GENETIC ASSOCIATION OF PE

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BACKGROUND

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.

METHODS

We conducted a 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.

RESULTS

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). Deficiencies in natural anticoagulant proteins such as protein C, protein S, and antithrombin further predispose individuals to clotting disorders (Table 1). 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.

RESULTS, CONTD.

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. 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 (Table 1, Figure 1).

CONCLUSIONS

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. These developments may pave the way for personalized treatments targeting genetic causes of clotting disorders, and management of PE.

Table 1: Inherited Causes of Blood Clots

Increased levels of natural procoagulants	Decreased levels of natural anticoagulants	Abnormal Fibrinolysis	Other Inherited Causes
Factor V Leiden mutation or activated protein C resistance*	Antithrombin	Decreased Levels of Tissue Plasminogen Activator (t-PA)	Paroxysmal nocturnal hemoglobinuria
Prothrombin 20210 mutation	Protein C	Increased levels of plasminogen activator inhibitor (PAI-1)	
Hyperhomocysteinemi	Protein S	Elevated Thrombin-Activatable Fibrinolysis Inhibitor (TAFI)	
FVIII, FIX, FXI, FVII, VWF	Thrombomodulin		
	Heparin Cofactor II		
	Tissue Factor Pathway Inhibitor (TFPI)		

*The Factor V Leiden mutation does not result in increased FV levels but a resistance to the anticoagulant action of activated protein C.

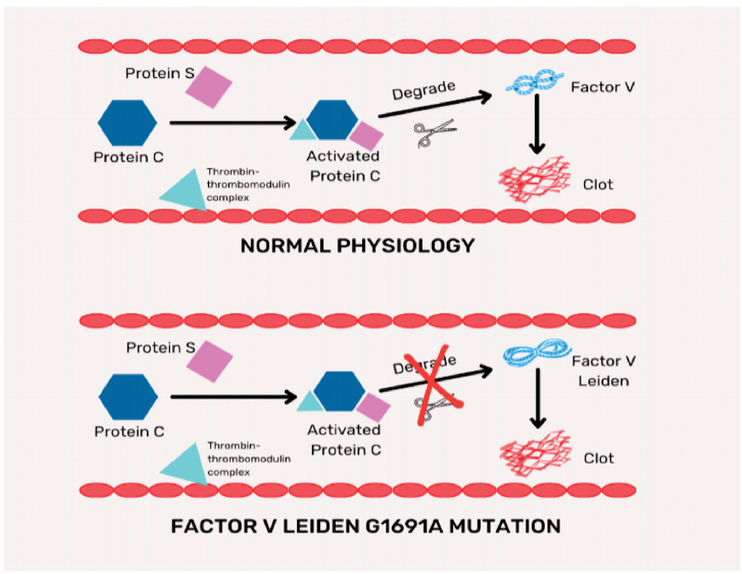

Figure 1: Pathophysiology of Factor V Leiden Mutation

The authors disclose no conflict of interest.

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