Case 1

- 65 year old smoker with COPD arrives in the emergency room with acute exacerbation of SOB.
- Thin, dyspneic and with productive cough and 30 pound weight loss over last 6 months
- Chest CTA: single sub-segmental pulmonary embolus
- Bilateral lower extremity venous dopplers are normal
- Medications: aspirin, atorvastatin, intermittent LD prednisone, and other COPD meds

Case 1

- Should this patient receive anticoagulation?
- If so, with what?
- What Dose?

Case 1

- **Frequency of PE in COPD during acute exacerbation**
  - **N=172 29.1%[1]**
  - **N=192 25%[2]**
  - **N=49 18%[3]**
  - **N=48 6.5%[4]**
- **Systemic Review[5]**
  - **Articles 2407**
    - **Hospitalized patients 19%**
    - **Emergency room patients 3.3%**

1.J Bras Pneumol. 2014;40(1):38-45
2. Ann Intern Med. 2006 Mar 21;144(6):390-6
3. Emerg Radiol. 2015 Jun;22(3):257-60
4. Thorax. 2007 Feb;62(2):121-5
5. Chest. 2009 Mar;135(3):786-793

Case 1

Hypercoagulability state in patients with COPD

- 37 COPD patients and in 30 controls matched for sex and age
  - Prothrombin F1 + 2 fragment
  - D-dimer
  - Fibrinogen
- COPD patients had significantly higher values of F1 + 2 ($p = 0.0001$) and fibrinogen ($p = 0.0005$) than healthy subjects.
- Heparin (5000 IU t.i.d.) significantly reduced F1 + 2 ($p = 0.03$)
- This study shows that COPD patients have an ongoing prothrombotic state which could potentially account for thrombosis occurring in pulmonary vessels

Thromb Haemost. 1994 Sep;72(3):343-6.

Thrombin generation in chronic obstructive pulmonary disease: dependence on plasma factor composition.

- COPD patients compared with controls:
  - Higher prothrombin (115 ± 16 vs 102 ± 10%, $p < 0.0001$)
  - FV (114 ± 19 vs 102 ± 12%, $p = 0.0002$)
  - FVII (111 ± 15 vs 102 ± 17%, $p = 0.002$)
  - FVIII (170 ± 34 vs 115 ± 27%, $p < 0.0001$)
  - FIX (119 ± 21 vs 107 ± 17%, $p = 0.003$)
  - Lower TFPI (17.7 ± 3.2 vs 18.9 ± 3.2 ng/ml, $p = 0.047$)
  - FX, AT, and PC were similar in both groups.
  - COPD patients had abnormal ETP ($p < 0.0001$)

Thromb Res. 2011 Oct;128(4):e24-8.

Is SSPE a distinct subset of thromboembolic disease compared with proximal PE?

- 3728 patients with clinically suspected PE.
  - SSPE patients were contrasted to patients with more proximal PE and to patients in whom suspected PE was excluded
  - PE was confirmed in 748 patients, 116 (16%) had SSPE; PE was ruled out in 2980 patients.
  - No differences were seen in the prevalence of VTE risk factors
  - The 3-month risk of recurrent VTE (3.6% vs 2.5%; P .42), and mortality (10.7% vs 6.5%; P .17) between patients with SSPE and those with more proximal PE.
  - When compared with patients without PE, aged >60 years, recent surgery, estrogen use, and male gender were independent predictors for SSPE
  - Patients with SSPE were at an increased risk of VTE during follow-up (hazard ratio: 3.8; 95% CI: (1.3-11.1).
- Patients with SSPE mimic those with more proximally located PE in regards to their risk profile and clinical outcome.

Blood. 2013;122(7):1144-1149

Case 1

- Does COPD predispose to thrombosis?
  - Chest CTA and conventional angiography
    - same diagnostic performance in patients with and without COPD. Prevalence of PE similar to other patient populations, suggesting equivalent sensitivity of the test and absence of association between PE and COPD
  - There is a similar distribution of D-dimer results in patients with and without COPD, suggesting COPD had no influence on the diagnostic accuracy of the test for thromboembolic disease
  - There is no increased prevalence of elevated D-dimer with COPD exacerbation.

Hartmann et al. Am J Respir Crit Care Med, 162:2232–37.

Case 1

- **This patient has a detected SSPE**
- **Can SSPE cause exacerbation of COPD**
- **Is SSPE incidental and unrelated to presentation**

Hartmann et al. Am J Respir Crit Care Med, 162:2232–37.

Case 2

- 64-year-old carpenter with no significant past medical history or smoking history
- Developed proximal DVT and treated with apixaban 10 mg twice daily and was compliant with the dose and frequency of administration
- The patient presented to the emergency room 3 days later with SOB
- The CTA + for PE The patient is compliant with taking the prescribed dose of apixaban.
- AntiXa levels were detectable on admission
- How should this patient be treated?

Case 2

- **AC prevents further thrombosis. It does not lyse or assist in the organization of the existing thrombi.**
- **It takes approximately 5-12 days for a clot to firmly attach to the vein wall to be endothelialized[1]**
- **Therefore early after thrombotic event the clot is friable and may fragment**
- **It takes a long time for thrombus to resolve with AC alone[2-5]**
- **Frequency of extension of thrombus within 7-10 days of starting AC[6-9]**
  - **LMWH – 6%; UFH-10%; apixaban-0.68%**

1. *J Vasc Surg*. 2008 March ; 47(3): 616–624.
2. Kearon et al. *Circulation*. 2003;107:I-22–I-30
3. Aghayev et al. AJR. 2013;200(4):791-797
4. Van Es et al. JTH. 2013;11:679-685
5. Stein et al. AJR. 2010;1263-1268
6. Circulation. 2003;107(23 Suppl 1):I22-30.
7. N Engl J Med. 1972;287(7):324-27.
8. Am J Med.1996;100:269-277
9. Thromb Haemost. 2016;115(4):809-16.

Case 3

- **69 year old physician asks whether he should continue anticoagulation and relates the following:**
  - Remote history of acute diverticulitis requiring partial colectomy and complicated by deep vein thrombosis.
  - Heterozygous Factor V Leiden mutation +
  - 7 month ago developed poorly controlled hypertension and SOB
  - Chest CTA: segmental and sub-segmental pulmonary emboli
  - Receiving rivaroxaban x 6 months
  - Self-diagnosed Cushing's Disease
  - S/P endoscopic, endonasal Pituitary adenectomy

Importance of Residual Venous thrombosis (RVT)

- 258 patients who received 3 months of AC were included and followed for at least one year
- 180 patients (70%) had RVT
- 78 (30%) did not have RVT
- Among patients with RVT
  - 88 patients continued AC x 12 months
  - 92 patients stopped AC X 3 months
  - Unprovoked (75%) vs provoked (25%)
- RVT+ 23.3% recurred vs RVT- 1.3% recurred
  - Unprovoked-RVT+ 21.1% recurred
  - Provoked-RVT+ 8.7% recurred

RVT is a risk factor for recurrence in both unprovoked and provoked VTE

Siragusa et al. Blood 2008; 112:511-515

Factors Suggesting Thrombophilia

- Age < 50 years
- Atypical site (hepatic, mesenteric, cerebral veins
- Previous thrombosis or family history of thrombosis
- No identifiable provoking risk factors
- Recurrent pregnancy loss
- Repeated evidence of intra-uterine growth retardation

Zhu et al. Arterioscler Thromb Vasc Biol 2009;(3): 298-310
Bates et al. Chest 2008; 133(6 suppl):8445-8865
Hansson et al Arch Intern Med; 160(6):769-774
Martinelli et al. Blood. 1998;92(7): 2353-2358

Importance of Residual Venous thrombosis (RVT)

Type of DVT	RVT cont. AC x 12 m		RVT stop AC at 3 m		No RVT stop AC at 3m	
	Events/total (%)	#/100 PY	Events/total (%)	#/100 PY	Events/total (%)	#/100 PY
Provoked	4/22 (18.2)	10.4	20	9.9	0	0
Unprovoked	13/66 (19.7)	10	29.2	16.9	3.6	1.9

Siragusa et al. Blood 2008; 112:511-515

D-dimer and Residual Vein Obstruction as Risk Factors for Recurrence after 1st Provoked DVT

	HR (95%CI)	
T0 (n=273)	**RVO (-)**	**RV (+)**
DD normal	1	1.13 (0.3-4.3) p=0.85
DD elevated	4.8 (0.7-31.3) p=0.10	4.4 (0.9-23) p=0.07
T1 (n=274)		
DD normal	1	4.2 (0.4-38) p=0.2
DD elevated	15 (1.7-139) p=0.01	6.8 (0.7-64) p=0.09

T0 – determined at AC withdrawal
T1 – determined 30 days after AC stopped

Cosimi et al. Thromb Haemost. 2011; 105:837-845