

## Review

# Incident and Risk of Pulmonary Embolism in Hospitalized Patients with Autoimmune Disorders

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### Abstract

Hospitalized patients with autoimmune disorders are at significantly heightened risk for pulmonary embolism due to a combination of chronic inflammation, immobility, and the effects of medications used to manage their conditions. Autoimmune conditions like systemic lupus erythematosus, rheumatoid arthritis, inflammatory bowel disease, and multiple sclerosis predispose individuals to thromboembolic events through mechanisms such as endothelial dysfunction, hypercoagulability, and reduced mobility. Diagnosis presents challenges due to overlapping symptoms with underlying autoimmune diseases, necessitating comprehensive clinical assessments and the use of diagnostic tools like D-dimer testing and computed tomography pulmonary angiography for accurate detection. Proactive management strategies include anticoagulation therapy, mechanical prophylaxis, and promoting mobility to effectively mitigate pulmonary embolism risk. Multidisciplinary care involving rheumatologists, hematologists, and pulmonologists is crucial for personalized treatment approaches and ongoing research to enhance the understanding and management of pulmonary embolism in hospitalized patients with autoimmune disorders. This review explores the incidence, underlying pathophysiological mechanisms, and optimal management strategies for pulmonary embolism in this vulnerable population.

### Keywords:

*Autoimmune disorders, pulmonary embolism, thromboembolism, risk assessment, management strategies*

## **Introduction**

Pulmonary embolism (PE) is a severe condition where thrombotic material obstructs pulmonary arteries, typically originating from deep vein thrombosis (DVT) in the legs. This obstruction can lead to significant morbidity and mortality, highlighting the critical need for effective prevention and management, especially in high-risk groups. Hospitalized patients with autoimmune disorders are notably vulnerable to PE due to their immune systems' abnormal responses against their own tissues, resulting in chronic inflammation and tissue damage. This chronic inflammatory state, exacerbated by factors like immobility and medication use, significantly increases their risk of thromboembolic events. Recognizing these risks and implementing proactive strategies for risk assessment, such as monitoring biomarkers like D-dimer levels, and preventive measures such as anticoagulation therapy and promoting mobility, are essential to mitigate the occurrence of PE and improve outcomes in this vulnerable population (1).

Autoimmune disorders encompass a wide range of conditions, including systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), inflammatory bowel disease (IBD), and multiple sclerosis (MS). Each of these conditions has unique pathophysiological mechanisms that contribute to an increased risk of PE.

The incidence of PE in patients with autoimmune disorders is significantly higher compared to the general population. Studies have demonstrated that patients with autoimmune diseases have a 2-3 times higher risk of developing PE (2). Specifically, the incidence rate of PE in patients with SLE can be as high as 10% over their lifetime (3). This heightened risk necessitates proactive management strategies to mitigate the occurrence of PE in these patients.

Effective risk assessment and prevention strategies play a crucial role in managing the risk of PE in hospitalized patients with autoimmune disorders. Regular assessment of thrombotic risk factors is essential, incorporating biomarkers such as D-dimer levels to identify those at considerable risk. This proactive approach allows healthcare providers to

intervene early, implementing appropriate preventive measures to reduce the likelihood of PE occurrence. Healthcare teams may adjust interventions to each patient's specific risk profile by closely monitoring these biomarkers and other clinical indicators. This improves overall management and outcomes for individuals with autoimmune conditions that increase susceptibility to thromboembolic strokes (4). Prophylactic measures, such as the use of anticoagulants, compression stockings, and intermittent pneumatic compression devices, can significantly reduce the risk of PE (5, 6). Encouraging mobility and physical activity, as appropriate for the patient's condition, also plays a vital role in preventing thromboembolic events (7). Close monitoring for signs and symptoms of PE, such as sudden onset of dyspnea, chest pain, and tachycardia, ensures prompt diagnosis and treatment, thereby improving patient outcomes (8). This review seeks to summarize the incidence, underlying pathological mechanisms, and best management practices for pulmonary embolism in populations at high-risk.

## **Methodology**

This study is based on a comprehensive literature search conducted on 27 June 2024, in the Medline and Cochrane databases, utilizing the medical topic headings (MeSH) and a combination of all available related terms, according to the database. To prevent missing any research, a manual search for publications was conducted through Google Scholar, using the reference lists of the previously listed papers as a starting point. We looked for valuable information in papers that discussed incidence and risk of pulmonary embolism in hospitalized patients with autoimmune disorders. There were no restrictions on date, language, participant age, or type of publication.

## **Discussion**

The relationship between autoimmune disorders and an increased risk of PE is a complex issue that necessitates a thorough understanding of the pathophysiological mechanisms, risk factors, clinical implications, and preventive strategies.

Autoimmune disorders such as SLE, RA, IBD, and MS involve chronic inflammation, which significantly contributes to the increased risk of thromboembolism. In SLE, the presence of antiphospholipid antibodies is a key factor in promoting a hypercoagulable state. These antibodies, including anticardiolipin antibodies and lupus anticoagulant, target phospholipid-binding proteins such as beta-2 glycoprotein I. This interaction leads to endothelial cell activation, disruption of normal anticoagulant pathways, and increased thrombus formation (9, 10). Lupus anticoagulant specifically interferes with the clotting cascade, further elevating the risk of thrombosis (11). The chronic inflammation in SLE also contributes to endothelial damage and subsequent thrombus formation, making regular monitoring and proactive management crucial.

RA is characterized by chronic inflammation that leads to endothelial dysfunction, impairing the vascular endothelium's normal anticoagulant properties. This dysfunction, combined with heightened platelet activation and aggregation, predisposes RA patients to thromboembolic events (12, 13). Inflammatory cytokines such as tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) and interleukin-6 (IL-6) produced in RA exacerbate the prothrombotic environment by inducing tissue factor expression on endothelial cells and monocytes, thus enhancing thrombosis risk (11). The use of certain biologic agents in RA treatment can also influence thromboembolic risk, requiring careful consideration of treatment options.

IBD, encompassing conditions like Crohn's disease and ulcerative colitis, creates a hypercoagulable state through chronic inflammation in the intestines. This inflammatory environment increases levels of procoagulant factors such as thrombin, fibrinogen, and factor VIII, while decreasing levels of natural anticoagulants like antithrombin and protein C. These imbalances promote thrombus formation and elevate the risk of PE, particularly during disease exacerbations or post-surgical periods (14, 15). Hospitalized IBD patients, especially those with active disease, are at significantly higher risk, necessitating preventive strategies like

pharmacological prophylaxis and early mobilization.

MS patients, especially in advanced stages, experience reduced mobility due to neurological impairment. This immobility contributes to venous stasis, a critical factor in the development of DVT and subsequent PE. Chronic inflammation characteristic of MS further exacerbates thrombotic risk by affecting blood flow dynamics and endothelial function (16, 17). Preventive measures, including mechanical prophylaxis (e.g., compression stockings) and promoting physical activity, are essential in managing thromboembolic risk in MS patients.

Risk factors contributing to the elevated risk of PE in patients with autoimmune disorders are multifaceted and underscored by several key factors. Chronic inflammation, a sign of autoimmune disorders, creates a prothrombotic environment by activating coagulation pathways and causing endothelial dysfunction, thereby increasing thrombus formation. Immobility, often due to hospitalization or disease severity, exacerbates PE risk by reducing venous return and promoting stasis in the lower limbs (18). The use of medications such as corticosteroids and immunosuppressants, which are commonly prescribed to manage autoimmune conditions, can further increase thrombotic risk. Corticosteroids, for instance, can cause endothelial damage and alter lipid profiles, leading to increased clotting potential (19).

Comorbidities such as cardiovascular diseases, which are more prevalent in patients with autoimmune disorders, also contribute to the increased risk of PE. These comorbid conditions often share common risk factors with thromboembolism, such as hypertension, hyperlipidemia, and smoking, further compounding the risk (20). Furthermore, genetic predispositions associated with thromboembolism and autoimmune illnesses are important and may work in conjunction to increase the risk of PE in patients who are susceptible. Understanding these interconnected risk factors is crucial for implementing effective

thrombo-prophylactic strategies and vigilant monitoring in clinical practice, aimed at mitigating the incidence and severity of PE in this vulnerable population.

The increased risk of PE in patients with autoimmune disorders has significant clinical implications. Early recognition and prompt management of thromboembolic events are crucial to improving patient outcomes. Healthcare providers must maintain a high index of suspicion for PE in patients with autoimmune conditions, especially those presenting with symptoms such as sudden onset of dyspnea, chest pain, and tachycardia (21).

Diagnosing PE in this population can be challenging due to the overlap of symptoms with those of the underlying autoimmune disease. For example, chest

pain and dyspnea are common in both PE and lupus-related pleuritis or pericarditis. Therefore, a thorough clinical evaluation, including detailed patient history and physical examination, is essential. Diagnostic tools such as D-dimer testing, which measures fibrin degradation products in the blood, can help assess the likelihood of thrombus formation (22). Imaging studies, such as computed tomography pulmonary angiography (CTPA), are critical for confirming the diagnosis of PE.

Specific autoimmune disorders like SLE and RA increase PE risk via unique mechanisms such as antiphospholipid antibodies and chronic inflammation. Effective management requires tailored prophylactic measures and interdisciplinary collaboration to mitigate thromboembolic complications in hospitalized patients (**Table 1**).

**Table 1: Summary of PE risk, mechanisms, and management strategies for autoimmune disorders, aiding effective preventive measures and improved outcomes.**

Autoimmune Disorder	PE Risk Factors	Thromboembolic Mechanisms	Management & Prophylactic Strategies
<b>Systemic Lupus Erythematosus (SLE)</b>	Presence of antiphospholipid antibodies interfering with coagulation pathways (9, 10, 23).	Antiphospholipid antibodies targeting phospholipid-binding proteins, leading to endothelial cell activation and disruption of normal anticoagulant pathways.	Regular monitoring for thrombotic events, prophylactic anticoagulation in high-risk patients, regular monitoring of antiphospholipid antibody levels.
<b>Rheumatoid Arthritis (RA)</b>	Chronic inflammation leading to endothelial dysfunction (12, 13).	Endothelial dysfunction, increased platelet activation and aggregation.	Use of anticoagulants, lifestyle modifications, careful use of biologic agents, weighing benefits and risks of disease-modifying antirheumatic drugs (DMARDs) and biologics.
<b>Inflammatory Bowel Disease (IBD)</b>	Chronic intestinal inflammation causing a hypercoagulable state (14, 15).	Elevated thrombin, fibrinogen, and factor VIII, decreased antithrombin and protein C.	Pharmacological prophylaxis, early mobilization, use of low-molecular-weight heparin (LMWH) or direct oral anticoagulants (DOACs) during hospitalization, ensuring early mobilization post-surgery.
<b>Multiple Sclerosis (MS)</b>	Reduced mobility and chronic inflammation increasing the risk of DVT and PE (16, 17).	Venous stasis due to reduced mobility and chronic inflammation.	Mechanical prophylaxis (e.g., compression stockings), encouraging physical activity, managing immobility within the patient's capabilities.

Managing PE in patients with autoimmune disorders requires a comprehensive approach that addresses these intertwined risk factors. Clinicians must prioritize strategies to mitigate chronic inflammation through targeted therapies aimed at controlling autoimmune disease activity and reducing systemic inflammation levels. Regular assessment and management of mobility issues, particularly in hospitalized patients, are essential to prevent venous stasis and subsequent thrombus formation. Moreover, careful consideration of medication choices and dosages is necessary to balance therapeutic benefits with thrombotic risks associated with corticosteroids and immunosuppressants. Anticoagulation therapy is the cornerstone of treatment, aiming to prevent further clot formation and promote the dissolution of existing thrombi. The choice of anticoagulant, whether it be heparin, warfarin, or direct oral anticoagulants (DOACs), should be tailored to the individual patient's risk profile and clinical condition. Monitoring for potential side effects, such as bleeding, is essential, particularly in patients with concurrent risk factors for hemorrhage. Concurrent management of cardiovascular comorbidities is crucial, involving aggressive control of hypertension and hyperlipidemia, along with smoking cessation interventions to reduce overall cardiovascular risk burden. Genetic screening and counselling may offer insights into individual predispositions, guiding personalized preventive measures against PE.

In clinical settings, implementing routine thromboprophylactic measures such as mechanical prophylaxis and pharmacological interventions based on risk stratification can significantly reduce PE incidence. Regular monitoring for signs and symptoms of PE, coupled with diagnostic vigilance using imaging modalities appropriate for detecting thromboembolic events in this high-risk population, remains paramount. Patient education on recognizing symptoms of PE and adherence to prescribed preventive measures are integral components of comprehensive management plans. By addressing these multifaceted risk factors holistically and tailoring interventions to individual

patient profiles, healthcare providers can optimize outcomes and minimize the impact of PE in patients with autoimmune disorders.

Preventive strategies play a pivotal role in mitigating the risk of PE among hospitalized patients with autoimmune disorders. Utilizing risk assessment tools like the Wells score enables clinicians to identify individuals at heightened risk for thromboembolic events, facilitating targeted application of prophylactic measures (23). Pharmacological prophylaxis represents a cornerstone of prevention, with guidelines advocating for the use of agents like LMWH or DOACs in high-risk patients, particularly those experiencing prolonged immobility or recovering from recent surgeries (24).

In addition to pharmacological approaches, mechanical prophylaxis methods such as compression stockings and intermittent pneumatic compression devices are instrumental in preventing deep vein thrombosis (DVT), an initial to PE. These interventions enhance venous circulation, thereby reducing stasis and lowering the risk of thrombus formation (25). Emphasizing early mobilization and tailored physical activity regimens further supports venous return and diminishes the likelihood of thromboembolic complications, aligning with individual patient capabilities and medical status. Educational initiatives form another critical component of preventive strategies, empowering patients with knowledge about the signs and symptoms indicative of DVT and PE. Timely recognition of these warning signs equips patients to seek prompt medical evaluation and intervention, potentially averting severe consequences associated with untreated thromboembolic events. Patient education also underscores the importance of adherence to prescribed preventive measures and therapeutic regimens, fostering active participation in their own healthcare management, and enhancing overall treatment outcomes.

By integrating these multifaceted preventive strategies into clinical practice, healthcare providers can effectively reduce the incidence and impact of PE in hospitalized patients with autoimmune

disorders. Comprehensive risk assessment coupled with targeted pharmacological and mechanical interventions optimizes thromboprophylaxis efforts, addressing both generalized and patient-specific risk factors. Moreover, ongoing patient education promotes early detection and proactive management of thromboembolic complications, reinforcing collaborative efforts between healthcare providers and patients to achieve favourable clinical outcomes.

Ongoing research is essential to further understand the relationship between autoimmune disorders and thromboembolic risk, and to develop targeted interventions to mitigate this risk. Studies exploring the molecular and genetic mechanisms underlying the prothrombotic state in autoimmune diseases can provide valuable insights into novel therapeutic targets.

The development of personalized medicine approaches, which consider individual patient characteristics such as genetic predispositions, comorbidities, and specific autoimmune disease manifestations, holds promise for improving the prevention and management of PE in this population. Additionally, exploring the role of novel anticoagulants and antiplatelet agents in patients with autoimmune disorders may offer new avenues for effective thromboembolism prevention.

The integration of multidisciplinary care teams, including rheumatologists, hematologists, cardiologists, and pulmonologists, is crucial for optimizing the management of thromboembolic risk in patients with autoimmune disorders. Such teams can provide comprehensive care, addressing both the underlying autoimmune disease and the associated thromboembolic risk.

## **Conclusion**

Hospitalized patients with autoimmune disorders face heightened pulmonary embolism risk due to chronic inflammation, immobility, and medication use. Crucial preventive measures include assessing thrombotic risk, using anticoagulants, promoting mobility, and vigilant symptom monitoring. Tailored protocols and research are vital for

effective management and improved outcomes, requiring multidisciplinary care integration.

## **Disclosures**

### ***Author Contributions***

The author has reviewed the final version to be published and agreed to be accountable for all aspects of the work.

### ***Ethics Statement***

Not applicable

### ***Consent for publications***

Not applicable

### ***Data Availability***

All data is provided within the manuscript.

### ***Conflict of interest***

The authors declare no competing interest.

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