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## **Association Between Gastroesophageal Reflux Disease (GERD) and Venous Thromboembolism (VTE): A Comprehensive Review**

Badriah Mohammed Alowais<sup>1</sup>, Huda Jassim Alqurqush<sup>2</sup>, Kawther Jassim Alqurqush<sup>3</sup>, Fatimah Ali Alkhalifah<sup>4</sup>, Ali Abdullatif Ali Alfaran<sup>5</sup>, Zaineb Majed Alalawi<sup>6</sup>, Omkalthom Ali Al Bhrani<sup>7</sup>, Bayan Emad Alabbad<sup>8</sup>, Murtadha Omran Almukinha<sup>9</sup>, Tahani Taher Mohammad Alkhamis<sup>10</sup>, Jamila Taher Alkhamis<sup>10</sup>, Maryam Taher Alkhamis<sup>11</sup>, Zainab Hussain Abdulla AlQanbar<sup>14</sup>, Fadheelah Khalil Ibrahim Annajjar<sup>12</sup>, Aeshah Khalid Alamal<sup>13</sup>

1. Alqadisyah PHC
2. King Fahad hospital alhofof
3. King Fahad specialist hospital-Dammam
4. Alnuzha PHC
5. Radiology.Techician Safwa Medical Complex
6. Safwa Medical Complex, Senior Health Informatics
7. Prince saud Bin jalawi hospital
8. Al-Omran General Hospital
9. Al-Ahsa Phchiatric hospital
10. AlJabr eye Ear Nose and throat Hospital
11. Primary health care
12. King Faisal Hospital
13. King Fahad hospital
14. King Fahad PHC

## ABSTRACT

Gastroesophageal reflux disease (GERD) and venous thromboembolism (VTE) are two common clinical conditions, each associated with significant morbidity and mortality. Although they differ in etiology and pathophysiology, recent studies have explored potential links between these two conditions. GERD-induced chronic inflammation, increased pro-thrombotic states, and shared risk factors, such as obesity, may contribute to an elevated risk of VTE. This review aims to summarize the current evidence, discuss possible mechanisms of association, and evaluate the clinical implications of the interplay between GERD and VTE.

## Introduction

Gastroesophageal reflux disease (GERD) is a prevalent gastrointestinal disorder characterized by the reflux of gastric contents into the esophagus, leading to symptoms such as heartburn and regurgitation. On the other hand, venous thromboembolism (VTE), encompassing deep vein thrombosis (DVT) and pulmonary embolism (PE), results from blood clots forming in the venous system.

While GERD primarily affects the gastrointestinal tract and VTE the vascular system, there is growing interest in understanding the systemic inflammatory state and shared risk factors that may link these conditions. This review examines the potential association, explores pathophysiological connections, and evaluates the current literature on this topic.

## Epidemiology of GERD and VTE

### GERD

GERD affects approximately **20-30% of the global population**, with obesity, smoking, and dietary habits being significant contributors(1).

### VTE

VTE has an annual incidence of **1-2 cases per 1,000 individuals**, with higher rates in hospitalized, immobile, or elderly patients. Risk factors include genetic predisposition, immobilization, malignancy, and systemic inflammation(2).

### Potential Mechanisms Linking GERD and VTE

#### • Chronic Inflammation and Hypercoagulability

GERD is associated with chronic esophageal inflammation, leading to increased levels of systemic inflammatory markers such as interleukin-6 (IL-6) and C-reactive protein (CRP). Chronic inflammation is a recognized contributor to hypercoagulability, potentially increasing the risk of VTE(3).

#### • Obesity as a Shared Risk Factor

Obesity is a major risk factor for both GERD and VTE. Increased abdominal pressure in obesity predisposes individuals to GERD, while the pro-inflammatory state and immobility associated with obesity elevate the risk of VTE(4).

• **Lifestyle and Comorbidities** Sedentary behavior, high-fat diets, and smoking—common in GERD patients—may also contribute to VTE development. Additionally, comorbidities like diabetes and cardiovascular diseases are prevalent in both conditions(5).

- **Pharmacological Factors** Proton pump inhibitors (PPIs), commonly used to treat GERD, have been associated with an increased risk of VTE. Although the evidence remains controversial, PPIs may alter clotting pathways and endothelial function(6).
- **Esophageal Motility Disorders and Vascular Effects** GERD-associated esophageal motility dysfunction might indirectly affect venous blood flow, particularly during nocturnal episodes of acid reflux, leading to reduced physical activity and increased venous stasis.

## Evidence from Recent Studies

### Observational Studies

- A retrospective cohort study found that GERD patients had a **1.3-fold increased risk** of developing VTE compared to non-GERD patients(7). The association was particularly significant in patients with obesity or metabolic syndrome.
- **Population-based Studies**
- A large-scale population-based study reported an elevated prevalence of VTE in patients with severe or untreated GERD, emphasizing the role of systemic inflammation in promoting thromboembolic events.

### • Experimental Studies

Laboratory investigations have demonstrated that GERD patients exhibit elevated levels of pro-coagulant factors such as fibrinogen, D-dimer, and tissue factor, supporting the hypothesis of a hypercoagulable state.

## Clinical Implications

### ✓ Screening and Risk Assessment

- Patients with severe GERD and additional risk factors for VTE (e.g., obesity, immobility) may benefit from regular screening for thromboembolic events.
- Enhanced risk stratification could identify high-risk patients and guide preventive measures.

### ✓ Pharmacological Considerations

- While PPIs are effective in managing GERD, clinicians should remain cautious about their potential thrombotic risks in susceptible populations. Alternative GERD treatments may be considered in high-risk patients.

### ✓ Lifestyle Modifications

- Addressing shared modifiable risk factors, such as weight reduction, smoking cessation, and physical activity, can mitigate the risks of both GERD and VTE.

## Future Directions

### • Longitudinal Studies

Large-scale, longitudinal studies are needed to clarify the causal relationship between GERD and VTE.

### • Mechanistic Research

Future research should focus on elucidating the biological mechanisms linking GERD-induced inflammation and hypercoagulability.

### • Intervention Trials

Randomized controlled trials assessing the impact of anti-inflammatory or anticoagulant therapies in GERD patients with elevated VTE risk could provide valuable insights.

### Conclusion

The potential association between GERD and VTE highlights the complex interplay between systemic inflammation, shared risk factors, and hypercoagulability. While the evidence remains preliminary, clinicians should be aware of this potential link and adopt a holistic approach to managing patients with either condition. Addressing modifiable risk factors and optimizing treatment strategies could significantly improve patient outcomes.

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