Prothrombin (F2) c.*97G>A (G20210A) Pathogenic Variant

The factor II c.*97G>A (prothrombin G20210A) gene variant is the second most common genetic defect influencing the risk of venous thromboembolism (VTE), with factor V Leiden being the most common. Although 6% of individuals with a first-time VTE carry the c.*97G>A variant,[1] its presence does not guarantee the occurrence or recurrence of VTE. In addition to genetic factors, VTE risk is affected by acquired and transient factors, such as pregnancy, surgery, malignancy, and oral contraceptive use.

Tests to Consider

Prothrombin (F2) c.*97G>A (G20210A) Pathogenic Variant 0056060

Method: Polymerase Chain Reaction/Fluorescence Monitoring

Use to detect the factor II c.*97G>A (prothrombin G20210A) pathogenic variant

See Testing Strategy

See Related Tests

Testing Strategy

Testing for factor II c.*97G>A is recommended[1] for individuals with any of the following criteria when results will affect patient management:

- One unprovoked VTE, particularly before age 50
- Recurrent VTE
- VTE in unusual locations
- Personal history of VTE and one family member with VTE before age 50 or two or more family members with VTE

Testing for factor II c.*97G>A can be considered[1] for individuals who:

- Have a sibling homozygous for c.*97G>A
- Are pregnant or plan to become pregnant and have a first-degree relative with unprovoked VTE or VTE linked to contraceptive use or pregnancy
- Are pregnant, plan to become pregnant, or plan to use estrogen-containing oral contraceptives or hormone replacement therapy and have a first-degree relative with VTE who carries the c.*97G>A variant
- Plan to become pregnant and have a previous unprovoked VTE
- Are female smokers <50 years of age and have a history of acute myocardial infarction

Testing for factor II c.*97G>A is currently not recommended in other clinical contexts, such as history of fetal loss or other pregnancy complications, family or personal history of arterial thrombosis, or population screening, particularly of asymptomatic minors.[1]

For detailed clinical recommendations for factor II c.*97G>A testing, refer to the American College of Medical Genetics and Genomics' 2018 technical standard.[1]

For more on the recommended testing for inherited thrombophilia, see the Hereditary Thrombophilia Consult topic.

Disease Overview

Prevalence

Heterozygosity[1]

- White Americans: 1-3%
- Hispanic Americans: 1%
- African Americans: 0.3%

Homozygosity[1]

- White Americans: 12/100,000
- Hispanic Americans: <1/100,000

Genetics

Gene

Factor II (*F2*)

Variant

c.*97G>A (formerly referred to as prothrombin G20210A or G20210G>A)

Inheritance

Semidominant; both heterozygotes and homozygotes are at increased risk for VTE

Penetrance

Low; most individuals with the c.*97G>A variant do not experience VTE

Test Interpretation

Sensitivity/Specificity

Analytical sensitivity/specificity: 99%

Results

Result	Variant(s) Detected	Interpretation
Negative	No copies of the variant detected	Does not exclude other hereditary risk factors
Heterozygous	One copy of the variant detected	Confers a two- to fourfold increase in thrombotic risk in the absence of other risk factors[1]
Homozygous	Two copies of the variant detected	Confers an increased thrombotic risk (not well characterized at this time)

Limitations

- Diagnostic errors can occur due to rare sequence variations.
- *F2* gene variants other than c.*97G>A will not be detected.

References

1. Zhang S, Taylor AK, Huang X, et al. Venous thromboembolism laboratory testing (factor V Leiden and factor II c.*97G>A), 2018 update: a technical standard of the American College of Medical Genetics and Genomics (ACMG). Genet Med. 2018;20(12):1489-1498.

Related Information

Hereditary Thrombophilia - Hypercoagulability

Related Tests

Factor II, Activity (Prothrombin) 0030007

Method: Electromagnetic Mechanical Clot Detection

Factor V Leiden (F5) R506Q Mutation 0097720

Method: Polymerase Chain Reaction/Fluorescence Monitoring

Thrombotic Risk, DNA Panel 0056200

Method: Polymerase Chain Reaction/Fluorescence Monitoring

Thrombotic Risk, Inherited Etiologies (Most Common) with Reflex to Factor V Leiden 0030133

Method: Electromagnetic Clot Detection/Quantitative Enzymatic/Polymerase Chain Reaction/Fluorescence Monitoring

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Content Review November 2021 | Last Update November 2021