Thromboembolic Disease

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Financial Disclosures

- None
Deep Vein Thrombosis

Venous thromboembolism is a major national health problem, with an overall incidence of more than 1-3 per 1,000 annually.

Deep Vein Thrombosis (DVT) is a potentially life-threatening pathology that can lead to pulmonary embolism (PE), and/or post-thrombotic syndrome (PTS).

The spectrum of DVT to pulmonary embolism can be referred to as venous thromboembolic disease (VTE).

Deep Vein Thrombosis is a major health problem

**900,000**

Americans are affected by DVT blood clots each year\(^1\)

**100,000**

People in the U.S. die each year from blood clots\(^1\)

Patients diagnosed with DVT and treated with the current standard of care (anticoagulation) have a **50%** chance of developing Post-Thrombotic Syndrome\(^2\)

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Diagnosing DVT

The Challenge - Approximately half of patients with DVT are asymptomatic.

Symptoms of DVT include swelling, pain, tenderness, warmth, and prominent superficial veins on the affected limb.

Patients with suspected DVT frequently present to hospital emergency departments. Since symptoms and signs of DVT can be non-specific and found in a wide variety of non-thrombotic disorders, timely diagnostic testing must be performed to correctly identify patients with VTE.
DVT: What we know

Venous thromboembolism (VTE) is manifested clinically by deep venous thrombosis (DVT) and pulmonary embolism (PE). DVT, usually of the lower extremity, nearly always precedes PE. The risk of VTE increases greatly after age 50.

Other Risk Factors
- Age
- Trauma
- Cancer
- Immobilization
- Surgery
- Medications-OCPs
- Inherited Coagulopathies- (Factor V Leiden, Protein S/C deficiency, Antiphospholipid, etc.)
- Infection/inflammatory Disorders

Occurrence
The disease most often occurs in hospitalized patients, particularly those with cancer or following surgical procedures, but also occurs sporadically in the community. In both settings, multiple risk factors are usually present.
No prophylaxis + routine objective screening for DVT

<table>
<thead>
<tr>
<th>Patient Group</th>
<th>DVT Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical patients</td>
<td>10 - 26 %</td>
</tr>
<tr>
<td>Major gyne/urol/gen surgery</td>
<td>15 - 40 %</td>
</tr>
<tr>
<td>Neurosurgery</td>
<td>15 - 40 %</td>
</tr>
<tr>
<td>Stroke</td>
<td>11 - 75 %</td>
</tr>
<tr>
<td>Hip/knee surgery</td>
<td>40 - 60 %</td>
</tr>
<tr>
<td>Major trauma</td>
<td>40 - 80 %</td>
</tr>
<tr>
<td>Spinal cord injury</td>
<td>60 - 80 %</td>
</tr>
<tr>
<td>Critical care patients</td>
<td>15 - 80 %</td>
</tr>
</tbody>
</table>

Heit – Mayo Clin Proc 2001;76:1102
May Thurner Syndrome

- An anatomical variant where the right common iliac artery compresses the left common iliac vein
- LEFT Thigh swelling common, PE rare
- Extensive iliofemoral DVT
- Iliac vein compression syndrome & ‘Cockett syndrome’
- High incidence of PTS
- Excellent 5 yr patency with thrombolysis and stents
- Think of it in young women
May-Thurner syndrome

Narrowed left iliac vein
(by pressure from right iliac artery)
24 yo female with left leg swelling
Tx with Stent
Anatomy

**The femoral vein is sometimes referred to as the "Superficial femoral vein." This can be confusing since the femoral vein is a deep vein and should be treated as such.**
U/S

- U/S Just checks CF vein to ankle (Does not see iliac veins)

- Direct signs of DVT=
  Noncompressible vein, clot in the vein, and lack of compressibility.

- Indirect Signs of DVT- Lack of augmentation and respiratory waveform.
Respiratory Variance

http://www.criticalecho.com/content/tutorial-10-vascular-ultrasound
www.jultrasoundmed.org
Augmentation

Heather L. Gornik, and Aditya M. Sharma Circulation. 2014;129:917-921
Treatment Options

- Anticoaguation
- Thrombolysis
- Thrombectomy
- IVC filters.
## Factor Xa Inhibitors

<table>
<thead>
<tr>
<th>Xarelto (Rivaroxaban)</th>
<th>Eliquis (Apixaban)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 15 mg x 2 for 21 days PO with food.</td>
<td>• 10 mg x 2 PO for 7 days</td>
</tr>
<tr>
<td>• 20 mg for remaining period of treatment</td>
<td>• 5 mg for remaining period of treatment</td>
</tr>
<tr>
<td>• Avoid in hepatic impairment (child class B and C), pregnancy/nursing.</td>
<td>• Avoid in severe hepatic impairment, pregnancy/nursing.</td>
</tr>
<tr>
<td>• Can be checked with anti-factor Xa activity assay.</td>
<td>• Can be checked with anti-factor Xa activity assay.</td>
</tr>
<tr>
<td>• Partially reverse with 4-factor PCC (Kcentra)</td>
<td>• Partially reverse with 4-factor PCC (Kcentra)</td>
</tr>
</tbody>
</table>

1. Xarelto.com
2. Eliquis.com
3. UW Guidelines for Reversal of Anticoagulation
## Factor Xa Inhibitors

### Savaysa (Edoxaban)
- 60 mg once daily PO
- Avoid in mechanical heart valves, nursing, mod/severe hepatic impairment.
- Reverse with 4-factor PCC (Kcentra) 50 Units/kg up to 5000 Units

### Arixtra (Fondaparinux)
- Dosed based on body weight-(5mg <50 kg, 7.5 mg-50kg-100kg, 10mg- >100kg) delivered SQ
- Used as bridging agent (avg time administered is 5-9 days)
- Contraindicated in severe renal impairment, bacterial endocarditis, and thrombocytopenia with + anti-platelet ab
- Reverse with rFVIIa (Novoseven) 90mcg/kg
Pradaxa- Dabigatran

- Direct Thrombin Inhibitor
- 150 mg X2 Daily after receiving 5-10 days of parenteral anticoagulation for 5-10 days.
- Contraindicated in severe active bleeding and prosthetic valves.
- Careful in patients with renal insufficiency.
- Can reverse with Praxbind ® (idarucizumab)

Lovenox (enoxaparin)

- LMWH
- Inpt: 1mg/kg SQ q 12 hrs vs 1.5mg/kg q day
- Outpt: 1mg/kg q 12 hrs
- Contraindicated with severe active bleeding, thrombocytopenia with antiplatelet ab, and hypersensitivity with heparin and pork
- Can partially reverse with protamine
**Warfarin (coumadin)**

- Vitamin K antagonist
- Individualized dosing to maintain INR between 2-3 with target of 2.5
- Contraindicated pregnancy (unless has mechanical valve), noncompliant pts without sufficient supervision, Malig HTN
- Can cause Tissue Necrosis
- Reverse with Vit K, FFP, and Kcentra.

**Heparin**

- Antithrombin III activator (blocks thrombin and Factor X)
- Inpt: Bolus 5000 U followed by 1300 units an hr infusion.
- Outpt: 17,500 Units SQ q 12 hrs
- Maintain PTT to 1/5-2.5 x normal control
- Avoid in severe thrombocytopenia
- Can cause HIT
- Reverse with protamine.
Lovenox/Heparin Injections
3 categories of patient

- **1st DVT with a major reversible risk factor (Factor Xa > VKA> LMWH (Level II evidence))***
  - Surgery, trauma, prolonged immobility, etc
  - 3 months treatment

- **Recurrent or unprovoked DVT**
  - Consider indefinite Rx
  - or 6 months and re-evaluate
  - Consider evaluation for coagulopathy.

- **Cancer patients**
  - 3-6 months LWMH
  - Or as long as cancer or cancer Rx is ongoing

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Interventional options in the treatment of DVT

<table>
<thead>
<tr>
<th>Catheter directed lytic use</th>
<th>Mechanical thrombectomy</th>
<th>Pharmacomechanical thrombus removal</th>
<th>IVC Filters</th>
</tr>
</thead>
<tbody>
<tr>
<td>Used for older thrombus or larger clot burden where thrombolytic is delivered directly to the site of thrombus</td>
<td>Mechanical removal of acute thrombus, to debulk and restore flow</td>
<td>Combination treatment utilizing lytics with mechanical thrombectomy for quicker and improved thrombus removal</td>
<td>Filter designed to capture an embolism; a blood clot that has broken loose</td>
</tr>
</tbody>
</table>
When to Use Interventional Therapies?

TABLE I. Indications for Pharmacomechanical Catheter-Directed Thrombolysis

<table>
<thead>
<tr>
<th>Clinical scenario—goal of therapy</th>
<th>Patient’s expected risk of bleeding</th>
</tr>
</thead>
<tbody>
<tr>
<td>DVT causing acute limb threat</td>
<td>Yes—Urgent</td>
</tr>
<tr>
<td>Progressive IVC thrombosis despite AC</td>
<td>Yes—Urgent</td>
</tr>
<tr>
<td>DVT symptoms markedly increased despite AC</td>
<td>Yes—Elective</td>
</tr>
<tr>
<td>Major anatomic DVT extension despite AC</td>
<td>Yes—Elective</td>
</tr>
<tr>
<td>Initially presenting acute iliopopliteal DVT (prevent PTS)</td>
<td>Yes—Elective</td>
</tr>
<tr>
<td>Initially presenting acute femoral/popliteal DVT (prevent PTS)</td>
<td>Usually no</td>
</tr>
</tbody>
</table>

*| Low | Moderate | High |
|-----|----------|------|


TABLE II. Contraindications to Thrombolytic Therapy for DVT

<table>
<thead>
<tr>
<th>Absolute or strong relative contraindications</th>
<th>Active bleeding</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of stroke within the previous 3 months</td>
<td>Intraocular trauma or hemorrhage</td>
</tr>
<tr>
<td>Recent (&lt;3 months) intracranial/intraspinal trauma or surgery</td>
<td>Intraparenchymal hypertrophy, aneurysm, or other lesion</td>
</tr>
<tr>
<td>Recent (&lt;3 months) internal eye surgery or hemorrhage</td>
<td>Recent gastrointestinal bleeding (&lt;10 days)</td>
</tr>
<tr>
<td>Intracranial/intraspinal mass, aneurysm, or other lesion</td>
<td>Other relative contraindications</td>
</tr>
<tr>
<td>Recent gastrointestinal bleeding (&lt;10 days)</td>
<td>Recent (&lt;10 days) major surgery, trauma, CPR, obstetrical delivery, or cataract surgery</td>
</tr>
<tr>
<td>Other relative contraindications</td>
<td>Recent (&lt;10 days) major invasive procedure or puncture of uncompressible vessel</td>
</tr>
<tr>
<td>Severe hypertension (systolic &gt; 180 mmHg; diastolic &gt; 110 mmHg)</td>
<td>Severe dyspnea or acute illness precluding ability to tolerate positioning on procedure table and/or conscious sedation</td>
</tr>
<tr>
<td>Hepatic failure, particularly in cases with coagulopathy</td>
<td></td>
</tr>
<tr>
<td>Bacterial endocarditis or septic thrombophlebitis</td>
<td></td>
</tr>
<tr>
<td>Pregnancy</td>
<td></td>
</tr>
<tr>
<td>Moderate or severe anemia or thrombocytopenia</td>
<td></td>
</tr>
<tr>
<td>Severe dyspnea or acute illness precluding ability to tolerate positioning on procedure table and/or conscious sedation</td>
<td></td>
</tr>
</tbody>
</table>
Acute Threatened Limb/Phlegmasia Cerulea Dolens
Acute Threatened Limb/Phlegmasia
Post 12 hours tPA @ 1 mg/hr
Phlegmasia - Consider Malignancy
Progressive IVC Thrombosis Despite AC

Recommendation:

- Urgently Treat even with moderate risk of bleeding.

Can Result In:

- Propagation to Renal and Hepatic Veins
- Phlegmasia
- Large PE

www.mypacs.net
Progression of Thrombus despite AC

- **Recommendation:** - Strongly consider tx with CDT -

- Avoid Propagation to IVC/Renal Veins, Phlegmasia, and Large PE -- (Class IIa, Level of Evidence C)

- Symptom Relief- (Class IIa, Level of Evidence B)
Initial Treatment of Ileofemoral DVT

• Recommendation:

Evidence supports treatment with CDT would benefit pt from preventing Post Thrombotic Syndrome if low risk of bleeding.
Mechanism of Post Thrombotic Syndrome

A. Normal Blood Flow
B. Damage to Leg Veins
C. Valve Becomes Leaky, Allowing Fluid to Pass Through
D. Leg Pain, Swelling, and Redness

Blood Clot and Inflammation

Sara R. Vazquez, and Susan R. Kahn Circulation.
2010;121:e217-e219
## PTS SYNDROME

<table>
<thead>
<tr>
<th>Leg symptoms</th>
<th>Signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heaviness</td>
<td>Oedema</td>
</tr>
<tr>
<td>Pain</td>
<td>Peri-malleolar telangiectasiae</td>
</tr>
<tr>
<td>Swelling</td>
<td>Venous ectasia</td>
</tr>
<tr>
<td>Itching</td>
<td>Hyperpigmentation</td>
</tr>
<tr>
<td>Cramps</td>
<td>Redness</td>
</tr>
<tr>
<td>Paresthesia</td>
<td>Dependent cyanosis</td>
</tr>
<tr>
<td>Bursting pain</td>
<td>Lipodermatosclerosis</td>
</tr>
<tr>
<td></td>
<td>Healed ulcer</td>
</tr>
<tr>
<td></td>
<td>Open ulcer</td>
</tr>
</tbody>
</table>

**Symptom pattern**

- Worse with activity, standing, walking
- Better with rest, recumbency

Post Thrombotic Syndrome

• Most Common cause is DVT—up to 50% of patients develop PTS from this

• Severe PTS seen in 5-10% of symptomatic DVT

• Significantly affects QOL and increase Healthcare Cost

Cost of PTS

- Direct Cost ~ 200 Million Dollars a year in the U.S.
- ~ 75% of cost of each DVT case.
- Loss of ~ 2 million workdays
- Poor QOL - considered worse than OA and COPD.

1. Heit et al, 2001)
2. (Bergqvist et al, 1997).
### CAVENT TRIAL

<table>
<thead>
<tr>
<th>CAVENT Trial</th>
<th>CDT + anticoagulation (101 pts)</th>
<th>Anticoagulation (108 pts)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td># with PTS after 24 mos</td>
<td>37</td>
<td>55</td>
<td>P=.047</td>
</tr>
<tr>
<td># with vein patency after 6 mos</td>
<td>58</td>
<td>45</td>
<td>p=.012</td>
</tr>
</tbody>
</table>

Enden et al, CAVENT study, Lancet 2012
<table>
<thead>
<tr>
<th>Procedure</th>
<th>Mean Change in Villalta Score over 2 Years (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Popliteal</td>
<td>-0.11 (-1.08 to +0.87)</td>
<td>0.83</td>
</tr>
<tr>
<td>Superficial femoral</td>
<td>+0.79 (-0.13 to +1.71)</td>
<td>0.091</td>
</tr>
<tr>
<td>Common femoral or iliac</td>
<td>+2.23 (+1.29 to +3.16)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Kahn et al, Annal Int Medicine, 2008
Ileofemoral DVT
What’s Coming?

- **ATTRACT TRIAL**
- Randomized control, NIH funded trial
- 692 pts from 56 hospitals
- Goal - Determine if the use of CDT in patients with acute proximal (DVT) prevents PTS and improves QOL.
Conclusion for CDT

- Phlegmaisa - Should treat urgently
- IVC thrombus - Should treat urgently
- Extension of clot while on AC - strongly consider treatment if low risk of bleeding.
- IFDVT - Evidence suggests greater benefit in hopes of preventing PTS if low risk of bleeding. (Attract Trial)
When to use IVC FILTERS

**Indications**

- PT with DVT/PE and cannot be anticoagulated or **Failed** anticoagulation therapy.

**Other Reasons Placed**

- Acute PE with cardiopulmonary compromise
- Prophylaxis for Surgery (Bariatric)
- Floating Thrombus within IVC/Iliac Vein
- DVT/PE and refuses anticoagulation
- Thrombectomy procedure

IVC filter History/Background

- PREPIC—Improved prevention of PE in first 12 days without significant benefit in comparison to anticoagulation over 2 years

- 8 year Followup—Similar incidence of venous thromboembolic dz with increase in LE DVT in the filter population.

- No significant change in post-thrombotic syndrome.


Increase Utilization

Filters Placed (1000's)
Other Potential Filter Complications

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FDA</strong></td>
<td><strong>08/2010</strong></td>
</tr>
<tr>
<td>Migration</td>
<td>328</td>
</tr>
<tr>
<td>Embolization</td>
<td>146</td>
</tr>
<tr>
<td>Fracture</td>
<td>56</td>
</tr>
<tr>
<td>Perforation</td>
<td>70</td>
</tr>
</tbody>
</table>

**Recommendations/Actions:**
The FDA recommends that physicians should consider removing the filter as soon as protection from pulmonary embolism is no longer needed.

References:
1. www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm221676
Pulmonary Embolism
Icoper: Cumulative Mortality After Diagnosis of PE

Categories of PE

- Non massive—Hemodynamically stable with no evidence of heart strain

- Submassive—Right heart strain/Acute MI with no hemodynamic instability.

- Massive—Hemodynamically unstable with hypotension and/or shock), pulselessness, and bradycardia.
PE: Indicators of Poor Outcome

<table>
<thead>
<tr>
<th>PE Criteria</th>
<th>Criteria</th>
<th>mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>High risk</td>
<td>Cardiovascular shock or persistent hypotension</td>
<td>&gt; 30 %</td>
</tr>
<tr>
<td>Intermediate risk</td>
<td>Lab (troponin, BNP) ↑ or RV dysfunction</td>
<td>1-30 %</td>
</tr>
<tr>
<td>Low risk</td>
<td>nl labs (troponin, BNP); nl RV function</td>
<td>&lt; 1 %</td>
</tr>
</tbody>
</table>

[Torbicki A et al. Eur Heart J 2008;2276-315]
VQ Scan

- Ventilation Phase (TcDTPA vs Xeon)
- Perfusion Phase (TcMAA)
- Looking for mismatch perfusion defects.
# VQ Scan Interpretation

<table>
<thead>
<tr>
<th>Result</th>
<th>Interpretation</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>No perfusion deficit</td>
<td>Excludes pulmonary thromboembolism</td>
</tr>
<tr>
<td>Low probability</td>
<td>Perfusion deficit with matched ventilation deficit</td>
<td>&lt; 20% probability of PE</td>
</tr>
<tr>
<td>Intermediate probability</td>
<td>Perfusion deficit that corresponds to parenchymal abnormality on chest x-ray</td>
<td>20% - 80% probability of PE</td>
</tr>
<tr>
<td>High probability</td>
<td>Multiple segmental perfusion deficits with normal ventilation</td>
<td>&gt; 80% probability of PE</td>
</tr>
</tbody>
</table>
Must Combine VQ with Clinical Findings/Score

<table>
<thead>
<tr>
<th>Wells</th>
<th>Score</th>
<th>Modified wells</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical signs of DVT</td>
<td>3.0</td>
<td>Clinical signs of DVT</td>
<td>1.0</td>
</tr>
<tr>
<td>Recent surgery or immobilization</td>
<td>1.5</td>
<td>Recent surgery or immobilization</td>
<td>1.0</td>
</tr>
<tr>
<td>Heart rate &gt; 100 beats/min</td>
<td>1.5</td>
<td>Heart rate &gt; 100 beats/min</td>
<td>1.0</td>
</tr>
<tr>
<td>Previous VTE</td>
<td>1.5</td>
<td>Previous VTE</td>
<td>1.0</td>
</tr>
<tr>
<td>Hemoptysis</td>
<td>1.0</td>
<td>Hemoptysis</td>
<td>1.0</td>
</tr>
<tr>
<td>Malignancy</td>
<td>1.0</td>
<td>Malignancy</td>
<td>1.0</td>
</tr>
<tr>
<td>Alternative diagnosis less likely than PE</td>
<td>3.0</td>
<td>Alternative diagnosis less likely than PE</td>
<td>1.0</td>
</tr>
</tbody>
</table>

Wells score three-level: < 2 points – low; 2-6 points – intermediate; > 6 points – high. Wells score two-level: PE unlikely < 4 points; PE likely > 4 points. Simplified Wells score: PE unlikely < 1 point; PE likely – 1 point. PE – pulmonary embolism, PTP – pretest probability
Acute Non-Massive PE

- Hemodynamically Stable
- No right heart strain
- Normal Troponin
- Tx-Anticoagulation—UFH vs LWMH

Acute Massive PE

- Systemic Hypotension- (<90 SBP for greater than 15 minutes, needing pressors, shock)
- Tx with IV TPA vs CDT-- if no major contra indication
Acute Submassive PE?
CT finding for Right Heart Strain

- RV to LV ratio

- If less than 1, then no heart strain.

- If greater than 1, then represents heart strain.
Submassive PE

<table>
<thead>
<tr>
<th>Trial</th>
<th>No. of normotensive patients with acute PE</th>
<th>Percentage of patients with RV dysfunction</th>
<th>Mortality [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>RV dysfunction</td>
</tr>
<tr>
<td>Grifoni et al. [3]</td>
<td>162</td>
<td>31%</td>
<td>4.6</td>
</tr>
<tr>
<td>Kasper et al. [4]</td>
<td>317</td>
<td>27%</td>
<td>12.6</td>
</tr>
<tr>
<td>Ribeiro et al. [5]</td>
<td>126</td>
<td>56%</td>
<td>12.9</td>
</tr>
</tbody>
</table>

Chronic thromboembolic pulmonary hypertension

-Mean pulmonary artery pressure greater than 25 mm Hg that persists 6 months after PE

-2-4% of patients after PE

http://radiopaedia.org/articles/chronic-pulmonary-embolism
## Submassive PE

<table>
<thead>
<tr>
<th>Source</th>
<th>No. of Events</th>
<th>No. of Patients</th>
<th>No. of Events</th>
<th>No. of Patients</th>
<th>OR (95% CI)</th>
<th>Favors Thrombolysis</th>
<th>Favors Anticoagulants</th>
<th>Weight, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Goldhaber et al, (^2) 1993</td>
<td>0</td>
<td>46</td>
<td>2</td>
<td>55</td>
<td>0.16 (0.01-2.57)</td>
<td></td>
<td></td>
<td>5.3</td>
</tr>
<tr>
<td>Konstantinides et al, (^3) 2002</td>
<td>4</td>
<td>118</td>
<td>3</td>
<td>138</td>
<td>1.58 (0.35-7.09)</td>
<td></td>
<td></td>
<td>18.4</td>
</tr>
<tr>
<td>TIPES, (^{29}) 2010</td>
<td>0</td>
<td>28</td>
<td>1</td>
<td>30</td>
<td>0.14 (0.00-7.31)</td>
<td></td>
<td></td>
<td>2.7</td>
</tr>
<tr>
<td>Fasullo et al, (^{11}) 2011</td>
<td>0</td>
<td>37</td>
<td>6</td>
<td>35</td>
<td>0.11 (0.02-0.58)</td>
<td></td>
<td></td>
<td>15.1</td>
</tr>
<tr>
<td>MOPETT, (^{10}) 2012</td>
<td>1</td>
<td>61</td>
<td>3</td>
<td>60</td>
<td>0.35 (0.05-2.57)</td>
<td></td>
<td></td>
<td>10.5</td>
</tr>
<tr>
<td>ULTIMA, (^{30}) 2013</td>
<td>0</td>
<td>30</td>
<td>1</td>
<td>29</td>
<td>0.13 (0.00-6.59)</td>
<td></td>
<td></td>
<td>2.7</td>
</tr>
<tr>
<td>TOPCOAT, (^9) 2014</td>
<td>1</td>
<td>40</td>
<td>1</td>
<td>43</td>
<td>1.08 (0.07-17.53)</td>
<td></td>
<td></td>
<td>5.3</td>
</tr>
<tr>
<td>PEITHO, (^8) 2014</td>
<td>6</td>
<td>506</td>
<td>9</td>
<td>499</td>
<td>0.66 (0.24-1.82)</td>
<td></td>
<td></td>
<td>40.0</td>
</tr>
<tr>
<td>Total</td>
<td>12</td>
<td>866</td>
<td>26</td>
<td>889</td>
<td>0.48 (0.25-0.92)</td>
<td></td>
<td></td>
<td>100.0</td>
</tr>
</tbody>
</table>

Heterogeneity: \(\chi^2 = 7.63; P = .37; I^2 = 8\%

Overall effect: \(z = 2.22; P = .03\)

Treatment for Acute PE

- Non-Massive Acute PE
- Submassive Acute PE
- Massive Acute PE

Anticoagulation UFH vs LMWH
IV TPA vs CDT + AC

Questions?