Factor V Leiden (F5) R506Q Variant

Factor V Leiden (FVL) thrombophilia is a blood-clotting disorder caused by an inherited genetic variant, c.1601G>A; p.Arg534Gln in the Factor 5 (F5) gene that may result in abnormal blood clots that can block blood vessels (venous thromboembolism [VTE]). Individuals with FVL thrombophilia have a higher risk of developing deep venous thrombosis (DVT), which occurs most often in the legs. However, DVTs can occur in other areas of the body, including the brain, eyes, liver, and kidneys.

Disease Overview

Prevalence

Most common genetic risk factor for VTE

- Heterozygosity for R506Q
- Caucasians – 5%
- Hispanics – 2%
- African-Americans – 1%
- Asians – 0.5%
- Homozygosity for R506Q – 1/1,500 Caucasians

Risk Estimates

- Lifetime risk of VTE
  - Heterozygotes – 10%
  - Homozygotes – 80%
- Risk of thrombosis among individuals with FVL is impacted by
  - Coexisting genetic thrombophilic disorders (eg, factor II G20210A variant, protein C deficiency, homocystinemia)
  - Acquired thrombophilic disorders (eg, malignancy, hyperhomocysteinemia, high factor VIII levels)
  - Nongenetic risk factors (eg, pregnancy, oral contraceptive use, HRT, selective estrogen-receptor modulators, travel, immobilization, central venous catheters, surgery, transplantation, advanced age)

Genetics

Variant

Factor V (F5) c.1601G>A; p.Arg534Gln. Legacy nomenclature R506Q (1691G>A).
Inheritance

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

Penetrance

Lifetime risk of VTE is 10 percent for heterozygotes and 80 percent for homozygotes.

Test Interpretation

Sensitivity/Specificity

Analytical sensitivity/ specificity – 99.9%

Limitations

- *F5* gene variants, other than R506Q, are not evaluated by this assay.
- Results of *F5* genotyping can be accurately determined for individuals on oral anticoagulant and standard heparin therapy.
- Rare diagnostic errors may occur due to primer-site variants.
- Not recommended for
  - Population screening and testing of asymptomatic minors for FVL
  - Routine testing for individuals with a personal or family history of arterial thrombotic disorders
  - Exceptions may include young female smokers who have experienced myocardial infarction or individuals <50 years with acute arterial thrombosis in the absence of other risk factors

References


Related Information

Hypercoagulable States - Thrombophilia
Deep Vein Thrombosis - Pulmonary Embolism

Related Tests

**APC Resistance Profile 0030127**

*Method*: Electromagnetic Mechanical Clot Detection

**APC Resistance Profile with Reflex to Factor V Leiden 0030192**

*Method*: Electromagnetic Mechanical Clot Detection/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

Factor V, R2 Mutation Detection by PCR 2014248

**Method:** Polymerase Chain Reaction