Factor V Leiden Associated with Inherited Predisposition to Venous Thrombosis

The UNC Molecular Genetics Laboratory performs a molecular test to detect FactorV gene mutation that is responsible, in part, for inherited predisposition to venous thrombosis. Heterozygosity for the Factor V R506Q mutation is quite prevalent in the general population (about 5%) and is associated with a 7 fold risk of venous thrombosis. Homozygosity imparts a 50-100 fold risk of thrombosis. Affected individuals are candidates for antithrombotic prophylaxis.

Biology of the disease: Factor V R506Q mutation results in resistance to activated protein C (APC-R) which promotes clot formation. However, most patients with the Factor V mutation will not experience thrombotic events unless they also have coexisting risk factors for thrombosis such as: oral contraceptive, pregnancy and perpeurium, perioperative, lupus anticoagulant, homocysteinuria, prothrombin gene mutation, or deficiency of selected coagulation factors such as protein S, protein C, or anti-thrombin III.

Clinical Indications for Factor V mutation testing:
Testing is recommended in patients with symptomatic venous thrombotic eventswho are young (age < 50 years), have unusual sites of thrombosis (e.g., hepatic mesenteric, cerebral), have had recurrent thrombotic events, have a strong familyhistory of thrombophilia, are pregnant or on oral contraceptive therapy, or have young family members (age < 50 years) with thrombotic events.
Testing should be considered in family members with a known Factor V Leiden mutation, older patients (age > 50 years) with a venous thrombotic event (except thosewith active cancer), and women with recurrent pregnancy loss or unexplained preeclampsia, intrauterine growth retardation, or stillbirth.

Laboratory Testing for Factor V mutations:
The preferred sample is 3 mL of blood in an ACD (yellow top) or EDTA (lavender-top),which may be refrigerated up to 48 hours. Molecular testing is performed using a TaqMan genotyping assay (Applied Biosystems). Genomic DNA is extracted from the blood sample, and targeted genomic regions are PCR amplified and detected by a TaqMan allelic discrimination assay.

Results are reported as heterozygous, homozygous, or normal genotype. Consider testing the same blood sample for prothrombin gene mutation (Factor II) which is also a risk factor for venous thrombosis.

References:

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