

Ishvari Mokadam, Ishanth Talanki, Atul Laddu, Global Thrombosis Forum, Suwanee, GA, USA.

Keywords: PE, Death Spiral, Pathophysiology of PE

## ABSTRACT

- PE is a life-threatening condition characterized by the blockage of blood vessels in the lungs due to emboli.
- Clotting disorders, including genetic variations, play a crucial role in the development of PE. Understanding the genetic associations of PE and clotting disorders is essential for risk assessment and management strategies.

## INTRODUCTION

- This project aims at our literature review to explore these genetic links while discussing recent advancements in gene therapies that hold promise for the treatment of thrombosis and clotting disorders.
- Mutations in genes such as factor V Leiden and prothrombin G20210A involved in coagulation pathways, increase the risk of clot formation, leading to PE.
- Figure 1 shows the mortality rate vs. age vs. gender.

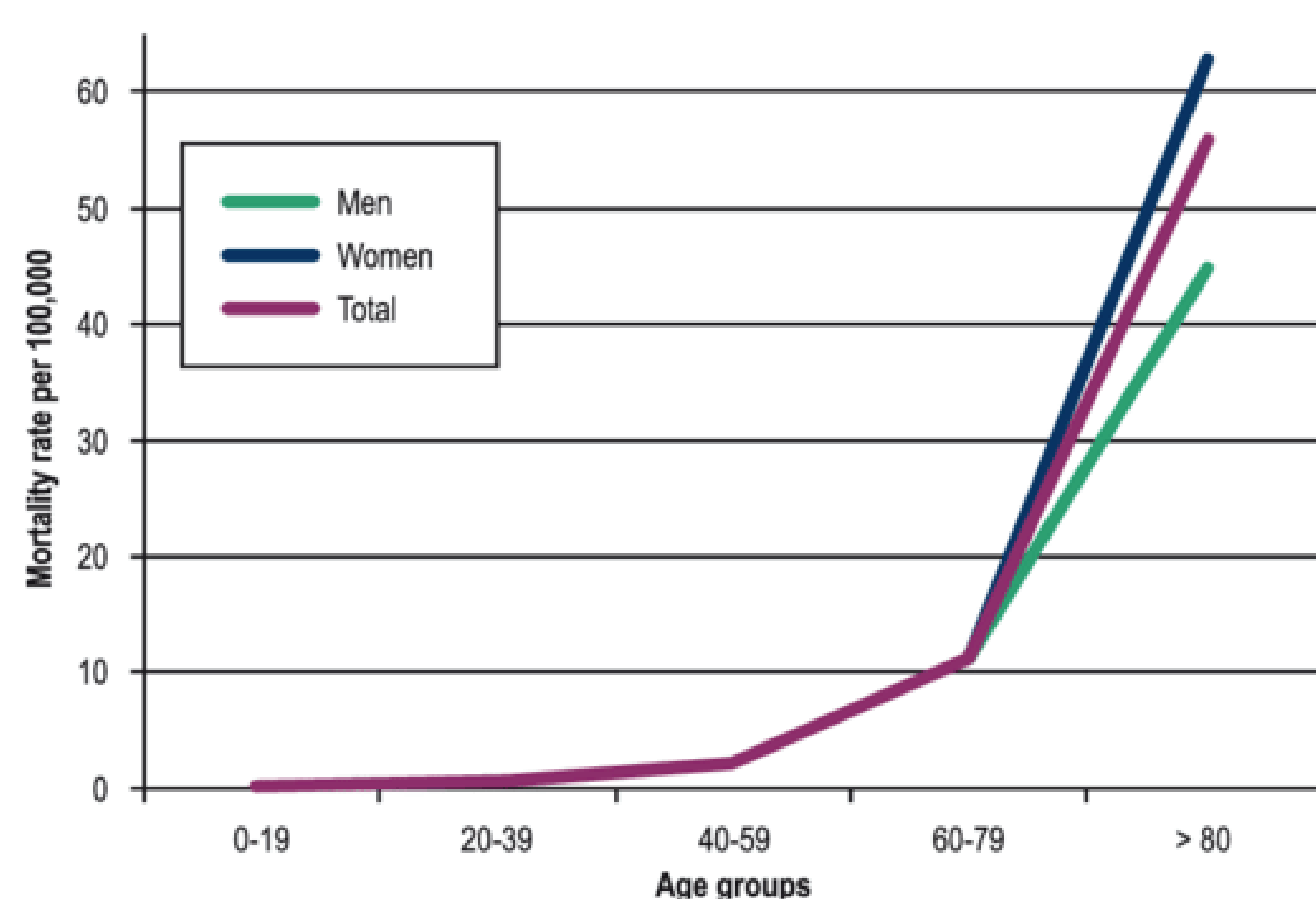


Figure 1: Mortality rate vs age vs gender

## RESULTS

- Deficiencies in natural anticoagulant proteins such as protein C, protein S, and antithrombin further predispose individuals to clotting disorders.

## RESULTS, cont.

- In a study by Meißner et al (2021), three single nucleotide polymorphisms (rs1800790, rs3813948, rs6025) showed evidence of association (EOA) in the main analysis, and five variants (rs169713, rs1801131, rs4524, rs5985 and rs8176592) demonstrated EOAs in subgroups, supporting the view that PE represents a complex disease with many factors contributing relatively small effect.
- Traditional treatments for thrombosis and clotting disorders primarily rely on anticoagulants, and recent advances have opened new avenues for gene therapies targeting clotting disorders.
- In preclinical studies, gene therapy approaches have shown promise in restoring the balance of coagulation factors and addressing underlying genetic abnormalities.
- Researchers have successfully used adeno-associated viral vectors to deliver therapeutic genes, such as those encoding natural anticoagulant proteins, into animal models with clotting disorders.
- These advances hold significant potential for personalized treatments that target the root genetic causes of clotting disorders, and new hope for patients with PE or recurrent thrombosis.
- Figure 2 indicates pulmonary embolism death spiral.

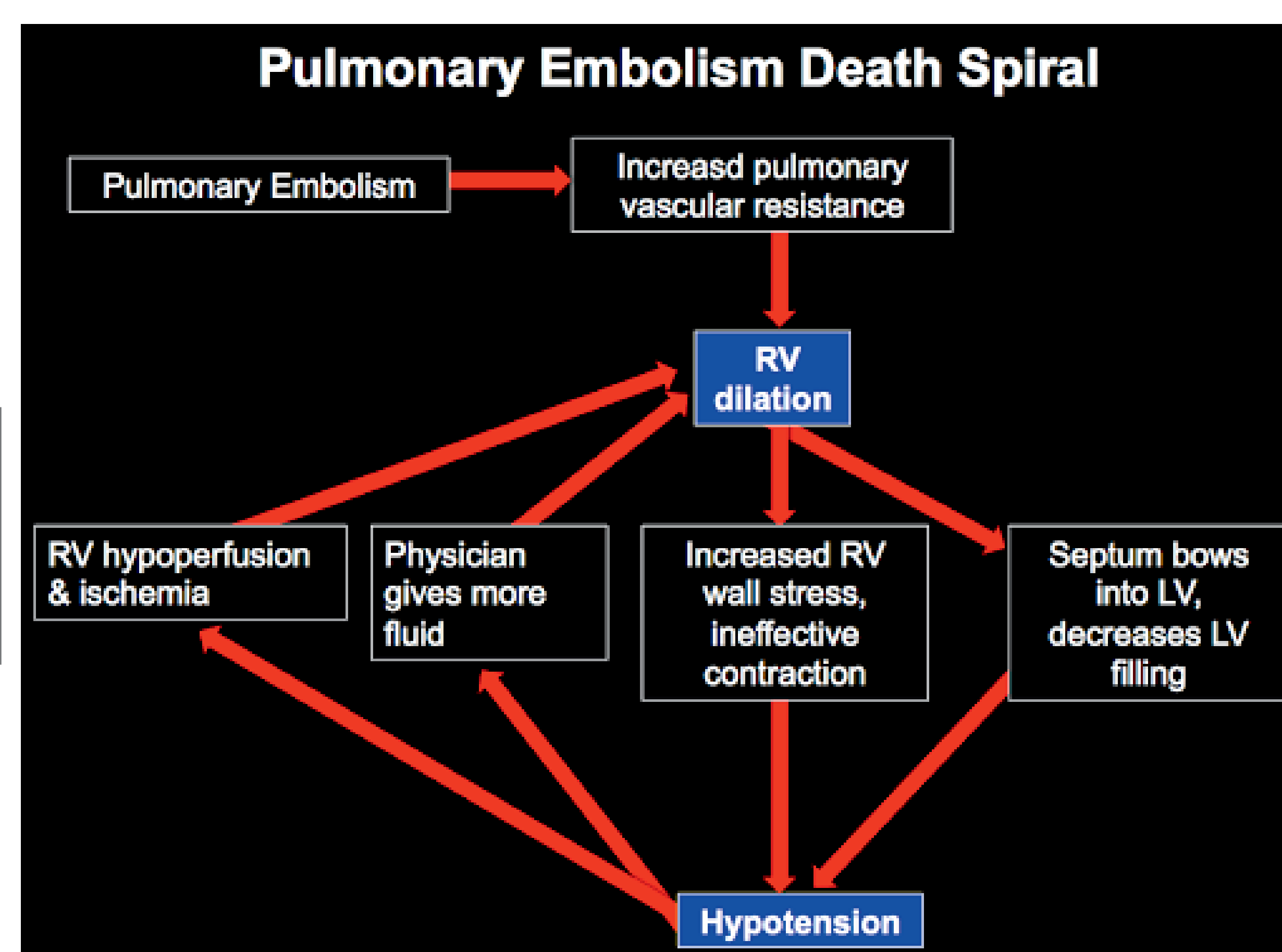


Figure 2: Death Spiral of PE

## CONCLUSION

- Understanding the genetic associations of clotting disorders and PE is crucial for risk assessment and management strategies.
- While traditional treatments primarily rely on anticoagulants, recent advancements in gene therapies offer promising approaches to address underlying genetic abnormalities. Preclinical studies have shown positive outcomes in restoring coagulation balance using gene therapy approaches.
- These developments may pave the way for personalized treatments targeting genetic causes of clotting disorders, and management of PE.

## IMPORTANCE OF OUR WORK

- Understanding the genetic associations of clotting disorders and PE is crucial for risk assessment and management strategies.
- While traditional treatments primarily rely on anticoagulants, recent advancements in gene therapies offer promising approaches to address underlying genetic abnormalities. Preclinical studies have shown positive outcomes in restoring coagulation balance using gene therapy approaches.
- These developments may pave the way for personalized treatments targeting genetic causes of clotting disorders, and management of PE.

The authors disclose no conflict of interest.

## REFERENCES

1. Goldhaber, Samuel Z. and Elliott, Gregory C: Acute Pulmonary Embolism: Part I: Epidemiology, Pathophysiology, and Diagnosis, Clinical Cardiology: New Frontiers, November 13, 2022.
2. Riedel, Martin: Acute pulmonary embolism 1: Pathophysiology, clinical presentation, and diagnosis. BMJ Journal, 2001.
3. Yang, P.; Li, H.; and Zhang, J: Research progress on biomarkers of pulmonary embolism: Clin Respir J.15,1046-1055, 2021