

Pulmonary Embolic Disease: Challenging the Conventional Wisdoms and Algorithms



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Disclosure

- No relevant financial disclosures

Lecture Objectives

- Briefly review the Pulmonary embolic Multispecialty literature & clinical “conventional wisdoms”
- Describe the Natural Fate of a DVT and the Lungs Role with the Emboli, With or Without Therapy
- Review the most relevant Imaging Clues regarding prognosis
- **“Where all think alike, no one thinks very much.” – Walter Lippmann**

Lecture Format

- Virchow’s triad & The lung’s function
- Risk factors for Thrombosis formation
- Patient symptoms, signs, chest radiograph
- Pulmonary CTA: Advantages & Problems
- Outcomes with versus without therapy

Qualifications?

- I am a *cardiopulmonary radiologist*, not a hematologist
- *Nor* do I even remotely enjoy looking over the coagulation cascade diagrams
- Just an Curious physician whose observations over the last decade *have not matched* much of the *common* teachings and *strongly* stated recommendations

Let’s Start With an example

- 28 year old female radiology resident developed sudden onset of shortness of breath with tachycardia (130) while on call...
- 88% O2 on room air & No chest pain
- Multiple sizable pulmonary emboli found on CT with heart strain (*She read her own CT*)
- Within 1 hour of IV heparin, her SOB resolved, O2 was 98% (RA) & Heart Rate was 80 (Then she went back to work in the Call Room!)

She was Pregnant

No...I lied

Well, she was on oral
contraceptive pills

No...I lied again

Why did she develop a large
DVT and Pulmonary Emboli?

Why did she Improve so quickly
with IV Heparin?

Would either of these questions have been posed *if she was actually pregnant or on Oral Contraceptive pills?*

**“The Greatest Obstacle to
Discovery is Not
Ignorance...It is The Illusion
of Knowledge”**

Daniel J. Boorstin

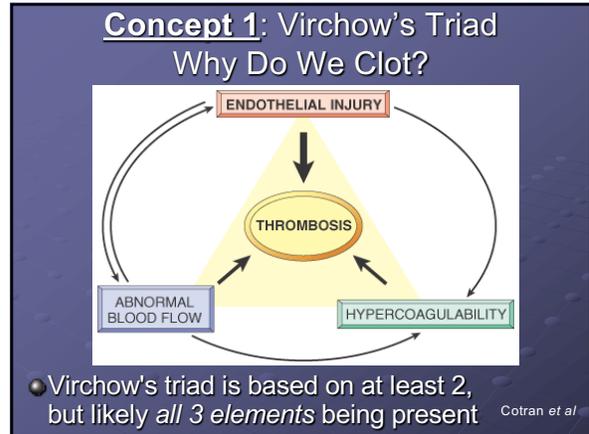
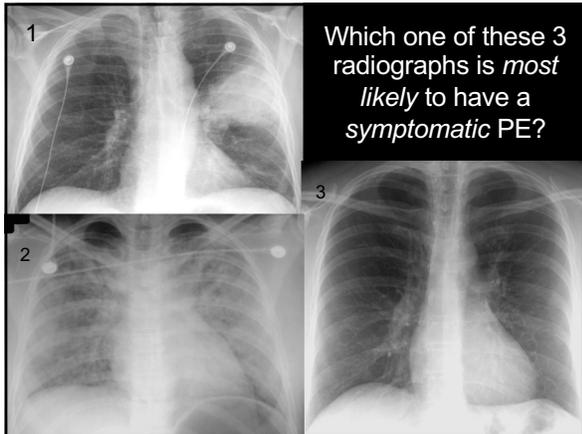
When **conventional wisdom/fear** is substituted for clinical judgment, observation and reason...

● **Emedicine:** Pulmonary Embolus

“Symptoms that should provoke a suspicion of PE must include chest pain, chest wall tenderness, back pain, shoulder pain, upper abdominal pain, syncope, hemoptysis, shortness of breath, painful respiration, new onset of wheezing, any new cardiac arrhythmia, or *any other unexplained symptom referable to the thorax.*”

“Eminence” Based Medicine



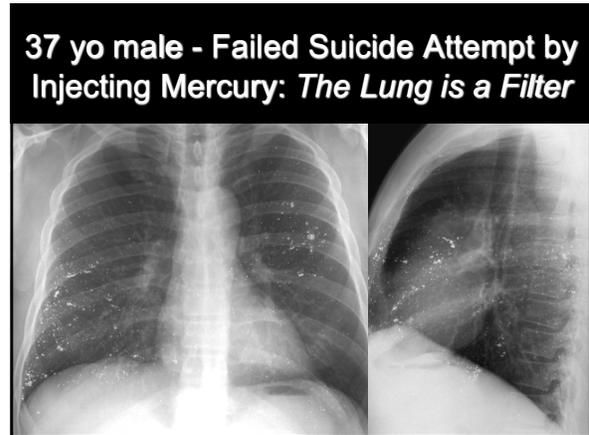


Concept 2: The Study of Evolution

- What is the function of the lung?
- **It is a Filter**

The *Liver & Lungs* are The Organs That Have A Dual Blood Supply.

Why?



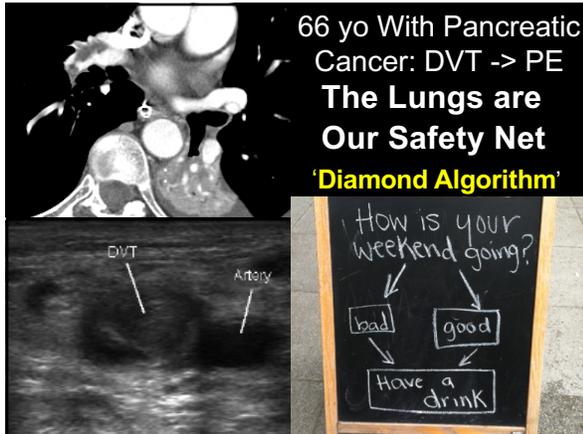
Concept 3: What Happens To The DVT?

- The venous endothelium *does not appear to use* fibrinolytic enzymes to break up the clot
- *Neutrophils & Monocytes* are important – It is handled via an **Inflammatory reaction** - 'Wound healing' & Where do the dislodged pieces of clot go?

● Mechanisms of Venous Thrombosis and Resolution
Arterioscler Thromb Vasc Biol 2008, 28:387-391

Lungs are often required for DVT clearance & resolution

- Pulmonary capillary endothelium has a **complete complement** of fibrinolytic enzymes to effectively break down clot
- In Essence – **DVT's Go To The Lung Where They Are Caught & Then Broken Down (Recycled)**



Beware: Renal Dialysis Patients

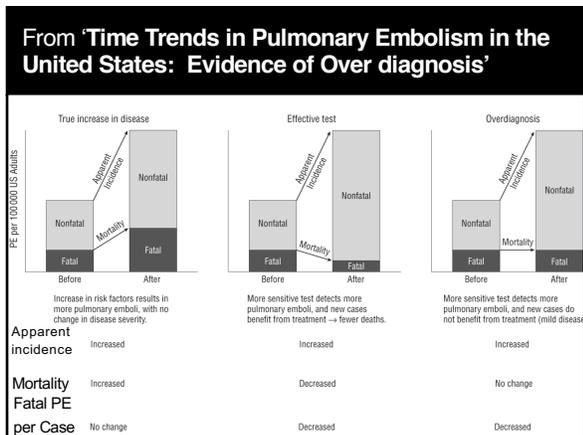
- **Fistula** is often the source of small PE's in these patients
- Do we treat these PE's?
- **Risks of Therapy** in these patients versus **Risks of Withholding Therapy**?
- How about looking in the legs and staying away from the lungs: Pandora's box!

Concept 4: Incidence of PE

- >70% of PE are incidental (Pathology)
- We *often* find multiple or even large incidental PE's on scans (1.5% outpatients, 6-9% inpatients, 9% with malignancy and 24% trauma patients)
- 5-9% positive rate with ED patients and 10-15% for inpatients when looking for PE
- The diagnosis is likely considered too quickly & with lower pretest probabilities
- "We do have an "easy" test to look for it"

Concept 5: Pulmonary Embolism in the United States; Evidence of Overdiagnosis

- *Arch Intern Med.* 2011;171(9):831-837
- The introduction of CTPA was associated with changes consistent with overdiagnosis: Rising incidence, minimal change in mortality, and *lower case fatality*.
- **Mortality changed little because many of the extra emboli may not have needed treatment at all.**



OHSU Data: Clinical Assessment

- 575 pulmonary CTA's done from ED or inpatients over 14 months
- Review of presenting symptoms & probabilities based on Well's criteria
- Clinical risk factors and the use of D-dimers were examined
- **9.6% had PE:** 12% inpatients & 8.5% of ED patients
- AJR. 2008; 191:471-474

Score by Wells et al. (11)	
Elements	Points
Previous PE or DVT	+1.5
Heart rate > 100/min	+1.5
Recent surgery or immobilization	+1.5
Clinical signs of DVT	+3
Alternative diagnosis less likely than PE	+3
Hemoptysis	+1
Cancer	+1
Clinical probability	
Low	0-1
Intermediate	2-6
High	>7

Pulmonary Embolism Prediction Model: Well's Criteria

Our retrospective evaluation of Well's criteria application found that **3 patients (NOT 3%)**, meet criteria for high probability

RESULTS (Note: 33% were women < 40 years old)						
Well's Criteria Clinical Probability	PE Positivity	D-dimer <0.5	D-dimer 0.5-2.0	D-dimer >2	D-dimer Not Obtained	SUM
High	PE NEG	0	0	0	1	33%
(0.5% of total)	PE POS	0	0	1	1	66%
Intermediate	PE NEG	8	20	15	91	85%
(28% of total)	PE POS	0	2	4	18	15%
Low	PE NEG	30	84	48	223	93%
(72% of total)	PE POS	0	1	10	17	7%
OVERALL RATE OF POSITIVE PE = 9.6%					61%	N=575

Conclusions

- We found a suboptimal use of validated clinical criteria (Well's or Geneva) and an *overestimation* of the probability of PE
- The CTA was more of a "screening" test rather than a diagnostic examination
- Risks of Radiation, contrast induced renal injury, Overdiagnosis and increased costs from unnecessary exams are often not deemed relevant

7 Step program to reduce CTA in the ED setting

- Step 1: Accept you can't identify every emboli
- Step 2: Recognize that any approach to detect All emboli does more harm than good.
- Step 3: Risk-Stratify & reduce testing
- Step 4: Try 'Watchful Waiting'
- Step 5: Document your decision-making
- Step 6: Be less afraid of litigation
- Step 7: Spread the word
- *'We will not always be right with individual patients, but aggressive testing for all only shifts who receives what bad event; it does not decrease harm universally.'*

Green, S & Yealy, D. Editorial on Article from Ann Emerg Med. 2012;59:524-526

D-Dimer adjustment

- Bayes Theorem Post test probability with the over sensitive D-dimer test
- Hirai, L et al found a 1.0 D-dimer threshold to be a more effective level to use in the ED
- Kline et al found using a variable D-dimer between .75 and 1.0 based on pre-test probability was effective for the ED

Hirai, L et al: J Vasc Interv Radiol 2007; 18:970-874

Kline, JA et al: Journal of Thrombosis and Haemostasis, 10 572-581

Concept 6: Right Ventricular Strain

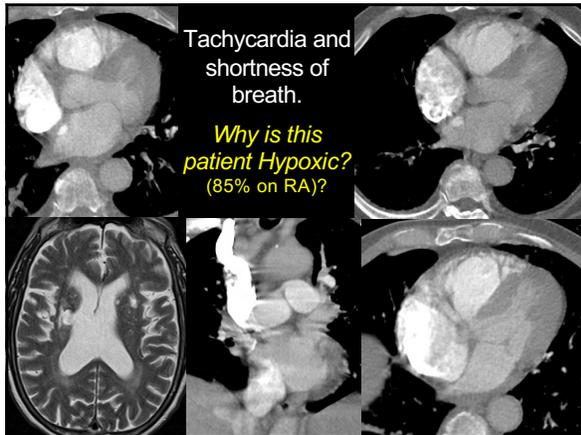
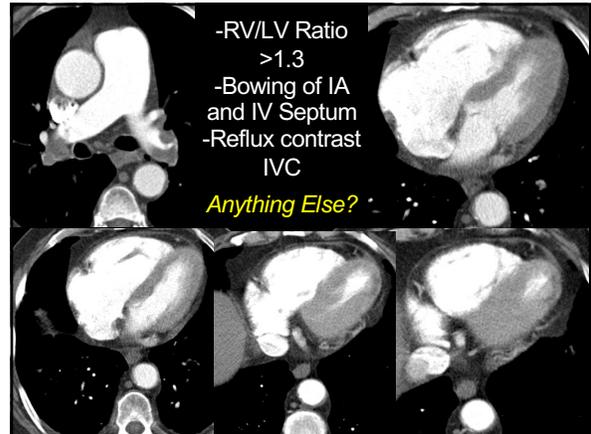
- ****Not associated with Clot burden****
- Tachycardia (B-blocker present?)
- PFO opens (pop off valve)
- **RV strain is the most important imaging finding** to look for, learn and document
- Also associated with RV Strain were PE in **Lobar arteries** and **increased troponin**
- Saddle Embolus **was not associated**

Chest 2102; 142: 1417-1424

Right Ventricular Strain

Look closely at the heart on All CTA's

- RV/LV chamber ratio >1.0 suggests it, but better specificity if >1.2
- Straightening of the IV septum is a very specific sign, although some interobserver variability
- Reflux of hyperdense contrast into IVC and hepatic veins
- Leftward bowing of IA septum helpful

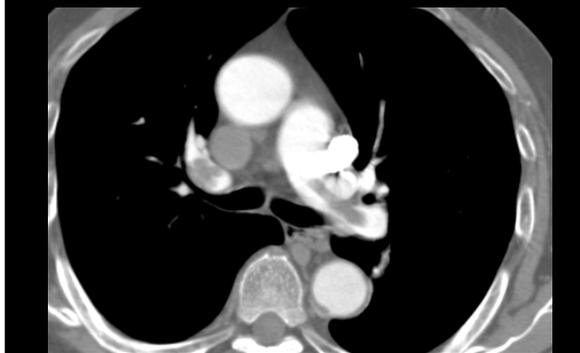


Concept 7: "Sufficient" Risk Factors

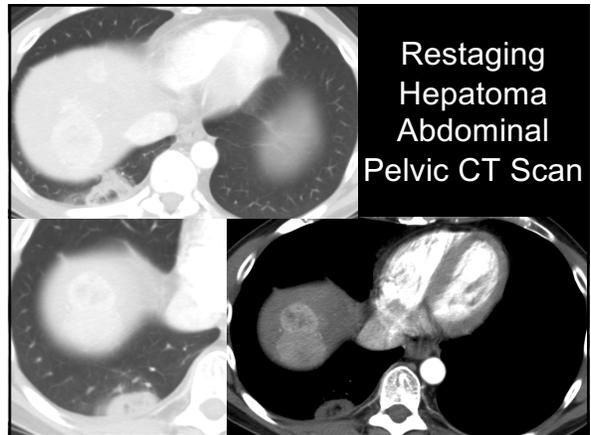
OHSU Study (51 out of 54)

- Major trauma
 - Neurological: Trauma, surgery or tumor
 - Major surgery: especially cardiovascular, abdominal or orthopedic (*C-section too*)
 - Active malignancy
 - Hyper-coagulation state - Transient vs. Life long, Provoked vs. Idiopathic, Inflammatory State* (Sepsis?) *Atheroscler Thromb
- Vasc Biol. 2008;28:387 Wakefield, Meyers & Henke

Metastatic Colon Cancer:
6 Weeks S/P Chemo Rx. - No Symptoms



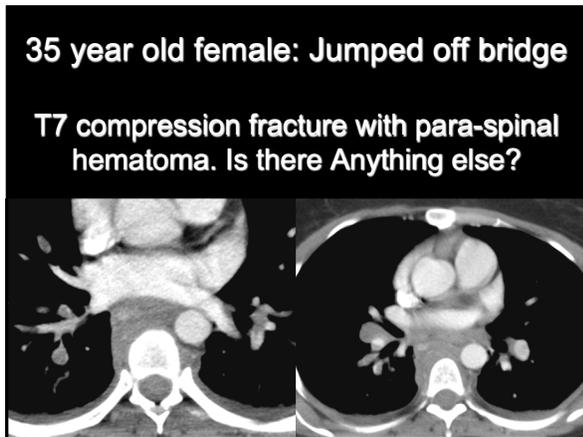
Restaging
Hepatoma
Abdominal
Pelvic CT Scan





Hypercoagulability Seen In Immediate Post-Trauma Setting

- Schreiber et al. Journal of Trauma 2005
- Use of the *Thrombelastograph analyzer* gives comprehensive functional evaluation of overall coagulation status
- “Activated” coagulation system highest in first 24 hours of injury
- Progressively decreases over next 3 days



Concept 8: “Trigger Events”

Component Causes

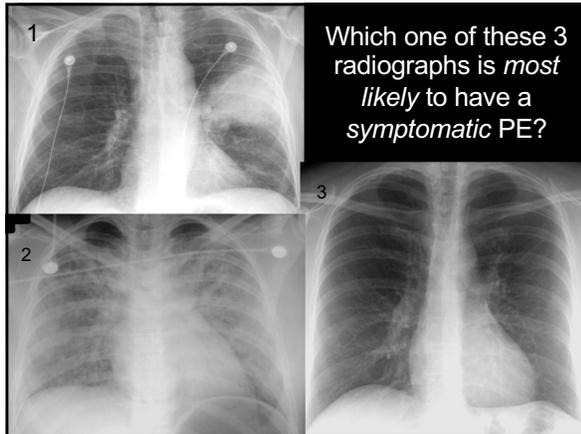
- Physiological states where clotting occurs *only in the presence* of other risk factors
- Increasing Age
- Immobilization: Plane or Car ride (or a Radiologist on call)
- Oral Contraceptives: Very, very small risk
- Pregnancy: 1/1000 *and* - the majority have an underlying thrombophilia (67%)
- Obesity?

Case 9: Symptomatic PE Common Exam & Vitals

- Acute onset of Shortness of breath (85%)
- Tachycardia (70%) (on B-blocker?)
- Chest radiograph often is normal (80%)
- Mild - moderate hypoxia on room air (65%)
- Differential: Asthma/small airways infection (Is there wheezing on auscultation?)

Acute dyspnea and mild hypoxia





Concept 10: The Ignored V/Q scan Excellent For Young Patients

Uniform distribution of Xenon gas
<0.01 mGy to fetus

Perfusion (Tc-99m) scan "High Probability"
0.9 -18 mGy to fetus

www.vh.org, Huda

CTA

A CT scan of the female thorax will give a dose of **250 CXRs** to the lungs and about **100 mammograms** to the breasts

0.14 mGy to fetus - Higher during 3rd trimester!

Patel et al, Huda, Milne

V/Q Scan Vs. CTA in Pregnant Women

- Ridge et al. AJR: 193 Nov 2009 (Ireland)
- V/Q diagnostic **96%** of the time
- CT diagnostic **64%** of the time
- V/Q exposes *mom* to *much less* radiation
- Fetus: Slightly more 1st trimester, slightly less in 3rd trimester
- V/Q less cost (especially if only perfusion)

Scanners are Too Good!

The Unexpected PE Problem

- We can not treat *everyone* ALL or Nothing
- Understanding which **subset of people** are most likely to benefit from therapy versus which are more likely to have an adverse affect is our future challenge
- **First, we need to release some conventional wisdoms & Eminence based teaching regarding PE's**

Concept 11: PE Mortality Exaggerated

- 1939-1961 work was retrospective, on inpatients & post surgical patients
- Data skewed as to mortality (18-35%), which is **still often quoted today***
- What is the natural evolution of VTE events
- 1960's saw a brief number of anticoagulation studies; most did *not* use a Control Group

* Calder: Mortality of Untreated Pulmonary Emboli in ED patients. Annals of Emerg Med; Vol 45; No. 3; March 2005

What Subset of Patients is PE Fatal?

Our Study: 2% **Symptomatic** PE were Fatal

- The vast majority of incidental PE in relatively healthy people (Cardiopulmonary function), even with large clot burden had good outcomes
- Average age-related death rates from PE is **2.3 (Caucasian) – 6.0 (African American) per 100,000 persons**
- Most deaths from pulmonary embolus occur in patients with Comorbid factors such as severely compromised cardiopulmonary function, cancer patients, increasing age and ICU setting

- Lilienfeld. International Journal of Epidemiology 2000;29:465-469.
- Calder – Annals of Emerg Medicine. Vol 45, No. 3 March 2005

Concept 12: Duration of Therapy

“People are like Snowflakes”

- **Not** All Thrombi, Emboli & Cardiopulmonary Functions are the same
- Algorithmic approach is based on faulty assumptions & inadequate studies
- **Idiopathic versus provoked thrombosis** seems to be the biggest determinant for risk of recurrent thrombosis

Nielson et al. 1994

- 87 ambulatory, relatively healthy patients with DVT (*Most* had asymptomatic PE)
- 46 randomly selected for therapy
- 41 randomly received *no* therapy
- Result after 60 days: **No difference in mortality, silent emboli, clot regression or progression**
- 1 patient died of PE, in the *treated* group

- J Intern Med 1994;235:457-461 (Cited by Cochrane Library)

Anticoagulation for Acute Venous Thromboembolism/PE

The NNT Website

In Summary, for those who got the anticoagulation:

- 100% saw no benefit
- 0% were helped by being saved from death
- 0.9% were harmed by a major bleeding event
- 0.9% were harmed by dying due to the bleeding

In Other Words:

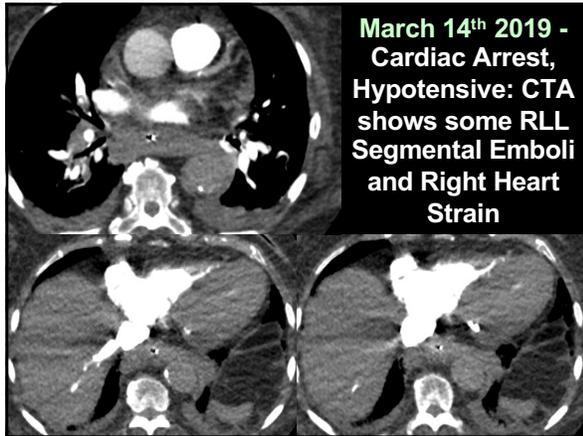
- None were helped (life saved, preventing PE)
- 1 in 50-111 were harmed (major bleeding event)
- 1 in >50 were harmed (death bleeding event)

Concept 13: How Does IV Heparin Improve Symptoms so Quickly?

- *Within 1-2 hours of starting IV Heparin; Symptoms often Improve*
- IV Heparin is a **Pulmonary Arterial Vasodilator** - Other Vasodilators found to have a similar Effect on Symptomatic PE
- **Pulmonary Vasoconstriction** appears to be common with Symptomatic patients
Cardiovascular Research 48 (2000) 23-33
- **Why bridge heparin for coumadin again?**

Question: When should one consider Thrombolytics/IR therapy?

- **Most** right heart strain relates to vasoconstriction
- **Small numbers** of patients the right heart strain is secondary to mechanical obstruction.
- What *could you suggest* to the ED physician when giving the CT report?



Summary

- Function of the lungs – *A Filter*
- Risk factors versus “Trigger” Events
- Signs, Symptoms, Radiograph & D-dimer
- CTA is not a screening study (*Overdiagnosis*)
- Pulmonary *Vasoconstriction*-Induced PVR Elevation From The Emboli.

Thank You

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