

# Pulmonary Embolism in AE-COPD How Common?

Amnon Ariel

Emek Med Ctr



# PE-AE-COPD - Introduction

## Is PE “common” in AE-COPD?

- PE is **difficult** to dx. & largely **under-dx**
- **AE-COPD problematic ddx. Scenario** for PE
  - Similar presentation
  - **VQ scan more commonly indeterminate**
- **Varied incidence** of PE in AE-COPD (**3-30%**)

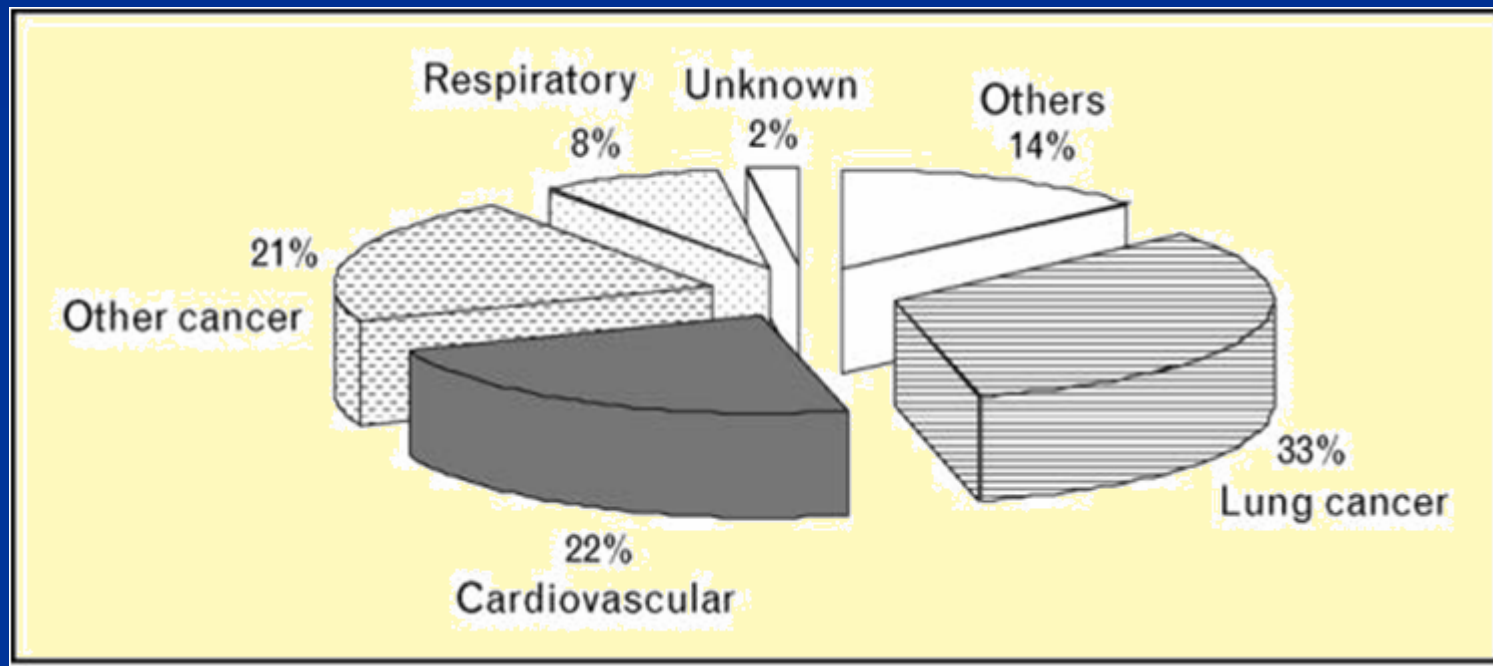
# PE in COPD – Issues/Outline

- **The Impact** of PE in COPD
- **How to dx. PE in AE-COPD?**
- **How common** is PE in AE-COPD
- **Implications;**
  - ? Investigate all AE-COPD of “unknown origin”?
  - ? VTE prophylaxis to all AE-COPD

# The Impact of PE in COPD

# Causes of Death in the Lung Health Study

Anthonisen NR, Skeans MA, Wise RA, et al. The effects of a smoking cessation intervention on 14.5-year mortality: a randomized clinical trial. *Ann Intern Med* 2005; 142:233–239.



# CVD & PE more common in COPD

- 1996-1999 Kaiser Permanente North California
- Database Case – Control study
- 46000 COPD vs 46000 Non-COPD Controls
- **PE-Hosp RR =2.5-3; PE-Mort RR=1.5-2.5**
- CHF-Hosp RR =3.5; CHF-Mort RR=3.5

**COPD and Incident Cardiovascular  
Disease Hospitalizations and Mortality:  
Kaiser Permanente Medical Care  
Program\***

*(CHEST 2005; 128:2068-2075)*

*Stephen Sidney, MD, MPH; Michael Sorel, MPH;  
Charles P. Quesenberry, Jr., PhD; Cynthia DeLuise, RPA-C, MPH;  
Stephan Lanes, PhD; and Mark D. Eisner, MD, MPH, FCCP*

**How to dx. PE in AE-COPD?**

# PE Clinical Suspicion Clinical Decision Rule (Wells Criteria)

## Difficult clinical prediction in AECOPD

Symptoms and signs of acute pulmonary embolism

	Frequency
<b>Symptom</b>	
Dyspnea	73 percent
Pleuritic chest pain	66 percent
Cough	37 percent
Hemoptysis	13 percent
<b>Sign</b>	
Tachypnea	70 percent
Rales	51 percent
Tachycardia	30 percent
Fourth heart sound	24 percent
Accentuated pulmonic component of second heart sound	23 percent
Circulatory collapse	8 percent

Data from Stein, PD, et al. Chest 1991; 100:598.

Data from Stein, PD, et al. Am J Cardiol 1991; 68:1723.

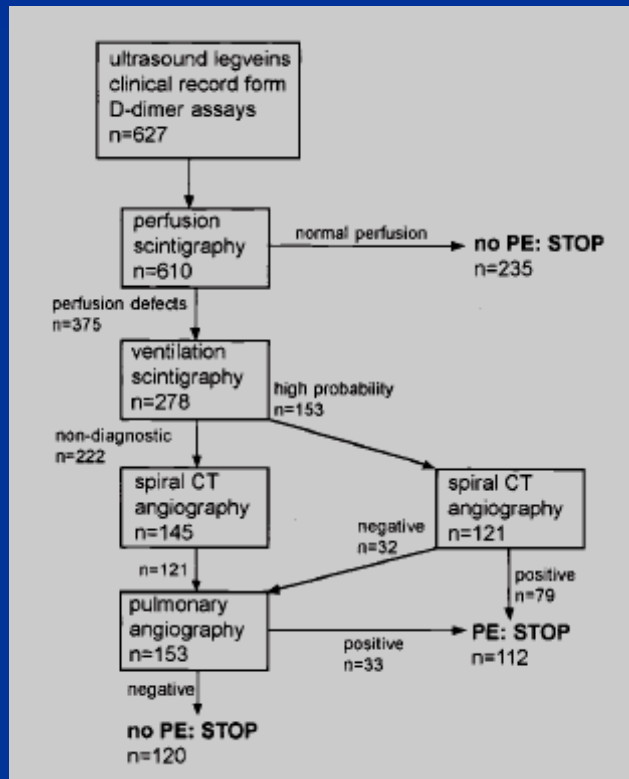
Modified Wells criteria: clinical assessment for pulmonary embolism

Clinical symptoms of DVT (leg swelling, pain with palpation)	3.0
Other diagnosis less likely than pulmonary embolism	3.0
Heart rate >100	1.5
Immobilization (≥3 days) or surgery in the previous four weeks	1.5
Previous DVT/PE	1.5
Hemoptysis	1.0
Malignancy	1.0
<b>Probability</b>	<b>Score</b>
<b>Traditional clinical probability assessment</b>	<b>VQ Scan Algorithm</b>
High	>6.0
Moderate	2.0 to 6.0
Low	<2.0
<b>Simplified clinical probability assessment*</b>	<b>CTA Algorithm</b>
PE likely	>4.0
PE unlikely	≤4.0

Data from van Belle, A, et al. JAMA 2006; 295:172.

# D-Dimer, VQ & sCT in PE-COPD

- ..COPD does not affect the dx performance of CPE, D-dimer, SCTA, or pulmonary angiography.
- ...although more nondiagnostic VQ scan results can be expected
- ...scintigraphy remains a valuable screening test in COPD.



PERFORMANCE OF VENTILATION/PERFUSION SCINTIGRAPHY, SPIRAL COMPUTED TOMOGRAPHIC ANGIOGRAPHY, AND D-DIMER TESTING IN DIAGNOSING PULMONARY EMBOLISM IN PATIENTS WITH AND WITHOUT CHRONIC OBSTRUCTIVE PULMONARY DISEASE

	COPD (n = 69)	No COPD (n = 448)	Difference (95% CI), p Value
<b>V/Q scintigraphy (high probability)</b>			
Sensitivity	79	88	9 (-10-28), 0.37
Specificity	92	96	4 (-4-12), 0.33
Positive predictive value	79	90	11 (-8-30), 0.24
Negative predictive value	92	94	2 (-5-11), 0.50
<b>D-dimer test</b>			
Sensitivity	82	82	0 (-24-24), 1.0
Specificity	65	63	-2 (-19-15), 0.83
Positive predictive value	43	52	9 (-14-32), 0.44
Negative predictive value	92	88	-4 (-17-8), 0.52
<b>SCTA</b>			
Sensitivity	53	70	17 (-9-44), 0.21
Specificity	91	85	-6 (-18-6), 0.34
Positive predictive value	73	84	11 (-16-39), 0.40
Negative predictive value	81	71	-10 (-25-5), 0.21

# How common is PE in AE-COPD

What do you think is the “true incidence” of  
AE-COPD/PE

**3% ?    30?**

# PE (CTA) in 22-25% of ER & in-Hosp Non-Infectious (Lille, France) “AE-COPD of unknown origin”

## Methods:

- Adm. AE-COPD with susp/pos PE → in 48hrs (CTA & US) → 3mo FU

## Results:

- 43/197 (22%) ; CTA+ (19/43, 44%- also US+)
- 25/197 (13%); US+ (19/76% - CTA+; 6/25, 24% - CTA-) 12% of VTE – CTA-
- 49/197 (25%); “PE” = (of these 1% CTA-/VTE+)

Annals of Internal Medicine 2006;144:390–396.

Pulmonary Embolism in Patients with Unexplained Exacerbation of Chronic Obstructive Pulmonary Disease: Prevalence and Risk Factors

Isabelle Tillie-Leblond, MD, PhD; Charles-Hugo Marquette, MD, PhD; Thierry Perez, MD; Arnaud Scherpereel, MD, PhD; Christophe Zanetti, MD; André-Bernard Tonnel, MD, PhD; and Martine Remy-Jardin, MD, PhD

PE-COPD↑↑

# PE (CTA) in 22-25% of ER & in-Hosp Non-Infectious (Lille, France) “AE-COPD of unknown origin”

## Limitations:

- Flexible, Non-Standard (MD based) AE-COPD
- PE – pretest evaluation CDR (Geneva) – retrospective
- D-Dimer not systematically used?/mentioned
- **Selection Bias: “non-infectious, non-icu” AE-COPD.**
- **Confounding effect of acute medical hospital admission: In-Hosp PE-Dx. Included.**
- **Not a true prospective study, Selection Bias**

Annals of Internal Medicine 2006;144:390-396.

Pulmonary Embolism in Patients with Unexplained  
Chronic Obstructive Pulmonary Disease: Prevalence and Risk Factors

Isabelle Tillie-Leblond, MD, PhD; Charles-Hugo Marquette, MD, PhD; Thierry Perez, MD; Arnaud Scherpereel, MD, PhD;  
Christophe Zanetti, MD; André-Bernard Tonnel, MD, PhD; and Martine Remy-Jardin, MD, PhD

**PE-COPD↑↑**

# PE (CTA) in 3.3% of ER-ADM

## “AE-COPD of unknown origin” (Geneva, Swiss.)

(no pneumonia, no CHF) D-Dimer+ Pts.

### Methods:

- ER-Adm. AE-COPD with 123/521 (other dx, not NOT URTI excluded) → Non-formal pretest eval. (all included) → D-Dimer > 500 → CTA & US

### Results:

- **Clinical Pretest** PE+ / PE- = 48 (39%) / 75 (61%)
- D-Dimer > 500 PE+ / PE- = 37 (77%) / 58 (77%) p=0.97
- US+ PE+ / PE- = 1 (2.1%) / 1 (1.3%) p=0.63
- **CTA+** PE+ / PE- = 6 (6.3%) / 1 (1.3%) p=0.13

THORAX

Should pulmonary embolism be suspected in exacerbation of chronic obstructive pulmonary disease?

Olivier T Rutschmann, Jacques Cornuz, Pierre-Alexandre Poletti, Pierre-Olivier Bridevaux, Olivier W Hugli, Salah D Qanadli and Arnaud Perrier

Thorax 2007;62:121-125; originally published online 13 Nov 2006;  
doi:10.1136/thx.2006.065557

PE-COPD ↓↓

# PE (CTA) in 3.3% of ER-ADM “AE-COPD of unknown origin” (Geneva, Swiss.)

(no pneumonia, no CHF) D-Dimer+ Pts.

## Limitations:

- High exclusion 41% (ATC Rx, Consent, Allergy, Creat., Mech Vent)
- Non-Formal CDR– but prospective!
- No 3 mo. Follow-up
- Vs. Tillie-Leblond:
  - ER Based
  - Pretest evaluation
  - D-Dimer - utilized

THORAX

Should pulmonary embolism be suspected in exacerbation of chronic obstructive pulmonary disease?

Olivier T Rutschmann, Jacques Cornuz, Pierre-Alexandre Poletti, Pierre-Olivier Bridevaux, Olivier W Hugli, Salah D Qanadli and Arnaud Perrier

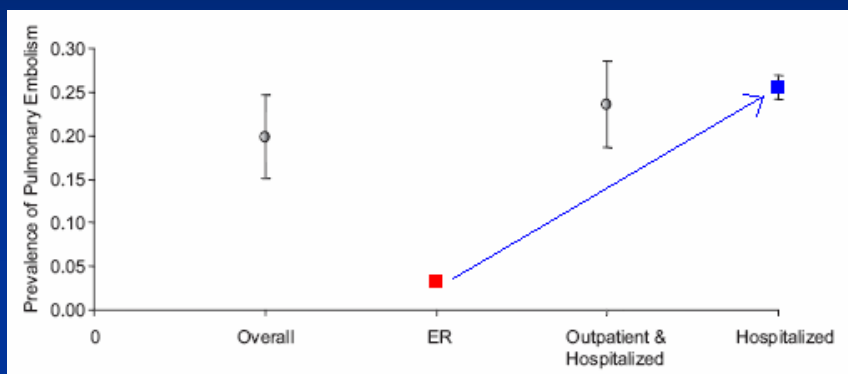
*Thorax* 2007;62:121-125; originally published online 13 Nov 2006;  
doi:10.1136/thx.2006.065557

PE-COPD ↓↓

# PE in “AE-COPD of unknown origin”

Systematic Review: **ER 3-6%/InPts? 20-30%**

Systematic Review (not really a Meta-Analysis, small no., heterogeneity)



	Tillie-Leblond	Rutchman
%PE+	25	1.3 CDR-/6.2 CDR+
Age [yrs]	61y	71y
% prev. VTE	25 PE+/7 PE-	3 all
% Surgery	4 PE+/2 PE-	2 all
% Cancer	43 PE+/24 PE-	5 all
% Travel Immobiliz	10 PE+/4 PE-	16 all
PE+ [RR]	Prev. VTE 2.4 Cancer 1.8	Chest pain, syncope, no sputum purulence

- ER & In-Hosp – different
- Validated CDR & Larger studies required

Prevalence of Pulmonary Embolism in  
Acute Exacerbations of COPD\*  
A Systematic Review and Metaanalysis

Jacques Rizkallah, MD; S. F. Paul Man, MD, FCCP;  
and Don D. Sin, MD, FCCP

(CHEST 2009; 135:786–793)

PE-COPD? ↓↓ ↑↑

# Implications & Summary

# Prevention of Venous Thromboembolism\*

## American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition)

William H. Geerts, MD, FCCP; David Bergqvist, MD, PhD;  
 Graham F. Pineo, MD; John A. Heit, MD; Charles M. Scamman, MD, PhD, FCCP;  
 Michael R. Lassen, MD; and Clifford W. Colwell, MD (CHEST 2008; 133:381S–453S)

### Prevention of Venous Thromboembolism\*

Table 4.

Approximate Risks of DVT in Hospitalized Patients (Section 1.2)\*

Patient Group	DVT Prevalence, %
Medical patients	10–20
General surgery	15–40
Major gynecologic surgery	15–40

Major urologic surgery
Neurosurgery
Stroke
Hip or knee arthroplasty
Major trauma
SCI
Critical care patients

Table 5—Levels of Thromboembolism Risk and Recommended Thromboprophylaxis in Hospital Patients (Section 1.3)\*

Levels of Risk	Approximate DVT Risk Without Thromboprophylaxis, %†	Suggested Thromboprophylaxis Options‡
<b>Low risk</b>		
Minor surgery in mobile patients	< 10	No specific thromboprophylaxis
Medical patients who are fully mobile		Early and “aggressive” ambulation
<b>Moderate risk</b>		
Most general, open gynecologic or urologic surgery patients	10–40	LMWH (at recommended doses), LDUH bid or tid, fondaparinux
Medical patients, bed rest or sick		
Moderate VTE risk plus high bleeding risk		Mechanical thromboprophylaxis§
<b>High risk</b>		
Hip or knee arthroplasty, HFS	40–80	LMWH (at recommended doses), fondaparinux, oral vitamin K antagonist (INR 2–3)
Major trauma, SCI		
High VTE risk plus high bleeding risk		Mechanical thromboprophylaxis§

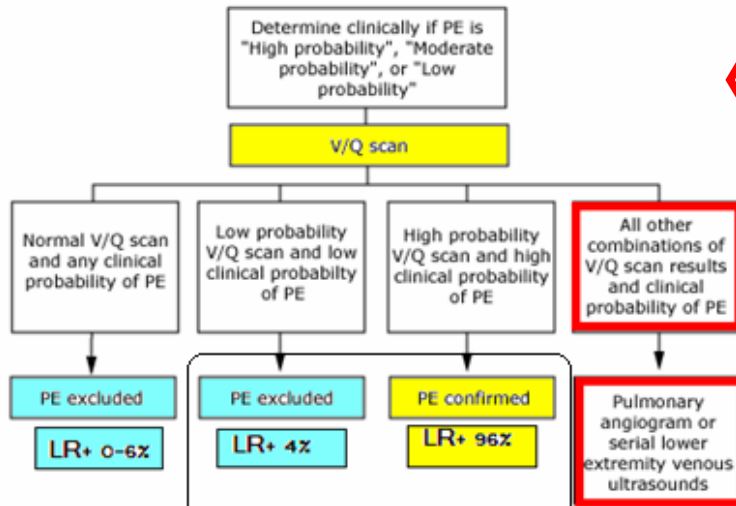
**Prevention of Venous Thromboembolism\***  
**American College of Chest Physicians Evidence-**  
**Based Clinical Practice Guidelines (8th Edition)**

*William H. Geerts, MD, FCCP; David Bergqvist, MD, PhD;  
Graham F. Pineo, MD; John A. Heit, MD; Charles M. Samama, MD, PhD, FCCP;  
Michael R. Lassen, MD; and Clifford W. Colwell, MD (CHEST 2008; 133:381S-453S)*

- ..hospitalization for an acute medical illness is independently associated with about an eight fold increased risk for VTE
- *6.0 Medical Conditions: 6.0.1. For acutely ill medical patients admitted to hospital with congestive heart failure or severe respiratory disease, ..., we recommend thromboprophylaxis with LMWH (Grade 1A)*
- ..study (683) compared a **LMWH**, nadroparin, to placebo in 223 pts who were receiving mechanical ventilation for exacerbations of COPD. **After a mean of 12 days, DVT was detected by routine venography in 28% of control subjects and 15% of LMWH recipients (RRR, 45%; p = 0.045). Major bleeding rates were 3% and 6%, respectively (p = 0.3)**

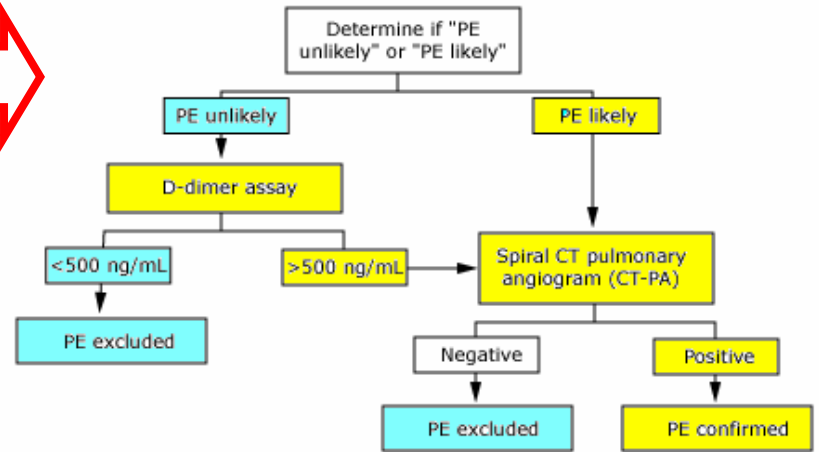
# Investigate AE-COPD/“unknown origin” who are “PE likely”

Diagnostic strategy used in patients with suspected pulmonary embolism



Hartman AJRCCM 2000  
46% vs 21% NonDx VQ  
in COPD vs non COPD

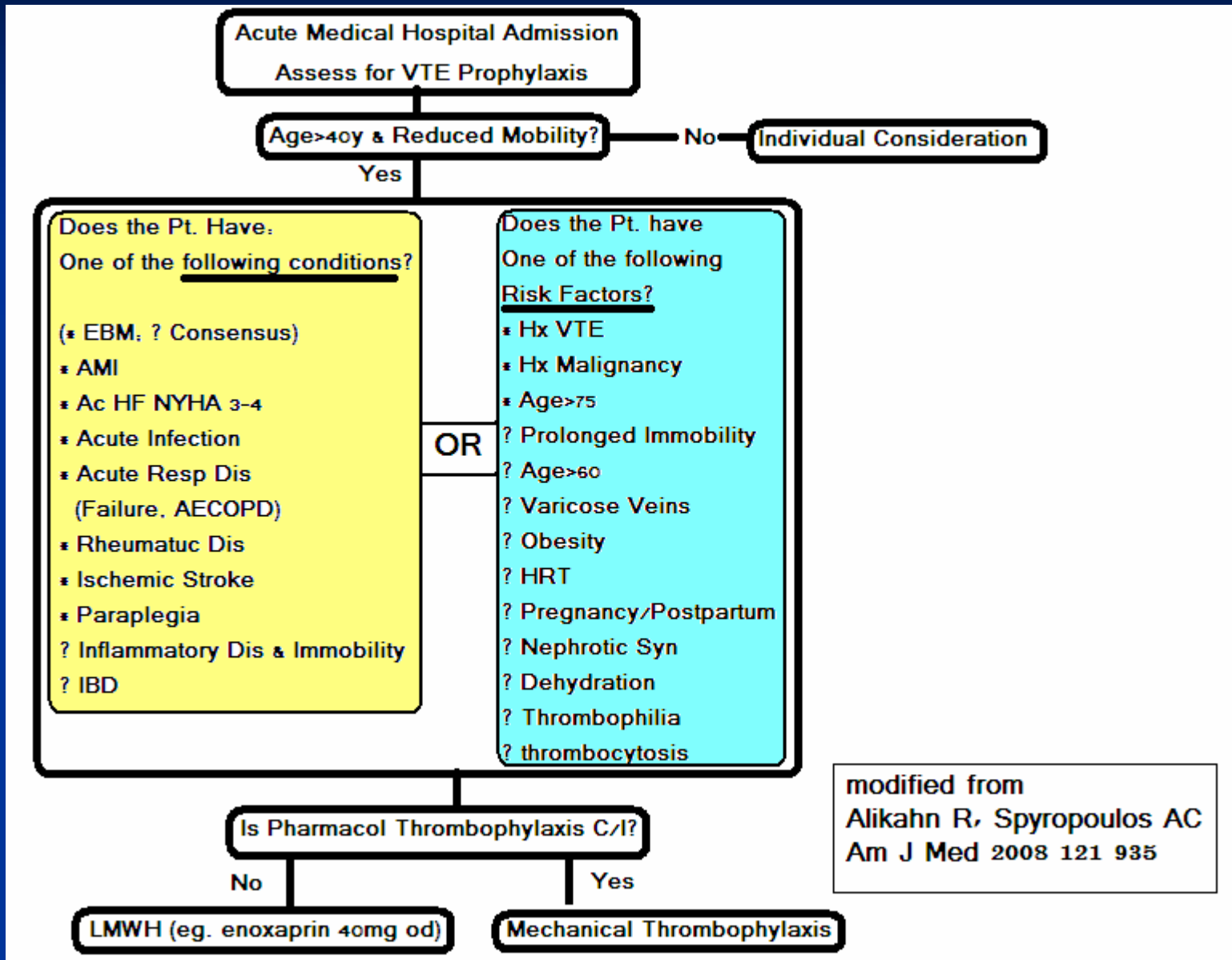
Diagnostic strategy used in patients with suspected pulmonary embolism



Adapted from van Belle, A, et al. JAMA 2006; 295:172.

Lower Extremity US (Serial 6/2wk)  
Pulmonary Angiogram  
MR Angiography  
3 mo. Follow-up

# Otherwise: VTE prophylaxis to all



# VTE-PE **cause** (5%) &/or **effect** (25%) of ADM-AE-COPD?

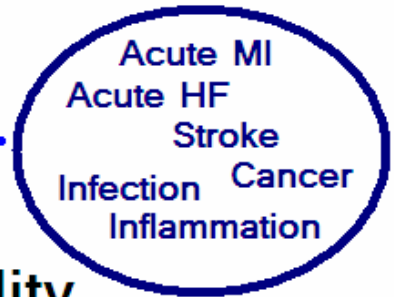
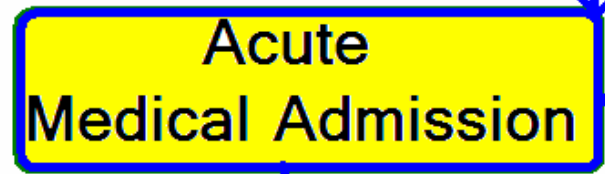
Smoking Genetics Inflammation Infection

Oxydative  
Stress

Hypercoagulability



immobilization  
hypoxia  
dehydration  
malignancy



Hypercoagulability



# Conclusion

- VTE Workup in AE-COPD  
In selected “PE-Likely” pts.
- VTE thromboprophylaxis  
in ADM-AE-COPD  
Yes – Unless C/I