopathic intracranial hypertension	Isolated headache, papilloedema; normal venous imaging excludes CVT
Intracerebral haemorrhage	More frequent in young patients; atypical or multifocal localisation
CNS infections	Meningitis, encephalitis, secondary ENT/mastoid infections
Complicated migraine	Unusual headache or aura with atypical neurological deficit
Other diagnoses	Dural arteriovenous fistula, PRES, vasculitis, convexity subarachnoid haemorrhage, vascular variants
Diagnostic pitfalls	Underestimation of headache severity, falsely reassuring normal CT scan, confusion with migraine, omission of venous imaging

Table n°6 : Differential diagnosis of CVT.

4.1.7. Complications and Prognosis:

The complications of CVT are classified into acute, potentially life-threatening events and long-term sequelae. Although the overall outcome is favourable in most cases, approximately 10–15% of patients die or remain functionally dependent despite intensive treatment (118,122). The complications of CVT are summarised in APPENDIX 21.

4.1.8. Diagnostic and Therapeutic Algorithm:

The diagnostic and therapeutic algorithm for CVT is provided in APPENDIX 22.

4.2. Jugular Vein Thrombosis (JVT):

4.2.1. Definition:

JVT is a rare form of DVT that mainly affects the internal jugular vein. It may be primary or secondary to predisposing factors, with variable clinical presentations.

Lemierre syndrome: a particular form of JVT corresponding to septic thrombophlebitis secondary to an otorhinolaryngological infection (most commonly *Fusobacterium necrophorum*). It classically associates pharyngitis, jugular vein thrombosis, and septic pulmonary emboli, mainly affecting young adults (125,128).

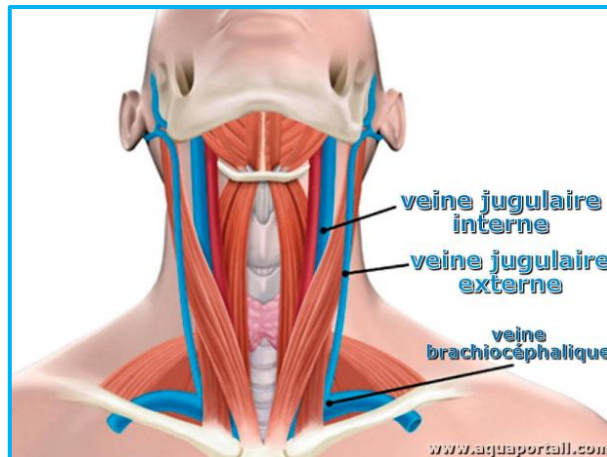


Figure n°14 : Superficial and Deep Veins of the Neck.

4.2.2. Anatomical Overview:

Internal jugular vein (IJV): the main deep cervical vein, draining blood from the brain, deep facial structures, and neck organs. It courses within the carotid sheath and joins the subclavian vein to form the brachiocephalic trunk.

External jugular vein (EJV): a superficial vein draining the superficial structures of the scalp and neck. It empties into the subclavian vein.

4.2.3. Etiology and Risk Factors:

JVT is most often secondary (approximately 79%) (123), mainly related to: Cancer, Central venous catheters, Implantable devices.

Other contributing factors include: Cervicofacial infections, Thrombophilia and antiphospholipid syndrome, Cervical surgery or trauma, Medications (e.g., oral contraceptives) (118,124).

4.2.4. Clinical and Paraclinical Diagnosis:

- **Clinical features:**

Unilateral neck pain and swelling (16,123).

Fever and infectious signs (especially in Lemierre syndrome) (126,130).

- **Imaging:**

Doppler ultrasound: first-line examination (73,133).

Contrast-enhanced cervical CT scan: confirms the diagnosis and evaluates complications (131).

MRI: in doubtful cases (61,73).

- **Laboratory tests:**

Blood cultures when infectious etiology is suspected (Lemierre syndrome) (126,127).

4.2.5. Differential Diagnosis:

Cervical lymphadenopathy, Cervicofacial abscesses, Cervical tumors, Post-traumatic hematoma, Subclavian vein thrombosis, Lemierre syndrome (infectious form).

4.2.6. Evolution and Complications:

JVT is associated with significant morbidity, with a risk of PE (10–16%) and post-thrombotic syndrome (approximately 41%) (123).

Thirty-day mortality depends on the underlying etiology and is higher in secondary forms (123).

In Lemierre syndrome, prognosis remains serious despite treatment because of infectious complications and long-term sequelae (128).

4.3. Upper Extremity Deep Vein Thrombosis (UEDVT):

4.3.1. Definition and Epidemiology:

UEDVT corresponds to the formation of a thrombus within the deep venous system of the upper limb. It accounts for 4 to 10% of all deep vein thromboses, with an incidence of 0.4 to 1 per 10,000 inhabitants per year. Its frequency is increasing due to the widespread use of central venous catheters and cardiac devices (35,36).

4.3.2. Anatomical Overview:

The deep venous system of the upper limb includes: Deep palmar venous arch, Radial and ulnar veins, Brachial vein, Axillary vein, Subclavian vein.

These veins drain into the superior vena cava. Their close relationship with osteoarticular structures explains certain compressive mechanisms.

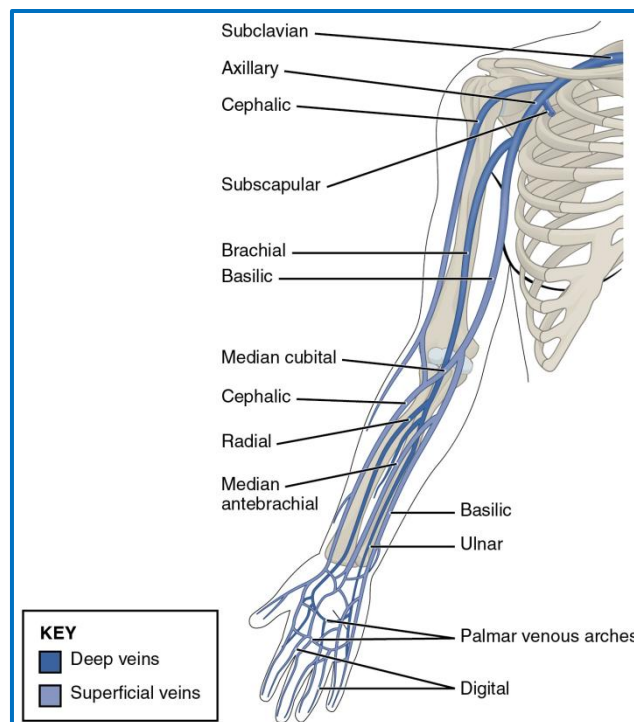


Figure n°15 : Superficial and Deep Venous Anatomy of the Upper Limb.

4.3.3. Classification and Etiology:

UEDVT is divided into two categories:

- ◆ **Secondary UEDVT (most common):** related to an identifiable triggering factor, mainly central venous catheters or pacemaker leads, intravascular devices, and cancer (35,135).
- ◆ **Primary UEDVT (Paget–Schroetter syndrome):** accounts for approximately one-third of cases and mainly affects young, active patients. It results from repeated microtrauma of the subclavian vein at the thoracic outlet, often after intense physical activity involving the dominant arm (35,136,137).

4.3.4. Clinical and Paraclinical Diagnosis:

UEDVT commonly presents with **pain, edema, erythema**, and **venous distension** of the affected limb. The diagnosis should be suspected in patients presenting with arm swelling, acute discomfort, and risk factors such as strenuous arm exercise, central venous catheterization, pacemaker implantation, previous DVT, or cancer (35,135,138).

Evaluation relies on an algorithm combining a clinical probability score, **D-dimer testing**, and **compression ultrasonography**, which has proven safe and effective. Doppler ultrasound remains the initial imaging modality of choice, although the mid-portion of the subclavian vein may be difficult to visualize. Contrast venography, although considered the gold standard, is now less frequently used in routine practice (135,136,139,140).

4.3.5. Differential Diagnosis:

Symptoms	Possible Etiologies
Isolated edema	Lymphedema
Redness, warmth	Infectious cellulitis
Hematoma	Trauma
Palpable mass	Arm tumor
Sudden exertional pain	Muscle rupture

Table n°7 : Differential Diagnosis of Upper Extremity Deep Vein Thrombosis.

4.3.6. Evolution and Complications:

Complications are less frequent than in lower limb DVT:

- Symptomatic pulmonary embolism: 6–8% (vs. 15–32%)
- Recurrence at 12 months: 2–5% (vs. 10%)
- Post-thrombotic syndrome: 5–21% (vs. up to 56%). (35,135)

4.4. Budd-Chiari syndrome (BCS):

4.4.1. Definition and Epidemiology:

Budd–Chiari syndrome (BCS) is a rare disorder characterized by partial or complete obstruction of the hepatic venous outflow tract, which may occur from the small hepatic veins up to the inferior vena cava, in the absence of cardiac obstruction. It is most often of thrombotic origin, occurring in a prothrombotic setting, and usually has a progressive onset (141,142).

Its prevalence is estimated at 11 cases per million inhabitants, with an annual incidence of 1 case per million. The mean age at diagnosis ranges between 35 and 40 years, with no clear sex predominance. In children, this condition is rare in Western countries (approximately 0.1% of liver diseases), but more frequent in Asia (up to 15%) (143).

4.4.2. Anatomical Overview:

The three main hepatic veins are: Right hepatic vein, Middle hepatic vein, Left hepatic vein.

They drain blood from the liver into the inferior vena cava, which returns blood to the heart (141).

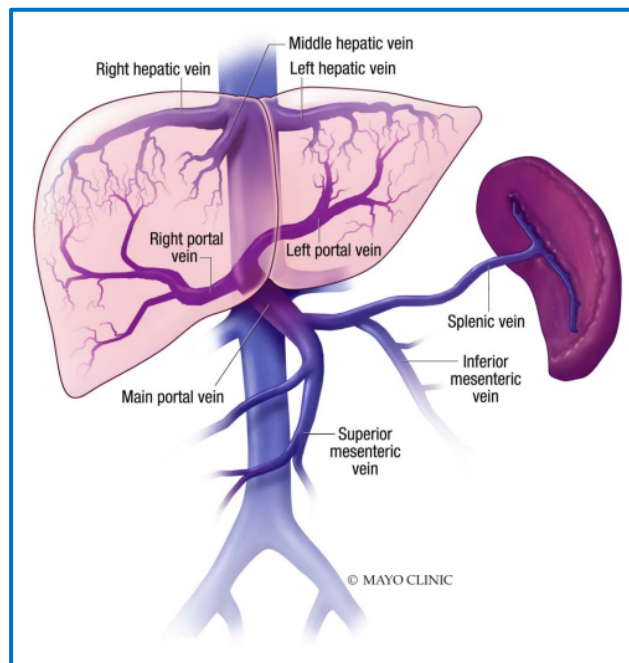


Figure n°16 : Anatomy of the portal and hepatic venous systems.

4.4.3. Physiopathology and Etiologies:

BCS is most often primary and thrombotic in origin, with a prothrombotic factor identified in 79–84% of cases, sometimes multiple (145).

Myeloproliferative neoplasms are the leading cause in Western countries (approximately 50%), often associated with the JAK2-V617F mutation. Other factors include oral contraceptives, inherited thrombophilias, and certain inflammatory diseases. (144,145) (APPENDIX 23)

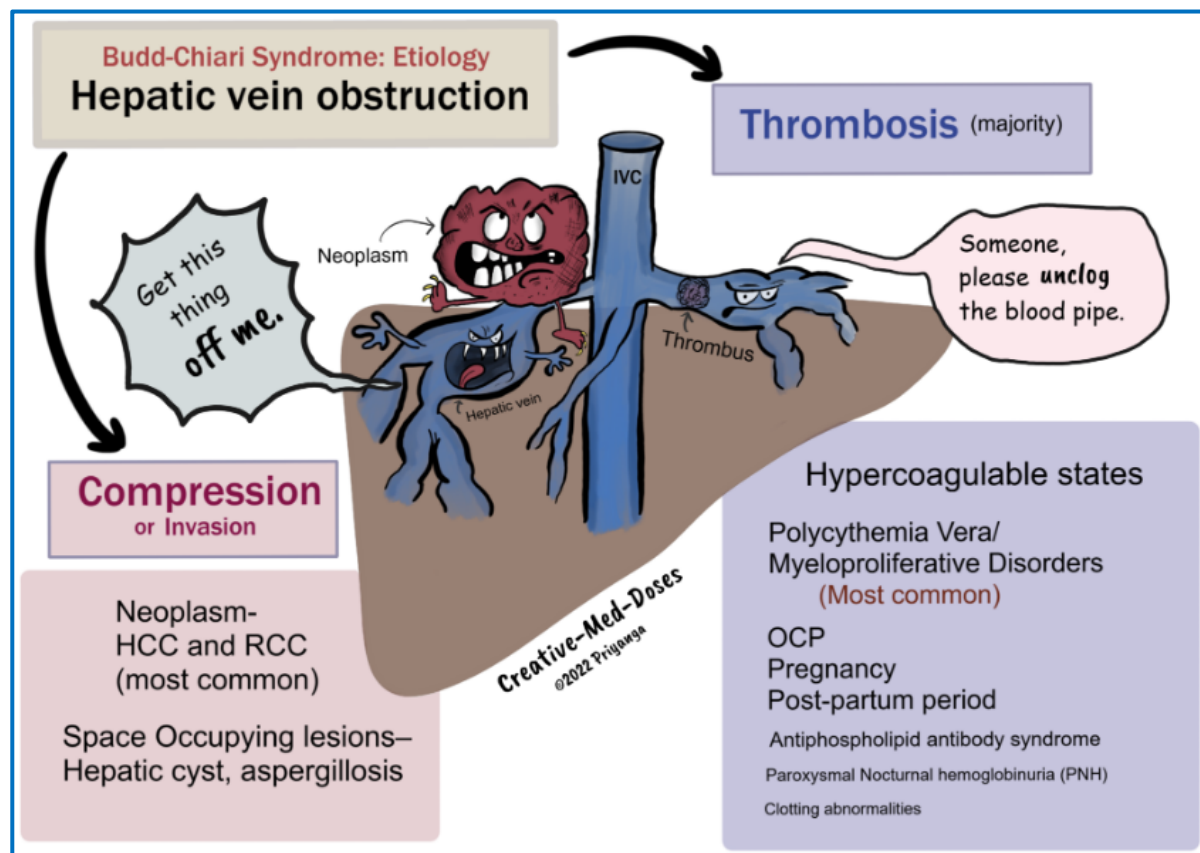


Figure n° 17: Pathophysiology of Budd-Chiari Syndrome: Compression vs. Thrombosis.

4.4.4. Clinical and Paraclinical Diagnosis:

Form	Clinical Features	Laboratory Findings	Particularities / Prognosis
Asymptomatic	No ascites, hepatomegaly, or pain; incidental diagnosis	Often normal or mildly abnormal	Effective collateral circulation (141,157)
Acute	Rapid onset; liver failure, ascites, painful hepatomegaly	Transaminases >5× normal	Rare, severe; obstruction of all 3 veins (141,142,158)
Subacute	Mixed presentation; rapid ascites, hepatomegaly, jaundice ± renal failure	Transaminases >5× normal, coagulopathy	Less favorable prognosis (141,142,159)
Chronic	Slow progression; ascites, portal hypertension, collaterals, cirrhosis	Transaminases <5× normal	Risk of HCC, varices (5–15%) (148,149,159,160)

Table n°8 : Form of Budd-Chiari syndrome (Clinical and Paraclinical Diagnosis).

Doppler ultrasound is the first-line imaging modality, allowing confirmation of hepatic venous obstruction or its consequences (142,147).

CT scan or MRI is indicated in cases of diagnostic uncertainty or for extension assessment and therapeutic planning (142,145,149).

Liver biopsy may be necessary when small-vein involvement is suspected (142).

An etiological work-up, particularly for myeloproliferative disorders, should always be performed (146,147).

4.4.5. Differential Diagnosis:

The differential diagnosis of Budd–Chiari syndrome includes:

Sinusoidal obstruction syndrome (SOS), Right-sided heart failure, Decompensated cirrhosis, Hepatic tumor infiltration.

Other liver diseases to consider:

Viral or alcoholic hepatitis, Hepatic steatosis, Wilson disease, Alpha-1 antitrypsin deficiency, Primary biliary cholangitis and primary sclerosing cholangitis. (148,149)

4.4.6. Evolution and Complications:

The course of BCS is variable, most often progressive, with alternating periods of stability and worsening. Without treatment, 3-year mortality reaches approximately 90%, mainly due to complications of portal hypertension and cirrhosis. With current treatments (anticoagulation, TIPS, transplantation), 5-year survival ranges from 70 to 90% (141,143,150,151).

The main complications are:

Ascites and portal hypertension, Gastrointestinal bleeding (varices), Liver failure, Infections.

In the long term, the risk of hepatocellular carcinoma justifies regular surveillance (143,150).

Treatment-related complications may also occur, particularly bleeding under anticoagulation and complications of interventional procedures (TIPS, angioplasty).

4.5. Portal Vein Thrombosis (PoVT):

4.5.1. Definition and Epidemiology:

Portal vein thrombosis (PVT) corresponds to a partial or complete thrombotic obstruction of the portal vein trunk, which may extend to its intrahepatic branches and even to the splenic and mesenteric veins (161,164). It may occur in either a healthy or cirrhotic liver, with variable clinical presentations depending on the underlying

context (162,163).

It is a relatively rare condition, with a lifetime risk of approximately 1% in the general population. It is more frequent in patients with cirrhosis (0.6 to 16%) and hepatocellular carcinoma (10 to 40%). It accounts for about 30% of portal hypertension cases in adults and up to 75% in children (161).

Its course may be acute or chronic, ranging from asymptomatic forms to complications of portal hypertension or, more rarely, intestinal ischemia (164).

4.5.2. Anatomical Overview:

The portal vein is formed by the confluence of the superior mesenteric vein and the splenic vein, posterior to the neck of the pancreas. It also receives the inferior mesenteric vein through the splenic vein.

It courses toward the liver, where it divides into right and left branches, providing approximately 75% of hepatic blood flow. It plays an essential role in draining digestive blood to the liver for detoxification and metabolism.

4.5.3. Etiology and Risk Factors:

In patients without cirrhosis, the main causes are thrombophilia (approximately 63%) and myeloproliferative neoplasms (approximately 25%) (161). Other factors include oral contraceptives, abdominal surgery, and intra-abdominal infections or inflammatory conditions (162).

In cirrhotic patients, PVT is related to portal hypertension and reduced portal blood flow, with a prevalence ranging from 1 to 20% (161,163). Hepatocellular carcinoma should always be ruled out (162).

4.5.4. Clinical and Paraclinical Diagnosis:

Clinical presentation varies according to the underlying condition:

- **Acute form (without cirrhosis):** acute abdominal pain, fever, nausea, ascites, and splenomegaly.
- **Septic form (pylephlebitis):** presentation of septicemia or septic shock.
- In cirrhotic patients: often asymptomatic, incidentally discovered on imaging .
- **Severe complication:** intestinal ischemia, suspected in the presence of severe pain disproportionate to clinical findings, with associated biological and radiological signs.
- **Chronic form:** progression to portal hypertension with cavernous transformation and esophagogastric varices (161,164).

Diagnosis relies on **Doppler ultrasound**, the first-line examination, showing a portal thrombus and absent flow. CT scan or MRI may further define the extent of thrombosis and assess for intestinal ischemia.

Biological findings are often nonspecific (elevated D-dimers). Blood cultures are useful when pylephlebitis is suspected, and thrombophilia screening should be performed systematically (165,166).

4.5.5. Differential Diagnosis:

- Non-thrombotic portal hypertension (cirrhosis without PVT).
- Portal vein tumor invasion (hepatocellular carcinoma).
- Extrinsic compression of the portal vein.
- Budd–Chiari syndrome.
- Non-venous mesenteric ischemia.
- Chronic liver diseases (hepatitis, steatosis).

4.5.6. Evolution and complications:

Long-term complications are mainly related to portal hypertension, particularly gastrointestinal bleeding (the most frequent), ascites, and portosystemic encephalopathy.

In cirrhotic patients, PVT is associated with increased mortality and may complicate liver transplantation. Spontaneous recanalization may occur in approximately 40% of cases (162).

4.6. Superficial Vein Thrombosis (SVT):

4.6.1. Definition and epidemiology:

Superficial vein thrombosis (SVT) is defined as the formation of a thrombus within the superficial venous system, mainly of the lower limbs. Its annual incidence is estimated between 64 and 131 cases per 100,000 person-years. It is generally considered a benign condition; however, approximately 10% of cases may progress to DVT or PE (167,168).

4.6.2. Clinical and Paraclinical Diagnosis:

SVT typically presents as a palpable, painful, and inflamed venous cord, most commonly located in the lower limbs. Risk factors are similar to those of DVT, including pregnancy, varicose veins, and active cancer, whereas upper-limb SVT is mainly related to venous catheters. The incidence is higher in women (169,172).

From a diagnostic perspective, D-dimer testing is unreliable for excluding SVT. Doppler ultrasound is the reference examination in doubtful cases, allowing confirmation of the diagnosis and assessment of thrombus extension. An associated DVT is found in approximately 18 to 25% of cases, with a non-negligible risk of PE (5,168).

4.6.3. Differential Diagnosis:

SVT should mainly be distinguished from:

- ◆ **Cellulitis / erysipelas:** diffuse febrile skin inflammation.
- ◆ **Deep vein thrombosis:** deeper pain with embolic risk.
- ◆ **Lymphangitis:** infectious erythematous streaking.
- ◆ **Local trauma or hematoma.**

In doubtful cases, Doppler ultrasound helps exclude deep venous involvement (5).

4.6.4. Evolution and complications:

SVT may extend into the deep venous system and progress to DVT, with a subsequent risk of pulmonary embolism. Approximately 25% of SVT cases are associated with deep venous involvement at diagnosis. PE may cause dyspnea and chest pain, sometimes severe.

The main risk factors for progression are: Male sex, Cancer, Previous history of DVT (168,170,171).

4.7. Other Rares Locations:

• Superior Vena Cava Thrombosis:

Usually associated with central venous catheters, mediastinal tumors, or implanted devices. It causes cervicofacial edema, dilated thoracic collateral veins, and dyspnea.

• Inferior Vena Cava Thrombosis:

A rare condition, often due to extension of iliofemoral DVT, tumor compression, or congenital anomalies. It typically causes bilateral lower limb edema.

• Mesenteric Venous Thrombosis:

This affects the mesenteric veins draining the intestine. It presents with severe abdominal pain, often disproportionate to physical findings, and may lead to intestinal ischemia.

• Splenic Vein Thrombosis:

Often related to pancreatitis, pancreatic cancer, or coagulation disorders. It may cause splenomegaly, hypersplenism, or segmental portal hypertension.

- **Renal Vein Thrombosis:**

A rare condition seen in nephrotic syndrome, dehydration, renal tumors, or thrombophilia. It may present with flank pain, hematuria, and renal impairment. (APPENDIX 24)(APPENDIX 25)

- **Ovarian Vein Thrombosis:**

Usually occurs postpartum, more commonly on the right side. It presents with pelvic pain, fever, and adnexal tenderness. It may be complicated by pulmonary embolism. (APPENDIX 24)(APPENDIX 25)

- **Uterine / Pelvic Vein Thrombosis:**

Associated with postpartum state, gynecologic surgery, pelvic infection, or cancer. It causes pelvic pain, fever, and inflammatory syndrome.

- **Penile Vein Thrombosis (Mondor's Disease):**

Superficial thrombosis of the dorsal vein of the penis. It presents as a painful palpable cord on the dorsal penile shaft. Prognosis is generally benign.

- **Retinal Vein Occlusion:**

Affects the central retinal vein or one of its branches. It causes sudden visual loss, especially in patients with hypertension, diabetes, or glaucoma.

- **Adrenal Vein Thrombosis:**

Rare, usually seen in sepsis, antiphospholipid syndrome, or severe hypercoagulable states. It may lead to acute adrenal insufficiency.

- **Digital / Palmar / Plantar Venous Thrombosis:**

Very rare thrombosis of the small veins of the fingers, hand, or foot. It presents with localized pain and a bluish tender nodule.

- **Multivisceral Venous Thrombosis:**

Some severe thrombophilias or cancers may cause simultaneous thrombosis in several territories (splanchnic, cerebral, limbs, renal, etc.).

Chapter 5:

Etiologies and Risk Factors of VTE

5. Etiology and risk factors of venous thromboembolism:

VTE is a multifactorial disease resulting from the interaction of multiple additive or synergistic risk factors, whose coexistence triggers the condition once a thrombosis threshold is reached. Its pathophysiology is based on Virchow's triad: venous stasis, vascular wall injury, and hypercoagulability. Approximately 20% of episodes are provoked by major transient factors (surgery, immobilization, trauma), 20% by active cancer, and the remainder by minor factors or without an identifiable cause (unprovoked VTE) (173). (APPENDIX 26)

5.1. Risk factors:

Risk factors for VTE are divided into two main categories according to their duration: permanent (persistent) factors and transient factors. This classification, established by the International Society on Thrombosis and Haemostasis, allows risk stratification and helps guide therapeutic decisions, particularly regarding the duration of anticoagulation (173).

5.1.1. Permanent (persistent) risk factors:

1) Advanced age :

Advanced age is one of the strongest risk factors for VTE, with incidence increasing exponentially from <1 per 10,000 per year in young adults to approximately 1% per year in the elderly (174). This is explained by multifactorial mechanisms, including increased coagulation factors, endothelial dysfunction, reduced mobility, and accumulation of comorbidities (175,177). In elderly patients, cancer is the leading risk factor (35% of cases), followed by chronic comorbidities (25%) (173).

2) Personal history of VTE :

A personal history of VTE is the strongest risk factor for recurrence, with a 3.5- to 4-fold increased risk (178). The recurrence rate is estimated between 10% and 30% within 5 years after discontinuation of anticoagulation, depending on whether the initial event was provoked or unprovoked (173). This high risk often justifies prolonged anticoagulation, particularly in cases of unprovoked VTE or associated thrombophilia (215,216).

3) Family history of venous thromboembolism (VTE) :

A first-degree family history of VTE significantly increases the risk of venous thrombosis and suggests a genetic predisposition, often related to undiagnosed inherited thrombophilias such as factor V Leiden mutation (prevalence 3–7% in Europe) and the prothrombin gene mutation (1–2%) (173,179). This risk is further increased when multiple family members are affected or when events occur before the age of 50 years (218).

4) Heart failure :

Congestive heart failure increases the risk of VTE by 1.5- to 3-fold, with an incidence of approximately 3.7% in hospitalized patients without thromboprophylaxis.

This increased risk is explained by Virchow's triad, combining blood stasis (low cardiac output), endothelial dysfunction (inflammation, oxidative stress), and hypercoagulability (activation of coagulation and impaired fibrinolysis) (180).

5) Respiratory failure :

Chronic respiratory failure increases the risk of VTE by 2- to 2.4-fold (173). Chronic hypoxia impairs the vascular endothelium and promotes tissue factor expression, while systemic inflammation increases acute-phase proteins (fibrinogen, factor VIII). Platelet activation and elevated D-dimer levels are observed even in stable patients with COPD. Acute exacerbations requiring hospitalization further increase this risk due to immobility and acute inflammation (214,215).

6) Chronic inflammatory diseases :

Inflammatory bowel diseases (Crohn's disease and ulcerative colitis) increase the risk of VTE by 2- to 5.5-fold, with an incidence of approximately 3% (182,183,184).

This increased risk is related to chronic inflammation leading to a hypercoagulable state mediated by pro-inflammatory cytokines (IL-6, TNF- α , IL-1 β). It is also associated with endothelial dysfunction promoting a prothrombotic state. Autoimmune diseases such as rheumatoid arthritis also show an approximately 3-fold increased risk of VTE through similar mechanisms (173,185).

7) Active cancer :

Active cancer is the main persistent risk factor for VTE, accounting for approximately 20% of cases and increasing the risk by 4- to 7-fold compared with the general population. The most thrombogenic sites include the pancreas, lung, stomach, brain, ovary, and hematologic malignancies (173,179).

Systemic chemotherapy further increases the risk by 4- to 6.5-fold, with an incidence of 5–10% in ambulatory patients and up to 30% in metastatic disease (186,187,188).

Certain treatments are particularly high-risk, notably Cisplatin ($\approx 8.5\%$ VTE) and Tamoxifen, which increases the risk by 2- to 5-fold (190,191,192,193).

8) Nephrotic syndrome :

The Nephrotic syndrome significantly increases the risk of VTE, with an incidence of approximately 3% in children and an even higher risk in adults, particularly within the first 6 months and in cases with serum albumin $< 2.5\text{--}2.9\text{ g/dL}$ (196,197,198)

This risk is explained by a hypercoagulable state related to urinary loss of natural anticoagulants (antithrombin III, protein C and S), combined with increased hepatic synthesis of procoagulant factors (V, VIII, fibrinogen, von Willebrand factor) and impaired fibrinolysis ($\uparrow$ PAI-1, $\downarrow$ plasminogen), as well as venous stasis (196,199,200).

9) Obesity:

Obesity ($\text{BMI} \geq 30\text{ kg/m}^2$) increases the risk of VTE by 1.5- to 2-fold, with a dose-dependent effect according to the degree of obesity (173,179). Abdominal obesity is a particularly strong risk factor, especially in women (risk $\times 1.8$) (202,203). The underlying mechanisms include low-grade chronic inflammation leading to a hypercoagulable state ($\uparrow$ tissue factor, $\uparrow$ PAI-1, $\uparrow$ fibrinogen, $\uparrow$ von Willebrand factor) (204,205,206,207), increased platelet activation, and venous compression by abdominal adipose tissue promoting stasis.

5.1.2. Transient risk factors:

● Major transient risk factors :

1) Recent surgery:

Major surgery (procedure lasting > 30 minutes under general anesthesia) accounts for approximately 15% of all VTE cases (179). The risk is highest in major orthopedic procedures (hip or knee replacement), as well as abdominal and pelvic surgeries, particularly in oncological settings. The underlying mechanisms correspond to Virchow's triad: tissue injury with direct endothelial damage, activation of the coagulation cascade through an acute inflammatory response (IL-6, IL-8, TNF- α), and venous stasis secondary to postoperative immobilization (208).

2) Major trauma:

The Major trauma markedly increases the risk of VTE, with an incidence ranging from 3% to 7.6% despite thromboprophylaxis. The pathophysiological mechanisms are similar to those observed in surgery but are often more pronounced due to the extent of tissue injury and systemic inflammation.

Specific risk factors include pelvic, lower limb, or spinal fractures; spinal cord injury (risk 5–6%); traumatic brain injury (risk 3–15% depending on timing of thromboprophylaxis); and the need for blood transfusions (209)

3) Prolonged immobilization:

Prolonged immobilization (bed rest ≥ 3 days) is a major risk factor for VTE, accounting for approximately 15% of cases. It concerns hospitalized patients or those immobilized at home, including cases of paralysis or paresis of the lower limbs (179,192,219).

This risk is mainly related to venous stasis due to the absence of the calf muscle pump, promoting thrombus formation at the level of venous valves (173).

4) Hospitalization for acute medical illness:

Hospitalization for an acute medical condition is a major risk factor for VTE, accounting for approximately 20% of cases. High-risk situations include severe infections, decompensated heart failure, acute respiratory failure, myocardial infarction, and ischemic stroke. The risk persists after hospital discharge, with 35–56% of events occurring in the post-hospitalization period (173,218).

5) Cesarean section:

Cesarean delivery increases the risk of VTE by 4- to 4.9-fold compared with vaginal delivery, with an estimated incidence of approximately 3 cases per 1,000 cesarean sections. The mechanisms involve surgical trauma, direct endothelial injury, and physiological changes in coagulation related to pregnancy and the postpartum period. The risk is highest during the first 2 to 6 weeks postpartum (178,208).

- **Minor transient risk factors :**

- 1) Prolonged travel (> 4–6 hours):**

Long-distance travel by air or car lasting more than 4 to 6 hours modestly increases the risk of VTE. The mechanisms include prolonged sitting leading to venous stasis in the lower limbs, dehydration causing hemoconcentration and increased blood viscosity, and compression of the popliteal veins by the seat, impairing venous return. Although considered a minor factor, the risk increases with travel duration and in the presence of additional risk factors (obesity, estrogen-containing contraception, thrombophilia, prior VTE) (173,179).

- 2) Pregnancy and postpartum:**

Pregnancy and the postpartum period are hypercoagulable states associated with a 4- to 5-fold increased risk of VTE, with an incidence of 0.5–2 per 1,000 pregnancies and a peak during the first 6 weeks postpartum.

This risk is related to coagulation changes ($\uparrow$ procoagulant factors, $\downarrow$ protein S, resistance to activated protein C), venous stasis due to pelvic and inferior vena cava compression by the gravid uterus, and the additional impact of postpartum factors (delivery-related trauma and inflammation) (178,210,211).

- 3) Estrogen-containing contraception and hormone replacement therapy:**

Estrogen-progestin contraception increases the risk of VTE by 3- to 4-fold, with an incidence of approximately 7–10 per 10,000 women-years compared with 2–10 per 10,000 in non-users. Menopausal hormone replacement therapy (HRT) also increases this risk by 1.5- to 2.5-fold, particularly with oral administration and in a dose-dependent manner (213,220,221).

This risk is related to the effects of estrogens on hemostasis, leading to increased procoagulant factors and decreased natural anticoagulants, resulting in a prothrombotic imbalance. Oral administration carries a higher risk than transdermal or vaginal forms, which appear less thrombogenic (222,223).

- 4) Acute infection and COVID-19 :**

Acute infections, particularly COVID-19, represent a major transient risk factor for VTE, with an incidence ranging from 7.7% to 31% in hospitalized patients, and higher rates in intensive care settings.

This risk is explained by involvement of Virchow's triad: endothelial dysfunction due to SARS-CoV-2-induced endotheliitis, hypercoagulability driven by systemic inflammation (activation of coagulation and imbalance of hemostatic factors), and venous stasis secondary to immobilization (224,225,226,227).

- 5)— Dehydration:**

Dehydration is an acquired risk factor for VTE, particularly in elderly individuals, hospitalized patients, and during prolonged travel (218,245,246).

It increases thrombotic risk by promoting hemoconcentration, leading to increased blood viscosity, and by inducing a hypercoagulable state with elevated hematocrit and coagulation factors (von Willebrand factor, fibrinogen). A serum osmolality > 297 mOsm/kg increases the risk of VTE by 4.7-fold in patients with ischemic stroke (247).

- 6) Venous catheterization:**

Central venous catheters increase the risk of upper extremity deep vein thrombosis, with an incidence ranging from 2% to 67%. The pathophysiological mechanisms involve direct endothelial injury occurring both at the time of insertion and from prolonged contact between the catheter and the venous wall, venous stasis resulting from partial obstruction of blood flow, and activation of the coagulation cascade induced by the presence of a foreign body (173).

The risk is further influenced by catheter-related factors (type, position, and duration of use) as well as patient-related factors, including cancer and thrombophilia (250,251).

5.2. Etiologies:

5.2.1. Constitutional thrombophilias:

Constitutional (hereditary) thrombophilias are genetic abnormalities that predispose to venous thrombosis. They are identified in approximately 30% to 50% of patients with unprovoked VTE (173,179) (APPENDIX 27)

1) Antithrombin III deficiency:

The Antithrombin III deficiency is the most severe inherited thrombophilia, with a prevalence of 0.02% to 0.2% in the general population and a 10- to 50-fold increased risk of VTE (179).

Antithrombin is the main inhibitor of thrombin and factors Xa, IXa, XIa, and XIIa; its deficiency results in excessive and uncontrolled thrombin generation. The deficiency may be quantitative (type I) or qualitative (type II). These patients exhibit relative resistance to Heparin, whose anticoagulant effect is mediated through potentiation of antithrombin (252,253,254,255).

2) Protein C deficiency:

Protein C deficiency has a prevalence of 0.2% to 0.5% in the general population and increases the risk of VTE by 7- to 10-fold (179). Activated protein C inactivates factors Va and VIIIa, thereby limiting thrombin generation. The deficiency may be quantitative (type I) or qualitative (type II).

Homozygous or compound heterozygous forms may present in the neonatal period with purpura fulminans, requiring lifelong anticoagulation. (256,257)

3) Protein S deficiency:

Protein S deficiency, with a prevalence of 0.03% to 0.13%, increases the risk of VTE by 5- to 10-fold (179).

Protein S acts as a cofactor for activated protein C and contributes to the inactivation of factors Va and VIIIa. The deficiency may be quantitative (types I and III) or qualitative (type II). Inflammatory states, pregnancy, and hypoxia reduce free protein S levels, thereby increasing thrombotic risk (266,267).

4) Factor V Leiden mutation / Activated protein C resistance:

Factor V Leiden is the most common inherited thrombophilia, with a prevalence of 3% to 7% in Europe. The G1691A mutation leads to resistance to inactivation by activated protein C, resulting in excessive thrombin generation. The risk of VTE is increased 3- to 8-fold in heterozygous individuals and 50- to 80-fold in homozygous individuals. Acquired resistance to activated protein C may also occur in certain conditions, including pregnancy, estrogen-containing contraception, and aPL syndrome (173,179,276).

5) Hyperhomocysteinemia:

Hyperhomocysteinemia (levels > 15–18 $\mu\text{mol/L}$) is associated with a 2- to 3-fold increased risk of VTE. It may be genetic (e.g., MTHFR C677T mutation) or acquired (vitamin B6, B9, or B12 deficiency, renal failure, hypothyroidism). The main mechanism involves endothelial toxicity mediated by oxidative stress, leading to endothelial dysfunction and inhibition of fibrinolysis. However, vitamin B supplementation has not been shown to reduce thrombotic risk in clinical trials (278).

5.2.2. Acquired thrombophilias:

1) Antiphospholipid syndrome:

APS is the most common acquired thrombophilia, characterized by the presence of persistent antiphospholipid antibodies associated with thrombotic or obstetric events. It is mediated by autoantibodies primarily directed against β_2 -glycoprotein I, leading to a prothrombotic state through endothelial and platelet activation, stimulation of tissue factor expression, and inhibition of natural anticoagulant pathways (228,230).

2) Cancer:

Cancer is a major cause of acquired thrombophilia, accounting for approximately 20% of VTE episodes. The risk varies according to tumor type, with strong associations for cancers of the pancreas, lung, stomach, brain, ovary, and hematologic malignancies. It results from multiple mechanisms, including tumor production of procoagulant factors, activation of endothelial cells, platelets, and leukocytes, as well as the effects of anticancer treatments and immobilization (173,179).

3) Behçet's disease:

Behçet's disease is a systemic vasculitis affecting vessels of all sizes, associated with a VTE prevalence of 15% to 40%, often revealing the disease.

Thrombosis in this condition is primarily inflammation-driven, related to neutrophil hyperactivation with

formation of neutrophil extracellular traps (NETs) and endothelial dysfunction, leading to highly adherent and poorly emboligenic thrombi (232,233,234).

4) Paroxysmal nocturnal hemoglobinuria:

PNH is a rare acquired clonal hematologic disorder characterized by complement-mediated intravascular hemolysis and a markedly increased risk of thrombosis, which represents the leading cause of morbidity and mortality. The incidence of thrombosis is approximately 21%, with events frequently occurring at atypical sites (Budd–Chiari syndrome, cerebral venous thrombosis, inferior vena cava thrombosis). The pathophysiological mechanisms are multifactorial and predominantly complement-mediated (236,237,238,239).

Chapter 6:

Therapeutic Management

6. Therapeutic Management:

6.1. Objectives :

- To limit thrombus extension and promote its resolution (recanalization) through anticoagulation, which inhibits thrombus formation and allows progressive venous and pulmonary recanalization.
- To prevent embolic migration and the occurrence of pulmonary embolism by inhibiting thrombus detachment and progression toward the pulmonary circulation.
- To reduce mortality, particularly in severe pulmonary embolism, especially in high-risk forms associated with shock or hypotension ($\approx 5\%$).
- To restore patency of the pulmonary arterial bed and improve cardiopulmonary function through vascular recanalization and symptomatic management of respiratory and hemodynamic failure.
- To prevent thromboembolic recurrence in the medium and long term, with recurrence rates reaching 10% at 1 year and 36% at 10 years in unprovoked cases.
- To prevent long-term functional sequelae, particularly post-thrombotic syndrome and CTEPH (279,280)

6.2. Therapeutic strategies:

6.2.1. Symptomatic treatment:

1) Oxygénothérapie:

Oxygen therapy is recommended in pulmonary embolism, even in the absence of hypoxemia, as it reduces pulmonary vascular resistance and right ventricular afterload; a FiO_2 of approximately 40% is generally sufficient. Hypoxemia, mainly related to ventilation/perfusion mismatch, usually responds to nasal oxygen therapy; in case of persistence, an intracardiac shunt should be investigated (102,281).

2) Fluid expansion:

Cautious fluid administration (≤ 500 mL) may improve cardiac output in selected hemodynamically stable patients. Excessive fluid loading may worsen right ventricular dysfunction, supporting a restrictive and individualized approach (102).

3) Inotropic and vasopressor therapy:

In cases of shock or hypotension, Norepinephrine is the vasopressor of choice due to its hemodynamic efficacy and minimal pulmonary effects. Dobutamine may be used in low cardiac output states, either alone or in combination, despite a potential decrease in systemic vascular resistance (102).

4) Pulmonary vasodilators:

Inhaled vasodilators (e.g., nitric oxide) reduce right ventricular afterload and improve right ventricular function, although no mortality benefit has been demonstrated. Systemic vasodilators such as Sildenafil and Epoprostenol have not shown clinical efficacy in acute PE (102).

6.2.2. Curative treatment:

• Medical treatment:

Medical management is based on anticoagulant therapy after exclusion of contraindications.

1) Anticoagulants:

1- Unfractionated Heparin (UFH): (APPENDIX 28)

2- Low Molecular Weight Heparin (LMWH): (APPENDIX 29)

Tinzaparin, an LMWH derived from unfractionated heparin, primarily acts through inhibition of factor Xa and, to a lesser extent, factor IIa. It is characterized by reduced dependence on renal clearance, allowing its use in patients with creatinine clearance ≥ 20 mL/min without dose adjustment, and generally does not require routine laboratory monitoring or dose modification in obese patients (282,284)

3- Vitamin K Antagonists (VKAs) :

3.1 General considerations:

Vitamin K antagonists (VKAs) are oral anticoagulants that inhibit vitamin K epoxide reductase, thereby

preventing the synthesis of vitamin K–dependent coagulation factors (II, VII, IX, X) as well as proteins C and S (285,286).

Their anticoagulant effect is delayed, requiring several days to become fully effective, particularly for agents with a long half-life.

- **Target INR:** 2.5 (range 2.0–3.0).
- **Monitoring:** Daily INR until stabilization, followed by progressive spacing (every 1–4 weeks, up to 12 weeks in stable patients).
- **Administration:** Once-daily intake at a fixed time (usually in the evening) (285,287,288).

3.2 VKA agents: (APPENDIX 30)

3.3 Adverse effects of VKAs:

The main complications include:

- **Hemorrhagic complications:** major bleeding (0.5%/year), intracranial hemorrhage (0.2%/year), epistaxis, hematomas, and gastrointestinal bleeding (286,291,292).
- **Paradoxical thrombotic events:** early skin necrosis (day 3–8), gangrene, and purple toe syndrome (3–8 weeks) (285).
- **Drug-specific effects:** severe hypersensitivity reactions with Phenindione (cutaneous and pulmonary manifestations, CD4+ T-cell–mediated immune mechanism) (289,290).
- **Chronic effects:** osteoporosis, vascular calcifications, reduced bone mineral density, gastrointestinal disorders, and allergic reactions (285,292).
- **Teratogenicity:** fetal skeletal abnormalities in case of exposure during pregnancy (285,293).

3.4 Contraindications of VKAs:

- **Absolute contraindications:** pregnancy (especially first trimester), active bleeding, severe hepatic impairment, hypersensitivity (notably to Phenindione).
- **Precautions:** severe renal impairment, elderly patients (reduced initial dose), protein C or S deficiency (increased risk of skin necrosis) (285,287,294,295).

3.5. Drug interactions: (APPENDIX 31)

NEW ANTICOAGULANTS

1. **Injectable forms:** (APPENDIX 32)
2. **DOACs (Direct Oral Anticoagulants):** (APPENDIX 33)
3. **Common contraindications of DOACs**

Direct oral anticoagulants (DOACs) are contraindicated in patients with mechanical heart valves, Antiphospholipid syndrome, pregnancy, or breastfeeding. Caution is required in cases of severe renal impairment (contraindicated for Dabigatran if creatinine clearance < 30 mL/min) or advanced hepatic disease (296,297,298).

4- Thrombolytic therapy:

Alteplase (rt-PA) is currently the reference agent for thrombolysis in pulmonary embolism, administered at the standard dose of 100 mg over 2 hours. Other agents are now rarely used in clinical practice, while reduced-dose regimens (25–50 mg) may decrease the risk of bleeding.

Thrombolysis is mainly indicated in high-risk pulmonary embolism, but its use is limited by the risk of major bleeding, particularly intracranial hemorrhage, estimated at approximately 1.7% (294,299,301).

6.2.3. Surgical treatment:

1) Inferior vena cava filter:

The Placement of an inferior vena cava (IVC) filter is indicated in cases of absolute contraindication to anticoagulation or recurrence of pulmonary embolism despite well-conducted anticoagulant therapy.

Retrievable filters are preferred, as they provide temporary protection while limiting long-term complications, provided they are removed early—ideally between 29 and 54 days after insertion. Routine use in adequately anticoagulated patients offers no clinical benefit and is not recommended (294,301)

2) Thrombectomy:

Mechanical thrombectomy is a percutaneous technique aimed at directly removing thrombi from the

pulmonary circulation. It is used in selected severe cases of pulmonary embolism, particularly when other therapeutic options are contraindicated or ineffective. Data from the FLAME and FLARE trials show improvement in hemodynamic parameters, with a low rate of major bleeding ($\approx 1\%$) (294,301).

3) Surgical embolectomy:

Surgical pulmonary embolectomy, performed under extracorporeal circulation, is an alternative in severe pulmonary embolism, particularly after failure or contraindication of thrombolysis.

Despite the severity of clinical presentations, outcomes are generally favorable, with mortality rates ranging from 1% to 15%, and particularly high survival in patients not requiring prior intensive care (249,301).

6.2.4. Non-pharmacological measures:

Elastic compression therapy:

Routine use of compression stockings for the prevention of post-thrombotic syndrome after DVT is no longer recommended due to lack of demonstrated benefit, particularly in the SOX trial. However, they retain a role in symptomatic management to reduce lower limb edema and discomfort. Below-knee stockings with 20–30 mmHg pressure are generally preferred due to comparable efficacy and better tolerance (288,311,312).

6.3. Indications and treatment strategy:

6.3.1. Deep vein thrombosis (DVT):

1) Compression stockings:

Current American Society of Hematology 2020 guidelines suggest not using compression stockings routinely in patients with DVT, regardless of post-thrombotic syndrome risk. However, they may help reduce edema and pain in selected patients with acute DVT (312).

2) Anticoagulant therapy:

DOACs are first-line treatment for most patients with DVT not associated with cancer. Rivaroxaban or Apixaban can be initiated immediately without prior parenteral anticoagulation. In patients treated with Warfarin, therapy can be initiated in the outpatient setting with bridging parenteral anticoagulation until the INR is stabilized within the target range (2–3) (287).

3) Duration of treatment:

For DVT provoked by a major transient risk factor, 3 months of anticoagulation are recommended, after which treatment may be discontinued (299,312). For unprovoked DVT or DVT associated with persistent risk factors, indefinite anticoagulation is suggested if bleeding risk is low and the patient prefers continuation.

The 2020 ASH guidelines suggest shorter primary treatment duration (3–6 months) rather than extended durations (6–12 months). After 6 months of full-dose anticoagulation, reduced-dose Apixaban (2.5 mg twice daily) or Rivaroxaban (10 mg once daily) may be considered for long-term secondary prevention (279). (APPENDIX 35)

4) Surgical treatment:

Surgical venous thrombectomy may be considered in selected patients with extensive acute iliofemoral DVT, particularly in cases of phlegmasia cerulea dolens (massive DVT with risk of venous gangrene) (8). However, this intervention is rarely performed in current practice.

5) Special situations:

◆ DVT and pregnancy:

Low Molecular Weight Heparin is the anticoagulant of choice during pregnancy due to the absence of placental transfer and fetal bleeding risk, whereas DOACs are contraindicated during pregnancy and breastfeeding (300,301). Treatment of acute DVT relies on weight-adjusted therapeutic LMWH (e.g., enoxaparin 1 mg/kg every 12 h or dalteparin 200 IU/kg/day). Treatment should be continued throughout pregnancy and for at least 6 weeks postpartum, with a minimum total duration of 3–6 months (300). In cases of severe renal impairment (creatinine clearance < 30 mL/min), Unfractionated Heparin is preferred (301).

◆ DVT and renal impairment:

In patients with creatinine clearance < 30 mL/min, LMWH is contraindicated due to accumulation risk.

Unfractionated Heparin or Warfarin are preferred options in this population.

Among DOACs, Apixaban may be used with caution in patients with creatinine clearance 15–29 mL/min at a reduced dose (2.5 mg twice daily if at least two of the following are present: age $\geq$ 80 years, weight $\leq$ 60 kg, serum creatinine $\geq$ 1.5 mg/dL) (294,302).

◆ **DVT and cancer:**

In patients with active cancer, LMWH or certain DOACs (edoxaban, rivaroxaban, apixaban) are recommended as first-line therapy if creatinine clearance $\geq$ 30 mL/min, with caution in gastrointestinal cancers due to increased bleeding risk. Anticoagulation should be continued for at least 6 months and then individualized, with extension in the presence of active cancer. Reduced-dose Apixaban after 6 months is an effective option with a lower bleeding risk (API-CAT 2025) (279,302,303,305,306).

6.3.2. Pulmonary Embolism (PE):

1) Risk Stratification and Treatment:

The management of pulmonary embolism depends on risk stratification according to the new AHA/ACC 2026 clinical categories (Categories A–E) (102). (APPENDIX 34)

2) Thrombolysis in Intermediate-Risk PE:

Systemic thrombolysis with tenecteplase reduced the incidence of the primary endpoint (all-cause mortality or hemodynamic collapse) from 5.6% to 2.6% in the PEITHO trial. However, this benefit was accompanied by a significant increase in major bleeding events (6.3% versus 1.5%). Consequently, routine systemic thrombolysis is not recommended for patients with intermediate-risk PE (279,308,309).

3) Management of Complications:

● **Post-Thrombotic Syndrome:**

Post-thrombotic syndrome affects 20 to 63% of patients following deep vein thrombosis. Although elastic compression stockings have historically been recommended, current guidelines do not advocate their routine use. Nevertheless, below-knee compression stockings of 20–30 mmHg may be considered to alleviate symptoms in symptomatic patients (8,299,280,310).

● **Chronic Thromboembolic Pulmonary Hypertension (CTEPH):**

Patients with a history of PE should be systematically queried regarding PE-related symptoms and functional limitations at each clinical visit for a minimum of one year, in order to screen for chronic thromboembolic pulmonary disease or other etiologies of dyspnea and functional impairment (102).

4) Monitoring:

● **Anticoagulation Monitoring:**

For DOACs: Routine coagulation monitoring is not required (65,287). However, periodic assessment of renal and hepatic function is recommended, particularly in elderly patients or those with pre-existing renal or hepatic impairment (279,65).

For VKAs: INR should be measured at least twice weekly during the transition from parenteral anticoagulation to oral therapy. Once the patient is maintained on VKA monotherapy with a stable INR between 2.0 and 3.0, INR testing frequency may be progressively reduced to a minimum of once monthly (302).

For LMWH: When administered at weight-adjusted therapeutic doses for the treatment or prevention of VTE, it remains unclear whether LMWH dosing requires upward adjustment during pregnancy. Some authorities advocate periodic measurement of anti-Xa levels 4 to 6 hours post-injection (target range: 0.6–1.0 IU/mL); however, other studies have demonstrated that few patients actually require dose escalation when weight-based dosing is employed (300).

For UFH: Coagulation parameters (aPTT, INR, platelet count) should be established at baseline, with aPTT monitored approximately every 4 hours upon initiation of continuous intravenous infusion and adjusted to maintain an aPTT of 1.5 to 2 times the control value (228,311,312).

● **Clinical Monitoring:**

All anticoagulated patients should be monitored for signs and symptoms of hemorrhage. Following anticoagulation initiation, hemoglobin, hematocrit, and platelet count should be measured at least every 2 to 3 days during the first 14 days of inpatient management, and subsequently every 2 weeks or as clinically indicated.

Patients should be reassessed at regular intervals to determine whether anticoagulation therapy should be continued beyond the initial treatment phase, taking into account the risk of VTE recurrence, hemorrhagic risk, renal and hepatic function, treatment adherence, and patient preferences.

In patients with a history of pulmonary embolism, systematic screening for PE-related symptoms and functional limitations should be performed at each clinical encounter for a minimum of one year, in order to identify potential chronic thromboembolic pulmonary disease (102,279,302).

Chapter 7:
**Prevention of Venous
Thromboembolism**

7. Prevention of Venous Thromboembolism:

7.1. Primary Prevention:

Primary prevention of VTE is based on identifying hospitalised patients at increased thromboembolic risk and adopting an individualised strategy balancing thrombotic and bleeding risks, rather than routine universal prophylaxis (313,314).

Pharmacological options include LMWHs, UFH, fondaparinux, and DOACs, depending on the patient's clinical profile, clinical context, and bleeding risk. When anticoagulation is contraindicated, mechanical methods such as intermittent pneumatic compression may be used (313).

In surgical patients, prophylaxis is particularly indicated after high-risk procedures, including major general, gynaecological, and orthopaedic surgeries such as hip and knee arthroplasty. In medical inpatients, validated tools such as the Padua and IMPROVE scores help guide prophylaxis decisions (315,316).

Preventive strategies should also address modifiable risk factors such as obesity, sedentary lifestyle, and smoking, particularly in individuals with additional thrombotic risk factors (317).

The tools used in the preventive strategy of VTE differ according to whether they are intended to assess the initial risk of occurrence or the risk of recurrence after a first event. The main scoring systems used in these settings, together with their interpretation, are presented in APPENDIX 36.

7.2. Secondary Prevention:

Secondary prevention is based on extending anticoagulant therapy beyond the initial treatment phase in order to reduce the risk of thromboembolic recurrence. The duration of anticoagulation mainly depends on whether the initial event was provoked or unprovoked, as well as on the individual bleeding risk assessment.

In patients with unprovoked VTE or persistent risk factors, long-term or even indefinite anticoagulation is often recommended when bleeding risk is considered acceptable, due to the higher risk of recurrence after treatment discontinuation. In contrast, when VTE is associated with a major transient risk factor such as surgery, trauma, or temporary immobilisation, treatment is generally limited to three months (318,319).

For extended prevention, reduced-dose direct oral anticoagulants (DOACs) may be considered in selected patients after the standard therapeutic phase. Long-term anticoagulation is particularly indicated after a second episode of VTE because of the significantly increased risk of recurrence (318,320).

Risk prediction tools may help estimate recurrence risk in specific clinical settings; however, they remain complementary and do not replace clinical judgement or guideline-based recommendations.

7.3. Tertiary Prevention:

Tertiary prevention aims to reduce the long-term consequences of venous thromboembolism (VTE), including functional sequelae, chronic complications, and their impact on quality of life. It is part of post-acute management and relies on structured clinical follow-up tailored to the initial thromboembolic event (321).

It may include monitoring symptom progression, management of post-thrombotic syndrome following deep vein thrombosis, screening for chronic thromboembolic pulmonary hypertension (CTEPH) after pulmonary embolism, as well as additional measures such as compression therapy or rehabilitation depending on the clinical context (322).

III. Materials and methods

1. Introduction:

Venous thromboembolic disease (VTE), encompassing deep vein thrombosis (DVT) and pulmonary embolism (PE), is a common and potentially severe condition resulting from thrombus formation within the venous circulation. It is associated with multiple acquired and inherited risk factors, including thrombophilia, malignancy, immobilization, surgery, trauma, inflammatory diseases, and hormonal factors. Clinical manifestations are heterogeneous and range from limb pain and edema to dyspnea and life-threatening complications.

Despite its clinical importance, epidemiological data regarding VTE remain limited in the Laghouat region, and comprehensive information concerning its epidemiological, clinical, etiological, therapeutic, and evolutionary characteristics is currently lacking.

2. Objectives:

2.1. Main objective:

To determine the in-hospital prevalence of venous thromboembolic disease in the Internal Medicine Department of Laghouat Mixed Hospital over a five-year period extending from January 1st, 2021 to December 31st, 2025.

2.2. Secondary objectives:

- To identify the main risk factors associated with VTE.
- To describe the characteristics and distribution of thrombotic localizations.
- To analyze the clinical presentation of affected patients.
- To determine the principal etiologies associated with thromboembolic disease.
- To evaluate the therapeutic modalities used in clinical practice.
- To assess clinical outcomes and complications observed during follow-up.

3. Materials and Methods:

3.1. Study design:

This was a descriptive retrospective study conducted in the Internal Medicine Department of Laghouat Mixed Hospital over a five-year period extending from January 1st, 2021 to December 31st, 2025. The study included all patients hospitalized for objectively confirmed venous thromboembolic disease during the study period.

Data were collected using a standardized case report form designed for the purposes of the study.

3.2. Study population:

Among the 5,968 hospitalizations recorded during the study period, all patients diagnosed with objectively confirmed venous thromboembolic disease based on clinical presentation, biological investigations, and imaging findings were included.

3.3. Inclusion criteria:

- Patients hospitalized for objectively confirmed VTE.
- Availability of complete and exploitable medical records.

3.4. Non inclusion criteria:

- Arterial thrombosis.
- Unconfirmed thrombotic diagnoses.
- Incomplete or non-exploitable medical records.

3.5. Study procedure:

Hospital archives were reviewed in order to identify patients diagnosed with venous thromboembolic disease during the study period. Data extracted from medical records included epidemiological, clinical, biological, radiological, etiological, therapeutic, and evolutionary characteristics.

Information was collected using a standardized case report form (Appendix 37). Missing data were supplemented whenever possible through patient follow-up consultations or by contacting treating physicians.

3.6. Statistical analysis:

- Data entered and analyzed using *IBM SPSS Statistics version 27.0.0*.
- Quantitative variables were expressed as mean $\pm$ standard deviation, median, or extremes according to data distribution. Qualitative variables were expressed as frequencies and percentages.
- Graphs and charts were created using *Microsoft Excel 2019*.
- Statistical analyses were performed using the Chi-square (χ^2) test and Fisher's exact test, according to the conditions of application.
- References were managed using *Zotero version 7.0.30*.

3.7. Ethical considerations:

Patient confidentiality and anonymity were strictly respected throughout the study. Data collection was performed exclusively for scientific and academic purposes.

3.8. Limitations of the study:

The principal limitations of this study were related to its retrospective design, including incomplete medical records, limited accessibility of archived files, and missing follow-up data for certain patients. These constraints may have introduced selection and information bias and limited the evaluation of etiological factors, clinical outcomes, and long-term disease evolution.

4. Outcome Measures:

4.1. Primary outcome:

Hospital prevalence of VTE:

Hospital prevalence = Number of patients with confirmed VTE / Total number of hospitalizations in Internal Medicine

4.2. Secondary outcomes:

4.2.1. Clinical and diagnostic profile:

- Circumstances of diagnosis and presenting symptoms.
- Distribution of thrombotic localizations, including lower-limb DVT, upper-limb thrombosis, pulmonary

embolism, cerebral venous thrombosis, abdominal thrombosis, and other atypical sites.

4.2.2. Risk factor profile:

- Prolonged immobilization.
- Recent surgery or trauma.
- Active malignancy.
- Hormonal factors (pregnancy, postpartum period, oral contraceptive use).
- Personal or family history of thromboembolic disease.
- Thrombophilia.
- COVID-19 infection.
- Associated comorbidities.

4.2.3. Paraclinical assessment:

Imaging investigations:

- Venous Doppler ultrasonography.
- CT angiography and/or MR angiography.

Biological investigations:

- D-dimer assay.
- Thrombophilia screening, including antithrombin deficiency, protein C and protein S deficiencies, Factor V Leiden mutation, prothrombin G20210A mutation, and antiphospholipid antibodies.

4.2.4. Etiological profile:

The principal etiologies investigated included:

- Immobilization.
- Surgery.
- Malignancy.
- Hormonal factors.
- Pregnancy and postpartum status.
- COVID-19 infection.
- Inflammatory and autoimmune diseases.
- Idiopathic forms.

4.2.5. Therapeutic management:

Therapeutic modalities included:

- Low-molecular-weight heparins (LMWH).
- Unfractionated heparin (UFH).
- Direct oral anticoagulants (DOACs).
- Vitamin K antagonists (VKA).

Both initial and long-term anticoagulant therapies were analyzed.

4.2.6. Clinical outcomes and prognosis:

Clinical evolution under treatment was assessed based on:

- Symptom regression.
- Stabilization or resolution of thrombosis.
- Occurrence of complications.

The complications evaluated included:

- Hemorrhagic events.
- Recurrence of thrombosis.
- Extension of thrombotic lesions.
- Post-thrombotic syndrome.
- Mortality.

IV. Results

5. Results and Statistical Analysis:

5.1. Hospital prevalence of venous thromboembolism:

5.1.1. Prevalence of venous thromboembolism in hospitalized patients:

Table 01: Hospital prevalence of VTE disease among all patients hospitalized in the Internal Medicine Department over the study period (from January 01, 2021, to December 31, 2025).

Parameter	Value
Number of hospitalized patients	5968
Number of confirmed VTE cases	267
Hospital prevalence formula	$(267 / 5968) \times 100$
Hospital prevalence (%)	4.47%

Commentary:

- This table summarizes the hospital prevalence of venous thromboembolic disease (VTE) among patients admitted to the Internal Medicine Department during the study period (January 2021 to December 2025). The overall prevalence was estimated at 4.47%.

5.1.2. Distribution of Patients According to Year of Hospitalization:

Table 02: Annual Distribution of VTE Cases During the Study Period.

Year	Frequency (n)	Percentage (%)
2025	61	22.8
2024	57	21.3
2023	57	21.3
2022	48	18.0
2021	44	16.5
Total	267	100.0

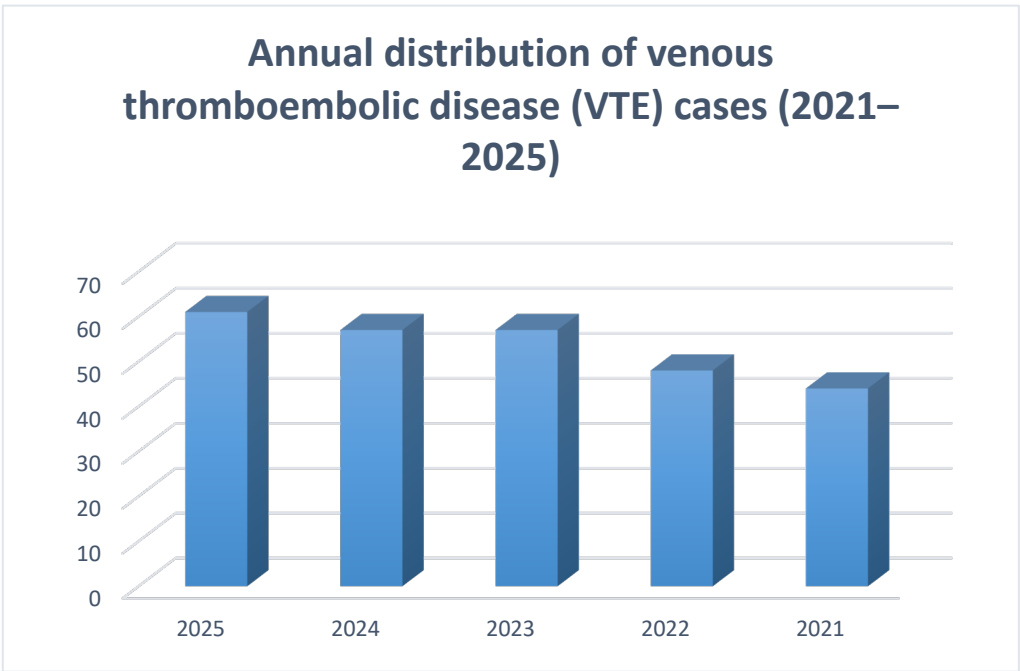


Diagram 01: Annual VTE Cases Overview: 2021–2025.

Commentary:

- The distribution of cases over the study period shows a relatively stable trend, with a slight predominance in 2025 (22.8%) n= 61, followed closely by 2023 and 2024 (21.3% each) n=57, suggesting no major annual fluctuation in case occurrence.
- A gradual decrease in the number of cases is observed when moving backward in time, reaching its lowest level in 2021 (16.5%) n= 44.
- The cumulative percentages indicate that more than half of the cases (65.5%) n= 175 were recorded during the last three years (2023–2025), highlighting a concentration of cases in the most recent period of the study.

5.2. Description of Socio-Demographic Characteristics:

5.2.1. Age Distribution: Descriptive Statistics and Categorization into Age Groups:

Table 03: Descriptive Statistics of Age.

Age (years)	Value
Mean	50.80
Median	46.00
Standard deviation	19.91
Minimum	16
Maximum	92

Commentary:

- The mean age of the study population was 50.80 years, indicating that the cohort is predominantly composed of middle-aged individuals.
- The median age (46 years) is slightly lower than the mean, suggesting a moderately right-skewed distribution, with the presence of older patients influencing the average.
- The relatively high standard deviation (19.91 years) reflects a wide dispersion of ages, highlighting substantial heterogeneity within the study population.
- The age range is broad, extending from 16 to 92 years, which indicates that the condition under investigation affects a wide spectrum of age groups, from adolescents to elderly individuals.

Table 04: Age-group distribution of the study population expressed in years.

Age group (years)	Frequency (n)	Percentage (%)
≤ 20	5	1.9
21 – 40	99	37.1
41 – 60	68	25.5
≥ 61	95	35.6
Total	267	100.0

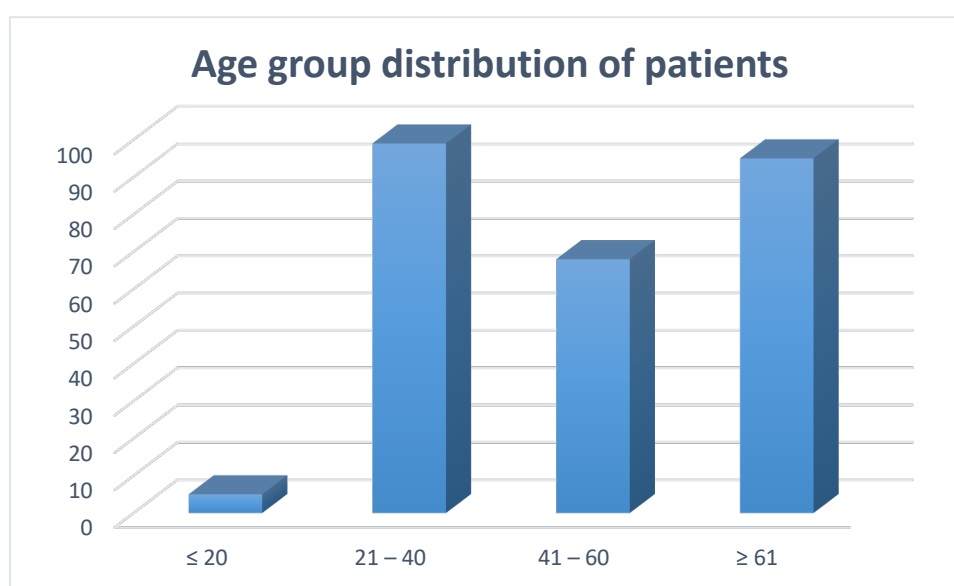


Diagram 02: Percentage Distribution of Patients by Age Group.

Commentary:

- The age group distribution shows that the majority of patients fall within the 21–40 years (36.8%) $n=99$ and ≥ 61 years (35.3%) $n=95$ categories, indicating a bimodal tendency with peaks in both young adult and elderly populations.
- Patients aged 41–60 years represent 25.3% $n=68$ of cases, while those aged ≤ 20 years constitute only a small proportion (1.9%) $n=5$, highlighting the low representation of younger individuals in the study.
- The cumulative percentages demonstrate that nearly two-thirds of patients (64.4%) are under 60 years of age, whereas more than one-third (35.6%) are aged 61 years and above.

5.2.2. Sex Distribution: Frequencies, Percentages, and Sex Ratio:

Table 05: Sex distribution of the study population.

Sex	Frequency (n)	Percentage (%)
Male	94	35.2
Female	173	64.8
Total	267	100.0

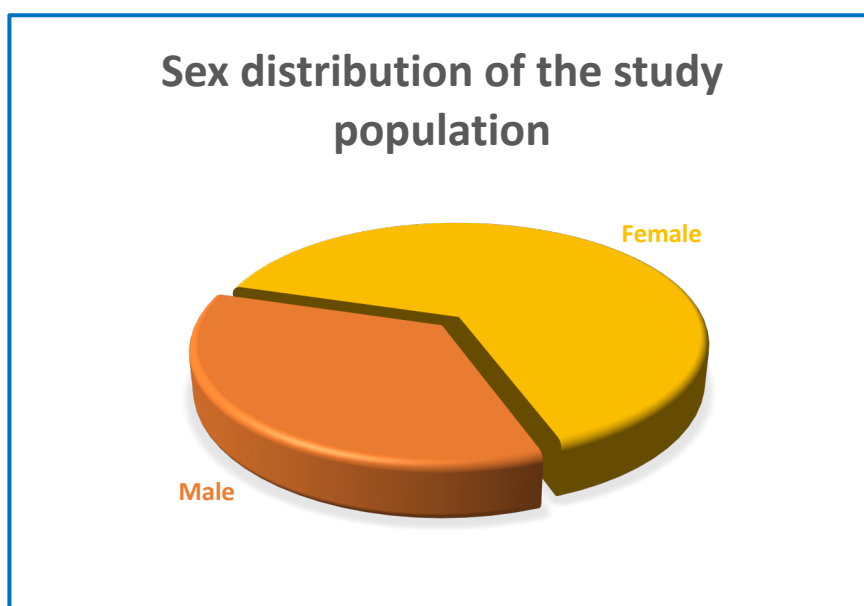


Diagram 03: Graphical representation of the sex distribution of the study population.

Sex Ratio:

The sex ratio, defined as the ratio of males to females, was calculated as $94/173$, yielding a value of 0.54. This indicates a clear female predominance in the study population, with approximately one male for every two females.

Sex ratio (Male/Female) = $94 / 173 = 0.54$ one male for every two females.

Commentary:

- The study population shows a clear predominance of female patients, accounting for 64.8% $n=173$ of cases, compared to 35.2% $n=94$ for males, indicating a marked imbalance in sex distribution.
- The graphical representation (diagram) visually confirms this disparity, with a substantially larger proportion of females, reinforcing the observation of female predominance within the cohort.
- The calculated sex ratio (Male/Female) is 0.54, reflecting that males are nearly half as numerous as females in this population. This further supports the significant female predominance observed.

5.3. Analysis of Medical History:

5.3.1. Personal History of Venous Thromboembolism:

Table 06: Distribution of medical history of VTE in the study population.

Category	Frequency (n)	Percentage (%)
No medical history of VTE	229	89.5
Positive medical history of VTE	27	10.5
Total	256	100

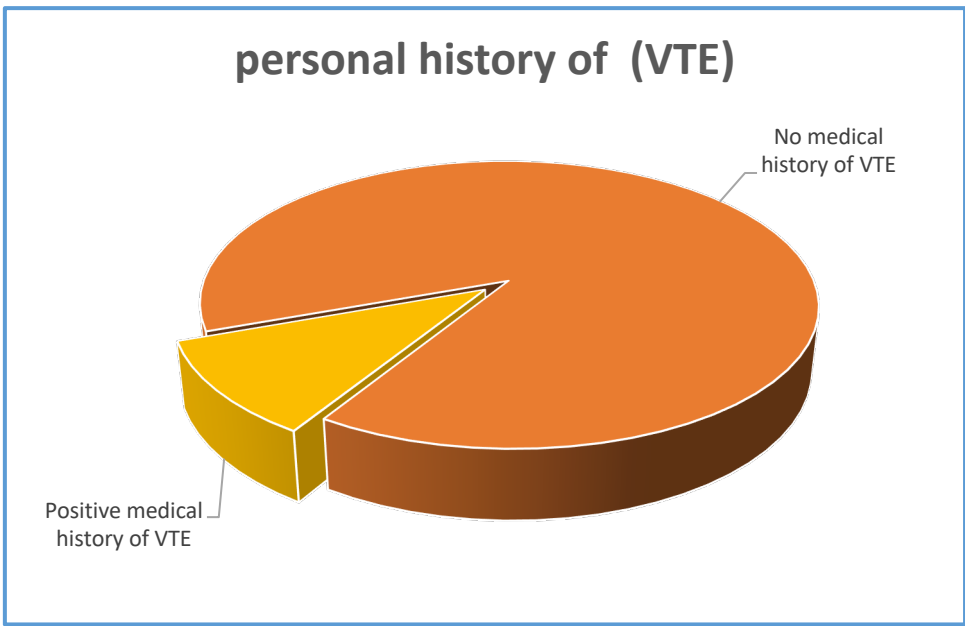


Diagram 04: Distribution of personal history of VTE in the study population.

Commentary:

- A medical history of VTE was absent in the majority of the study population, accounting for 229 patients (89.5%), indicating that most participants had no prior thromboembolic events.
- Conversely, a positive medical history of VTE was observed in a relatively small proportion of cases, involving 27 patients (10.5%), suggesting a low prevalence of previous thromboembolic disease within the studied cohort.
- Notably, a small proportion of data was missing (4.1%, n = 11).

Table 07: Distribution of personal history of VTE components in the study population.

Variable	Category	Frequency (n)	Percentage (%)
Lower limb DVT	No	247	95.4
	Yes	12	4.6
Upper limb DVT	No	259	99.6
	Yes	1	0.4
Pulmonary Embolism (PE)	No	255	98.1
	Yes	5	1.9
Cerebral Venous Thrombosis (CVT)	No	255	98.1
	Yes	5	1.9
Other VTE History	No	253	97.3
	Yes	7	2.7
Total		267	100

Table 08: Prevalence of positive personal history of VTE by subtype.

Variable	Frequency (n)	Percentage (%)
Lower limb DVT	12	40
Upper limb DVT	1	3.33
Pulmonary Embolism (PE)	5	16.67
Cerebral Venous Thrombosis (CVT)	5	16.67
Other VTE history	7	23.33
Total	30	100

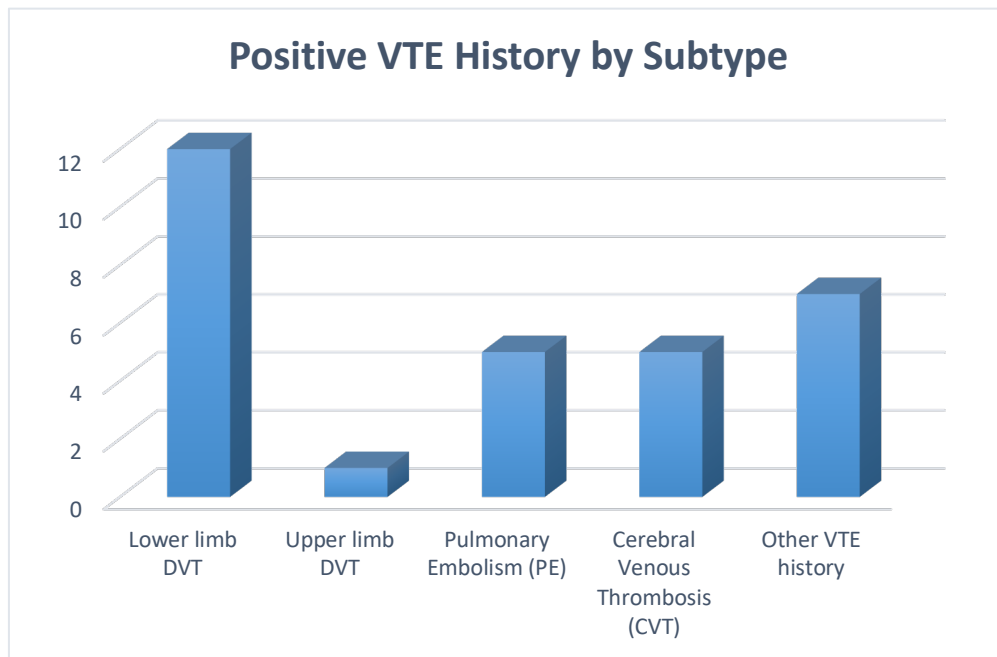


Diagram 05: Distribution of positive personal history of VTE according to clinical subtype.

Commentary:

- The analysis of prior VTE history demonstrates a clear predominance of patients with no previous thromboembolic events across all categories, ranging from 95.4% in lower limb DVT to 99.6% in upper limb DVT, confirming the rarity of antecedent VTE in this cohort.
- When present, prior VTE events were uncommon. Lower limb DVT was the most frequent previous event (4.6%), followed by “other VTE history” (2.7%), which included atypical venous thromboses such as renal vein thrombosis, portal vein thrombosis, inferior vena cava thrombosis, ovarian vein thrombosis, right atrial thrombosis, as well as splenic, mesenteric, and portal system thromboses. Pulmonary embolism and cerebral venous thrombosis each accounted for 1.9%, while upper limb DVT remained rare (0.4%).
- Overall, lower limb DVT represents the main prior VTE manifestation, whereas other subtypes remain infrequent. The corresponding table and diagram consistently reflect this distribution, emphasizing the dominance of lower limb DVT and the minimal contribution of upper limb DVT.

5.3.2. Family History of Venous Thromboembolism:

Table 09: Distribution of family history of VTE in the study population.

Category	Frequency (n)	Percentage (%)
No family history of VTE	159	93.5
Positive family history of VTE	11	6.5
Total	170	100

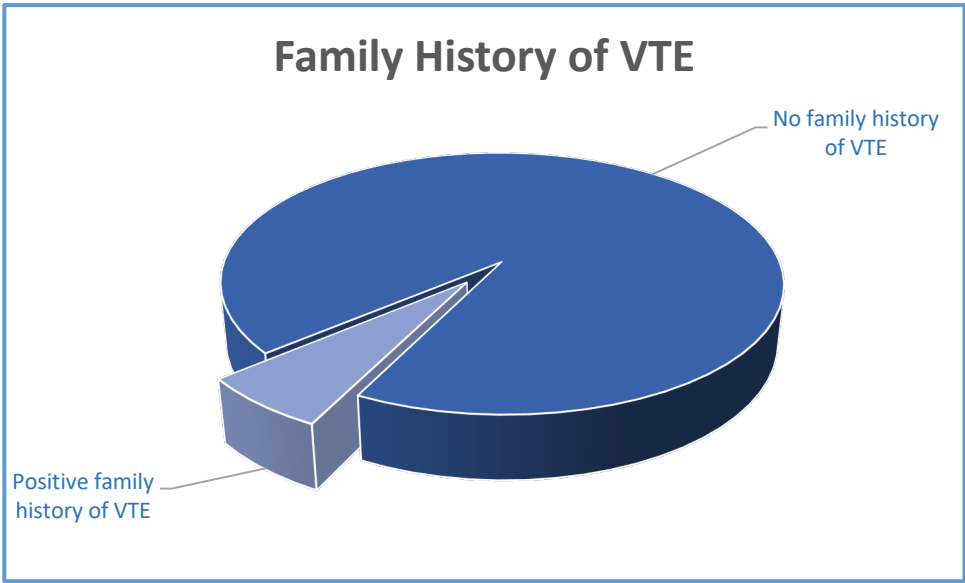


Diagram 06: Distribution of positive personal history of VTE according to clinical subtype.

Commentary:

- The majority of patients had no family history of VTE, representing 159 cases (93.5% of valid data), indicating a low frequency of reported familial thromboembolic risk.
- A positive family history of VTE was observed in a small proportion of patients (11 cases, 6.5%), suggesting that hereditary predisposition was uncommon in this cohort.
- A considerable proportion of data was missing (36.3%, n = 97).
- The associated diagram confirms the clear predominance of patients without a family history of VTE and highlights the low occurrence of positive familial cases.

5.3.3. Medical history of hypertension and diabetes in the study population:

Table 10: Distribution of hypertension and diabetes medical history in the study population.

Variable	Frequency (n)	Percentage (%)
Hypertension (HBP)	61	22.8
Diabetes	55	20.6

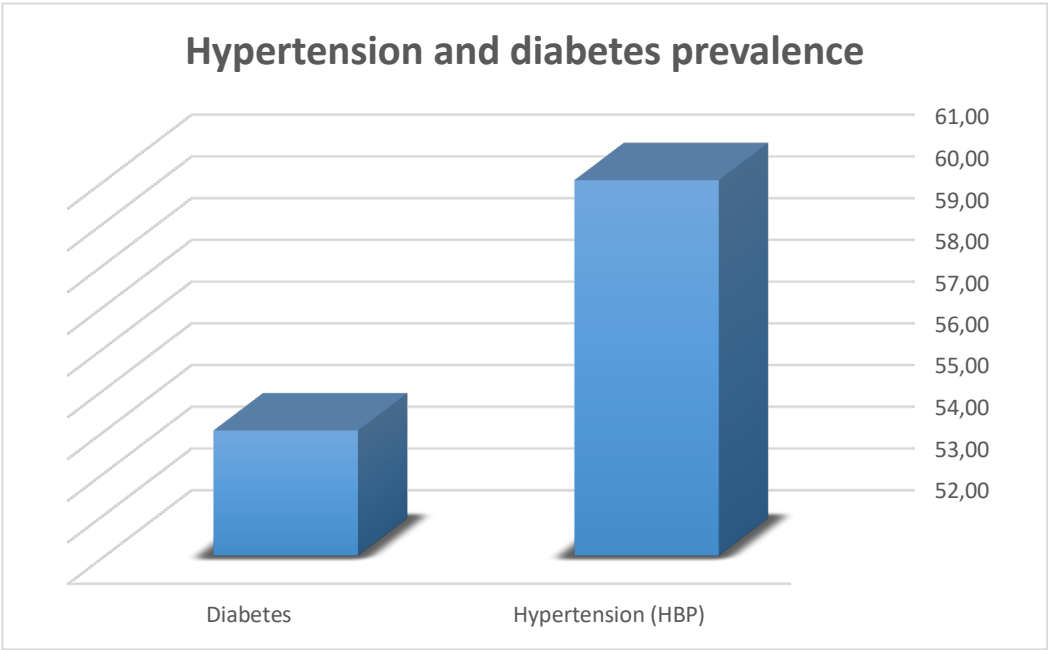


Diagram 07: Distribution of hypertension and diabetes prevalence in the study population.

Commentary:

- The distribution of cardiometabolic comorbidities shows that hypertension was present in 61 patients (22.8%), while diabetes was reported in 55 patients (20.6%), indicating comparable frequencies of these two conditions within the study population.
- Both conditions affected approximately one-fifth of the patients, reflecting a moderate prevalence of these comorbidities in the cohort.
- The associated diagram provides a clear visual comparison of the two variables, illustrating the slightly higher prevalence of hypertension compared to diabetes, although the difference between them remains limited.
- Overall, the graphical representation highlights the relatively similar distribution of these two major comorbid conditions among the study participants.

5.4. Distribution of toxic habits in the study population:

Table 11: Distribution of tabaco as a risk behavior in the study population.

Tobacco Smoking (Risk Behavior)	Frequency (n)	Percentage (%)
Non-smoker	158	83.6
Smoker	31	16.4
Total	189	100.0

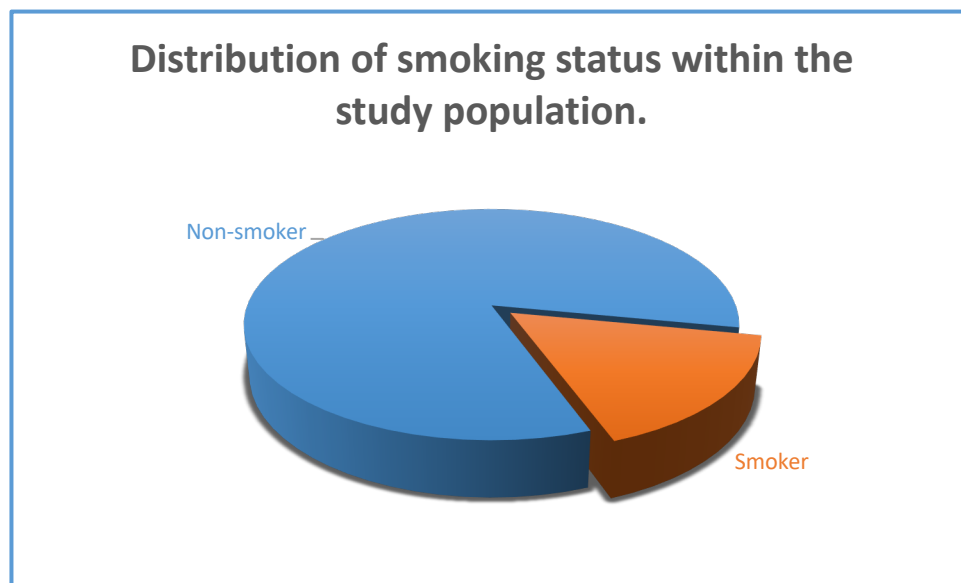


Diagram 08: Distribution of tabaco as a risk factor in the study population.

Commentary:

- Risk behaviors were absent in the majority of the study population, accounting for 158 patients (58.7%), indicating that more than half of the participants did not exhibit identifiable behavioral risk factors.
- Conversely, risk behaviors were present in a relatively small proportion of cases, observed in n= 31 patients (11.5%), suggesting a limited contribution of these behaviors within the studied cohort.
- Notably, a substantial proportion of data was missing (29.7%, n = 80).

Table 12: Distribution of Alcohol Consumption as a Risk Behavior in the Study Population.

Alcohol Consumption (Risk Behavior)	Frequency (n)	Percentage (%)
No alcohol use	188	97.92
Alcohol use present	4	2.08
Total	192	100.0

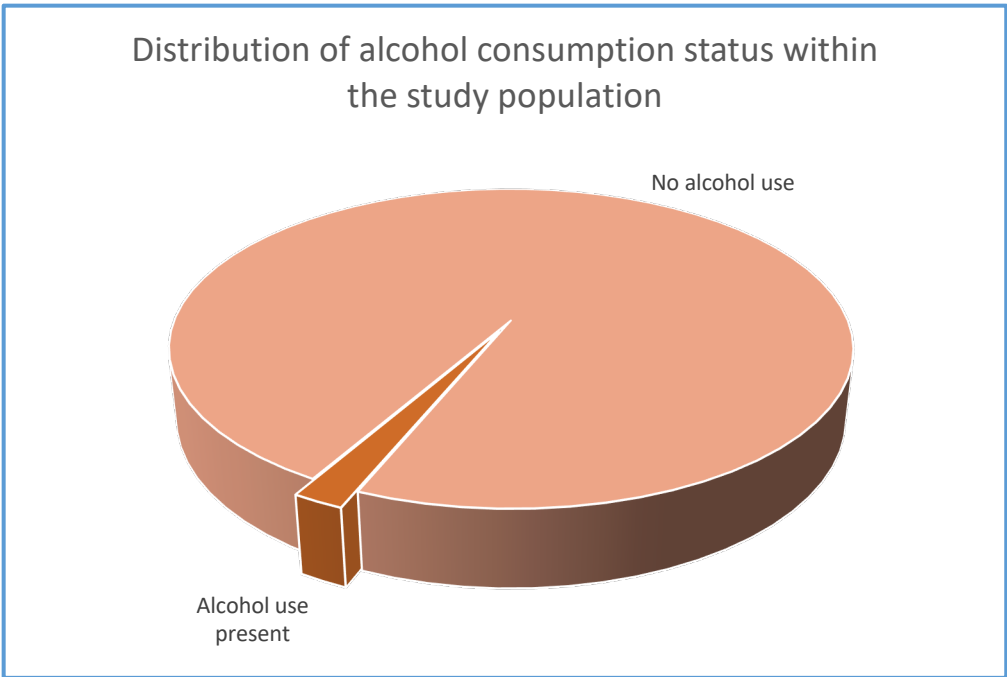


Diagram 09: Distribution of Alcohol Consumption as a Risk Behavior in the Study Population.

Commentary:

- Alcohol consumption was absent in the majority of the study population, accounting for 188 patients (69.9%), indicating that most participants did not report alcohol use as a behavioral risk factor.
- Conversely, alcohol consumption was present in a very small proportion of cases, observed in only 4 patients (1.5%), suggesting a low prevalence of this exposure within the studied cohort.
- Notably, a considerable proportion of data was missing (28.6%, n = 77).

5.5. Risk Factors:

5.5.1. Associated Clinical and Acquired Risk Factors:

Table 13: Distribution of acquired and clinical risk factors for VTE.

Risk factor	Category	Frequency (n)	Percentage (%)
Cancer	No	234	89.3
	Yes	28	10.7
Recent major surgery	No	229	87.4
	Yes	33	12.6
Prolonged immobilization	No	221	84.4
	Yes	41	15.6
Heart failure	No	256	97.7
	Yes	6	2.3
Recent long-distance travel	No	262	100
	Yes	0	0
Chronic inflammatory disease	No	244	93.1
	Yes	18	6.9
Nephrotic syndrome	No	261	99.6
	Yes	1	0.4
Congenital heart disease	No	262	100
	Yes	0	0
Other risk factors	No	225	85.9
	Yes	37	14.1
Total		267	100

Table 14: Prevalence of positive VTE risk factors.

Risk factor	Frequency (n)	Percentage (%)
Cancer	28	17.07
Recent major surgery	33	20.12
Prolonged immobilization	41	25
Heart failure	6	3.66
Recent long-distance travel	0	0
Chronic inflammatory disease	18	10.98
Nephrotic syndrome	1	0.61
Congenital heart disease	0	0
Other risk factors	37	22.56
Total	164	100

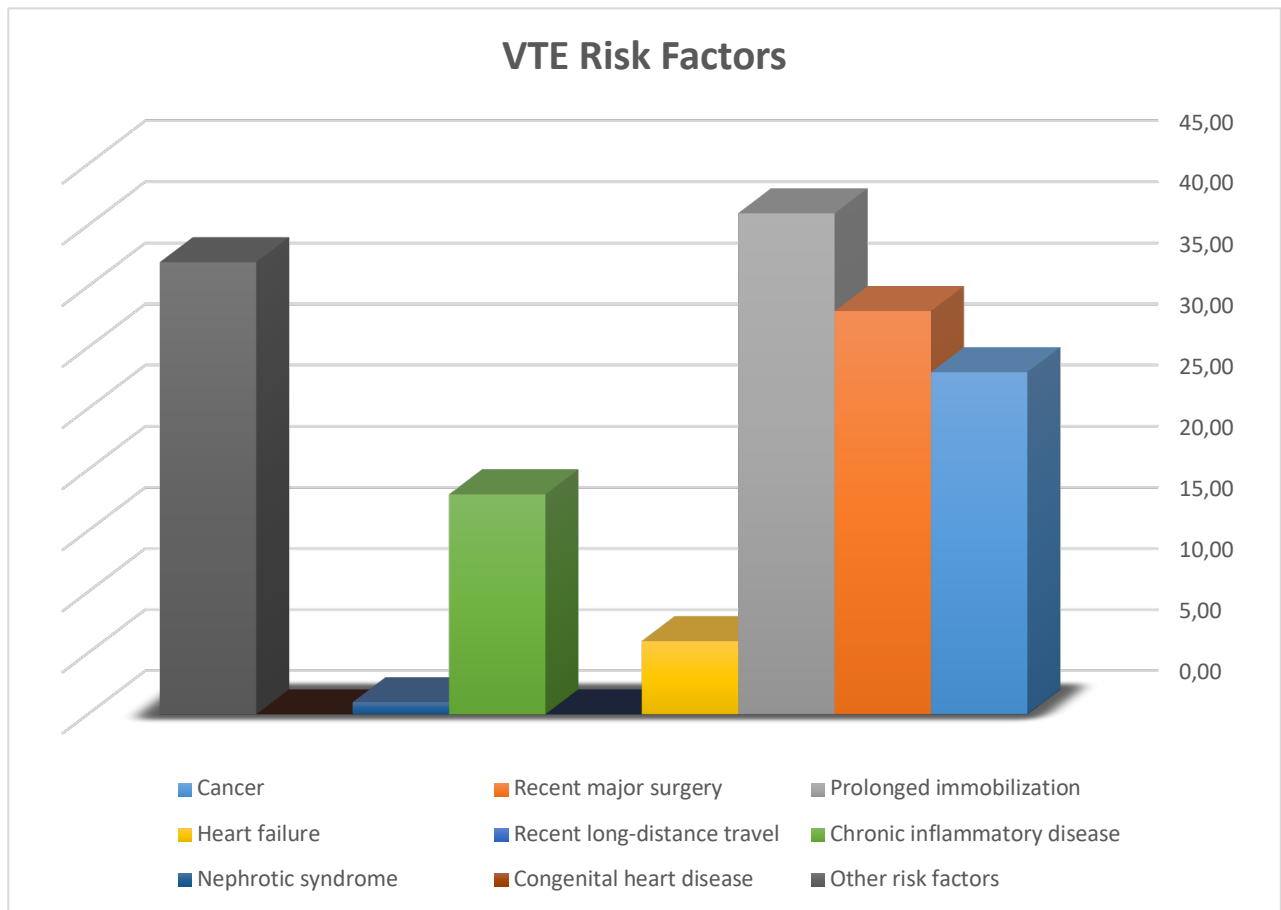


Diagram 10: Distribution of positive VTE risk factors in the study population.

Commentary:

- In the total study population (n = 267), cancer (10.7%), recent major surgery (12.6%), and prolonged immobilization (15.6%) were the most frequently observed risk factors, whereas chronic inflammatory disease, heart failure, and nephrotic syndrome were less common. No cases were related to recent long-distance travel or congenital heart disease, indicating their negligible contribution in this cohort.
- In the subgroup of patients with at least one identified risk factor (n = 164; 61.4%), the distribution shows a clear predominance of prolonged immobilization (25%), followed by “other risk factors” (22.56%), recent major surgery (20.12%), and cancer (17.07%). Chronic inflammatory diseases accounted for a moderate proportion (10.98%), while heart failure (3.66%) and nephrotic syndrome (0.61%) remained rare.
- The corresponding diagram of the second table visually confirms this pattern, highlighting immobilization, surgery, and malignancy as the leading contributors to the risk profile, with a relatively heterogeneous distribution among the remaining factors.
- The “other risk factors” category was heterogeneous, chronic renal failure (IRC/IRCT), malignancy (KT), hepatopathy with hypertension, cirrhosis, COVID-19, HIV infection, obesity, and absence of anticoagulant treatment (non-AC use). This reflects a mixed group of clinical conditions contributing variably to thrombotic risk.

5.5.2. Female-Specific Risk Factors:

Table 15: Distribution of female-specific risk factors in the study population.

Variable	Category	Frequency (n)	Percentage (%)
Contraception use	No	88	65.7
	Yes	46	34.3
Ongoing pregnancy	No	143	98.6
	Yes	2	1.4
Postpartum status	No	118	80.8
	Yes	28	19.2
Total		173	100

Table 16: Prevalence of positive female-specific risk factors.

Variable	Frequency (n)	Percentage (%)
Contraception use	46	60.53
Ongoing pregnancy	2	2.63
Postpartum status	28	36.84
Total	76	100

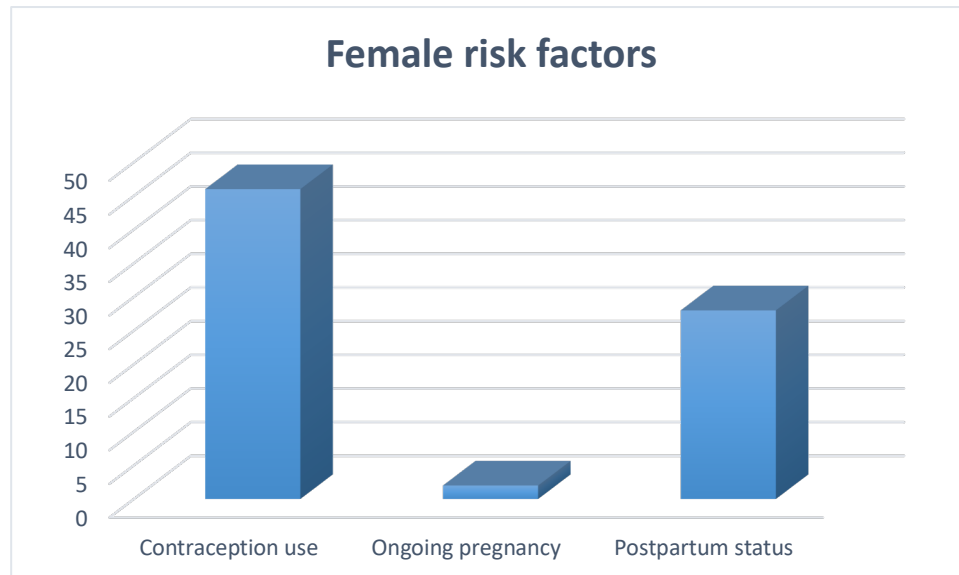


Diagram 11: Distribution of positive female-specific risk factors in the study population.

Commentary:

- The first table describes the distribution of female-specific risk factors in the study population. Contraceptive use was reported in 46 women (34.3%), while 88 women (65.7%) did not use contraception. Ongoing pregnancy was rare, observed in only 2 cases (1.4%), whereas 143 women (98.6%) were not pregnant. Postpartum status was present in 28 women (19.2%), while 118 (80.8%) were not in the postpartum period.
- The distribution of reproductive status shows that contraception use was the most frequent category (60.53%), followed by postpartum status (36.84%), while ongoing pregnancy was uncommon (2.63%).
- Overall, out of 173 female patients included in the study, 76 presented specific female-related risk factors, indicating that approximately 43.9% of the female population had at least one reproductive or hormonal risk exposure.

5.5.3. Number of venous thromboembolism risk factors per patient:

Table 17: Distribution of the number of VTE risk factors per patient.

Number of risk factors	Frequency (n)	Percentage (%)
0	95	35.58
1	116	43.44
2	46	17.23
≥3	10	3.75
Total	267	100

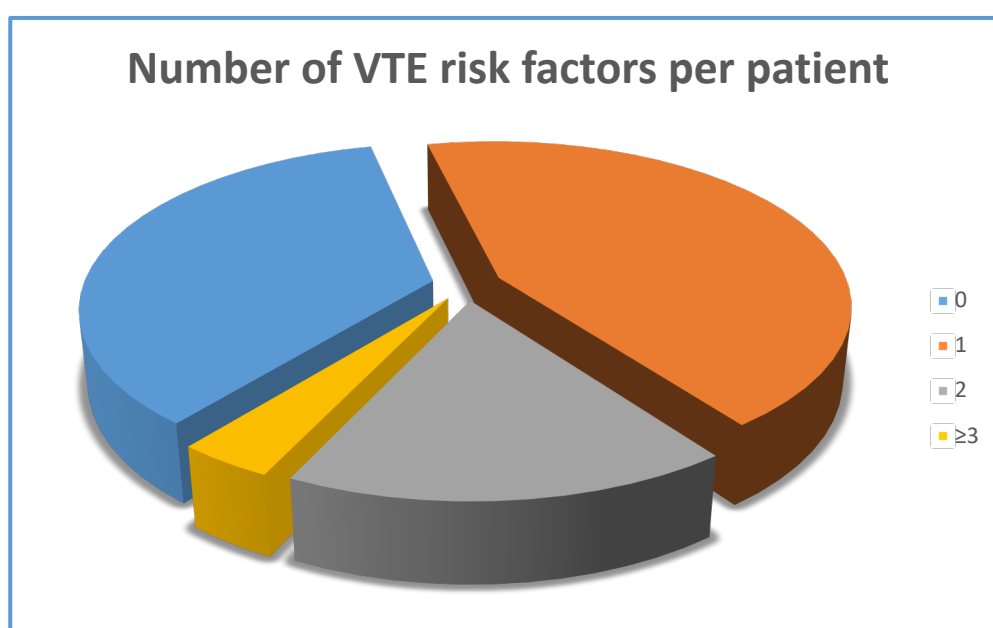


Diagram 12: Distribution of the cumulative number of VTE risk factors per patient in the study population.

Commentary:

- The distribution of the number of venous thromboembolism (VTE) risk factors per patient shows that the majority of patients had at least one risk factor. Specifically, 116 patients (43.6%) presented with one risk factor, representing the most frequent category.
- A substantial proportion of patients had no identified risk factors, accounting for 94 cases (35.3%). Meanwhile, 46 patients (17.3%) had two risk factors
- Patients with three or more risk factors were relatively uncommon, representing only 10 cases (3.8%).
- The associated diagram clearly illustrates this distribution, highlighting the predominance of patients with one risk factor, followed by those with no risk factors, while higher numbers of risk factors are progressively less frequent.

5.5.4. Distribution of Venous Thromboembolism Risk Factors According to Sex:

Table 18: Distribution of risk factors according to sex.

Risk factor	Male	Female	p-value	Significance
Cancer risk factor	7 (12.7%)	21 (15.4%)	0.204	Not significant
Recent major surgery	5 (9.1%)	28 (20.6%)	0.008	Significant
Prolonged immobilization	5 (9.1%)	36 (26.5%)	0.001	Significant
Heart failure	2 (3.6%)	4 (2.9%)	0.895	Not significant
Chronic inflammatory disease	9 (16.4%)	9 (6.6%)	0.196	Not significant
Nephrotic syndrome	1 (1.8%)	0 (0.0%)	0.180*	Not significant
Other risk factors	13 (23.6%)	24 (17.6%)	0.919	Not significant
No identifiable risk factor	13 (23.6%)	14 (10.3%)	—	—
Total patients	55 (100%)	136 (100%)	—	—

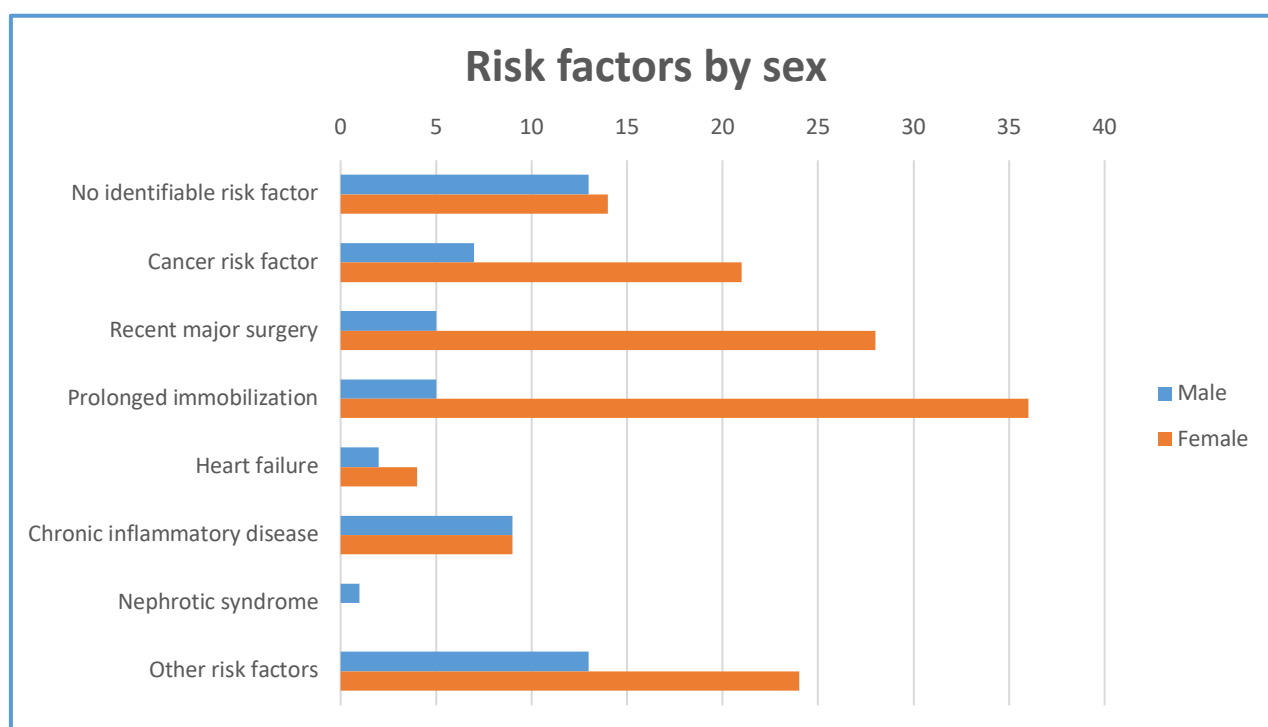


Diagram 13: Distribution of the cumulative number of VTE risk factors per patient in the study population.

Commentary:

- Female patients showed significantly higher frequencies of transient acquired thromboembolic risk factors, particularly recent major surgery (20.6% vs 9.1%; $p = 0.008$) and prolonged immobilization (26.5% vs 9.1%; $p = 0.001$), compared with male patients. In contrast, no statistically significant sex-related differences were observed for cancer-associated risk factors, heart failure, chronic inflammatory disease, nephrotic syndrome, or other miscellaneous risk factors ($p > 0.05$). Moreover, males more frequently presented without identifiable risk factors (23.6% vs 10.3%).
- The diagram confirms these findings by showing a clear predominance of females in categories related to surgery and prolonged immobilization, whereas males were more represented among patients without identifiable risk factors.

5.5.5. History of COVID-19 Infection as a Potential Risk Factor for Venous Thromboembolic Disease:

Table 19: History of COVID-19 Infection Among Patients Hospitalized for VTE.

History of COVID-19 Infection	Frequency (n)	Valid Percentage (%)
Documented previous COVID-19 infection	20	8.6
No documented history of COVID-19 infection	213	91.4
Total valid cases	233	100.0

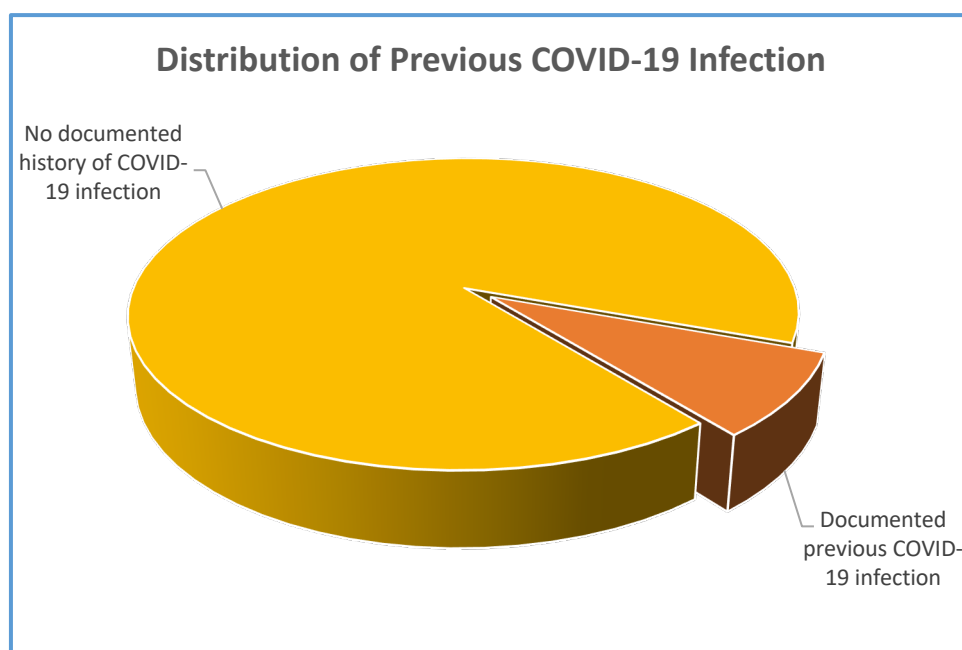


Diagram 14: Distribution of Patients According to Documented History of Previous COVID-19 Infection in the VTE Cohort

Commentary:

- A documented previous history of COVID-19 infection was identified in 20 patients, accounting for 8.6% of valid cases. In contrast, 213 patients (91.4%) had no documented prior SARS-CoV-2 infection. Data regarding COVID-19 history were missing in 34 patients out of the total study population (267 cases).
- The associated diagram demonstrates a clear predominance of patients without a previous history of COVID-19 infection, while only a small proportion of the cohort reported documented prior infection.

5.6. Comparison of Risk Factors According to Type of Venous Thromboembolism:

5.6.1. Lower-limb deep vein thrombosis:

Table 20: Association between lower limb thrombosis and risk factors.

Risk Factor	DVT Positive (n=139)	Percentage (%)	p-value	significance
No identified risk factor	69	49.6%	—	—
Cancer risk factor	15	10.8%	0.464	Not significant
Recent major surgery	15	10.8%	0.349	Not significant
Prolonged immobilization	32	23.0%	<0.001	Significant
Chronic inflammatory disease	8	5.8%	0.448	Not significant
Other risk factors	23	16.5%	0.231	Not significant

Commentary:

- Among patients with lower limb DVT, 139 cases were included in the analysis, with 3 missing observations. Nearly half (49.6%) had no identifiable risk factors, suggesting a substantial proportion of idiopathic cases.
- Prolonged immobilization was the most frequent risk factor (23.0%) and the only variable significantly associated with DVT ($p < 0.001$), highlighting its major role in thrombosis development.
- In contrast, cancer, recent major surgery, chronic inflammatory diseases, and other risk factors were less frequent and showed no statistically significant association ($p > 0.05$).
- Overall, these findings emphasize the predominance of immobilization as a key modifiable risk factor, while a large proportion of cases remain unexplained.
- It is important to note that the total percentages cannot be summed to 100% because several patients had multiple concurrent risk factors, leading to overlapping categories rather than mutually exclusive groups.

5.6.2. Pulmonary Embolism:

Table 21: Association between pulmonary embolism and risk factors.

Risk Factor	PE Positive (n=55)	Percentage (%)	p-value	Statistical significance
No identified risk factor	28	50.0%	—	—
Cancer risk factor	8	14.3%	0.173	Not significant
Recent major surgery	12	21.4%	0.025	Significant
Prolonged immobilization	12	21.4%	0.179	Not significant
Chronic inflammatory disease	5	8.9%	0.492	Not significant
Other risk factors	7	12.5%	0.694	Not significant

Commentary:

- Among patients with pulmonary embolism (n = 56), half of the cases (50.0%) had no identifiable risk factors, indicating a substantial proportion of idiopathic events.
- Recent major surgery was the only factor significantly associated with pulmonary embolism (21.4%, p = 0.025), supporting its role as a major transient precipitating factor.
- Although prolonged immobilization and cancer-related factors were relatively frequent (21.4% and 14.3%, respectively), their associations were not statistically significant (p > 0.05).
- Other factors, including chronic inflammatory diseases and risk factors, were less prevalent and did not show any significant relationship with pulmonary embolism.
- Overall, these findings highlight the predominance of recent surgery as the main significant risk factor, while emphasizing the high proportion of unexplained cases.
- It should be noted that percentages do not add up to 100%, as several patients presented multiple concomitant risk factors. Therefore, the categories are overlapping rather than mutually exclusive.

5.6.3. Cerebral vein thrombosis:

Table 22: Association between cerebral venous thrombosis and risk factors.

Risk Factor	CVT Positive (n=43)	Percentage (%)	p-value	Statistical significance
No identified risk factor	37	86.0%	—	—
Cancer risk factor	2	4.7%	0.232	Not significant
Recent major surgery	9	20.9%	0.072	Not significant (trend)
Prolonged immobilization	2	4.7%	0.030	Significant
Chronic inflammatory disease	2	4.7%	0.529	Not significant
Other risk factors	6	14.0%	0.972	Not significant

Commentary:

- The analysis of risk factors for cerebral venous thrombosis (CVT) shows no statistically significant association for cancer, recent major surgery, chronic inflammatory diseases, or other risk factors, except for prolonged immobilization, which is significantly associated with CVT ($p = 0.030$).
- The majority of CVT patients had no identified risk factor (86.0%), suggesting a substantial proportion of idiopathic or multifactorial cases not documented in this cohort.
- It is important to note that only one missing case was recorded in the entire dataset, with no meaningful impact on the overall robustness of the analysis.
- The sum of percentages exceeds 100% because patients could have more than one risk factor simultaneously; thus, the variables are not mutually exclusive.

5.7. Analysis of Thrombotic Localization:

Table 23: Distribution of VTE Disease According to Anatomical Localization.

Localization	Frequency (n)	Percentage % (Responses)	Percentage % (of Patients)
Pulmonary embolism	56	17.9%	21.0%
Cerebral venous thrombosis	44	14.1%	16.5%
Portal abdominal thrombosis	17	5.4%	6.4%
Mesenteric abdominal thrombosis	11	3.5%	4.1%
Budd-Chiari syndrome	4	1.3%	1.5%
Other locations	28	9.0%	10.5%
DVT lower limb	142	45.5%	53.2%
DVT upper limb	10	3.2%	3.7%
Total	312	100%	116.9%

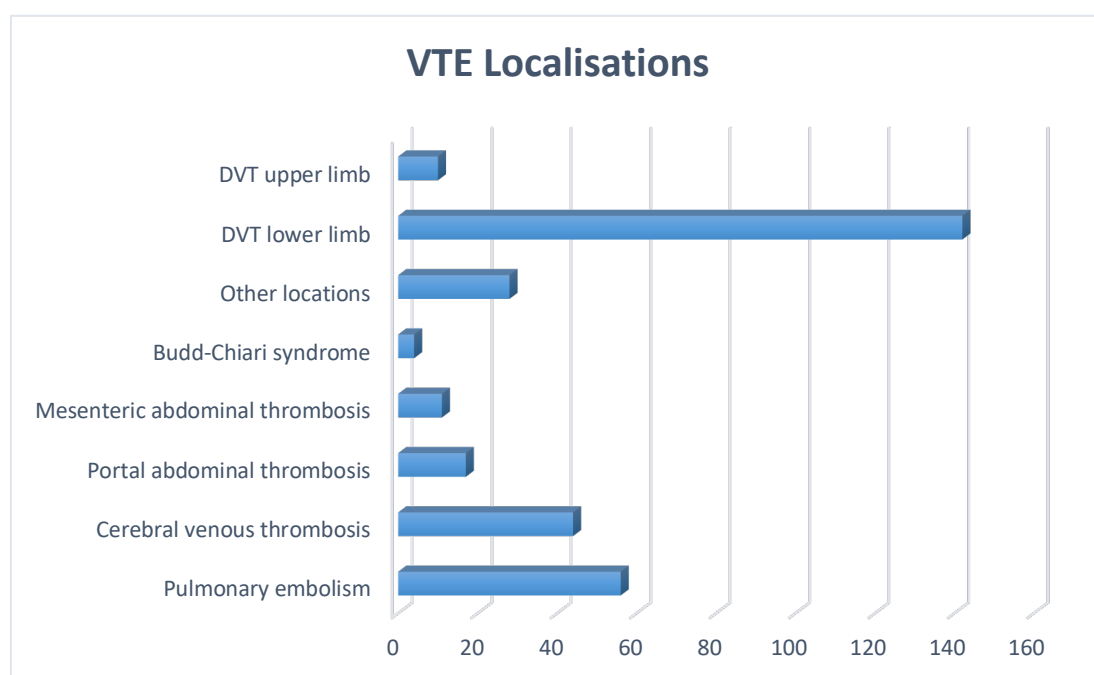


Diagram 15: Anatomical Distribution of VTE Disease.

Commentary

- A total of 312 thrombotic events were recorded across 267 patients (116.9%), confirming that a proportion of patients presented with multiple simultaneous localizations.
- Lower limb DVT was the most frequent localization (45.5%, n = 142; 53.2% of patients), followed by pulmonary embolism (17.9%, n = 56; 21.0% of patients) and cerebral venous thrombosis (14.1%, n = 44; 16.5% of patients).
- Visceral thromboses collectively represented 10.2% of events, comprising portal vein thrombosis (5.4%, n = 17), mesenteric vein thrombosis (3.5%, n = 11), and Budd–Chiari syndrome (1.3%, n = 4).
- Upper limb DVT accounted for 3.2% (n = 10) and other localizations for 9.0% (n = 28).

5.7.1. Laterality of Lower Limb DVT:

Table 24: Distribution of DVT According to Lower Limb Laterality.

DVT Laterality	Frequency (n)	Valid Percentage (%)
Left lower limb	77	54.2%
Right lower limb	61	43.0%
Bilateral lower limb	4	2.8%
Total	142	100%

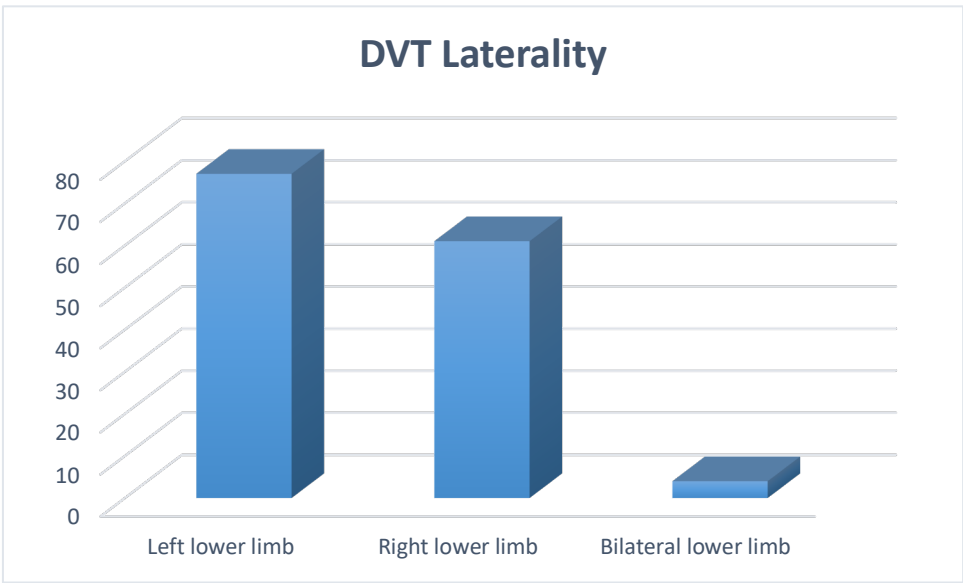


Diagram 16: Laterality Distribution of Lower Limb Deep Vein Thrombosis.

Commentary:

- Left lower limb was the most frequently affected site of DVT, representing 54.2% of cases.
- Right lower limb involvement accounted for 43.0%, while bilateral lower limb thrombosis was uncommon, observed in 2.8% of patients.
- Overall, unilateral DVT predominated over bilateral presentation in the study population.

5.7.2. Classification of Thromboembolic Events:

Table 25: Classification of VTE Disease Cases According to Clinical Presentation (Isolated DVT, Isolated PE, and Concomitant DVT–PE).

VTE Type	Frequency (n)	Valid Percentage (%)
Isolated DVT	126	69.6%
Isolated PE	39	21.5%
DVT with concomitant PE	16	8.8%
Total	181	100.0%

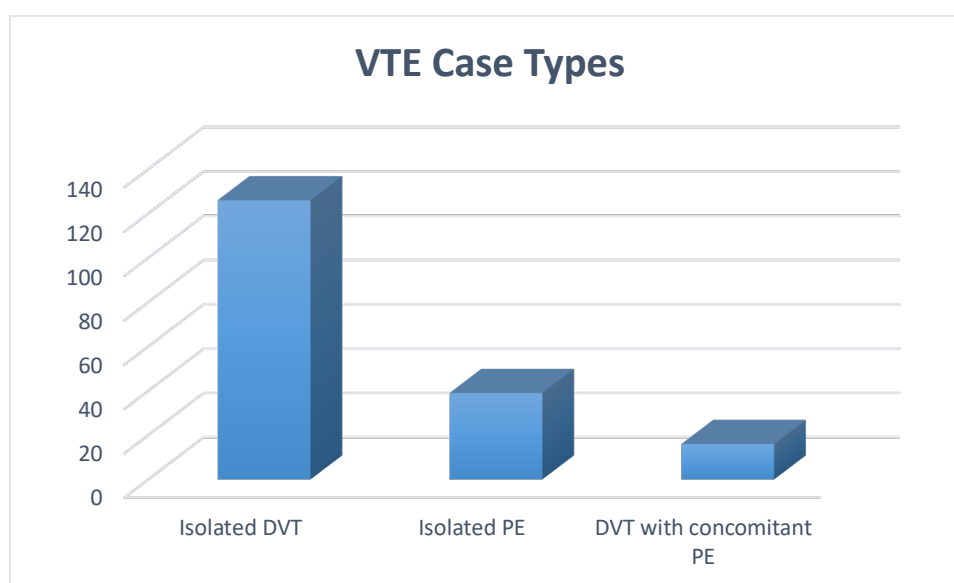


Diagram 17: Distribution of VTE Disease According to Clinical Presentation Type.

Commentary:

- Isolated deep vein thrombosis (DVT) was the predominant clinical presentation, representing 69.6% of all venous thromboembolic disease cases.
- Isolated PE accounted for 21.5% of patients, while concomitant DVT and PE was observed in 8.8% of cases.
- These findings indicate that isolated DVT constituted the most common presentation of venous thromboembolic disease in the study population.

5.8. Distribution of Thrombotic Sites According to Sex :

Table 26: Distribution of thrombotic locations according to sex.

Thromboembolic localization	Male	Female	p-value	Significance
Lower limb DVT	48 (51.1%)	94 (54.7%)	0.575	Not significant
Upper limb DVT	5 (5.3%)	5 (2.9%)	0.323	Not significant
Abdominal thrombosis	17 (18.1%)	10 (5.8%)	0.006	Significant
Pulmonary embolism	17 (18.1%)	39 (22.7%)	0.380	Not significant
Cerebral venous thrombosis	6 (6.4%)	38 (22.1%)	0.001	Significant
Other localizations	15 (16.0%)	13 (7.6%)	0.033	Significant
Total patients	94 (100%)	172 (100%)	—	—

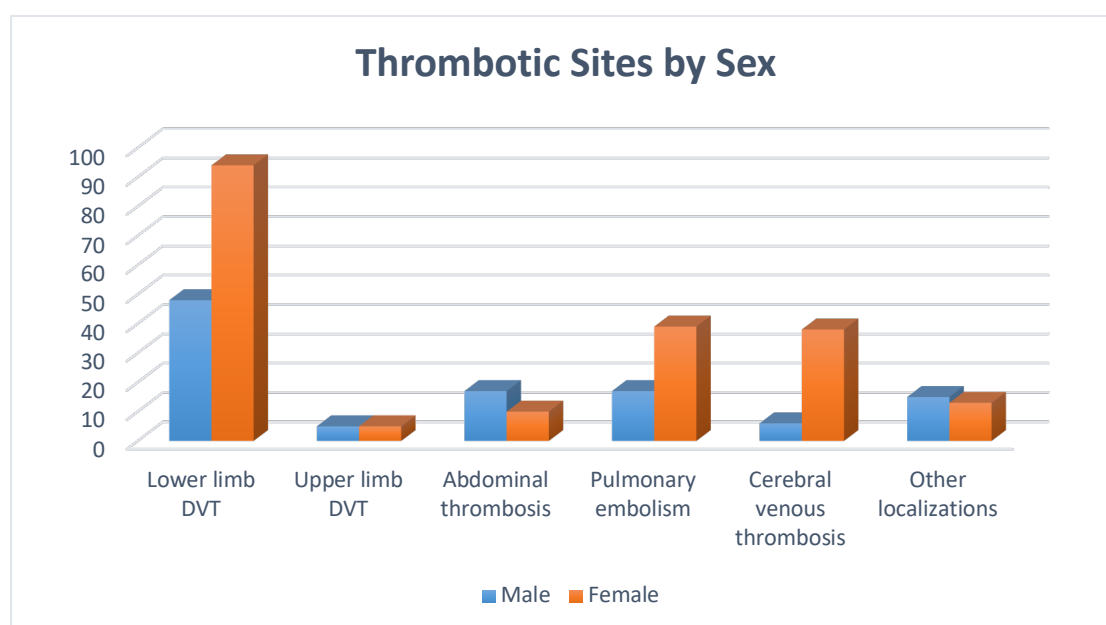


Diagram 18: Distribution of Thrombotic Sites According to Sex in the Study Population.

Commentary:

- The most frequent thromboembolic localization in both sexes was lower limb DVT, with no significant sex difference. Pulmonary embolism and upper limb DVT were also similarly distributed between males and females.
- Significant differences were observed for atypical sites: cerebral venous thrombosis was more frequent in females, while abdominal thrombosis and other rare localizations were more common in males.
- However, some patients had multiple thrombotic sites
- These results are based on thrombotic events rather than individual patients, as some patients had multiple localizations.

5.9. Analysis of Clinical Presentation:

Table 27: Distribution of Clinical Presentations in Patients with VTE Disease.

Clinical Presentation	Frequency (n)	Percentage % of Responses	Percentage % of Patients (N=267)
Limb edema, warmth, and redness	142	33.1%	54.8%
Limb pain	76	17.7%	29.3%
Other symptoms	55	12.8%	21.2%
Dyspnea	41	9.6%	15.8%
Sudden abnormal headache	31	7.2%	12.0%
Chest pain	25	5.8%	9.7%
Acute abdominal pain	22	5.1%	8.5%
Seizure (FNS)	19	4.4%	7.3%
Neurological deficit (FNS)	18	4.2%	6.9%

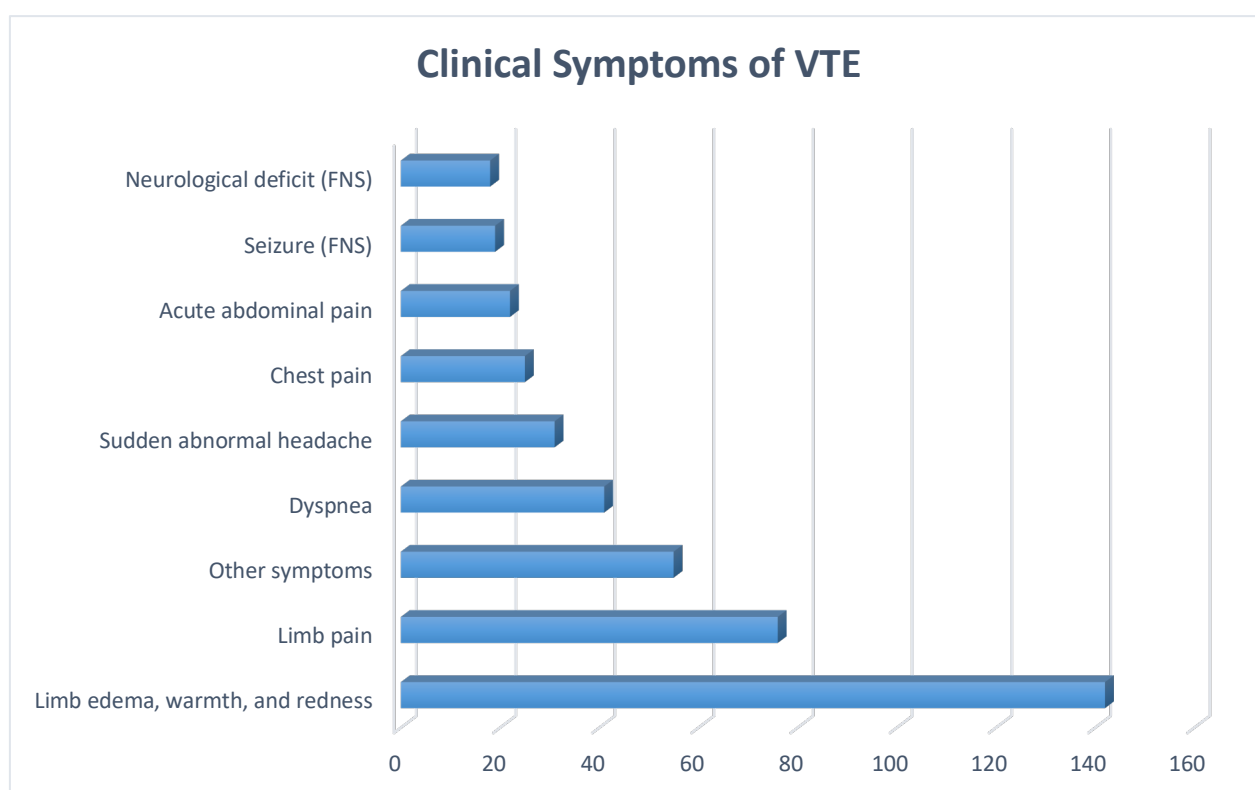


Diagram 19 : Distribution of Clinical Presentations and Symptoms Among Patients With VTE Disease.

Commentary:

- A total of 429 clinical presentations were recorded across 267 patients, yielding an observation percentage of 165.6%, confirming that the majority of patients presented with multiple simultaneous symptoms.
- Limb oedema with warmth and redness was the most frequent presentation (33.1%, n = 142; 54.8% of patients), followed by limb pain (17.7%, n = 76; 29.3% of patients) and dyspnoea (9.6%, n = 41; 15.8% of patients).
- Sudden severe headache accounted for 7.2% of responses (n = 31; 12.0% of patients), whilst chest pain represented 5.8% (n = 25; 9.7% of patients).
- Acute abdominal pain was recorded in 5.1% of responses (n = 22; 8.5% of patients).
- Neurological manifestations comprised focal neurological deficits (4.2%, n = 18; 6.9% of patients) and seizures (4.4%, n = 19; 7.3% of patients).
- Other symptoms accounted for 12.8% of responses (n = 55; 21.2% of patients).

5.10. Analysis of paraclinical investigations:

Table 28: Frequency and distribution of paraclinical investigations.

Paraclinical Investigations	Frequency (n)	Percentage % of Investigations	Percentage % of Patients
Venous Doppler ultrasound	155	36.6%	58.7%
Thrombophilia workup	106	25.1%	40.2%
Chest CT angiography	56	13.2%	21.2%
Other paraclinical investigations	46	10.9%	17.4%
Cerebral CT angiography	31	7.3%	11.7%
Cerebral MRI angiography	25	5.9%	9.5%
D-dimer assay	4	0.9%	1.5%
Total	423	100.0%	160.2%

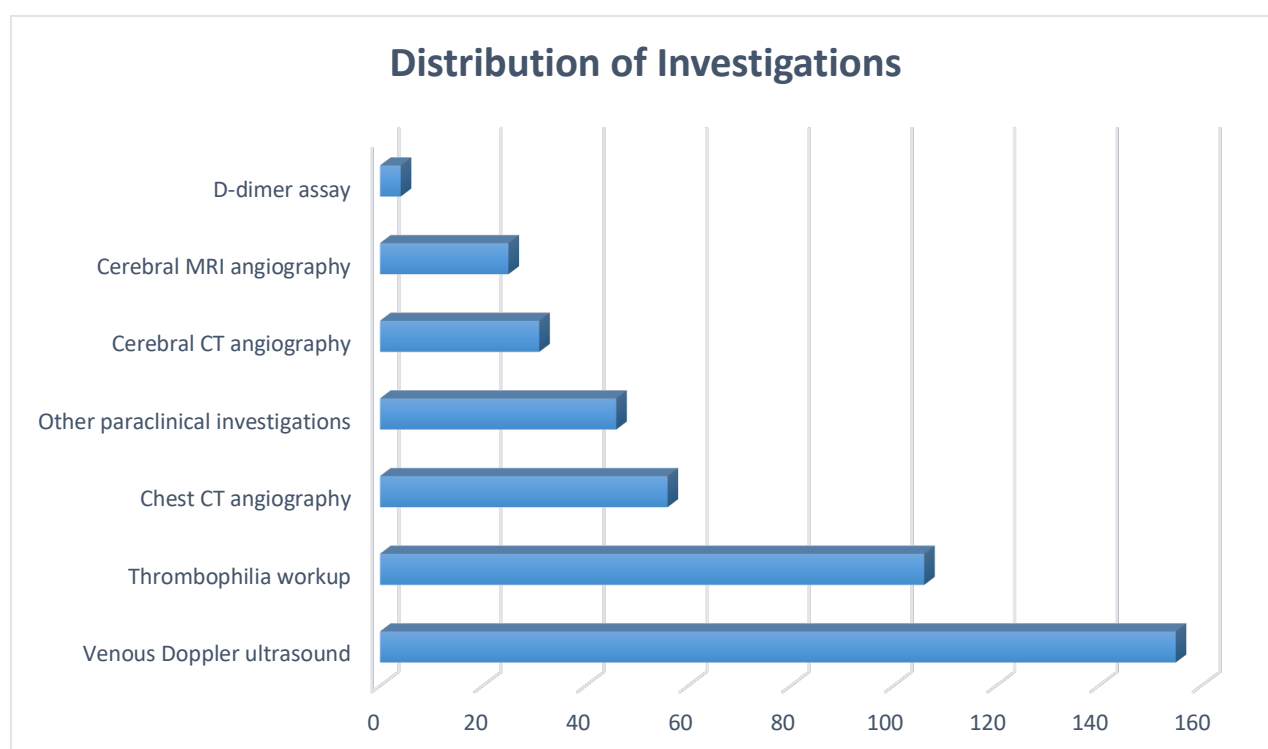


Diagram 20: Frequency Distribution of Paraclinical Investigations Among Patients With VTE Disease.

Commentary:

- Venous Doppler ultrasound was the most frequently performed investigation, accounting for 36.6% of all investigations and being used in 58.7% of patients.
- Thrombophilia workup represented the second most common examination (25.1%), followed by chest CT angiography (13.2%).
- Cerebral imaging techniques, including cerebral CT angiography and cerebral MRI angiography, were less frequently performed. D-dimer assay was rarely requested, representing only 0.9% of all investigations.
- The percentage of patients exceeded 100% because several patients underwent multiple paraclinical investigations during hospitalization.

5.11. Etiological Analysis:

5.11.1. Distribution of Etiologies:

Table 29: Distribution of etiologies of venous thromboembolism

Etiology	Frequency (n)	Percentage %
Thrombophilia (congenital or acquired)	29	14,3%
Active cancer (under treatment)	35	17,2%
Immobilization / Major surgery / Recent trauma	34	16,7%
Pregnancy / Postpartum	16	7,9%
Combined oral contraceptives (Estrogen-progestin)	6	3%
Idiopathic cause (no identified triggering factor)	63	31%
Other causes	20	9,9%
Total	203	100%

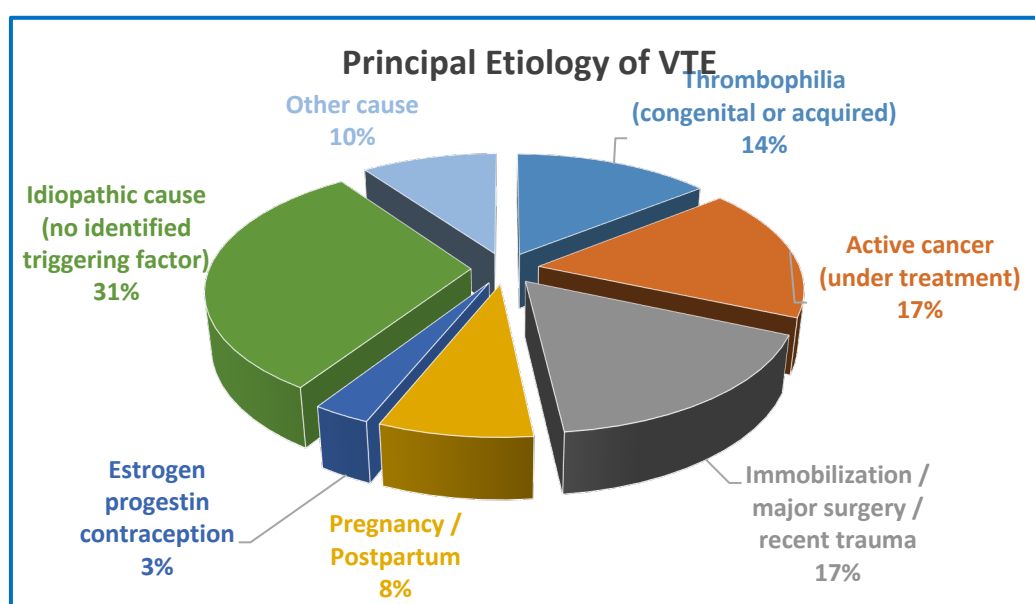


Diagram 21: Distribution of etiologies of venous thromboembolism.

Commentary:

- Among the 267 patients included, etiological data were available for 203 cases (76%), while 64 cases (24%) had missing data. The category of other causes included less frequent and heterogeneous conditions such as central venous catheterization, Sjögren syndrome, poor adherence or absence of postoperative / postpartum anticoagulant prophylaxis, Behçet disease, inflammatory myositis.
- Among the 203 patients with available etiological data, idiopathic causes were the most frequent, identified in 63 cases (31%). This was followed by active cancer in 35 cases (17.2%), immobilization / major surgery / recent trauma in 34 cases (16.7%), and thrombophilia in 29 cases (14.3%).
- Hormonal factors were less common, with pregnancy / postpartum reported in 16 cases (7.9%) and combined oral contraceptive use in 6 cases (3%). Other causes accounted for 20 cases (9.9%).

5.11.2. Distribution of Etiologies according to age group:

Table 30: Distribution of Principal Etiologies According to Age Groups

Principal Etiology	≤20 years	21–40 years	41–60 years	≥61 years	Total	p-value	Significance
Thrombophilia (congenital or acquired)	1 (33.3%)	13 (14.8%)	12 (22.2%)	3 (5.2%)	29 (14.3%)	<0.001	Significant
Active cancer (under treatment)	1 (33.3%)	1 (1.1%)	15 (27.8%)	18 (31.0%)	35 (17.2%)	<0.001	Significant
Immobilization / major surgery / recent trauma	0 (0.0%)	10 (11.4%)	6 (11.1%)	18 (31.0%)	34 (16.7%)	<0.001	Significant
Pregnancy / Postpartum	0 (0.0%)	15 (17.0%)	1 (1.9%)	0 (0.0%)	16 (7.9%)	<0.001	Significant
Estrogen-progestin contraception	0 (0.0%)	6 (6.8%)	0 (0.0%)	0 (0.0%)	6 (3.0%)	<0.001	Significant
Idiopathic cause (no triggering factor identified)	1 (33.3%)	37 (42.0%)	17 (31.5%)	8 (13.8%)	63 (31.0%)	<0.001	Significant
Other causes	0 (0.0%)	6 (6.8%)	3 (5.6%)	11 (19.0%)	20 (9.9%)	<0.001	Significant
Total	3	88	54	58	203	-	-

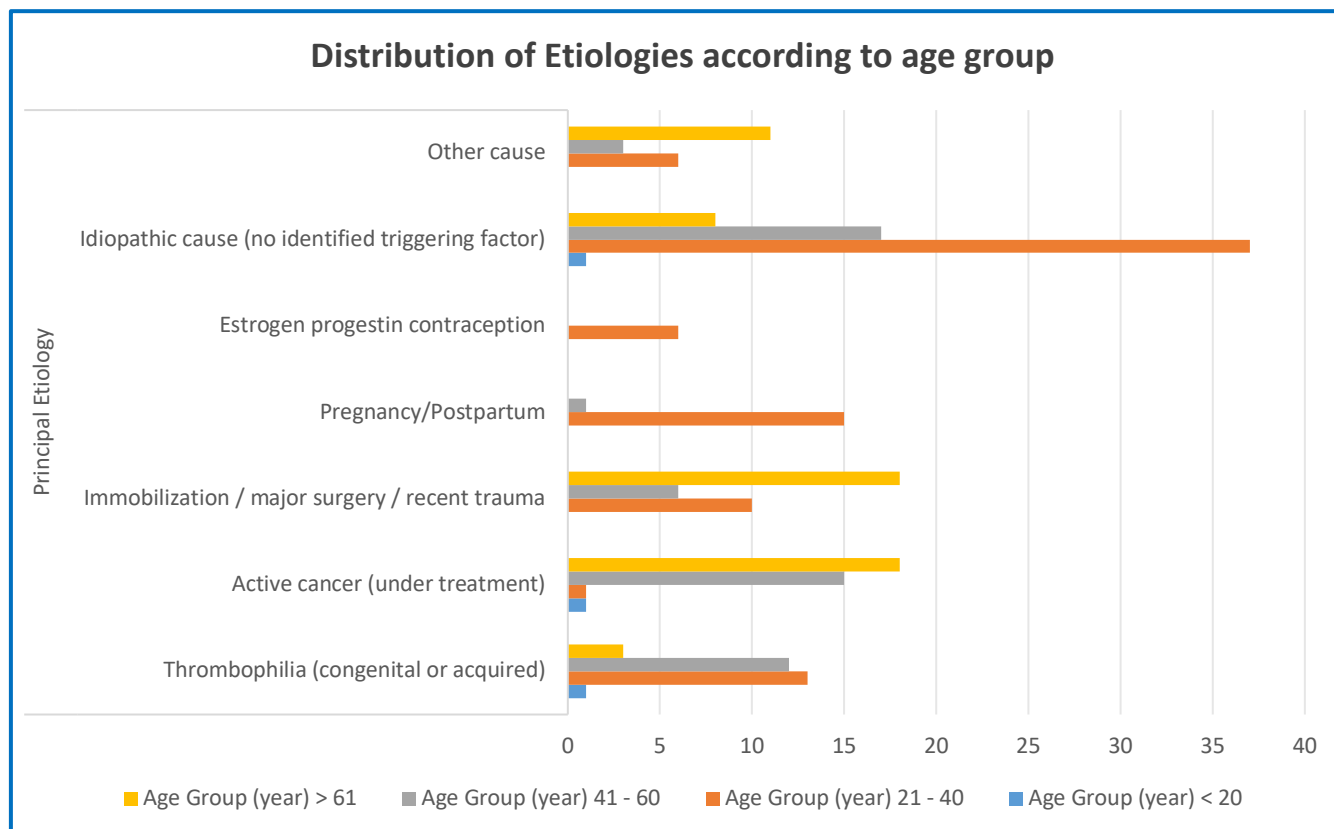


Diagram 22: Distribution of etiologies according to age group.

Commentary:

- Among the 267 patients enrolled in the study, 203 cases (75.9%) had a documented principal etiology and were retained for etiologic analysis. The remaining 64 cases (24.1%) were excluded due to incomplete data or absence of identifiable etiology.
- Idiopathic VTE was the leading cause among analyzed cases (31.0%; n = 63), predominating in the 21–40 year group (42.0%). Active cancer (17.2%; n = 35) and immobilization/surgery/trauma (16.7%; n = 34) were the next most frequent etiologies, both markedly concentrated in patients aged ≥ 41 years, peaking in the ≥ 61 year cohort (31.0% each).
- Thrombophilia accounted for 14.3% of cases (n = 29), with higher rates in the younger and middle-aged groups.
- Pregnancy/postpartum was identified in 7.9% of cases (n = 16), exclusively in the 21–40 year group. Estrogen-progestin contraception represented 3.0% (n = 6), restricted to the same age group. Other causes accounted for 9.9% (n = 20), with a predominance in older patients (19.0% in ≥ 61 years).
- The distribution of all etiologies across age groups was statistically significant ($p < 0.001$ for all categories).

5.11.3. Distribution of Etiologies according to sex:

Table 31: Distribution of etiologies according to sex.

Principal Etiology	Male	Female	Total	p-value	Significance
Thrombophilia (congenital or acquired)	16 (21.6%)	13 (10.1%)	29 (14.4%)	<0.001	Significant
Active cancer (under treatment)	13 (17.6%)	22 (17.1%)	35 (17.2%)	<0.001	Significant
Immobilization / major surgery / recent trauma	9 (12.2%)	25 (19.4%)	34 (16.8%)	<0.001	Significant
Pregnancy / Postpartum	0 (0.0%)	16 (12.4%)	16 (7.9%)	<0.001	Significant
Estrogen-progestin contraception	0 (0.0%)	6 (4.7%)	6 (3.0%)	<0.001	Significant
Idiopathic cause (no identified triggering factor)	23 (31.1%)	40 (31.0%)	63 (31.2%)	<0.001	Significant
Other causes	13 (17.6%)	7 (5.4%)	20 (9.9%)	<0.001	Significant
Total	74	129	203	-	Significant

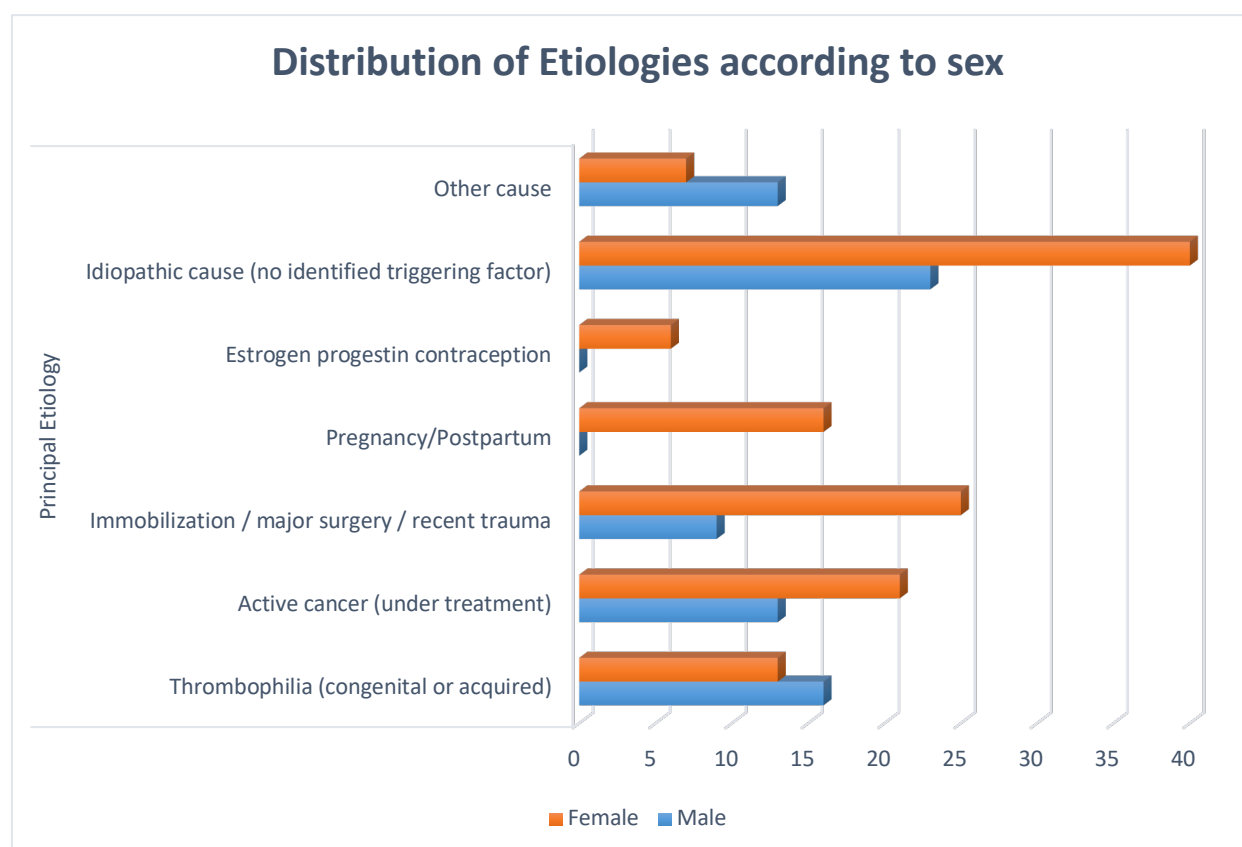


Diagram 23: Distribution of etiologies according to sex.

Commentary:

- Among the 203 patients retained for etiologic analysis, 74 were male (36.5%) and 129 were female (63.5%).
- Idiopathic VTE was the most frequent etiology in both sexes, with virtually identical proportions in males and females (31.1% vs. 31.0%). Active cancer accounted for 17.2% of cases (n = 35), with a slightly higher proportion among males (17.6% vs. 17.1%).
- Immobilization/surgery/trauma was more prevalent in females (19.4% vs. 12.2%). Thrombophilia was notably more frequent in males (21.6% vs. 10.1%).
- Pregnancy/postpartum (12.4%) and estrogen-progestin contraception (4.7%) were exclusively observed in females, collectively representing 17.1% of all female cases. Other causes were more frequent in males (17.6% vs. 5.4%).
- The distribution of all etiologies across sexes was statistically significant ($p < 0.001$ for all categories).

5.12. Comparison of etiologies according to thrombotic location:

5.12.1. Lower-limb deep vein thrombosis:

Table 32: Distribution of etiologies in Lower-limb deep vein thrombosis.

Principal Etiology	Frequency (n)	Percentage %
Thrombophilia (congenital or acquired)	17	16.5%
Active cancer (under treatment)	21	20.4%
Immobilization / major surgery / recent trauma	20	19.4%
Pregnancy / Postpartum	9	8.7%
Estrogen–progestin contraception	1	1%
Idiopathic cause (no identified triggering factor)	27	26.2%
Other cause	8	7.8%
Total	103	100%

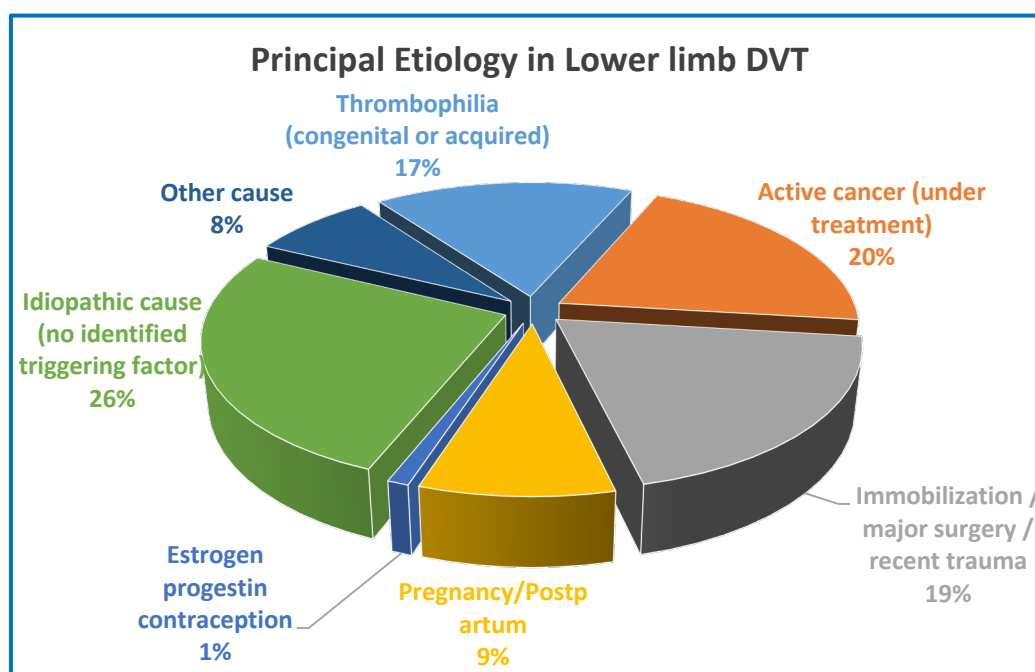


Diagram 24: Distribution of etiologies in Lower-limb deep vein thrombosis.

Commentary:

- Among patients with lower-limb DVT (n = 103), idiopathic causes were the most frequent etiology, identified in 27 cases (26.2%), followed by active cancer in 21 cases (20.4%) and immobilization / surgery / trauma in 20 cases (19.4%).
- Thrombophilia was reported in 17 cases (16.5%). Hormonal factors were less common, including pregnancy / postpartum in 9 cases (8.7%) and estrogen–progestin contraception in 1 case (1.0%).
- Overall, lower-limb DVT was mainly associated with idiopathic forms and acquired provoking factors.

5.12.2. Pulmonary Embolism:

Table 33: Distribution of etiologies in Pulmonary Embolism.

Principal Etiology	Frequency (n)	Percentage %
Thrombophilia (congenital or acquired)	5	11,1 %
Active cancer (under treatment)	9	20 %
Immobilization / major surgery / recent trauma	12	26,7 %
Pregnancy / Postpartum	2	4,4 %
Estrogen–progestin contraception	1	2,2 %
Idiopathic cause (no identified triggering factor)	13	28,9 %
Other cause	3	6,7 %
Total	45	100%

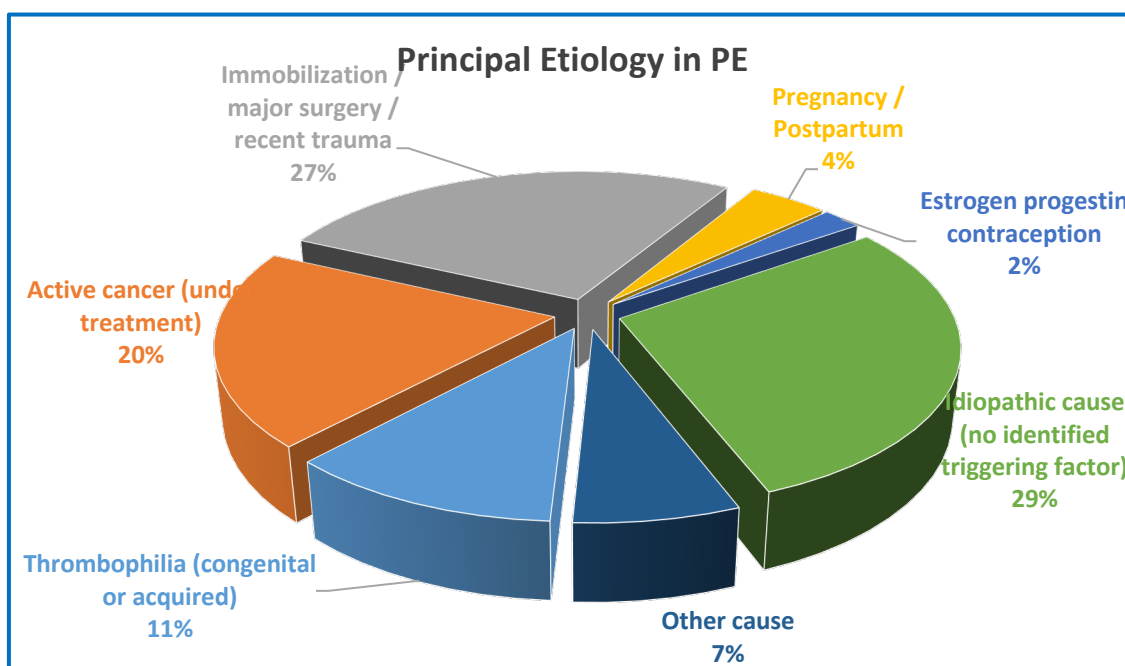


Diagram 25: Distribution of etiologies in Pulmonary Embolism.

Commentary:

- Among patients with pulmonary embolism (n = 45), idiopathic causes were the most frequent etiology, identified in 13 cases (28.9%), followed by immobilization / surgery / trauma in 12 cases (26.7%) and active cancer in 9 cases (20.0%).
- Thrombophilia was reported in 5 cases (11.1%). Hormonal factors were less common, including pregnancy/postpartum in 2 cases (4.4%) and estrogen–progestin contraception in 1 case (2.2%). Other causes accounted for 3 cases (6.7%).
- Overall, pulmonary embolism was mainly associated with idiopathic forms and acquired provoking factors.

5.12.3. Cerebral vein thrombosis:

Table 34: Distribution of etiologies in Cerebral vein thrombosis.

Principal Etiology	Frequency (n)	Percentage %
Thrombophilia (congenital or acquired)	6	15 %
Active cancer (under treatment)	2	5 %
Immobilization / major surgery / recent trauma	4	10 %
Pregnancy / Postpartum	6	15 %
Estrogen–progestin contraception	5	12,5 %
Idiopathic cause (no identified triggering factor)	15	37,5 %
Other cause	2	5 %
Total	40	100%

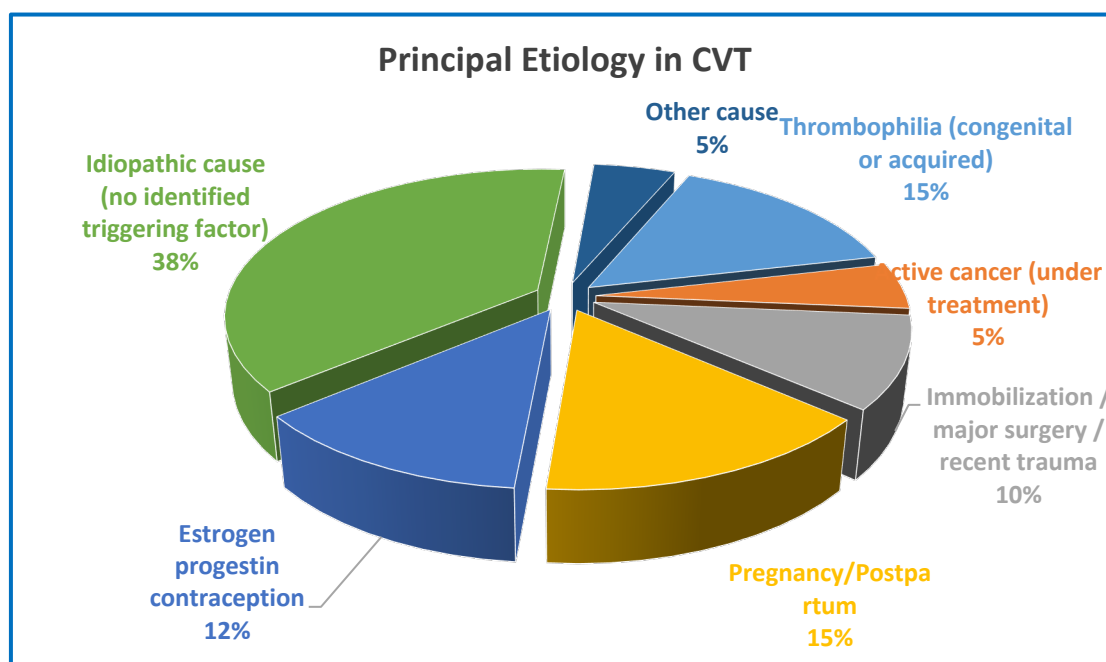


Diagram 26: Distribution of etiologies in Cerebral vein thrombosis (CVT)

Commentary:

- Among patients with cerebral venous thrombosis (n = 40), idiopathic causes were the most frequent etiology, identified in 15 cases (37.5%). This was followed by thrombophilia and pregnancy/postpartum, each reported in 6 cases (15.0%), while estrogen–progestin contraception accounted for 5 cases (12.5%).
- Immobilization / surgery / trauma was identified in 4 cases (10.0%), whereas active cancer and other causes were less common, with 2 cases each (5.0%).
- Overall, cerebral venous thrombosis was mainly associated with idiopathic and hormonal risk factors.

5.12.4. Upper-limb deep DVT:

Table 35: Distribution of etiologies in Upper-limb DVT.

Principal Etiology	Frequency (n)	Percentage %
Thrombophilia (congenital or acquired)	1	14,3 %
Active cancer (under treatment)	0	0 %
Immobilization / major surgery / recent trauma	2	28,6 %
Pregnancy / Postpartum	0	0 %
Estrogen–progestin contraception	0	0 %
Idiopathic cause (no identified triggering factor)	2	28,6 %
Other cause	2	28,6 %
Total	7	100%

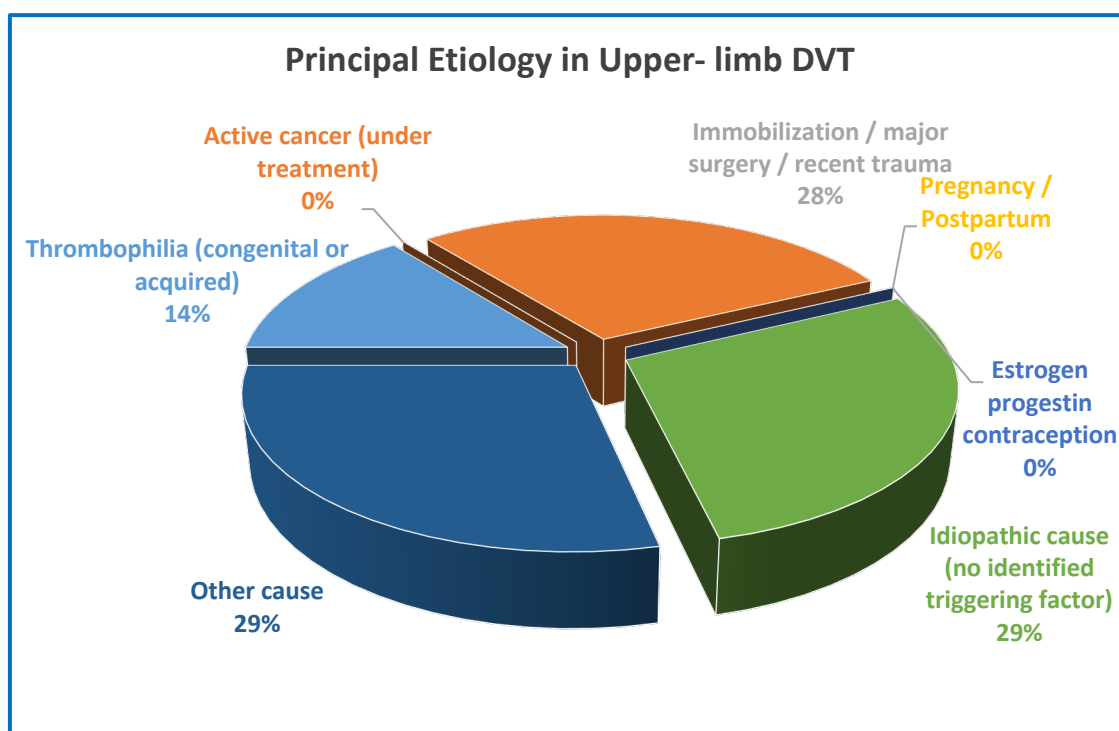


Diagram 27: Distribution of etiologies in Upper-limb DVT.

Commentary:

- Among patients with upper-limb deep vein thrombosis (n = 7), the most frequent etiologies were immobilization / surgery / trauma, idiopathic causes, and other causes, each identified in 2 cases (28.6%).
- Thrombophilia was reported in 1 case (14.3%), while no cases were related to active cancer, pregnancy/postpartum, or estrogen–progestin contraception.
- Overall, upper-limb DVT showed a heterogeneous etiological profile, although interpretation remains limited due to the small number of cases.

5.12.5. Splanchnic vein thrombosis:

Table 36: Distribution of etiologies in SpVT, (including mesenteric vein thrombosis, portal vein thrombosis, and Budd–Chiari syndrome).

Principal Etiology	Frequency (n)	Percentage %
Thrombophilia (congenital or acquired)	3	14,3 %
Active cancer (under treatment)	6	28,6 %
Immobilization / major surgery / recent trauma	1	4,8 %
Pregnancy / Postpartum	0	0 %
Estrogen–progestin contraception	0	0 %
Idiopathic cause (no identified triggering factor)	7	33,3 %
Other cause	4	19 %
Total	21	100%

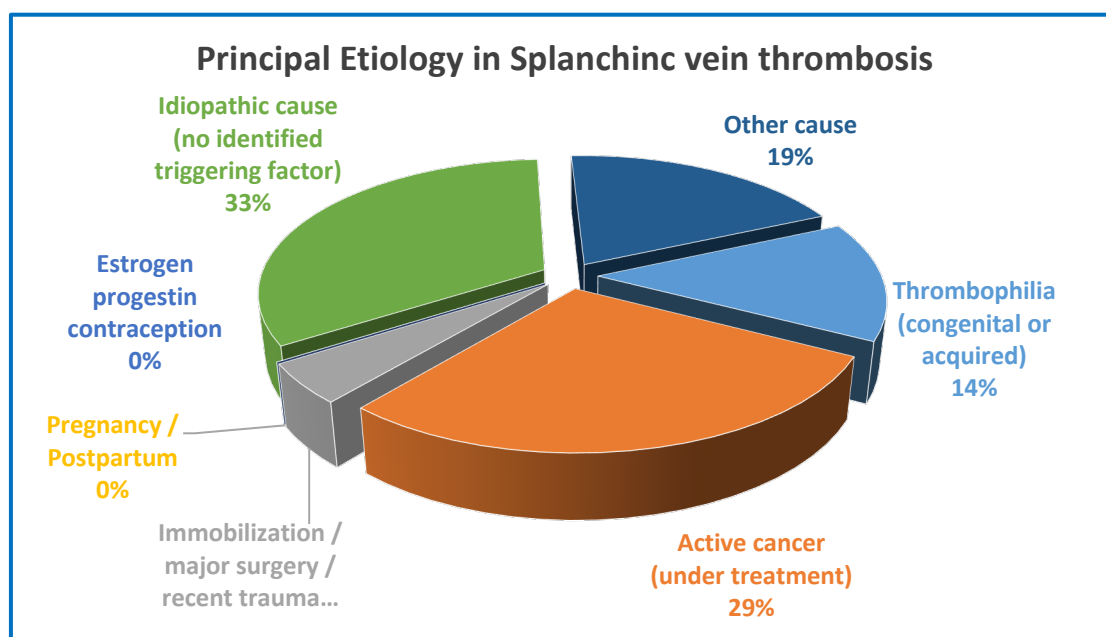


Diagram 28: Distribution of etiologies in Splanchnic vein thrombosis.

Commentary:

- Among patients with splanchnic vein thrombosis (SVT) (n = 21), including mesenteric vein thrombosis, portal vein thrombosis, and Budd–Chiari syndrome; idiopathic causes were the most frequent etiology, identified in 7 cases (33.3%).
- This was followed by active cancer in 6 cases (28.6%) and other causes in 4 cases (19.0%). Thrombophilia was reported in 3 cases (14.3%), while immobilization / surgery / trauma accounted for 1 case (4.8%).
- No cases were related to pregnancy/postpartum or estrogen–progestin contraception. Overall, SVT was mainly associated with idiopathic forms, malignancy, and less common heterogeneous risk factors.

5.12.6. Other Location of vein thrombosis:

Table 37: Distribution of etiologies in Other Location of vein thrombosis.

Principal Etiology	Frequency (n)	Percentage %
Thrombophilia (congenital or acquired)	6	25 %
Active cancer (under treatment)	1	4,2 %
Immobilization / major surgery / recent trauma	3	12,5 %
Pregnancy / Postpartum	2	8,3 %
Estrogen–progestin contraception	1	4,2 %
Idiopathic cause (no identified triggering factor)	9	37,5 %
Other cause	2	8,3 %
Total	24	100%

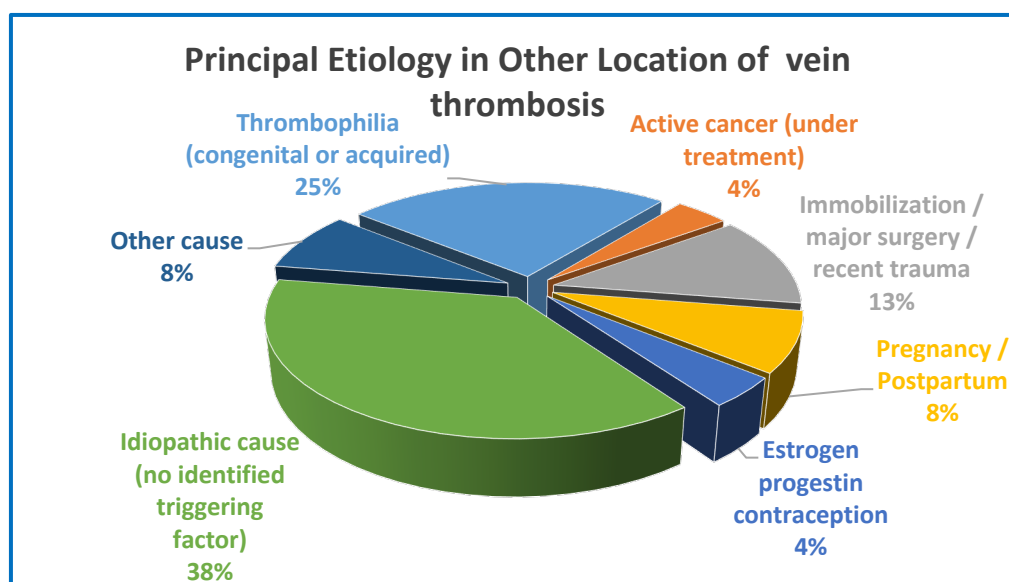


Diagram 29: Distribution of etiologies in Other Location of vein thrombosis.

Commentary:

- Among patients with other locations of venous thrombosis (n = 24), idiopathic causes were the most frequent etiology, identified in 9 cases (37.5%). This was followed by thrombophilia in 6 cases (25.0%), suggesting an important role of underlying prothrombotic disorders in unusual thrombosis sites.
- Immobilization / surgery / trauma accounted for 3 cases (12.5%), while pregnancy / postpartum and other causes were each reported in 2 cases (8.3%). Active cancer and estrogen–progestin contraception were less frequent, with 1 case each (4.2%).
- Overall, thrombosis at other venous sites was mainly associated with idiopathic causes and thrombophilia.

5.13. Therapeutic Analysis:

5.13.1. Initial Treatment:

Table 38: Distribution of initial treatment strategies.

Initial Traitement	Frequency (n)	Percentage %
Low-molecular-weight heparin (LMWH)	224	85,8%
Unfractionated heparin (UFH)	20	7,7%
Direct oral anticoagulant (DOAC)	8	3,1%
Other	6	2,3%
None	3	1,1%
Total	261	100%

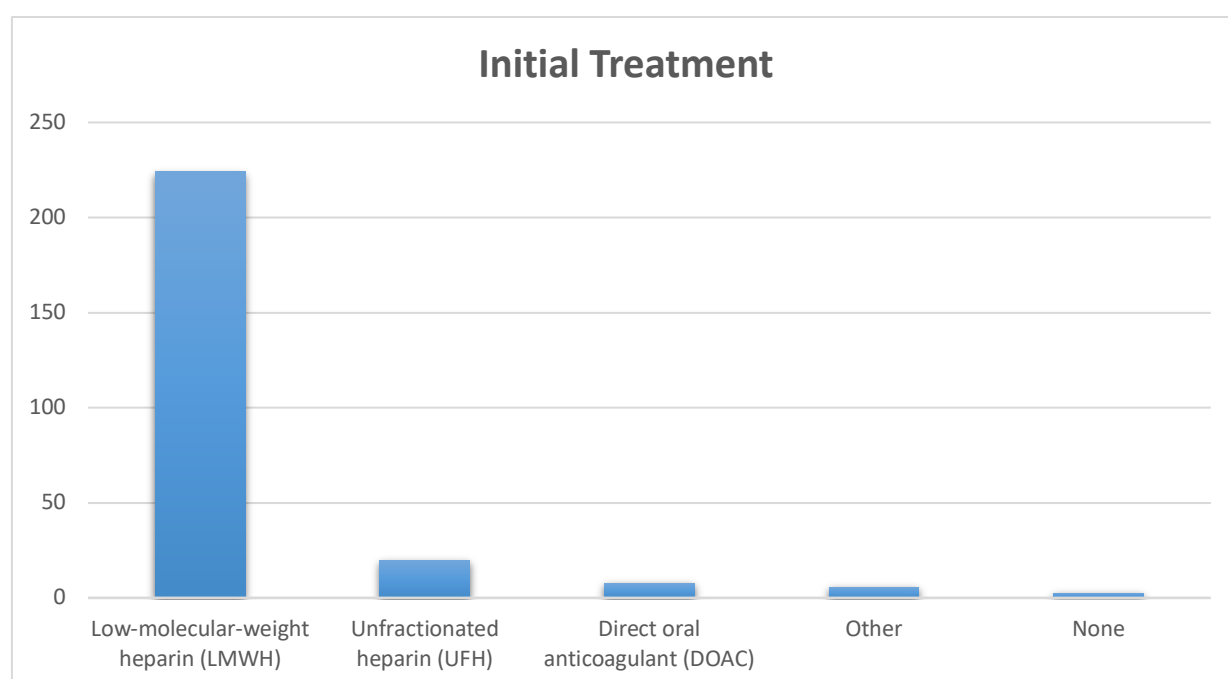


Diagram 30: Distribution of initial treatment strategies.

Commentary:

- Data on initial treatment were available for 261 patients (97.8%), while 6 patients (2.2%) had missing information. The category of other treatments included less commonly prescribed therapies such as antiplatelet agents (clopidogrel), nonsteroidal anti-inflammatory drugs (aspirin), vitamin B12 supplementation, and other supportive medications according to the clinical situation.
- Among the 261 patients with available data, low-molecular-weight heparin (LMWH) was the most frequently used initial treatment, prescribed in 224 cases (85.8%). Unfractionated heparin (UFH) was administered in 20 cases (7.7%), whereas direct oral anticoagulants (DOACs) were used in 8 cases (3.1%). Other treatments accounted for 6 cases (2.3%), and no initial treatment was reported in 3 cases (1.1%).

5.13.2. Other Treatment :

Table 39: Distribution of other treatment.

Other Traitement	Frequency (n)	Percentage %
None	194	73,2%
Graduated compression stockings	47	17,7%
Other	24	9,1%
Total	265	100%

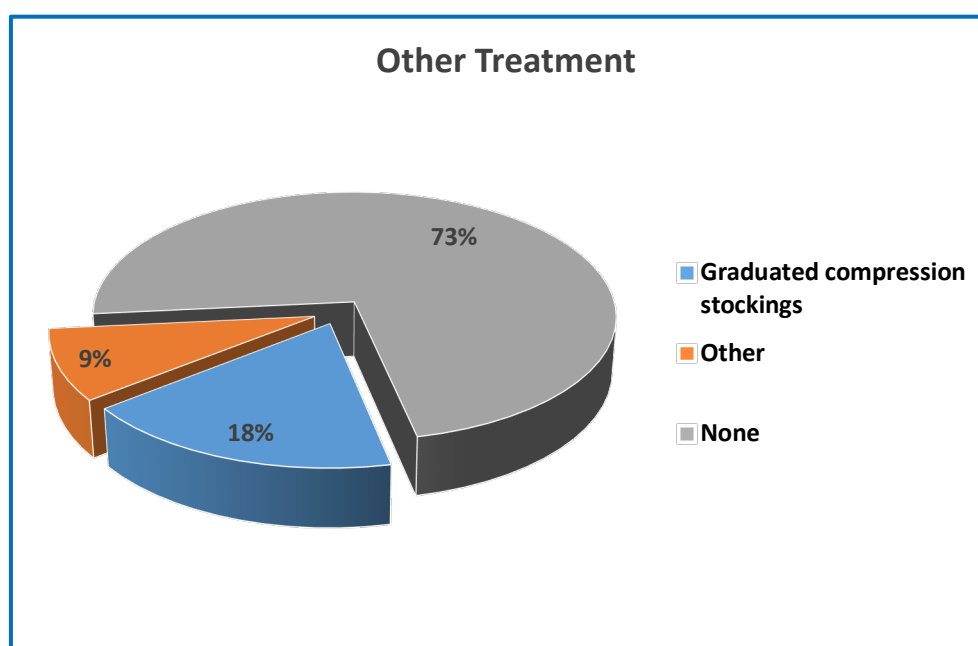


Diagram 31: Distribution of other treatment.

Commentary:

- Among the 265 patients with available data, no additional treatment was reported in 194 cases (73.2%). Graduated compression stockings were prescribed in 47 cases (17.7%), while other supportive treatments were used in 24 cases (9.1%).

5.13.3. Maintenance Treatment:

Table 40: Distribution of maintenance treatment.

Maintenance Traitement	Frequency (n)	Percentage %
Vitamin K antagonist (VKA)	130	53,5%
Direct oral anticoagulant (DOAC)	52	21,4%
Low-molecular-weight heparin (LMWH)	45	18,5%
None	11	4,5%
Other	5	2,1%
Total	243	100%

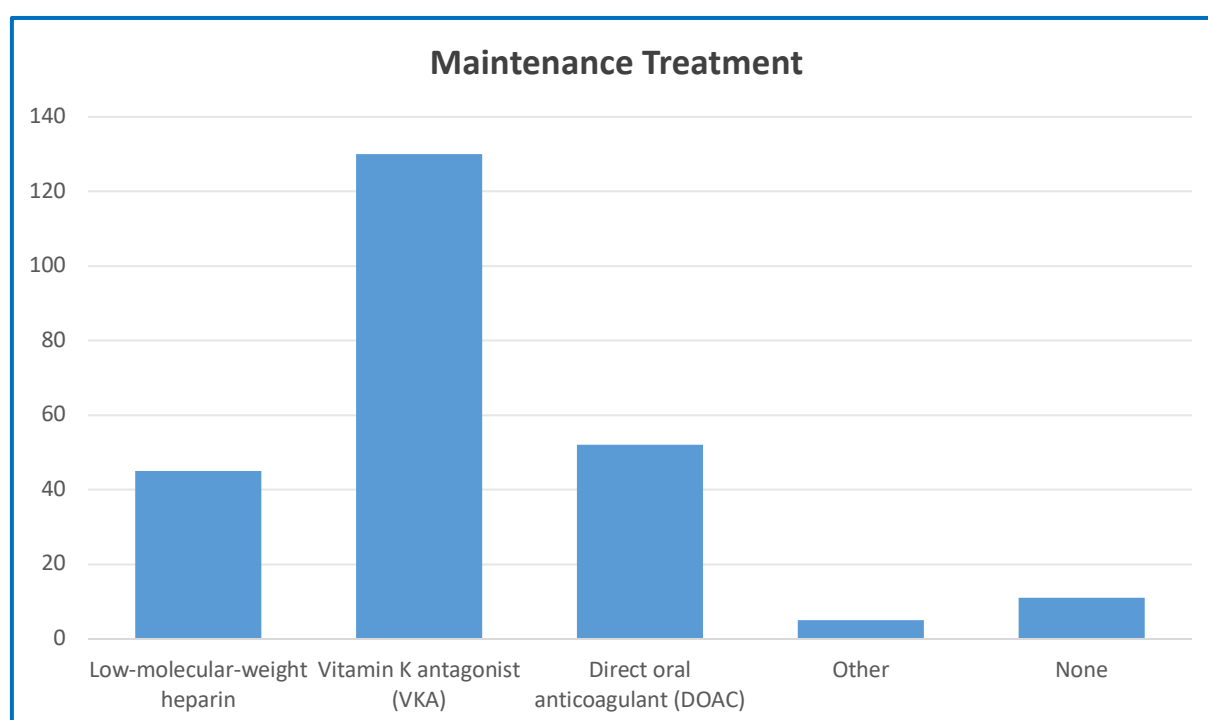


Diagram 32: Distribution of maintenance treatment.

Commentary:

- Among the 243 patients with available data, vitamin K antagonists (VKA) were the most commonly prescribed maintenance treatment, used in 130 cases (53.5%). This was followed by direct oral anticoagulants (DOACs) in 52 cases (21.4%) and low-molecular-weight heparin (LMWH) in 45 cases (18.5%). No maintenance treatment was reported in 11 cases (4.5%), while other treatments accounted for 5 cases (2.1%).

5.14. Outcome Analysis:

5.14.1. In-hospital Outcome:

Table 41: In-hospital outcomes of patients.

Outcome	Frequency (n)	Percentage %
Favorable (symptom regression)	213	79,8%
Death	19	7,1%
Hemorrhagic complication	3	1,1%
Worsening / extension of thrombosis	3	1,1%
Thrombotic recurrence	2	0,7%
Messing data	27	10,1%
Total	267	100%

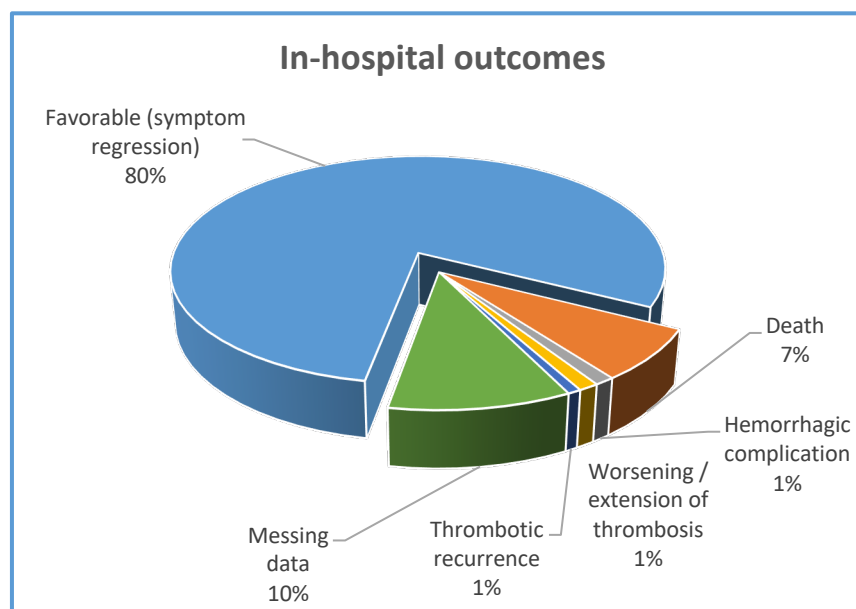


Diagram 33: In-hospital outcomes of patients

Commentary:

- Among the 240 patients with available outcome data, the clinical evolution was favorable (symptom regression) in 213 cases (79,8%), indicating a generally good short-term prognosis. Death occurred in 19 cases (7.1%). Hemorrhagic complications and worsening/extension of thrombosis were each observed in 3 cases (1.1%), while thrombotic recurrence was reported in 2 cases (0.7%).

5.14.2. Mortality and Complication Rate :

◆ Mortality Rate:

Formula:

$$\text{Mortality rate} = (\text{Number of deaths} / \text{Total number of patients}) \times 100$$

Calculation:

$$\text{Mortality rate} = (19 / 267) \times 100 = 7.1\%$$

Results:

The in-hospital mortality rate was 7.1%.

◆ Complication Rate:

Formula:

$$\text{Complication rate} = (\text{Number of complications} / \text{Total number of patients}) \times 100$$

Calculation:

$$\text{Complication rate} = (27 / 267) \times 100 = 10,1\%$$

Results:

The in-hospital complication rate was 10,1%.

5.15. Comparison of Therapeutic Strategy and In-Hospital Outcomes:

5.15.1. Initial treatment:

Table 42: Comparison of Initial treatment and In-Hospital Outcomes.

In-Hospital Outcomes	None	LMWH	UFH	DOAC	Other	Total	p-value	Significance
Favorable (symptom regression)	2 (100%)	190 (91.3%)	15 (83.3%)	4 (66.7%)	2 (40.0%)	213 (89.1%)	<0.001	Significant
Hemorrhagic complication	0 (0.0%)	2 (1.0%)	1 (5.6%)	0 (0.0%)	0 (0.0%)	3 (1.3%)	<0.001	Significant
Worsening / extension of thrombosis	0 (0.0%)	3 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (1.3%)	<0.001	Significant
Thrombotic recurrence	0 (0.0%)	1 (0.5%)	0 (0.0%)	0 (0.0%)	1 (20.0%)	2 (0.8%)	<0.001	Significant
Death	0 (0.0%)	12 (5.8%)	2 (11.1%)	2 (33.3%)	2 (40.0%)	18 (7.5%)	<0.001	Significant
Total	2 (0.8%)	208 (87.0%)	18 (7.5%)	6 (2.5%)	5 (2.1%)	239 (100%)	-	-

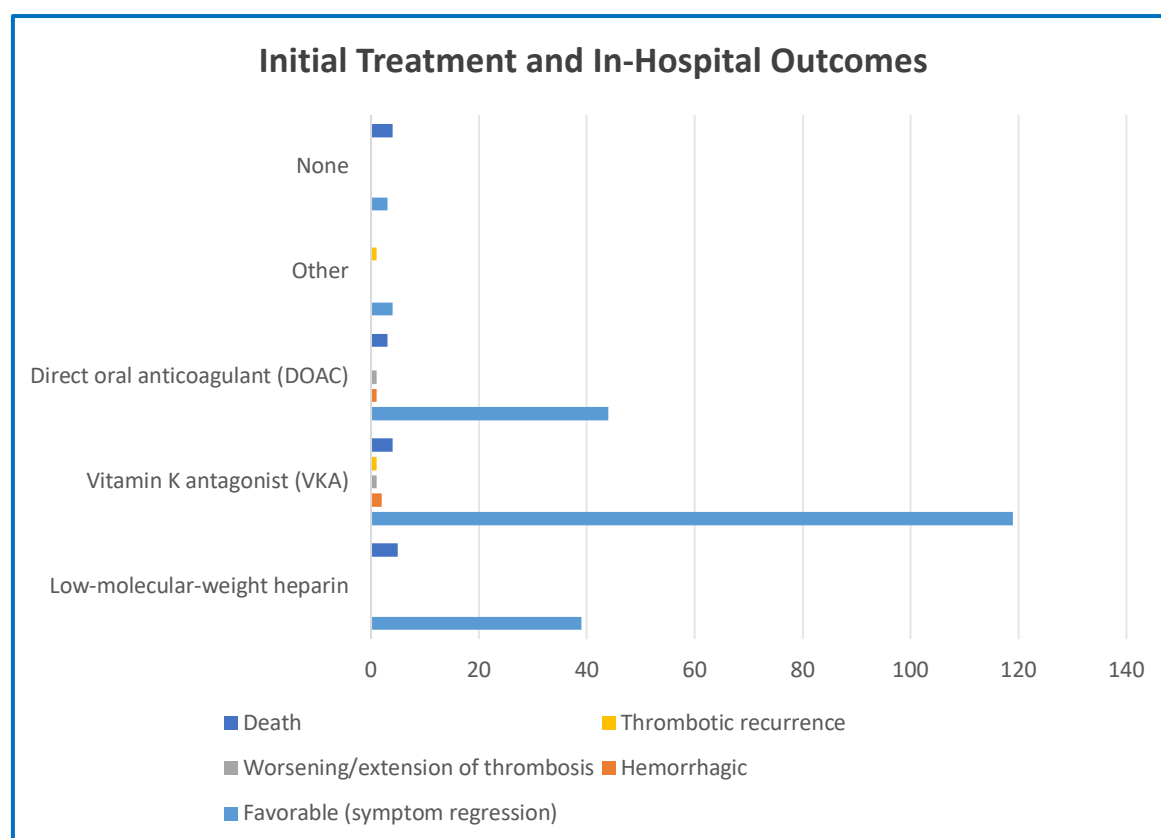


Diagram 34: Comparison of Initial treatment and In-Hospital Outcomes.

Commentary:

- Among the 239 patients assessed for in-hospital outcomes, the majority received low molecular weight heparin (LMWH) as the primary anticoagulant (n = 208; 87.0%), followed by unfractionated heparin (UFH) (n = 18; 7.5%), direct oral anticoagulants (DOAC) (n = 6; 2.5%), and other treatments (n = 5; 2.1%). Two patients received no treatment (0.8%).
- Favorable outcome defined as symptom regression was the most frequently observed outcome overall (89.1%; n = 213), with the highest rate recorded in the no-treatment group (100%) and LMWH group (91.3%), followed by UFH (83.3%), DOAC (66.7%), and other treatments (40.0%).
- In-hospital mortality was recorded in 18 patients (7.5%), with the highest case-fatality rates observed in the other treatment group (40.0%) and DOAC group (33.3%), compared to UFH (11.1%) and LMWH (5.8%). Hemorrhagic complications occurred in 3 patients (1.3%), predominantly under UFH (5.6%) and LMWH (1.0%). Worsening or extension of thrombosis was noted in 3 cases (1.3%), exclusively in the LMWH group. Thrombotic recurrence was rare, affecting only 2 patients (0.8%), observed under LMWH and other treatments respectively.
- The distribution of all in-hospital outcomes across treatment groups was statistically significant ($p < 0.001$ for all categories).

5.15.2. Maintenance treatment:

Table 43: Comparison of Maintenance treatment and In-Hospital Outcomes.

In-Hospital Outcomes	LMWH	VKA	DOAC	Other	None	Total	p-value	Significance
Favorable (symptom regression)	39 (88.6%)	119 (93.7%)	44 (89.8%)	4 (80.0%)	3 (42.9%)	209 (90.1%)	<0.001	Significant
Hemorrhagic complication	0 (0.0%)	2 (1.6%)	1 (2.0%)	0 (0.0%)	0 (0.0%)	3 (1.3%)	<0.001	Significant
Worsening / extension of thrombosis	0 (0.0%)	1 (0.8%)	1 (2.0%)	0 (0.0%)	0 (0.0%)	2 (0.9%)	<0.001	Significant
Thrombotic recurrence	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (20.0%)	0 (0.0%)	2 (0.9%)	<0.001	Significant
Death	5 (11.4%)	4 (3.1%)	3 (6.1%)	0 (0.0%)	4 (57.1%)	16 (6.9%)	<0.001	Significant
Total	44 (19.0%)	127 (54.7%)	49 (21.1%)	5 (2.2%)	7 (3.0%)	232 (100%)	-	-

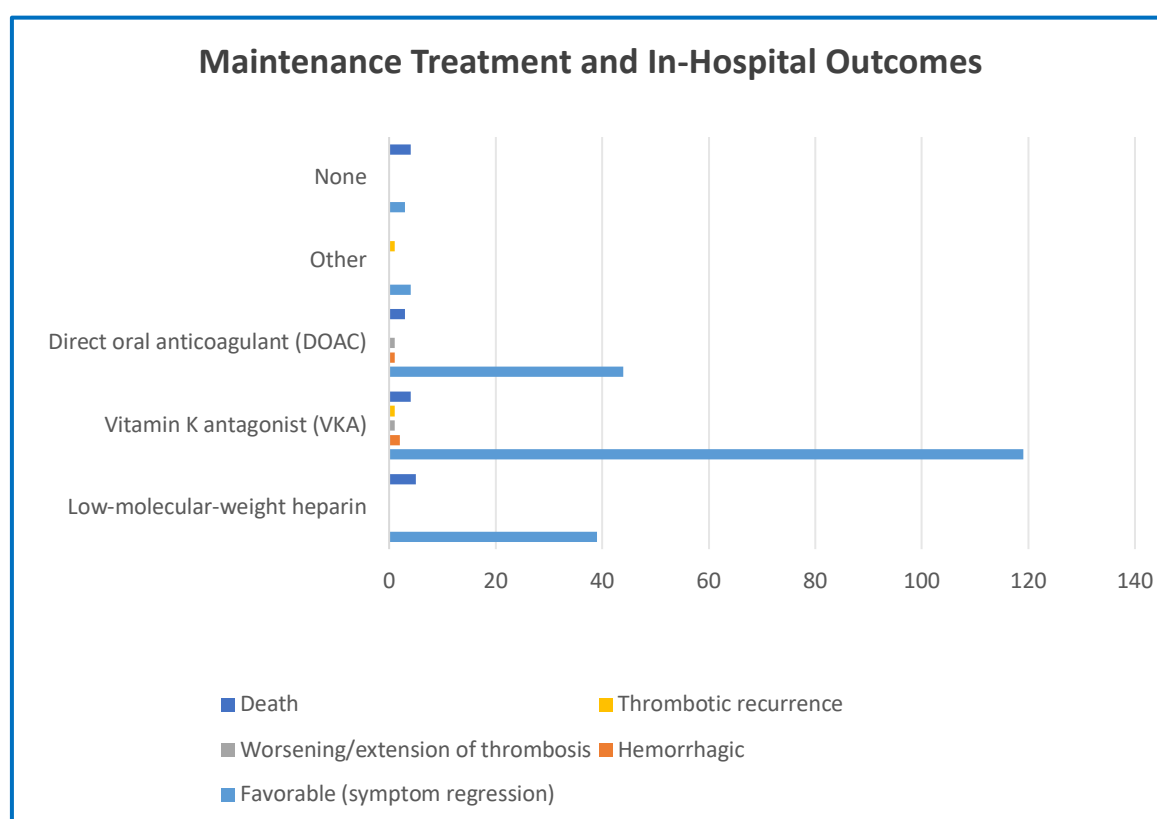


Diagram 35: Comparison of Maintenance treatment and In-Hospital Outcomes.

Commentary:

- Among the 232 patients assessed for in-hospital outcomes, vitamin K antagonists (VKA) constituted the most frequently used treatment (n = 127; 54.7%), followed by direct oral anticoagulants (DOAC) (n = 49; 21.1%), low molecular weight heparin (LMWH) (n = 44; 19.0%), other treatments (n = 5; 2.2%), and no treatment (n = 7; 3.0%).
- Favorable outcome defined as symptom regression was observed in 90.1% of cases (n = 209), with the highest rates recorded under VKA (93.7%) and DOAC (89.8%), followed by LMWH (88.6%) and other treatments (80.0%). The no-treatment group showed a markedly lower favorable outcome rate (42.9%).
- In-hospital mortality was recorded in 16 patients (6.9%), with the highest case-fatality rate observed in the no-treatment group (57.1%), followed by LMWH (11.4%), DOAC (6.1%), and VKA (3.1%). No deaths were recorded in the other treatment group. Hemorrhagic complications occurred in 3 patients (1.3%), noted under VKA (1.6%) and DOAC (2.0%). Worsening or extension of thrombosis was observed in 2 cases (0.9%), exclusively under VKA (0.8%) and DOAC (2.0%). Thrombotic recurrence was rare, affecting only 2 patients (0.9%), recorded under VKA (0.8%) and other treatments (20.0%).
- The distribution of all in-hospital outcomes across treatment groups was statistically significant ($p < 0.001$ for all categories).

5.16. Outcome during Hospitalisation According to Principal etiology of VTE.

Table 44: Distribution of in-hospital outcomes according to the principal aetiology of VTE.

Principal Etiology	Favorable outcome n (%)	Unfavorable outcome n (%)	Total (n)	p-value	Significance
Thrombophilia (congenital/acquired)	27 (96.4%)	1 (3.6%)	28	0.011	Significant
Active cancer	21 (72.4%)	8 (27.6%)	29	0.011	Significant
Immobilization / surgery / trauma	27 (87.1%)	4 (12.9%)	31	0.011	Significant
Pregnancy / Postpartum	16 (100%)	0 (0%)	16	0.011	Significant
Estrogen–progestin contraception	5 (83.3%)	1 (16.7%)	6	0.011	Significant
Idiopathic etiology	59 (98.3%)	1 (1.7%)	60	0.011	Significant
Other causes	15 (100%)	0 (0%)	15	0.011	Significant
Total	170 (91.9%)	15 (8.1%)	185		

Commentary:

- Of the 267 patients in the total cohort, 185 were included in this analysis, the remaining 82 being excluded due to missing aetiological data.
- The overall favourable outcome rate was 91.9% (n = 170), with unfavourable outcomes in 8.1% (n = 15). Idiopathic aetiology was the most frequent category (32.4%, n = 60), with a favourable outcome in 98.3% of cases. Thrombophilia (15.1%, n = 28) and pregnancy/post-partum (8.6%, n = 16) similarly achieved excellent outcomes (96.4% and 100% respectively). Immobilisation/surgery/trauma (16.8%, n = 31) recorded a mortality of 6.5% (n = 2). Active cancer (15.7%, n = 29) carried the worst prognosis, with the lowest favourable outcome rate (72.4%) and the highest in-hospital mortality (24.1%, n = 7), alongside a thrombotic recurrence of 3.4%.

- The chi-square test demonstrated a statistically significant association between principal aetiology and in-hospital outcome ($p = .011$), confirmed by all complementary statistical tests performed. This association was driven primarily by the markedly adverse prognosis of active cancer-associated VTE. The exclusion of 82 patients with missing data represents a limitation that should be acknowledged in interpreting these results.

V. DISCUSSION

The present retrospective study, conducted over a period of five years (January 2021 – December 2025) in the Internal Medicine Department of Laghouat Mixed Hospital, identified 267 cases of venous thromboembolic disease (VTE), confirmed clinically, biologically, and by imaging.

The overall hospital prevalence of (VTE) in our cohort was 4.47%, which is within the lower range reported in European internal medicine studies (3.65–14.9%) (323). This difference is probably related to disparities in diagnostic resources rather than true epidemiological variation. In high-income countries systematic use of CT pulmonary angiography and venous Doppler ultrasound allows detection of both symptomatic and incidental VTE, whereas diagnosis in our setting remains mainly symptom-oriented, potentially leading to underestimation.

The concentration of cases during 2023–2025 (65.5%) may indicate improved detection over recent years, consistent with trends observed in American cohorts (324). In contrast, the lower number of cases during 2021–2022 may be explained by the COVID-19 pandemic, since patients with COVID-associated VTE were managed in dedicated units and were not included in our cohort (325).

The mean age of patients was 50.8 years, lower than that reported in international registries such as PREFER in VTE (Europe, Barco et al, 2021), where the mean age was approximately 60 years (327), probably explained by demographic characteristics, as Western populations are generally older. French epidemiological data showed that a substantial proportion of VTE cases occurred in patients aged ≥ 85 years (324). In contrast, the younger Algerian population structure shifts the burden of disease toward younger age groups. The bimodal age distribution observed in our study suggests the coexistence of two clinical profiles: younger patients exposed mainly to transient factors and older patients with age-related comorbidities. Similar findings were reported in the Algerian cohort (328).

Women represented 64.8% of cases (sex ratio 0.54), contrasting with data from high-income countries where VTE is generally more frequent in men or equally distributed between sexes. French national estimates (Sanchez et al, 2024) reported a higher incidence in men, while Canadian studies showed only a slight female predominance (324,329). This difference is probably explained by the higher frequency of hormonal and obstetric exposures among women in our population.

A previous history of VTE was identified in 10.5% of patients, suggesting that most cases represented first thromboembolic events. This proportion is within the lower range reported internationally in USA, Sweden 2024, who showed that recurrence risk depends mainly on the persistence of underlying risk factors (323,330). Lower limb DVT was the most frequent previous event, consistent with the findings of KSA (331). Unusual thromboses, including splanchnic and caval thrombosis, were also observed and may suggest underlying systemic disorders (332).

A positive family history of VTE was reported in only 6.5% of cases, although interpretation is limited by the high proportion of missing data. International studies nevertheless support a strong familial contribution to thrombotic risk. Recent studies highlighted the importance of hereditary predisposition, particularly in younger patients (332,333).

Behavioural risk factors were absent in 58.7% of patients, while smoking and alcohol consumption were reported in 11.5% and 1.5% of cases, respectively. This pattern is consistent with the socio-cultural context of southern Algeria, where alcohol consumption is limited. Large cohort studies found no clear association between moderate alcohol consumption and VTE risk (334,335). Smoking is recognised as a modest prothrombotic factor but probably had only a limited impact in our cohort.

The majority of patients presented with a single identifiable risk factor (43.6%), with general VTE risk factors mainly dominated by prolonged immobilisation (15.6%), recent major surgery (12.6%), and active malignancy (10.7%). This distribution is consistent with the classical Virchow triad and aligns with international literature

(336,337), the association between active cancer and VTE has also been confirmed in North African (338). Similar observations emphasised that thrombotic risk depends not only on the number of risk factors but also on their interaction with individual patient characteristics (341), while 38.6% of patients presented without any recognised provoking factor.

Among women, 43.9% presented at least one sex-specific risk factor, with contraceptive use being the most frequent (60.53%), followed by the postpartum period (36.84%). Combined oral contraceptives are well-recognised prothrombotic factors, as reported by Kapczyńska et al. (2025, Poland) (339), and the postpartum period is associated with a markedly increased VTE risk, particularly during the first six weeks after delivery, according to Bates et al. (2022, Canada) (340). The relatively high proportion of postpartum cases may also reflect the higher fertility rate in Algeria compared with many Western countries. The small number of pregnancy-related cases is likely due to referral to obstetric services. This strongly contributes to female predominance.

A sex-related difference in risk factor distribution was observed, with women more frequently exposed to surgery and immobilisation, whereas men more often had no identifiable risk factors. This distribution is consistent with international literature (342,343).

Lower limb DVT was significantly associated with prolonged immobilisation (23.0%), consistent with the RECOVERY DVT/PE study and the Merck Manual (2023), which identify venous stasis secondary to immobilisation as a major trigger for thrombosis (344,345). Pulmonary embolism was significantly associated with recent major surgery (21.4%), in agreement with Kristoffersen et al. (2023, Norway) and StatPearls (2023), which highlighted postoperative hypercoagulability and immobilisation as major precipitating factors for PE (337,346). Cerebral venous thrombosis was significantly associated with immobilisation; however, this finding should be interpreted cautiously since female-specific hormonal and obstetric risk factors were not included in the present analysis (347).

Hypertension (22.8%) and diabetes (20.6%) were the most common comorbidities. However, their independent role in VTE remains controversial. American study reported no independent association between hypertension and VTE after adjustment for confounding factors (323). Their high prevalence in our cohort therefore probably reflects the epidemiological transition currently occurring in Algeria rather than a direct causal role in thrombosis.

COVID-19 was identified in 20 patients (8.6% of valid cases), with 34 missing data. This prevalence is lower than that reported by a Turkish study (30.4% in PTE patients) (348). This difference is mainly explained by the fact that during the COVID-19 period in our institution, SARS-CoV-2-positive patients were managed in dedicated COVID units and therefore not included in the Internal Medicine VTE cohort, in addition to possible underdiagnosis of asymptomatic infections due to limited RT-PCR availability and retrospective data collection in a resource-limited setting. Similar underreporting was highlighted by SATH (2020) in Algeria (349) and Tazi Mezalek et al. (2021) in Morocco (350). Nevertheless, COVID-19 remains a well-established prothrombotic condition, with Clavijo et al. (2021) showing increased VTE risk after mild infection (351). and Katsoularis et al (352). and Xie et al (353). confirming a persistent post-infectious thrombotic risk over weeks to months. The 8.6% rate in our cohort likely underestimates the true contribution of prior COVID-19 infection to VTE.

Lower limb DVT remained the most frequent localisation (53.2%), in agreement with international epidemiological data (323,325,326). However, the proportion of CVT (16.5%) was higher than typically reported in Western cohorts, possibly due to the hospital-based recruitment and the role of internal medicine departments in managing atypical thrombotic presentations. Similar trends have been described in North African studies and in the Algerian CHU Béni Messous experience (331,332).

Likewise, the frequency of splanchnic thrombosis (10.2%) exceeded that reported in most European series, likely reflecting the systematic inclusion of unusual thrombotic localisations in our cohort, as noted in recent reviews (332,333).

Regarding DVT laterality, the predominance of left-sided involvement (54.2%) is consistent with international data and may be explained by haemodynamic asymmetry of the iliofemoral venous system, as described in May–Thurner syndrome (325).

This distribution also showed some variations according to sex. Lower limb DVT remained the predominant localisation in both men and women, whereas CVT was more frequently observed in females, likely related to hormonal risk factors such as oral contraception, pregnancy, and the postpartum period, as reported in previous studies. In contrast, abdominal and other atypical thromboses were more common in males, possibly reflecting a greater contribution of underlying conditions such as thrombophilia, malignancy, and systemic diseases. These findings should nevertheless be interpreted cautiously, since the analysis was based on thrombotic events rather than individual patients, and some patients presented with multiple localisations.

Isolated DVT was the predominant clinical form (69.6%), followed by isolated PE (21.5%) and combined DVT–PE (8.8%). Compared with international registries, this suggests a relatively lower proportion of PE, possibly reflecting limited access to thoracic imaging in routine practice (323,326). Similarly, the low frequency of concomitant DVT–PE may be explained by the absence of systematic screening for associated localisations (324,327).

The clinical presentation of VTE disease in our cohort was predominantly characterised by lower limb manifestations, particularly oedema with warmth and redness (54.8%) and limb pain (29.3%), consistent with the classical presentation of DVT described in the literature. Similar findings have been reported in recent European studies (323).

Neurological manifestations «such as sudden severe headache (12.0%), seizures (7.3%), and focal deficits (6.9%)» were relatively more frequent than in Western series mainly focused on DVT and pulmonary embolism (PE). This likely reflects the substantial proportion of cerebral venous thrombosis (CVT) in our cohort, as also observed in Maghrebian studies (331).

Venous Doppler ultrasound was the most frequently performed investigation (58.7%), consistent with current recommendations identifying compression ultrasonography as the first-line test for suspected DVT (323,327). In contrast, the very low use of D-dimer testing (0.9%) diverges from standard diagnostic algorithms, where it plays a central role in excluding VTE prior to imaging (324). This likely reflects limited assay availability and reliance on imaging-based diagnosis.

Despite the notable burden of CVT, the limited use of cerebral imaging suggests infrastructural constraints that may have impacted diagnostic accuracy. Similar limitations have been reported in Maghrebian studies (323).

In our study, etiological data were available for 76% of patients, while 24% were missing due to the retrospective design. This limitation is frequently reported in similar Algerian studies. It's mainly dominated by idiopathic causes (31%), followed by active cancer, immobilization, surgery, trauma, and thrombophilia, while hormonal and other causes were less frequent. This pattern is consistent with Algerian studies (357,358), the Saudi KFMC registry, and French data such as the REMOTEV registry. Similar distributions are reported in international literature (25–50%) (360,361). Compared with Western European series, the higher proportion of idiopathic causes may reflect under-diagnosis of transient risk factors, incomplete screening for occult malignancy, and the retrospective nature of data collection. The relatively higher rate of thrombophilia likely reflects selective testing in younger patients and possible selection bias, while the lower proportion of postoperative VTE may be related to differences in surgical activity, thromboprophylaxis practices, and healthcare organization (361,362).

According to sex and age, idiopathic VTE was similarly distributed between men and women, in agreement with most international studies. Thrombophilia was more frequently identified in males in our cohort, consistent with data showing a higher intrinsic VTE risk in men after adjustment for hormonal exposure, partly related to inherited thrombophilic states (359). Immobilization and surgery related VTE were more frequent in females, likely reflecting gynecological procedures, pregnancy, and postpartum hospitalizations, which are more

prevalent in our setting. Hormonal factors were confined to women aged 21–40 years and appeared slightly more frequent than in some Western cohorts, possibly due to higher fertility rates and wider use of hormonal contraception (360). With increasing age, the rise in cancer and immobilization related VTE was consistent with international data, although the relatively high burden in elderly patients may reflect delayed cancer diagnosis and a higher prevalence of comorbidities (362).

Regarding localization, lower-limb DVT and pulmonary embolism were mainly associated with idiopathic causes, cancer, and immobilization, in line with classical epidemiological patterns described in ESC guidelines and international registries (362). The slightly higher proportion of idiopathic cases may reflect under-recognition of provoking factors or limited per-hospital diagnostic evaluation. CVT was more frequently associated with idiopathic, thrombophilia, and hormonal factors, particularly in young women, consistent with Maghrebian studies (356), which may be related to regional prothrombotic conditions, including Behçet disease and antiphospholipid syndrome, as well as greater exposure to hormonal treatments. Splanchnic vein thrombosis was mainly linked to cancer and idiopathic causes, similar to international data, although the higher idiopathic proportion may reflect incomplete screening for myeloproliferative disorders or occult malignancy. Unusual thrombosis sites showed a higher prevalence of thrombophilia compared with European cohorts, suggesting either a stronger underlying prothrombotic predisposition or selective testing in these patients (359).

In terms of outcomes, prognosis varied according to etiology. The best outcomes were observed in pregnancy-related and miscellaneous causes, followed by idiopathic and thrombophilia associated VTE. In contrast, cancer-associated VTE had the worst prognosis, with the highest mortality, consistent with the RIETE registry and other international studies (355). However, mortality in the cancer subgroup was higher than that reported in Western cohorts, likely due to advanced cancer stage at diagnosis, limited access to direct oral anticoagulants, and delayed initiation of treatment. Immobilization and surgery related VTE showed intermediate outcomes, with occasional complications such as bleeding and thrombus extension, reflecting variability in anticoagulation strategies and monitoring. Overall, differences in outcomes compared with other studies are mainly explained by healthcare system factors, access to early diagnosis, and heterogeneity in therapeutic management (354,361,362).

LMWH was the predominant initial treatment in our cohort (85.8%), similar to several Algerian and North African hospital series where parenteral anticoagulation remains the standard first-line approach (365). This contrasts with international data from the GARFIELD-VTE registry, where DOACs represented nearly half of initial treatments, especially in Europe (363,369). UFH was used in 7.7% of cases, comparable to other studies where it is reserved for unstable patients or severe renal impairment (362,364). Overall, our results show persistent reliance on heparins, unlike Western countries where DOACs are increasingly preferred.

Adjunctive treatments were less frequent in our study. Compression stockings were prescribed in 17.7% of patients with lower-limb DVT, a lower rate than that reported in French and Belgian series where their use after proximal DVT is more systematic (366,367). This difference may be explained by variations in prescribing habits, limited access, or lower adherence. Similar low utilisation has also been described in Maghrebian retrospective studies (365). Most of our patients received no additional supportive treatment besides anticoagulation.

For maintenance therapy, VKA remained the most common regimen (53.5%), which is consistent with many Algerian and regional studies but differs from Western European cohorts where DOACs have become the leading long-term treatment (365,368). DOACs accounted for 21.4% of our prescriptions, still lower than international registries, suggesting slower adoption in our setting (363,370). LMWH was continued in 18.5% of patients, a proportion higher than in European series and likely related to cancer-associated thrombosis (371). These findings indicate a transitional pattern, with traditional anticoagulants still dominant but gradual integration of DOACs.

The in-hospital clinical evolution was generally favorable, with symptom regression observed in nearly 9 out of 10 cases. This finding is consistent with the literature, where early improvement is typically reported when VTE is promptly diagnosed and managed according to current guidelines (362,372). In our series, better outcomes were seen in patients receiving standard anticoagulation, particularly initial LMWH followed by VKA or DOACs, whereas poorer outcomes in untreated patients or those receiving alternative therapies were likely related to more severe clinical conditions or contraindications to anticoagulation.

In-hospital complications were relatively uncommon. Bleeding events accounted for only 1.1% of cases, confirming the overall safety of anticoagulant therapy when appropriately monitored (368). Thrombus progression and recurrence were also rare (<2%), in line with international data under effective anticoagulation. Overall, these findings confirm that VTE has a favorable short-term outcome in most patients when appropriately managed.

In-hospital mortality remained significant, ranging from 6.9% to 7.5% across groups. These rates are comparable to those reported in North African series but higher than in large European registries, where improved healthcare organization and wider use of DOACs have contributed to lower mortality (372,373). Deaths were mainly observed in untreated patients or those receiving non-standard therapies, suggesting a major influence of baseline severity, comorbidities, or inability to initiate anticoagulation.

VI. CONCLUSION

In conclusion, this retrospective study provides one of the few comprehensive overviews of venous thromboembolic disease (VTE) in southern Algeria and highlights the growing burden of this pathology in internal medicine practice. The estimated hospital prevalence observed in our cohort remains lower than that reported in international registries; however, this figure is probably underestimated because of persistent diagnostic limitations, restricted access to advanced imaging, and the absence of systematic screening strategies, particularly in peripheral regions.

From an epidemiological perspective, our findings confirm that VTE in our population predominantly affects relatively younger patients compared with Western cohorts, with a marked female predominance largely related to hormonal and obstetric exposures. Lower-limb deep vein thrombosis remained the most frequent localization, while the relatively high proportion of cerebral and splanchnic thrombosis reflects the specific clinical profile encountered in internal medicine departments and the importance of atypical thrombotic presentations in our setting.

The study also confirms the major contribution of classical provoking factors, particularly prolonged immobilization, surgery, and active malignancy, while a substantial proportion of cases remained idiopathic. This finding underlines the probable under-recognition of transient risk factors, limited thrombophilia investigations, and insufficient screening for occult cancer. The coexistence of idiopathic and unusual thrombotic forms further suggests that underlying prothrombotic conditions may remain insufficiently explored in routine practice.

Therapeutically, our results demonstrate that anticoagulation remains largely based on traditional regimens, especially low-molecular-weight heparin and vitamin K antagonists, whereas the use of direct oral anticoagulants (DOACs) remains limited compared with international standards. Despite generally favorable short-term outcomes, in-hospital mortality remains significant, particularly among cancer-associated VTE and severe untreated forms, emphasizing the impact of delayed diagnosis, comorbidities, and therapeutic inequalities.

In light of these findings, this study highlights several major public health priorities and calls for a structured national strategy aimed at improving VTE prevention, diagnosis, and management. It is essential to:

- Strengthen early detection strategies for VTE, particularly in high-risk patients, through systematic risk assessment and improved screening practices,
- Facilitate equitable access to modern diagnostic tools, including Doppler ultrasonography, CT pulmonary angiography, D-dimer testing, and neurovascular imaging across all healthcare levels,
- Promote wider accessibility to newer therapeutic options, especially direct oral anticoagulants, in order to align national practice with current international recommendations,
- Develop national evidence-based protocols for VTE diagnosis, thromboprophylaxis, and therapeutic management adapted to the Algerian healthcare system,
- Encourage multidisciplinary collaboration involving internists, hematologists, cardiologists, neurologists, radiologists, oncologists, emergency physicians, pharmacists, and healthcare policymakers.
- Organize national scientific meetings, awareness campaigns, and continuous medical education programs dedicated to VTE prevention and management,
- Reinforce the training of general practitioners and frontline healthcare professionals to improve early recognition of thromboembolic manifestations and reduce diagnostic delay,
- Promote therapeutic education programs for patients and their families in order to improve treatment adherence, awareness of recurrence risk, and long-term follow-up,
- Encourage prospective multicenter studies and national registries to obtain more accurate epidemiological data, reduce missing information, and better evaluate long-term outcomes and therapeutic practices,
- Expand research on thrombophilia, cancer-associated thrombosis, and unusual thrombotic localizations in

the Algerian population to better identify regional specificities and optimize personalized management.

Although venous thromboembolic disease remains a potentially preventable and treatable condition, it continues to represent a major source of morbidity and mortality in our setting. A coordinated national effort integrating early diagnosis, modernization of therapeutic strategies, physician training, and patient education is essential to improve prognosis, reduce complications, and optimize the quality of care for patients with VTE in Algeria

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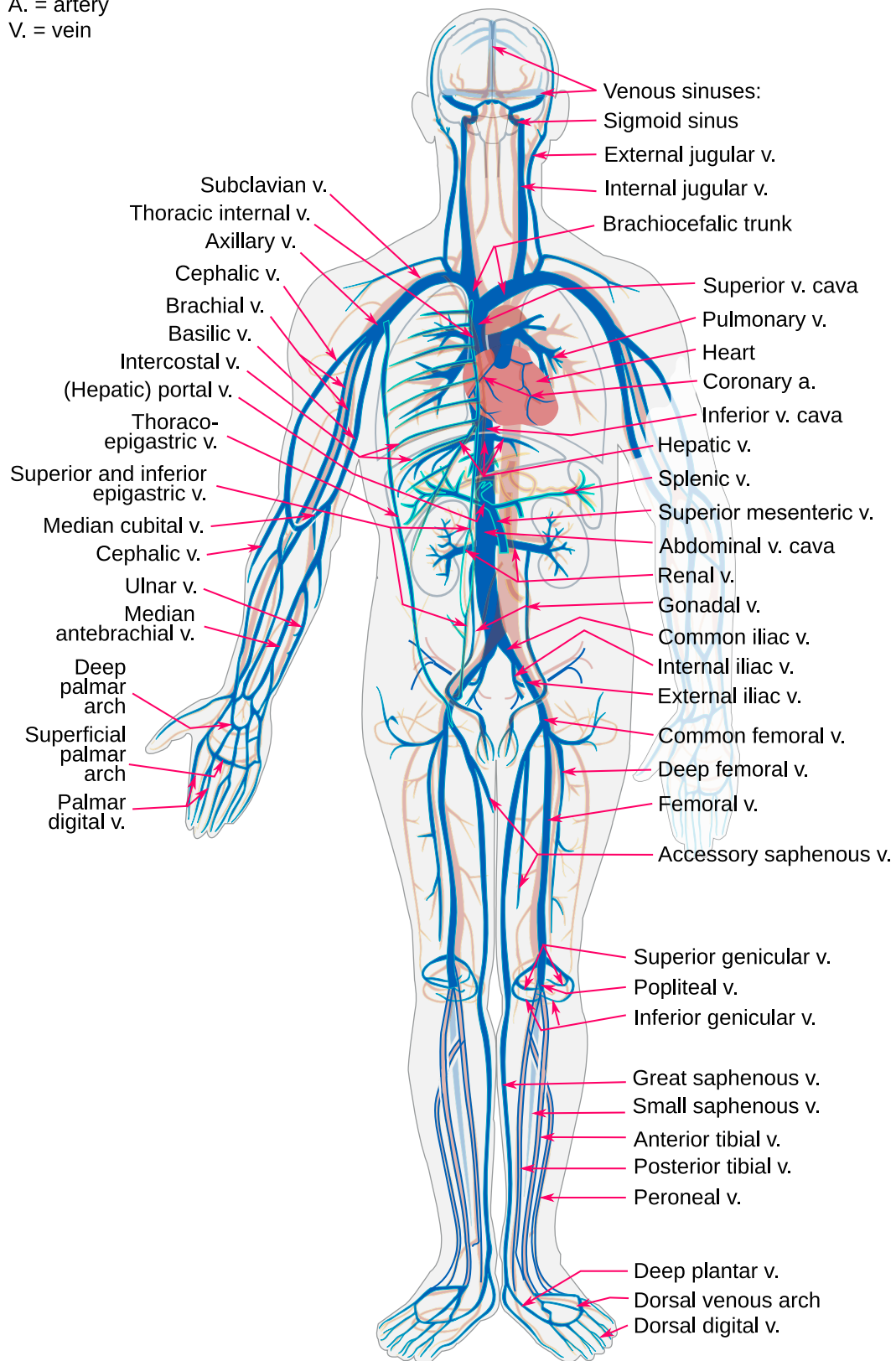
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VIII. APPENDIX

APPENDIX 01: Systemic Venous Anatomy of the Human Body.

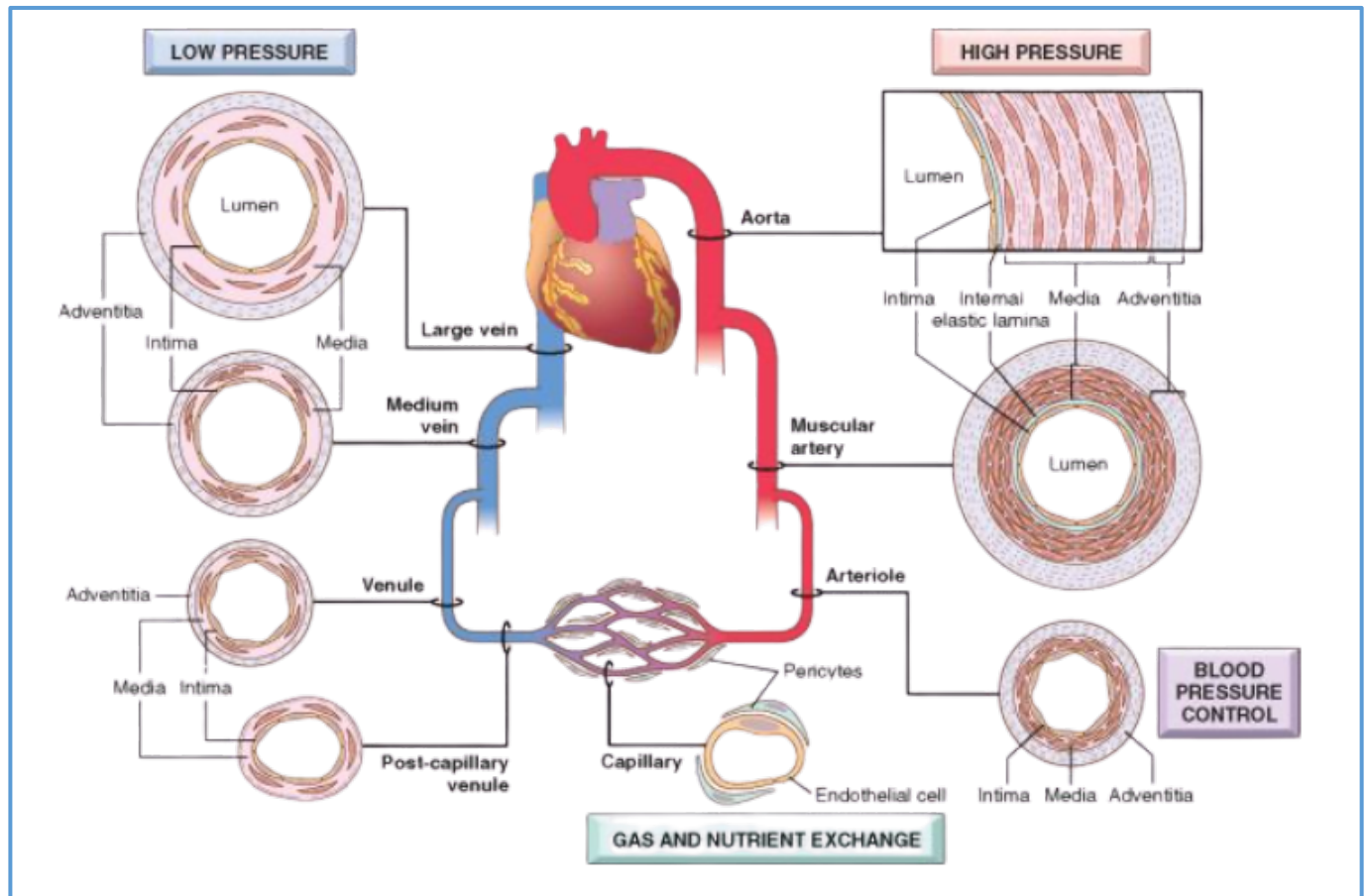
A. = artery
V. = vein



APPENDIX 02: Classification of Veins According to Circulation and Anatomical Location.

	Classification of veins
01	Pulmonary veins carry oxygenated blood from the lungs to the left atrium of the heart.
02	Systemic veins return deoxygenated blood from the rest of the body to the right atrium of the heart.
03	Superficial veins are located close to the skin surface and are not accompanied by a corresponding artery.
04	Deep veins are located within the muscular tissues and are usually accompanied by a corresponding artery.

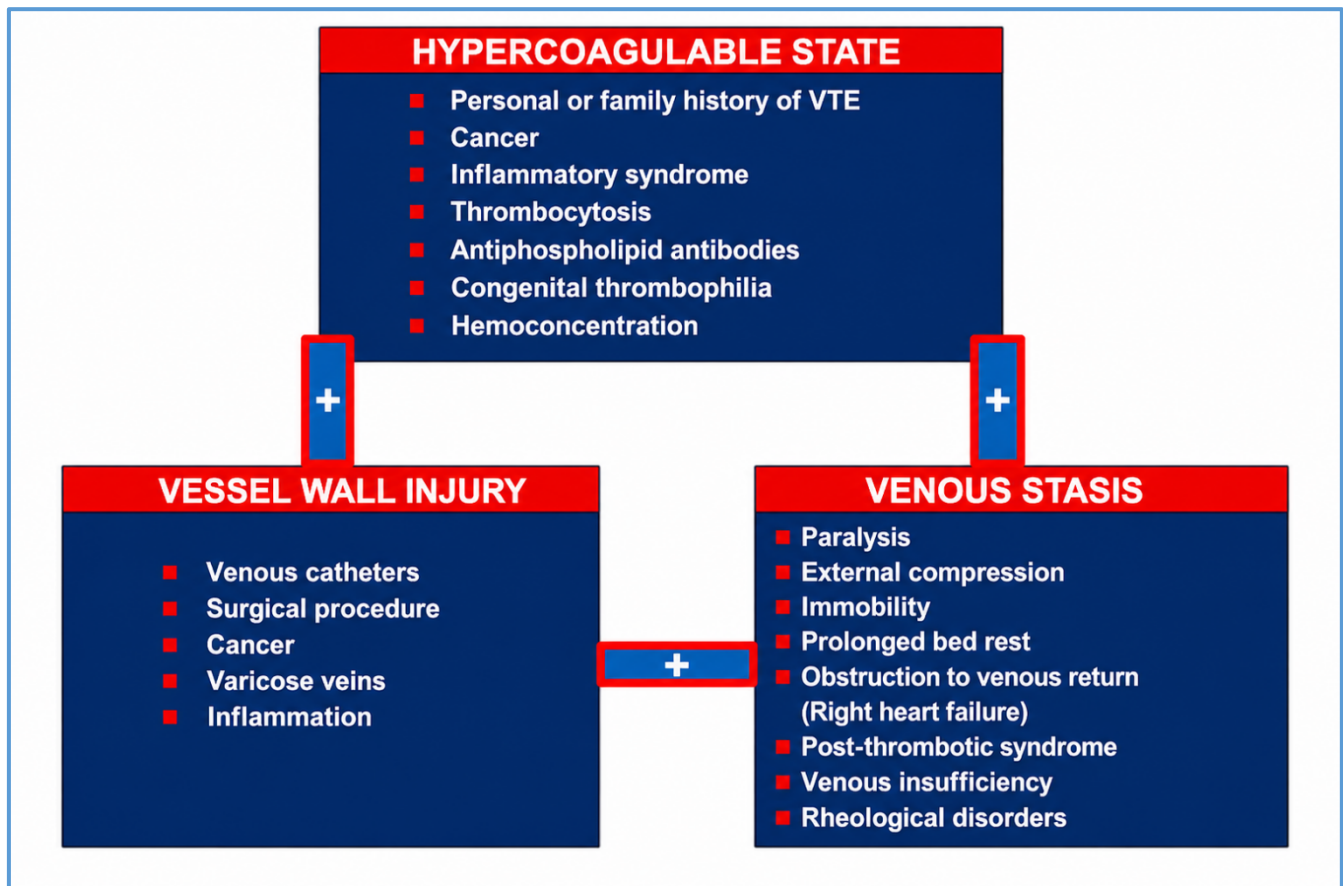
APPENDIX 03: Structural and Functional Differences Between Arteries and Veins.



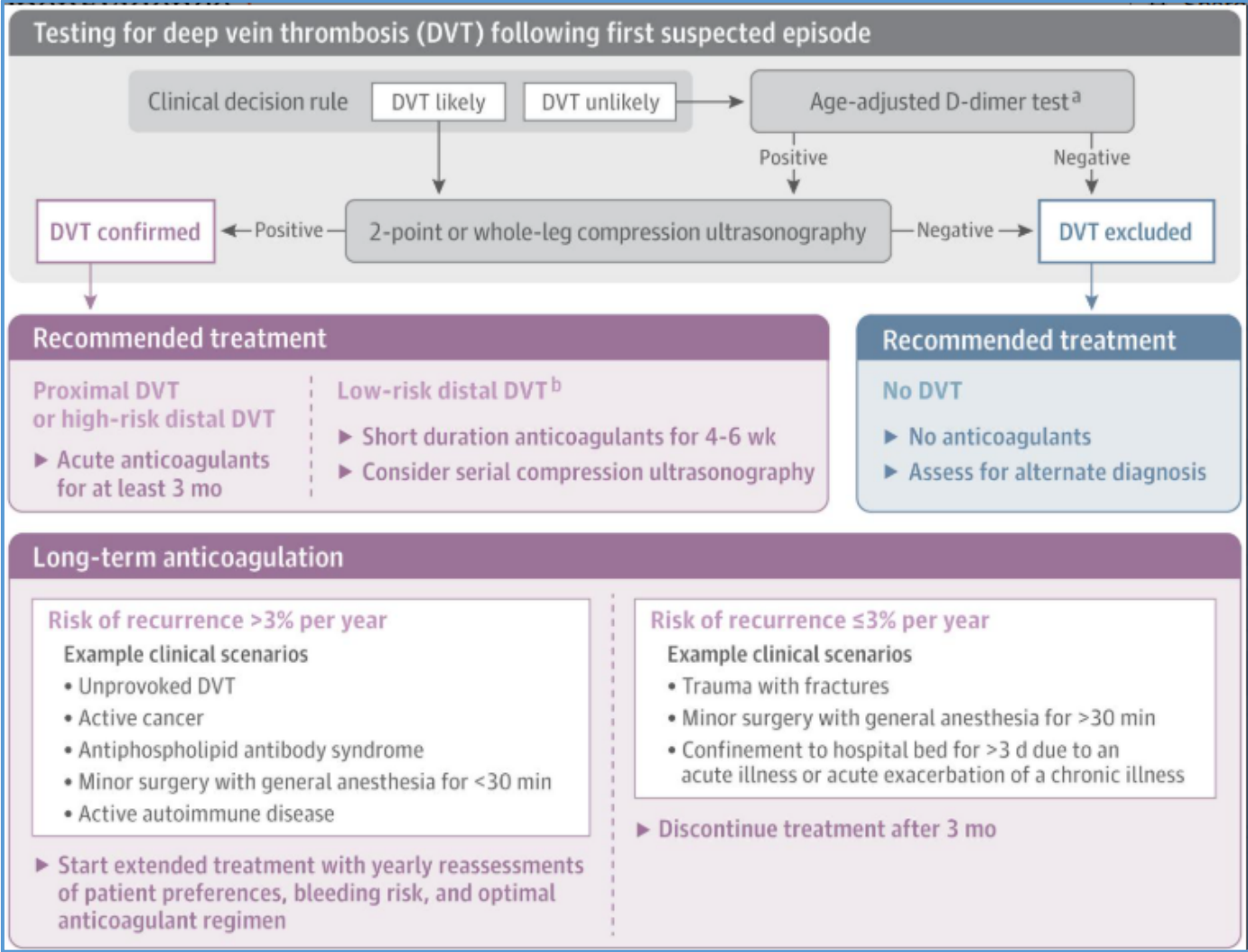
APPENDIX 04: Table of Coagulation Factors (Modified) (Pavie and G  r  me, 2013).

Factor	Function
I (Fibrinogen)	Substrate of thrombin
II (Prothrombin)	Activates I, V, VIII, XIII, protein C, platelets
III (Tissue factor)	Activates factor VII
IV (Calcium)	Link between phospholipids and factors
V (Proaccelerin, labile factor)	Increases enzymatic activity of Xa (cofactor)
VI	Not assigned
VII (Proconvertin, stable factor)	Activates IX, X
VIII (Antihemophilic factor A)	Increases enzymatic activity of IXa (cofactor)
IX (Christmas factor or Antihemophilic factor B)	Activates X
X (Stuart–Prower factor)	Activates II
XI (Rosenthal factor, plasma thromboplastin antecedent)	Activates XII, IX and prekallikrein
XII (Hageman factor or contact factor)	Activates prekallikrein and fibrinolysis
XIII (Fibrin-stabilizing factor)	Covalent bonds between fibrin monomers
von Willebrand factor	Mediates platelet adhesion
Prekallikrein (Fletcher factor)	Activates XII and prekallikrein, cleaves HMWK
High-molecular-weight kininogen (HMWK)	Transport and binding of XI and prekallikrein (cofactor)

APPENDIX 05: Risk Factors for Venous Thrombosis (Virchow's Triad Components).



APPENDIX 06: Clinical Management Algorithm for Suspected Deep Vein Thrombosis (DVT).



APPENDIX 07: Table of Wells Clinical Prediction Score for PE.

Criterion	Points
Clinical signs of DVT	3
PE more likely than an alternative diagnosis	3
Heart rate > 100/min	1.5
Immobilization or recent surgery	1.5
Previous DVT/PE	1.5
Hemoptysis	1
Active cancer	1

Interpretation:

table: Wells score – Interpretation

Classification	Score
Low	< 2
Intermediate	2–6
High	> 6

table: Simplified version of Wells score

Classification	Score
PE unlikely	≤ 4
PE likely	> 4

APPENDIX 08: Table of the Revised Geneva Clinical Prediction Score for PE (Simplified Version).

Criterion	Points (simplified)
Previous DVT/PE	1
Heart rate 75–94/min	1
Heart rate ≥ 95 /min	2
Recent surgery	1
Hemoptysis	1
Active cancer	1
Unilateral lower limb pain	1
Pain + lower limb edema	1
Age > 65 years	1

Interpretation:

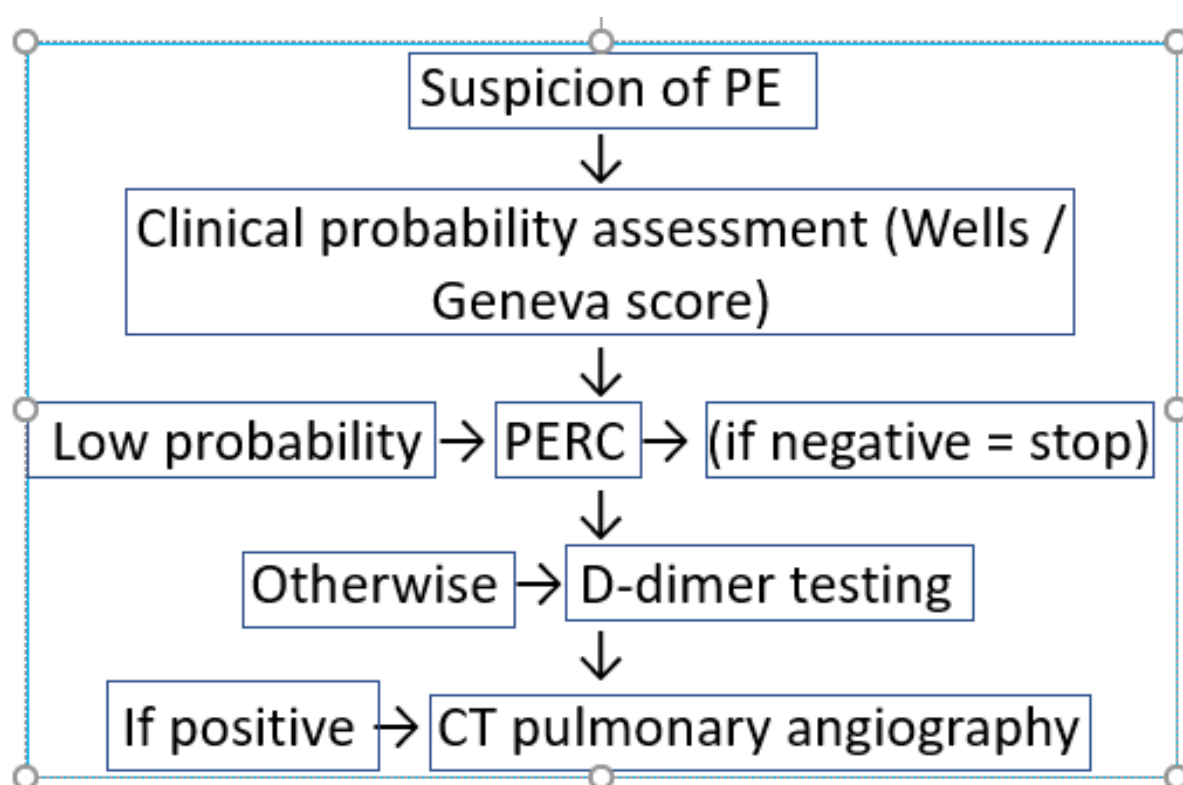
Classification	Score
Low	0–1
Intermediate	2–4
High	≥ 5

Simplified version	Score
PE unlikely	≤ 2
PE likely	≥ 3

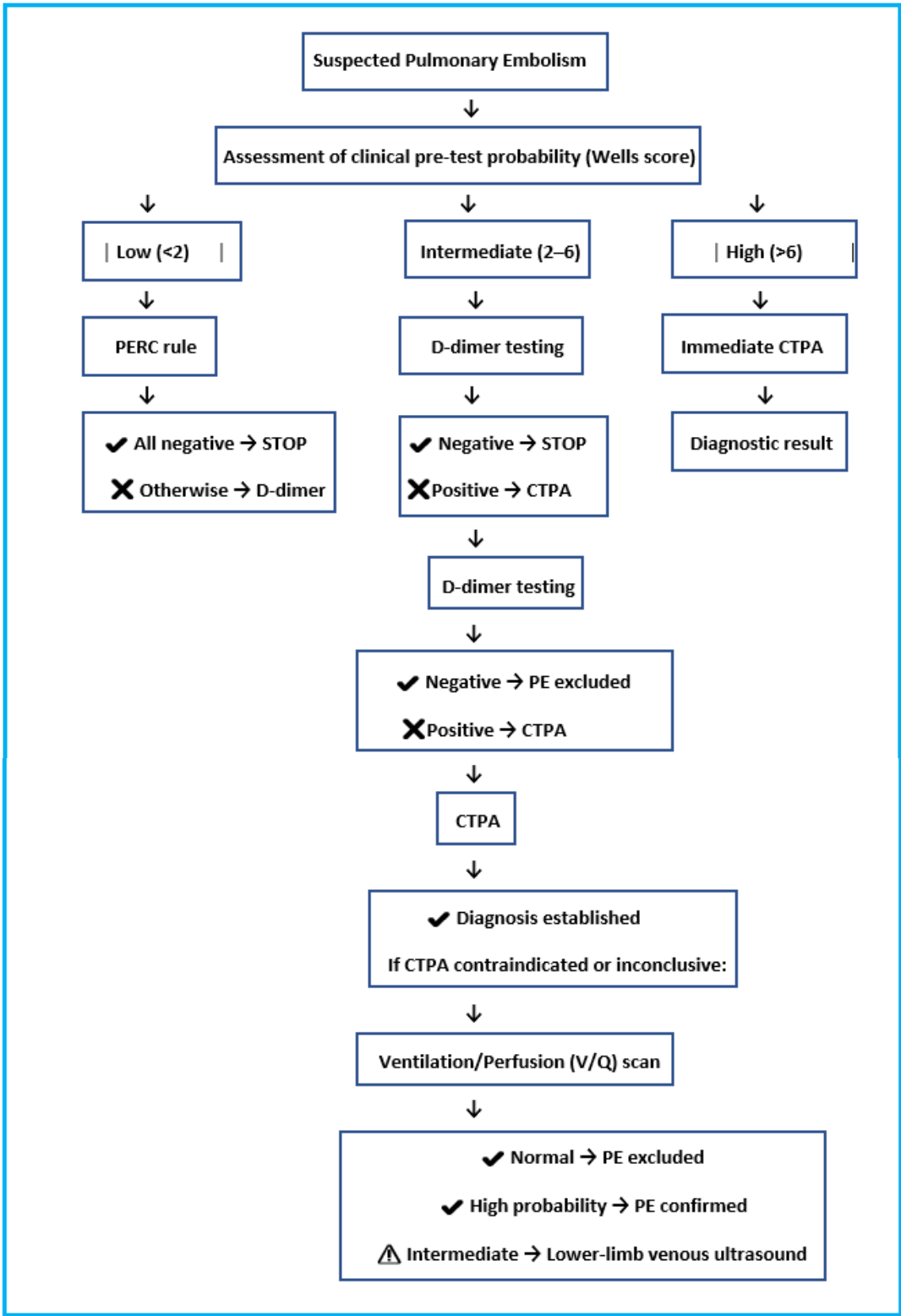
APPENDIX 09: Table of Pulmonary Embolism Rule-out Criteria (PERC).

Criterion
Age < 50 years
Heart rate < 100/min
SaO₂ > 94%
No lower limb edema
No hemoptysis
No recent surgery/trauma
No history of VTE
No hormonal therapy

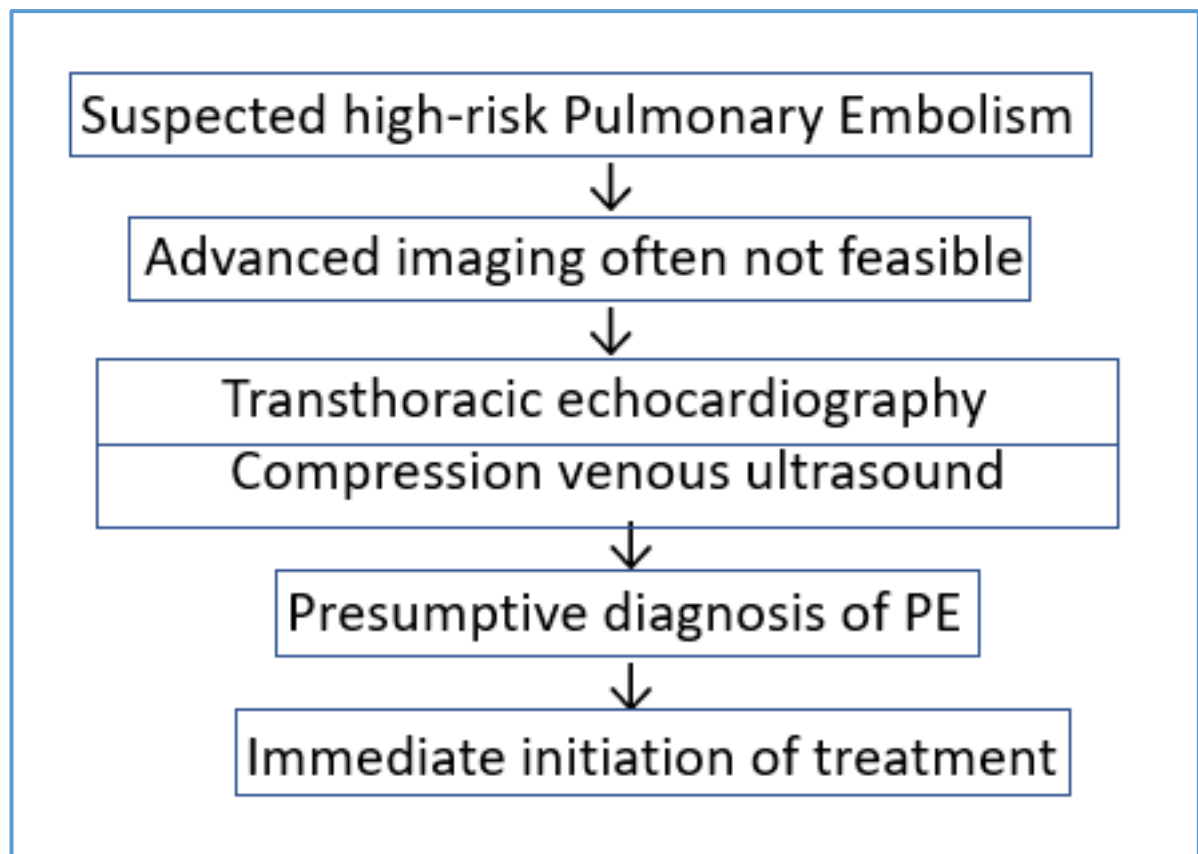
APPENDIX 10: Simplified Diagnostic Algorithm for Suspected Pulmonary Embolism.



APPENDIX 11: Comprehensive Diagnostic Algorithm for Suspected PE in Hemodynamically Stable Patients.



APPENDIX 12: Diagnostic Approach for Suspected High-Risk PE in Hemodynamically Unstable Patients.



APPENDIX 13: Prognostic Scores and Risk Stratification in Pulmonary Embolism (PESI and sPESI).

Parameter	PESI	sPESI
Age > 80 years	✓	1
Male sex	✓	–
Cancer	✓	1
Heart failure	✓	1
Chronic pulmonary disease	✓	1
Heart rate ≥ 110 bpm	✓	1
Systolic BP < 100 mmHg	✓	1
Respiratory rate > 30/min	✓	–
Temperature < 36°C	✓	–
Altered mental status	✓	–
SpO ₂ < 90%	✓	1

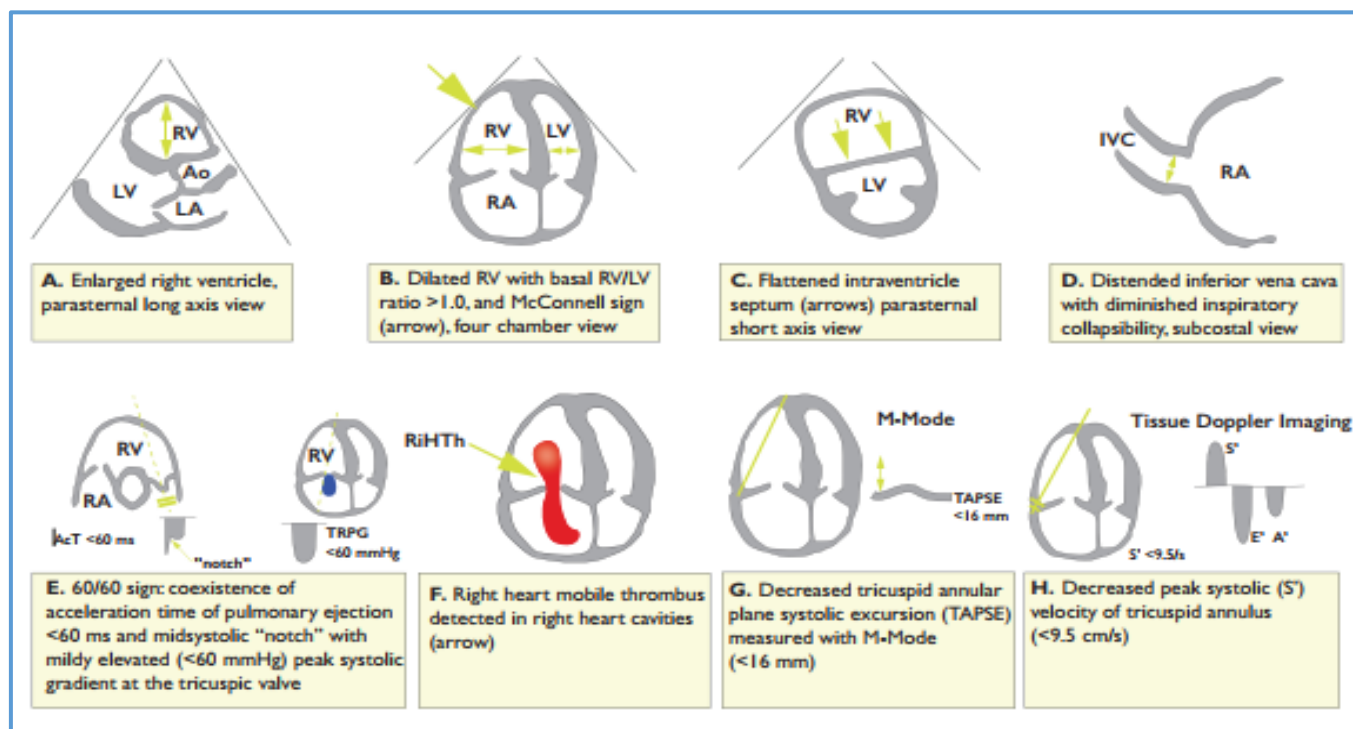
Risk stratification :

Score	Risk of mortality
PESI I–II	Low (≈ 1 –6%)
PESI III–V	Moderate to high
sPESI = 0	$\approx 1\%$
sPESI ≥ 1	$\approx 10.9\%$

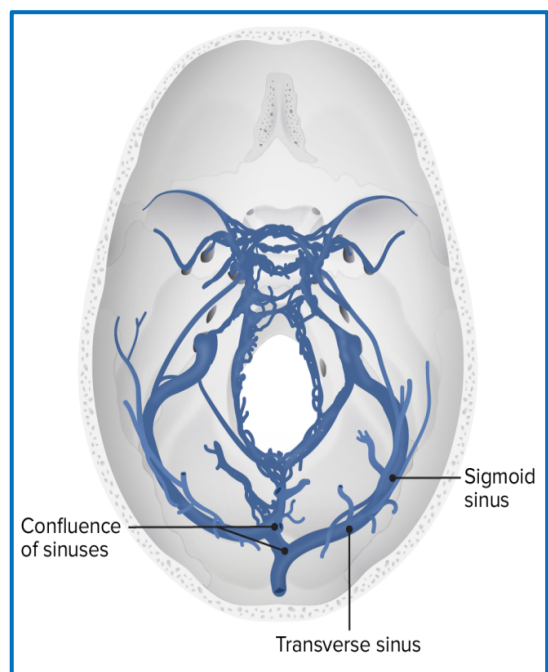
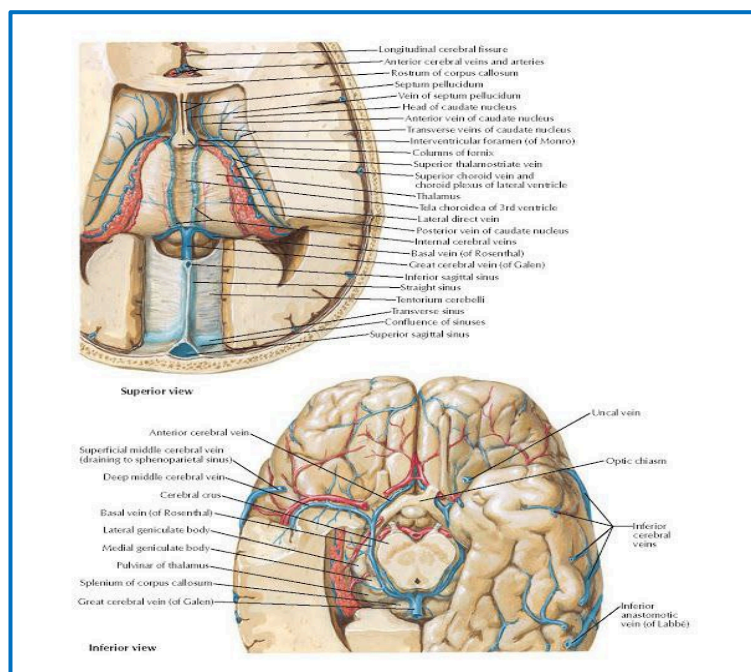
APPENDIX 14: Table of Severity Classification of PE.

Type of PE	Characteristics
Massive PE (high risk)	Hemodynamic instability (SBP < 90 mmHg, shock)
Intermediate PE (submassive)	Hemodynamically stable with right ventricular dysfunction and/or elevated biomarkers
Low-risk PE	Hemodynamically stable without right ventricular dysfunction or elevated biomarkers

APPENDIX 15: Echocardiographic Signs of Right Ventricular Dysfunction in Pulmonary Embolism.



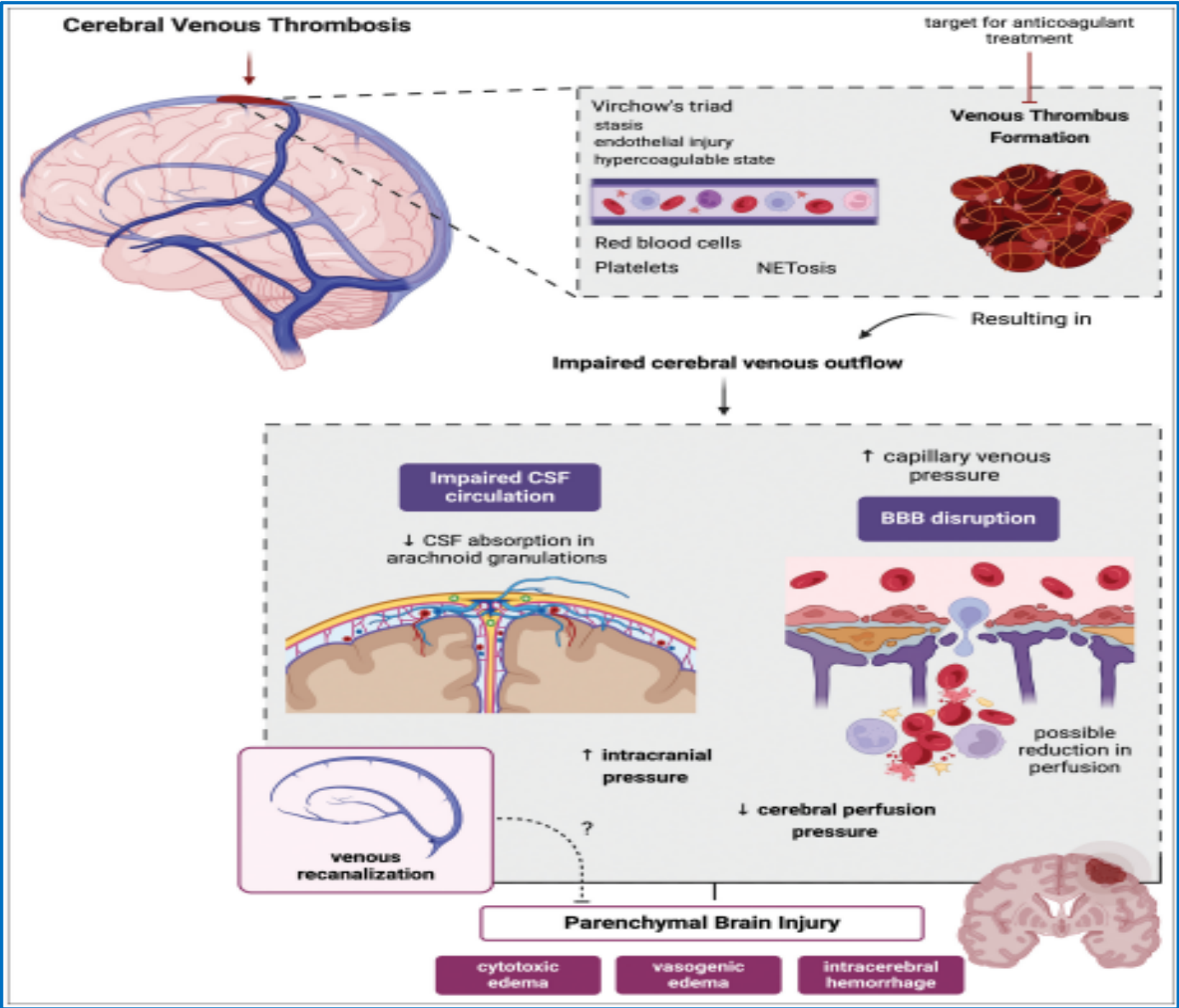
APPENDIX 16: Anatomy of the Cerebral Venous System and Dural Sinuses.



APPENDIX 17: Principal pathophysiological mechanisms, consequences, and resulting effects of CVT.

Consequence	Mechanism	Result
Vasogenic oedema	Disruption of the blood–brain barrier	Increased hydrostatic pressure
Cytotoxic oedema / venous infarction	Reduction in cerebral perfusion pressure	Cellular injury and neuronal dysfunction
Intracranial hypertension	Impairment of LCS resorption	Involvement of the dural sinuses, particularly the superior sagittal sinus
Haemorrhagic transformation	Rupture of small cerebral vessels	Associated intracerebral haemorrhages

APPENDIX 18: Pathophysiology of cerebral venous thrombosis (CVT).



APPENDIX 19: Table of the CVT-Risk Score Clinical Variables and Probability Interpretation.

Clinical variables	Points
Seizure(s) at onset	4
Known thrombophilia	4
Oral contraception	2
Symptom duration > 6 days	2
Worst headache of life	1
Focal neurological deficit	1

Score Interpretation :

Total score	Probability of cerebral venous thrombosis (CVT)
0 – 2	Low
3 – 5	Intermediate
6 – 12	High

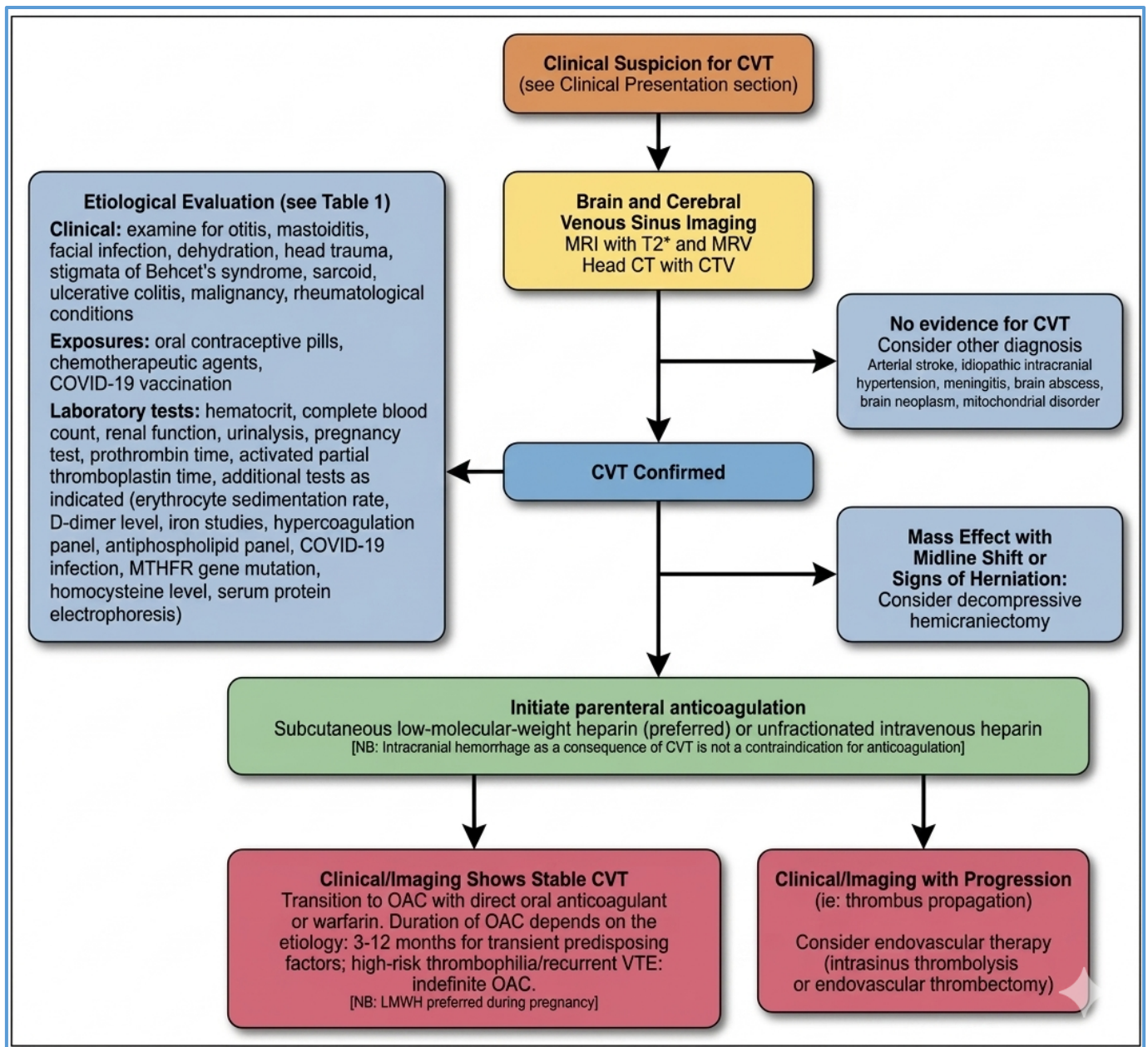
APPENDIX 20: Non-Contrast CT Findings in Cerebral Venous Thrombosis (CVT).

Direct Signs	Indirect Signs
Spontaneous hyperdensity of a thrombosed sinus or vein	Parenchymal hypodensities not restricted to an arterial territory
Cord sign	Bilateral lesions
Dense triangle sign	Hemorrhagic infarcts
	Mass effect or cerebral oedema

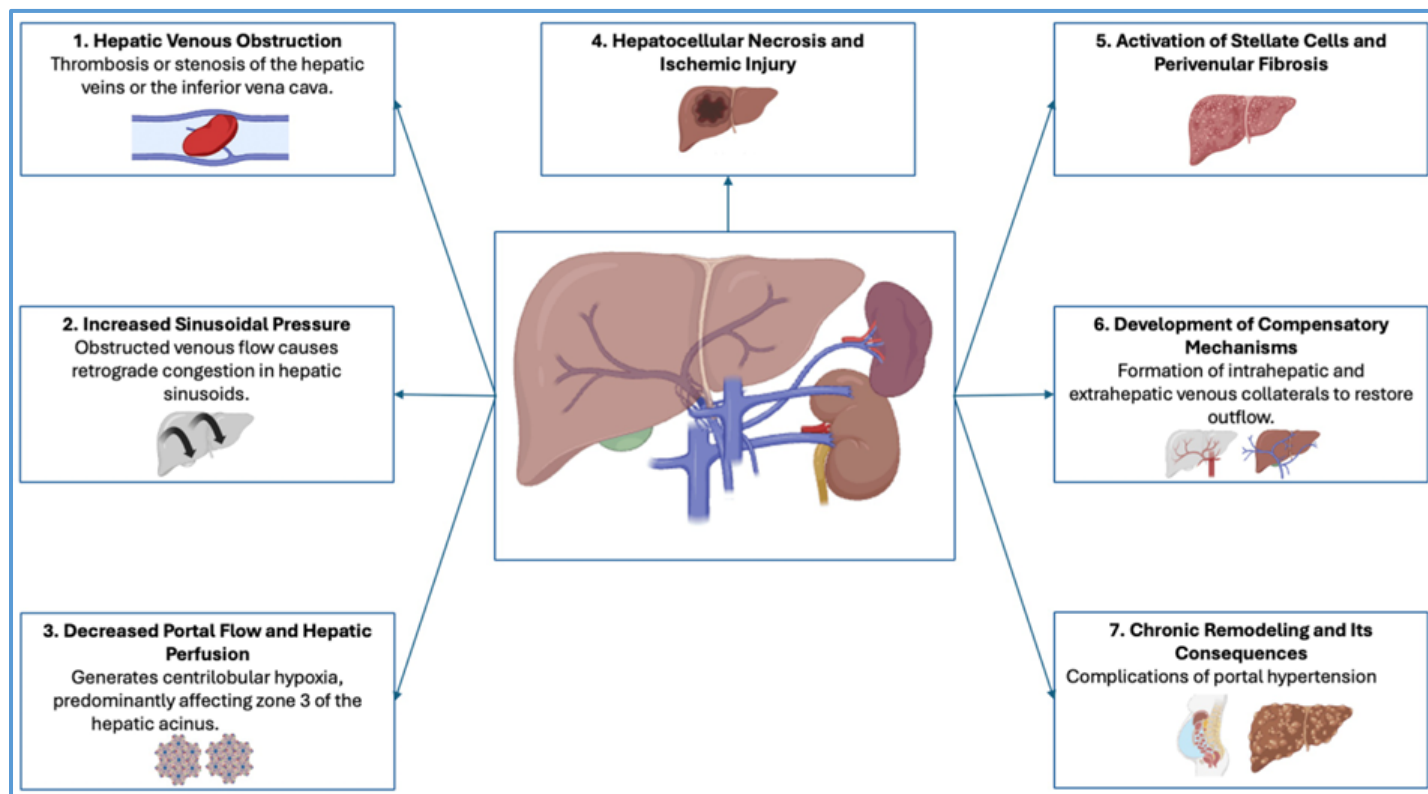
APPENDIX 21: Complications and Prognostic Factors in Cerebral Venous Thrombosis (CVT).

Category	Manifestations / Factors
Acute complications	Cerebral oedema, intracranial haemorrhages, seizures, impaired consciousness, cerebral herniation (1,2,4)
Functional complications / sequelae	Post-CVT epilepsy, chronic headaches, persistent fatigue, cognitive impairment, anxiety and depressive disorders (1,3,4,5)
Poor prognostic factors	Advanced age, initial coma, extensive haemorrhagic lesions, deep venous involvement, active malignancy, specific causes (e.g. VITT) (1,2)
Overall prognosis	Generally better than arterial strokes, provided there is early diagnosis and prompt anticoagulant treatment (1,2,3,6)

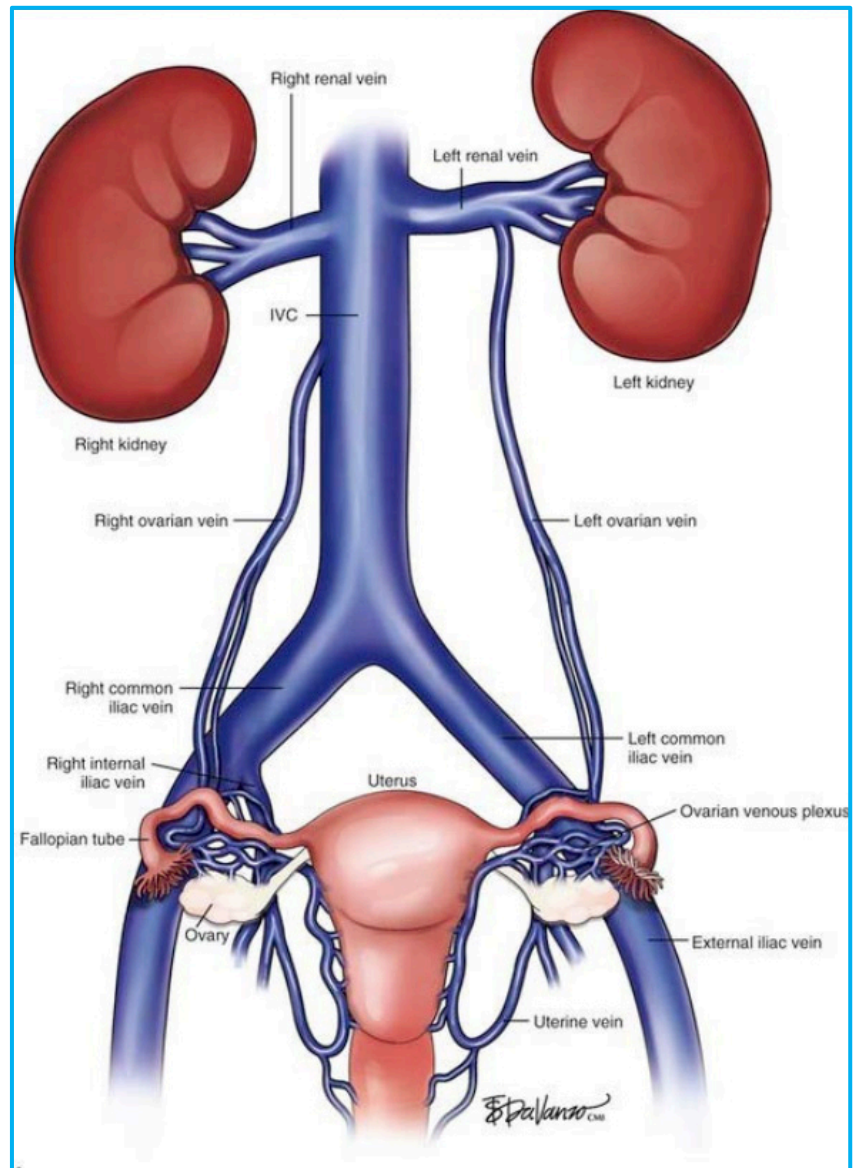
APPENDIX 22: Proposed algorithm for the management of CVT.



APPENDIX 23: The Pathophysiological Sequence of Budd-Chiari Syndrome.



APPENDIX 24: Anatomy of the female renal and pelvic venous systems: focus on ovarian drainage.



APPENDIX 25: Clinical overview of Renal Vein Thrombosis (RVT) and Ovarian Vein Thrombosis (OVT).

	Renal Vein Thrombosis ²⁴	Ovarian Vein Thrombosis ²⁵
Epidemiology	• Limited data • High variability in prevalence (5% to 60% of patients with nephrotic syndrome may have RVT)	• Rare; limited data • Occurs in less than 0.2% of pregnancies • Incidence higher after C-section (0.1%) than after vaginal delivery (0.02%) • Age: 30s to 60s • Right ovarian vein commonly involved (~75%), bilateral (10%)
Risk Factors	• 12% unprovoked • Nephrotic syndrome • Malignancy (RCC) • Surgery • Abdominal trauma • Infections	• Pelvic infections - related to septic pelvic thrombophlebitis • Pregnancy or post partum period • Malignancy (ovarian & uterine) • Recent abdomen-pelvic surgery • Inherited thrombophilia • Idiopathic
Presentation	• Triad of flank pain, hematuria, and AKI. Often asymptomatic, and incidentally discovered on imaging	• Abdominal pain • Palpable cord-like abdominal mass • Nausea, vomiting • Anorexia, malaise, ileus • Triad of fever, pelvic pain, abdominal mass -> septic pelvic thrombophlebitis
Diagnosis	• Renal venography – gold standard • CT angiography – test of choice due to feasibility (sensitivity & specificity ~100%) • MR venography (if AKI) – equal sensitivity as CT	• Doppler Ultrasound – first line • Contrast-enhanced CT or CT venography • MR venography (highest sensitivity/specificity)
Complications	• Propagation into IVC, CKD, HTN, and PE	• Rare complications including thrombus extension to the IVC or rarely PE
Treatment	• Start LMWH (renally dosed) or UFH followed by VKA with INR goal 2-3 • Consider degree of renal function when choosing anticoagulant • Duration of treatment: 6 – 12 months, longer if nephrotic syndrome • Systemic thrombolysis NOT recommended due to bleeding risk • Local thrombolytic therapy with or without thrombectomy for acute bilateral RVT and acute renal failure	• Parenteral antibiotics are mainstay of therapy due to underlying infectious etiology • Asymptomatic OVT may not need treatment • LMWH, VKAs, or DOACs (latter if not breastfeeding) can be used for treatment Duration • Optimal duration of AC is unclear • 3 months of AC is reasonable especially if provoked by postpartum state or other prothrombotic risk factor • Longer duration can be considered in patients with persistent risk factors • Subset of patients may do well with shorter duration (2-6 weeks)

APPENDIX 26: Risk Factors and Etiological Classification of Venous Thromboembolism.

Category	Risk factors	Relative risk
Permanent	Advanced age, history of VTE, active cancer, thrombophilia, heart/respiratory failure, inflammatory bowel disease, nephrotic syndrome, obesity	High to very high
Major transient	Major surgery, trauma, immobilization > 3 days, hospitalization, cesarean section	High
Minor transient	Pregnancy, oral contraception, travel > 4 hours, acute infection, dehydration, venous catheter	Moderate
Inherited thrombophilias	Antithrombin III, protein C, protein S deficiency; Factor V Leiden; prothrombin mutation	Variable depending on abnormality
Acquired thrombophilias	Antiphospholipid syndrome, cancer, Behçet's disease, paroxysmal nocturnal hemoglobinuria	High

APPENDIX 27: Inherited thrombophilias: prevalence, relative risk, and main mechanisms.

Abnormality	General prevalence	Relative risk of VTE	Main mechanism
Antithrombin III deficiency	0.02–0.2%	×10–50	↓ inhibition of thrombin and factors Xa, IXa
Protein C deficiency	0.2–0.5%	×7–10	↓ inactivation of factors Va and VIIIa
Protein S deficiency	0.03–0.13%	×5–10	↓ cofactor activity of activated protein C
Factor V Leiden mutation	3–7% (Europe)	×3–8 (heterozygous) / ×50–80 (homozygous)	Resistance to activated protein C
Prothrombin gene mutation	1–2%	×2–3	↑ prothrombin generation
Hyperhomocysteinemia	Variable	×2–3	Endothelial toxicity, ↓ fibrinolysis

APPENDIX 28: Unfractionated Heparin (UFH): Pharmacological characteristics.

Category	Data
Presentation	Parenteral anticoagulant (IV or SC), acting via antithrombin III to inhibit thrombin and factor Xa [7][8]
Dose	Bolus 80 IU/kg followed by 18 IU/kg/h IV (aPTT 1.5–2× control) OR 5,000 IU then 20,000–40,000 IU/24 h OR SC 333 IU/kg followed by 250 IU/kg every 12 h [7–9]
Monitoring	aPTT (every 4 h initially), INR, platelet count [7][8]
Adverse effects	Heparin-induced thrombocytopenia (HIT; anti-PF4 IgG), bleeding, skin necrosis, alopecia, hypersensitivity, ↑ transaminases [11–13]
Contraindications	HIT, heparin/pork allergy, active bleeding [12–14]
Major precautions	Recent stroke (delay ~14 days) [36–41], malignant hypertension [36–37][42][44–45]
Interactions	Increased bleeding risk with NSAIDs, aspirin, and antiplatelet agents [46–48]

APPENDIX 29: Low Molecular Weight Heparin: Pharmacological characteristics.

Category	Data
Advantages	Subcutaneous administration, 1–2 injections/day, bioavailability ~90%, no routine monitoring required, ↓ risk of HIT [15][49]
Efficacy	↓ VTE recurrence and bleeding compared with Unfractionated Heparin [10][16]
Examples & doses	Enoxaparin 1 mg/kg every 12 h (0.8 if BMI ≥ 40); Dalteparin 200 IU/kg/day then 150 IU/kg/day; Tinzaparin 175 IU/kg/day [17][18][51–54]
Adverse effects	HIT (less frequent), bleeding, increased risk in renal impairment [15][17]
Contraindications	HIT, severe renal impairment (<30 mL/min), pork allergy [16][17]
Interactions	Same as Unfractionated Heparin

APPENDIX 30: Vitamin K Antagonists: Pharmacokinetic characteristics and dosing.

Drug	Half-life	Dosage	Specific features
Acenocoumarol	8–11 h	11–21 mg/week	Once-daily administration
Phenindione	5–10 h	50–150 mg/day	Hypersensitivity (1.5–3%)
Warfarin	36–42 h	2–10 mg/day	Effect reached in 5–10 days
Phenprocoumon	96–104 h	14.4 mg/week	Stable anticoagulation
Fluindione	31 h	20 mg then 5–30 mg	Gradual dose adjustment

APPENDIX 31: Table: Vitamin K Antagonists: Drug interactions.

Effect	Drugs / factors
↑ INR	Amiodarone, metronidazole, TMP-SMX, cephalosporins, NSAIDs, prolonged paracetamol
↓ INR	Rifampicin, carbamazepine, barbiturates, cholestyramine
Diet	Vitamin K intake, chronic alcohol consumption, St. John's Wort

APPENDIX 32: Indirect factor Xa inhibitors: pharmacological characteristics.

Molecule	Mechanism	Pharmacology	Indications	Contraindications
Fondaparinux	Anti-Xa via antithrombin III (×300)	Bioavailability 100%, t½ 17–21 h, once-daily SC	VTE prophylaxis and treatment	CrCl < 30 mL/min
Indaparinix	Long-acting pentasaccharide	t½ 80–130 h	Limited use	Limited data

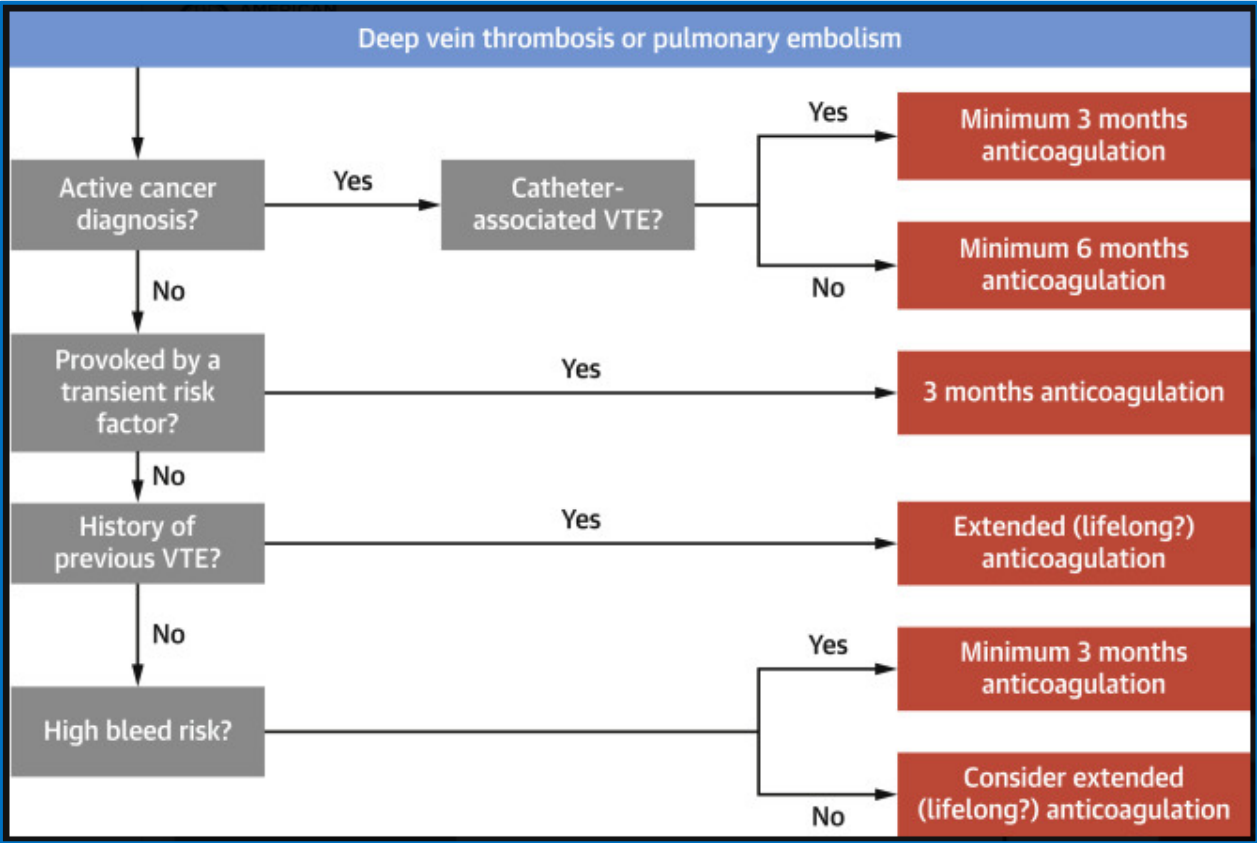
APPENDIX 33: Direct oral anticoagulants (DOACs): pharmacological characteristics.

Molecule	Target	Half-life	Elimination	Dosing	Main contraindications
Rivaroxaban	Xa	9–11 h	33% renal	Once daily	CYP3A4 drug interactions
Apixaban	Xa	9–11 h	25% renal	Twice daily	Use with caution in renal impairment
Dabigatran	Ila	12–14 h	80% renal	Twice daily	CrCl < 30 mL/min

APPENDIX 34: Risk stratification and management of pulmonary embolism.

Category	Clinical description	Management
A (Asymptomatic PE)	Asymptomatic patients	Outpatient management without hospitalization is possible [12][13]. Oral anticoagulation with Direct Oral Anticoagulants as monotherapy.
B (Low-risk symptomatic PE)	Symptomatic PE without severity criteria	Early discharge is recommended [12][13]. Direct Oral Anticoagulants as first-line therapy [12][13]. Rivaroxaban or Apixaban can be initiated directly without parenteral bridging [14].
C (Intermediate-risk PE)	Elevated severity score, increased biomarkers and/or right ventricular dysfunction	Hospitalization is recommended [12][13]. Low Molecular Weight Heparin preferred over Unfractionated Heparin, followed by transition to DOACs [2][15]. Close monitoring required ($\approx 5\%$ progress to shock) [2]. Thrombolysis not systematic due to bleeding risk [2][16][17].
D (Early cardiorespiratory failure)	Initial signs of decompensation	Intensive care unit admission [12][13]. Consider advanced therapies: catheter-directed thrombolysis, mechanical thrombectomy, or surgical embolectomy [12][13].
E (High-risk PE)	Cardiorespiratory failure with persistent hypotension	Advanced therapies indicated [12][13]. Systemic thrombolysis recommended if bleeding risk acceptable [2][12][13]. Alternatives: catheter-based therapy, thrombectomy, or surgery.

APPENDIX 35: Decision-Making Algorithm for the Duration of Anticoagulation in VTE.



APPENDIX 36: Principal Scoring Systems Used in the Prevention of VTE.

A. Padua Prediction Score:

Risk Factor	Points
Active cancer	3
Previous VTE	3
Reduced mobility	3
Known thrombophilia	3
Recent trauma or surgery	2
Age ≥ 70 years	1
Heart and/or respiratory failure	1
Acute myocardial infarction or ischaemic stroke	1
Acute infection and/or rheumatological disease	1
Obesity (BMI ≥ 30 kg/m ²)	1
Hormonal therapy	1

- **Score ≥ 4 :** high risk of VTE
- **Score < 4 :** low risk of VTE

B. IMPROVE Score:

Risk Factor	Points
Previous VTE	3
Known thrombophilia	2
Lower limb paralysis	2
Active cancer	2
Immobilisation ≥ 7 days	1
Intensive care unit stay	1
Age > 60 years	1

- Higher scores indicate an increased risk of VTE.

C. HERDOO2 Score:

Criterion	Points
Hyperpigmentation, oedema, or redness of the lower limb	1
Elevated D-dimer level	1
Obesity (BMI ≥ 30 kg/m ²)	1
Age ≥ 65 years	1

- **0–1 point** : low risk of recurrence → treatment discontinuation may be considered .
- **≥ 2 points** : higher risk of recurrence → extended anticoagulation should be considered .

D. DASH Score:

Variable	Points
Abnormal D-dimer after treatment discontinuation	+2
Age < 50 years	+1
Male sex	+1
Hormone-associated VTE in women	-2

- The higher the score, the greater the risk of recurrence.

APPENDIX 37: Standardized Data Collection Form for Patients Hospitalized with VTE.

• **English Version :**

Internal Medicine Department – Mixed Hospital of Laghouat
Dr F. Benmediouni

Patient Code: _____ File No.: _____ Date of hospitalization: //____

I. SOCIO-DEMOGRAPHIC DATA AND MEDICAL HISTORY

1. Age: years
2. Sex: ☐ Male ☐ Female
3. Toxic habits:
☐ Tobacco ☐ Alcohol ☐ Other (specify): _____ ☐ None
(If the patient is a woman)
4. Gyneco-obstetrical status:
☐ Oral contraception: ☐ Yes ☐ No
☐ Current pregnancy: ☐ Yes ☐ No ☐ N/A
☐ Postpartum (< 6 weeks): ☐ Yes ☐ No ☐ N/A
5. Personal history of VTE:
☐ Yes ☐ No
→ If YES, specify:
 - Location: ☐ LL ☐ UL ☐ Pulmonary ☐ Cerebral ☐ Other: _____
 - Suspected/known etiology: _____
 - Treatment received: _____
6. Family history of VTE in first-degree relatives:
☐ Yes ☐ No ☐ Unknown
7. Other medical history or risk factors (check all that apply):
 - ☐ Cancer (active or previous) ☐ Recent major surgery (< 3 months)
 - ☐ Prolonged immobilization (> 3 days) ☐ Recent prolonged travel (> 4h)
 - ☐ Heart failure ☐ Chronic inflammatory disease
 - ☐ Nephrotic syndrome ☐ Congenital heart disease
 - ☐ Other: _____

II. CLINICAL DATA OF THE CURRENT EPISODE

8. Presenting symptom(s) (check all that apply):
 - ☐ Unilateral limb edema (warmth, redness) ☐ Acute abdominal pain
 - ☐ Dyspnea (shortness of breath) ☐ Chest pain
 - ☐ Sudden abnormal headache ☐ Focal neurological signs (deficit, seizure)
 - ☐ Other: _____
9. Location(s) of thrombosis (confirmed by imaging):
 - ☐ Lower Limb (LL): ☐ Right ☐ Left ☐ Bilateral
 - ☐ Upper Limb (UL): ☐ Right ☐ Left
 - ☐ Pulmonary Embolism (PE)
 - ☐ Cerebral venous thrombosis
 - ☐ Abdominal thrombosis (portal, mesenteric) ☐ Budd–Chiari syndrome
 - ☐ Other location (specify): _____

III. PARACLINICAL INVESTIGATIONS AND ETIOLOGY

10. Imaging examinations performed (check all that apply):

- ☐ Venous Doppler ultrasound
- ☐ CT pulmonary angiography (CTPA)
- ☐ MR angiography
- ☐ Other (specify): _____

11. Thrombophilia workup performed (if applicable):

- ☐ No ☐ Yes → If YES, check the investigations performed:
- ☐ Antithrombin assay ☐ Protein C assay
- ☐ Protein S assay ☐ Factor V Leiden testing
- ☐ Prothrombin G20210A mutation testing
- ☐ Antiphospholipid antibody testing (LAC, anticardiolipin, anti-β2GP1)
- ☐ Other: _____

12. Etiology retained for this VTE episode (check the main cause):

- ☐ Thrombophilia (congenital or acquired) ☐ Active cancer (under treatment)
- ☐ Immobilization/Major surgery/Recent trauma
- ☐ Hormonal triggering factor: ☐ Pregnancy/Postpartum ☐ Estroprogestative contraception
- ☐ Idiopathic cause (without identified triggering factor)
- ☐ Other cause (specify): _____

IV. TREATMENT INITIATED AND OUTCOME

13. Initial treatment:

- ☐ Low Molecular Weight Heparin (LMWH) – Type: _____ Dose: _____
- ☐ Unfractionated Heparin (UFH)
- ☐ Direct Oral Anticoagulant (DOAC) – Molecule: _____
- ☐ Other (specify): _____

14. Maintenance treatment at hospital discharge:

- ☐ LMWH
- ☐ Vitamin K Antagonist (VKA)
- ☐ Direct Oral Anticoagulant (DOAC) – Molecule: _____
- ☐ Other (specify): _____

15. Outcome during hospitalization period:

- ☐ Favorable (regression of symptoms)
- ☐ Complication(s):
- ☐ Hemorrhagic (specify grade and location): _____
- ☐ Worsening/extension of thrombosis
- ☐ Thrombotic recurrence
- ☐ Death

Observations / Free comments:

Name of the clinician who completed the form: _____ Date: //____

• **French Version :**

FICHE DE RECUEIL DE DONNÉES - ÉTUDE MTEV

Service de Médecine Interne - Hôpital Mixte de Laghouat

Dr F. Benmediouni

Code Patient : _____ N° du dossier : _____ Date de l'hospitalisation : __/__/____

I. DONNÉES SOCIO-DÉMOGRAPHIQUES ET ANTÉCÉDENTS

1. Âge : ans
2. Sexe : ☐ Masculin ☐ Féminin
3. Habitudes toxiques :
☐ Tabac ☐ Alcool ☐ Autre (préciser) : _____ ☐ Aucun
(Si le patient est une femme)
4. Statut gynéco-obstétrical :
☐ Contraception orale : ☐ Oui ☐ Non
☐ Grossesse en cours : ☐ Oui ☐ Non ☐ N/A
☐ Post-partum (< 6 semaines) : ☐ Oui ☐ Non ☐ N/A
5. Antécédents personnels de MTEV :
☐ Oui ☐ Non
→ Si OUI, précisez :
- Localisation : ☐ MI ☐ MS ☐ Pulmonaire ☐ Cérébrale ☐ Autre : _____
- Étiologie suspectée/connue : _____
- Traitement reçu : _____
6. Antécédents familiaux de MTEV au 1er degré :
☐ Oui ☐ Non ☐ Non connu
7. Autres antécédents ou facteurs de risque (cocher tout ce qui s'applique) :
☐ Cancer (actif ou antérieur) ☐ Chirurgie majeure récente (< 3 mois)
☐ Immobilisation prolongée (> 3 jours) ☐ Voyage prolongé (> 4h) récent
☐ Insuffisance cardiaque ☐ Maladie inflammatoire chronique
☐ Syndrome néphrotique ☐ Cardiopathie congénitale
☐ Autre : _____

II. DONNÉES CLINIQUES DE L'ÉPISODE ACTUEL

8. Signe(s) fonctionnel(s) révélateur(s) (cocher tout ce qui s'applique) :
☐ Œdème unilatéral d'un membre (chaleur, rougeur) ☐ Douleur abdominale aiguë
☐ Dyspnée (difficulté respiratoire) ☐ Douleur thoracique
☐ Céphalées brutales anormales ☐ Signes neurologiques focaux (déficit, crise)
☐ Autre : _____
9. Localisation(s) de la thrombose (confirmée par imagerie) :
☐ Membre Inférieur (MI) : ☐ Droit ☐ Gauche ☐ Bilatéral
☐ Membre Supérieur (MS) : ☐ Droit ☐ Gauche
☐ Embolie Pulmonaire (EP)
☐ Thrombose veineuse cérébrale
☐ Thrombose abdominale (porte, mésentérique) ☐ Syndrome de Budd-Chiari
☐ Autre localisation (préciser) : _____

III. EXAMENS PARACLINIQUES ET ÉTIOLOGIE

10. Examens d'imagerie réalisés (cocher tout ce qui s'applique) :

- ☐ Échodoppler veineux
- ☐ Angio-scanner thoracique (angio-TDM)
- ☐ Angio-IRM
- ☐ Autre (préciser) : _____

11. Bilan de thrombophilie réalisé (si applicable) :

- ☐ Non ☐ Oui → Si OUI, cocher les éléments réalisés :
 - ☐ Dosage de l'Antithrombine ☐ Dosage de la Protéine C
 - ☐ Dosage de la Protéine S ☐ Recherche du Facteur V Leiden
 - ☐ Recherche de la mutation G20210A de la Prothrombine
 - ☐ Recherche des Anticorps Antiphospholipides (LAC, anti-cardiolipine, anti-β2GP1)
 - ☐ Autre : _____

12. Étiologie retenue pour cet épisode de MTEV (cocher la principale) :

- ☐ Thrombophilie (congénitale ou acquise) ☐ Cancer actif (en cours de traitement)
- ☐ Immobilisation/Chirurgie majeure/Traumatisme récent
- ☐ Facteur déclenchant hormonal : ☐ Grossesse/Post-partum ☐ Contraception œstroprogestative
- ☐ Cause idiopathique (sans facteur déclenchant identifié)
- ☐ Autre cause (préciser) : _____

IV. TRAITEMENT INSTAURÉ ET ÉVOLUTION

13. Traitement d'attaque initial :

- ☐ Héparine de Bas Poids Moléculaire (HBPM) - Type : _____ Dose : _____
- ☐ Héparine Non Fractionnée (HNF)
- ☐ Anticoagulant Oral Direct (AOD) - Molécule : _____
- ☐ Autre (préciser) : _____

14. Traitement d'entretien au départ de l'hospitalisation :

- ☐ HBPM
- ☐ Antivitamine K (AVK)
- ☐ Anticoagulant Oral Direct (AOD) - Molécule : _____
- ☐ Autre (préciser) : _____

15. Évolution durant la période d'hospitalisation :

- ☐ Favorable (régression des symptômes)
- ☐ Complication(s) :
 - ☐ Hémorragique (préciser le grade et la localisation) : _____
 - ☐ Aggravation/extension de la thrombose
 - ☐ Récidive thrombotique
- ☐ Décès

Observations / Commentaires libres :

Nom du clinicien ayant rempli la fiche : _____ Date : __/__/__