Pulmonary Embolism
Treatment Challenges

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Outline

Treatment
- How and when to anticoagulate?
- Can we discharge home from ED?
- Should we use the new oral anticoagulants?
- Who gets thrombolytics?
- Should we give half dose thrombolytic?

Case #1 – Recurrent Pleurisy

- 38 y.o. F w/ recurrent “pleurisy” x several days. Is obese, takes OCP’s, and smokes
- Exam: Normal vitals except HR=102
  - PEx: unremarkable
  - ECG and CXR – Normal
- Something just not right - D-dimer sent and elevated.
  - CTPA shows multiple subsegmental PE’s

How would you treat this patient?

1. Admit and anticoagulate in hospital until INR therapeutic?
2. Admit for initial anticoagulation. If stable, discharge early and complete anticoagulation as outpatient?
3. Discharge directly from ED on LMWH + Coumadin?
Guidelines

- ACEP 2011 – Fesmire, Ann Emerg Med,
  - Level A = Generally accepted/ high degree of clinical certainty
  - Level B = Moderate clinical certainty
  - Level C = Strategies based on Class III studies or panel consensus

- ACCP 2012 – Kearon, Chest, 2012
  - Recommendation: Grade 1 = strong, Grade 2 = weak
  - Quality of evidence: A = High, B = moderate, C = Low

Approach to Anticoagulation

ACCP Guidelines 2012

- Anticoagulate with once daily Tinzaparin or Fondaparinux, or twice daily Enoxaparin (Grade 2C). Use IV Unfractionated heparin if subQ absorption will be unreliable.
- Begin warfarin (Coumadin) the same day as parenteral anticoagulation (Grade 1B).
- Continue parenteral anticoagulation for at least 5 days, even if the INR reaches 2.0 earlier (Grade 1B).
- Continue parenteral anticoagulation until the INR is at least 2.0 for 24 hours or more (Grade 1B).

Entirely Outpatient Treatment?

ACCP guidelines 2012

- Not an official recommendation
  - "Evidence suggests that treating appropriately selected patients with acute PE at home does not increase recurrent VTE, bleeding, or mortality."
- In ACCP’s web discussion of guidelines, recommend more strongly.
- Hull et al. Arch IM 1997
- CAREFUL! Risk of recurrent PE was 25 percent if PTT was sub-therapeutic in first 24 hours in pooled analysis of 3 trials
Entirely Outpatient Treatment?

1st RCT!
* RCT of outpt vs inpt Rx in 344 low risk PE pts

* PESI class 1 and 2

* Rx’d with BID enoxaparin

* => No difference in safety!

Aujesky, Lancet, 2011

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**PESI 1 or 2: Score < 86**

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<table>
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<tbody>
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<td>Respiratory rate ≥30 breaths per min</td>
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<td>Altered mental status†</td>
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<tr>
<td>Arterial oxygen saturation &lt;90%‡</td>
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Aujesky, Lancet, 2011
Entirely Outpatient Treatment?

The Implications

- Average ED stay was 12 hrs
- Probably more consistent with safety of 23 hour obs and expedited discharge?

Aujesky, Lancet, 2011

Entirely Outpatient Treatment?

- Prospective, web-based registry of 1,515 hemodynamically stable patients with confirmed PE in Italy
- 3.4% mortality
- HR for death/clinical deterioration was 7.9 for either troponin elevation or RV dysfunction
- If neither was present, no death and 1 deterioration

Becattini, Chest, 2013

Entirely Outpatient Treatment?

Acute Pulmonary Embolism
External Validation of an Integrated Risk Stratification Model

Cecilia Becattini, MD, PhD; Franco Caruza, MD; Chiara Frezzato, MD; Fernanda Fergonzi, MD; Branco Meric Felicio, MD; Alessandro Sturli, MD; Alessandra Lapina, MD; Luca Conti, MD; Filippo Spena, MD; Anna Maria Bongiorni, MD, and Giancarlo Agosti, MD

Becattini, Chest, 2013

Treatment Pearls

- Consider early discharge in PE patients with stable vital signs and without significant co-morbidities.
- Entirely Outpatient Treatment is based on a single randomized study of 344 patients with lots of caveats – Not Quite Ready for Prime Time
Case #2 - New Anticoagulants

- 65 y.o. M with minor head trauma on “new” blood thinner for PE.
- Head CT shows SAH
- What to do?

The New Blood Thinners

- Rivaroxaban = Xarelto (10a)
  - A Fib
  - VTE prophylaxis AND treatment
- Dargabatran = Pradaxa (DTI)
  - A Fib
  - VTE prophylaxis post joint surgery
- Apixaban = Eliquis (10a)
  - A Fib

Xarelto = Rivaroxaban

- Oral Factor 10a inhibitor
- Approved for
  - Non-valvular Afib
  - Rx AND Prophylaxis of PE/DVT
- T1/2 is 6 hrs in healthy and 12 in elderly
- Elevates PT

Rivaroxaban vs Coumadin

Einstein-PE
- 4832 PE pts randomized, open label
- Not inferior to Lovenox and Coumadin
**Xarelto = Rivaroxaban**

**Issues**
- The patient with bleeding!!!
  - *PCC (2, 7, 9, 10) reversed the lab abnormalities*
- Black Box - Nov 2012 Stopping it increases stroke – need to transition to something else first!!!!!

  *Eerenberg Circulation. 2011*

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**Xarelto = Rivaroxaban**

**COST**
- 6 month = $1600
- Coumadin
  - 6 months Coumadin = $150
  - 7 days Lovenox = $250
  - INR x 5 - $110

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**Pradaxa = Dabigatran**

- Oral Direct Thrombin Inhibitors
- Approved for Non-valvular AFib – not for Rx of PE
- Most common adverse reactions (>15%) are gastritis-like symptoms and bleeding

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**Pradaxa = Dabigatran**

- Elevates PTT
- *NO REVERSAL – dialysis may help*
- Stopping it increases stroke – need to transition to something else first!!!!!

  *Eerenberg Circulation. 2011*
Reversing New Blood Thinners

- If Rx is for PE = likely Rivaroxaban
  - If bleed is life-threatening:
  - Check PT and start Prothrombin Complex Concentrates

- If Rx is for Afib = likely Dabigatran
  - If bleed is life-threatening:
  - Check PTT and initiate dialysis

Case #3 – Recurrent Pleurisy

- 38 y.o. F w/ recurrent “pleurisy” x several days
- Risk factors: Obese, takes OCP’s, smokes
- Exam: 100/80, 102, 20, 37.1, 90%
  - NAD - o/w unremarkable
  - ECG – Normal
  - CXR - Clear

Indications for thrombolitics

ACEP Clinical Policy 2011
- Level B: For patients with confirmed PE and hemodynamic instability
  - For whom benefits of treatment outweigh risks of life-threatening bleeding complications.
  - Procedural intervention, if available, may be used as an alternative.
Indications for thrombolytics

ACEP Clinical Policy 2011

- Level C: For patients with high clinical suspicion for PE and hemodynamic instability
  - For whom the diagnosis of PE cannot be confirmed in a timely manner (too unstable to CT)

Insufficient evidence to make any recommendations regarding use of thrombolytics in any subgroup of hemodynamically STABLE patients.

Thrombolytics have been demonstrated to result in faster improvements in right ventricular function and pulmonary perfusion, but these benefits have not translated to improvements in mortality.

Indications for thrombolytics

PEITHO (Pulmonary Embolism Thrombolysis)

- Presented at American College of Cardiology 2013 Summer Sessions
  - Randomized pts with submassive PE to Full dose thrombolytics vs heparin in 1006 pts over a 10 year period.
  - Significant benefit (absolute risk reduction of 3% in death or hemodynamic collapse) which was balanced by significantly higher rates of major bleeding.

1/2 Dose Thrombolytics

- Standard dose t-PA = 100mg in 2 hrs
- Unlike heart (5%) or brain (15%), 100% flows to lungs
- MOPETT = Sharifi, AmJ C, 2012
  - Moderate Pulmonary Embolism Treated with Thrombolysis
  - 121 pts with “moderate” PE (>1 lobar clot)
  - All got heparin
  - Randomized to 50 mg TPA over 2 hrs
½ Dose Thrombolitics

- Population
  - 66% had BNP or Trop I elevation
  - RV enlargement in 20%
  - RV hypokinesia in 5%

½ Dose Thrombolitics

Results of ½ dose TPA v Usual

- Pulmonary HTN at 28 months
  - 9 (16%) vs. 32 (57%) p<0.001
- Pulmonary HTN + recurrent PE at 28 months
  - 9 (16%) vs 35 (63%) p<0.001
- Hospital Stay (days)
  - 2.2 vs 4.9 p <0.001

Vena Cava Filters?

ACCP Guidelines 2012

- NOT routinely (1A)
- IF acute prox DVT AND anticoagulation not possible then IVC filter (1C)

Summary

Initiate immediate treatment with one of the following:

- Twice daily enoxaparin + Coumadin
- Once daily Tinzaparin + Coumadin
- Once daily Fondaparinux + Coumadin
- Oral Rivaroxaban
Summary

- 23 hour observation and discharge is safe for low risk patients
- Oral Xa inhibitors look good – if you aren’t the one paying
- TPA for hemodynamically unstable PE patients
- Half dose TPA for moderate size PE is not yet recommended, but may be around the corner…

Bibliography