

# The Role of Genetic Factors in the Development of Chronic Venous Insufficiency

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## DESCRIPTION

Chronic Venous Insufficiency (CVI) is a condition in which the veins in the legs are unable to efficiently return blood to the heart, leading to symptoms such as leg swelling, varicose veins, pain and in severe cases, ulcers. While environmental factors, such as prolonged standing, obesity and pregnancy, are well-established risk factors for CVI, there is increasing evidence that genetic factors play a significant role in the development of this condition. Understanding the genetic underpinnings of CVI may offer new insights into its prevention, early detection and treatment, as well as provide a framework for personalized therapeutic strategies.

The concept that genetics contribute to CVI has been supported by several twin and family studies. These studies have shown that CVI tends to cluster in families, suggesting a genetic predisposition to the condition. In fact, a large percentage of patients with CVI report a family history of the disorder. Twin studies, in particular, have indicated that there is a higher concordance of CVI among monozygotic (identical) twins compared to dizygotic (fraternal) twins, further emphasizing the role of genetic factors in its development. This hereditary pattern suggests that genetic factors may predispose individuals to the anatomical and physiological changes that lead to CVI, such as weakened vein walls and dysfunctional venous valves.

Research into the genetic basis of CVI has identified several candidate genes and genetic variations that may contribute to the development of the condition. These genetic factors are thought to influence the structural integrity of the veins, the function of venous valves and the inflammatory processes that underlie CVI. One of the key genetic factors associated with CVI is collagen, a protein that provides structural support to blood vessels. Variations in genes encoding for collagen, such as, have been linked to an increased risk of venous insufficiency. Defects in collagen synthesis or structure can weaken the walls of veins, making them more susceptible to dilation and failure. Additionally, mutations in (encoded by the gene) have been implicated in venous insufficiency, as elastin is another essential

protein that contributes to the elasticity of blood vessels. Reduced elastin function can lead to the inability of veins to return blood efficiently to the heart, contributing to venous stasis and eventual valve failure.

Another important genetic factor is the regulation of Matrix Metalloproteinases (MMPs), enzymes that break down the extracellular matrix in blood vessels. Excessive MMP activity can lead to the degradation of the vein wall, contributing to venous dilation and valve incompetence. Variants in genes encoding MMPs, such as MMP9, have been associated with an increased risk of venous insufficiency. These genetic variations may influence the body's ability to repair venous damage, thereby promoting the development of chronic venous disease.

In addition to structural proteins, genetic variations that modulate the body's inflammatory response have also been implicated in CVI. Chronic venous insufficiency is often associated with low-grade inflammation, which can damage the endothelial lining of blood vessels and disrupt normal venous function. Variations in genes that regulate the inflammatory response, such as (a cytokine involved in systemic inflammation) and (interleukin-6), may predispose individuals to the development of venous insufficiency. These genetic variations may enhance the inflammatory response to venous stasis, contributing to the progression of CVI and the development of complications such as venous ulcers.

While genetic factors play a major role in the development of CVI, environmental influences cannot be overlooked. Studies suggest that the interaction between genetic predisposition and environmental factors, such as physical activity, obesity and occupational hazards (e.g., prolonged standing), contributes to the onset and progression of the disease. For instance, individuals who carry genetic variants that predispose them to venous insufficiency may be more vulnerable to environmental risk factors, leading to an increased likelihood of developing CVI. Moreover, hormonal changes, particularly during pregnancy or menopause, can exacerbate the effects of genetic predisposition. Pregnancy, for example, is a known risk factor for

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**Received:** 19-Nov -2025, Manuscript No. AOA-25-40121; **Editor assigned:** 21-Nov-2025, PreQC No. AOA-25-4014012120 (PQ); **Reviewed:** 05-Dec-2025, QC No. AOA-25-40121; **Revised:** 12-Dec -2025, Manuscript No. AOA-25-40121 (R); **Published:** 19-Dec -2025. DOI: 10.35841/2329-9495.25.13.591

**Citation:** Mitchell J (2025). The Role of Genetic Factors in the Development of Chronic Venous Insufficiency. Angiol Open Access. 13. 591.

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CVI due to the increased blood volume and pressure on the veins. Women with a family history of venous insufficiency may experience more severe symptoms during pregnancy, highlighting the interplay between genetics and hormonal factors.

The growing understanding of the genetic factors that contribute to CVI opens up new avenues for personalized medicine. Advances in genetic testing may eventually allow healthcare providers to identify individuals at high genetic risk for CVI, enabling early intervention and highlighted treatment strategies. For example, individuals with genetic variants that affect collagen production or elastin function could benefit from early lifestyle modifications, such as weight management, exercise and compression therapy, to reduce the burden on their veins.

Additionally, genetic research could lead to the development of targeted therapies aimed at addressing the underlying genetic causes of CVI. For example, drugs or gene therapies that enhance collagen production or modulate MMP activity could potentially strengthen vein walls and improve venous function.

Furthermore, personalized approaches to the management of CVI could involve genetic screening to determine the most effective treatments for individual patients based on their unique genetic makeup.

## CONCLUSION

Chronic venous insufficiency is a multifactorial condition with a significant genetic component. Genetic variations in structural proteins, inflammatory mediators and matrix-modulating enzymes play a key role in the development of CVI by influencing vein wall integrity, valve function and the inflammatory response. While environmental factors remain important, the recognition of genetic predisposition offers valuable insights into the pathophysiology of the disease and paves the way for personalized treatment strategies. Continued research into the genetic underpinnings of CVI will be essential for the development of more effective prevention and therapeutic approaches, ultimately improving patient outcomes and quality of life.