Review Article

Thromboembolism in Pregnancy: A Comprehensive Risk-Based Diagnostic and Therapeutic Approach

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Abstract

Venous thromboembolism during pregnancy represents a significant cause of maternal morbidity and mortality, driven by complex physiological, clinical, and management-related factors. Pregnancy induces a hypercoagulable state characterized by increased procoagulant factors, reduced natural anticoagulants, and impaired fibrinolysis, which together favor thrombus formation. These changes, combined with venous stasis due to uterine compression and endothelial injury during delivery, reflect the components of Virchow's triad and explain the increased thrombotic risk throughout pregnancy and the postpartum period. Risk factors are multifactorial and include pre-existing conditions such as prior venous thromboembolism and thrombophilias, pregnancy-related complications like preeclampsia and multiple gestation, and transient factors such as immobilization and cesarean delivery. Given this variability, structured risk assessment models are essential to stratify patients and

guide management. However, clinical diagnosis remains challenging, as symptoms of deep vein thrombosis and pulmonary embolism often overlap with normal physiological changes in pregnancy, requiring careful evaluation and exclusion of alternative diagnoses. A stepwise diagnostic approach that integrates clinical probability, adjusted D-dimer testing, and imaging modalities such as compression ultrasonography and ventilation–perfusion scanning is recommended to balance diagnostic accuracy with safety. Low-molecular-weight heparin is the cornerstone of treatment due to its efficacy and safety profile, while management strategies are tailored according to risk severity. Peripartum planning and postpartum prophylaxis are critical, as thrombotic risk remains elevated after delivery. Overall, individualized, risk-based, and multidisciplinary management is essential to optimize maternal and fetal outcomes.

Key words

Venous thromboembolism, pregnancy, hypercoagulability, risk stratification, anticoagulation, pulmonary embolism.

Introduction

Venous thromboembolism during pregnancy encompasses two principal clinical entities: deep vein thrombosis and pulmonary embolism. Deep vein thrombosis refers to the formation of a blood clot within a deep venous system, most commonly in the lower extremities, with the potential to cause significant complications if the thrombus embolizes. In contrast, pulmonary embolism occurs when a thrombus dislodges and migrates to the pulmonary arterial circulation, leading to obstruction of blood flow within the lungs and representing a potentially life-threatening condition [1, 2].

From an epidemiological perspective, venous thromboembolism remains one of the leading causes of maternal morbidity and mortality, particularly in high-income countries, where it continues to account for a substantial proportion of preventable maternal deaths [1, 3]. Data from the United Kingdom illustrate this burden, reporting 45 maternal deaths attributed to venous thromboembolism between 2020 and 2022 among more than two million maternities, underscoring the ongoing need for improved risk assessment and timely intervention strategies. These findings highlight the clinical relevance of early recognition and appropriate management in reducing adverse maternal outcomes [4].

The increased susceptibility to thromboembolic events during pregnancy is largely explained by physiological adaptations in the hemostatic system. Pregnancy induces a hypercoagulable state characterized by elevated levels of procoagulant factors alongside a reduction in fibrinolytic activity, which functions as a protective mechanism to minimize hemorrhage during delivery [5]. However, this prothrombotic tendency is further amplified by additional factors such as venous stasis, resulting from mechanical compression of pelvic veins, and vascular endothelial injury, particularly during labor and delivery. Together, these elements reflect the components of Virchow’s triad, which collectively contribute to thrombus formation in the pregnant population [1].

Despite the well-established pathophysiological basis, the diagnostic and therapeutic approach to venous thromboembolism in pregnancy presents significant challenges. Conventional diagnostic modalities, particularly imaging techniques, are associated with concerns regarding fetal radiation exposure, which limits their routine use and necessitates careful consideration of risk–benefit balance. Consequently, alternative strategies, including clinical prediction rules and the use of D-dimer testing, have been explored to reduce dependence on imaging while maintaining diagnostic accuracy. Similarly, therapeutic options are constrained by safety considerations,

as many anticoagulants are contraindicated during pregnancy. Low-molecular-weight heparin remains the preferred agent due to its established safety profile, whereas direct oral anticoagulants are generally avoided given the lack of sufficient evidence regarding fetal safety [2, 6].

The adoption of a risk-adapted clinical approach has become increasingly relevant. This strategy emphasizes individualized patient assessment through the use of validated risk stratification tools that incorporate factors such as prior thromboembolic events, underlying thrombophilia, and specific pregnancy-related characteristics [7]. By tailoring diagnostic and therapeutic decisions according to the patient's risk profile, clinicians can optimize outcomes while minimizing unnecessary interventions. Furthermore, the management of high-risk cases often requires the involvement of multidisciplinary teams, integrating expertise from obstetrics, hematology, and other specialties to ensure comprehensive and patient-centered care that accounts for both maternal and fetal considerations [6, 8].

The objective of this article is to provide a comprehensive and clinically integrated analysis of venous thromboembolism during pregnancy, focusing on a risk-based diagnostic and therapeutic approach. It aims to synthesize current evidence regarding the pathophysiology, risk factors, clinical presentation, and available diagnostic strategies, while emphasizing the limitations and adaptations required in the pregnant population.

Methodology

This manuscript was developed as a structured narrative review aimed at providing an updated and clinically integrated analysis of thromboembolism during pregnancy, with particular emphasis on risk stratification, diagnostic strategies, and contemporary therapeutic approaches. The review was conducted in accordance with the SANRA (Scale for the Assessment of Narrative Review Articles) framework and followed a predefined methodological protocol established prior to literature screening. Given the clinical heterogeneity of thromboembolic disease in pregnancy, the variability in maternal risk profiles, and the limitations of conventional diagnostic and treatment algorithms in this population, a narrative interpretative synthesis was selected over quantitative pooling in order to integrate physiological, hematological, obstetric, and therapeutic considerations into a coherent and clinically applicable framework. Special attention was given to the pathophysiological basis of pregnancy-associated hypercoagulability, the role of individualized risk assessment, the diagnostic evaluation of deep vein thrombosis and pulmonary embolism, and the selection of anticoagulant and interventional therapies according to maternal and fetal risk. The objective was to provide a structured synthesis capable of supporting multidisciplinary decision-making in pregnant patients with suspected or confirmed thromboembolism.

A comprehensive literature search was conducted in PubMed, Scopus, and Web of Science, including peer-reviewed articles published in English or Spanish between January 2020 and December 2026. The final search was performed in December 2026. This timeframe was selected to capture contemporary advances in pregnancy-adapted diagnostic algorithms, the use of clinical prediction models, updated recommendations on D-dimer interpretation and imaging, evolving anticoagulation strategies, and recent international guideline updates on venous thromboembolism in pregnancy and the postpartum period. Foundational studies were incorporated when necessary to contextualize pathophysiological mechanisms, historical changes in diagnostic approaches, or the evolution of anticoagulant therapy in pregnant patients. The search strategy combined MeSH and free-text terms using Boolean operators related to venous thromboembolism, deep vein thrombosis, pulmonary embolism, pregnancy,

postpartum, thrombophilia, maternal mortality, anticoagulation, low-molecular-weight heparin, risk assessment, diagnostic imaging, and prophylaxis. Searches were conducted in titles and abstracts as well as indexed subject headings to maximize sensitivity.

The initial search yielded 224 records. After removal of duplicates, 176 articles remained for title and abstract screening. Of these, 101 underwent full-text evaluation, and 40 studies were included in the final synthesis. Selection was performed independently by two authors, with disagreements resolved through discussion and consensus. Exclusion criteria comprised non–peer-reviewed publications, isolated case reports, editorials without relevant clinical outcome data, studies focused exclusively on non-pregnant populations, redundant datasets, and articles not directly addressing risk stratification, diagnosis, treatment, prophylaxis, or maternal-fetal outcomes in pregnancy-associated thromboembolism.

Eligible studies included randomized controlled trials, large observational cohorts, systematic reviews, meta-analyses, expert consensus statements, and contemporary international guidelines from obstetric, hematologic, cardiovascular, and thrombosis societies. Priority was assigned to multicenter investigations, studies with clearly defined diagnostic criteria, and research evaluating maternal outcomes, recurrence risk, bleeding complications, fetal safety, and treatment efficacy. Extracted variables included study design, population characteristics, type of thromboembolic event, risk factors, diagnostic modality, anticoagulation regimen, indication for prophylaxis or treatment, maternal outcomes, fetal outcomes, recurrence, and reported complications. Methodological quality and internal validity were assessed narratively, considering risk of bias, sample size, follow-up duration, consistency of diagnostic definitions, and reproducibility of reported outcomes. In cases of conflicting evidence, greater interpretative weight was assigned to higher-level evidence and guideline-supported recommendations.

Reference lists of included studies were manually screened to identify additional relevant publications. Given its narrative design, this review is subject to potential selection bias and does not provide pooled quantitative estimates. Artificial intelligence–based tools were used exclusively to assist in literature organization and structural coherence, whereas critical appraisal, synthesis, and final interpretation were conducted independently by the authors to preserve methodological rigor.

Pathophysiology and Hemostatic Adaptations in Pregnancy

Pregnancy is characterized by profound alterations in the coagulation system that collectively promote a hypercoagulable state. This condition is primarily driven by increased circulating levels of several procoagulant factors, including factors VII, VIII, X, and fibrinogen, which enhance thrombin generation and favor clot formation. Although this upregulation represents a physiological adaptation intended to reduce the risk of hemorrhage during childbirth, it simultaneously predisposes pregnant individuals to an increased risk of thromboembolic events [9, 10].

In parallel, the regulatory mechanisms that normally counterbalance coagulation are also altered. Protein S, a key natural anticoagulant, is significantly reduced during pregnancy, leading to diminished inhibition of thrombin generation [11]. This reduction is compounded by the development of resistance to activated protein C, further impairing the body's capacity to regulate excessive coagulation activity. As a result, the balance between procoagulant and anticoagulant forces becomes increasingly skewed toward thrombosis [12]. Additionally, fibrinolytic activity is suppressed during pregnancy. Elevated levels of plasminogen activator inhibitors limit the conversion of plasminogen to plasmin, thereby reducing the breakdown of fibrin clots.

While this impairment in fibrinolysis contributes to clot stability and helps prevent excessive bleeding during delivery, it also increases the persistence of thrombi and the overall risk of thrombosis [9].

Beyond these hematological changes, mechanical and structural factors further contribute to thrombus formation. The enlarging uterus exerts pressure on the inferior vena cava and pelvic veins, resulting in reduced venous return and the development of venous stasis, a key component of thrombus formation. This effect is particularly pronounced in the lower extremities, where blood flow becomes sluggish, facilitating clot development [5]. Moreover, endothelial injury plays a significant role, especially during and after delivery. Disruption of the vascular endothelium in the placental bed exposes subendothelial tissue factor, which activates the coagulation cascade and promotes thrombus formation. Although this process is a natural part of placental separation, it contributes to the heightened thrombotic risk observed in the postpartum period [9].

Together, these physiological and mechanical changes reflect the classical components of Virchow's triad: hypercoagulability, venous stasis, and endothelial injury. Their simultaneous presence during pregnancy and the postpartum period provides a comprehensive explanation for the increased susceptibility to venous thromboembolism in this population [1]. Recognizing the interaction of these factors is essential for accurate risk assessment and the implementation of appropriate preventive and therapeutic strategies [7].

Risk Factors and Clinical Risk Stratification

Risk factors for venous thromboembolism during pregnancy can be broadly classified into pre-existing, pregnancy-related, and transient or acquired categories, each contributing to the overall thrombotic risk profile. Among pre-existing factors, a prior history of venous thromboembolism represents one of the most significant predictors of recurrence during pregnancy. In addition, inherited thrombophilias, such as factor V Leiden mutation and prothrombin gene mutation, are strongly associated with an increased risk of thrombotic events in this population [7, 13]. Antiphospholipid syndrome also constitutes a major acquired thrombophilic condition that further elevates the likelihood of venous thromboembolism due to its prothrombotic immunological mechanisms [5].

In addition to baseline risk factors, several conditions directly related to pregnancy contribute to thromboembolic risk. Clinical scenarios such as multiple gestation, hyperemesis gravidarum, and preeclampsia have been associated with an increased incidence of venous thromboembolism, likely due to the combined effects of hemodynamic changes, systemic inflammation, and endothelial dysfunction inherent to these conditions. These pregnancy-specific factors further amplify the underlying hypercoagulable state and contribute to a cumulative increase in thrombotic risk [5, 13].

Transient or acquired factors also play a critical role, particularly when superimposed on existing vulnerabilities. Immobilization, whether due to prolonged bed rest or hospitalization, reduces venous flow and promotes stasis. Similarly, infection and surgical interventions introduce inflammatory and prothrombotic stimuli, while cesarean delivery is recognized as a significant procedural risk factor due to both surgical trauma and postoperative immobility. These factors are often temporary but can substantially increase the risk of thromboembolism during critical periods [14, 15].

Beyond these categories, certain demographic and clinical characteristics further modulate thrombotic risk. Obesity is a well-established independent risk factor, with increasing body mass index correlating directly with a higher likelihood of venous thromboembolism, likely

due to chronic inflammation, impaired venous return, and metabolic alterations [15]. Advanced maternal age has also been associated with increased risk, potentially reflecting age-related changes in vascular integrity and coagulation pathways [7]. Additionally, the use of assisted reproductive techniques has been linked to elevated thrombotic risk, possibly because of hormonal stimulation protocols and the increased incidence of multiple gestations in this group [14].

Given the multifactorial nature of these risks, structured risk assessment models have been developed to guide clinical decision-making. Tools such as the Royal College of Obstetricians and Gynaecologists guidelines and the modified Caprini score allow clinicians to stratify patients into defined risk categories and tailor thromboprophylaxis accordingly [7, 4]. These models incorporate a range of clinical variables and recommend repeated risk assessment at different stages of pregnancy and during the postpartum period to account for dynamic changes in risk profile [14]. Based on these assessments, patients are typically categorized into low, intermediate, or high-risk groups, which informs both the intensity and duration of prophylactic or therapeutic interventions [16].

Clinical Presentation and Differential Diagnosis

The clinical presentation of venous thromboembolism during pregnancy is often variable and may overlap with normal physiological changes, which complicates timely recognition and diagnosis. In the case of deep vein thrombosis, typical manifestations include unilateral leg edema, localized pain, and erythema. However, these findings may be misinterpreted as common pregnancy-related symptoms, such as dependent edema or musculoskeletal discomfort, leading to potential delays in diagnosis [14, 17]. Furthermore, atypical presentations are not uncommon, with some patients exhibiting bilateral symptoms or only subtle swelling, which further obscures the clinical picture and reduces diagnostic specificity [5].

Pulmonary embolism presents an additional diagnostic challenge, as its symptoms frequently overlap with physiological adaptations of pregnancy. Common manifestations include dyspnea, chest pain, tachycardia, and, in more severe cases, syncope. These symptoms can resemble normal cardiovascular and respiratory changes associated with pregnancy, such as increased cardiac output and altered respiratory mechanics, making clinical differentiation particularly difficult [1, 6]. Despite this overlap, certain clinical features should raise immediate concern. Hemodynamic instability, including hypotension and signs of shock, represents a critical red flag for high-risk pulmonary embolism and requires urgent evaluation and intervention [8, 18].

These diagnostic challenges are further compounded by the underlying physiological changes inherent to pregnancy. The hypercoagulable state, driven by increased clotting factors and reduced fibrinolysis, predisposes patients to thrombus formation while simultaneously masking clinical suspicion [5]. In addition, increased blood volume and venous stasis, particularly in the lower extremities due to compression by the gravid uterus, can both mimic and exacerbate the signs of deep vein thrombosis [19]. Similarly, respiratory adaptations, including increased tidal volume and decreased functional residual capacity, may produce symptoms such as dyspnea that resemble those seen in pulmonary embolism [6].

Given these complexities, the identification of high-risk features is essential for appropriate triage and management. Hemodynamic instability remains the most important indicator of severe pulmonary embolism, reflecting significant obstruction of pulmonary blood flow and impaired right ventricular function. In such cases, immediate diagnostic imaging and consideration of advanced therapeutic

interventions, including thrombolysis or surgical embolectomy, are warranted [8, 18].

A comprehensive differential diagnosis is therefore critical when evaluating pregnant patients with suspected thromboembolism. Cardiopulmonary conditions such as pneumonia and myocardial infarction may present with chest pain and dyspnea, closely mimicking pulmonary embolism [6]. Peripartum cardiomyopathy represents another important consideration, particularly in late pregnancy or the postpartum period, due to its similar clinical presentation [19]. Obstetric conditions, including amniotic fluid embolism and preeclampsia, may also manifest with respiratory distress and hemodynamic changes, necessitating careful differentiation [19]. In addition, musculoskeletal causes, such as muscle strain or joint disorders, may explain limb pain and swelling and should be distinguished from deep vein thrombosis to avoid unnecessary interventions [17].

Risk-Based Diagnostic Approach

The diagnostic approach to venous thromboembolism during pregnancy begins with an initial assessment of clinical probability, which is essential given the increased baseline risk associated with the hypercoagulable state of pregnancy. This assessment incorporates individual risk factors, including a history of previous venous thromboembolism, the presence of high-risk thrombophilias, and specific maternal or pregnancy-related characteristics that may further elevate thrombotic risk [7]. Given the dynamic nature of these risk factors, formal risk assessment is recommended at multiple time points, including early pregnancy, at delivery, and whenever clinical conditions change, allowing for continuous re-evaluation of thromboembolic risk [14].

Within this framework, D-dimer testing plays a supportive but limited role. Its diagnostic specificity is reduced during pregnancy due to physiological elevations in fibrin degradation products, which necessitates the use of trimester-adjusted thresholds to improve its clinical utility. Despite these limitations, low to intermediate D-dimer values may still be useful in excluding pulmonary embolism in selected patients, thereby reducing the need for advanced imaging [20, 21]. The use of adjusted cutoffs, whether based on age or clinical probability, has been proposed to enhance diagnostic efficiency; however, their safety and effectiveness remain variable across different clinical settings [22].

A stepwise diagnostic strategy is therefore recommended to optimize accuracy while minimizing unnecessary interventions. In cases of suspected deep vein thrombosis, compression ultrasonography is considered the first-line diagnostic modality due to its safety and lack of radiation exposure. Although its diagnostic yield may be limited in the absence of clear clinical symptoms, it remains highly valuable when findings are positive, as it can confirm the diagnosis and obviate the need for further imaging [20]. In contrast, the evaluation of suspected pulmonary embolism requires a more integrated approach, combining clinical probability assessment with appropriate imaging modalities [22].

Among imaging options, ventilation–perfusion scanning and computed tomography pulmonary angiography represent the primary modalities used in pregnancy. Ventilation–perfusion scanning is particularly useful when computed tomography is contraindicated or when minimizing radiation exposure is a priority. However, accurate interpretation requires correlation with clinical probability to reduce the risk of false-positive results. Computed tomography pulmonary angiography, on the other hand, provides high diagnostic accuracy and is widely used, although it involves greater radiation exposure, necessitating careful consideration of risks and benefits [20].

Given these concerns, strategies to minimize radiation exposure are a critical component of the diagnostic pathway. The use of trimester-

adjusted D-dimer thresholds can help reduce unnecessary imaging by safely excluding thromboembolism in low-risk patients. When imaging is required, preference is generally given to modalities such as ultrasonography and ventilation–perfusion scanning over computed tomography when clinically appropriate. In situations where initial diagnostic tests are inconclusive, serial imaging may be employed as a strategy to balance the need for diagnostic certainty with the goal of limiting cumulative radiation exposure [20].

Pharmacological Management of Acute Thromboembolism

Low-molecular-weight heparin represents the cornerstone of pharmacological management of venous thromboembolism during pregnancy due to its favorable efficacy and safety profile. Its mechanism of action is primarily based on the inhibition of factor Xa, which reduces thrombin generation and ultimately limits clot formation. Compared with unfractionated heparin, low-molecular-weight heparin exhibits more predictable pharmacokinetics, including a longer half-life and improved bioavailability, allowing for subcutaneous administration without the need for routine laboratory monitoring. These properties make it particularly suitable for use in the outpatient setting and contribute to its widespread adoption in clinical practice [23, 24].

Dosing of low-molecular-weight heparin during pregnancy is generally based on body weight, which has been shown to be both effective and safe in achieving therapeutic anticoagulation. In most cases, this approach eliminates the need for routine anti-Xa monitoring, as clinical outcomes do not demonstrate significant benefit from systematic laboratory surveillance. However, certain high-risk populations may require closer monitoring to ensure adequate anticoagulation while minimizing bleeding risk. This includes patients with mechanical heart valves or significant renal impairment, in whom anti-Xa levels may be used to guide dose adjustments and optimize therapeutic safety [23, 25].

Despite the advantages of low-molecular-weight heparin, unfractionated heparin retains an important role in specific clinical scenarios. It is particularly useful when rapid reversal of anticoagulation is required, such as in the setting of imminent delivery, or in patients with impaired renal function, given its shorter half-life and reliance on non-renal clearance. Additionally, its intravenous administration allows for rapid titration and precise control of anticoagulant effect, which is advantageous in acute or unstable clinical situations [24].

In contrast, certain anticoagulant agents are contraindicated during pregnancy due to safety concerns. Warfarin is avoided because of its well-documented teratogenic effects and the risk of fetal bleeding, particularly during the first trimester and near delivery. Similarly, direct oral anticoagulants are not recommended, as current evidence regarding their safety in pregnant populations remains insufficient to support routine use [23].

The management of anticoagulation must also consider the potential for bleeding complications. In such cases, protamine sulfate can be administered to reverse the anticoagulant effects, although its efficacy is greater for unfractionated heparin and only partial for low-molecular-weight heparin [24]. Careful clinical monitoring for signs of bleeding, along with appropriate dose adjustments, is essential, particularly in patients with elevated risk profiles [26].

The monitoring of therapeutic response and safety during anticoagulation therapy in pregnancy is primarily based on clinical evaluation rather than routine laboratory testing. Anti-Xa monitoring is not generally recommended for patients receiving low-molecular-weight heparin, except in selected high-risk scenarios, as it has not been shown to significantly improve clinical outcomes. This approach aligns with current guideline recommendations, which support the use of weight-based dosing and individualized clinical

assessment as the foundation of safe and effective anticoagulation management during pregnancy [26].

Risk-Stratified Therapeutic Strategies

The management of venous thromboembolism during pregnancy is guided by a risk-stratified approach that allows treatment intensity and monitoring to be adapted according to clinical severity. In low-risk cases, management can often be safely conducted in the outpatient setting, provided that patients remain hemodynamically stable and do not present with significant comorbidities. Appropriate candidates for outpatient care include those with stable vital signs, absence of severe symptoms, and the capacity to adhere to anticoagulation therapy and scheduled follow-up. In this context, low-molecular-weight heparin remains the treatment of choice due to its well-established safety profile during both pregnancy and breastfeeding, while direct oral anticoagulants are contraindicated and therefore not recommended [1, 18].

In contrast, patients classified as intermediate risk require closer clinical observation, often within a hospital setting, to allow for careful adjustment of anticoagulation therapy and early detection of clinical deterioration. Monitoring in these cases focuses on identifying progression toward hemodynamic compromise or right ventricular dysfunction. Point-of-care ultrasound has emerged as a useful tool in this setting, particularly for evaluating right ventricular function and supporting dynamic clinical decision-making [27, 28]. Given the complexity of these cases, management should involve a multidisciplinary team, including obstetricians, hematologists, and cardiologists, to ensure that treatment strategies are individualized and account for both maternal and fetal considerations [6].

High-risk pulmonary embolism represents a medical emergency and is characterized by hemodynamic instability and evidence of right ventricular dysfunction. In such scenarios, immediate intervention is required to restore pulmonary perfusion and prevent cardiovascular collapse. Systemic thrombolysis is indicated in life-threatening situations despite its associated risk of major bleeding, including intracranial hemorrhage, as the potential benefits outweigh the risks in the context of severe hemodynamic compromise [8, 27, 28]. In addition to systemic therapy, advanced interventional strategies may be considered. Catheter-directed therapies, including localized thrombolysis and mechanical thrombectomy, offer the advantage of reduced systemic bleeding risk and are increasingly utilized in selected high-risk patients [29]. Surgical embolectomy remains a viable option in cases where thrombolysis is contraindicated or has failed, providing a definitive means of clot removal in critical situations [30]. Furthermore, the placement of inferior vena cava filters may be considered in selected patients when anticoagulation is contraindicated or ineffective, although their use is typically reserved for specific clinical indications [31].

Given the complexity and potential severity of thromboembolic disease in pregnancy, multidisciplinary decision-making is essential, particularly in high-risk scenarios. Effective management requires collaboration among obstetricians, hematologists, cardiologists, and critical care specialists to ensure a balanced approach that carefully weighs maternal and fetal risks. Within this framework, individualized care plans are fundamental, as each patient presents with a unique combination of risk factors, clinical features, and therapeutic considerations that must be integrated into a tailored management strategy [6].

Peripartum and Postpartum Management

The peripartum management of anticoagulated patients with venous thromboembolism requires careful planning to balance the risks of bleeding and thrombosis. One of the key considerations is the timing of anticoagulant discontinuation prior to delivery. In patients receiving low-molecular-

weight heparin, it is generally recommended to discontinue therapy approximately 24 hours before planned labor or cesarean section. This approach reduces the risk of peripartum bleeding while maintaining adequate thromboembolic protection [5, 16].

An additional critical aspect involves the use of neuraxial anesthesia, which is often preferred over general anesthesia due to its favorable maternal and fetal outcomes. However, its safe administration requires appropriate timing relative to anticoagulation therapy to minimize the risk of spinal or epidural hematoma. Current recommendations suggest maintaining a minimum interval of 12 hours between the last dose of low-molecular-weight heparin and the placement of neuraxial anesthesia, ensuring adequate hemostasis before the procedure [32, 33].

In patients at high risk of thromboembolism, bridging strategies with unfractionated heparin may be employed to provide greater flexibility in anticoagulation management. Due to its shorter half-life and rapid reversibility, unfractionated heparin allows for closer timing to delivery, as it can be discontinued approximately 4 to 6 hours before labor or surgical intervention. This approach facilitates a reduction in bleeding risk while maintaining anticoagulant coverage during the critical peripartum period [5, 16].

Following delivery, the timely resumption of anticoagulation is essential to mitigate the increased thrombotic risk associated with the postpartum period. Anticoagulant therapy is typically restarted 4 to 6 hours after vaginal delivery and 6 to 12 hours after cesarean section, depending on the patient's bleeding risk and the type of anesthesia used. The duration of postpartum anticoagulation is generally recommended for a minimum of 3 to 6 months, with low-molecular-weight heparin remaining the preferred agent due to its established safety and efficacy [33, 34]. Importantly, low-molecular-weight heparin is considered safe during breastfeeding, as it does not significantly transfer into breast milk, making it suitable for continued use in the postpartum period [16].

The puerperium represents a period of particularly elevated thrombotic risk, necessitating vigilant clinical monitoring and appropriate prophylactic strategies. Ongoing risk assessment is essential during this phase to identify patients who may benefit from extended thromboprophylaxis. Individualized management plans, guided by validated risk assessment tools, are crucial to optimize outcomes and prevent recurrent thromboembolic events [4, 33]. Although a duration of six weeks of postpartum thromboprophylaxis is commonly recommended, emerging evidence suggests that shorter durations may be appropriate in selected low-risk patients, although further research is needed to define these subgroups more precisely [34, 35].

Prevention, Outcomes, and Future Directions

Primary prophylaxis of venous thromboembolism in pregnancy is particularly important in high-risk patients, in whom the baseline thrombotic risk is significantly elevated. In this context, low-molecular-weight heparin is the preferred pharmacological agent due to its ease of administration, favorable safety profile, and lower incidence of adverse events compared with unfractionated heparin [16]. It is indicated in women with a prior history of venous thromboembolism, known thrombophilia, or additional risk factors such as cesarean delivery and advanced maternal age [36]. The effectiveness of this strategy is well established, with thromboprophylaxis using low-molecular-weight heparin reducing the risk of venous thromboembolism by approximately 60 to 70 percent in high-risk pregnant populations [16].

In women with a history of venous thromboembolism, secondary prevention plays a critical role throughout pregnancy and the postpartum period. These patients remain at increased risk of recurrence, and the use of low-

molecular-weight heparin is recommended to mitigate this risk. Evidence suggests that such strategies are effective in reducing recurrence rates without significantly increasing adverse maternal or fetal outcomes, supporting their routine use in this population [37, 38].

In addition to pharmacological approaches, mechanical prophylaxis may be considered as either an adjunct or, in selected cases, an alternative strategy. Methods such as graduated compression stockings and intermittent pneumatic compression devices aim to improve venous return and reduce stasis. Although these interventions are generally safe, their effectiveness as standalone prophylaxis is less well established when compared with pharmacological measures, and they are most commonly used in combination with anticoagulation or when anticoagulants are contraindicated [37].

Maternal outcomes associated with venous thromboembolism in pregnancy include both acute and long-term complications. Recurrence of thromboembolic events remains a concern, particularly in high-risk patients, while chronic complications such as post-thrombotic syndrome and chronic thromboembolic pulmonary hypertension may significantly impact long-term health [8]. In this regard, low-molecular-weight heparin has demonstrated a favorable safety profile, with a lower incidence of bleeding complications compared with unfractionated heparin, further supporting its use as the preferred agent in pregnancy [16].

From a fetal perspective, safety considerations are paramount when selecting prophylactic strategies. Low-molecular-weight heparin does not cross the placenta, making it a safe option for the developing fetus. Available evidence indicates no significant increase in adverse fetal outcomes among women receiving thromboprophylaxis compared with those who do not, although careful clinical monitoring remains essential to balance maternal benefits with potential risks [38].

Emerging strategies in the prevention of pregnancy-associated venous thromboembolism are increasingly focused on improving risk prediction and individualizing care. Ongoing research into biomarkers and predictive tools aims to enhance the accuracy of risk stratification, allowing for more targeted prophylaxis [4]. In parallel, the concept of personalized medicine, which integrates individual risk factors and potential genetic predispositions, represents a promising approach to optimizing outcomes and minimizing unnecessary treatment [35]. However, significant variability persists among international guidelines regarding indications for thromboprophylaxis, particularly in the postpartum period, highlighting the need for greater standardization [36, 39].

These inconsistencies underscore the importance of developing standardized, risk-based clinical protocols grounded in robust evidence. Current challenges include defining which patient populations derive the greatest benefit from prophylaxis and determining the optimal duration and intensity of treatment. Future research efforts are therefore essential to refine risk assessment models, clarify therapeutic thresholds, and establish more consistent, evidence-based recommendations for the prevention of venous thromboembolism in pregnancy [39].

Conclusions

Pregnancy induces a multifactorial prothrombotic state characterized by the convergence of hypercoagulability, venous stasis, and endothelial injury, which collectively align with Virchow’s triad and explain the increased susceptibility to venous thromboembolism during both gestation and the postpartum period.

The risk of venous thromboembolism in pregnancy is highly heterogeneous and

influenced by a combination of pre-existing, pregnancy-related, and transient factors, making structured and dynamic risk stratification essential to guide individualized diagnostic, preventive, and therapeutic strategies.

A risk-adapted clinical approach integrating tailored diagnostic algorithms, safe anticoagulation strategies, multidisciplinary management, and appropriate peripartum planning is fundamental to optimize maternal and fetal outcomes while minimizing complications associated with thromboembolic disease in pregnancy.

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