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The Emergency Department Management of Pulmonary Embolism

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Goals

- PE is complication of venous thrombosis
- PE is very, very common
- Diagnosing only a very small % of PEs
- The classic symptoms are uncommon

20 y.o Male College Student with Hypotension & Questionable Syncope

- Found knocking at neighbors door
- BP=60/p P=125 R=24
- EMS with MAST-trousers
- PMH= none

Pulmonary Embolism

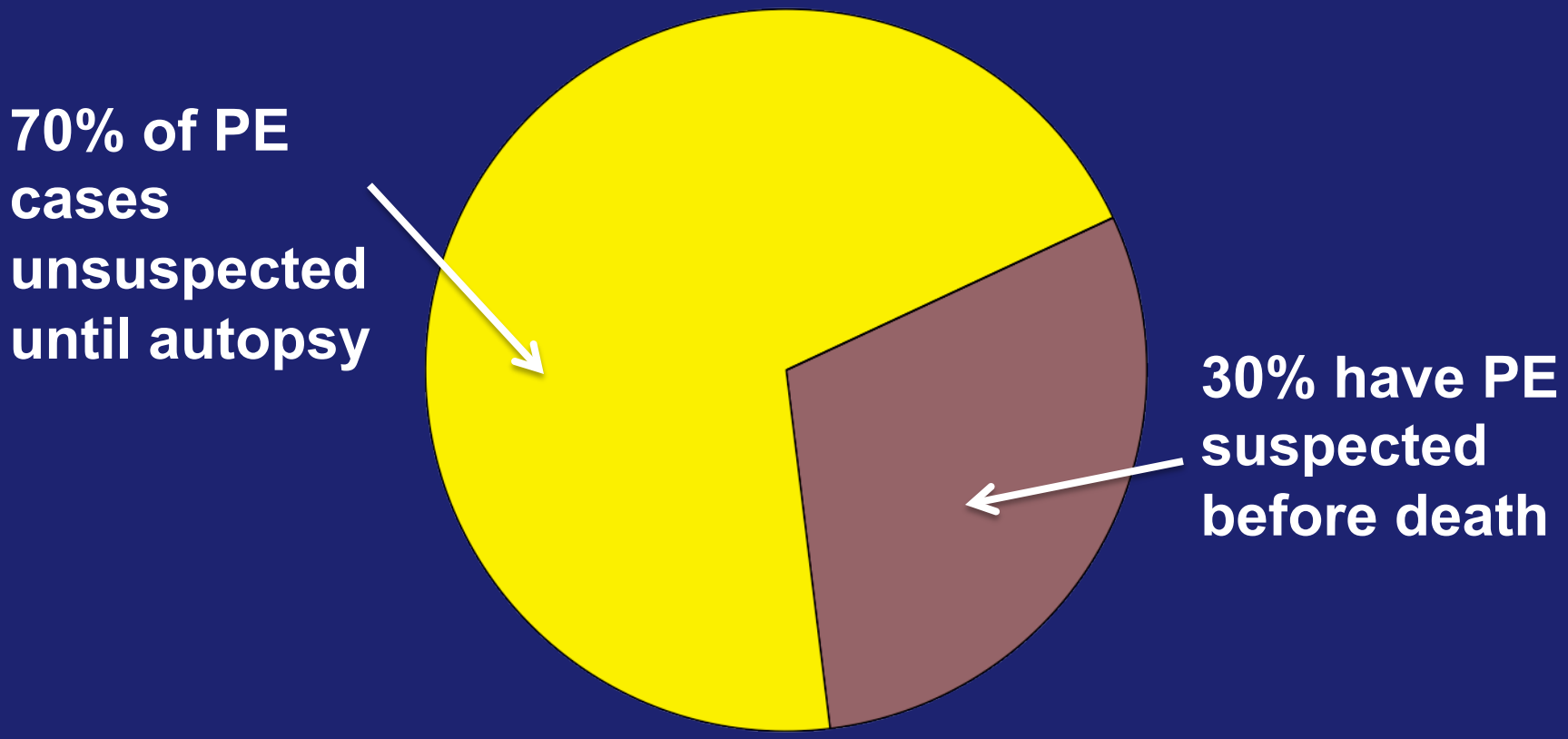
3rd most common cause of death

- Most common fatal missed diagnosis
- **#2** cause of unanticipated death (after MI)
- **#1** cause of unexpected death on ventilator
- **#1** cause of death in orthopedics
- **#1** cause of death in pregnancy

Papadakis: JAMA 1991; 265
Hecht: Zentralbl Allg Pathol 1984; 129

Fatal PE in-hospital

70% misdiagnosed antemortum



Reference: Coon: Arch Surg 1976;111

Mayo inpatient PE deaths
Autopsies between 1985 - 1989

- Listed cause of death correct in only 32%
- Only 22% had a diagnostic workup for PE
- 'Classic' symptoms absent in most cases
- 64% had no prophylaxis
- 46% had inadequate prophylaxis

Reference: Morgenthaler: Mayo Clin Proc 1995; 70

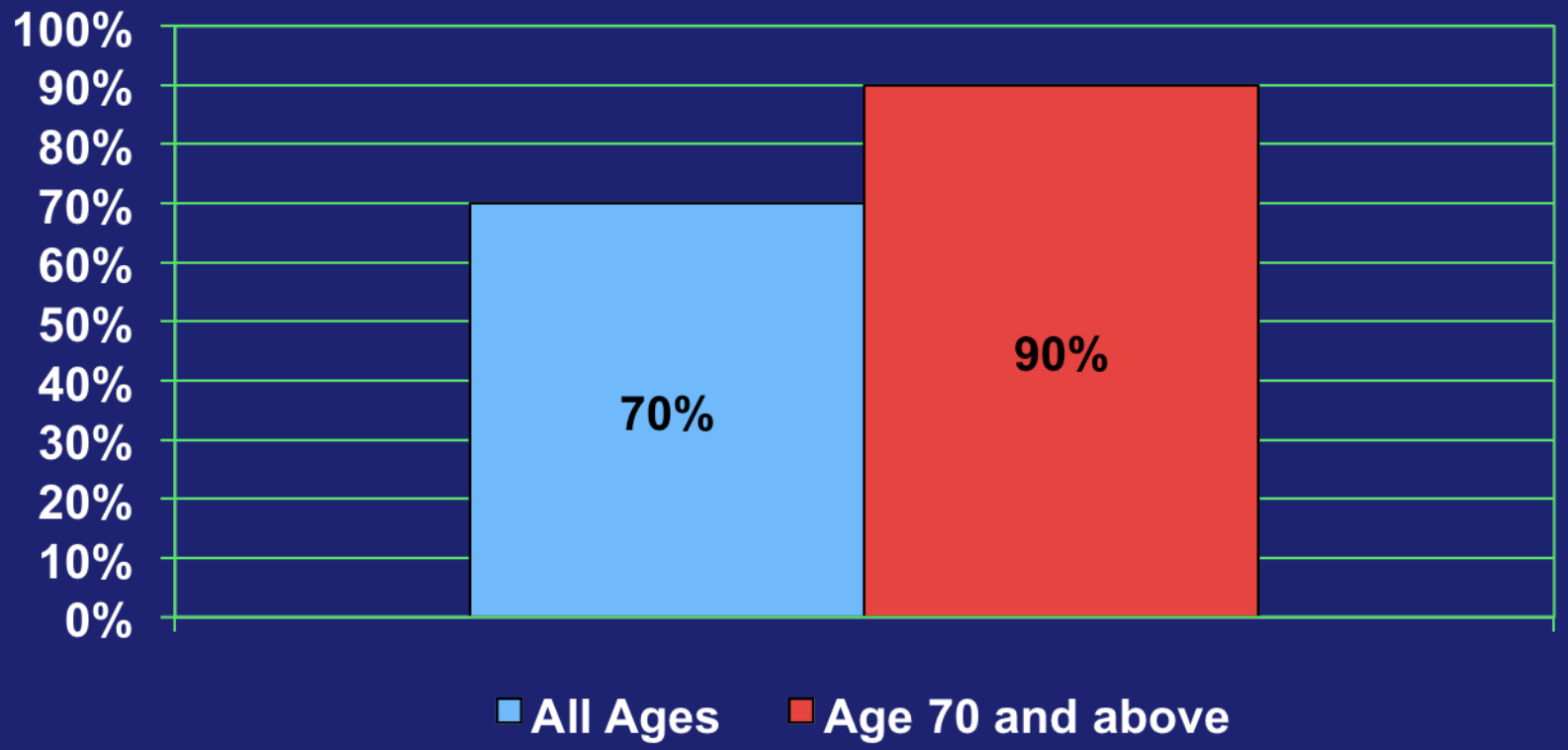
Missed PE: autopsy incidence
33 published autopsy studies

- 33 studies between 1980 - 1995
- 150,000 autopsies
- Fraction w/ missed diagnosis
  - 100% (highest)
  - 85% (average)
  - 55% (lowest)

References too numerous to list

Fatal PE: missed Dx by age

Dx missed in 90% of older patients



Reference: Goldhaber: Am J Med 1982; 73

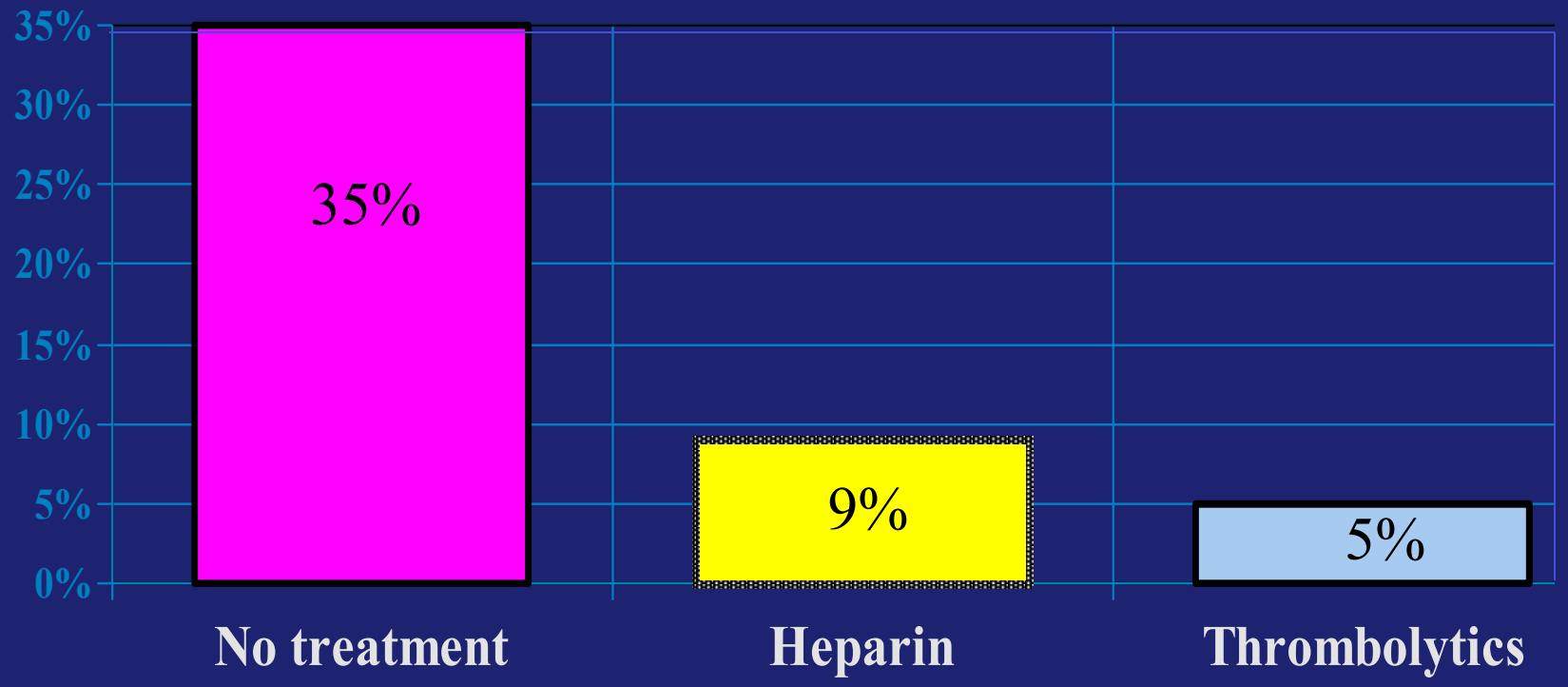
Inpatients vs out-of-hospital

No difference in the incidence of PE found at autopsy

Sperry: Hum Pathol 1990; 21

Mortality in PE

By treatment type



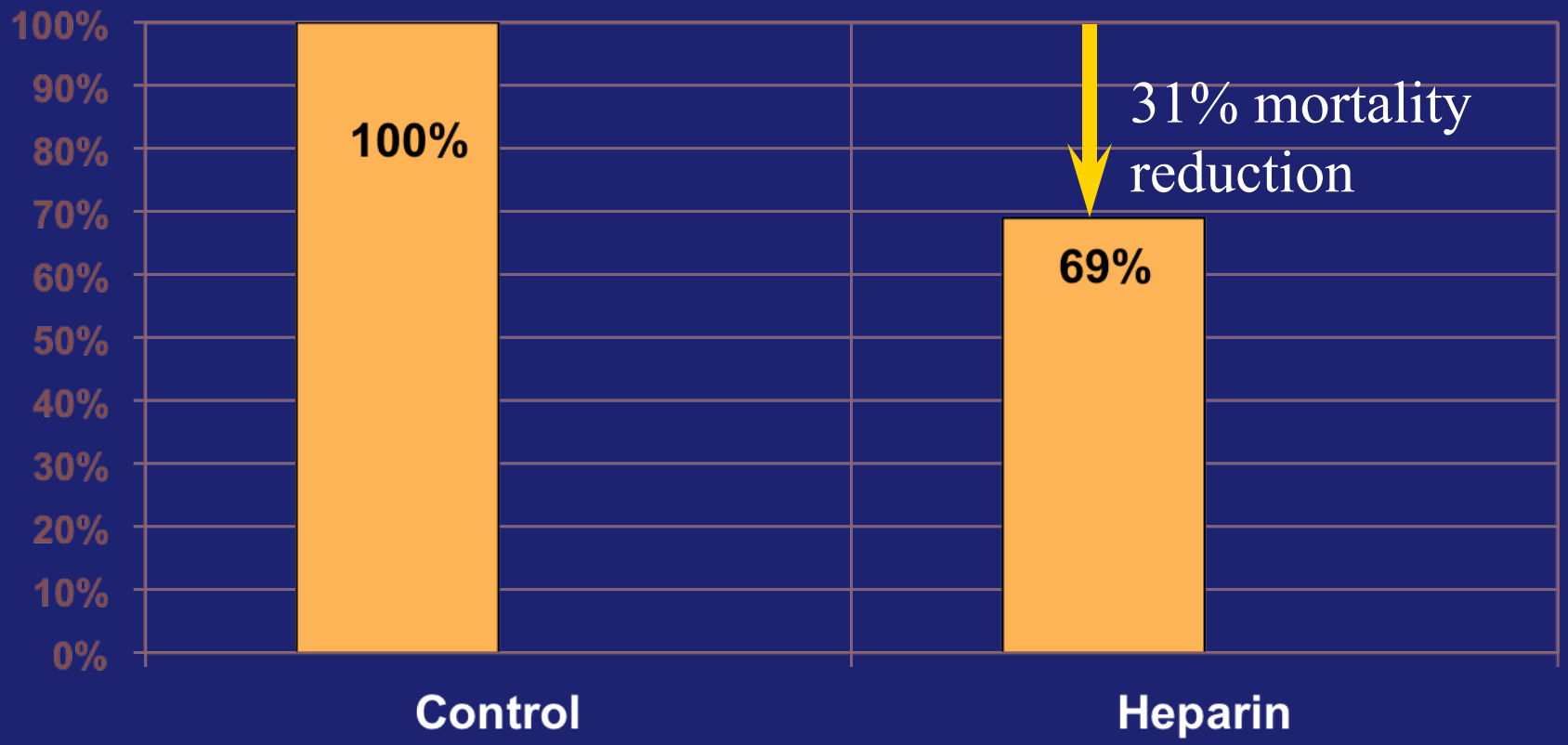
References:

Bell: Am Heart J 1982;103

The Urokinase Pulmonary Embolism Trial: Circulation 1973;47

Mortality reduction w/ heparin

1358 medical admissions randomized



Reference: Halkin:Ann Intern Med1982; 96

Risk Factors for PE & DVT

Virchow's Triad

- Hypercoaguable state
  - Protein S & C def -Anti-Thrombin III def*
  - Pregnancy -BCP (>35 yo & smoker)
  - Malignancy (colon & ovarian)
- Venostasis
  - Obesity -Immobilization
  - Heart disease (CHF, MI)
- Vessel injury
  - Surgery (especially pelvic surgery)
  - Trauma

Risk Factors for PE

	Clinical Trial (n=117)	Autopsy* (n=92)
Immobile	66 (56%)	56 (61%)
Surgery	63 (54%)	33 (36%)
Malignancy	27 (23%)	36 (39%)
Thrombophlebitis	16 (14%)	22 (24%)
Trauma	12 (10%)	7 (8%)
Post-Partum <3 mos.	5 (4%)	NA
No Risk Factors	21 (18%)	11 (12%)

References: Stein Chest 1991:100:598; Morgenthaler: Mayo Clin Proc 1995:70:417

Pathophysiology of PE

- Majority caused by DVT
  - 15-30X more common
  - 50-90% with pelvic/lower ext. clot

- Patent foramen ovale
- Air embolus (barotrauma, gyn surgery)
- Fat embolus (trauma)

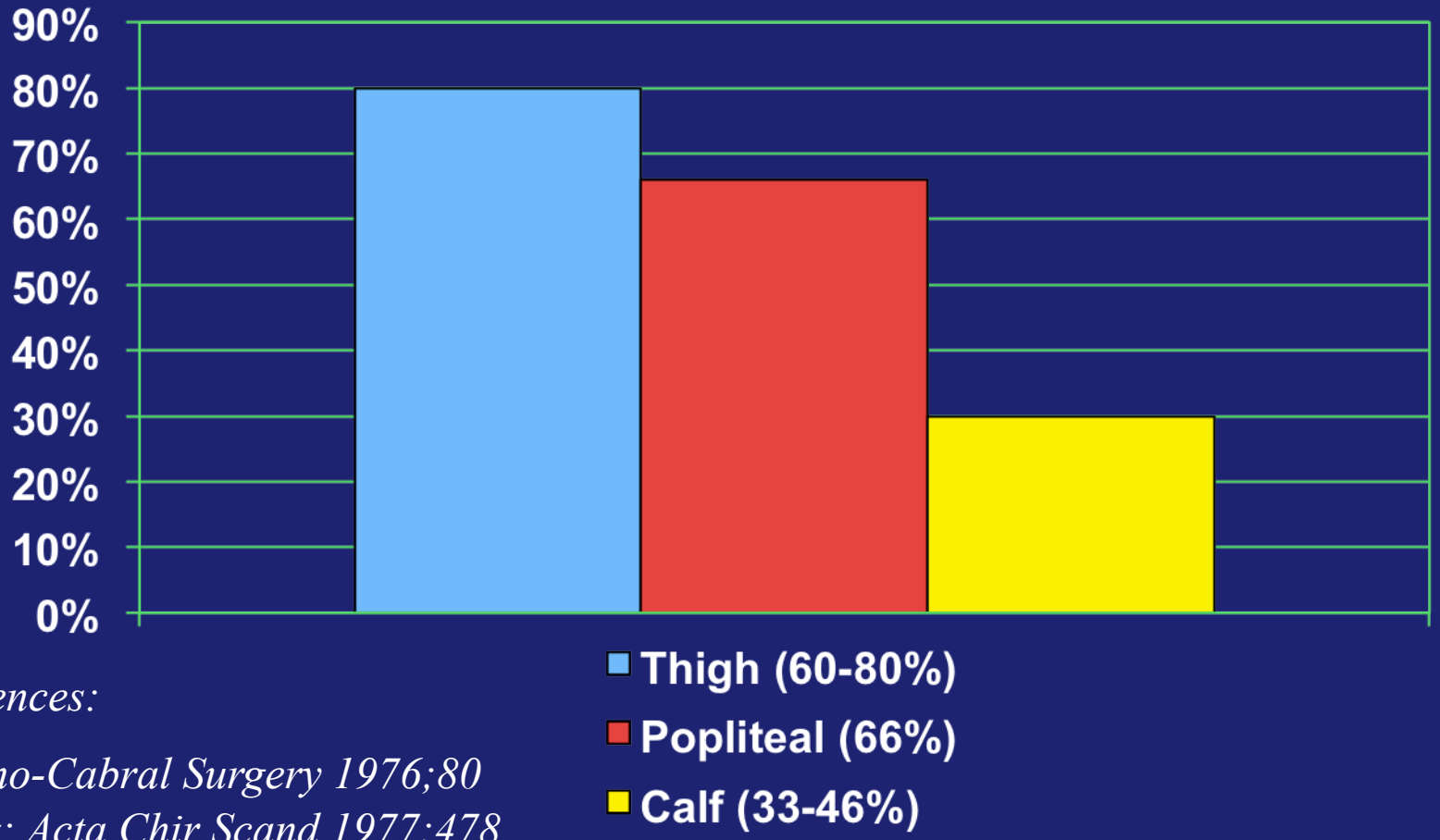
Incidence of PE in patients with DVT

Level	No PE	Asymp. PE	Symp. PE	Total PE
Distal (n=72)	40 (56.5%)	4 (6.5%)	28 (39%)	32(45.5%)
Proximal (n=292)	160 (55%)	72 (25%)	60 (20%)	132 (45%)
Total (n=364)	200 (55%)	76 (21%)	88 (24%)	164 (45%)

Reference: Monreal:Chest 1992102:677

PE from calf vein DVT

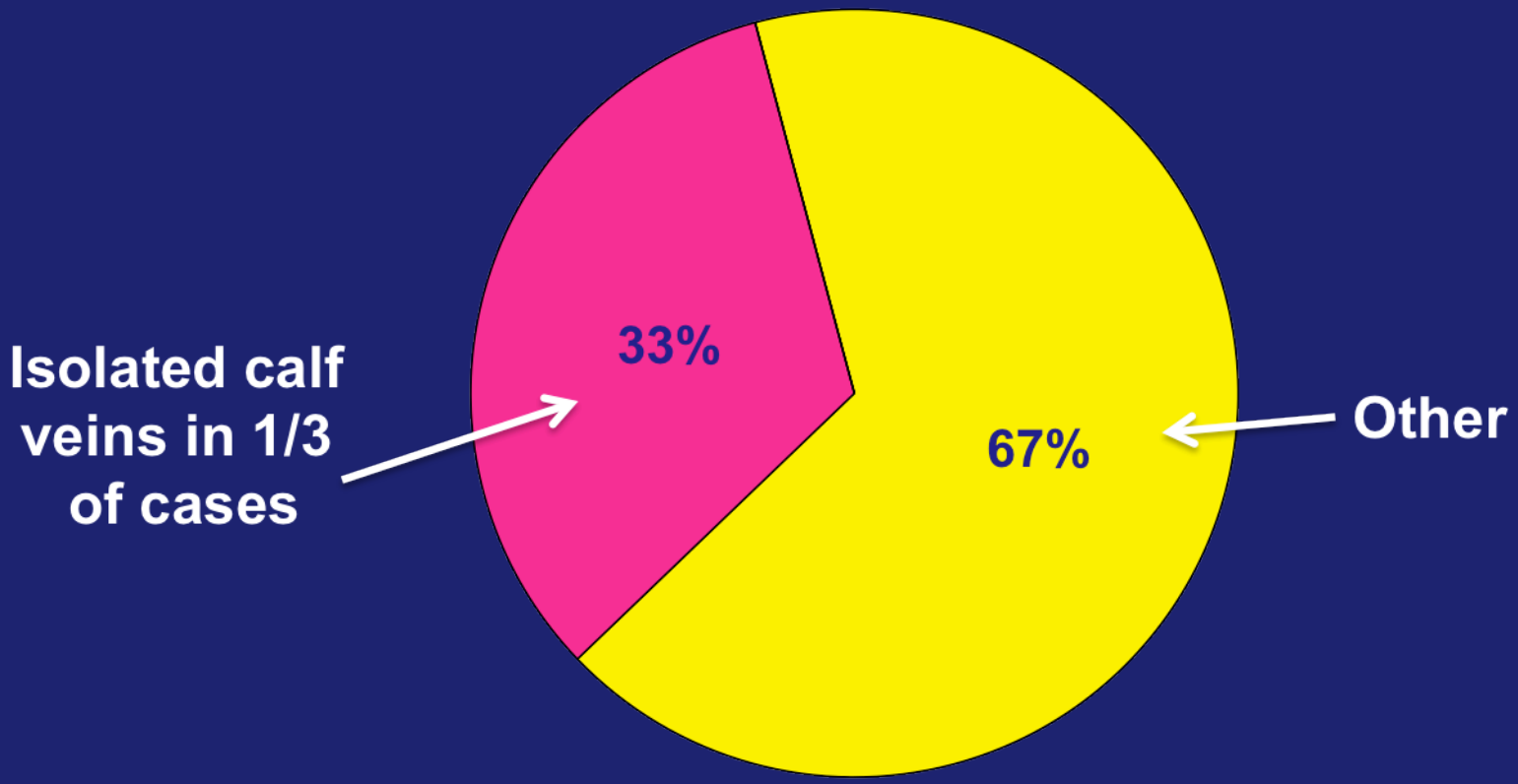
Common and often fatal



References:

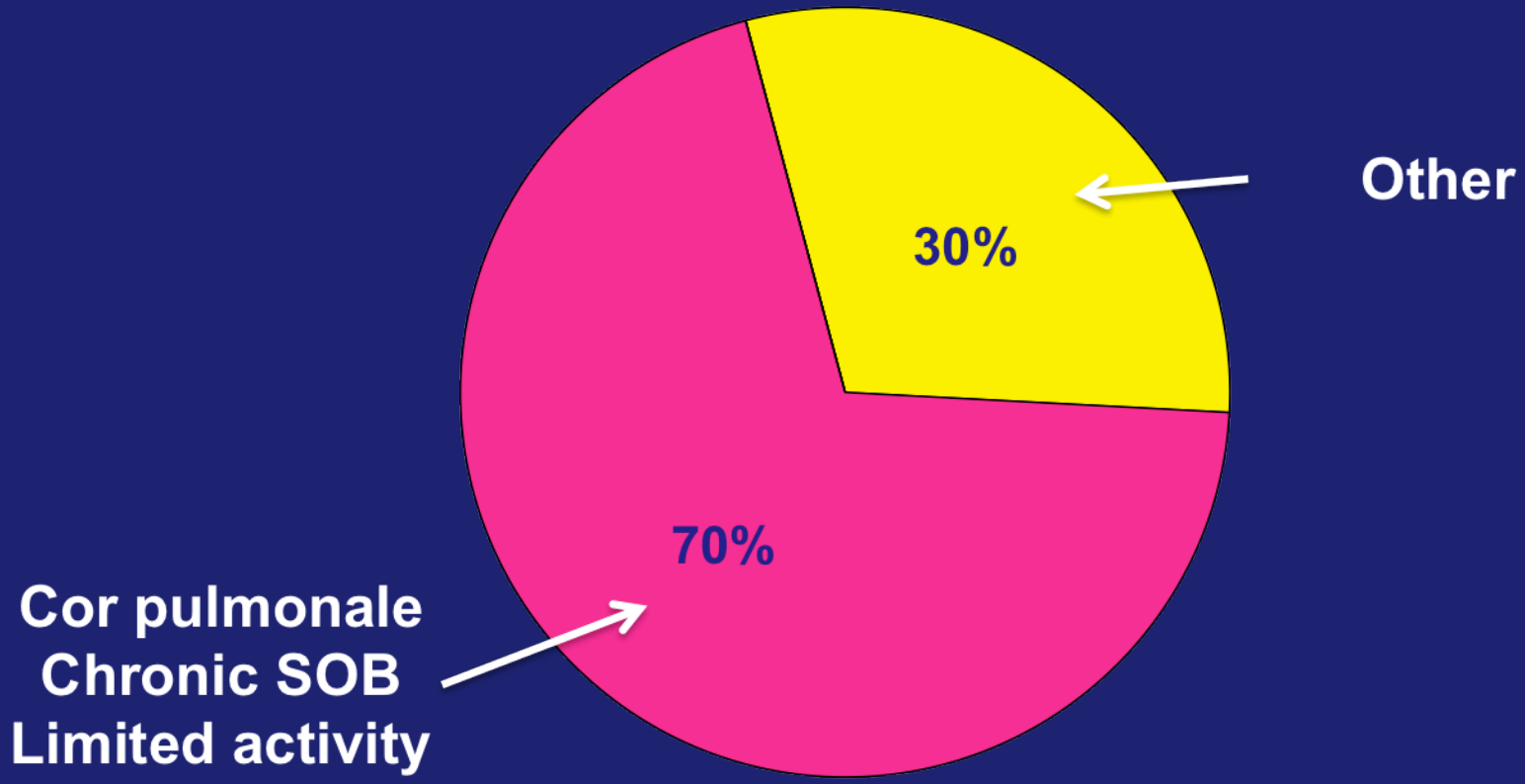
Moreno-Cabral Surgery 1976;80
Havig: Acta Chir Scand 1977;478
Kohn: Eur J Nucl Med 1987; 13

Autopsy source of PE



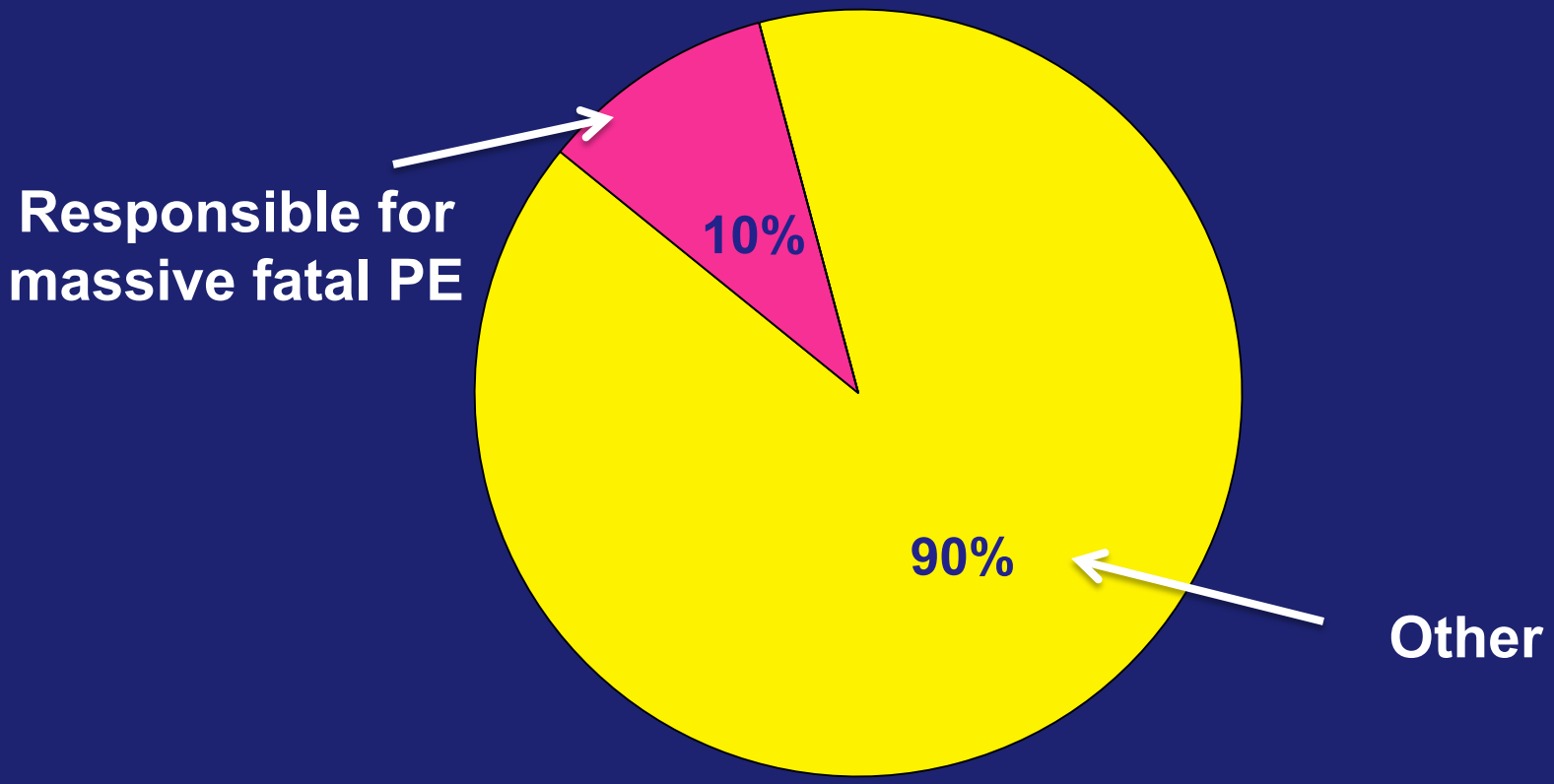
Reference: Havig: Acta Chir Scand 1977;478

Chronic pulmonary HTN
In 70% of those with recurrent PE



Reference: Riedel: Chest 1982;81

512 autopsy cases
With isolated upper-extremity DVT



Reference: Diebold: Pathol Res Pract 1991; 187

Catheter-associated DVT
One-year autopsy study of PE

- Autopsies with catheter DVT at one hospital
- 10 fatalities from massive PE
- Source of embolus:
  - Innominate vein
  - Subclavian vein
  - Superior vena cava

Muller: Dtsch Med Wochenschr 1976; 101

PE from catheter-related DVT

20 cases of upper-extremity DVT associated with indwelling catheters

- 6/20 had PE
- 1 died from massive PE

Monreal: Chest 1991; 99

Pathophysiology (cont)

- Obstructs pulmonary vasculature
- Increased physiologic deadspace in lung
- Increases PA & RV pressures
  - May cause Mitral regurg & cor pulmonale
- Poor filling of L Ventricle causing hemodynamic compromise/collapse

Clinical Presentation

Symptom	Clinical Trials[1]	Autopsy[2]
Dyspnea	84%	59%
Pleuritic Chest Pain	74%	8%
Hemoptysis	27%	3%
Apprehension	59%	17%
Cough	53%	3%

[1] *UPET & USPET*

[2] *Morgenthaler: Mayo Clin Proc 1995:70:417*

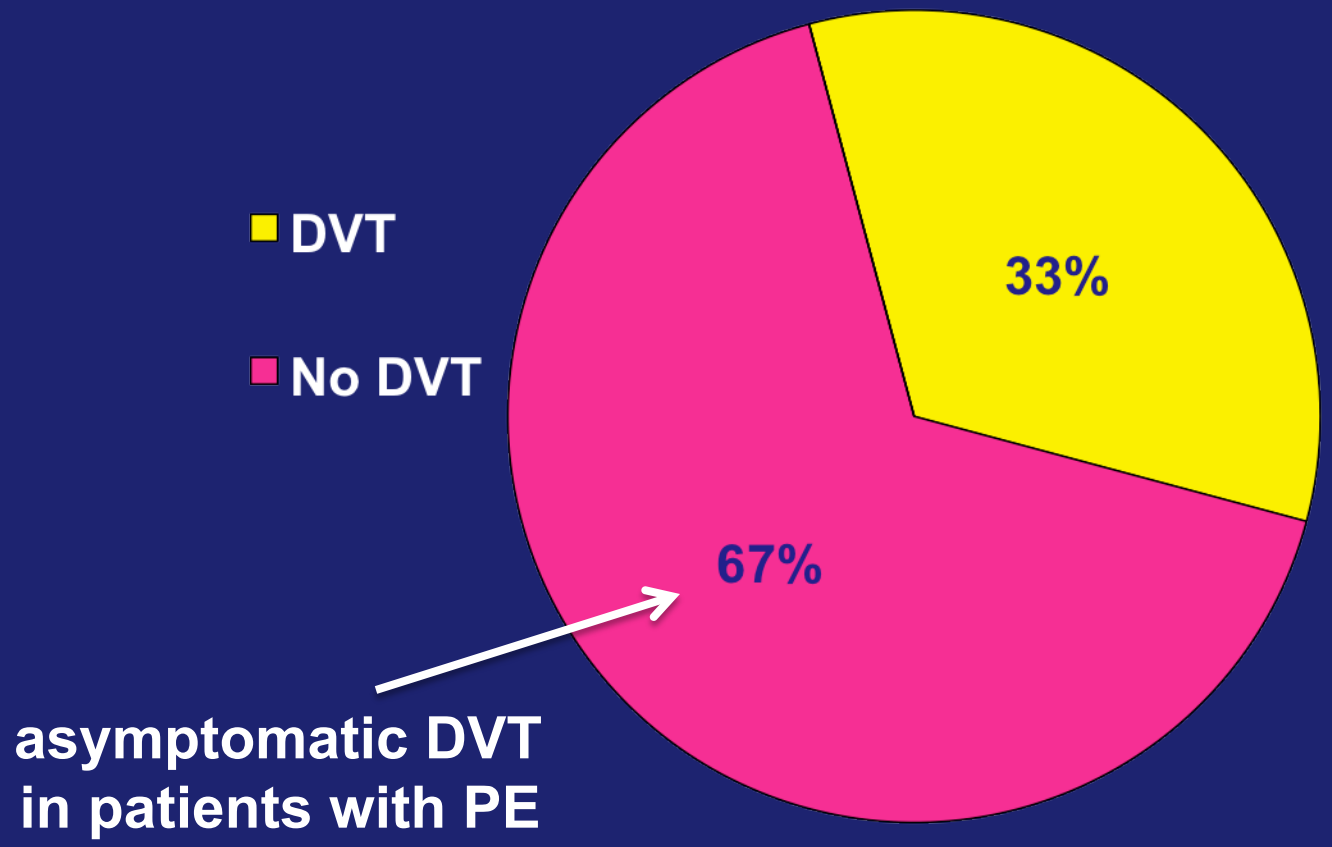
Signs of PE

Sign	Clinical Trials	Autopsy*
Tachypnea >16	92%	66%
Tachypnea >20	70%	NA
Tachycardia >100	30%	54%
Fever >37.5 C	43%	30%
Low. Ext. edema	24%	26%
Homan's sign	4%	NA

**Morgenthaler: Mayo Clin Proc 1995:70:417*

PE & asymptomatic DVT

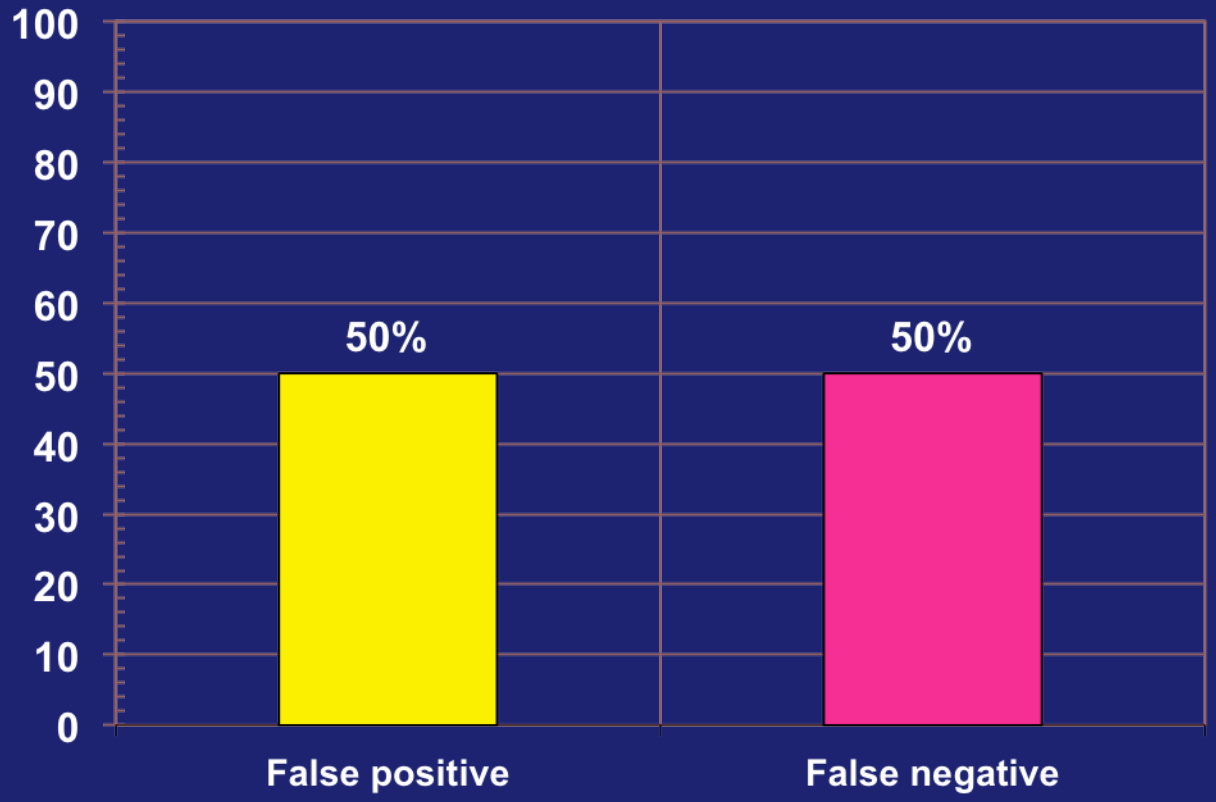
2/3 with PE have no DVT symptoms



Reference: Walsh: J Obstet Gynaecol Br Commw 1974; 81

Clinical Dx of DVT unreliable

50% false positives and negatives



In asymptomatic patients and in patients with pain, tenderness, and unilateral leg swelling

Reference: Richards: Arch Int Med 1976; 136

ED Evaluation of PE

- Prospective, all pleuritic chest pain (n=173)
- EKG, CXR, V/Q,
- Angio (low, intermed., & high prob V/Q)
- 23% had PE

- Immobilization, hx DVT, phlebitis, effusion*
- 20% had none of these risk factors*

Tierney: Med Dec Making 6:12. 1986
**Branch: Am J Med 75:671. 1983*

Laboratory Tests

- CXR
- EKG
- ABG
- D-Dimer

Chest X-ray

- Non-specific & insensitive
- Findings:
  - Normal 30%
  - Elevated hemi-diaphram 50%
  - Focal infiltrate (w/in 3 days) indistinguishable from pneumonia 30-50%
  - Effusion 40-50%
  - Atelectasis 50-60%
- Classic findings:
  - Hampton's hump
  - Westermark Sign 7%

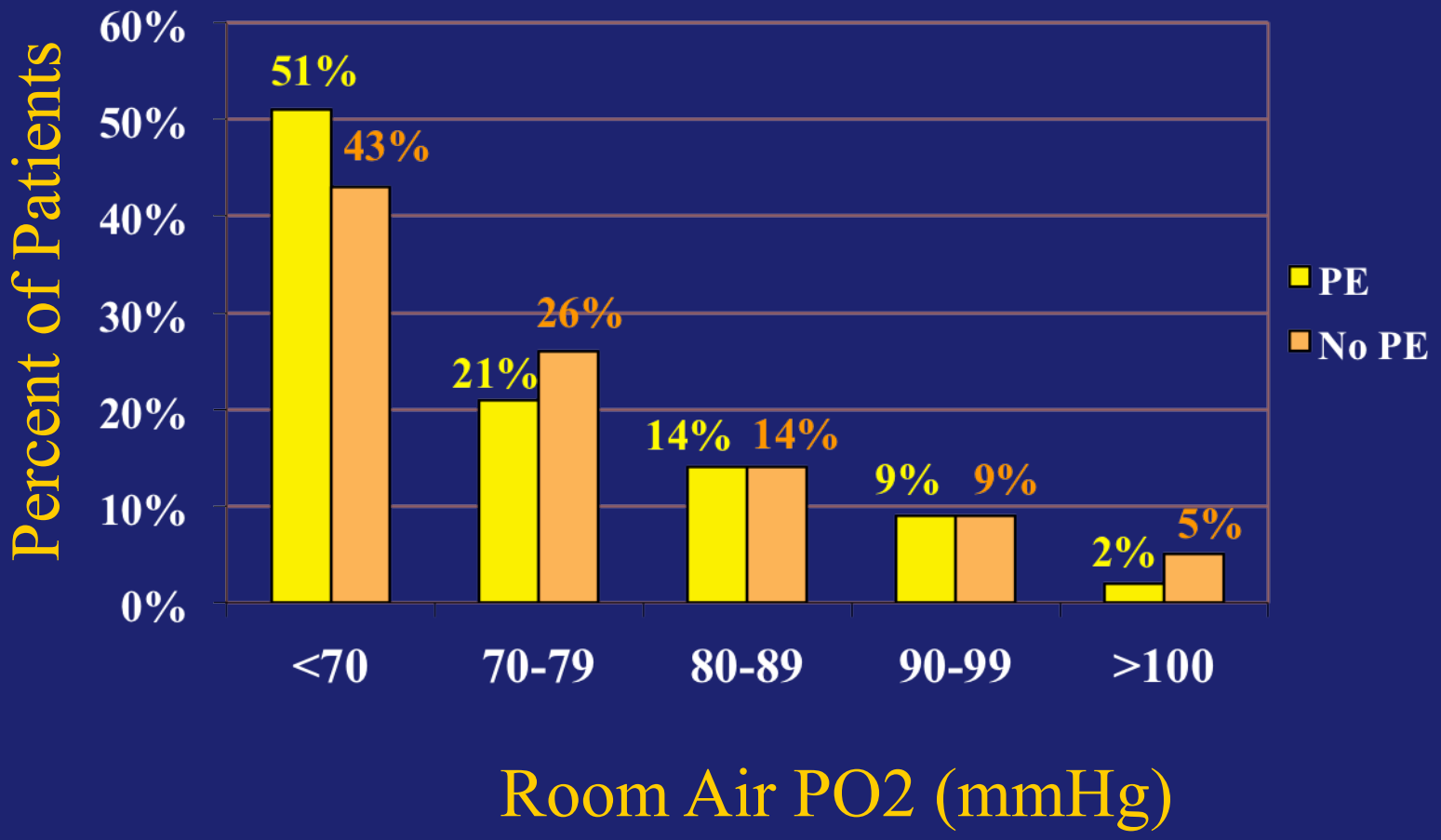
Electrocardiogram

- Poor sensitivity & specificity
- Findings:
  - Tachycardia
  - Non-specific ST-T wave changes
  - Rt or Lt axis deviation
  - P-pulmonale
  - Atrial fibrillation
  - $S_1Q_3T_3$
  - $S_1S_2S_3$

20%

Reference: Bell: Am J Med: 62:355:1977

PO_2 in Patients with & without PE
(no prior history of Cardiac or Pulmonary disease)



Reference: Stein Chest 1991:100:598

Arterial Blood Oxygen

- 0% predictive value
- 17% $PO_2 > 80$ mmHg
- 5% $PO_2 > 100$ mmHg

ABG does not predict PE

(120 possible PE, 54 with PE)

PO_2	Incidence of PE below level	Incidence of PE above level
80 mm Hg	45/101 (44.6%)	9/19 (47.4%)
70 mm Hg	39/87 (44.8%)	15/33 (45.5%)
65 mm Hg	29/69 (42%)	25/51(49%)

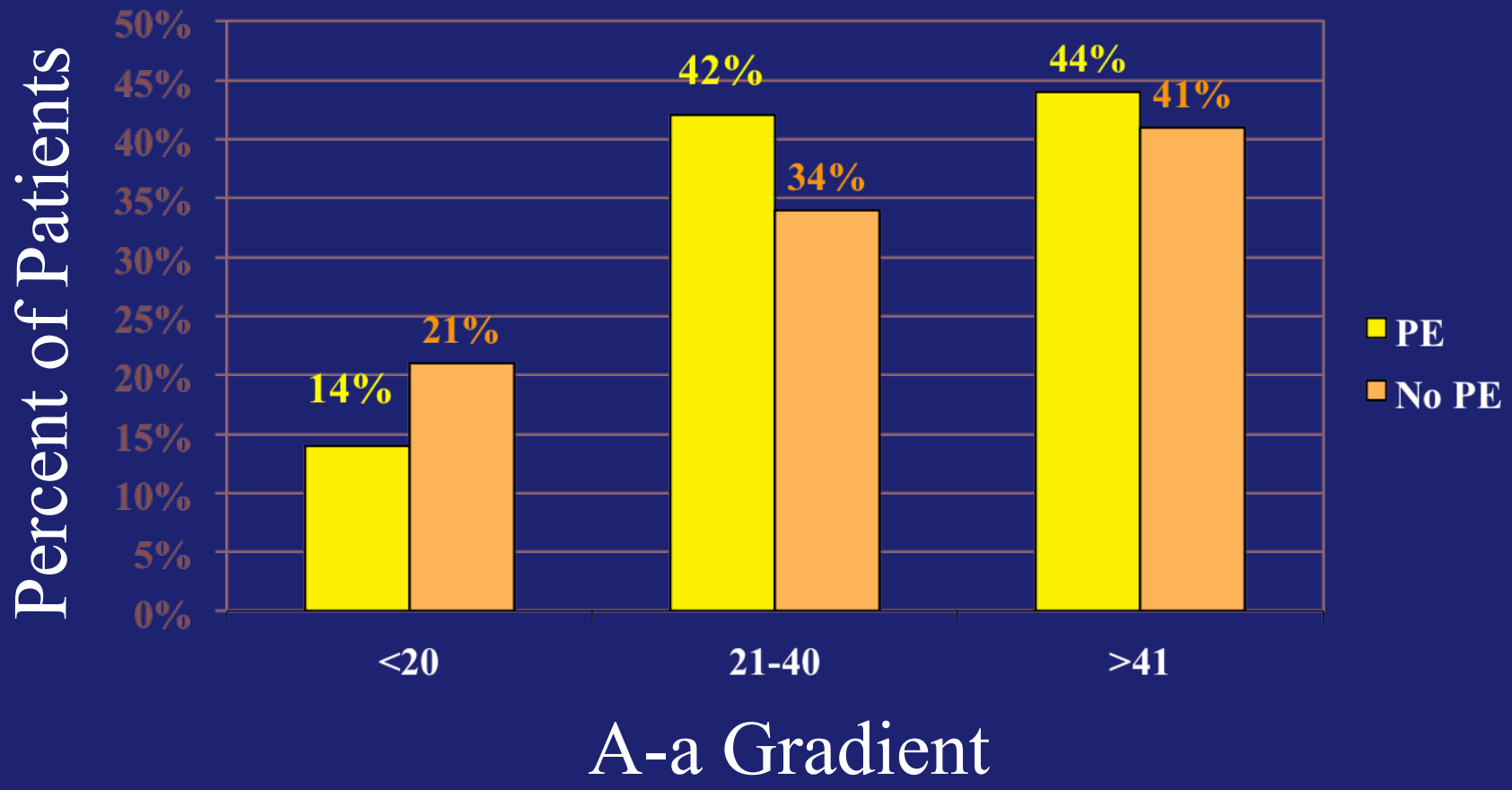
Reference: Menzolan: Am J Surg 137:543:1979

A-a Gradient

- A-a grad=(Calc PO_2)-(Measured PO_2)
- A-a grad=150-(PCO_2 /.8)- PO_2
- Normal =10-20

- 23% will have normal A-a gradient

A-a Gradient in Patients with & without PE
(no prior history of Cardiac or Pulmonary disease)



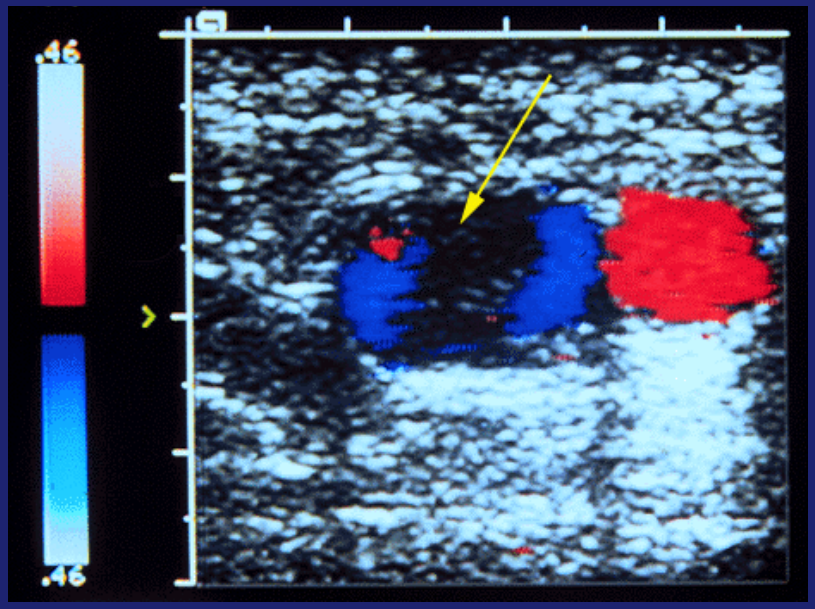
Reference: Stein Chest 1991:100:598

D-Dimer

- A degradation product of fibrin
- Monoclonal Ab test (RIA* & latex)
- NPV 90% (misses 1/10)
- PPV 30% (incorrect 7/10)

Lower Extremity Dopplers

- PPV=78% NPV=88%
- Advantages
  - noninvasive
  - inexpensive
- Disadvantages
  - diff. with acute on chronic
  - worse PPV & NPV if asymp
  - leg pain
  - casts
  - calf DVT's (52% sens)



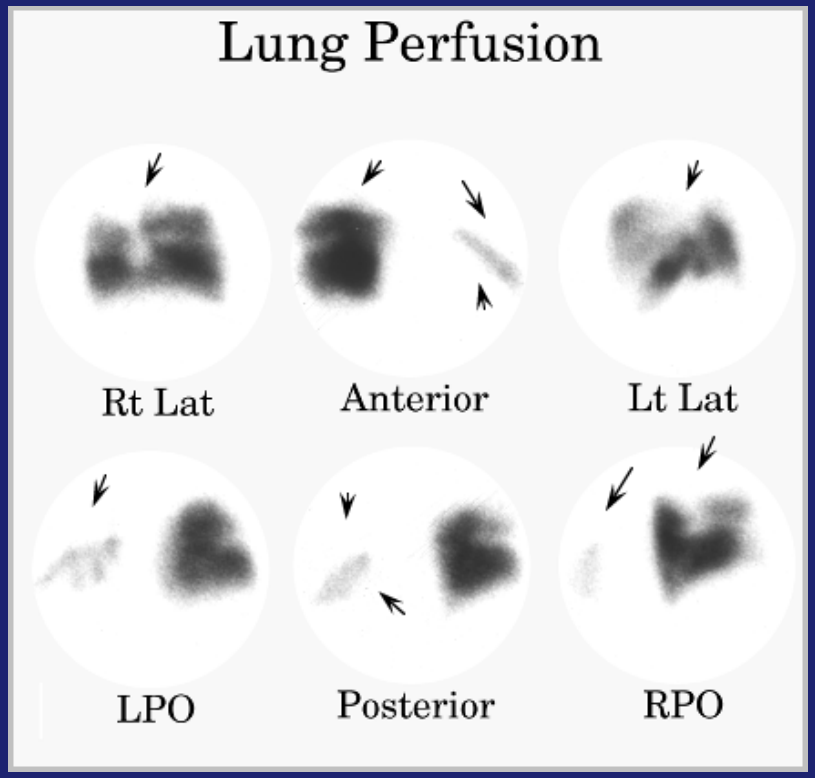
PD-INEL Source undetermined

Ventilation Perfusion Scans

	Clinical Probability 80-100%	20-79%	0-19%
Hi	96%	88	56%
Int	66%	28%	16%
Low	40%	16%	4%
Nl	0%	6%	2%

73% had Int/Low prob scans

High prob scans have PPV 88%



PD-INEL Source undetermined

PIOPED 90

Ventilation Perfusion Scan

- PIOPED, ‘90
  - Interobserver agreement for V/Q readings 95%, 92%, 94% for high, VLP, & NL scans but dropped to 75% & 70% for IP & LP scans
- *Schugler et al ‘94*
  - 78% of intermediate scans & 92 % of low probability scans had no further testing
  - But 35% of the former and 20% of the latter received anticoag.
  - Leaving the decision to anticoagulate based on clinical grounds
- *Stein et al ‘91*
  - Clinical evaluation of PE is non-specific

Pulmonary Angiogram

- Advantages
  - gold standard
- Disadvantages
  - invasive, $$$$
  - internists reluctance
- PIOPED ‘90
  - 2.5% mortality
  - 66% interobserver agreement for subsegmental PE’s
- Stein ‘92
  - 6% morb., 0.5% mortality
- Sustman ‘82 12% requiring PA underwent procedure

CT Angiograms

- Remy-Jardin, *Radiology* '96
  - 75 conseq. Pts referred for PA prospectively
  - Sensitivity 91%, specificity 78%, PPV 100%, NPV 89%
  - 188 central PE's on CT corresponded to PA
  - Found isolated subsegmental clots in 5% on PA

	Angiography			
CT Findings	Negative	Positive	Inconclusive	Total
Negative	25	1	0	26
Positive	0	39	0	39
Inconclusive	4	3	0	7
Suboptimal	3	0	0	3
Total	32	43	0	75

Goodman et al., 1995

PA of Central Vessels Only

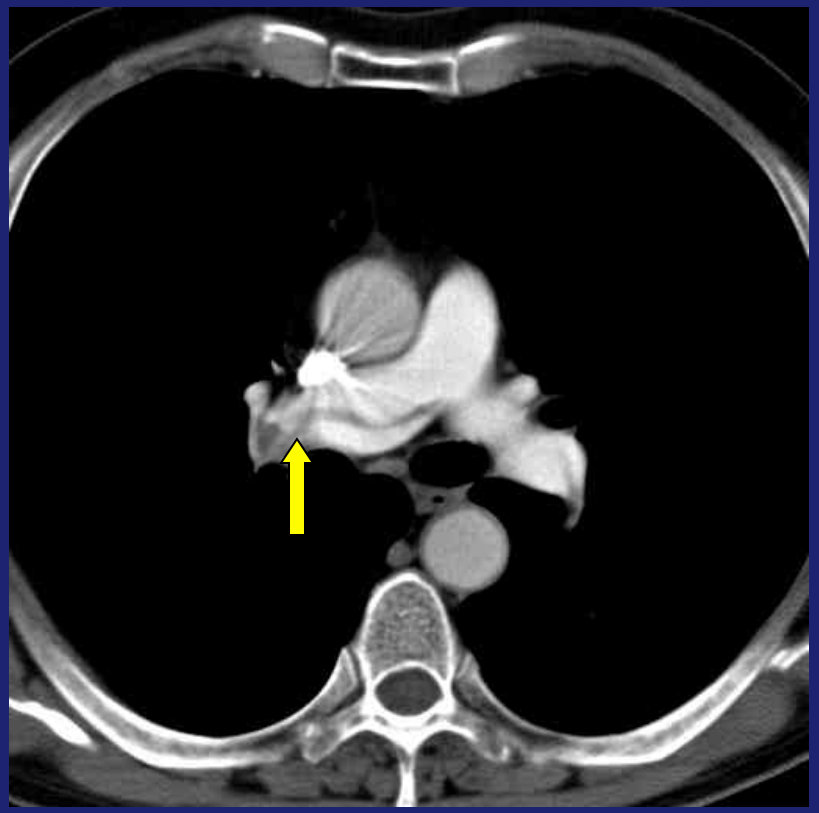
CT	PE	No PE	Total
Embolism present	6	1	7
Embolism absent	1	12	13
Total	7	13	20

PA of All Vessels

CT	PE	No PE	Total
Embolism present	7	1	8
Embolism absent	4	8	12
Total	11	9	20

CT Angiograms

- General Observations
  - Sensitivities 53-97%
  - Specificity 78-97%
- Advantages
  - Cost
  - Fast
  - Close proximity to ED
  - Alternative Dx
- Disadvantages
  - ? Misses subseg. PE's
  - Not standard of care;yet
  - IVP dye



Treatment

- Unfractionated Heparin
  - 5000 U bolus followed by 1250 U/hr
  - Maintain aPTT 2 - 2.5 normal
  - Recommend concurrent heparin tx for 48 hr when starting Coumadin
  - Most recommend 3 - 6 months of coumadin, or longer if they have a clotting disorder Agnelli et al., *Int'l J. of Card.*; 1998
- LMWH
  - Prospective randomized study have found nadroparine as safe and effective as unfrac. heparin for submassive PE
  - Similar double blinded studies using tinzaprin

Thery et al., Circ.; 1992 & Simonnneau et al, Haemostasis; 1996

Thrombolytic Therapy

- Studies
  - Jerjes-Sanchez et al., *J Thrombosis*; 1995
    - Pts with hypotension & CHF were randomized to anticoag or thrombolytics and anticoag
    - Stopped after 8 pts b/c all 4 anticoag alone died, & all 4 thrombolytics and anticoag survived
  - Wolfe et al., *Am Heart J*; 1994
    - 101 pts (nl BP, RV dysfxn) randomized to rt-PA plus heparin or heparin alone
    - No rt-PA pts had recurrent PE or died
    - Of the 55 receiving heparin alone, 5 recurrent PE (2 fatal)

Thrombolytic Therapy of PE

- Standard Regimen*
  - 100 mg tPA infusion over 2 hours
- Unstable patients
  - .6mg/kg (max=50mg) over 15 min

**FDA approved*

The bad news
about thromboembolic disease

- Most DVT's are asymptomatic
- Most DVT's produce PE
- Most PE's are asymptomatic
- DVT & PE causes death and disability

  even when there are no recognizable symptoms

Risk Factors for PE in patients without Cardiac or Pulmonary disease

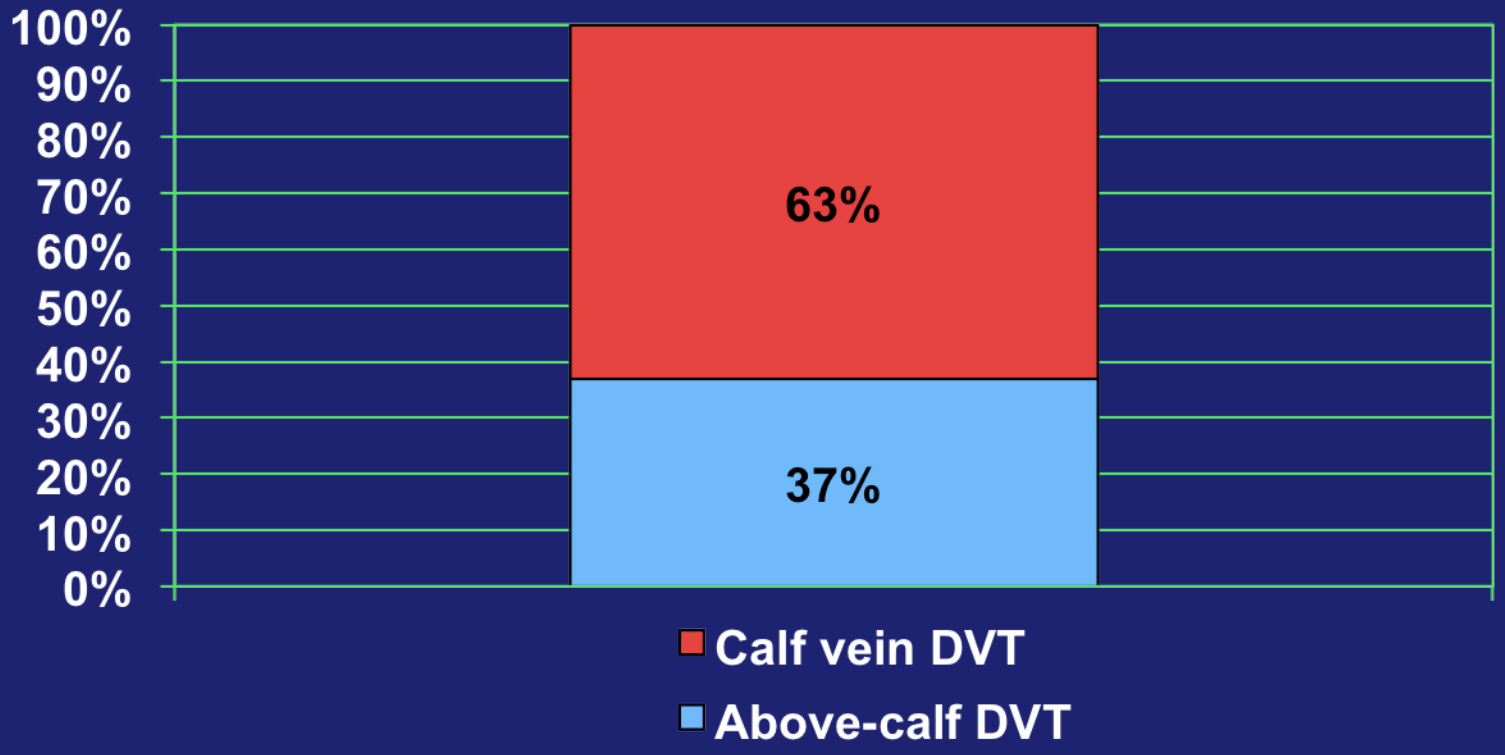
	PE (n=117)	No PE (n=248)
Immobile	66 (56%)	81 (33%)*
Surgery	63 (54%)	78 (31%)*
Malignancy	27 (23%)	38 (15%)
Thrombophlebitis	16 (14%)	19 (8%)
Trauma	12 (10%)	25 (10%)
Post-Partum <3 mos.	5 (4%)	8 (3%)

**p<.001*

Stein Chest 1991:100:598

Paradoxical embolism

Source most often in the calf



Reference: Stollberger: Ann Intern Med 1993;119

Electrocardiogram

- Normal Sinus or Sinus Tachycardia 80%
- QRS axis change
  - Acute RAD 15%*
  - RBBB 8%
- T-wave abnormality 40%*
- Depressed ST 25%
- Elevated ST 16%*

**Significantly more common in massive PE* *Stein:Progr. Cardiovasc Dis. 1974;17:247*

CT Angiogram

- Mayo et al., *Radiology*; 1997
  - 139 nonconseq. pts. underwent CT, V/Q, & PA (if indicated)
  - 16% were outpts
  - 46/139 pts had a PE and 93/139 did not
    - High prob V/Q in 30/46 (sens 65%)
    - + CT in 40/46 (sens 87%), - CT in 88/93 (spec 95%)
  - Overall, V/Q correct in 103/139 (74%) pts & CT was correct in 128/139 (92%) of cases
  - Interobserver agreement (K) 0.61 for V/Q and 0.85 for CT