

Acute Pulmonary Oedema and Pulmonary Embolism

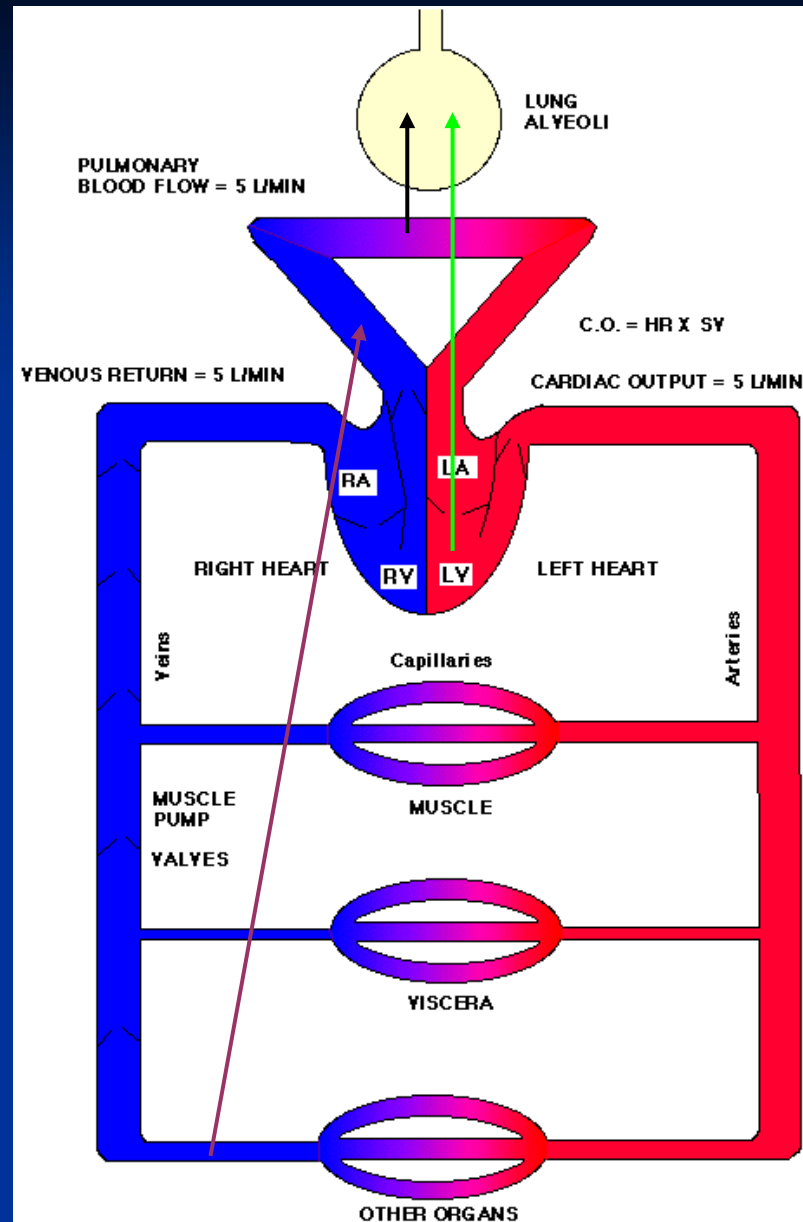
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25 August 2008



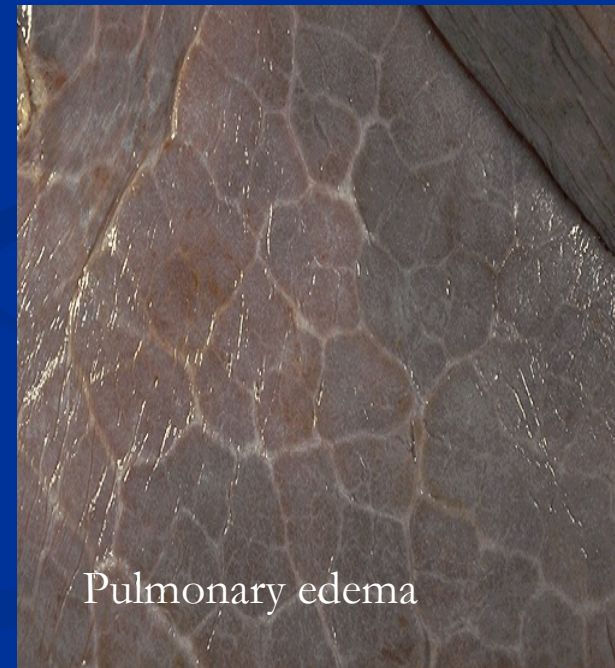
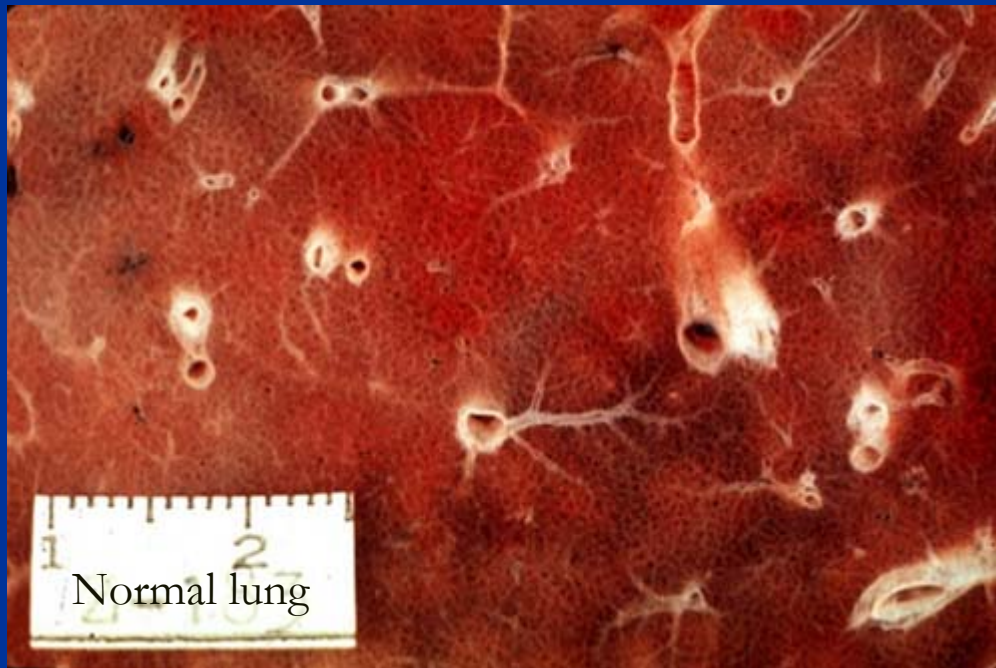
Pathogenesis

1. Pulmonary edema

- Cardiogenic
- Non-cardiogenic (e.g. acute lung injury (ALI), acute respiratory distress syndrome (ARDS))

2. Pulmonary embolism

Cardiogenic pulmonary edema



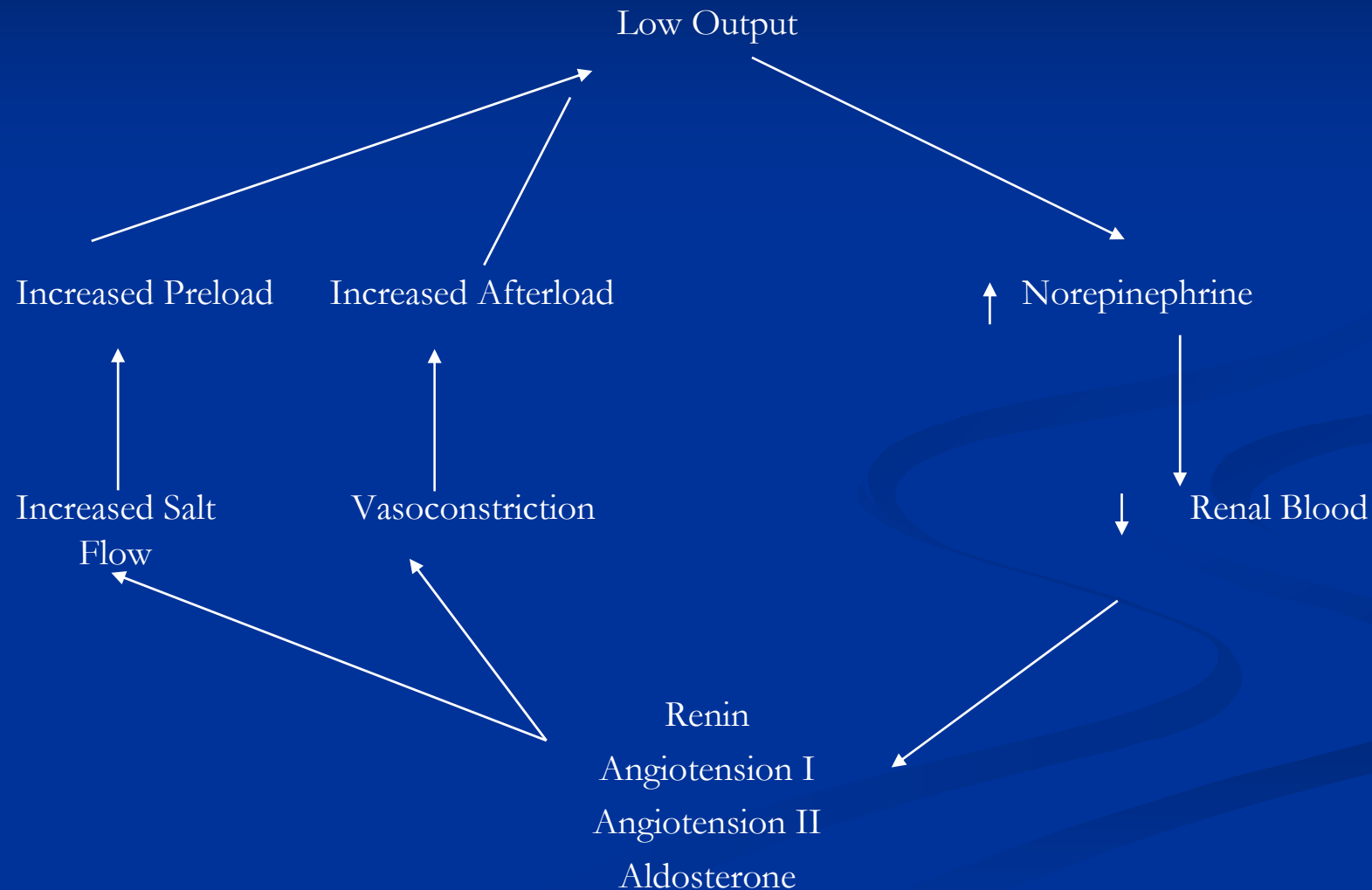
Case

- M/62
- C/o progressive SOB, non-productive cough, low grader fever x 3 days
- Past health: CHF 2 years ago
- P/E:
 - BP 95/55 mmHg, P 110, T 37.9°C, SpO2 96% in RA
 - Chest: bilateral rales and rhonchi

Common causes of APO/CHF

Acute	Chronic	Both
Myocardial infarction	Coronary artery disease	Hypertension 
Myocarditis	Diabetes: systolic and diastolic dysfunction	
Dysrhythmias	Alcoholic cardiomyopathy	
	Valvular heart disease (esp aortic and mitral)	

CHF Vicious Cycle



Symptoms

- Ankle edema
- Severe resp. distress: orthopnea, dyspnea, paroxysmal nocturnal dyspnea.
- Severe apprehension, agitation, confusion, diaphoresis: Results from sympathetic stimulation

Signs

■ Vitals

- increase in sympathetic discharge to compensate.
- BP — elevated
- Pulse rate — elevated to compensate for decreased stroke volume.
- Respirations — rapid and labored, desaturation and cyanosis
- Diaphoresis

■ Pulmonary congestion

- Rales—especially at the bases.
- Rhonchi—associated with fluid in the larger airways
- Wheezes

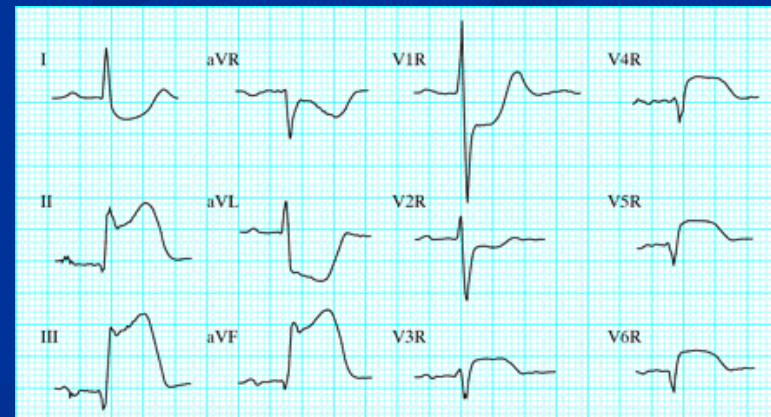
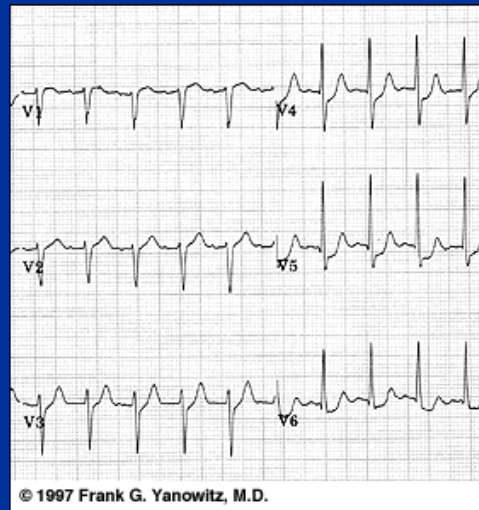
■ Jugular Venous Distention

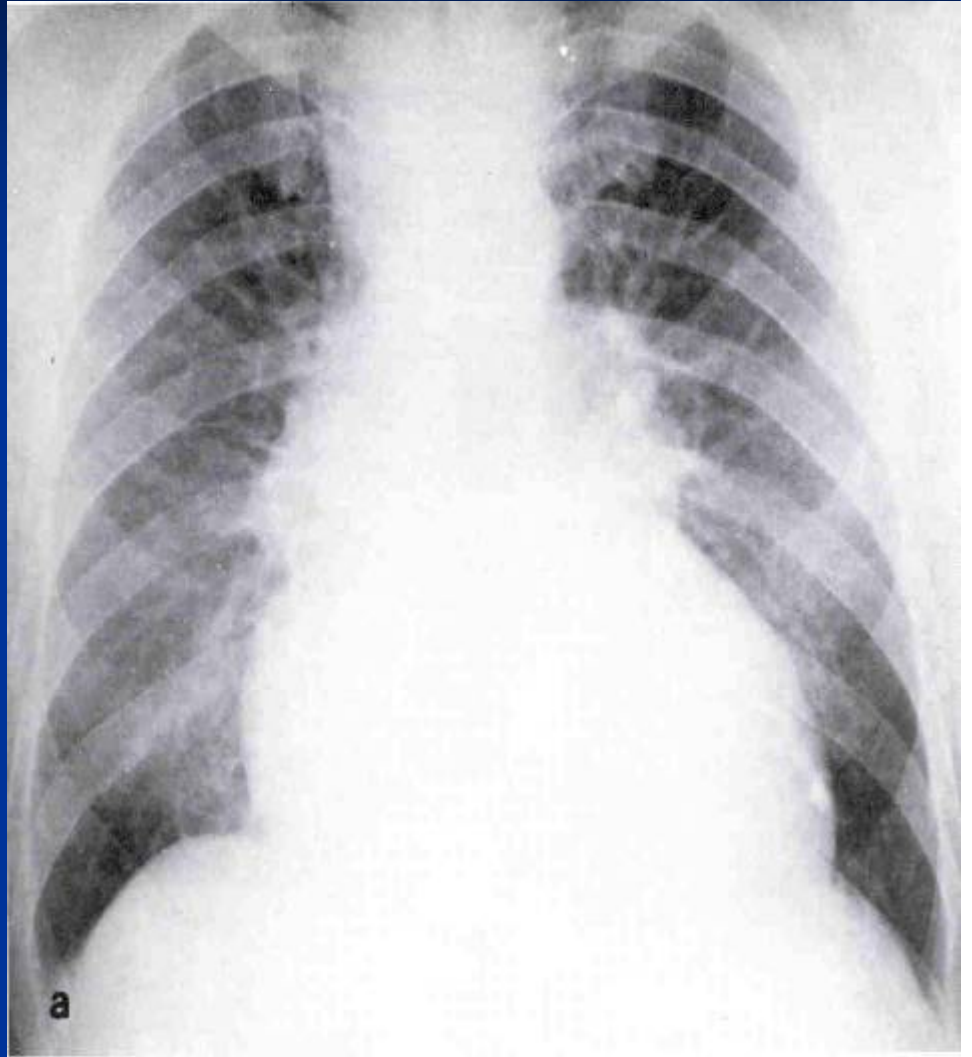
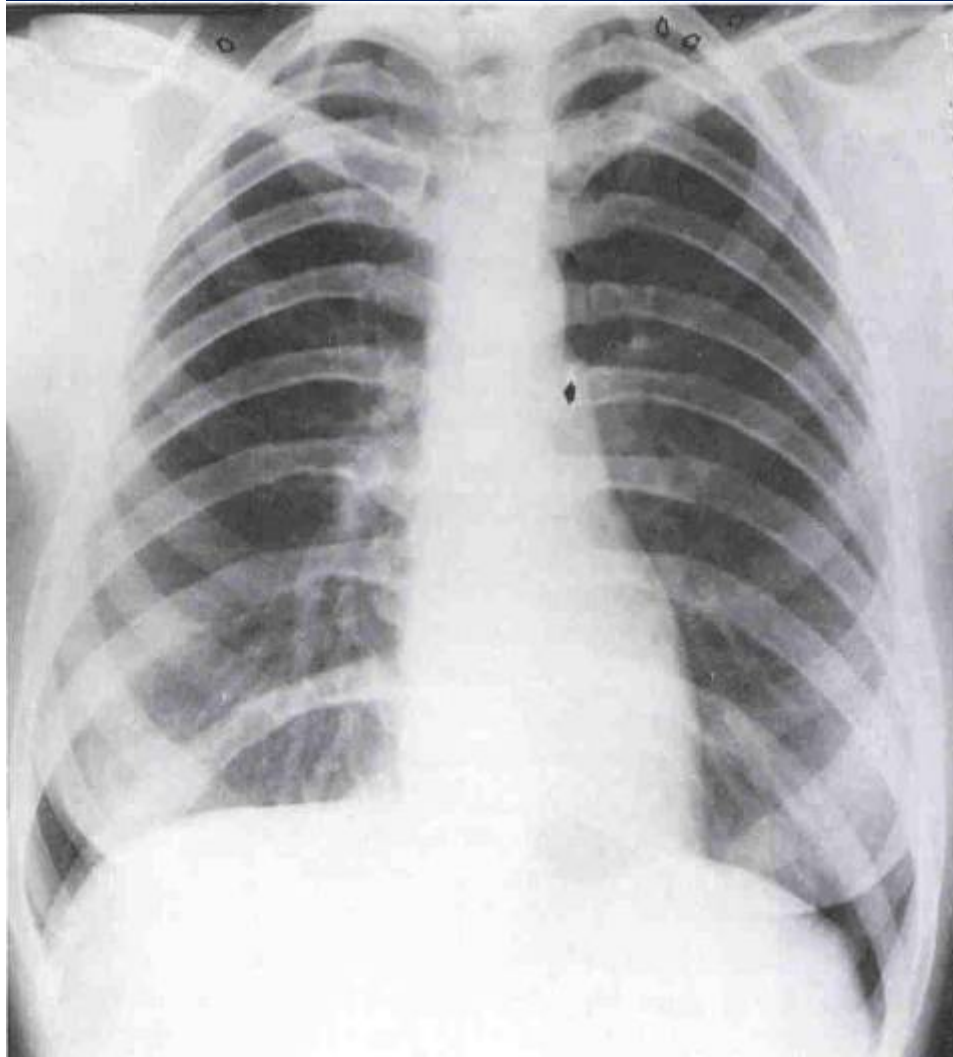
- Comes from back pressure building from right heart into venous circulation

■ Ankle edema, congested liver

Investigations

- ECG: look for cardiac ischaemia
- Echo: check cardiac function, valvular function
- B-type Natriuretic Peptide (BNP): low levels of BNP (<100 pg/ml) make a cardiac cause very unlikely







Left vs Right-side HF

- Left-sided is associated with dyspnea, fatigue, weakness, cough, PND, orthopnea and JVD
- Right-sided is associated with peripheral edema, JVD, RUQ pain, hepatojugular reflex

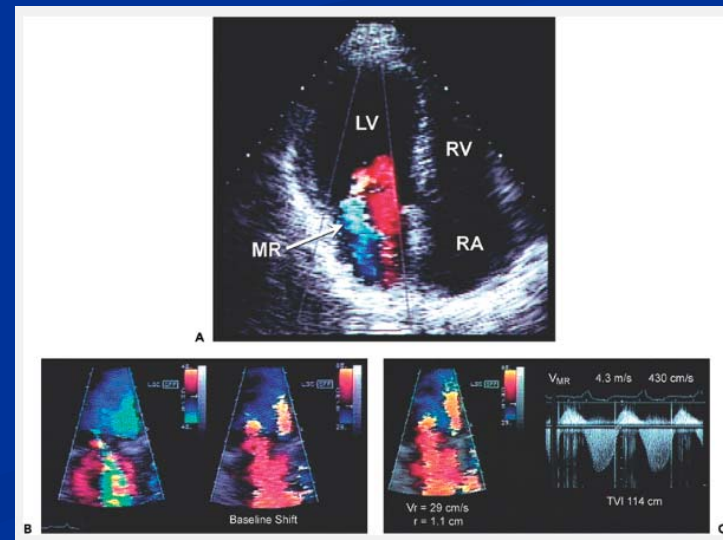
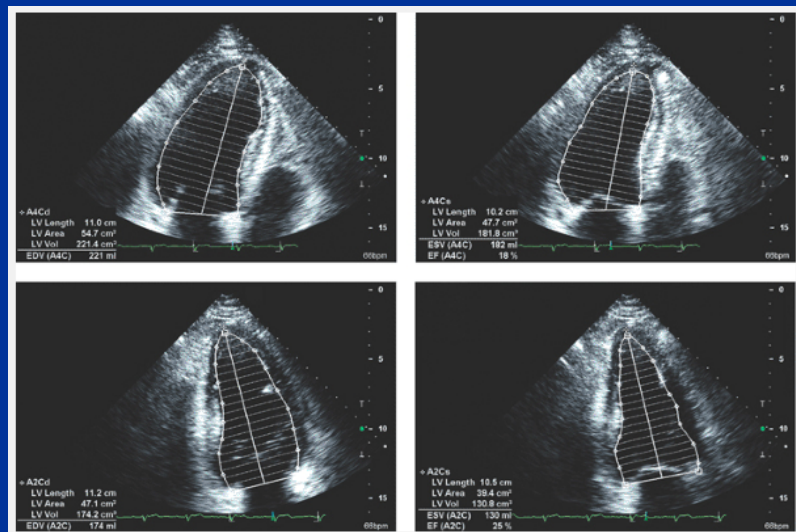
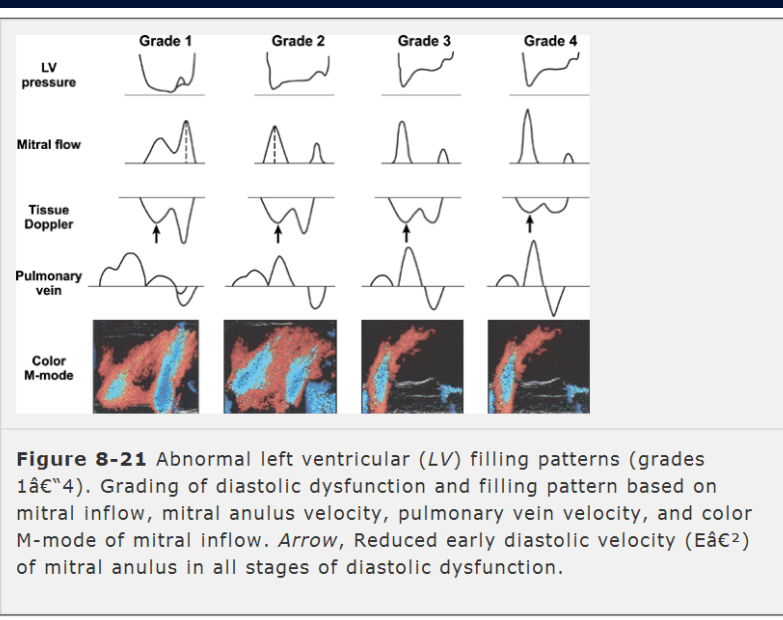
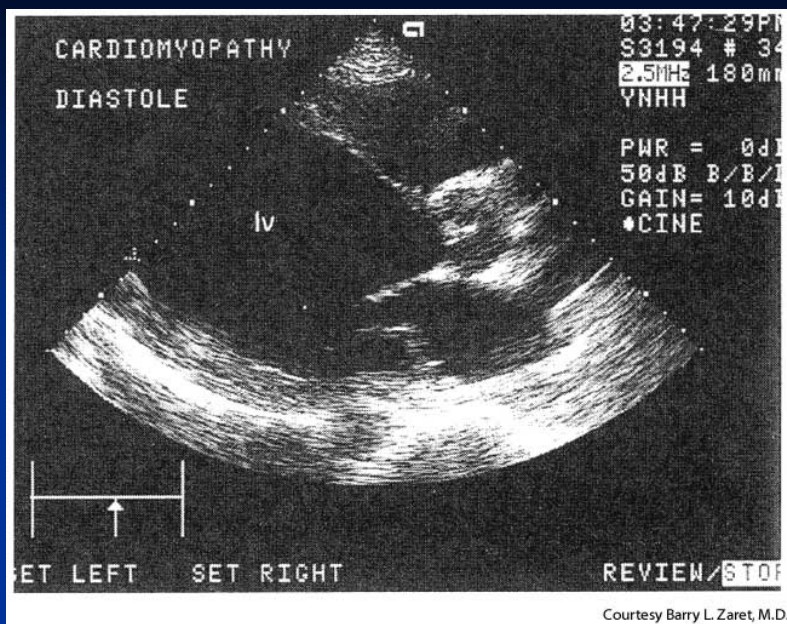
Systolic vs Diastolic HF

■ Systolic HF

- impaired contractility leads to increased cardiac volumes and pressure, and afterload sensitivity
- With stress, failure to improve cardiac contractility, despite increasing venous return results in increased cardiac pressures, pulmonary congestion and edema

■ Diastolic HF

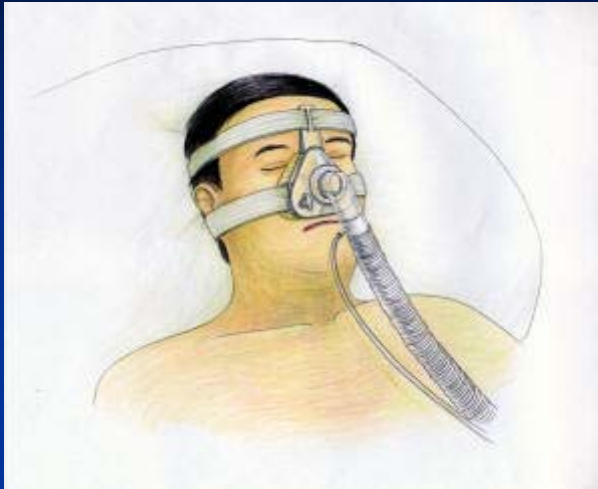
- decreased LV compliance and higher atrial pressures results in preload sensitivity
- Decreased LV compliance necessitates higher atrial pressures to ensure adequate diastolic LV filling



Treatment

- 100% O₂ by face mask to obtain saturation >95%
- Airway control and adequate ventilation: NIV or MV
- Sit up 45 degrees
- Promotion of rest, Relief of anxiety
- Diuretics: e.g. lasix 40-80 mg IV
- Control myocardial ischaemia: aspirin, thrombolytic agents, nitrate, beta-blocker
- Vasodilators: nitrates, ACEI, Ca channel blocker
- Control hypertension: nitrate, ACEI, nitroprusside, Ca channel blockers, hydralazine
- If hypotensive or need for inotropic support: dopamine 5-10 ug/kg/min, dobutamine, digoxin
- Treat coexisting arrhythmia or electrolyte disturbance
- Morphine use PRN
- Fluid removal in renal shutdown: haemofiltration, haemodialysis
- Intraaortic balloon pump
- LV remodelling: ACEI

Nasal



Facial



Nasal pillow



Total face



Vasodilator

- Dilate blood vessels
- Often constricted due to activation of the sympathetic nervous system and the renin-angiotensin-aldosterone system.
- Common ACE inhibitors
 - Perindopril
 - Lisinopril
 - Captopril
- Nitrates

Diuretics

- Lasix
 - Hydrochlorothiazide(HCTZ)
 - Spironolactone
-
- These inhibit reabsorption of Na^+ into the kidneys

Calcium channel blocker

- Used to dilate blood vessels
- Used mostly with CHF in the presence of ischemia
- Examples
 - Nifedipine
 - Diltiazem
 - Verapamil
 - Amlodipine
 - Felodipine

Beta blockers

- Useful by blocking the beta-adrenergic receptors of the sympathetic nervous system, the heart rate and force of contractility are decreased → could actually worsen CHF
- Examples
 - Metoprolol
 - Atenolol
 - Propranolol
 - Amiodarone

Inotropic agents

- Dopamine
 - Dobutamine
 - Digoxin
-
- Increases the contractility of the heart → increasing the cardiac output

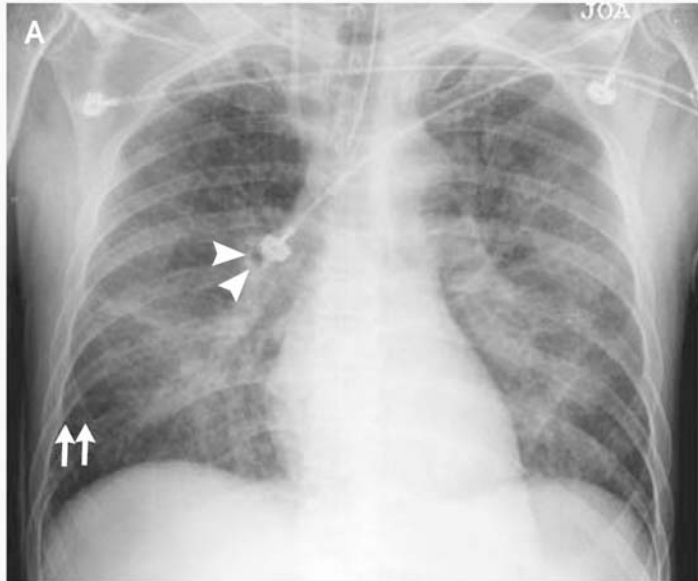
ACE Inhibitors

- Prevent the production of the chemicals that causes blood vessels to narrow
- Resulting in blood pressure decreasing and the heart pumping easier

Non cardiogenic pulmonary edema

Causes of non-cardiogenic APO (= ALI, ARDS)

- Inhalation of toxic gases
- Multiple blood transfusions
- Severe infection
- Pulmonary contusion, i.e.,
- Multitrauma, e.g., severe car accident
- Neurogenic, e.g., subarachnoid hemorrhage
- Aspiration, e.g., gastric fluid or in case of drowning
- Certain types of medication
- Upper airway obstruction
- Arteriovenous malformation
- Reexpansion, i.e. post pneumectomy or large volume thoracentesis
- Reperfusion injury, i.e. postpulmonary thromboendartectomy or lung transplantation
- Ascent to high altitude occasionally causes high altitude pulmonary edema (HAPE)[\[2\]](#)



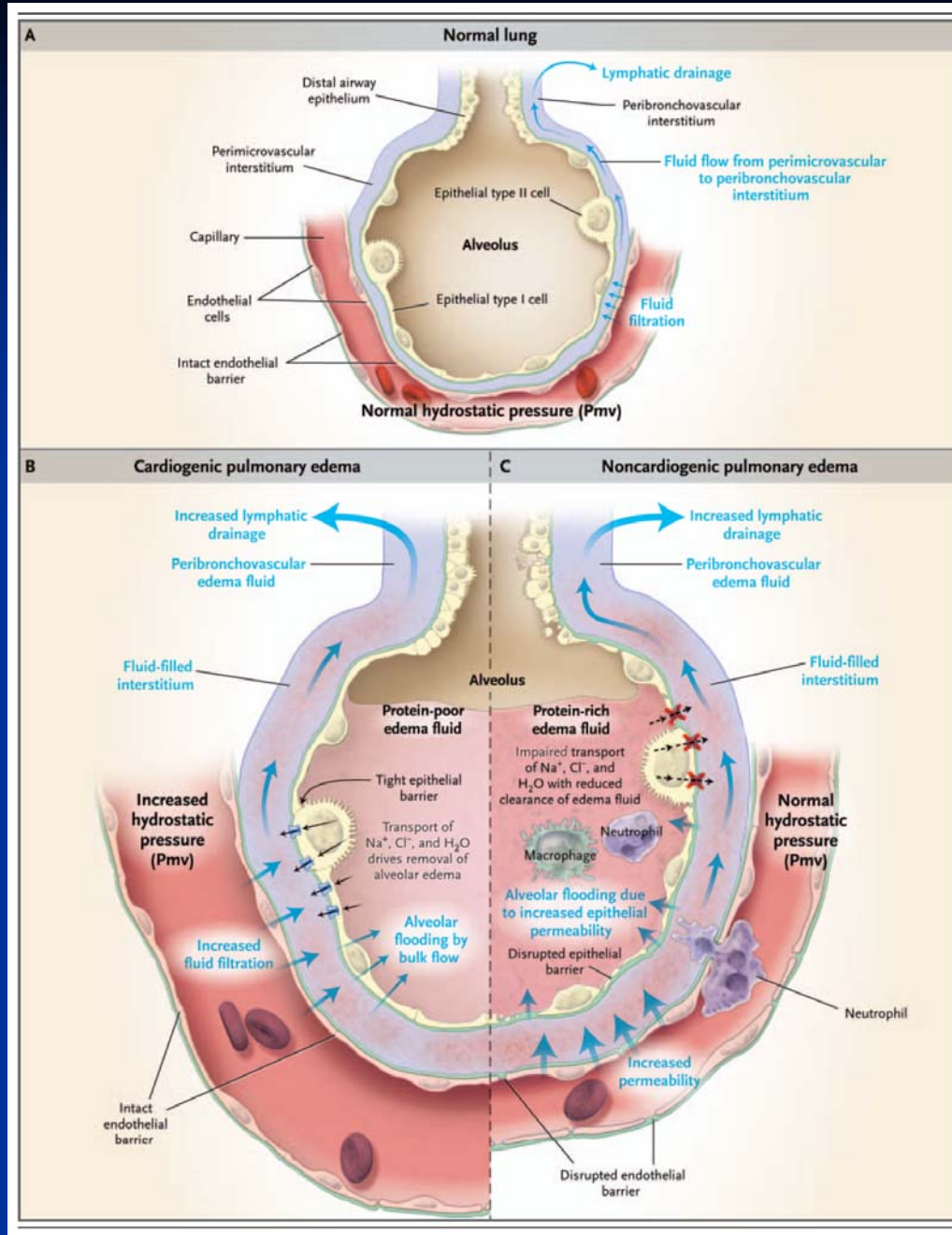
Cardiogenic pulmonary edema

- Enlargement of peribronchial vascular space
- Kerley's B lines



Non- cardiogenic pulmonary edema

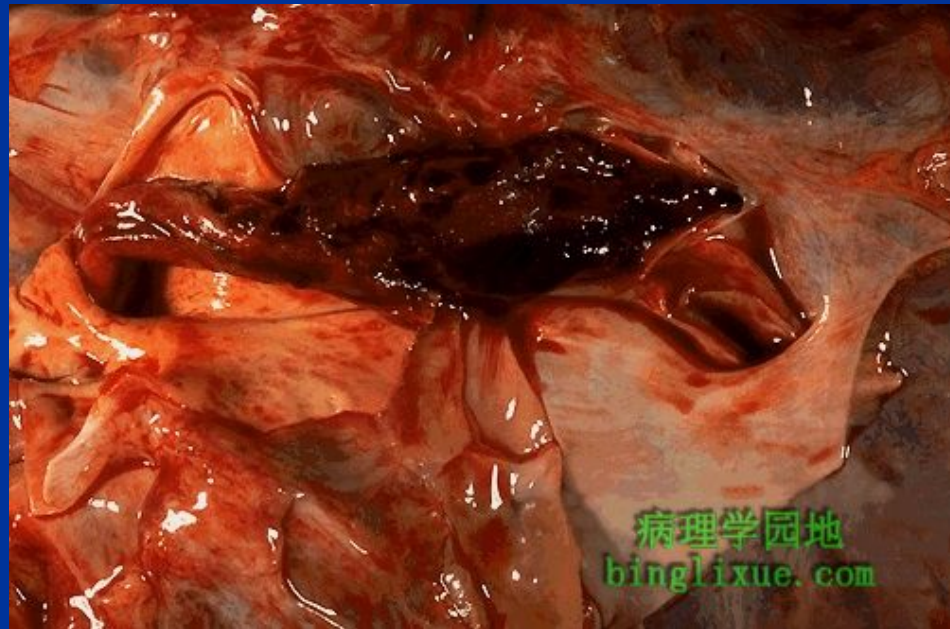
- E.g. pneumococcal septicaemia
- Air-bronchograms
- Acute lung injury/acute respiratory distress syndrome



Treatment

- Ventilatory support
- Direct to underlying cause

Pulmonary embolism



Investigations

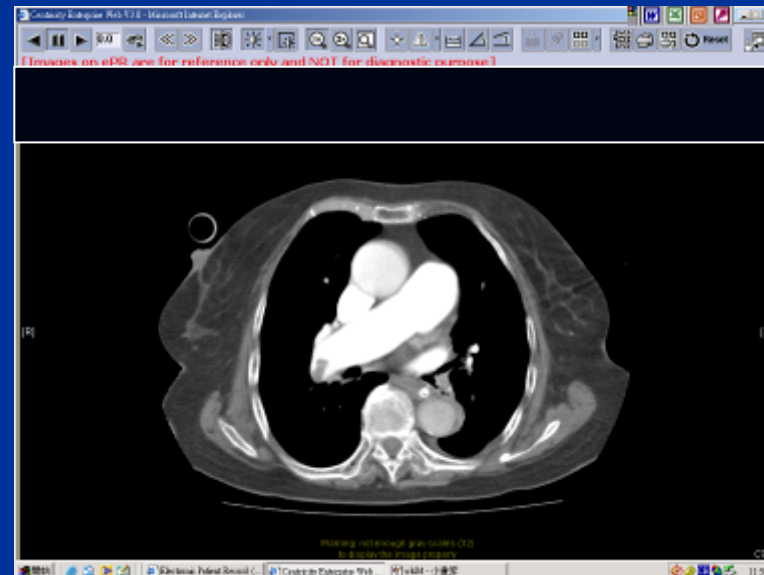
- 1837 First case report of PE
- 1922 Description of signs at CXR
- 1963 Pulmonary angiography
- 1964 Lung scintigraphy
- 1992 Spiral CT

Case 1: F/80, WK

- HT / IHD / CHF / Bronchiectasis
- Slipped and fell, sustained # left NOF.
- OT postponed for 2 weeks due to an episode of HAP and fast AF.
- Intra-op hypotension with PEA.
- Echo: Grossly dilated RV
- Spiral CT thorax

Spiral CT thorax

- Filling defects in right superior / inferior and left superior PA and subsegmental branches.



Progress

- Clexane (low molecular weight heparin) 60mg Q12H SC.
- Not for thrombolytic / embolectomy in view of unstable haemodynamics and extensive involvement.
- Subsequent ARF with anuria.
- Succumb on D1 ICU stay.

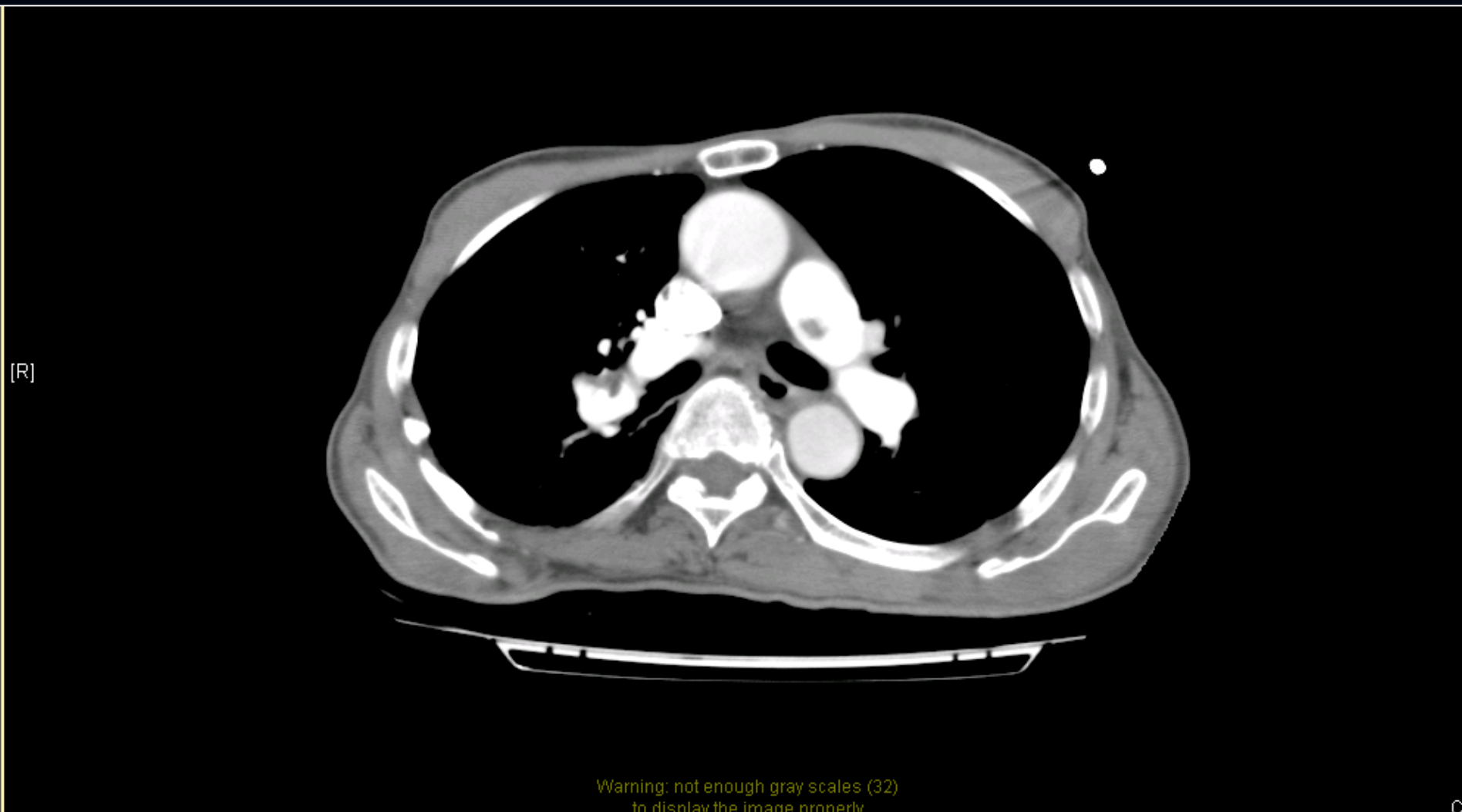
M/64, HYK

- History of old TB with right lobectomy.
- Slip and fell from a flight of stairs
- CT C-spine: No fracture but cord impingement in C6/7.
- MRI C-spine: Spinal stenosis at C4/5.
Heterogeneous signals in pre / paravertebral region, could be oedema / haemorrhage.

Rehabilitation

- Able to walk wth frame.
- Increased SOB with desaturation.
- Difference in calves circumference.
- ECG: Sinus tachycardia. RBBB.
- CXR: Clear lung fields.
- Echo: Dilated RA / RV with paradoxical septal motion and D-shaped LV during diastole; TR.



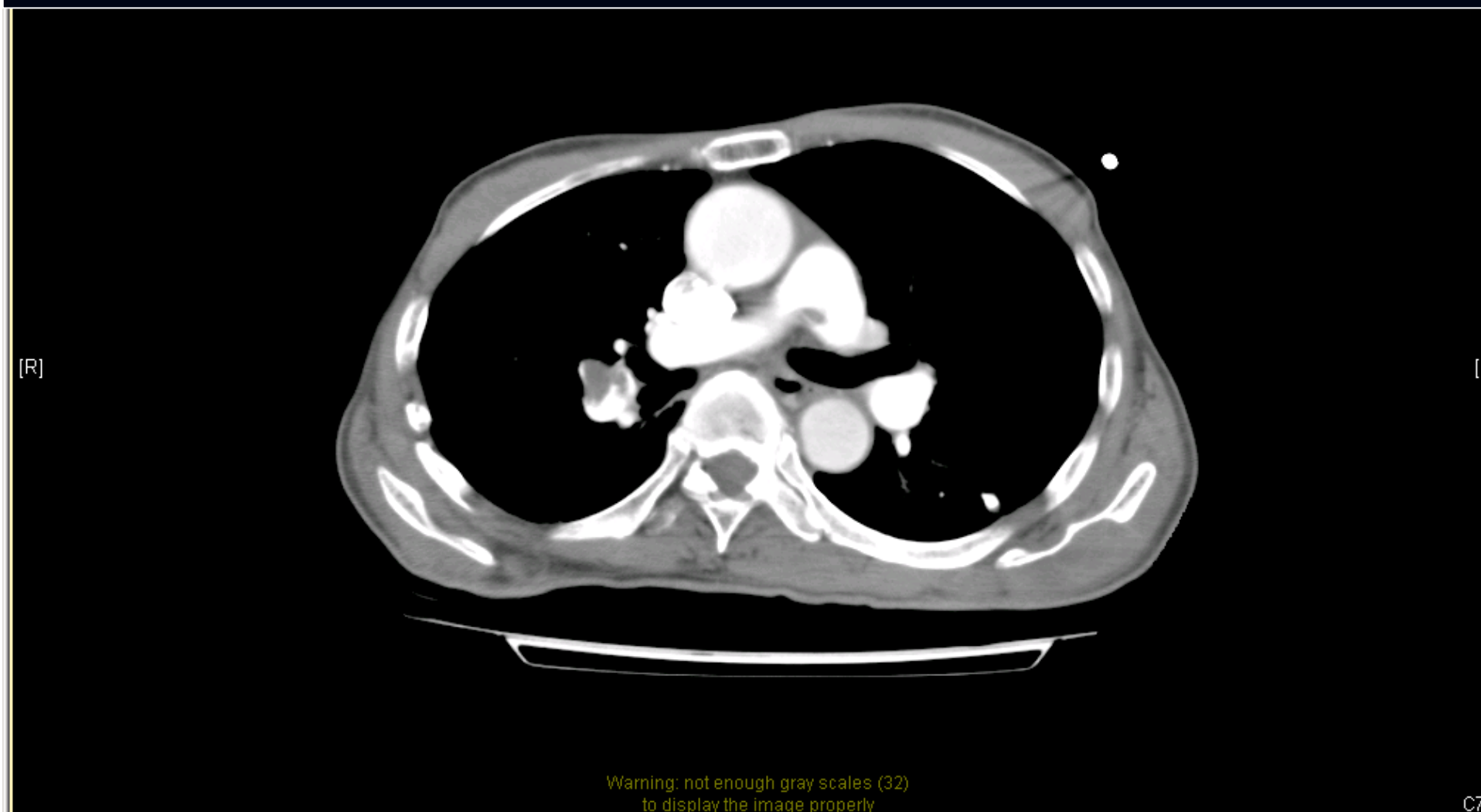


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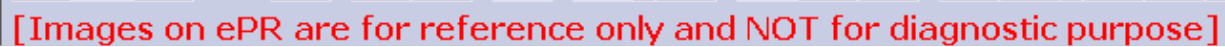
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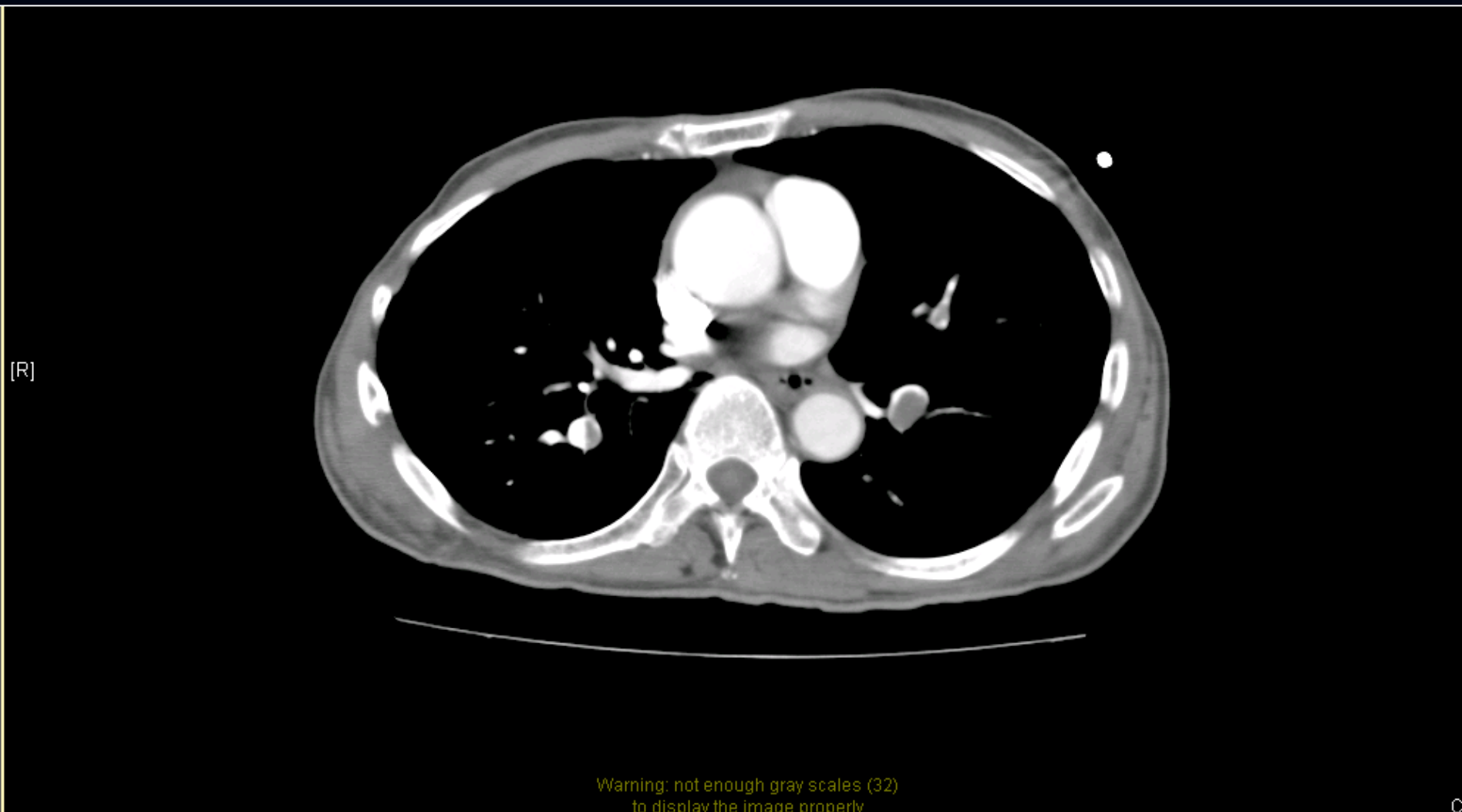


[Images on ePR are for reference only and NOT for diagnostic purpose]

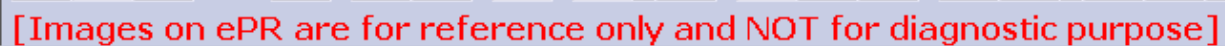








C



Progress

- Spiral CT: Filling defects in pulmonary trunk, bilateral pulmonary arteries and their segmental branches.
- Enoxaparin 60mg Q12H SC + warfarin.
- Thrombolytics not given **in view of MRI findings suspicious of oedema / haemorrhage over C-spine.**
- Weaned off all O2.
- Haemodynamics remained stable.
- INR 1.4 before discharge.

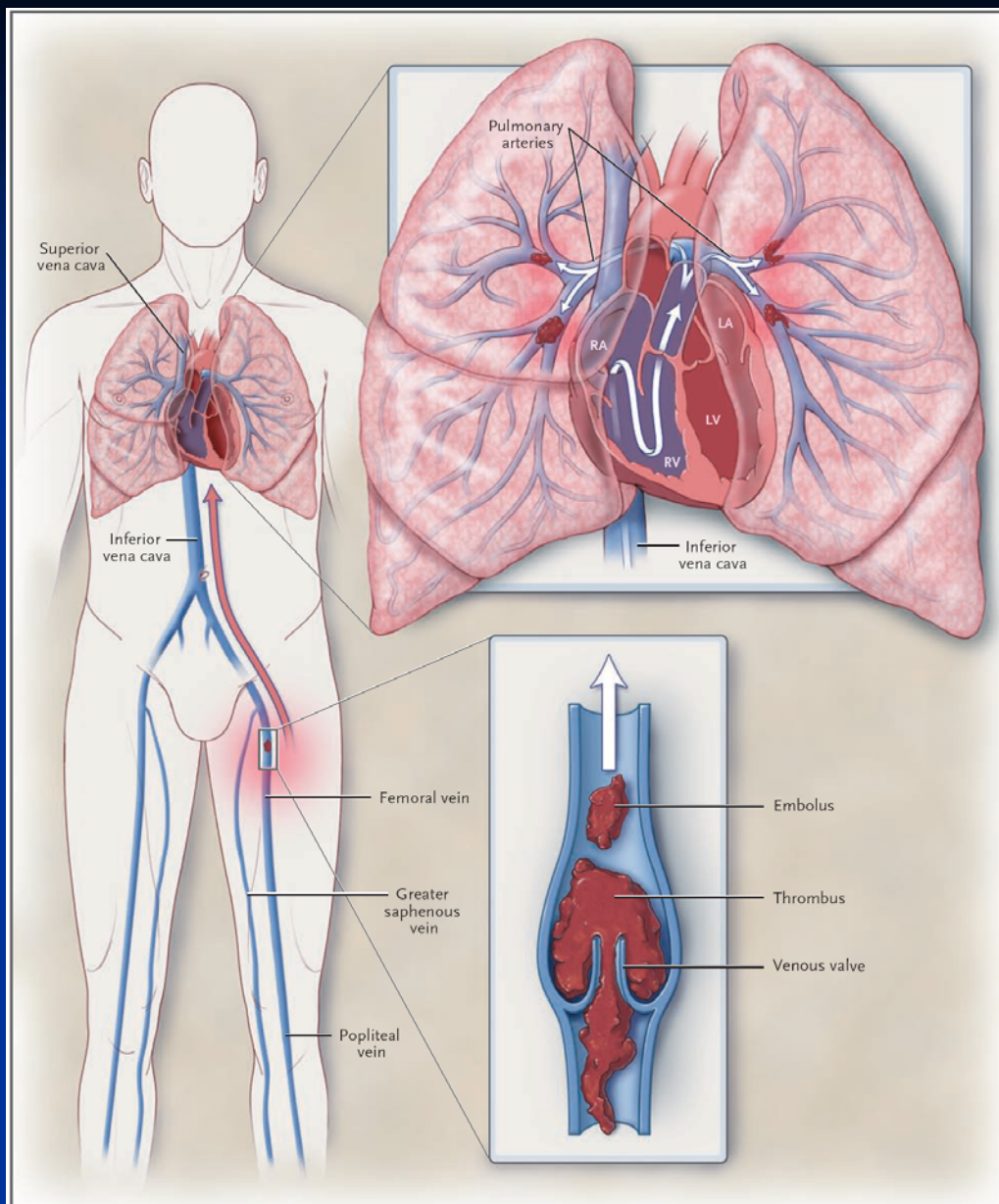
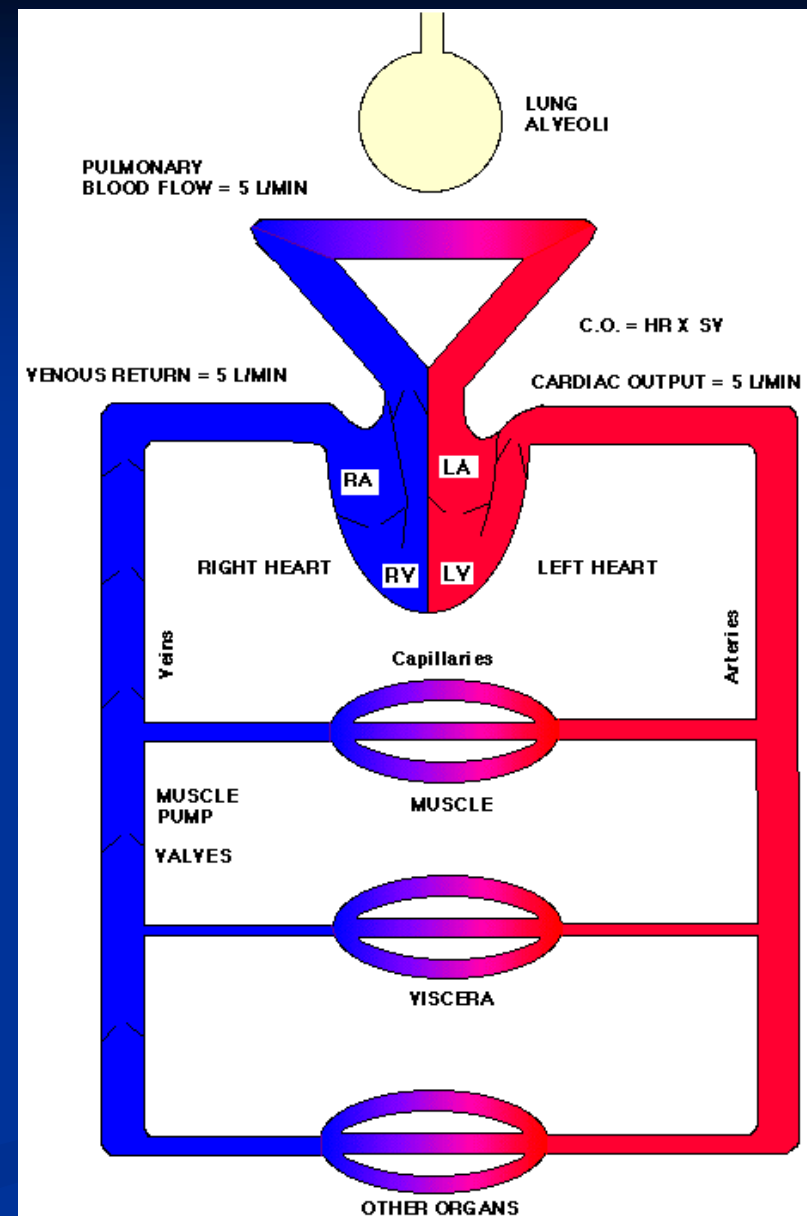
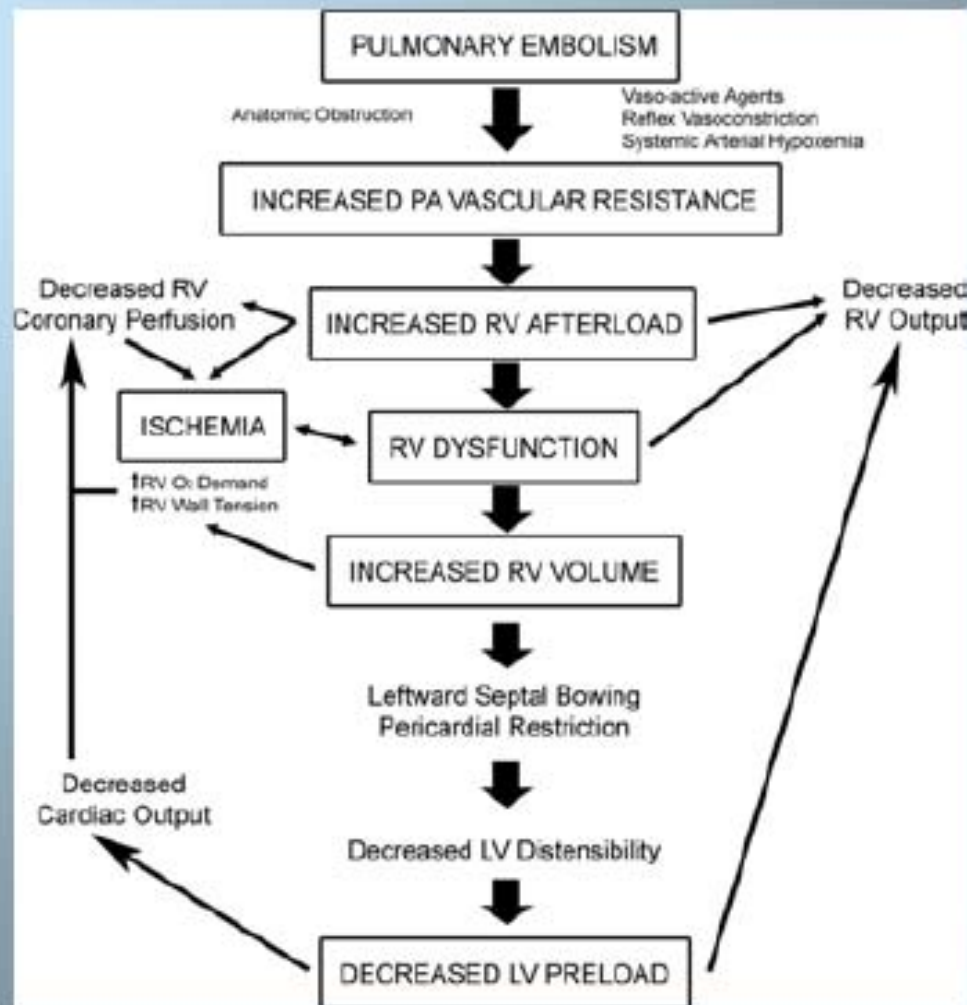


Figure 1. Pathophysiology of Pulmonary Embolism.

Pulmonary embolism usually originates from the deep veins of the legs, most commonly the calf veins. These venous thrombi originate predominantly in venous valve pockets and at other sites of presumed venous stasis (inset, bottom). If a clot propagates to the knee vein or above, or if it originates above the knee, the risk of embolism increases. Thromboemboli travel through the right side of the heart to reach the lungs. LA denotes left atrium, LV left ventricle, RA right atrium, and RV right ventricle.



PATHOPHYSIOLOGIC CYCLE OF MAJOR PE



Hong Kong Data

Data of VTE in Chinese population

Mok et al 2005 Arthritis Rheuma	N=625 HK SLE	VTE: 13/1000 pt-yrs Cumulative hazards at 60M after dx: 3.7% Chinese (c/w 6.6% in African-Americans, 10.3% in Caucasians)
Cheuk BL 2004 Br J Surg	Hong Kong Chinese 6.7 million population	All - DVT: 17.1 per 100,000; PE: 3.9 per 100,000 65 yrs old - DVT: 81.1 per 100,000; PE: 18.6 per 100,000 Hospital mortality – DVT 7.3%, PE 23.8% Surgical (N = 120140) – DVT 0.13%/yr; PE: 0.04%/yr
Lee AC 2003 HKMJ	N = 8 HK children	4 with DVT + PE; others SVC thrombosis, CV thrombosis, pr C def, pr S def, anti-cardiolipin, malignancy Rates similar to Caucasians
Liu HS 2002 HKMJ	N = 376 Hong Kong	352 peripheral DVT, 5 deep DVT (cerebral sinus and portal v), 40 PE (26 with concomitant DVT), 6 fatal PE at autopsy Projected VTE rate in the population: 16.6 per 100,000
You JHS 2005 Br J Pharmacol	Hong Kong	Events vs INR (see graph), aim 1.8 – 2.4 for Chinese
Chau KY 1991 Pathology	Hong Kong	Retrospective review of 15 years' autopsies Incidence of significant PE: 0.58% in first 5 yr period; 2.08% in recent yrs Conclusion: increasing incidence of pul TE
Joynt GM 2000 Chest	Hong Kong N = 124 femoral v cats	14 out of 124 femoral venous catheterizations ■12 line-related; 2 in the uncannulated leg ■Onset 1 day to 1 week after catheterization
Chau KY 1995 J Clin Pathol	N = 3446 necropsies from 1987 - 1992 Hong Kong	Overall rate 3.77% Seasonal changes noted (see graph) ■Troughs in June, July, Nov, Dec: 1.6 – 2.4% ■Rest of months: 4.0 – 5.5%

PULMONARY EMBOLISM

- 90% of clinically important PE results from leg DVT
- 96% of patients with DVT or PE have one or more risk factors
- The risk increases in proportion to the # of risk factors

Table 1. Risk Factors for Venous Thromboembolism.*

Hereditary factors

Antithrombin deficiency

Protein C deficiency

Protein S deficiency

Factor V Leiden

Activated protein C resistance without factor V Leiden

Prothrombin gene mutation

Dysfibrinogenemia

Plasminogen deficiency

Acquired factors

Reduced mobility

Advanced age

Cancer

Acute medical illness

Major surgery

Trauma

Spinal cord injury

Pregnancy and postpartum period

Polycythemia vera

Antiphospholipid antibody syndrome

Oral contraceptives

Hormone-replacement therapy

Heparins

Chemotherapy

Obesity

Central venous catheterization

Immobilizer or cast

Probable factors

Elevated levels of lipoprotein(a)†

Low levels of tissue factor–pathway inhibitor

Elevated levels of homocysteine; factors VIII, IX, and XI;
fibrinogen; and thrombin-activated fibrinolysis in-
hibitor

Proportion of patients with clinically suspected DVT in whom Dx Was confirmed

# of DVT risk factors	Confirmed DVT(%)
0	11%
1	24%
2	36%
3	50%
4 or more	100%

Diagnosis of pulmonary embolism

Based on:

- Relevant SYMPTOMS & SIGNS
- Associated RISK FACTORS
- Probability of ALTERNATIVE
Diagnosis
- OBJECTIVE Confirmation

Canadian (Wells) prediction score

Variable and score

DVT symptoms and signs — 3.0

PE as likely as or more likely than alternative diagnosis — 3.0†

Heart rate >100 beats/min — 1.5

Immobilization or surgery in previous 4 wk — 1.5

Previous DVT or PE — 1.5

Hemoptysis — 1.0

Cancer — 1.0

Total score‡

<2.0 — low pretest probability

2.0 to 6.0 — moderate pretest probability

>6.0 — high pretest probability

Dichotomized Wells score§

≤4 — PE unlikely

>4 — PE likely

Original Geneva (Wicki) score¶

Variable and score

Age

60–79 yr — 1

≥80 yr — 2

Previous DVT or PE — 2

Recent surgery — 3

Heart rate >100 beats/min — 1

PaCO₂

<36.2 mm Hg (<4.8 kPa) — 2

36.2–38.9 mm Hg (4.8–5.19 kPa) — 1

PaO₂

<48.8 mm Hg (<6.5 kPa) — 4

48.8–59.9 mm Hg (6.5–7.99 kPa) — 3

60–71.2 mm Hg (8.0–9.49 kPa) — 2

71.3–82.4 mm Hg (9.5–10.99) — 1

Chest radiograph

Platelike atelectasis — 1

Elevation of hemidiaphragm — 1

Revised Geneva score¶

Variable and score

Age >65 yr — 1

Previous DVT or PE — 3

Surgery or lower limb fracture in previous wk — 2

Active cancer — 2

Unilateral lower limb pain — 3

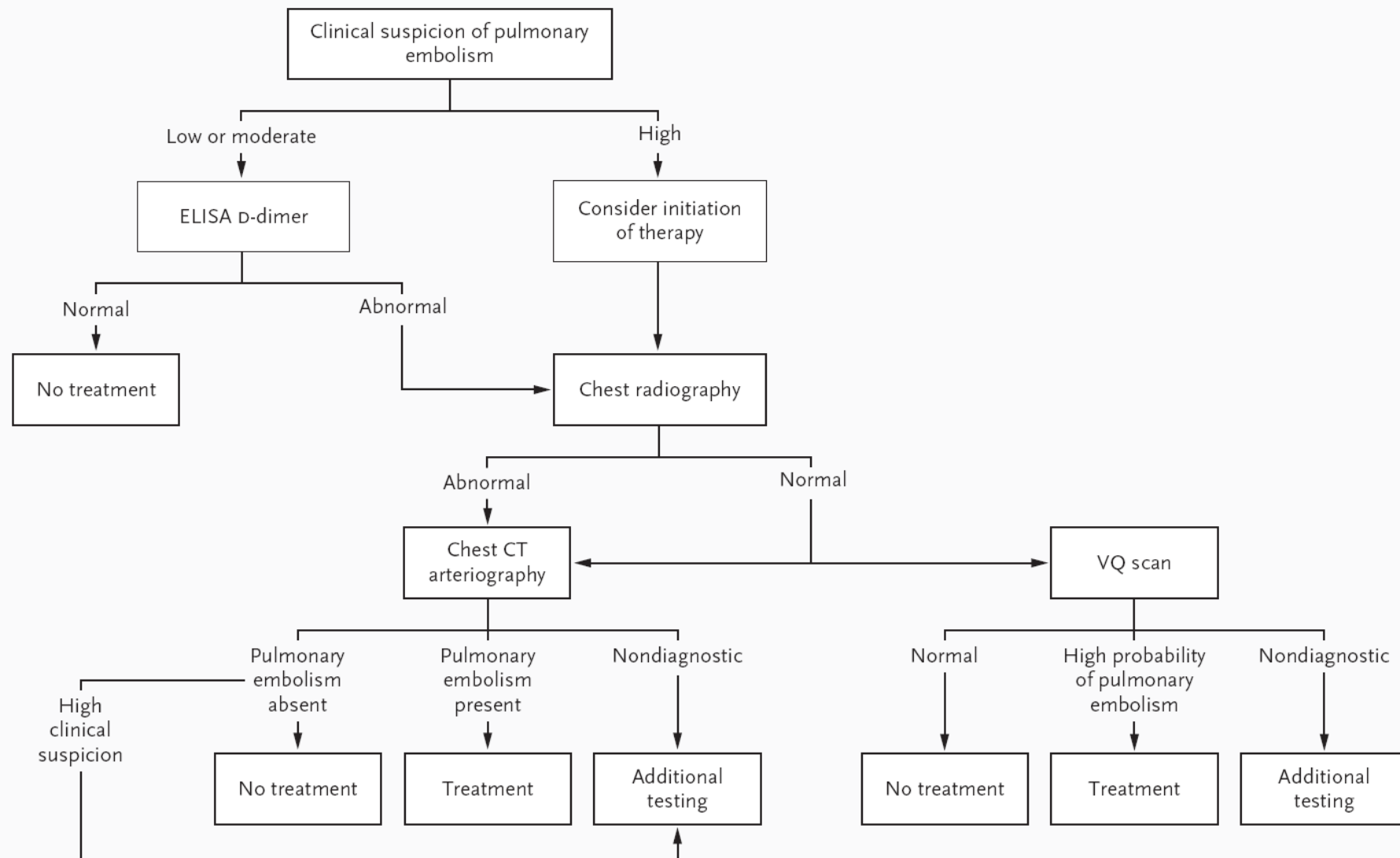
Hemoptysis — 2

Heart rate

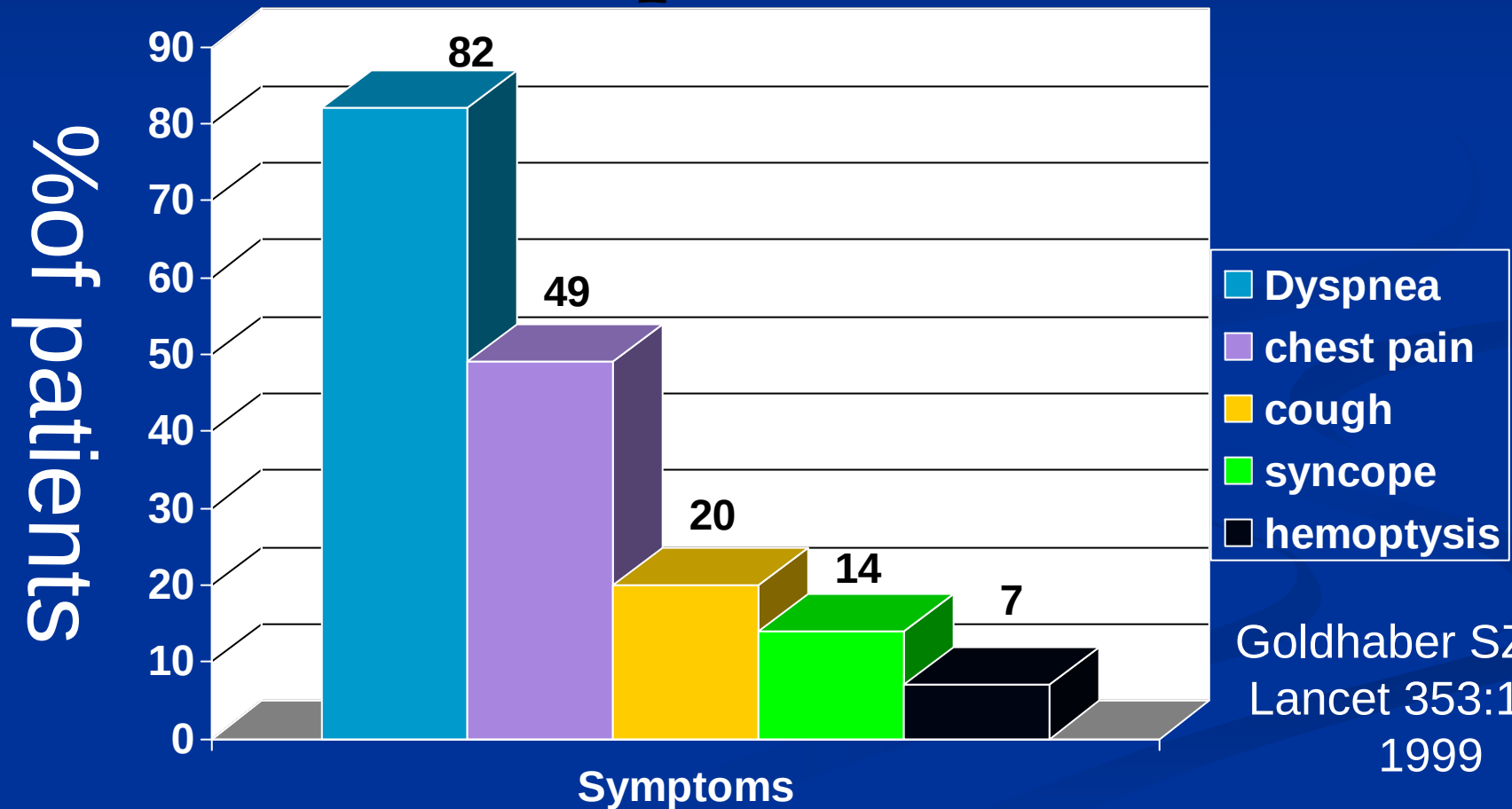
75–94 beats/min — 3

≥95 beats/min — 5

Pain on leg palpation or unilateral edema — 4



Symptoms & Signs of Pulmonary Embolism in 2110 patients



Goldhaber SZ et al.
Lancet 353:1386
1999

PULMONARY EMBOLISM SIGNS

■ Tachypnea	92%
■ Crackles	58%
■ Tachycardia	44%
■ Fever	43%
■ Increased “P ₂ ”	53%
■ Phlebitis	32%

Blood investigations

■ ABGs:

- Hypoxaemia and hypocapnia
- E.g. pH 7.48 PaO₂ 52 PaCO₂ 29

■ D-dimer by ELISA

- A degradation product of crosslinked fibrin
- Has a high negative predictive value:
R/O PE in low clinical probability

ECG FINDINGS

■ Sinus Tachycardia	43%
■ “T” wave inversion	40%
■ ST segment depression	33%
■ Low voltage	16%
■ L axis	12%
■ S1 Q3 T3	11%
■ ST elevation	11%
■ R Bundle Branch Block	11%

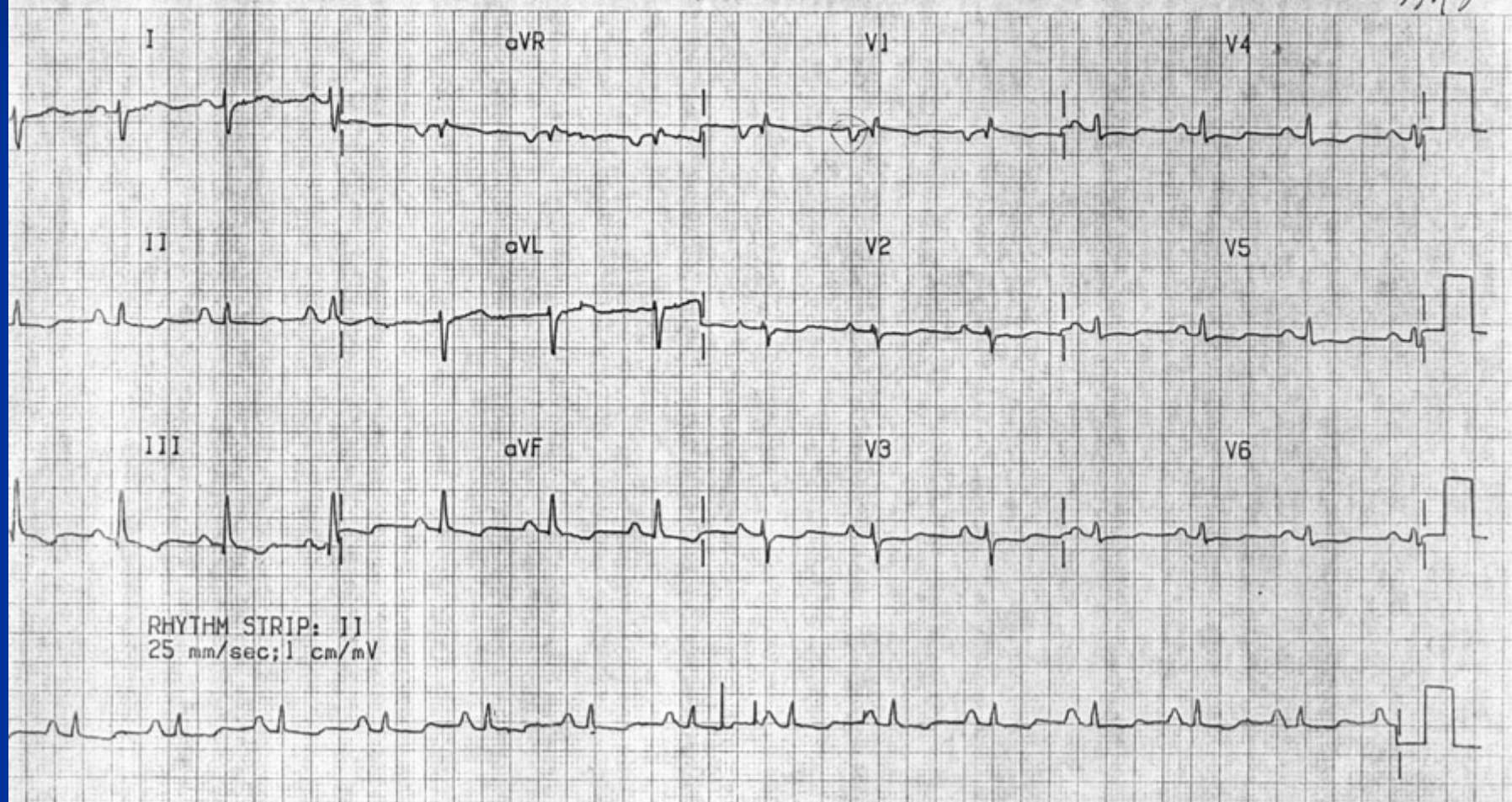
60 yo pt. on Labs had AHct(58).
Echo showed >RA, >RV, TR. Cor pulmonale
Secondary polycythemia was observed.

PE: S, Q3T3

P pulmonar.

S, T3 Q3 → pathognomonic for pulm HTN/PE

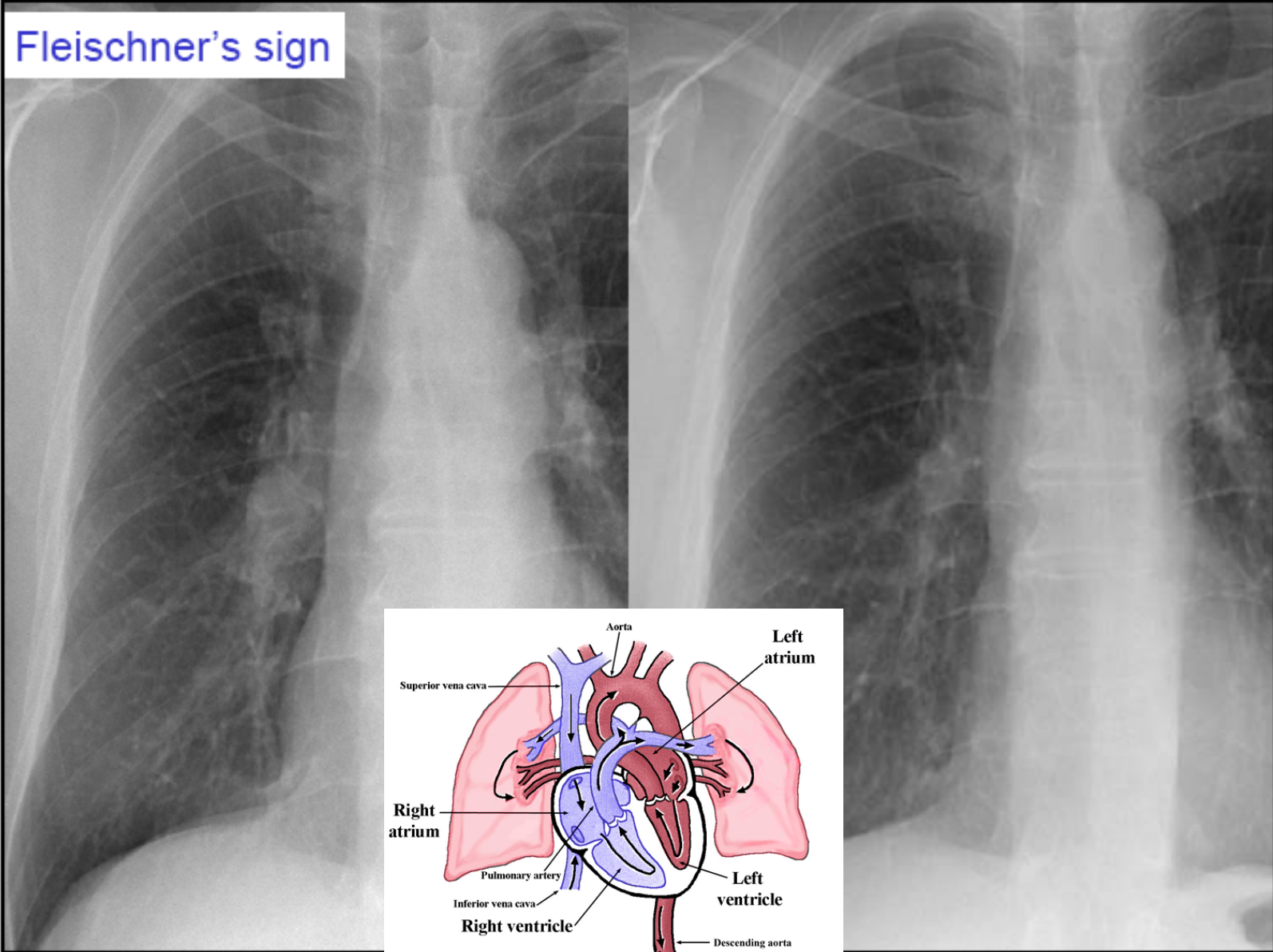
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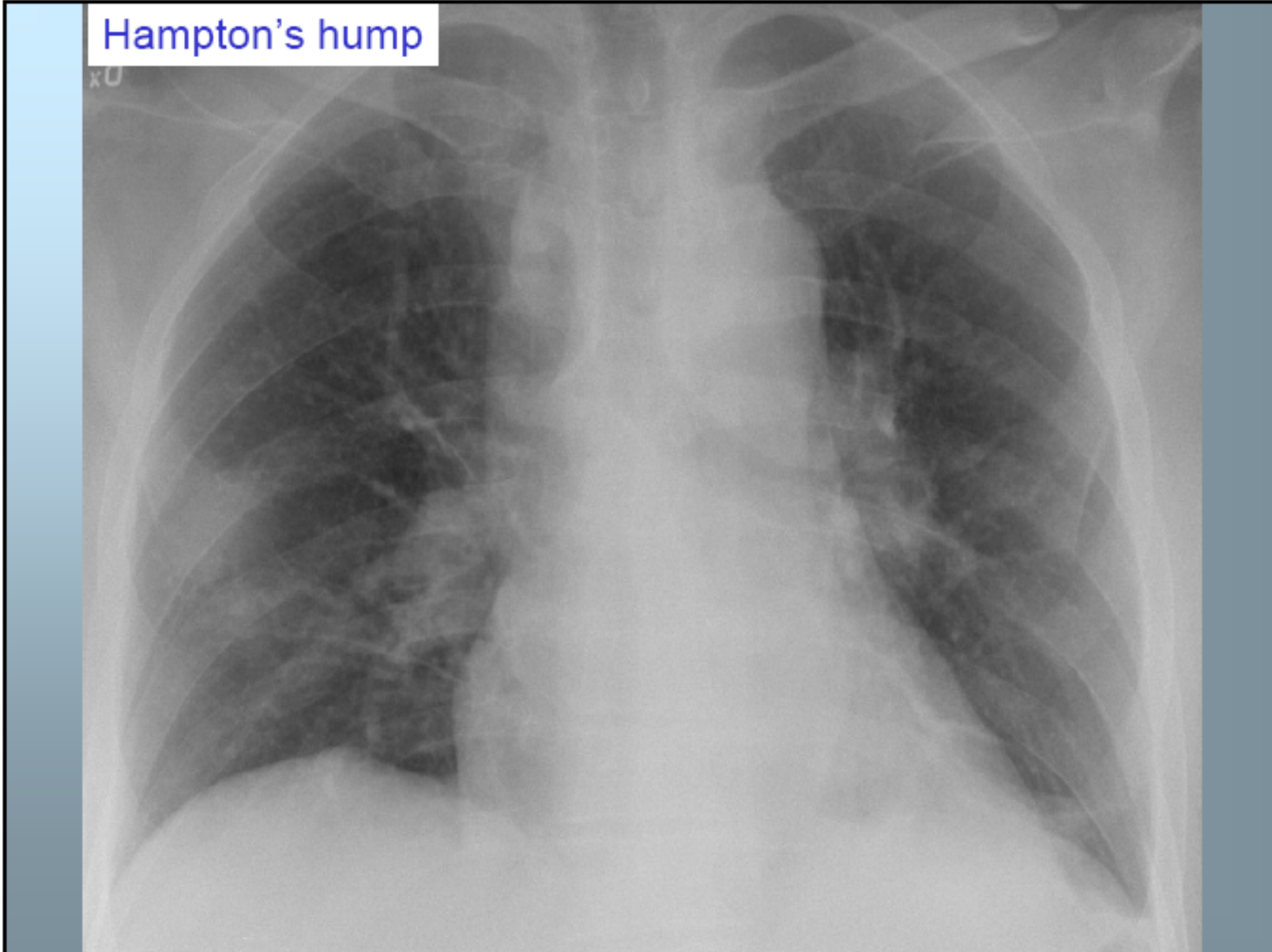
X-RAY FINDINGS

Diaphragm elevation	41%
Consolidation	40%
Pleural effusion	28%
Distended prox. Pulm art (Fleischner's sign)	23%
Atelectasis/infiltrates	20%
Oligemia (Westermarck's sign)	15%
Lung infarct (Hampton's hump)	

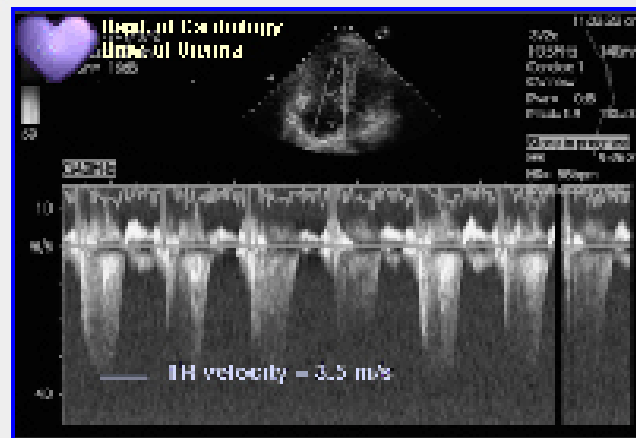
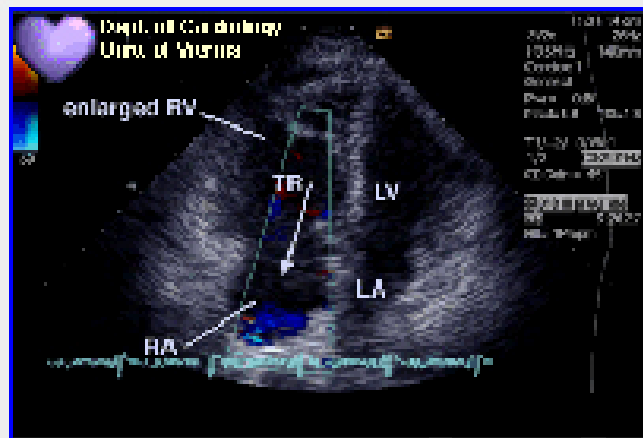
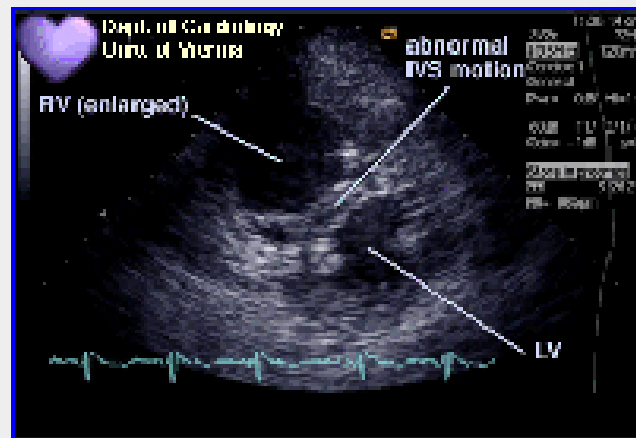
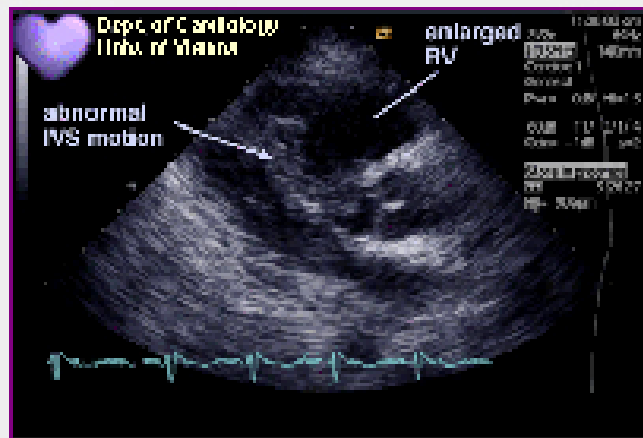
Fleischner's sign



Hampton's hump



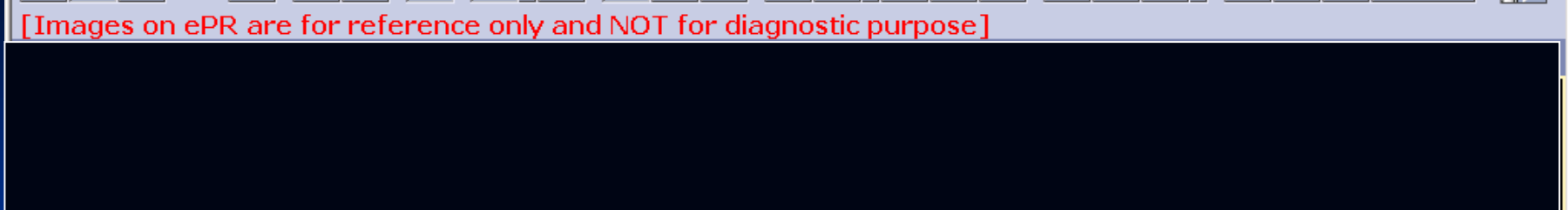
Echocardiogram



QuickTime required to view videos

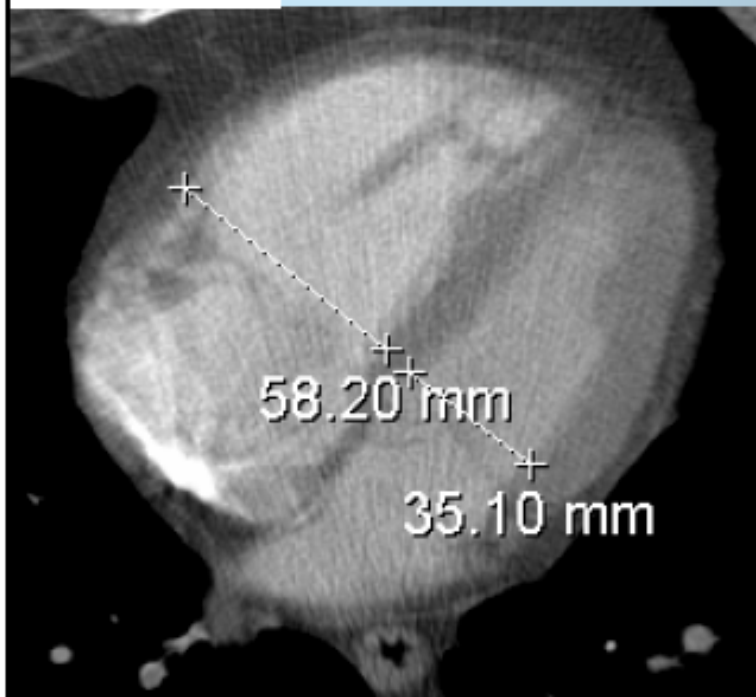
Spiral CT Scan

- Easily done non invasive test with few complications
- Requires proper equipment and experienced readers
- Rarely cannot perform e.g. allergy, SVC syn. Renal insufficiency, Approximately 10-13%
- Sensitivity 90%, specificity 95%, with multidetector CT in experienced hands

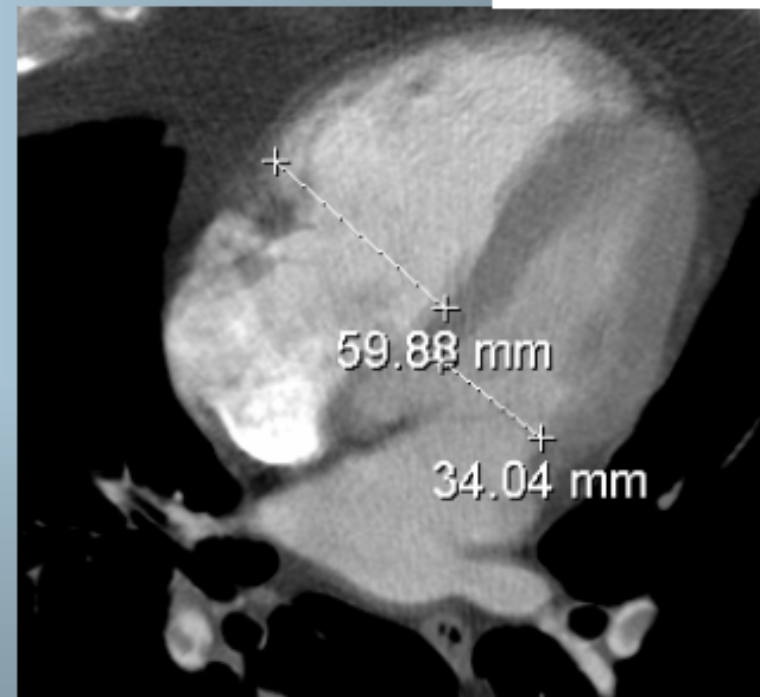


REFORMATED FOUR-CHAMBER VIEW

RV/LV=1.65



RV/LV=1.74

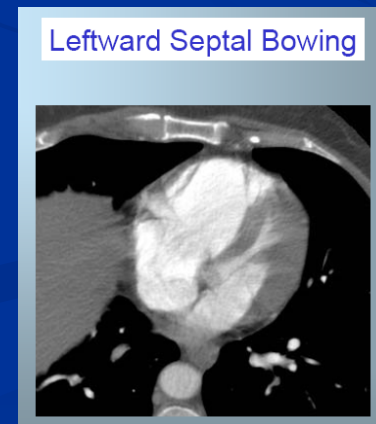


Quiroz et al
Circulation (2004) 109:2401-2404

An RV/LV diameter ratio greater than 0.9 was associated with a higher mortality rate compared to an RV/LV diameter ratio less than or equal to 0.9 calculated on a four-chamber view in 431 patients with PE.

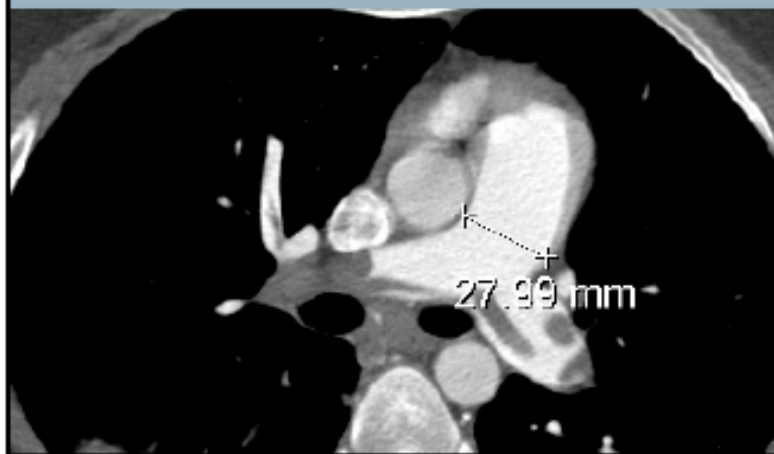
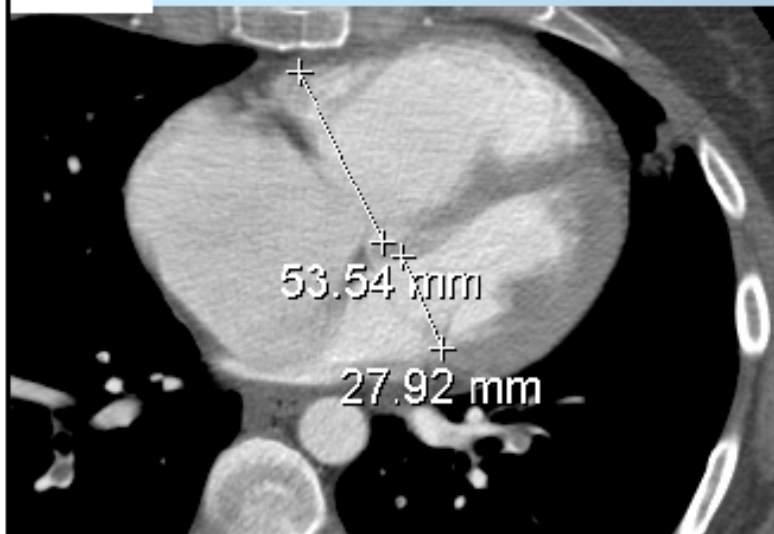
Right ventricular failure

- Increased risk of sudden death
- Dilated RV and normal or small LV
- RV/LV short axes ratio > 1
- RV/LV short axis ratio > 1.5 indicates a severe episode of PE
- Leftward septal bowing

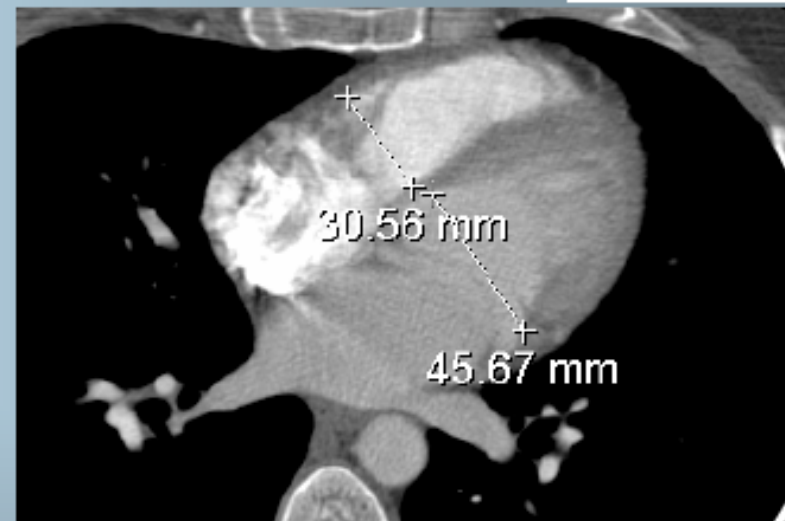


Regression of RV failure and pulmonary hypertension

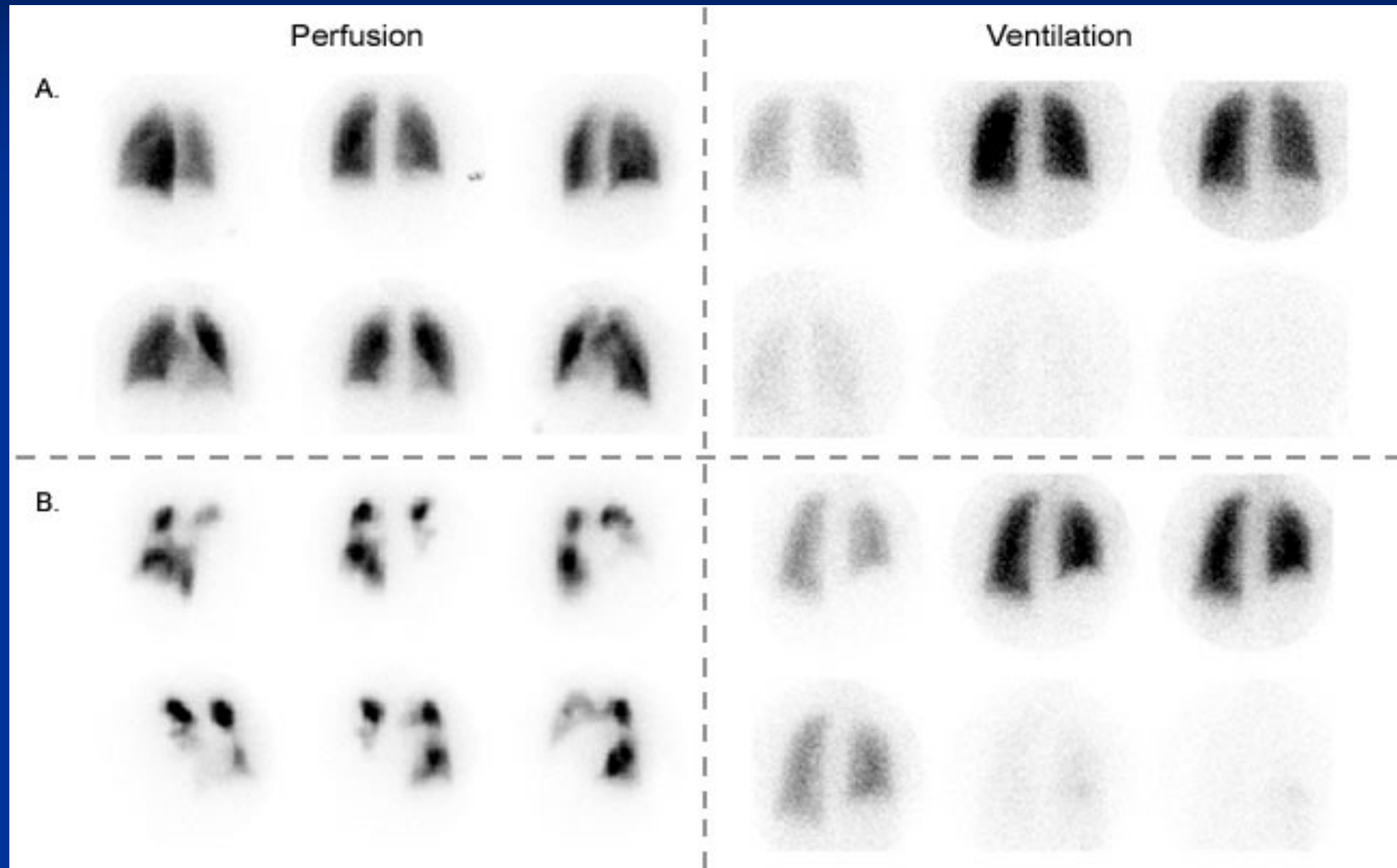
Acute



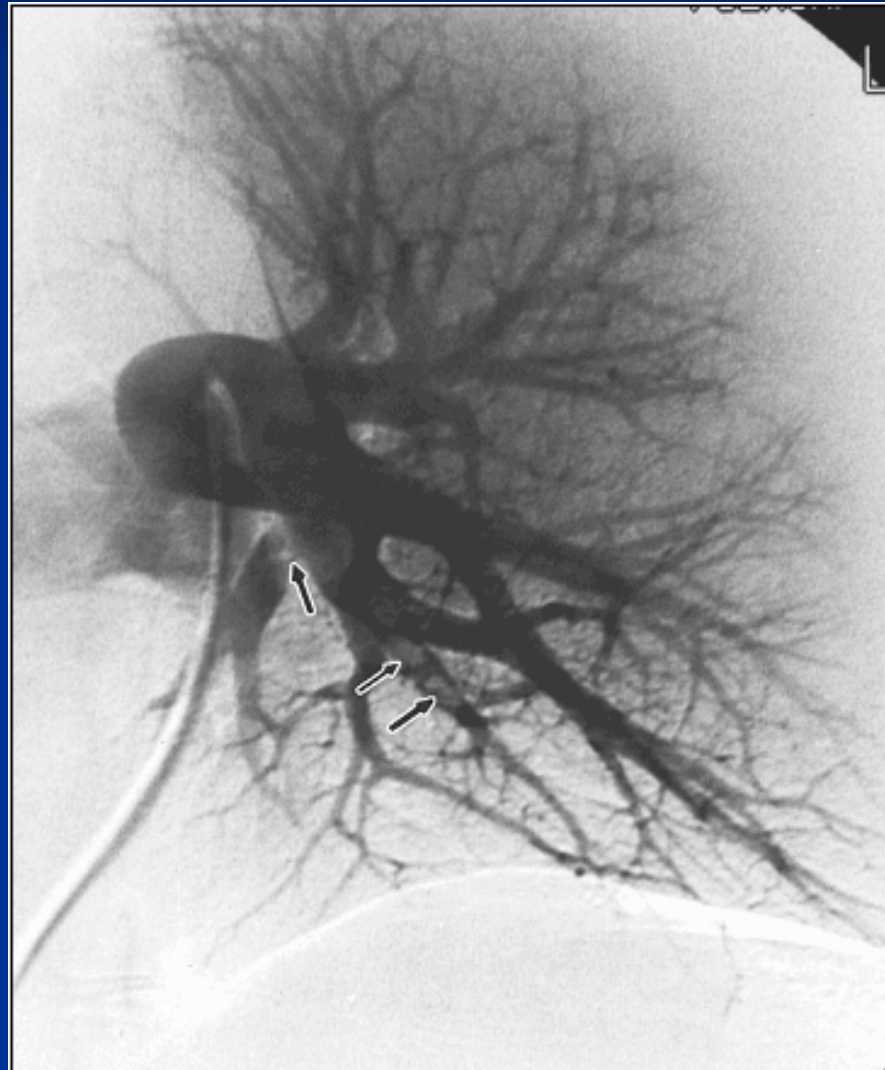
Follow-up



V/Q scan



Pulmonary angiography

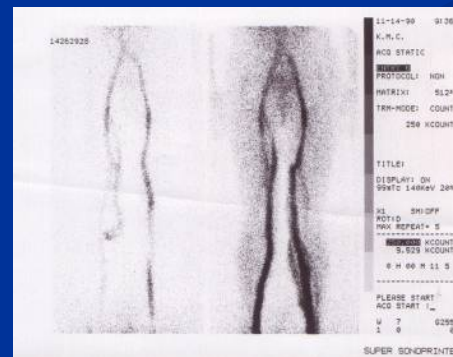
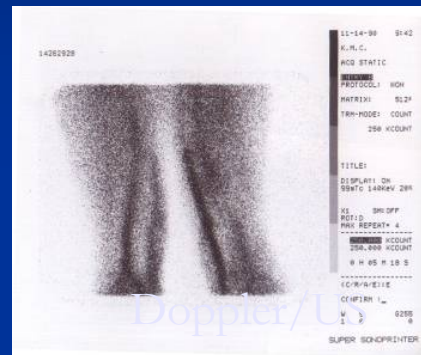


Work up for DVT

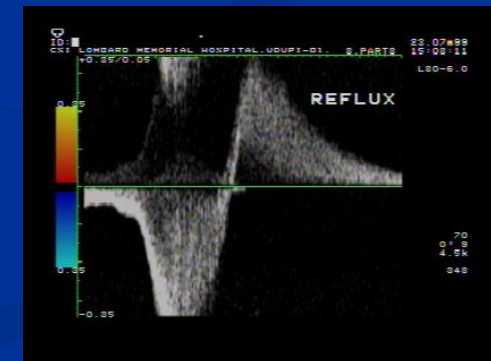
Contrast venography



Radionuclide venography

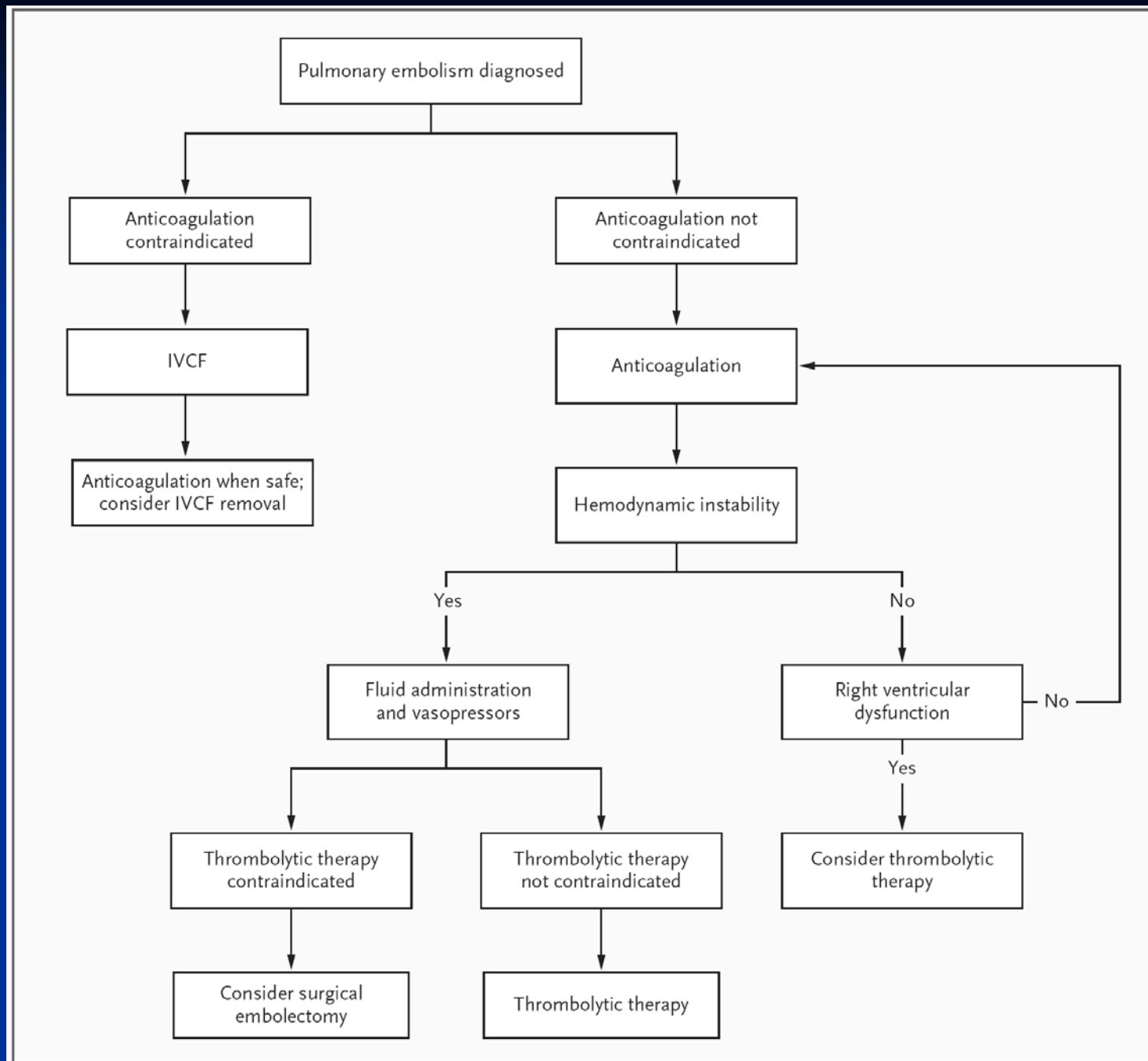


Doppler USG



Treatment

- Anticoagulation
 - unfractionated heparin
 - Low molecular weight heparin
 - warfarin
- IVC filter
- Thrombolytic
- Embolectomy



TREATMENT of PULMONARY EMBOLISM

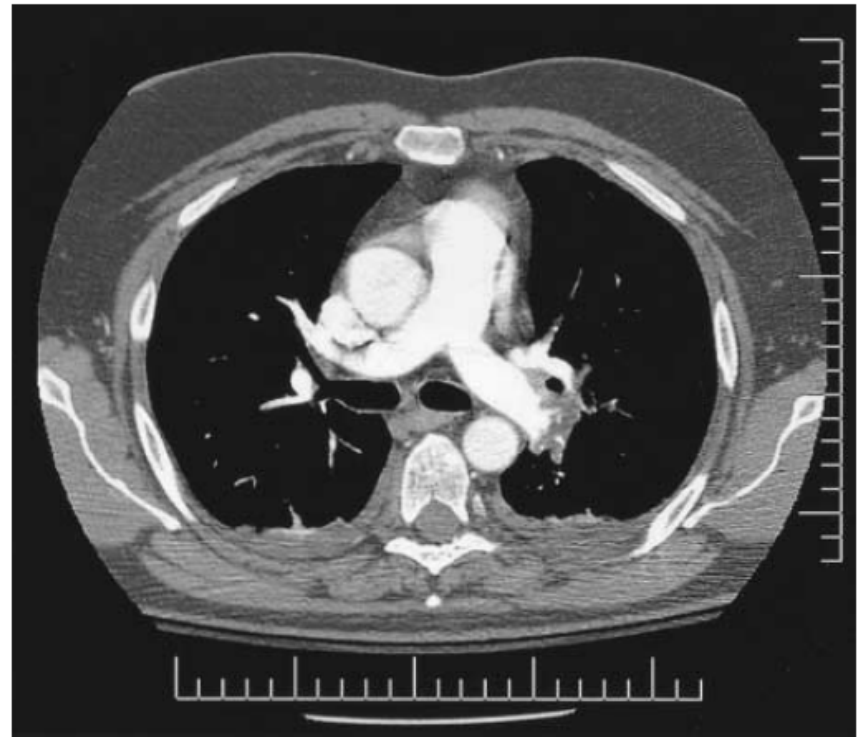
- Start oral anticoagulants in 24 -72 hrs.
with $\approx$ 5 day crossover with heparin
- Duration: - 3 - 6 months if
correctable cause e.g. surgery
 - indefinitely if no known cause or
recurrent or ongoing risk e.g cancer

Thrombolytic therapy

- More rapid in effect
- Can be considered in patients hemodynamically compromised or with RV dysfunction
- R-tPA 10mg bolus then 90mg ivi over 2 hours, plus heparin

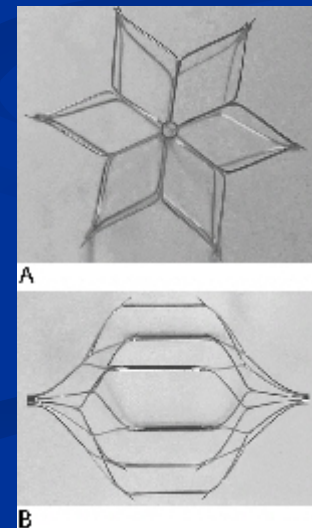
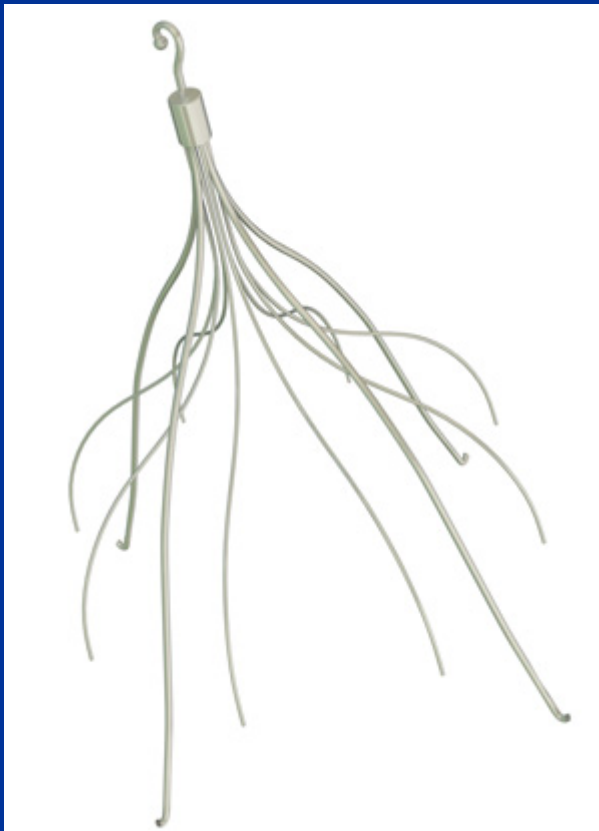
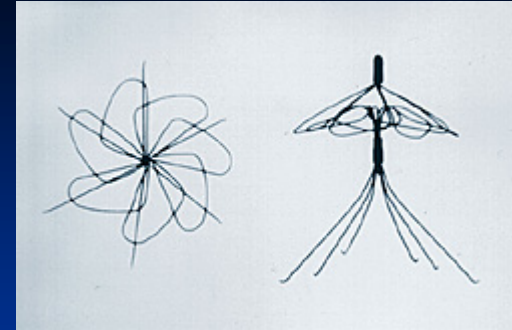


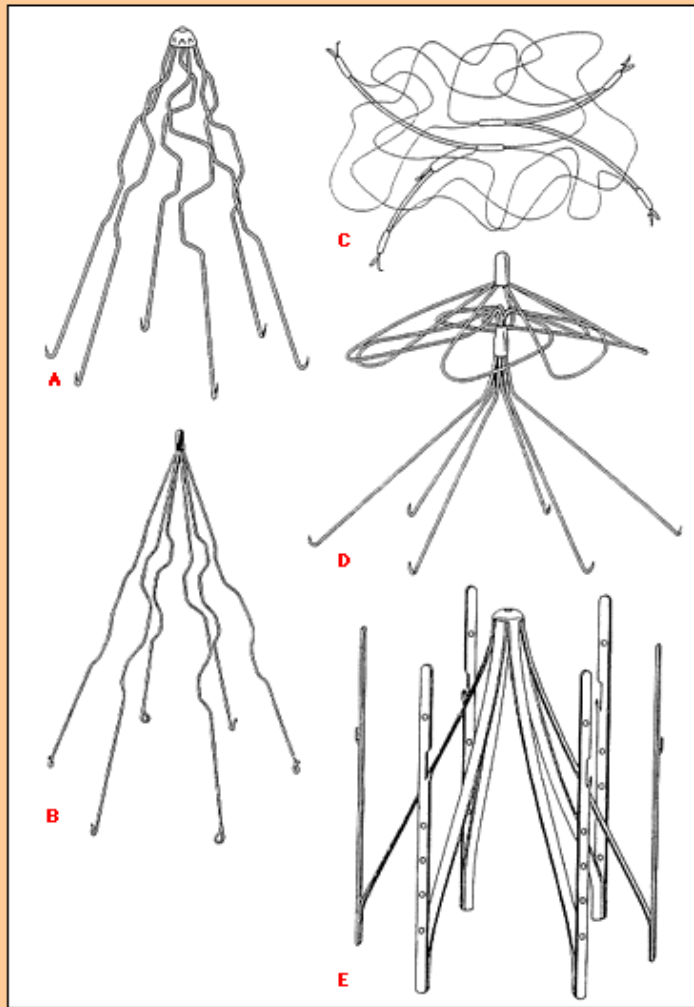
A



B

IVC filter





Inferior vena caval filter models A, Stainless steel Greenfield filter. B, Modified-hook titanium Greenfield filter. C, Bird's nest filter. D, Simon nitinol filter. E, Vena Tech filter. Reproduced with permission from Streiff, MB. Vena caval filters: a comprehensive review. *Blood* 2000 Jun 15;95(12):3669-77. (Copyright 2000 by American Society of Hematology).

Case: F/83, HSC

- DM / HT/ IHD
- Slipped and fell with # right NOF.
- OT postponed for 2 weeks.
- Clexane 30mg Q12H SC in ortho unit.
- Also on aspirin 80mg daily PO.

Progress

- Post-op hypotension with drop in Hb.
- Extensive bruising over both arms.
- Echo: Poor LV. LVH with collapsed RV. Small rim of pericardial effusion.
- Persistent oozing from wound.
- Significant blood-stained output from redivac drain.
- Hb topped up but slowly drop to 7 again.

Outcome

- Oozing gradually stopped
- Clear up of blood-stained wound discharge after 2 days.
- Weaned off inotrope and extubated.

Event rate vs INR

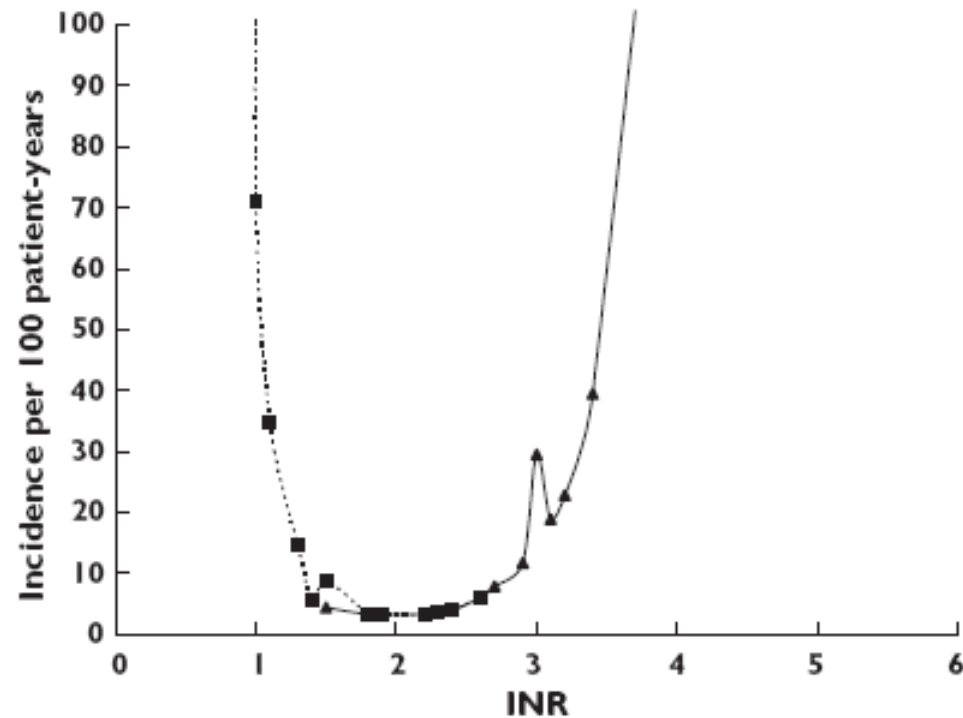


Figure 2

Incidence of major events at specific INR levels. Bleeding event (▲); thromboembolic event (■)

Prevention protocol

	Low	Medium	High
Proximal vein thrombosis	~ 0.4%	~ 2-4%	~ 10-20%
Fatal PE	< 0.2%	~ 0.2 – 0.5%	~ 1-5%
Others	< 40 years old Major surgery (>30 mins) but with no other risk factors. Minor surgery (>30 mins) but with no other risk factors. Minor trauma or illness	> 40 years old: Major general, urological, gynaecological, cardiothoracic, vascular, or neurosurgical operation. < 40 years old: Major operation and with one or more other risk factors. Major trauma. Minor surgery, trauma, or illness, and with one or more other risk factors. Plaster cast immobilisation of leg. Major acute medical illness.	Major surgery, trauma, or illness, with previous DVT / PE / thrombophilia. Major pelvic or abdominal surgery for cancer Critical leg ischaemia or major leg amputation. Major orthopaedic surgery / pelvis, hip, or knee # / SC injury. Ischaemic stroke.

	<i>General surgery</i>			<i>Severely ill medical illness</i>	<i>Elective hip replacement</i>	<i>Elective knee replacement</i>	<i>Elective neuro-surgery</i>	<i>Acute spinal cord injury</i>
	<i>Low risk</i>	<i>Moderate risk</i>	<i>High risk</i>					
Compression elastic stockings	✓	✓	✓	✓	✓	✓	✓	
Intermittent pneumatic compression	✓	✓	✓	✓	✓	✓	✓	
Early mobilization, if feasible	✓	✓	✓	✓	✓	✓	✓	
Unfractionated heparin 5000iu/dose SC		✓ (Q12H)	✓ (Q8H)	✓	✓(Q8H) or ✓ or ✓			
Enoxaparin 20mg (0.2ml)-40mg (0.4ml) daily SC		✓	✓			✓ or	✓	✓
Tinzaparin 3500iu daily SC		✓	✓			✓		



Contraindications

- Compression Elastic Stocking / Intermittent pneumatic compression (IPC)
 - Local leg condition : Dermatitis, post venous ligation operation, gangrene and recent skin graft.
 - Severe atherosclerosis or other ischaemic vascular disease.
 - Massive edema of legs or pulmonary edema due to congestive heart failure.
 - Extreme deformity of leg.
 - Suspected / confirmed DVT.
- Anticoagulation: bleeding tendency
- Antithrombotic Agent: Evidence or high risk of active bleeding

Table 2. Medications and Doses for Prophylaxis of Venous Thromboembolism in Hospitalized Medical Patients.*

Drug†	Dose	Comment
Unfractionated heparin	5000 U subcutaneously, every 8 hr‡	
Low-molecular-weight heparins		
Enoxaparin (Lovenox)	40 mg subcutaneously, once daily	More expensive than heparin; 20 mg daily not effective
Dalteparin (Fragmin)	5000 U subcutaneously, once daily	More expensive than heparin
Fondaparinux (Arixtra)§	2.5 mg subcutaneously, once daily	More expensive than heparin

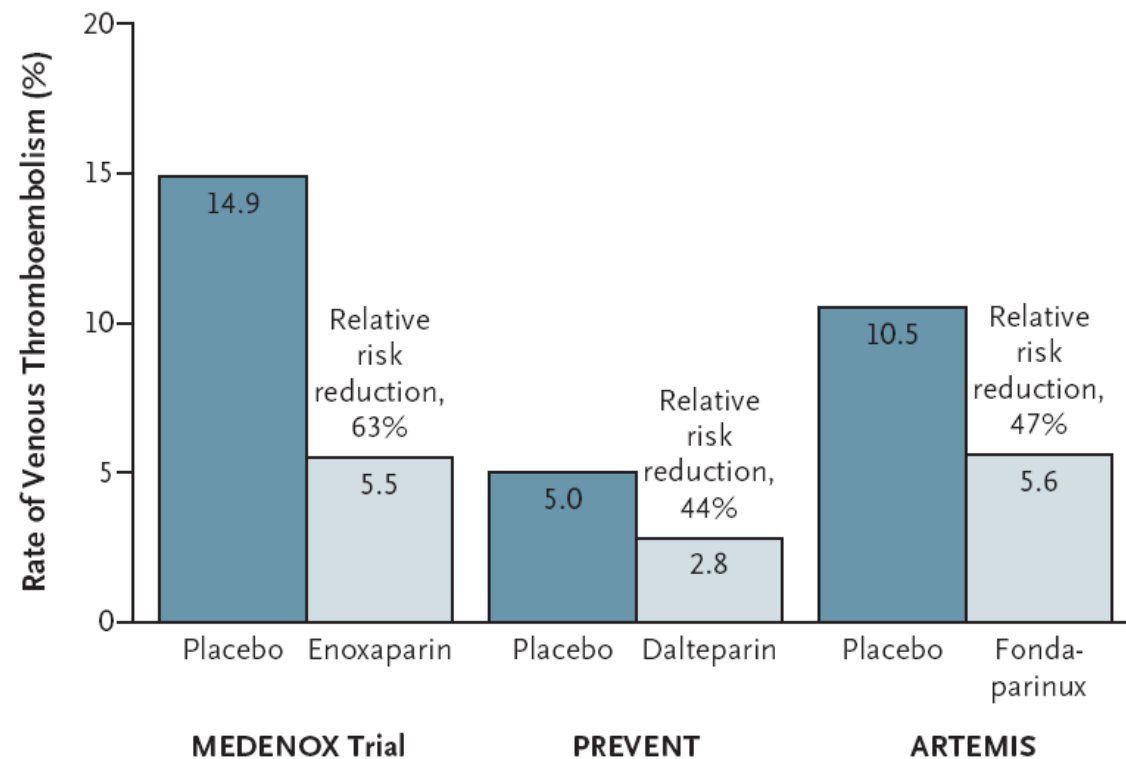


Figure 1. Results of Trials of Prophylaxis for Venous Thromboembolism in High-Risk Hospitalized Patients.

In three randomized, double-blind trials, enoxaparin, dalteparin, or fondaparinux was compared with placebo for the prevention of venous thromboembolism. The use of the anticoagulant resulted in significantly decreased rates of thromboembolism in the Prophylaxis in Medical Patients with Enoxaparin (MEDENOX) trial ($P < 0.001$),⁷ the Prospective Evaluation of Dalteparin Efficacy for Prevention of VTE in Immobilized Patients Trial (PREVENT) ($P = 0.002$),⁸ and the Arixtra for Thromboembolism Prevention in a Medical Indications Study (ARTEMIS) ($P = 0.03$).⁶ Relative risk reductions are shown for patients receiving each prophylactic drug as compared with those receiving placebo.

Thank you