

Factor II (*F2*) G20210A Mutation

ASSESS GENETIC RISK FOR THROMBOSIS ASSOCIATED WITH INCREASED PLASMA PROTHROMBIN

Disease Overview

- The factor II (*F2*) gene mutation, G20210A, is associated with increased prothrombin levels.
- Higher concentrations of prothrombin lead to increased rates of thrombin generation, resulting in excessive growth of fibrin clots.
- Increased plasma prothrombin is a risk factor for venous thromboembolism (VTE), which most often presents in adults as deep-vein thrombosis in the legs or pulmonary embolism.
- The predicted risk for prothrombin thrombophilia increases when other genetic risk factors (e.g., factor V Leiden carrier status), acquired thrombotic risk factors (e.g., malignancy, hyperhomocysteinemia), and circumstances, including pregnancy, oral-contraceptive use, hormone-replacement therapy, selective estrogen-receptor modulators, travel, central venous catheters, surgery, and transplantation, are present
- Among adults with a first VTE, approximately 6–14 percent carry the G20210A mutation.
- It is unclear whether G20210A heterozygosity increases the risk of recurrent VTE after a first episode.
- Prothrombin thrombophilia may have a mild increase on the risk of pregnancy loss and preeclampsia.
- The prothrombin gene mutation is not a major risk factor for arterial thrombosis.
- No convincing association has been demonstrated for heterozygosity or homozygosity for G20210A and myocardial infarction and stroke.
- Treatment of individuals experiencing prothrombin thrombophilia is dependant upon clinical circumstances and may include oral anticoagulation therapy.

Epidemiology

- Prevalence of *F2* G20210A heterozygotes in the United States is 2–5 percent in Caucasians, 0.3 percent in African-Americans, and rare in Asians and Native Americans.
- Homozygosity for G20210A occurs in approximately one in 10,000 individuals.
- The G20210A mutation increases thrombotic risk in all age groups and in both sexes.

Genetics

- Incomplete autosomal dominant inheritance.
- *F2* G20210A is the second most common genetic defect influencing genetic risk for VTE, with factor V Leiden being the most common.
- Variable penetrance; many adult patients who are heterozygous or homozygous for G20210A do not experience VTE.
- Adult heterozygotes for G20210A have a two to fourfold increase in thrombotic risk.
- Homozygosity for G20210A is rare, but it increases thrombotic risk above that seen in G20210A heterozygotes.
- Patients heterozygous for *F2* G20210A who also carry factor V Leiden R506Q have an earlier age of VTE and a higher risk of recurrent thrombosis than heterozygotes for either single gene mutation. Coinheritance of both mutations occurs in approximately one in 1,000 individuals in the general population and in 1–5 percent of individuals with VTE.

Indications for Ordering

- Diagnostic testing for patients with VTE (especially before age 50) or an unprovoked VTE at any age.
- Women with VTE associated with pregnancy, use of oral contraceptives, or HRT.
- Women with unexplained pregnancy loss after the first trimester.

Contraindications

- General population screening
- Fetal testing

Interpretation

- If the prothrombin G20210A mutation is not detected, this does not exclude elevated prothrombin levels and hereditary forms of venous thrombosis due to other causes.
- Detection of one or two copies of the prothrombin G20210A mutation is associated with increased prothrombin levels and risk for venous thrombosis.
- If the prothrombin mutation is identified, testing for other inherited or acquired thrombophilic disorders, including DNA testing for the factor V Leiden mutation, measurement of total plasma homocysteine concentration, serological assays for anticardiolipin antibodies, and multiple phospholipid-dependent coagulation assays for lupus inhibitor, is recommended.

Limitations

- Genetic causes of thrombosis, other than the prothrombin G20210A mutation, will not be detected.
- Rare diagnostic errors may occur due to primer-site mutations.
- Non-genetic factors may contribute to the etiology of thrombosis.

Methodology

- Polymerase chain reaction (PCR) and fluorescence monitoring to detect the F2 c.20210G>A mutation.
- Clinical sensitivity for venous thrombosis is approximately 10 percent.
- Analytical sensitivity and specificity are 99 percent.

Related Tests

- Factor II, Activity (Prothrombin) ([0030007](#))
- Factor V Leiden (F5) R506Q ([0097720](#))
- Methylene tetrahydrofolate Reductase Mutation Detection (Thermolabile Form (C677T & A1298C)) ([0055655](#))
- Thrombotic Risk, DNA Panel ([0056200](#))
- Thrombotic Risk, Inherited Etiologies (Most Common) with Reflex to Factor V Leiden ([0030133](#))

References

1. Online GeneTests: Prothrombin Thrombophilia. <http://www.genetests.org> (accessed April 1, 2009).
2. Poort SR, et al. A common genetic variation in the 3'-untranslated region of the prothrombin gene is associated with elevated plasma prothrombin levels and an increase in venous thrombosis. *Blood* 1996;88(10):3698–703.
3. Rey E, et al. Thrombotic disorders and fetal loss: a meta-analysis. *Lancet* 2003;15(9361):901–8.
4. Martinelli I, et al. The risk of venous thrombosis in family members with mutations in the genes of factor V or prothrombin or both. *Br J Haematol* 2000;111:1223–9.

Test Information

0056060

Prothrombin Nucleotide 20210 G/A Gene Mutation (Factor II)

For specific collection, transport, and testing information, refer to the ARUP Web site at www.aruplab.com.

For information on test selection, ordering, and interpretation, refer to ARUP Consult® at www.arupconsult.com.