Genetics, OCs Up Venous Thromboembolism Risk

BY GIANCARLO LA GIORGIA
Contributing Writer

TORONTO — A combination of inherited and acquired risk factors puts certain women in danger of developing venous thromboembolism (VTE), said Dr. Susan R. Kahn at the annual meeting of the Society of Interventional Radiology.

The VTE incidence rate in women of child-bearing age with genetic thrombophilia who also take oral contraceptives is 2.85 per thousand—35 times higher than women of the same group with neither risk factor, whose incidence rate is a comparatively low 8 per 100,000.

"A woman between the ages of 28 and 45 with [genetic thrombophilia], such as the factor V Leiden mutation, and who also uses oral contraceptives has an increased risk of thrombosis, but she may ultimately manage to avoid having a thrombotic episode. However, if she happens to undergo knee surgery at age 35, the added risk factor may tip her over the thrombosis threshold, and she may develop clinical VTE," said Dr. Kahn, a researcher of thromboembolic disorder epidemiology at McGill University, in Montreal.

The clinical complications from VTE—which is manifested as either deep-vein thrombosis (DVT) or pulmonary embolism (PE)—include death from PE, postphlebitic syndrome, and recurrent VTE. Some of the long-term complications include postthrombotic syndrome, which develops in 30%–40% of DVT patients despite treatment with anticoagulants, as well as chronic pulmonary hypertension, which develops in about 2% of PE patients.

Despite advances in thromboprophylaxis and treatment, the annualized incidence of VTE in the general population has remained one to two patients per 1,000 persons over the last 25 years. On average, a person can expect a 5% chance of developing VTE in their lifetime, and the incidence increases twofold with each decade of age. The incidence is also far greater in black and white populations than in those of Asian descent.

According to Dr. Kahn, understanding the etiology of VTE is essential in improving outcomes in high-risk patients. She pointed out the tendency of VTE risk factors to interact: "In oncology patients, cancer itself activates coagulation factors, the patient is often immobilized, and there may be a tumor obstructing or invading the veins, leading to a thrombotic episode."

In a woman who has the factor V Leiden mutation and uses OCs, a knee surgery at age 35 'may tip her over the thrombosis threshold,' bringing on VTE.

The multifactorial pathogenesis of VTE was first described by German pathologist Rudolf Virchow over a century ago as a combination of venous stasis (such as with iliac vein stenosis), blood vessel damage (during the replacement of a central venous catheter, for example) and hypercoagulation (due to hereditary causes, such as factor V Leiden, or acquired factors, such as the lupus anticoagulant or exposure to estrogen).

Dr. Kahn noted that much of the recent interest in VTE has focused on the inherited factors discovered in the last decade predisposing patients to venous thrombosis. Known generically as genetic thrombophilia, these relatively common factors occur through one or more biochemical defects. Genetic thrombophilia affect 8%-10% of the population, though in patients presenting with idiopathic VTE, incidence of genetic thrombophilia rises to 40%-50%.

The factor V Leiden mutation is the most common genetic thrombophilia: the heterozygous form, found in 5%-8% of the normal population, increases the risk of VTE five-fold, whereas the rarer homozygous form confers an 18-fold risk increase. The second most common genetic thrombophilia is the heterozygous form of the prothrombin 20210 mutation, affecting 2% of the population, and doubling the risk of VTE. Other, rarer thrombophilias—that arise from multiple genetic mutations that cause deficiencies in natural anticoagulant proteins, such as protein C, protein S, or antithrombin III—occur in less than 1% of the population, yet are associated with a much higher risk of VTE. ■

Pages 48a—48d