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.

For detailed clinical recommendations for factor II c.*97G>A testing, refer to the 2018 technical standard update from the American College of Medical Genetics and Genomics (ACMG).[1] For more on the recommended testing strategy for inherited thrombophilia, refer to the ARUP Consult Hereditary Thrombophilia - Hypercoagulability topic.

Featured ARUP Testing

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.

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

Analytic 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

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