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# **CONTEMPORARY MANAGEMENT OF VENOUS THROMBOEMBOLISM: CLINICAL RISK STRATIFICATION, THROMBOPROPHYLAXIS, AND ANTICOAGULATION WITH ORAL ANTICOAGULANTS**

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## **NARRATIVE LITERATURE REVIEW**

### **ABSTRACT**

Venous thromboembolism (VTE), encompassing deep vein thrombosis and pulmonary embolism, remains a major global health concern due to its high morbidity and mortality. Over the past decades, significant advances in the understanding of its pathophysiology and management have led to a shift from standardized therapeutic approaches to more individualized strategies. This narrative review aims to analyze contemporary VTE management, focusing on clinical risk stratification, thromboprophylaxis, and the use of direct oral anticoagulants (DOACs). A narrative literature review was conducted using PubMed/MEDLINE, Scopus, Web of Science, and ScienceDirect, including studies published between 2015 and 2026. Clinical trials, systematic reviews, and international guidelines were analyzed to synthesize current evidence. Findings highlight the central role of risk stratification tools, such as the Pulmonary Embolism Severity Index (PESI), in guiding clinical decisions, including outpatient management for low-risk patients. Thromboprophylaxis strategies have evolved with the implementation of validated risk assessment models, particularly in hospitalized populations. The introduction of DOACs represents a major advancement, offering comparable or superior efficacy to vitamin K antagonists, with improved safety profiles and greater convenience. However, their use requires careful consideration in specific populations, including patients with renal impairment, cancer, or pregnancy. Overall, contemporary VTE management reflects a paradigm shift toward personalized medicine, integrating clinical assessment, evidence-based protocols, and patient-



centered decision-making. Despite these advances, challenges remain in guideline implementation and treatment individualization. Future research should focus on optimizing long-term outcomes and refining risk stratification models to further enhance clinical care.

**Keywords:** Venous thromboembolism; Risk stratification; Thromboprophylaxis; Direct oral anticoagulants; Personalized medicine.

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## **1 INTRODUCTION**

Venous thromboembolism (VTE), encompassing deep vein thrombosis (DVT) and pulmonary embolism (PE), remains one of the leading causes of morbidity and mortality worldwide, being recognized as a multifactorial condition associated with genetic, environmental, and clinical factors. Its clinical relevance lies not only in its high incidence but also in potentially fatal complications, such as massive pulmonary embolism, as well as chronic sequelae including post-thrombotic syndrome and chronic thromboembolic pulmonary hypertension (Lutsey; Beckman, 2023; Tsiamita et al., 2023).

Historically, the management of VTE has been based on the use of parenteral anticoagulants, such as unfractionated heparin and low-molecular-weight heparins, followed by oral anticoagulation with vitamin K antagonists. However, over the past two decades, significant advances in pharmacology and in the understanding of the pathophysiology of thromboembolism have led to a paradigm shift, particularly with the introduction of direct oral anticoagulants (DOACs), which offer greater pharmacokinetic predictability, reduced need for monitoring, and a more favorable safety profile (Ortel et al., 2020; Stevens et al., 2021).

In parallel, risk stratification has become a central component of clinical decision-making, enabling the individualization of treatment based on the probability of adverse events, disease severity, and bleeding risk. Clinical tools and prognostic scores have been widely used both in diagnosis and in guiding therapeutic management, as well as determining the need for hospital admission (Konstantinides et al., 2020; Leidi et al., 2022).

Within this context, this narrative review aims to analyze the contemporary management of venous thromboembolism, with emphasis on clinical risk stratification, thromboprophylaxis strategies, and the use of oral anticoagulants, discussing their implications for evidence-based clinical practice (Ortel et al., 2020; Stevens et al., 2021).

## **2 METHOD**

This study consists of a narrative literature review of a descriptive and analytical nature, conducted with the aim of synthesizing and discussing the most recent evidence regarding the management of venous thromboembolism. This

methodological approach allows for an interpretative and critical analysis of the scientific literature, facilitating the integration of diverse clinical and therapeutic perspectives.

The literature search was performed in the PubMed/MEDLINE, Scopus, Web of Science, and ScienceDirect databases, including articles published between 2015 and 2026. English-language descriptors were used in combination with Boolean operators, such as “venous thromboembolism,” “risk stratification,” “thromboprophylaxis,” and “direct oral anticoagulants.” Clinical studies, systematic reviews, international guidelines, and expert consensus statements were included. Duplicate publications, studies with low methodological rigor, and those not directly addressing the scope of this review were excluded.

### **3 RESULTS**

The analyzed evidence demonstrates a significant evolution in the management of venous thromboembolism, particularly with regard to clinical risk stratification and the use of novel anticoagulant therapies. The use of clinical prediction scores, such as the Wells and Geneva scores, has contributed to the estimation of pre-test probability, supporting more rational use of diagnostic tests and guiding initial therapeutic decision-making (Thomas *et al.*, 2024; Konstantinides *et al.*, 2020).

In the context of pulmonary embolism, tools such as the Pulmonary Embolism Severity Index (PESI) and its simplified version (sPESI) have been widely employed to classify mortality risk and guide clinical management, including the possibility of outpatient treatment for low-risk patients. In addition, laboratory biomarkers and imaging studies complement this assessment, enabling a more precise and individualized approach (Jiménez *et al.*, 2010; Konstantinides *et al.*, 2020; Ortel *et al.*, 2020).

Regarding thromboprophylaxis, there has been substantial progress in identifying at-risk patients, particularly in hospital settings. Institutional protocols based on validated risk assessment models, such as the Padua Prediction Score, have been implemented to guide pharmacological prophylaxis, primarily with low-molecular-weight heparins or DOACs when indicated. In surgical patients, prophylaxis

remains strongly recommended, with strategies tailored to the type of procedure and individual risk profile (Barbar *et al.*, 2010; Stevens *et al.*, 2021; Lutsey; Beckman, 2023).

With respect to anticoagulation, direct oral anticoagulants—including rivaroxaban, apixaban, dabigatran, and edoxaban—have become established as first-line therapy for VTE across a wide range of clinical scenarios. Comparative studies have demonstrated efficacy comparable to or greater than that of vitamin K antagonists, with a lower risk of intracranial bleeding and greater convenience for patients. However, their use requires careful consideration in specific populations, such as those with renal impairment, pregnant women, and patients with active malignancy (Ortel *et al.*, 2020; Stevens *et al.*, 2021; Bauersachs *et al.*, 2010; Büller *et al.*, 2012; Agnelli *et al.*, 2013; Schulman *et al.*, 2009; Hokusai-VTE Investigators, 2013).

The integrated analysis of the studies indicates that contemporary VTE management is guided by an individualized approach, grounded in risk stratification, appropriate selection of prophylactic strategies, and the rational use of oral anticoagulants. These elements reflect a significant shift toward personalized medicine, with direct implications for clinical outcomes (Leidi *et al.*, 2022; Ortel *et al.*, 2020; Stevens *et al.*, 2021).

Given the diversity of therapeutic approaches and management strategies identified in the literature, it is essential to systematically synthesize the main findings in a comparative manner, highlighting clinical criteria, therapeutic indications, and the specific characteristics of the anticoagulants used (Konstantinides *et al.*, 2020; Stevens *et al.*, 2021).

**Table 1.** Summary Table of Included Studies on Contemporary Management of Venous Thromboembolism

Author (Year)	Study Type	Population	Main Focus	Key Findings
Konstantinides <i>et al.</i> (2020)	Clinical Guideline (ESC)	Patients with acute pulmonary embolism	Risk stratification and management	Established risk-based management using PESI/sPESI; supports outpatient care for low-risk patients and guides reperfusion strategies for high-risk cases.
Ortel <i>et al.</i> (2020)	Clinical Guideline (ASH)	Patients with VTE	Anticoagulation strategies	Recommends DOACs as first-line therapy in most patients; emphasizes

				individualized treatment based on bleeding risk and comorbidities.
Stevens <i>et al.</i> (2021)	Clinical Guideline (CHEST)	Patients with VTE	Antithrombotic therapy	Reinforces DOAC preference over vitamin K antagonists; highlights duration of therapy based on provoked vs unprovoked VTE.
Barbar <i>et al.</i> (2010)	Cohort Study	Hospitalized medical patients	Thromboprophylaxis	Developed Padua Prediction Score to identify patients at high risk for VTE, supporting targeted prophylaxis.
Jiménez <i>et al.</i> (2010)	Cohort Study	Patients with acute pulmonary embolism	Risk stratification	Validated simplified PESI (sPESI) for mortality prediction and clinical decision-making.
Leidi <i>et al.</i> (2022)	Narrative Review	Patients with pulmonary embolism	Risk assessment	Highlights integration of clinical, imaging, and biomarker data for improved stratification.
Lutsey & Beckman (2023)	Review	General population	Epidemiology and prevention	Emphasizes importance of preventive strategies and risk-based prophylaxis in clinical practice.
Bauersachs <i>et al.</i> (2010)	Randomized Clinical Trial	Patients with acute VTE	Rivaroxaban	Demonstrated non-inferiority to standard therapy with improved convenience and safety profile.
Büller <i>et al.</i> (2012)	Randomized Clinical Trial	Patients with pulmonary embolism	Rivaroxaban	Showed efficacy comparable to standard anticoagulation with reduced bleeding risk.
Agnelli <i>et al.</i> (2013)	Randomized Clinical Trial	Patients with VTE	Apixaban	Confirmed effective anticoagulation with lower bleeding rates compared to conventional therapy.
Hokusai-VTE Investigators (2013)	Randomized Clinical Trial	Patients with VTE	Edoxaban	Demonstrated non-inferiority to warfarin with improved safety profile.
Schulman <i>et al.</i> (2009)	Randomized Clinical Trial	Patients with acute VTE	Dabigatran	Established efficacy comparable to warfarin with predictable pharmacokinetics.
Thomas <i>et al.</i> (2024)	Review	Patients with suspected PE	Diagnostic strategies	Supports evidence-based diagnostic pathways integrating clinical scores and imaging.
Tsiamita <i>et al.</i> (2023)	Review	Patients with VTE complications	Long-term outcomes	Highlights chronic complications such as post-thrombotic



				syndrome and CTEPH, reinforcing need for follow-up.
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Note: Data synthesized from the studies included in this review.

#### 4. DISCUSSION

Contemporary management of venous thromboembolism reflects a paradigm shift from protocol-driven medicine toward an approach centered on dynamic risk stratification and therapeutic individualization. This transformation does not occur in a linear manner but rather emerges from the progressive incorporation of robust clinical evidence alongside the practical need to optimize outcomes across heterogeneous care settings (Konstantinides et al., 2020; Ortel et al., 2020).

##### 4.1 Risk Stratification as a Structuring Element of Clinical Decision-Making

Risk stratification in VTE extends beyond its diagnostic function and assumes a structuring role in the organization of care, directly influencing decisions regarding hospitalization, therapeutic intensity, and clinical follow-up. Scores such as the Pulmonary Embolism Severity Index (PESI) and its simplified version (sPESI), initially developed as prognostic tools, have evolved into instruments of clinical governance, guiding care pathways and optimizing resource allocation (Konstantinides et al., 2020; Leidi et al., 2022).

Within this context, an important conceptual shift can be observed: risk is no longer merely a marker of disease severity but becomes an organizing axis of care. Patients classified as low risk may be safely managed in outpatient settings, reducing healthcare costs and potentially improving patient experience without compromising clinical safety (Konstantinides et al., 2020). This approach reinforces the integration between scientific evidence and healthcare system organization.

However, the application of these scoring systems is not without limitations. The heterogeneity of study populations and the presence of complex comorbidities pose challenges to the generalizability of findings. Consequently, clinical judgment remains indispensable, acting as a mediating element between prognostic tools and the individual patient context (Ortel et al., 2020; Thomas et al., 2024).

Furthermore, the increasing incorporation of biomarkers and imaging findings into risk assessment suggests a trend toward the development of hybrid models that integrate clinical, laboratory, and technological data. This perspective points to a future in which risk stratification will become progressively more refined, potentially integrated with artificial intelligence systems, thereby enhancing the precision of clinical decision-making (Leidi *et al.*, 2022).

#### **4.2 Anticoagulation and Thromboprophylaxis: From Standardized Therapy to Personalized Medicine**

The introduction of direct oral anticoagulants represents one of the most significant advancements in the management of VTE, not only due to their clinical efficacy but also because of their transformative impact on the care model. By reducing the need for routine monitoring and simplifying therapeutic regimens, DOACs enhance patient autonomy and improve treatment adherence (Ortel *et al.*, 2020; Stevens *et al.*, 2021).

Pivotal clinical trials have demonstrated that these agents provide efficacy comparable to or greater than that of vitamin K antagonists, with a lower risk of major bleeding, particularly intracranial hemorrhage (Bauersachs *et al.*, 2010; Büller *et al.*, 2012; Agnelli *et al.*, 2013; Hokusai-VTE Investigators, 2013; Schulman *et al.*, 2009). This body of evidence has established DOACs as first-line therapy across a wide range of clinical scenarios.

However, the adoption of these agents does not eliminate the complexity inherent to therapeutic decision-making. Factors such as renal function, drug–drug interactions, the presence of active malignancy, and specific conditions such as pregnancy continue to require careful evaluation. In this context, the selection of an anticoagulant should be understood as a relational process that integrates scientific evidence, clinical characteristics, and the patient’s individual context (Ortel *et al.*, 2020; Stevens *et al.*, 2021).

In the field of thromboprophylaxis, a persistent gap remains between recommendations and real-world practice. Although clinical guidelines strongly emphasize the importance of prophylaxis in hospitalized patients, adherence remains inconsistent, revealing challenges in the implementation of scientific knowledge.



Protocols based on validated risk assessment models, such as the Padua Prediction Score, represent important advances; however, their effectiveness depends on institutional integration and team engagement (Barbar *et al.*, 2010; Lutsey; Beckman, 2023).

Finally, a clear shift toward personalized medicine is evident, in which VTE management extends beyond the mere application of guidelines to encompass shared and context-sensitive decision-making. This transition requires not only technical expertise but also expanded clinical competencies, including communication skills, risk assessment, and ethical decision-making (Leidi *et al.*, 2022).

## **5 CONCLUSION**

Contemporary management of venous thromboembolism has been profoundly transformed by advances in risk stratification, thromboprophylaxis, and the development of novel anticoagulant therapies. The incorporation of clinical tools and the use of direct oral anticoagulants have contributed to a safer, more effective, and patient-centered approach.

Nevertheless, important challenges remain, particularly regarding the implementation of prophylactic protocols, adherence to clinical guidelines, and the individualization of treatment in specific populations. In this context, continuing education of healthcare professionals and the strengthening of institutional policies are essential to improve the quality of care.

Finally, there is a clear need for further studies exploring personalized management strategies, as well as long-term evaluation of clinical outcomes associated with different therapeutic approaches, thereby consolidating progress toward increasingly evidence-based and patient-centered medicine.

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