Disclosures

I have no relevant or non-relevant financial relationship with a commercial interest in this subject or other subject matter.

I have no financial relationships to disclose.

I will not discuss off label use or investigational use in my presentation.

I will discuss the following off label use and/or investigational use in my presentation:

Learning Objectives

Describe issues related to VTE that occur frequently & frustrates everyone.

Analyze the current data, formulate the best treatment for this problem.

Review some new data that will help us make an improved decision on similar cases – which we will likely see tomorrow on the medical wards remembering not to go back to our old habits.
Case Presentation

Mr. Med al CoError is a 57-year-old man present with left-sided chest pain for the past 5 to 6 days. He has no history of cancer, but has HTN, OSA, DM, and CAD without MI. On questioning symptoms started gradually & progressively worsened; He reports pressure-like pain but no radiation. Pain Scale: 8/10; Cough or body movement make the pain worse, lying still feels better.


You suspect a pulmonary embolism.

Question 1

What is the next best step in the evaluation of this patient?

A. Do nothing  
B. Risk stratification  
C. Yell for help  
D. Start Treatment and order D-Dimer

Risk Stratification

Suspect Acute Pulmonary Embolism

Low Risk: Check D Dimer  
Intermediate Risk: (+) D Dimer Begin treatment  
High Risk: (+) D Dimer Start treatment & Confirm diagnosis

European Heart Journal (2014) doi 10.1093
**Venous Thromboembolism Primary Care Criteria**

*Primary Care Diagnostic Rule to Estimate the Probability of Deep Vein Thrombosis (DVT)*

<table>
<thead>
<tr>
<th>Clinical Features</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male Gender</td>
<td>1</td>
</tr>
<tr>
<td>Oral Contraceptive Use</td>
<td>1</td>
</tr>
<tr>
<td>Presence of cancer/malignancy</td>
<td>1</td>
</tr>
<tr>
<td>Recent surgery (4 wk)</td>
<td>1</td>
</tr>
<tr>
<td>Absence of trauma</td>
<td>1</td>
</tr>
<tr>
<td>Vein distension</td>
<td>1</td>
</tr>
<tr>
<td>Call circumference &gt;= 3</td>
<td>2</td>
</tr>
<tr>
<td>Abnormal D-dimer</td>
<td>8</td>
</tr>
</tbody>
</table>


**Venous Thromboembolism Modified Wells Criteria**

*Modified Wells Rule for Use to Estimate the Probability of Venous Thrombosis*

<table>
<thead>
<tr>
<th>Clinical Features</th>
<th>Score</th>
<th>Traditional Clinical Probability Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active Cancer</td>
<td>1</td>
<td>High &gt; 6 points</td>
</tr>
<tr>
<td>Clinical Signs of DVT</td>
<td>3</td>
<td>Intermediate 2 to 5 points</td>
</tr>
<tr>
<td>Immobilization or major surgery &lt; 4 wks</td>
<td>1.5</td>
<td>Low &lt; 2 points</td>
</tr>
<tr>
<td>Heart Rate &gt; 100</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Hemoptysis</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Previously documented deep vein thrombosis</td>
<td>1.5</td>
<td></td>
</tr>
<tr>
<td>Alternative diagnosis as likely than that of DVT</td>
<td>3</td>
<td></td>
</tr>
</tbody>
</table>

Simplified Clinical Probability Assessment

*Scores of > 4 indicated that the probability of pulmonary embolism is high.
*Score of < 4 indicated that the probability of pulmonary embolism is low.

Van Belle A et al. JAMA 2006;295:172

**Thrombosis Risk Factor(s)**

*Siri Study*

<table>
<thead>
<tr>
<th>Risk Factor(s)</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malignant neoplasm</td>
<td>18</td>
<td>13.4 - 22</td>
</tr>
<tr>
<td>History of VTE</td>
<td>15</td>
<td>8.77 - 35.8</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>12</td>
<td>1.40 - 99.2</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>10</td>
<td>3.3 - 15.8</td>
</tr>
<tr>
<td>Neurologic disease with paresis</td>
<td>7</td>
<td>3.5 - 10.2</td>
</tr>
<tr>
<td><em>Exogenous female hormones</em></td>
<td>5.75</td>
<td>2.2 - 15.0</td>
</tr>
<tr>
<td>Immobilization</td>
<td>5.61</td>
<td>2.30 - 13.6</td>
</tr>
<tr>
<td>Venous insufficiency</td>
<td>5</td>
<td>3.10 - 6.9</td>
</tr>
<tr>
<td>Obesity (BMI&gt;30)</td>
<td>2.39</td>
<td>1.48 - 3.87</td>
</tr>
</tbody>
</table>

OR = Odds Ratio

Samama MM. Arch Intern Med 2000; 160: 3415-3420
Rodendal FR. Thorax Heart 1998;43:129-130
Question 2

Your colleague asks you, “What are you thoughts on a D-dimer test?” for this patient for which you reply….

A. Come on dude, D dimer are useless
B. The D dimer test is < 500 (negative) but you know your going to do a CTA anyway (as you laugh and walk away)
C. The D dimer test confirms a diagnosis
D. A D dimer test is reasonable in low/intermediate risk patient but it should be above the age-adjusted cutoff

Thromboembolism Cutoff Level

Study:
- 103 patients suspected of PE
- 34% confirmed via angiogram.

Latex Agglutination Assays:
- Sensitive of > 97%
- Specificity of 29%
- Negative predictive value > 94%

Age-Adjusted D-Dimer Cutoff Levels

The ADJUST-PE Study

2809 patients pulmonary embolism unlikely or non-high-clinical probability

- 817 patients D-Dimer < 500
- 337 patients D-Dimer > 500 but < age-adjusted cutoff
- 1744 patients Levels > age-adjusted cutoff
Question 3

The patient age adjusted D-dimer was 680 (+), what is the best next step in the management of your patient?

A. No more testing is needed
B. Order a CT Angiogram
C. Admit & Start Apixaban [Eliquis]
D. Discharge home with NOAC agent
E. Order a V/Q and US legs bilaterally

Case Presentation

Radiographic Images
Question 4

What is the next best step in for this patient?

A. Do nothing  
B. Start Treatment with a thrombolytic  
C. Again, Risk stratification  
D. Now, yell for help (really loud)

Risk Assessment Score  
Pulmonary Embolism Severity Index

<table>
<thead>
<tr>
<th>Pulmonary Embolism Severity Index [PESI]</th>
<th>Our case</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>Age 57</td>
</tr>
<tr>
<td>Male sex</td>
<td>SSB 135</td>
</tr>
<tr>
<td>Cancer</td>
<td>+30 points</td>
</tr>
<tr>
<td>CHF/CHF</td>
<td>+10 points</td>
</tr>
<tr>
<td>Chronic lung disease</td>
<td>+10 points</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>+60 points</td>
</tr>
<tr>
<td>Pulse = 110 b/p/m</td>
<td>+20 points</td>
</tr>
<tr>
<td>Systolic BP &lt; 100 mmHg</td>
<td>+30 points</td>
</tr>
<tr>
<td>Respiratory rate &gt; 30 b/min</td>
<td>+20 points</td>
</tr>
<tr>
<td>Temperature &gt; 36 C</td>
<td>+20 points</td>
</tr>
<tr>
<td>Arterial Oxygen SaO2 &lt; 90%</td>
<td>+20 points</td>
</tr>
</tbody>
</table>

Risk Class for Mortality

<table>
<thead>
<tr>
<th>Class</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>&lt; 65</td>
</tr>
<tr>
<td>II</td>
<td>66-85</td>
</tr>
<tr>
<td>III</td>
<td>86-105</td>
</tr>
<tr>
<td>IV</td>
<td>106-125</td>
</tr>
<tr>
<td>V</td>
<td>&gt;125</td>
</tr>
</tbody>
</table>

Risk Strata PESI Scores

- Class I < 65 points: Very low 30 day mortality risk (0 - 1.6%)
- Class II 66 - 85 points: Low mortality risk (1.7 - 3.5%) NPV 99%
- Class III > 86 - 105 points: Moderate mortality risk (3.2 - 7.1%)
- Class IV > 106 - 125 points: High mortality risk (4.0 - 14.4%)
- Class V > 125 points: Very high risk (10 to 24.5%)

Our case

Age 57  
SSB 135  
SaO2 > 90 %  
P + COPD  
P = 112  
RR = 22

**Risk Assessment Score**  
**Simplified PESI**

- **sPESI = Retrospective analysis of RIETE registry**

<table>
<thead>
<tr>
<th>Risk Category</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low risk</td>
<td>0</td>
</tr>
<tr>
<td>High risk</td>
<td>1</td>
</tr>
</tbody>
</table>

**Risk Scores**
- Age >80: 1 point
- History of Cancer: 1 point
- Chronic cardiopulmonary disease: 1 point
- Pulse > 110 b/min: 1 point
- Systolic BP < 100 mmHg: 1 point
- Arterial Oxygen $\text{SaO}_2 <$ 90%: 1 point

**Risk Stratification sPESI Scores**
- 0 points: low 30 day mortality risk (1.2% 95% CI 0.0-2.1%)
- >1 point(s): 30 day mortality risk 10.9% (95% CI 8.5-13.2%)

Konstantinides SV et al. Thrombosis & Haemostasis 2015; 113:1202-1209.

**Question 5**

Based on this information where would you admit the patient?

A. The Palm Springs 'Bates' Hotel  
B. General Medical Ward  
C. Hospital (Step down/ICU)  
D. Discharge home with treatment

Home Treatment of Pulmonary Embolism
In the Era of Novel Oral Anticoagulants

<table>
<thead>
<tr>
<th>Study Design</th>
<th>N</th>
<th>Cancer (%)</th>
<th>Risk Stratification</th>
<th>Rx &amp; Tx</th>
<th>Mortality (%)</th>
<th>Fatal PE (%)</th>
<th>Fatal ICH (%)</th>
<th>Recurrent Event (%)</th>
<th>Major Bleeding (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retrospective Cohort Study</td>
<td>18 years of age, pulmonary embolism, 5 Emergency Departments.</td>
<td>983 (+)</td>
<td>Unstable or Hypoxic</td>
<td>237 Ineligible for home treatment</td>
<td>746 eligible for home treatment</td>
<td>Home 13 (1.7%)</td>
<td>Admitted 733 (96.3%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
CONCLUSION: Even in the era of novel oral anticoagulants, the vast majority of patients with acute pulmonary embolism were hospitalized, and only a small proportion were discharged in 2 days. Although home treatment has been found to be safe in carefully selected patients, and scoring systems have been derived to identify those at low risk of adverse events, home treatment was infrequently selected.

746 eligible for home treatment
13 (1.7%) Admitted
733 (98.3%) Home

Home Treatment Be Careful

- In patients with acute thrombosis whose home circumstances are adequate, we recommend initial treatment at home over treatment in hospital (Grade 1B).

- Remarks: The recommendation is conditional on the adequacy of home circumstances:
  - well-maintained living conditions,
  - strong support from family or friends,
  - phone access, and
  - ability to quickly return to the hospital if there is deterioration.

  It is also conditional on the patient feeling well enough to be treated at home (eg, does not have severe symptoms or comorbidity).

Risk Stratification
Echocardiogram

Transthoracic echocardiograph reveals evidence of acute right heart strain, with a poorly contracting right ventricle

Also, tricuspid regurgitation with pulmonary hypertension (PSP 55 mm Hg) and bowing of the interventricular septum towards the left ventricle
Question 6

Based on the abnormal echocardiogram, you are able to tell the patient and family what important information?

A. Risk of fatal & non-fatal embolism is high
B. The risk of recurrent events is low
C. Risk of death from pulmonary embolism is low
D. He will be ‘Ok’ in 3 months

Case Questions
Discussion
Cumulative incidence of recurrent venous thromboembolism. RVD indicates right ventricular dysfunction.

Echocardiography was used to assess RVD on admission and before hospital discharge in 301 consecutive patients with the first episode of acute pulmonary embolism.

Right ventricular dysfunction was diagnosed in the presence of 1 or more of the following: right ventricular dilation (without hypertrophy), paradoxical septal systolic motion, and Doppler evidence of pulmonary hypertension.

Patients were followed up at 2, 6, and 12 months and yearly thereafter.

The primary end point was symptomatic, recurrent fatal or nonfatal VTE.


doi:10.1001/archinte.166.19.2151

<table>
<thead>
<tr>
<th>Year</th>
<th>No. of Patient</th>
<th>No. of VTE</th>
<th>No. of RVD</th>
<th>No. of Recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>32</td>
<td>12</td>
<td>16</td>
<td>4</td>
</tr>
<tr>
<td>6</td>
<td>36</td>
<td>11</td>
<td>15</td>
<td>3</td>
</tr>
<tr>
<td>12</td>
<td>44</td>
<td>6</td>
<td>20</td>
<td>5</td>
</tr>
<tr>
<td>1</td>
<td>36</td>
<td>9</td>
<td>18</td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td>30</td>
<td>6</td>
<td>15</td>
<td>1</td>
</tr>
<tr>
<td>5</td>
<td>24</td>
<td>5</td>
<td>12</td>
<td>2</td>
</tr>
</tbody>
</table>

Case Questions
Discussion

Table 2. Follow-up Subscores in Study Patients Based on In-Hospital Course of VTE

<table>
<thead>
<tr>
<th>Subscores</th>
<th>In-Hospital</th>
<th>Follow-up 1 yr</th>
<th>Follow-up 2 yr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>21/106</td>
<td>11/136</td>
<td>10/126</td>
</tr>
<tr>
<td>MI</td>
<td>18/106</td>
<td>14/136</td>
<td>12/126</td>
</tr>
<tr>
<td>Stroke</td>
<td>15/106</td>
<td>11/136</td>
<td>2/126</td>
</tr>
<tr>
<td>Hospital Stay</td>
<td>21/106</td>
<td>12/136</td>
<td>10/126</td>
</tr>
<tr>
<td>VTE</td>
<td>21/106</td>
<td>11/136</td>
<td>10/126</td>
</tr>
</tbody>
</table>


doi:10.1001/archinte.166.19.2151
Medication Options

Question 7

In this patient, what would be the best treatment to start?

A. Nothing
B. LMWH
C. High dose heparin gtt / per nomogram
D. Coumadin (Warfarin)
E. Altapace (tpa)
F. Surgical embolectomy

Treatment Options

- Enoxaparin (low molecular weight heparin)
  - Xa inhibitor
  - Weight-based dosing
  - Anti-Xa level for monitoring
  - Peak 3 - 5 hours, Half-life about 6 hours
  - Dosing in low weight, obese patients is challenging
  - Clearance reduced with renal disease (CrCl<30)
Treatment Options

- Fondaparinux [Arixtra]
  - Binds anti-thrombin
  - Lowest risk of HIT (Heparin Induced Thrombocytopenia)
  - Peaks at 2 hours, half-life 17 hours
    - Stop 4 days before major procedure
    - No antidote
  - Clearance reduced with renal disease
    - Reduce 50% in CrCl < 50
    - Contraindicated in CrCl <30

Risk Stratification
Acute Pulmonary Embolism

Low Risk
- LMWH or Fondaparinux + Rivaroxaban
- Non-inferior to standard treatment in stable patients

Intermediate Risk
- LMWH + Dabigatran and Rivaroxaban
- Non-inferior to standard treatment in stable patients

High Risk
- LMWH or Fondaparinux > Unfractionated heparin
- Sub-massive?
- Risk
- Mass?
- Risk

Question 8
This patient appears to have a unprovoked pulmonary embolism thus would you recommend cancer screening.

A. I will ask Susan Stacy, she know everything
B. Yes
C. Maybe
D. No
Prevalence of Occult Cancer in Unprovoked Clot

Prevalence of Occult Cancer in Unprovoked Clot: SOME Study

- Prevalence of occult cancer was low.
- Routine screening with CT of the abdomen and pelvis did not provide a clinically significant benefit.
- CT included a virtual colonoscopy and gastroscopy, biphasic enhanced CT of the liver, parenchymal pancreatography, and uniphasic enhanced CT of the distended bladder.

Kaplan–Meier Curves for Time to Detection of Missed Occult Cancer.

<table>
<thead>
<tr>
<th>Group</th>
<th>Cancer</th>
<th>Percentage</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Limited Screening</td>
<td>14/431</td>
<td>3.2%</td>
<td>1.9 – 5.4</td>
</tr>
<tr>
<td>Limited (+) CT</td>
<td>19/423</td>
<td>4.5%</td>
<td>2.9 – 6.9</td>
</tr>
</tbody>
</table>

No significant between-group difference in the mean time to cancer diagnosis (4.2 m limited-screening group vs. 4.0 m in the limited-screening plus CT group. (P=0.88).

Secondary outcome analyses:
- Rate of recurrent events (3.3% and 3.4%, p=1.0),
- Overall mortality (1.4% and 1.2%, p=1.0),
- Cancer-related mortality (1.4% and 0.9%, p=0.75),
- Rate of detection of early cancers (p=0.37).
- 0.23% in the limited-screening group
- 0.71% in the limited-screening plus CT group
Question 9

What about Catheter related treatment for this patient?

A. Benefits (> 2 weeks) are in question.
B. Helps everyone who gets it.
C. Sure, there is no risk.
D. I really need to find Susan.

Interventions for Pulmonary Embolism

- Ultrasound Assisted Thrombolysis (EKOS)
  - Technically similar to catheter directed dripping.
  - Ultrasound potentially reduced drug administration time and tPA dose.
  - Potential lower rated of bleeding complications.

Back to Background Information

<table>
<thead>
<tr>
<th>Massive PE</th>
<th>Submassive PE</th>
<th>Minor/Nonmassive PE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>High risk</strong></td>
<td><strong>Moderate/Intermediate risk</strong></td>
<td><strong>Low risk</strong></td>
</tr>
<tr>
<td>Sustained hypotension (systolic BP &lt;90 mmHg for &gt;15 min)</td>
<td>Systemically normotensive (systolic BP &gt;90 mmHg)</td>
<td>Systemically normotensive (systolic BP &gt;90 mmHg)</td>
</tr>
<tr>
<td>Inotropic support</td>
<td>RV dysfunction</td>
<td>No RV dysfunction</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>Myocardial necrosis</td>
<td>No myocardial necrosis</td>
</tr>
<tr>
<td>Persistent profound bradycardia (HR &lt;40 bpm with signs or symptoms of shock)</td>
<td>Echocardiogram RV/LV ratio &gt;0.9 or RV systolic dysfunction</td>
<td>Echocardiogram RV/LV ratio &gt;0.9 on CT</td>
</tr>
<tr>
<td>Sustained hypotension (systolic BP &lt;90 mmHg for &gt;15 min)</td>
<td>Elevation of BNP (&gt;90 pg/mL)</td>
<td>Elevation of NTproBNP (&gt;500 pg/mL)</td>
</tr>
<tr>
<td>Systemically normotensive (systolic BP &gt;90 mmHg)</td>
<td>ECG changes: new complete or incomplete RBBB</td>
<td>ECG changes: anteroseptal ST elevation or depression</td>
</tr>
<tr>
<td>No RV dysfunction</td>
<td>RV/LV ratio &gt;0.9 on CT</td>
<td>RV/LV ratio &gt;0.9 on CT</td>
</tr>
<tr>
<td>No myocardial necrosis</td>
<td>Myocardial necrosis</td>
<td>Myocardial necrosis</td>
</tr>
</tbody>
</table>

• Retrospective analysis of 120 patients with hemodynamically stable PE based on CT

• PE-related mortality at 3 months:
  • 17% if RV/LV ≥ 1.5
  • 8% if 1.0 ≤ RV/LV < 1.5
  • 0% if RV/LV < 1.0


Ultrasound Accelerated Thrombolysis

Mechanism of Action

Ultrasound Pulses  Fibrin Separation  Active Drug Delivery by Acoustic Streaming

US delivered in High freq (2.2Mhz) Low power (0.5 W/per element Pulses of varying waveforms

Interventional Summary

• Lysis vs. Placebo
  • 13 placebo controlled, randomized trials of lysis vs placebo
  • Minority for massive PE, total 480 patients.
  • Variable drugs, dosing, timing and adjunctive therapies
  • No independent mortality effect
  • Meta-analyses reduction in death/recurrent PE
  • Improvement in RV size/function, mPA pressures

• EKOS vs. Heparin
  • No study large enough to evaluate death/recurrent PE
  • Improved RV size-function at 24hrs, catch up at 90days
  • Improved RV function at 90 days
Question 10

How long would you recommend treatment for this patient.

A. Stop at hospital discharge
B. Life-long
C. Minimum of three month
D. Again, I will ask Susan

who should be treated for 3 months and who should indefinitely

Isolated event
- Stop at 3 months

Reversible Factors
- Stop at 3 months

Unprovoked
- Next Step

Cancer
- Indefinite or until inactive + 6 months

High Bleed Risk
- Stop at 3 months

Others
- Next Step

Low Bleed Risk
- Stop at 3 months

Second VTE
- Indefinite

- D dimer
  - (-) Stop Rx
  - (+) D dimer
    - Extended Rx

Question 10

What would you do after three months? More importantly how would/do you decide?

A. Use a validated risk score
B. Rock, Paper, Scissors
C. Guess
D. Stop treatment after 3 months
VTE Recurrence Risk Assessment Scores

**HERDOO-2 Score**
- HER =
  - Hyperpigmentation or
  - Edema or
  - Redness
- D = D-dimer positivity (on warfarin)
- O = Obesity, BMI ≥ 30
- D = Older age, ≥ 65 years

Scoring:
- HER = 1 point
- D = 1 point
- O = 1 point
- D = 2 points

> 2 points: Continue warfarin
≤ 1 point: Discontinue anticoagulation

**DASH Score**

DASH Rule
- D = D-dimer positivity (off warfarin)
- A = Age < 50 years
- S = Sex (male)
- H = Hormone use

Annual VTE recurrence rate:
- ≤ 1: 3.1%
- 2: 6.4%
- ≥ 3: 12.3%

Predicting disease recurrence in unprovoked venous thromboembolism: a proposed prediction score (DASH)

<table>
<thead>
<tr>
<th>DASH Score</th>
<th>Annualized Recurrence Rate (95% CI)</th>
<th>Cumulative Recurrence, % 1-year</th>
<th>2-years</th>
<th>3-years</th>
</tr>
</thead>
<tbody>
<tr>
<td>-2</td>
<td>1.8 (0.5-7.6)</td>
<td>2.4</td>
<td>5.2</td>
<td>5.2</td>
</tr>
<tr>
<td>-1</td>
<td>1.0 (0.4-2.6)</td>
<td>1.9</td>
<td>1.5</td>
<td>5.7</td>
</tr>
<tr>
<td>0</td>
<td>2.4 (1.4-4.4)</td>
<td>4.2</td>
<td>5.4</td>
<td>9.5</td>
</tr>
<tr>
<td>1</td>
<td>3.9 (2.9-5.3)</td>
<td>5.1</td>
<td>8.7</td>
<td>15.9</td>
</tr>
<tr>
<td>2</td>
<td>6.3 (5.0-8.1)</td>
<td>8.4</td>
<td>12.8</td>
<td>25.3</td>
</tr>
<tr>
<td>3</td>
<td>10.6 (8.7-13.4)</td>
<td>14.6</td>
<td>20.5</td>
<td>40.9</td>
</tr>
<tr>
<td>4</td>
<td>19.9 (13.9-28.2)</td>
<td>21.9</td>
<td>33.6</td>
<td>61.3</td>
</tr>
</tbody>
</table>

Six Months vs Extended Oral Anticoagulation After a First Episode of Pulmonary Embolism: The PADIS-PE Randomized Clinical Trial

Randomized, double-blind trial treatment period: 18 months; median follow-up: 24 months. 271 adult patients who had experienced a first episode of symptomatic untreated pulmonary emboli (PE) with no major risk factors for hemorrhage and had been hospitalized initially for a minimum of 6 months to 2 years. A vitamin K antagonist was randomized and followed up between Interventions: Warfarin or placebo for 38 months.

Probability of the Composite Outcome of Recurrent Venous Thromboembolism and Major Bleeding Throughout the Study Period. The unadjusted hazard ratios for warfarin-placebo were 0.23 (95% CI, 0.09-0.55) during the treatment period and 0.74 (95% CI, 0.47-1.17) for the entire study period. The y-axis that is shown in blue indicates the range of estimated cumulative risk from 0% to 10%.


Effect of a Retrievable Inferior Vena Cava Filter Plus Anticoagulation vs Anticoagulation Alone on Risk of Recurrent Pulmonary Embolism: A Randomized Clinical Trial

Consecutive patients aged ≥18 years or older, hospitalized for acute, symptomatic clot, ≥1 additional criterion for severity: Standard care (UFH, LMWH or Fondaparinux +/- fibrinolytic treatment) <72 hours 3 months IVC Removal 6 months = On anticoagulation

PREPIC 2 Trial 399 patients Randomized IVC Filter Group + anticoagulation Control (anticoagulation only) Group n = 200 n = 199

Data Analysis


Effect of a Retrievable Inferior Vena Cava Filter Plus Anticoagulation vs Anticoagulation Alone on Risk of Recurrent Pulmonary Embolism: A Randomized Clinical Trial

<table>
<thead>
<tr>
<th>Clinical Outcomes For Patients With at Least 1 Event in the PREPIC2 Trial</th>
<th>Group</th>
<th>No. With Events (%)</th>
<th>Event Rate</th>
<th>Relative Risk (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Patients</td>
<td>Recurrent pulmonary embolism</td>
<td>12 (6.0)</td>
<td>3 (1.5)</td>
<td>2.69 (0.95-7.29)</td>
<td>58</td>
</tr>
<tr>
<td>Total</td>
<td>Recurrent deep vein thrombosis</td>
<td>1 (0.5)</td>
<td>1 (0.5)</td>
<td>1.00 (0.09-11.1)</td>
<td>1.00</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>1 (0.5)</td>
<td>9 (4.6)</td>
<td>1.75 (0.81-3.88)</td>
<td>36</td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>24 (12.0)</td>
<td>0 (0.0)</td>
<td>0.00 (0.00-0.00)</td>
<td>35</td>
<td></td>
</tr>
</tbody>
</table>

Clinical Trials with DOAC in the Treatment of Venous Thromboembolism

<table>
<thead>
<tr>
<th>Study/Phase</th>
<th>DOAC</th>
<th>N (pts)</th>
<th>Age (yrs.)</th>
<th>Male (%)</th>
<th>Sex (pts)</th>
<th>Drug Treatment</th>
<th>Clinical Outcomes</th>
<th>Duration of Treatment</th>
<th>TTR (%)</th>
<th>Risk of Bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute Treatment Venous Thromboembolism</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RE-COVER I (Dabigatran)</td>
<td>2,564</td>
<td>55 years</td>
<td>56%</td>
<td>826 (31%)</td>
<td>NR</td>
<td>UFH + DAB</td>
<td>Post-index</td>
<td>6 months</td>
<td>60%</td>
<td>Low</td>
</tr>
<tr>
<td>RE-COVER II (Dabigatran)</td>
<td>2,589</td>
<td>55 years</td>
<td>61%</td>
<td>816 (32%)</td>
<td>NR</td>
<td>UFH + DAB</td>
<td>Post-index</td>
<td>6 months</td>
<td>57%</td>
<td>Low</td>
</tr>
<tr>
<td>EINSTEIN (Rivaroxaban)</td>
<td>3,449</td>
<td>56 years</td>
<td>57%</td>
<td>23 (1%)</td>
<td>NA</td>
<td>UFH + RIV</td>
<td>Post-index</td>
<td>3,6,12 months</td>
<td>57.7%</td>
<td>Unclear</td>
</tr>
<tr>
<td>EINSTEIN PE (Rivaroxaban)</td>
<td>5,400</td>
<td>57</td>
<td>59</td>
<td>4,833 (100%)</td>
<td>Intermediate: 24</td>
<td>UFH + RIV</td>
<td>Post-index</td>
<td>3,6,12 months</td>
<td>62.7%</td>
<td>Unclear</td>
</tr>
<tr>
<td>AMPLIFY (Apixaban)</td>
<td>5,400</td>
<td>57</td>
<td>59</td>
<td>1,836 (35%)</td>
<td>Extensive: 37</td>
<td>UFH + EDO</td>
<td>Post-index</td>
<td>3,6,12 months</td>
<td>63.5%</td>
<td>Low</td>
</tr>
<tr>
<td>HOKUSAI-VTE (Edoxaban)</td>
<td>8,292</td>
<td>56</td>
<td>58</td>
<td>3,319 (40%)</td>
<td>Extensive: 46</td>
<td>UFH</td>
<td>Post-index</td>
<td>3 to 12 months</td>
<td>63.5%</td>
<td>Low</td>
</tr>
</tbody>
</table>

• Treated with Hep gtt in ICU
• Coumadin for 3 months.
• Continues on treatment with coumadin

Conclusion

• There is no “ideal way” to diagnosis a VTE
• Can be managed safety when can’t reach a definitive diagnosis.
• Risk stratification is need and often patients need to be followed longitudinally.
• Deliberate efforts are needed to assess thromboembolic risk in all patients.