Annals of Reviews and Research

Juniper Publishers key to the Researchers

Review Article
Volume 12 Issue 1 - September 2024
DOI: 10.19080/ARR.2024.12.555829

Ann Rev Resear

The Role of Factor V Leiden Deficiency in Venous Thromboembolism: A Comprehensive Review

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Submission: September 19, 2024; **Published:** September 24, 2024

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Abstract

Factor V Leiden deficiency is one of the most common inherited thrombophilias, significantly increasing the risk of venous thromboembolism (VTE). This comprehensive review explores the pathophysiology underlying Factor V Leiden mutation, emphasizing its role in dysregulating coagulation and enhancing thrombotic risk. Clinical presentations of VTE in individuals with this deficiency range from asymptomatic cases to life-threatening conditions, including deep vein thrombosis and pulmonary embolism. Genetic testing and risk stratification are essential for diagnosis and management, while anticoagulation therapy remains the cornerstone of treatment. Advances in personalized medicine and genetic counseling are improving patient outcomes, particularly in populations with concurrent risk factors such as pregnancy or surgery. Understanding the interplay between Factor V Leiden and other thrombotic risk factors is crucial for optimizing prevention and treatment strategies in at-risk populations.

Keywords: Factor V Leiden; Venous thromboembolism; Thrombophilia; Treatment strategies; Anticoagulation therapy

Abbreviations: DVT: Deep Vein Thrombosis; PE: Pulmonary Embolism; VTE: Venous Thromboembolism; FVL: Factor V Leiden; F5: Coagulation Factor V; APC: Activated Protein C; OCPs: Oral Contraceptive Pills; BMI: Body Mass Index; CTPA: Computed Tomography Pulmonary Angiography; V/Q: Ventilation-Perfusion; CVT: Cerebral Vein Thrombosis; FVR506Q: Factor V Leiden Mutation (Arg506Gln); LMWH: Low Molecular Weight Heparin; DOACs: Direct Oral Anticoagulants; INR: International Normalized Ratio

Introduction

Factor V Leiden deficiency, also known as Owren disease, is a rare genetic blood clotting disorder that increases the risk for abnormal blood clots and is the most common inherited form of thrombophilia. Factor V Leiden deficiency is caused by a mutation in the coagulation factor V (F5) gene inherited in an autosomal recessive manner [1]. The F5 gene regulates the production of a protein called factor V, which plays a role in helping your blood clot when necessary, such as after an injury. The Factor V Leiden mutation alters the structure of this protein, making it resistant to other proteins that normally prevent excessive clotting [2]. Consequently, this can cause your blood to clot more easily than normal, potentially leading to severe complications in the legs or lungs, respectively known as deep vein thrombosis (DVT) and pulmonary embolism (PE). Approximately 5% of the Caucasian population carry one copy of the mutation, while fewer have two copies, leading to a more significant risk of clotting disorders [3]. Figure 1 shows the coagulation cascade pathway during cell-surface-directed hemostasis [2].

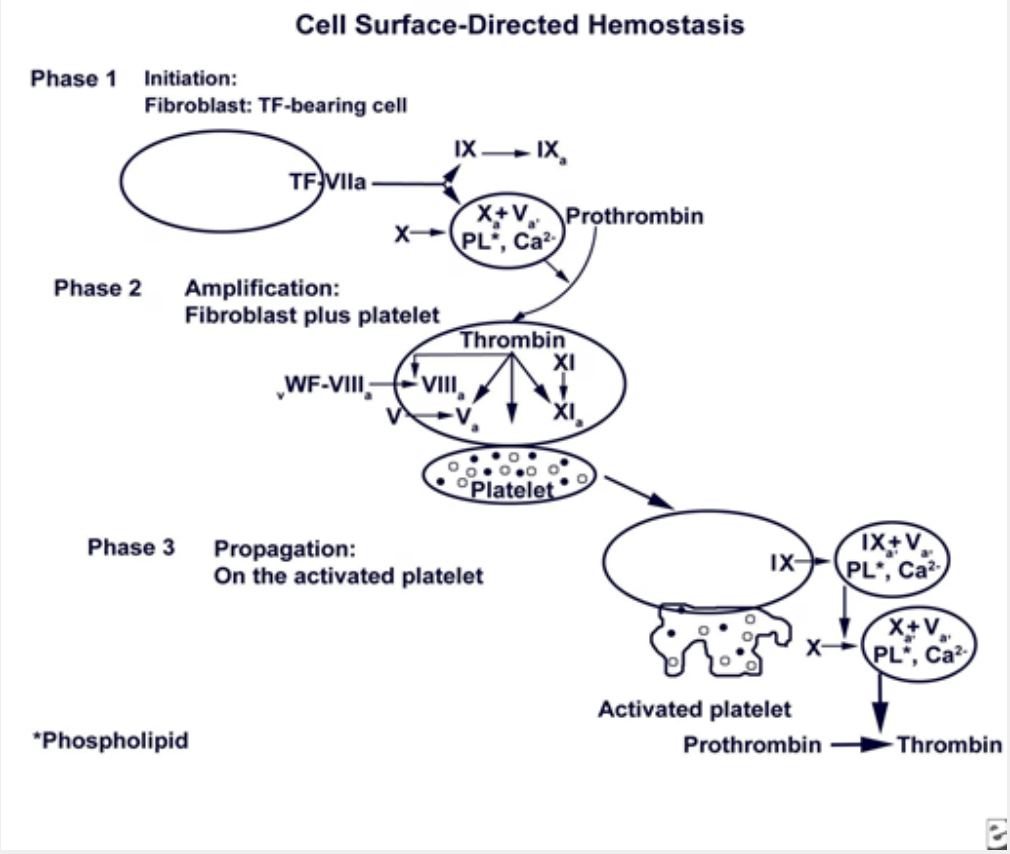

Figure 1: Coagulation Cascade Pathway During Cell Surface-Mediated Hemostasis Cell surface-directed hemostasis. Initially, a small amount of thrombin is generated on the surface of the tissue factor (TF)-bearing cell. Following amplification, the second burst generates a larger amount of thrombin, leading to fibrin (clot) formation. Burgess, R., & Patel, P. (2021). Factor V Leiden thrombophilia. Medscape.

Most individuals with Factor V Leiden do not experience abnormal blood clots. However, in those who do, these clots can result in serious long-term health complications or pose a life-threatening risk. Factor V Leiden deficiency is clinically important due to its association with DVT and PE. Clinical management revolves around assessing the risk of thrombosis, mainly when additional risk factors like surgery, trauma, pregnancy, or the use of oral contraceptives are present, for individuals with the Factor V Leiden mutation [4]. Individuals carrying the mutation may need prophylactic anticoagulation therapy during high-risk periods. Factor V Leiden should be included in the differential diagnosis for patients with unexplained or recurrent thrombotic events. Due to its hereditary nature, genetic counseling is also a critical aspect for families with a history of this condition [4].

Venous thromboembolism (VTE), which includes deep vein thrombosis and pulmonary embolism, is the primary clinical complication linked to Factor V Leiden deficiency. VTE occurs when a blood clot forms in deep veins, usually in the legs, and can travel to the lungs, leading to a potentially life-threatening pulmonary embolism. Individuals with Factor V Leiden are more likely to develop a first-time VTE than the general population, with the risk increasing significantly in those with two copies of the mutation [5]. Factor V Leiden is one of the most common genetic predispositions for VTE, making it crucial to understand this risk for tailored preventive and therapeutic interventions, especially in high-risk clinical settings.

Pathophysiology of Factor V Leiden Deficiency

Genetic Basis

Activated protein C is a natural anticoagulant that cleaves Factor Va at three different amino acid positions: R (Arginine) 306, R 506, and R 679 [5]. Factor V Leiden refers to a point mutation at nucleotide 1691 in the Factor V gene, which substitutes adenine for guanine. It replaces arginine with glutamine at the Arg506 APC (Activated protein C) cleavage site. The mutated gene is usually referred to as FVR506Q. As a result of this substitution, Factor Va is cleaved at a slower rate by APC, leading to a diminished anticoagulant response [6].

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Factor V Leiden is inherited in an autosomal dominant fashion with incomplete penetrance, which means that not every person who carries the disease-causing mutation will develop the disease [7]. Factor V Leiden is the most common inherited form of thrombophilia, but its prevalence differs across populations. It is most frequent among individuals of European descent, with 3 to 8% being heterozygous carriers on average. The highest rates are found in Greece, where up to 15% of people carry the mutation. On the other hand, this mutation is infrequent in African, Asian, and Australasian (indigenous) people [8]. In addition, 1 in 5000 people of European ancestry are homozygous, i.e., they carry two mutated copies of the gene [6].

Mechanism Leading to Thrombosis

Factor V is postulated to have dual functions, procoagulant and anticoagulant [9]. They are induced by differential proteolysis of Factor V at sites of vascular injury. Thrombin and Factor Xa cleave Factor V to form procoagulant Factor Va, further degraded by APC (activated protein C). In contrast, APC reveals anticoagulant properties of Factor V (FVac). Furthermore, anticoagulant functions of Factor Va are lost upon further proteolysis by Thrombin or Factor Xa, forming a tightly regulated loop. Factor Vac (anticoagulant fraction of Factor V), along with APC and protein S, assists in the degradation of Factor VIIIa in the tenase complex (Factor IXa, Factor VIIIa, phospholipids, and Ca2+) [10].

Based on its physiological properties, mutations in Factor V can have dual effects, decreased degradation of Factor Va by APC and impaired destruction of Factor VIIIa [9]. Typically, inactivation of Factor V involves initial cleavage at Arg506 followed by sequential cleavage at Arg306 [11]. However, Factor V Leiden (FVR506Q), is only cleaved by APC at Arg306, which is insufficient to completely inactivate FVa, resulting in a 10 times slower cleavage of FVa, leading to resistance to APC [12]. All these factors contribute to a mildly increased lifelong risk of venous thrombosis in these individuals [13].

Interaction with Other Risk Factors

According to Vandenbroucke et al., the risk of venous thrombosis is higher in women who use oral contraceptive pills (OCPs) and carry the Factor V Leiden mutation compared to those without the mutation [14]. This increased risk occurs because OCP alone increases the likelihood of venous thrombosis, and when combined with the Factor V Leiden mutation, the two risk factors amplify each other's effects [15]. In addition, Factor V Leiden may also be responsible for pregnancy-related VTE (venous thromboembolism) in the postpartum period, especially in its homozygous form [16].

Other risk factors for VTE, such as recent surgery, trauma, and immobilization for more than 7 days, can further increase the risk of thrombotic events in individuals who carry the Factor V Leiden mutation, though the added risk is relatively small and does not justify prolonged anticoagulation prophylaxis [17]. Patients who are homozygous or compound heterozygous for Factor V Leiden and Prothrombin G20210A gene mutations are at increased risk of thromboembolic events, in particular, when predisposing factors such as pregnancy, or recent surgery are present [18]. Additionally, double heterozygosity for Factor V Leiden and HR2 haplotype (a complex haplotype in exon 13 of Factor V gene: A4070G; His1299Arg) elicited a 3- to 4-times increase in the relative risk of venous thromboembolism compared with Factor V Leiden alone [19,20]. These findings suggest that Factor V Leiden works together with other risk factors to increase the likelihood of thromboembolic events.

Factor V Leiden and Venous Thromboembolism

Factor v leiden is the most common inherited form of thrombophilia. Although factor V Leiden thrombophilia increases the risk of blood clots, only about 10 percent of individuals with the factor V Leiden mutation ever develop abnormal clots [21]. Factor V Leiden mutation is found in 4% to 6% of the U.S. population [22]. The mutation is found in 3.8% of individuals in France, but the frequency ranges from 1.3% in southwestern regions to 7.1% in northeastern France. In the United States of America, there are different prevalences per ethnicity; 5.2% of white Americans; 2.2% of Hispanic Americans; 1.2% of African Americans; 0.45% of Asian Americans; 1.25% of native Americans [23,24]. Table 1 reflects the prevalence of the mutation in the world.

Table 1: Prevalence of the Factor V Leiden Mutation worldwide. Hirschhorn JN, Kunkel LM (1992) Factor V Leiden thrombophilia. Genet Med 4(2): 112-115.

Population	Prevalence (%)[9-11,12-17]
European whites	3-15
Spain	3.3
France	3.8
Germany	4
Iceland	5.2
United Kingdom	8.8
Greece	15
Sweden	11

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Africa	Absent
Southeast Asia	Absent
Asia minor	1.2
Australia (indigenous)	Absent
Japan	Absent
Jordanian Arabs	12.2
Lebanon	14
Western Iran	2.97
Canada	5.3
United States	
Whites	5.2
Hispanic Americans	2.2
African Americans	1.2
Asian Americans	0.45
Native Americans	1.25
[a]Healthy individuals with no history of venous thromboembolism.	
[b]Includes heterozygous and homozygous individuals.	

Risk factors for VTE in heterozygous vs. homozygous carriers

The chance of developing an abnormal blood clot depends on whether a person has one (heterozygous) or two copies (homozygous) of the factor V Leiden mutation in each cell (Tables 2 & 3). People who inherit two copies of the mutation have a higher risk of developing a clot than people who inherit one copy of the mutation. The presence of one copy of the factor V Leiden mutation increases that risk to 3 to 8 in 1,000, and having two copies of the mutation may raise the risk to as high as 80 in 1,000 [25]. Many individuals with the factor V Leiden variant never develop thrombosis. Most individuals with factor V Leiden thrombophilia are heterozygous for the factor V Leiden variant, which they inherited from a parent who is also heterozygous for the factor V Leiden variant. Each child of a heterozygous parent has a 50% chance of inheriting the factor V Leiden variant from the parent (heterozygote inheritance) [26].

Table 2: Risk of thrombotic complications in heterozygotes individuals with Factor V Leiden Mutation. Miller T, Dinsmore J (2021) Factor V Leiden thrombophilia. Genet Med 23(1): 1-16.

Thrombotic complication	Estimated risk (odds ratio)[a]
First VTE[61-64]	3-8
Cerebral vein thrombosis[46.59]	3-5
Primary upper extremity thrombosisb[43,45]	3-6
CVC-associated thrombosis[65]	2-3
Superficial vein thrombosis[60]	6
Pregnancy-associated VTE[66,67]	8-52
Recurrent VTE[42,68]	1.4-1.6
Pregnancy loss66,69-71	2-4
[a]Risk relative to individuals without Factor V Leiden.	
[b]Not related to malignancy or a central venous catheter.	
VTE, venous thromboembolism; CVC, central venous catheter.	

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Table 3: Risk of thrombotic complications in homozygotes individuals with Factor V Leiden Mutation. Miller T, Dinsmore J (2021) Factor V Leiden thrombophilia. Genet Med 23(1): 1-16.

Thrombotic complication	Risk (odds ratio)[a]
First VTE[4,33,62]	10-80
Pregnancy-associated VTE[66,73,74]	20-40
Oral contraceptive-associated VTE[75]	100
Recurrent VTE[33]	2-3
Surgery-associated VTE[76]	20
Early fetal loss[66]	3
Late fetal lossb[77]	11
[a]Risk relative to individuals without Factor V Leiden allele.	
[b]Occurring after 12 weeks gestation.	
VTE, venous thromboembolism.	

Interaction between Factor V Leiden and other thrombophilic conditions

There are many factors that increase thromboembolic conditions in Factor V Leiden deficiency. Factor V Leiden is only one of many risk factors for developing DVT or PE. Usually, the effect of risk factors is additive: the more risk factors you have, the higher the risk. Sometimes, however, the effects of multiple risk factors are more than additive.

OCPS: A woman who has factor V Leiden and takes OCPs, for example, has a 35-fold increased risk of developing a DVT, which is higher than the increased risk associated with simply adding together the risk of factor V Leiden (5-fold increased risk) and OCP use (4-fold increased risk) [25]. The risk for VTE is increased more than 100-fold in women homozygous for Factor V Leiden who use oral contraceptives. Oral contraceptives containing third-generation progestagen and desogestrel are associated with a 2-fold higher risk for VTE than second-generation preparations, and the risk is especially high in Factor V Leiden heterozygotes [26].

Age: Thrombotic incidences increase as one age, and the incidence increases more with factor v Leiden mutation. It was also complicated by obesity and smoking. The 10-year risk for VTE among heterozygotes was 10% in smokers older than 60 years with a BMI >30 kg/m^2, in contrast to a <1% risk in nonsmokers younger than 40 years who were not overweight. The corresponding absolute 10-year thrombotic risks for Factor V Leiden homozygotes with and without these risk factors were 51% and 3%, respectively [26].

Obesity: Obesity is a known risk factor for venous thrombotic embolism. Obesity (BMI >30 kg/m^2) has been associated with a double-fold (2.5) increased risk of VTE. The risk was increased 8-fold in obese individuals with Factor V Leiden and approximately 6-fold in overweight (BMI ≥25 and <30 kg/m^2) individuals with the mutation [27].

Pregnancy: Factor V Leiden is found in 20-46% of women with pregnancy-associated VTE [24]. It is usually made worse if the women have other risk factors like obesity and have the habit of smoking. Pregnancy increases estrogen, which makes the patients more prone to venous thromboembolism.

Clinical Manifestations of VTE in Factor V Leiden Carriers

Deep Vein Thrombosis (DVT)

Deep vein thrombosis (DVT) is one of the most common clinical manifestations of venous thromboembolism (VTE) in individuals with Factor V Leiden deficiency. DVT typically occurs in the lower extremities, most commonly in the deep veins of the legs. The symptoms include pain, swelling, warmth, and redness in the affected limb. However, many cases of DVT can be asymptomatic or present with mild symptoms, leading to delayed diagnosis. The definitive diagnosis of DVT is made through imaging studies such as duplex ultrasonography, which is the gold standard for detecting thrombi in the deep veins [28-30]. The incidence of DVT in Factor V Leiden carriers is significantly elevated compared to the general population. Heterozygous carriers have a 3- to 8-fold increased risk of developing DVT, while homozygous individuals have a much higher predisposition, with a 50- to 100-fold increased risk. The mutation leads to resistance to activated protein C (APC), which prevents the proper regulation of the coagulation cascade, resulting in a hypercoagulable state that favors clot formation [29,30].

Pulmonary Embolism (PE)

Pulmonary embolism (PE) occurs when a thrombus, typically originating from a DVT, dislodges and travels through the venous circulation to the lungs. PE is a life-threatening condition characterized by the obstruction of the pulmonary arteries, leading to impaired oxygen exchange. In Factor V Leiden carriers, the clinical presentation of PE can range from mild to severe. Symptoms may include shortness of breath, chest pain, cough,

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tachycardia, and, in severe cases, hemodynamic instability or sudden death. The severity of PE in individuals with Factor V Leiden is similar to that of the general population; however, the mutation increases the overall likelihood of experiencing a PE [28-32]. The diagnosis of PE is usually confirmed through imaging techniques such as computed tomography pulmonary angiography (CTPA) or ventilation-perfusion (V/Q) scans. Factor V Leiden carriers, mainly homozygous individuals, are at an elevated risk for PE, especially when additional risk factors, such as immobilization, surgery, or oral contraceptive use, are present [30].

Recurrent Thrombosis

One of the significant concerns in individuals with Factor V Leiden deficiency is the increased risk of recurrent thrombosis. Once an individual has experienced a thrombotic event, such as DVT or PE, the likelihood of a subsequent event is significantly higher, especially in those with the Factor V Leiden mutation. Heterozygous carriers of the mutation are at a 3- to 5-fold increased risk of recurrent VTE compared to non-carriers, while homozygous individuals face an even greater recurrence risk. Recurrent thrombotic events follow a similar pattern to the initial thrombosis, often involving the same venous territory [29-32]. Additional risk factors, such as prolonged immobilization or pregnancy, further increase the recurrence risk. Long-term anticoagulation therapy is often required to prevent recurrent events, but the duration and intensity of treatment need to be carefully balanced to minimize the risk of bleeding complications [30].

Other Associated Complications

In addition to DVT and PE, Factor V Leiden deficiency has been associated with other less common but thrombotic severe complications. One such complication is cerebral vein thrombosis (CVT), a rare but potentially life-threatening condition involving clot formation in the venous sinuses of the brain. Symptoms of CVT include headache, visual disturbances, seizures, and focal neurological deficits. While CVT is rare, Factor V Leiden carriers are at an increased risk compared to the general population, mainly when other risk factors, such as oral contraceptive use or pregnancy, are present [31]. Pregnancy-related complications are another concern in women with Factor V Leiden. The mutation has been linked to an increased risk of pregnancy loss, preeclampsia, and placental abruption. Pregnant women with the mutation are also at higher risk for developing VTE, particularly in the postpartum period. Prophylactic anticoagulation may be considered in high-risk pregnancies to prevent adverse outcomes [28-32].

Management and Treatment Strategies

Anticoagulation Therapy

Anticoagulation therapy is the cornerstone of managing Factor V Leiden deficiency and preventing venous thromboembolism (VTE). Anticoagulants such as low molecular weight heparin (LMWH), unfractionated heparin, or fondaparinux are used as initial treatment in acute settings. These agents act quickly to inhibit clot propagation and are typically administered for several days before transitioning to long-term anticoagulation therapy. Warfarin has historically been the standard oral anticoagulant for long-term management for VTE prevention. However, frequent international normalized ratio (INR) monitoring is required to ensure therapeutic efficacy. Direct oral anticoagulants (DOACs), such as rivaroxaban, apixaban, and dabigatran, are increasingly preferred due to their predictable pharmacokinetics, reduced need for monitoring, and efficacy in preventing VTE in individuals with Factor V Leiden use long-term anticoagulation in Factor V Leiden carriers depends on the individual's risk profile. Heterozygous carriers with a history of VTE may benefit from extended anticoagulation therapy, mainly if additional risk factors are present. Due to their significantly higher risk of recurrence, homozygous carriers often require indefinite anticoagulation following an initial thrombotic event. However, the reactions must be weighed carefully against the risk of recurrent thrombosis [28-34].

Prophylactic Measures

In high-risk situations, such as surgery, pregnancy, or prolonged immobility, prophylactic anticoagulation is an important strategy for preventing VTE in individuals with Factor V Leiden deficiency. Surgical patients, especially those undergoing orthopedic procedures or extended hospital stays, are at high risk for developing DVT. In these cases, perioperative anticoagulation with LMWH or DOACs is commonly employed. Similarly, pregnant women with the mutation are often given prophylactic anticoagulation throughout pregnancy and the postpartum period due to the heightened risk of thrombotic complications during these times. Stocking compression devices during immobilization or hospitalization can further reduce the risk of VTE. Additionally, careful attention to hydration and mobilization strategies can mitigate thrombotic risks in high-risk individuals [25,17,33].

Lifestyle and Supportive Therapies

Life stcations and patient education are crucial in the long-term management of Factor V Leiden carriers. Regular physical activity, weight management, and smoking cessation are essential lifestyle changes that can reduce thrombotic risk. Obesity and smoking are well-known risk factors for VTE, and addressing these through lifestyle interventions can reduce the overall burden of thrombosis. Additionally, patients should be educated about the importance of staying hydrated and avoiding prolonged periods of immobility, particularly during travel or hospitalization. Patients should also know the potential interactions between anticoagulant therapy and certain medications or supplements. Regular monitoring and close communication with healthcare providers can help to manage these risks. In women, it is essential

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to discuss the use of hormonal contraceptives, which can increase the risk of thrombosis in Factor V Leiden carriers [28-34].

Emerging Therapies

Recent advancements in the treatment have introduced new and experimental therapies that hold promise for patients with Factor V Leiden deficiency. Novel anticoagulants with different mechanisms of action are currently under investigation, aiming to provide more effective and safer options. For example, inhibitors targeting Factor XI are being explored as potential anticoagulants that may reduce bleeding risk while protecting against clot formation [33]. Gene therapy and other molecular approaches that address the underlying genetic mutation V Leiden carriers are also being investigated. While these therapies are still experimental, they represent a potential future avenue for reducing the lifelong thrombotic risk associated with the mutation. In addition, research into personalized medicine strategies, such as genetic profiling, may allow tailored approaches to anticoagulation and risk management [30-34].

Prognosis and Outcomes

Factor V Leiden deficiency is a significant genetic risk factor for venous thromboembolism (VTE), profound vein thrombosis, and pulmonary embolism [35]. Studies have shown that patients with Factor V Leiden have a markedly increased risk of VTE recurrence. For example, a study by Kahn et al. showed that the recurrence rate of VTE in individuals with Factor V Leiden is approximately 8-10% annually, compared to a lower recurrence rate in those without the mutation [36]. Eppenberger et al. deducted through a systematic review and meta-analysis, "the association of heterozygous FVL mutation and recurrent VTE in 30 prospective cohort studies and 24 publications summarizing 13,571 patients of which a 42% increased risk of recurrence was found in patients with heterozygous FVL mutation" [37].

Several factors influence the prognosis of VTE in patients with Factor V Leiden. Coexisting genetic mutations, such as prothrombin gene mutations or deficiencies in proteins C and S, significantly increase the risk of VTE [38]. Also, health behaviors and lifestyle factors such as smoking, lack of exercise, alcoholism, and obesity exacerbate the risk, as do comorbid conditions such as cancer or chronic inflammatory diseases [39]. Research has elaborated that "FV Leiden is a genetically determined and disease-independent parameter, hence associated with VTE in cancer patients" [40,41]. These combined risk factors necessitate a personalized approach to management.

Long-term anticoagulation therapy, while crucial for preventing VTE recurrence, has implications for quality of life and bleeding risk. Studies indicate that patients on prolonged anticoagulation often face challenges related to bleeding complications, such as gastrointestinal bleeding or hemorrhagic stroke. However, the benefits of preventing VTE recurrence generally outweigh these risks [42,43]. Furthermore, patients report a reduced quality of life due to the inconvenience and anxiety associated with long-term anticoagulant use, highlighting the need for careful management and patient education [44].

Controversies and Future Directions

One of the main controversies in the management of Factor V Leiden (FVL) deficiency relates to the need for lifelong anticoagulation in patients who have experienced venous thromboembolism (VTE). While anticoagulation is well-established in reducing the risk of recurrent VTE, there is significant debate about whether lifelong therapy is warranted in all patients, especially those who are heterozygous for FVL and have experienced a single VTE event. The long-term use of anticoagulants poses a substantial risk of bleeding, which must be balanced against the risk of recurrent thrombosis. Studies suggest that, in heterozygous FVL patients, the risk of recurrent VTE may not justify lifelong anticoagulation for all, mainly if the initial VTE was provoked by transient risk factors such as surgery or pregnancy. However, patients with homozygous FVL or those with recurrent VTE are at a much higher risk, and indefinite anticoagulation is often recommended; this has sparked ongoing debate in the clinical community regarding risk stratification and individualized treatment protocols [45].

The emergence of new therapies has significantly shaped the management of VTE in FVL patients. The development of direct oral anticoagulants (DOACs) has provided an alternative to traditional anticoagulants like warfarin. DOACs offer several advantages, including fewer dietary restrictions, reduced need for monitoring, and lower bleeding risks in some cases. Nonetheless, long-term safety data for DOACs, particularly in the specific context of hereditary thrombophilias such as FVL, are still evolving. Another promising area is gene-based therapies, such as CRISPR, which hold the potential to correct the FVL mutation at its source, although this approach remains in the experimental stages. Personalized medicine also plays a growing role, with increasing attention being given to genetic testing and individualized risk assessments to guide anticoagulation decisions. Tailoring treatment based on a patient's genetic profile, family history, and additional risk factors can better manage VTE risk while minimizing the adverse effects associated with anticoagulation [46].

Future research should focus on several critical areas. First, large-scale, randomized trials are needed to clarify which patients with FVL benefit most from lifelong anticoagulation and to better define the optimal duration of therapy. Given the variable risk of recurrence based on FVL status and other risk factors, more data are needed to guide personalized treatment strategies. Additionally, research should continue exploring the safety and efficacy of DOACs in the long-term management of FVL-associated VTE, particularly in comparison to traditional therapies such as warfarin. Emerging technologies such as gene editing

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should also be investigated for their potential to offer curative treatment options in hereditary thrombophilias. Finally, a better understanding of biomarkers and genetic profiles that predict recurrence risk could further inform individualized treatment plans, optimizing the balance between preventing thrombosis and minimizing bleeding risks [47,48].

Conclusion

Factor V Leiden deficiency significantly contributes to the risk of venous thromboembolism, highlighting the need for heightened awareness and proactive management. The mutation leads to a hypercoagulable state by impeding the inactivation of factor V, which results in an increased propensity for thrombus formation. This review underscores the importance of early detection through genetic testing, particularly in individuals with a family history of thrombotic events or those presenting with unexplained VTE. Effective management involves a combination of lifestyle modifications, risk assessment, and tailored anticoagulation therapy, with a focus on mitigating risks associated with surgery, pregnancy, and other high-risk conditions. Emerging research into novel anticoagulants and personalized treatment strategies offers hope for improved patient outcomes. Future studies should aim to further elucidate the interaction between Factor V Leiden and other genetic and environmental factors, enhancing our ability to predict, prevent, and treat venous thromboembolism.

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How to cite this article: Rishita D, Lilian R Diaz R, Chinyere P, Linda Boahemaah-K, Arashdeep S, et al. The Role of Factor V Leiden Deficiency in Venous Thromboembolism: A Comprehensive Review. Ann Rev Resear. 2024; 12(1): 555829. DOI: 10.19080/ARR.2024.12.555829

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DOI:10.19080/ARR.2024.12.555829

How to cite this article: Rishita D, Lilian R Diaz R, Chinyere P, Linda Boahemaah-K, Arashdeep S, et al. The Role of Factor V Leiden Deficiency in Venous Thromboembolism: A Comprehensive Review. Ann Rev Resear. 2024; 12(1): 555829. DOI: 10.19080/ARR.2024.12.555829