

Hypercoagulable Work-up for the Living Liver Donor

Authors: Ben Samstein, MD and Matthew R. Kappus, MD

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ISSUE

Situational risk for venous thromboembolism occurs at the time of living liver donation. Possible inherited prothrombotic conditions include protein C, protein S, or antithrombin deficiencies, procoagulant factor accumulation (e.g., prothrombin G20210A), or resistance to coagulation factor inactivation by a natural anticoagulant (e.g., factor V G1691A, also known as factor V Leiden).

DATA

In the general population, venous thromboembolic disease, including deep vein thrombosis (DVT) and pulmonary embolism, constitutes a large proportion of cardiovascular disease after atherosclerotic heart disease and stroke in the United States. Risk factors for venous thromboembolic events (VTE) can be divided into situational, inherited, and acquired categories. A situational event includes among other things surgery and prolonged immobilization. These are well-defined events that are transient clinical circumstances associated with a higher risk for VTE. Inherited factors represent genetic mutations and polymorphisms that result in deficiency of inherent anticoagulants (e.g., protein C, protein S, or antithrombin), procoagulant factor accumulation (e.g., prothrombin G20210A, thermolabile variant of methylenetetrahydrofolate reductase), or resistance to coagulation factor resistant to inactivation by a natural anticoagulant (e.g., factor V G1691A, also known as factor V Leiden)(1). Acquired risk factors occur in the setting of non-inherited hematologic abnormalities that can occur in the setting of hyperviscosity syndrome, antiphospholipid antibodies, etc.

Studies have indicated an association between obesity, oral contraceptive medications(2), smoking and age with development of venous thromboembolism. In a study of over 1 million women in the United Kingdom, current smokers had a relative risk of 1.38 compared to never smokers(3). Many living donor liver transplant (LDLT) programs stop oral contraception for 6-8 weeks prior to surgery and resume 6-8 after surgery.

Studies in surgical populations have revealed an increased incidence of hereditary prothrombotic events in patients with personal or familial history of VTE, where preoperative evaluation by a hematologist has been considered(4). Patients undergoing hepatectomy have a relatively high incidence of VTE events. In the National Surgical Quality Improvement Program (NSQIP) database, the rate of VTE after hepatectomy has been reported to be 2.9%(5). Thus, efforts to prevent VTE events in living liver donors appear warranted. As testing for inherited and acquired thrombophilias have become widely available, some programs have introduced these tests for the purpose of screening healthy donors(6). Prothrombin 20210A mutation has been associated with an increased risk for venous thromboembolism. In asymptomatic carriers, there was a non-significant increase in VTE and studies concluded that routine testing was not justified(7). Factor V Leiden mutation has an overall prevalence of 5% in a Caucasian population(8) and a several fold increase in venous thromboembolism in heterozygous carriers(9). However, the American College of Chest Physicians does not give guidance on thrombophilia testing(10). A negative thrombophilia work up does not indicate that the risk of VTE is low. Perhaps the most important guidance for donors is assessing a patient's personal and family history of VTE. Thrombosis at a young age (<50 year), multiple first-degree family members, and VTE in splanchnic or cerebral veins are suggestive of thrombophilia(11).

RECOMMENDATIONS

Evaluation for hypercoagulable states prior to donor surgery is not uniform nor supported by society recommendations. Careful attention to personal and family history of VTE is necessary. VTE prophylaxis is a standard for all major abdominal operations, including living liver donation. Heparin can be given pre-operatively to living liver donors, however intra-operative heparin is not routinely given at the time of donation. A prophylactic approach with the use of classic or low-molecular-weight heparin (LMWH), anti-Xa factors, antithrombotic stocking, intermittent pneumatic compression stocking, and early mobilization is recommended(12).

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