Testing for Cancer and Other Hypercoagulable States in PE

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Disclosures

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Venous Thromboembolism: Scope of the Problem

Venous Thromboembolism: The Third Leading Cause of Cardiovascular Death

Incidence of Pulmonary Embolism
How can we change these statistics?

Will looking for occult malignancy or testing for thrombophilia help?

Case 1: Unprovoked VTE

- 55F avid tennis player who presented with sudden onset SOB and RLE swelling.
- CT: bilateral main stem emboli and right ventricular dilation.
- Vitals: HR 102; BP 151/106; O2 95% on 15L.
- Troponin: minimally elevated.
- Echo: demonstrated RV strain.

Case 1: Unprovoked VTE

- There was no identifiable cause for her PEs.

Should she undergo extensive search for occult malignancy?

Epidemiology: Cancer and Thrombosis

- ~5-10% of patients presenting with idiopathic VTE will be diagnosed with cancer within next 12-24 months.
Screening for Occult Malignancy in Idiopathic VTE

- Carner
  - 845 pts: limited occult-cancer screening or limited PLUS abdominal pelvic CT.
  - No difference in number of cancers detected at baseline or 1-year follow up.
- Prandoni
  - 195 patients: limited occult-cancer screening or limited PLUS CT CAP.
  - No difference in number of cancers at baseline or 1-year follow up.
- Robin
  - 399 patients: limited occult-cancer screening or limited PLUS PET scan.
  - Results: 2.0% limited and 5.5% in limited/PET (p=0.07).
  - At 2-year follow up, more cancers in limited (4.7% vs 0.5%; p=0.01).
- No difference in survival

Carrier et al. NEJM. 2015.

Available data do not support an extensive search for occult malignancy; however, it is important to perform complete Hx/PE/Labs and pursue symptoms or signs which suggest an underlying malignancy and to ensure that age-appropriate cancer screening tests have been performed.

**Case 1: Unprovoked VTE**

- Signs or symptoms of malignancy: None
- Labs: normal
- Colonoscopy: up to date
- Mammogram: up to date
- Pap smear: up to date


**What is the data?**

- Should we test her for hypercoagulable states?
### DVT/PE Risk Factors

<table>
<thead>
<tr>
<th>Thrombophilia</th>
<th>Prevalence (%)</th>
<th>Relative risk of a first episode of VTE compared with controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>AT deficiency</td>
<td>0.02 to 0.2%</td>
<td>1 to 7%</td>
</tr>
<tr>
<td>Protein C deficiency</td>
<td>0.2 to 0.5%</td>
<td>2 to 5%</td>
</tr>
<tr>
<td>Protein S deficiency</td>
<td>1%</td>
<td>6-fold increased</td>
</tr>
<tr>
<td>Factor V Leiden*</td>
<td>4 to 5%</td>
<td>12 to 18%</td>
</tr>
<tr>
<td>Prothrombin G20210A*</td>
<td>2%</td>
<td>5 to 8%</td>
</tr>
</tbody>
</table>

Is thrombophilia testing useful?

### What is the data?

- Will testing change management?
  - Effect duration of anticoagulation?
  - Predict recurrence?
  - Guide thromboprophylaxis?
  - Identify family members at risk?
  - Avoid estrogen
- Will testing cause harm?

### Who to test?

- Routine testing is NOT warranted for everyone
- **Testing Not Warranted:**
  - First provoked VTE

### Role of hypercoagulable testing

- Published guidelines: thrombophilia testing does not assist clinical decision making in provoked VTE
- American Society of Hematology (ASH) and Society for Vascular Medicine (SVM) recommended against testing in these cases in their Choosing Wisely© initiatives.

### Despite these recommendations ....

**An Electronic Best Practice Alert based on Choosing Wisely Guidelines Reduces Thrombophilia Testing in the Outpatient Setting**

- Best Practice Alert (BPA) was triggered if any thrombophilia test was ordered. ASH on line Chose Wisely recommendations showed up.
- Non-hematology specialists and general medicine providers were more likely to follow the alert compared to hematologists.
  - 50% and 44% vs 10% (p<0.001)

### Who to test?

**First unprovoked VTE**

- Up to 42% will have inherited disorder
- **The inherited disorder did not cause VTE**
- Unprovoked nature of VTE predicts risk of future VTE and dictates length of AC
VIENNA Prediction Model

Cumulative rate of recurrence in patients with first unprovoked VTE who stopped anticoagulation

Key points:
1. At 5 years, risk is 25%
2. Increases with time


Prediction Models

- DASH
  - Ddimer, age, sex, hormones
- HERDOO2
  - Hyperpigmentation, edema, Ddimer, obesity, age
- Vienna

None of them have thrombophilia status in their model

Will testing help family members?

Primary prevention

- Guidelines: variable
- Studies show higher incidence of VTE with inherited risks.
- BUT... Family history alone carries increased risk of VTE even in absence of positive thrombophilic test (ppx).
- MEGA showed: positive FHX increased risk of VTE > 2-fold and up to 4-fold if more than one family member VTE.

Negative thrombophilia screening does not equate to normal VTE risk.


MEGA: Multiple Environmental and Genetic Assessment

Whom should we test?

- Consider testing for inherited thrombophilies and APS:**
  - Young patient, strong family history, (female) - inherited
  - Recurrent or extensive thrombosis – APS
  - Thrombosis in multiple venous or unusual vascular beds (portal, hepatic, mesenteric, or cerebral veins).
  - MPD (JAK2), APS, paroxysmal nocturnal hemoglobinuria.
  - Warfarin-induced skin necrosis - protein C deficiency.
  - Arterial thrombosis – APS or MPD.
  - Patient with unprovoked VTE and low bleeding risk planning to stop anticoagulation, test if results change decision.

** Only if it is going to change management of pt/family member

What do I do?

- Provoked – no role for testing
- If results will change management of pt/family and through shared decision making, consider:
  - Unprovoked
    - Young, strong FHX ... stepwise (FVL, PTGM)
  - Unusual sites
    - Antiphospholipids
    - Paroxysmal Nocturnal Hemoglobinuria.
    - Myeloproliferative disorders
  - Arterial events
  - Recurrent VTE

FVL = Factor V Leiden
PTGM = Prothrombin Gene Mutation
Case 1: Unprovoked VTE

- She did well.
- One month after presentation, reappeared with new RLE swelling.
- She had been compliant with anticoagulation.
- US showed new DVT.
- CT abd/pelvis showed ovarian cancer.

Closing Reflections

- Extensive screening for cancer in idiopathic VTE is not indicated. However, ensure age specific cancer related screening and pursue any abnormalities on history, physical exam or labs.
- Thrombophilia testing
  - is not indicated in many situations
  - should be performed if will influence management of patient or family member, and benefits outweigh potential risks of testing.

Be thoughtful about testing

Thank you

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