



Are We Really Addressing Hypercoagulability?

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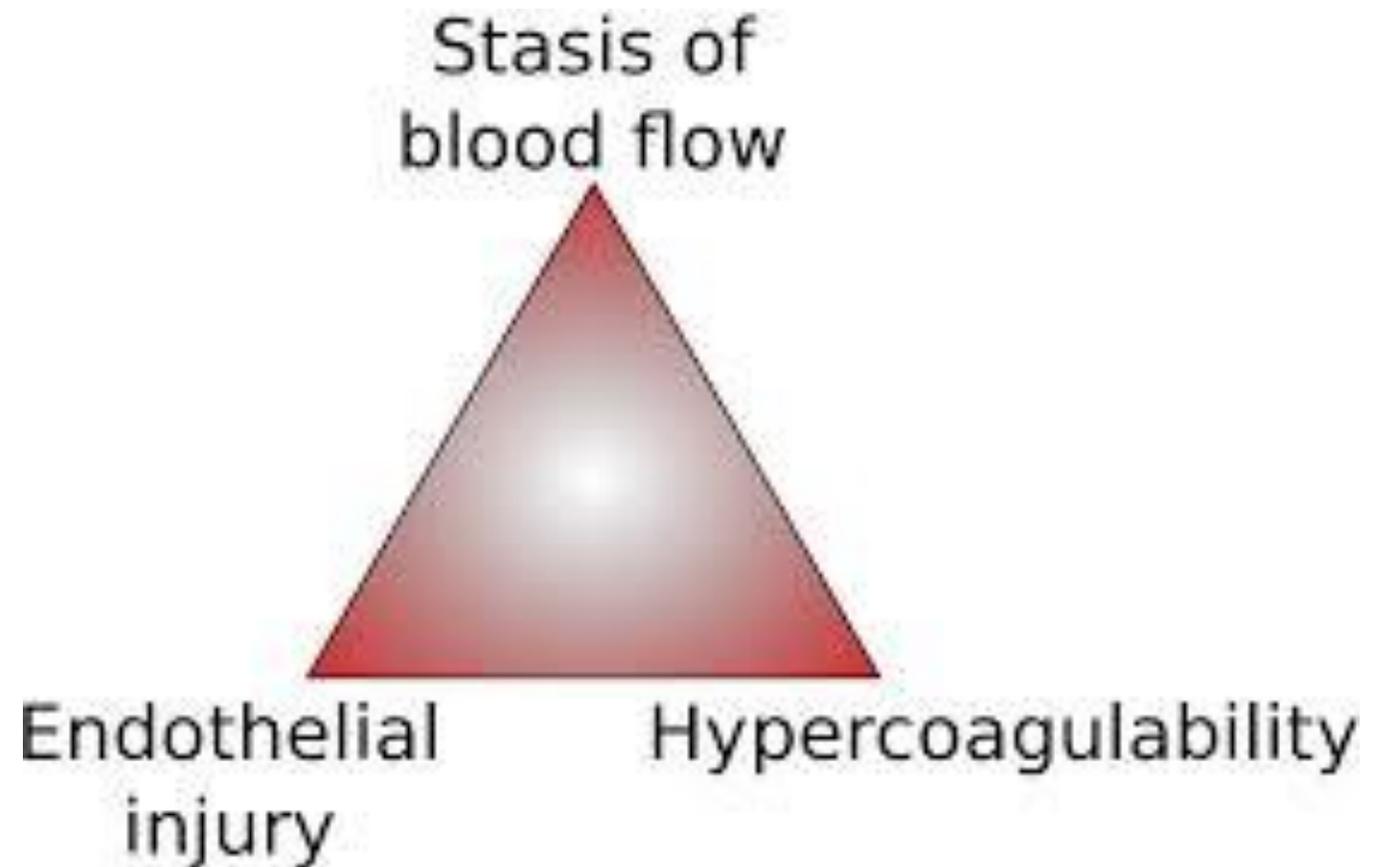


Definition of Thrombophilia

- ▶ An imbalance in hemostasis with an increased tendency to form intravascular pathologic venous or arterial thrombus
- ▶ Predisposing factors are either inherited or acquired and is considered a multifactorial disease
- ▶ Virchow's triad includes endothelial injury or activation, reduced blood flow, and hypercoagulability of the blood

Virchow's Triad

- ▶ Virchow's Triad is important to understand, as it is THE basis of thrombosis



Common Presentations of Hypercoagulable States

- ▶ Deep Vein Thrombosis
- ▶ Pulmonary Embolism
- ▶ miscarriage
- ▶ Arterial Clot
- ▶ thrombophlebitis

Common Causes of Acquired Hypercoagulability

- ▶ BMI >30 kg/m²
- ▶ Immobilization (such as flight >6 hours)
- ▶ Trauma
- ▶ Surgery
- ▶ Pregnancy
- ▶ Certain medications (OCP's and some chemotherapies)
- ▶ APLA's
- ▶ Lupus Anticoagulant
- ▶ Malignancy
- ▶ Infection
- ▶ Myeloproliferative Disorders (PV, ET)
- ▶ Smoking
- ▶ PNH

Causes of Inherited Hypercoagulability

- ▶ Antithrombin Deficiency (1st one identified in 1965)
- ▶ Protein C Deficiency
- ▶ Protein S Deficiency
- ▶ Factor V Leiden
- ▶ Factor II G20210A Mutation
- ▶ Elevated Factor VIII
- ▶ Homocystinemia
- ▶ Dysfibrinogenemia

Who Should Be Screened?

- ▶ First, idiopathic thrombophilia is a diagnosis of exclusion. All other factors must be first ruled out to determine this is truly idiopathic. However, it must be ruled out, as it determines length of therapy, especially in younger people
- ▶ A careful medical and family history, acquired risk factors, associated diseases, prognosis and therapy's adverse effects should be carefully considered prior to laboratory testing
- ▶ For instance, not every woman going on oral contraceptives should be considered for screening

Who should be screened (continued)

- ▶ In patients with first symptomatic thrombotic event, generally, it is not recommended that screening should be done for inheritable defects, as the prevalence is still very low in the general population
- ▶ Physiologic changes in hemostasis and physical changes in women during pregnancy are responsible for a prothrombotic state and increase in blood stasis. The risk of an event is 4 times higher in pregnancy than in non-pregnant women. This number is even higher with a positive family history of clotting (when asking women about clotting, this should also include asking about prior miscarriages personally, as well as women in their families)*

Common Tests

- ▶ Protein C&S
- ▶ Lupus Anticoagulant
- ▶ APLA's (cardiolipin, beta-2-glycoprotein 1, phosphatidylserine)
- ▶ Factor V Leiden (activated Protein C resistance*)
- ▶ Factor II G20210A mutation
- ▶ Homocysteine
- ▶ Antithrombin III
- ▶ Factor VIII levels
- ▶ CBC, CMP, INR, PTT

Case Example

- ▶ 33 year old female presents with plans to get pregnant, and has never had a DVT. She has 1 child and 3 prior miscarriages. Her sister had 1 miscarriage and her mother had 2 prior miscarriages, as well as a DVT at an older age following a long cross country car ride

Case 2

- ▶ 66 year old male presents with leg swelling in his left calf. It is painful, and was of sudden onset. He is a heavy smoker, and has no prior history of DVT or other thrombotic events personally or in his family. He has hypertension and hyperlipidemia. He also explains he has been feeling more fatigued lately, and has had an increase in cough compared to normal and even relates occasional blood tinged sputum

Outpatient Treatment Options

- ▶ Unfractionated heparin
- ▶ Low molecular weight heparin (Lovenox or enoxaparin)
- ▶ Warfarin
- ▶ Factor Xa inhibitors (Arixtra*, Eliquis, Xarelto, Pradaxa)
- ▶ IVC filter (only suggested in patients with high risk of bleeding due to other disease processes or general safety of other anticoagulation is in question)

Special Considerations

- ▶ Pregnancy alone is an acquired risk factor. As a general rule of thumb, Protein C&S and Antithrombin become deficient by rule of 3's as pregnancy progresses toward term. Coupled with other hypercoagulability, the risk is significantly higher for a thrombotic event, both during pregnancy AND up to ~8 weeks following pregnancy when the woman is still in a hypercoagulable state
- ▶ Certain patient populations should be carefully monitored and anticoagulation should be low on decision making tree, and those are those with high fall risks, hepatic and/or renal failure, chronic GI bleeding such as angiodysplasia

Conclusions

- ▶ Thrombotic events are considered multifactorial. Not all patients who have hereditary hypercoagulability develop thrombosis.
- ▶ There are numerous risk factors that come into play, both on the acquired and hereditary trees
- ▶ Careful assessment must also include a family history of DVT, PE, miscarriages, arterial clots
- ▶ There are special considerations to understand in certain populations, such as pregnancy, as well as patients at high risk for bleeding problems

Conclusions (continued)

- ▶ There are numerous treatment options available, and it is important to understand the oral Factor Xa inhibitors have been shown to have a better safety profile than warfarin (Pradaxa is only medication to have a commercially available antidote—Praxbind [idarucizumab injection])
- ▶ Hypercoagulability and thrombosis should always be high on the list of differential diagnoses in patients with limb swelling, sudden onset chest pain, shortness of breath and/or weakness and dizziness, or in women with numerous miscarriages
- ▶ Not all patients need to be evaluated for hereditary hypercoagulable states, even in thrombotic events, such as first DVT or first miscarriage

Conclusions (yet again)

- ▶ There are many variables that go into treatment, and currently Eliquis is the only factor Xa inhibitor that is approved for front line outpatient treatment following <5 days of LMWH. If patient in hospital or on LMWH for 5 days or greater, then Xarelto or Pradaxa could be considered
- ▶ Warfarin still has a role and is still used in patients with chronic atrial fibrillation in many cases, or in patients with heart valve replacements, and is still the least expensive alternative, but requires the highest amount of surveillance

