



Pulmonary embolism:

**Does every patient with PE need hospitalisation?
Am Westen nichts neues???**

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Lugano, 8 mars 2006*

Outpatient treatment of PE

- What do the guidelines say?
 - Current organisation for outpatient management of DVT should be extended to include stable patients with PE. [C]

British Thoracic Society, Thorax 2003

Outpatient treatment of PE

CHEST
College of Chest Physicians

Not a single word!

**Antithrombotic Therapy for Venous
Thromboembolic Disease: The Seventh
ACCP Conference on Antithrombotic and
Thrombolytic Therapy**

Harry R. Büller, Giancarlo Agnelli, Russel D. Hull, Thomas M. Hyers,
Martin H. Prins and Gary E. Raskob

Chest 2004;126:401-428
DOI 10.1378/chest.126.3_suppl.401S

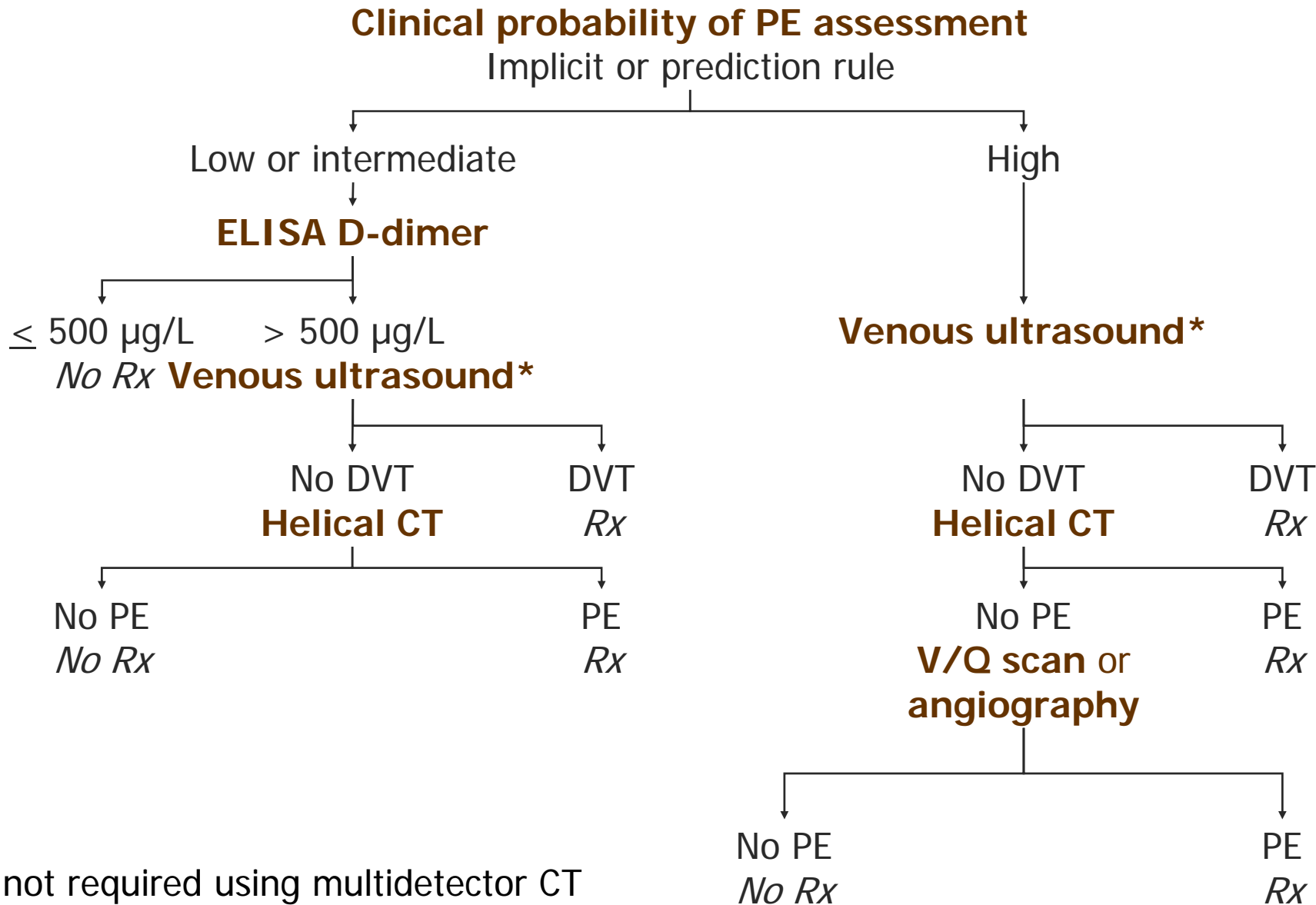
Prerequisites for outpatient treatment of PE

- Rapid and safe outpatient diagnosis of PE
- Safe and effective outpatient treatment
- Identification of low risk patients (risk stratification)

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Validated algorithm for diagnosing PE



*not required using multidetector CT

Prediction rules for PE

Thromb Haemost 2000;83:416-20. Ann Intern Med 2006;144:65-71

Wells score

Previous DVT or PE + 1,5

Immobilization or surgery +
1,5
(< 4 weeks)

Cancer + 1

Alternative Dx less probable +
3

Hemoptysis + 1

Heart rate > 100 /min + 1,5

Revised Geneva score

Age > 65 years +1

Previous DVT or PE +3

Surgery or fracture
(< 1 month) +2

Cancer +2

Unilateral lower limb pain +3

Hemoptysis +2

Heart rate

75 to 94 beats per minute

D-dimer for suspected PE: summary of outcome studies

	N patients evaluated	Clinical probability	NNTest
Vidas DD	2165	low/intermediate	3
Tinaquant	833	low	3
SimpliRed	1912	low	2 to 3

3-month thromboembolic risk in patients with negative D-dimer 0 to 0.5%

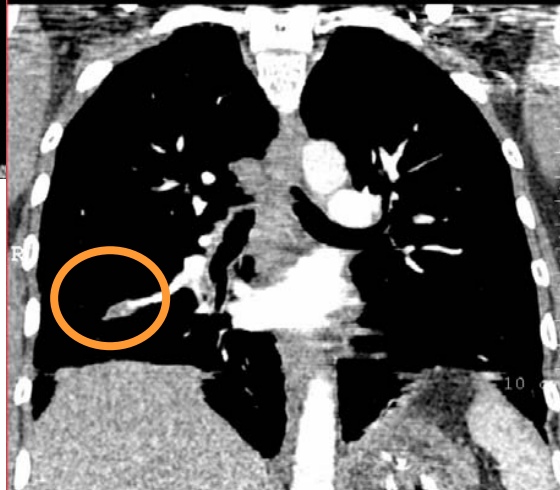
CT in suspected PE: a story of evolution



2-slice CT

1992

2 x 2.7 mm
25 sec

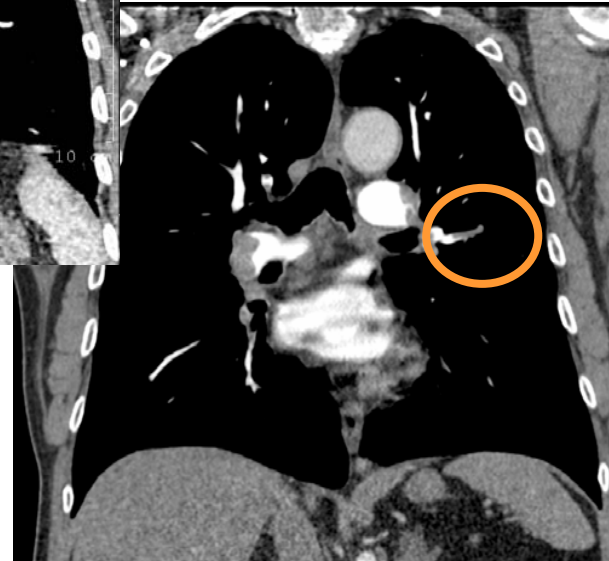


4-slice CT

1998

4 x 1 mm
25 sec

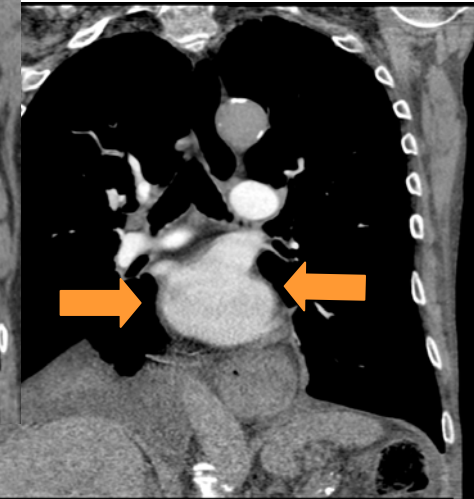
16 x 0.75 mm
10 sec



16-slice CT

2002

64 x 0.625 mm
4 sec



64-slice

2004

PIOPED II study

N Engl J Med 2006;354:2317-27

- **Objective:** assess the sensitivity and specificity of multidetector CT angiography in suspected PE
- **Design:** accuracy study comparing CT with a reference diagnosis
- **Population:**
 - 1090 patients (of 3262 eligible patients).
 - Analysed: 824 with a reference diagnosis, 90% outpatients
- **CT:** 4-detector mainly

Results: Sensitivity 83%; specificity 96%

PIOPED II study: results

N Engl J Med 2006;354:2317-27

23% of positive CTs

Clinical probability	Prevalence of PE, n/n (%)	
	CT positive	CT negative
Low	22/38 (58%)	8/164 (4%)
Intermediate	93/101 (92%)	15/136 (11%)
High	22/23 (96%)	6/15 (40%)

2% of negative CTs

Does using inappropriate diagnostic criteria for PE influence patient outcome?

Roy PM et al., Ann Intern Med 2006;144:157-164

Annals of Internal Medicine

ARTICLE

Appropriateness of Diagnostic Management and Outcomes of Suspected Pulmonary Embolism

Pierre-Marie Roy, MD, PhD; Guy Meyer, MD; Bruno Vielle, MD, PhD; Catherine Le Gall, MD; Franck Verschuren, MD; Françoise Carpentier, MD; Philippe Leveau, MD; and Alain Furber, MD, PhD, for the EMDEPU Study Group*

- 1529 patients with suspected in 116 emergency departments
- **Appropriate diagnostic workup:** PE rule in or out by validated diagnostic criteria
- Examples of inappropriate diagnostic criteria:
 - PE ruled out by single-detector CT alone
 - Low probability V/Q lung scan without clinical probability assessment

Does using inappropriate diagnostic criteria for PE influence patient outcome?

Roy PM et al., *Ann Intern Med* 2006;144:157-164

Table 3. Patient Outcomes at 3 Months after Exclusion of Pulmonary Embolism*

Diagnostic Work-up	Patients Receiving Appropriate Management (n = 418)	Patients Receiving Inappropriate Management (n = 506)	P Value
Total thromboembolic events, n (%)	5 (1.2)	39 (7.7)	<0.001
Nonfatal thromboembolic event, n	2	10	0.045
Unexplained sudden death, n	3	29	<0.001

* Patients who received anticoagulation for reasons other than thromboembolic disease were excluded from follow-up analysis.

Outpatient diagnosis of PE

- Possible in less than 24 hours nearly everywhere
 - Clinical probability
 - D-dimer
 - Multidetector CT angiography
 - (Lower limb venous ultrasonography)

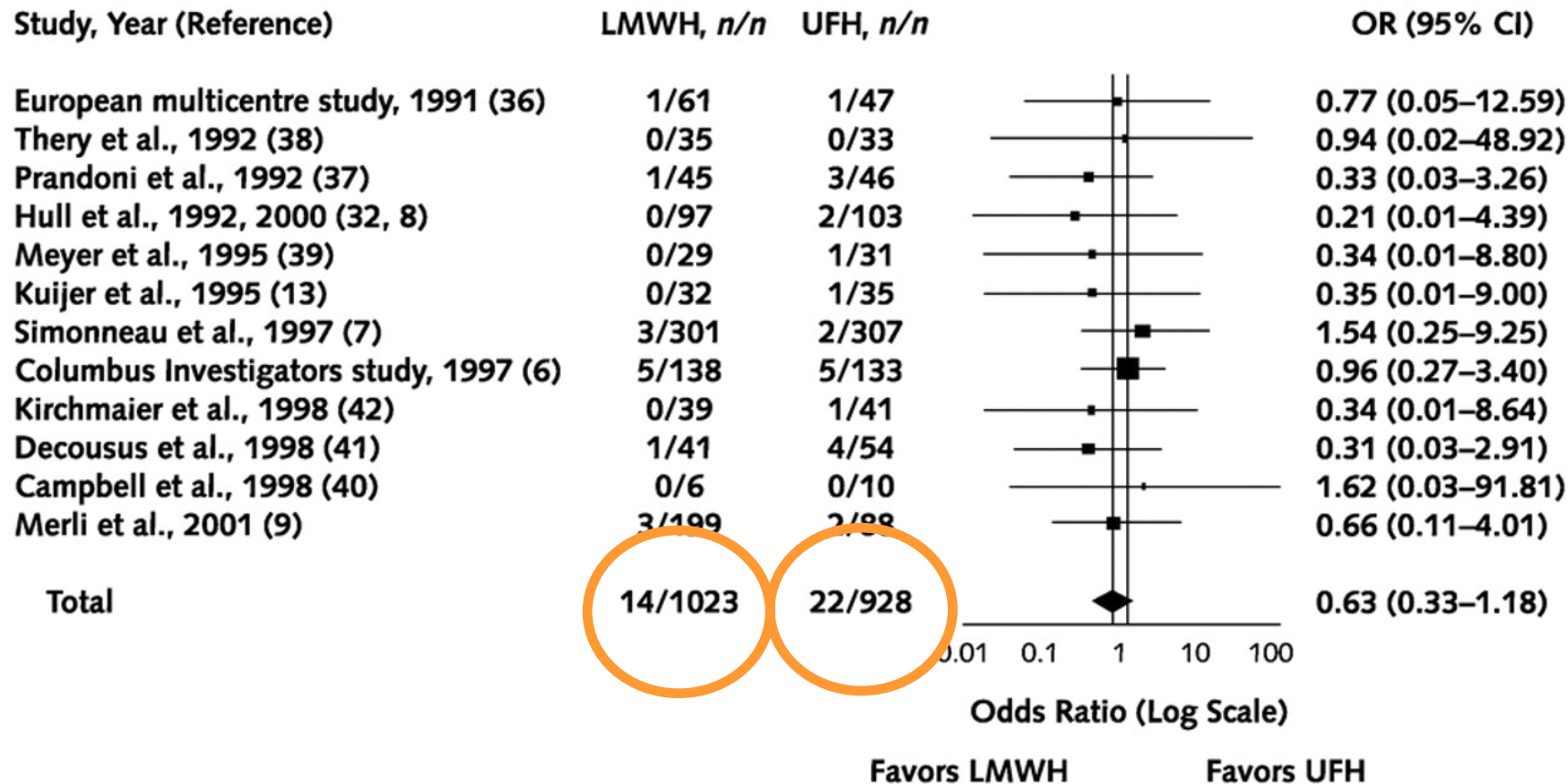
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LMWH or UFH for PE:

DVT or PE recurrence at end of heparin therapy

Quinlan DJ et. al. *Ann Intern Med* 2004;140:175-183



LMWH or UFH for PE:

DVT or PE recurrence at end of heparin therapy

Quinlan DJ et. al. Ann Intern Med 2004;140:175-183

	LMWH, % n=1023	UFH, % n=928	Odds ratio
DVT/PE recurrence	1.4	2.4	0.6 (0.3 à 1.2)
Death	1.4	1.2	1.2 (0.6 à 2.4)
Major bleeding	1.2	2.3	0.7 (0.4 à 1.3)

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Clinical spectrum of PE

Mortality

1-2%

4-10%

25-50%



Non massive PE

- Normal Blood Pressure
- No RV strain

Submassive PE

- Normal BP
- RV strain

Massive PE

- Shock

Prognostic score for PE

Wicki J et al. Thromb Haemost 2000; 84: 548-52.

Nendaz M. et al. Thromb Haemost 2004;91:1232-6.

Odds ratio

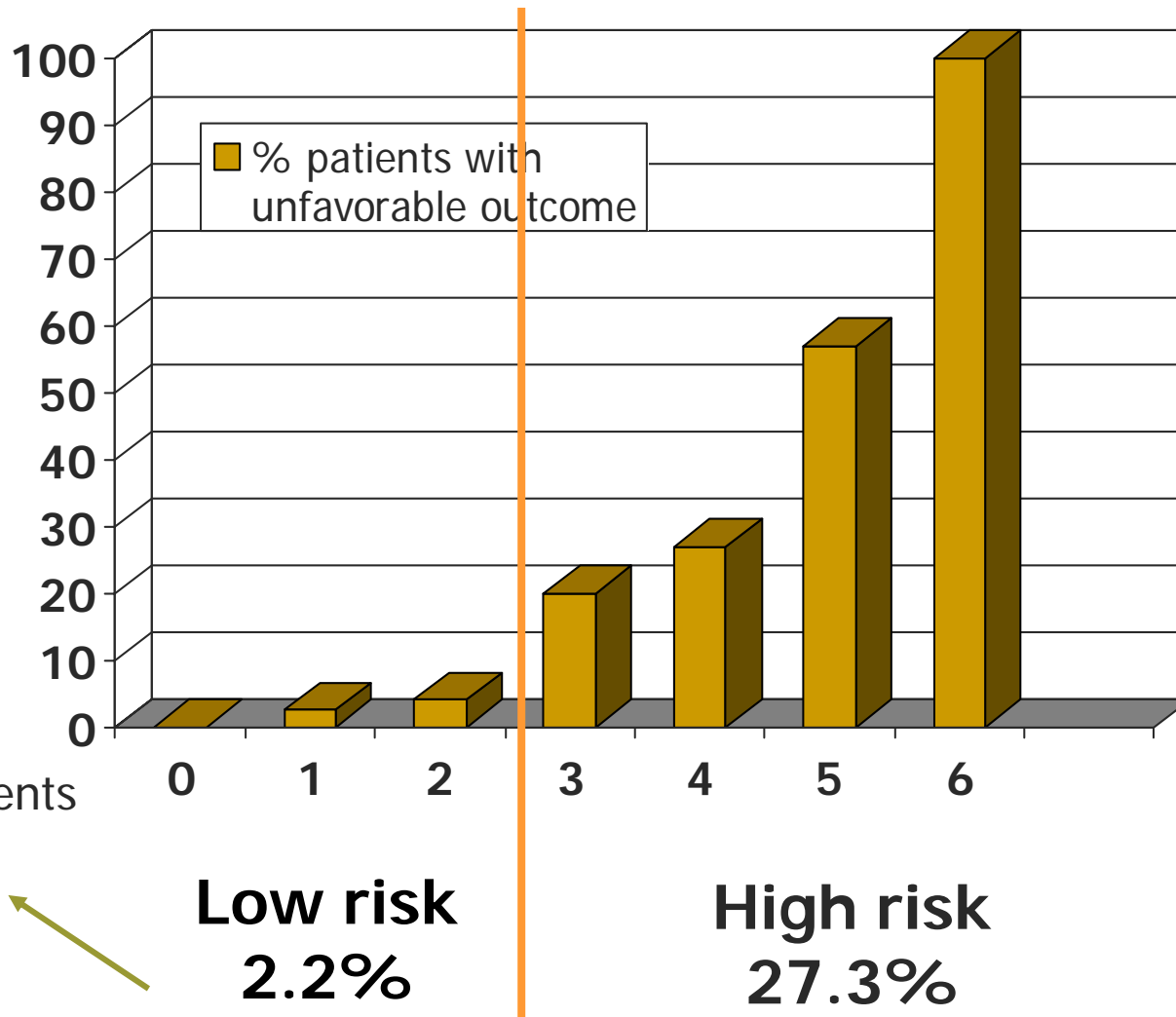
Points

Cancer	8.8	2
Heart failure	2.8	1
Previous DVT	3.2	1
SBP < 100 mmHg	15.5	2
PaO ₂ < 8 kPa	2.9	1
DVT (ultrasound)	2.9	1
Score		0-8

Prognostic score for PE

Wicki J et al. Thromb Haemost 2000; 84: 548-52.

Nendaz M. et al. Thromb Haemost 2004;91:1232-6.



Limits of the Geneva prognostic score

- Predict unfavorable outcome at 3 months
- Requires lower limb venous ultrasonography

Prognostic score for PE

Aujesky et al., AJRCCM 2005;172:1041-6

- Pennsylvania Health Care Cost Containment Council (PHC4) database (11).
- Inpatients 18 years or older discharged with a primary ICD-9-CM diagnosis of PE
- 15,531 discharged patients with PE treated at 186 hospitals.
 - randomly selected 10,354 patients (67%) for the derivation
 - 5,177 (33%) for the internal validation sample.
- Outcome: 30-day mortality

Prognostic score for PE

Aujesky et al., AJRCCM 2005;172:1041-6

Variables	Points
Age	Age, in years
Male gender	+10
Cancer (Previous or active)	+30
Chronic heart failure	+10
Chronic lung disease	+10
Heart rate ≥ 110 per min	+20
Systolic BP < 100 mmHg	+30
Respiratory rate ≥ 30 per min	+20
Temperature $< 36^{\circ}\text{C}$	+20
Altered mental status	+60
Arterial oxygen saturation $< 90\%$	+20
class I < 65 points; class II 66-85 points; class III 86-105 points; class IV 106-125 points; and class V > 125 points. Low risk = classes I et II.	

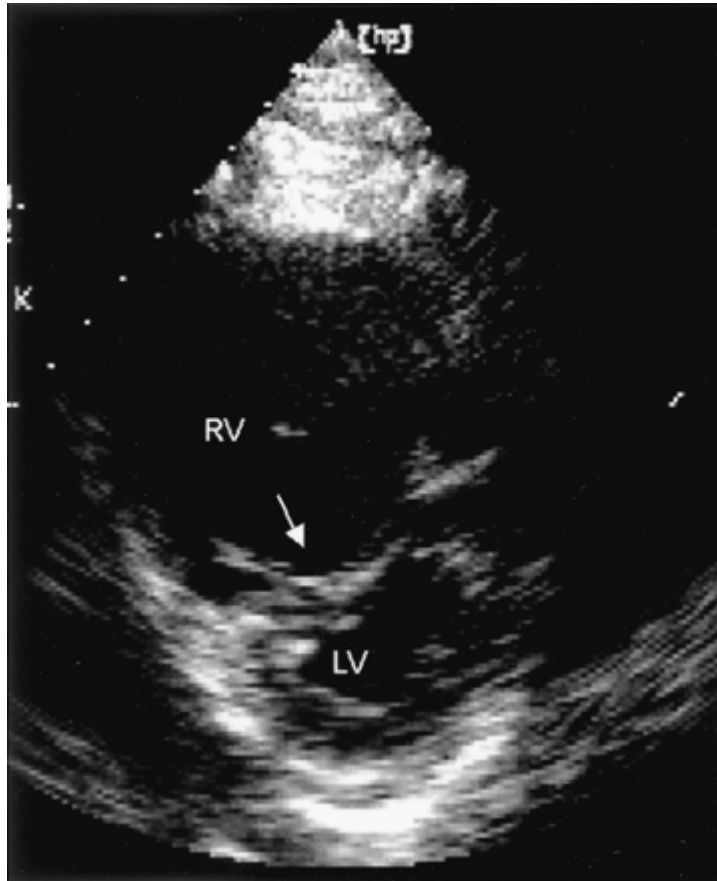
Prognostic score for PE

Aujesky et al., AJRCCM 2005;172:1041-6

Medical Outcomes	Derivation sample, % (<i>n</i> = 10,354)	Validation internal, % (<i>n</i> = 5,177)	Validation external, % (<i>n</i> = 221)
30-day mortality			
Class I	1.1 (0.7–1.7)	1.6 (0.9–2.6)	0 (0–6.6)
Class II	3.1 (2.5–4.0)	3.5 (2.5–4.7)	1.7 (0–8.9)
Class III	6.5 (5.5–7.6)	7.1 (5.7–8.7)	3.2 (0.4–11.2)
Class IV	10.4 (9.0–11.9)	11.4 (9.3–13.8)	4.0 (0.1–20.4)
Class V	24.5 (22.7–26.4)	23.9 (21.4–26.5)	10.0 (1.2–31.7)

Around 40% of patients

Echocardiographic signs of right ventricular strain



Qualitative

- RV hypokinesis (mild, moderate, severe)

Quantitative

RV dilatation

- RV:LV end-diastolic diameter > 1.0
- RV end-diastolic diameter > 30 mm

Pulmonary hypertension

- PA systolic pressure > 30 mm Hg
- Tricuspid regurgitant velocity > 2.8 m/s
- PA mean pressure > 20 mm Hg

Prognosis of PE and echocardiography

ten Wolde et al., Arch Intern Med. 2004;164:1685-1689.

Source	No. of Patients	Mean Age, y	Hemodynamic Status	Thrombolytic Treatment, No. (%)
Goldhaber et al, ⁸ 1993	101	59	Stable	46 (46)
Ribeiro et al, ⁹ 1997	157	>65	Not reported	37 (24)
Kasper et al, ¹⁰ 1997	317	59	Not reported	49 (15)
Goldhaber et al, ⁷ 1999	2454	62	2182 Stable, 169 no symptoms	49 (15)
Grifoni et al, ¹¹ 2000	209	65	162 Normotensive, 19 hypotensive, 28 shock	31 (15)
Grifoni et al, ¹⁸ 2001	117	63	Not reported	NDA
Jerjes-Sanchez et al, ¹⁹ 2001	40	47	Large/massive PE, 24 normotensive	40 (100)

Prognosis of PE and echocardiography

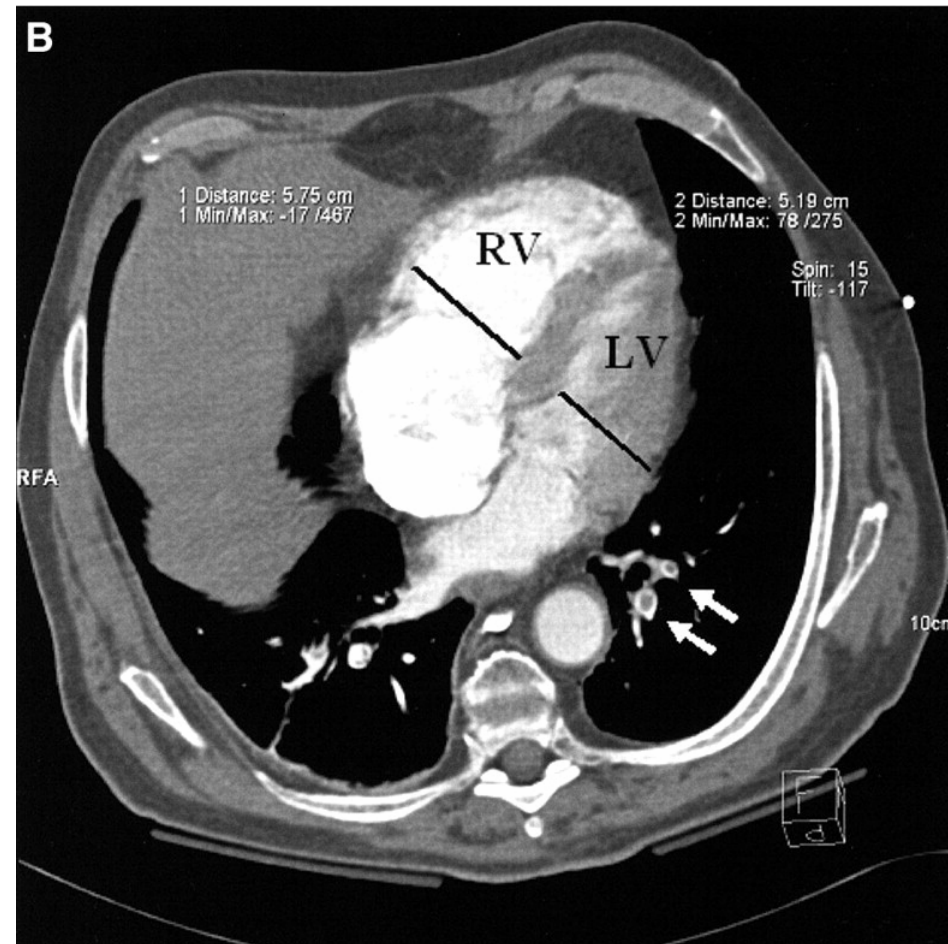
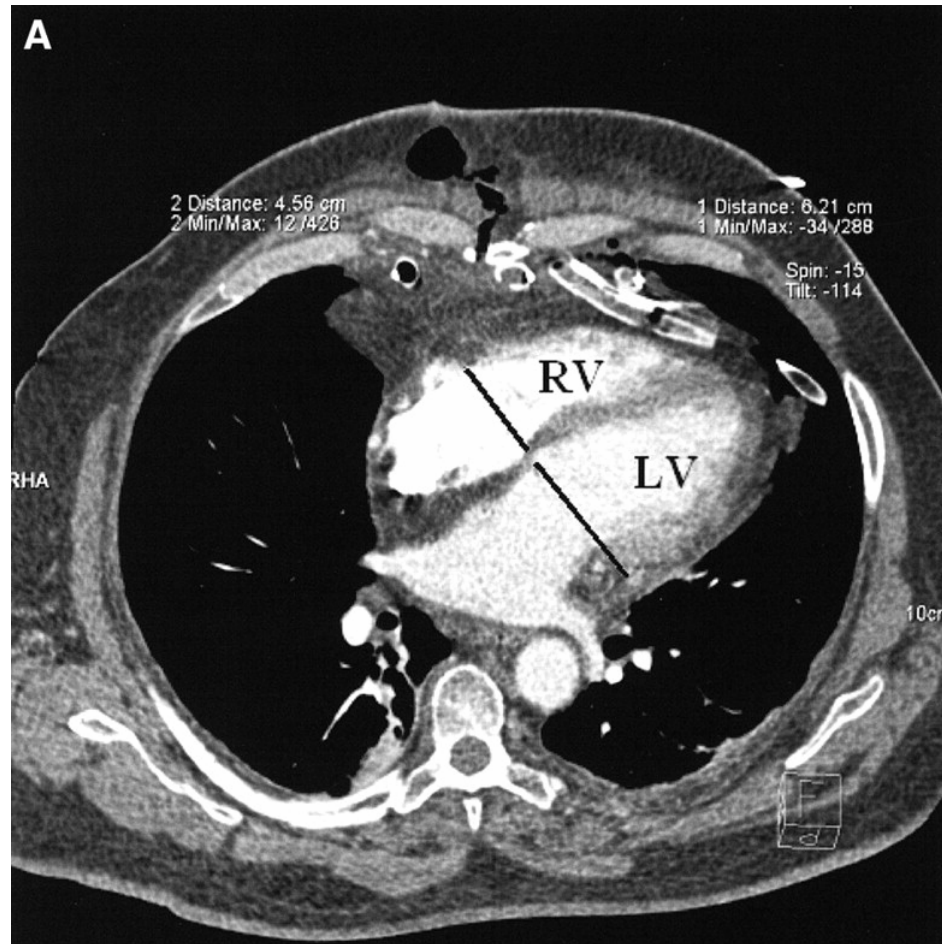
Kreit et al. Chest. 2004;125:1539-1545

Source	Patients, n	Mortality, %	
		RV strain	Normal RV
Goldhaber et al	101	4.3	0
Kasper et al	317	12.6	0.9
Ribeiro et al	126	12.8	0
Grifoni et al	162	4.6	0
Total	706	9.3	0.4

NB: Mortality difference less big after exclusion of hemodynamically unstable patients

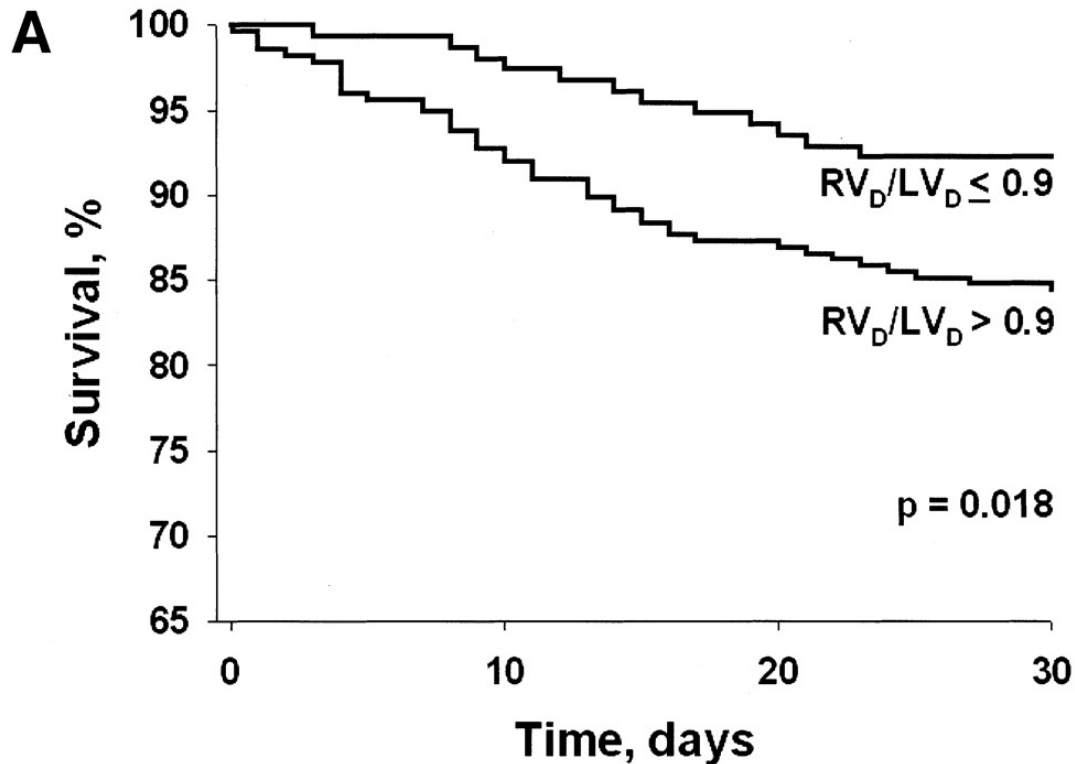
CT and RV strain

Schoepf et al., Circulation. 2004;110:3276-3280



RV strain on CT and mortality

Schoepf et al. Circulation 2004;110:3276-3280



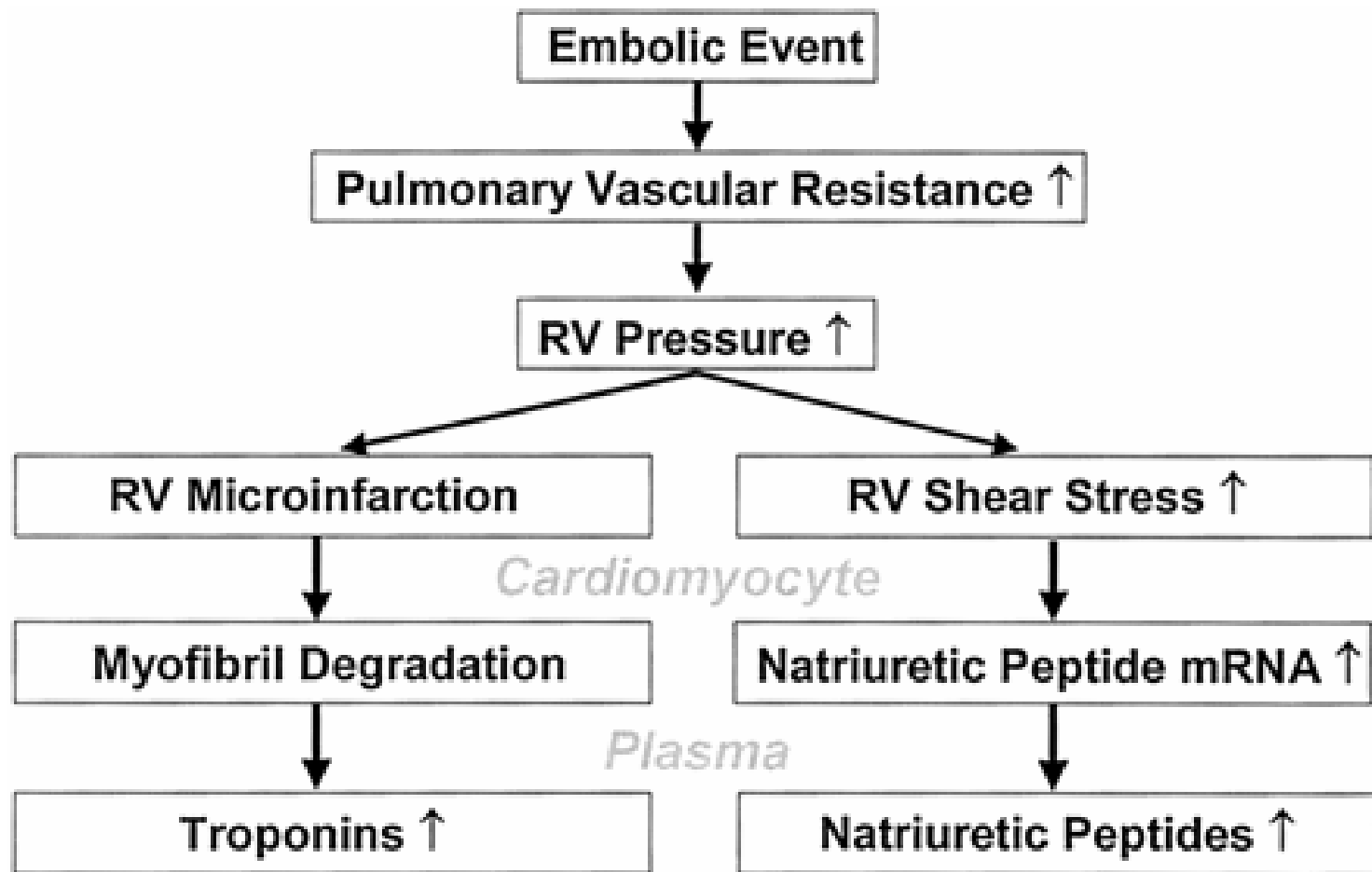
No. at risk
 RV_D/LV_D

≤ 0.9	155	152	146	144
> 0.9	276	256	241	234

64% →

Prognosis of PE: biomarkers

Kucher et al. Circulation. 2003;108:2191



Prognosis of PE: biomarkers

Reference	n	Bio-markers	Assay	Cutoff value	Test + %	NPV %	PPV %
<i>Troponine</i>							
Konstantinides et al	106	cTnI	Centaur	0.07 ng/mL	41	98	14
Konstantinides et al	106	cTn	TElecsys	0.04 ng/mL	37	97	12
Giannitsis et al	56	cTnT	TropT	0.10 ng/mL	32	97	44
Janata et al	106	cTnT	Elecsys	0.09 ng/mL	11	99	34
Pruszczyk et al	64	cTnT	Elecsys	0.01 ng/mL	50	100	25
<i>BNP</i>							
ten Wolde et al	110	BNP	Shionoria	21.7 pmol/L	33	99	17
Kucher et al	73	NT-proBNP	Elecsys	500 pg/mL	58	100	12
Kucher et al	73	BNP	Triage	50 pg/mL	58	100	12
Pruszczyk et al	79	NT-proBNP	Elecsys	153 to 334* pg/mL	66	100	23

Outpatient treatment of PE

- What is the actual evidence?



Outpatient treatment of PE

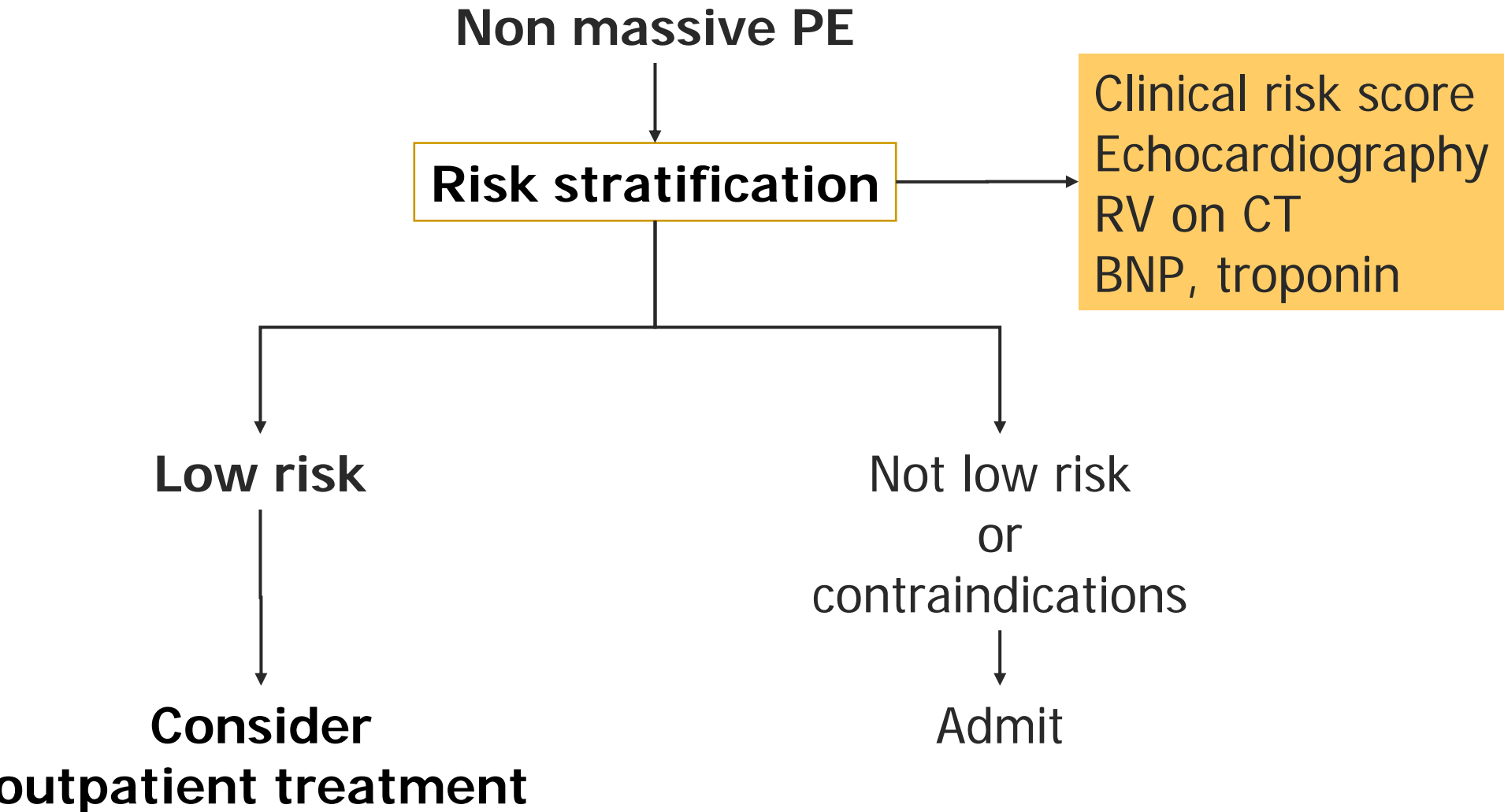
	HBPM	n patients	n PE (%)
Wells 1998	dalteparin 1x/j	194	34 (17%)
Kovacs 2000	dalteparin 1x/j	81	81 (100%)
Beer 2003	nadroparin 1x/j	43	43 (100%)
Wells 2005	dalteparin vs. tinzaparin	505	90 (18%)
Siragusa 2005	not specified	127	36 (28%)
Total			284

Outpatient treatment of PE

	Patients, n	Recurrences DVT/PE, n(%)	Major bleeds, n(%)	Death n(%)
Wells 1998	194	7 (3.6)	4 (2.1)	14 (7.2)
Kovacs 2000	81	5 (6.2)	1 (1.2)	4 (4.9)
Beer 2003	43	1 (2.3)	0 (0)	0 (0)
Wells 2005	90	2 (2.2)	0 (0)	3 (3.3)
Siragusa 2005	36	2 (5.6)	1 (2.8)	11 (30.6)

Outpatient treatment of PE

Pragmatic approach in 2007



OTPE study

Goals:

Randomised control trial (outpatient vs. inpatient treatment of PE by LMWH):

- Recurrence rate of symptomatic DVT/PE
- Major bleeding risk and global mortality
- Resource use and patient satisfaction

OTPE study

INTERVENTION

OUTCOMES At 3 months

Eligible patients
at low risk and
consenting

Randomisation

Outpatient Rx (LMWH)
Discharge from ER within
24 hours of randomisation

Inpatient Rx (HBPM)
Discharge at discretion of
Physician in charge

DVT/PE recurrence
Major bleeding
All-cause mortality
Resource use
Patient satisfaction

Outpatient treatment of PE

- Certainly advisable for low-risk patients
- Standardization of risk stratification required
- Low level of evidence
 - Further studies required