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Massive PE

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Massive PE: *Outline*

- 1. Prognosis in acute PE, massive PE**
- 2. Supportive therapy**
- 3. Embolus reduction therapy**
 - IV thrombolytic therapy**
 - catheter-directed interventions**
- 4. Management of submassive PE**

Mrs. C.R.

- ▶▶ 53 yo with hypertension
- ▶▶ 4 weeks PTA → Lt ankle # → below-knee cast
- ▶▶ Sudden syncope, SOB, chest pain

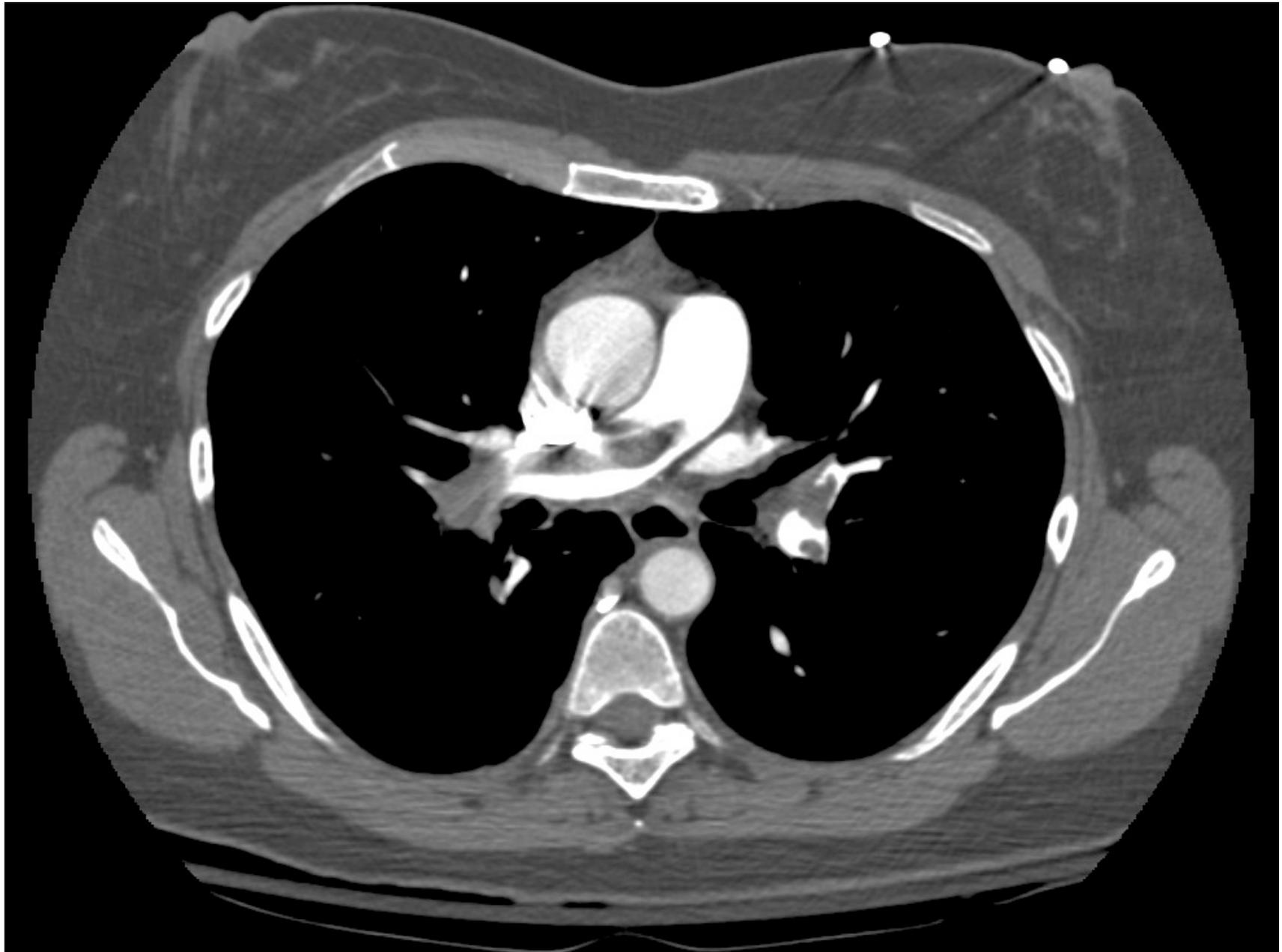
O/E: HR=140 RR=34 BP=50/30 $\xrightarrow[\text{dopamine}]{\text{Saline}}$ 100/60

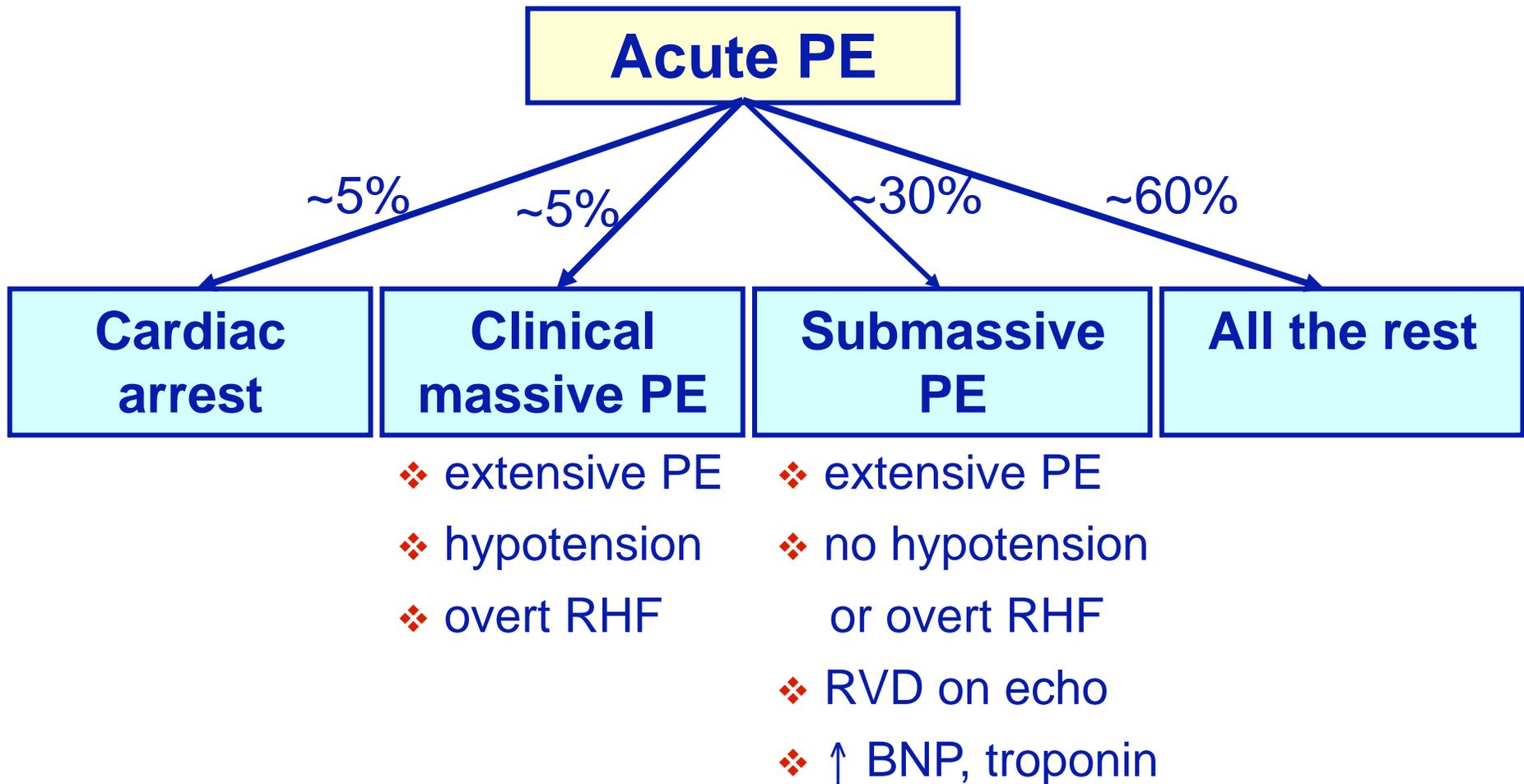
JVP ↑

ECG: ST at 130, S_IQ_{III}T_{III}, RBBB, T_{inv} V₁₋₃

SCT: saddle PE with multiple bilateral emboli
Lt popliteal DVT

53 yo woman with massive PE after ankle #





Mortality:

70-95%

20-50%

5-10%

≤ 3%

Goals of PE Treatment

1. Reduce mortality
2. Reduce symptoms
3. Shorten acute illness
4. Prevent recurrent VTE
5. [Prevent thromboembolic pulmonary hypertension]

PE Treatment Options

Anticoagulation

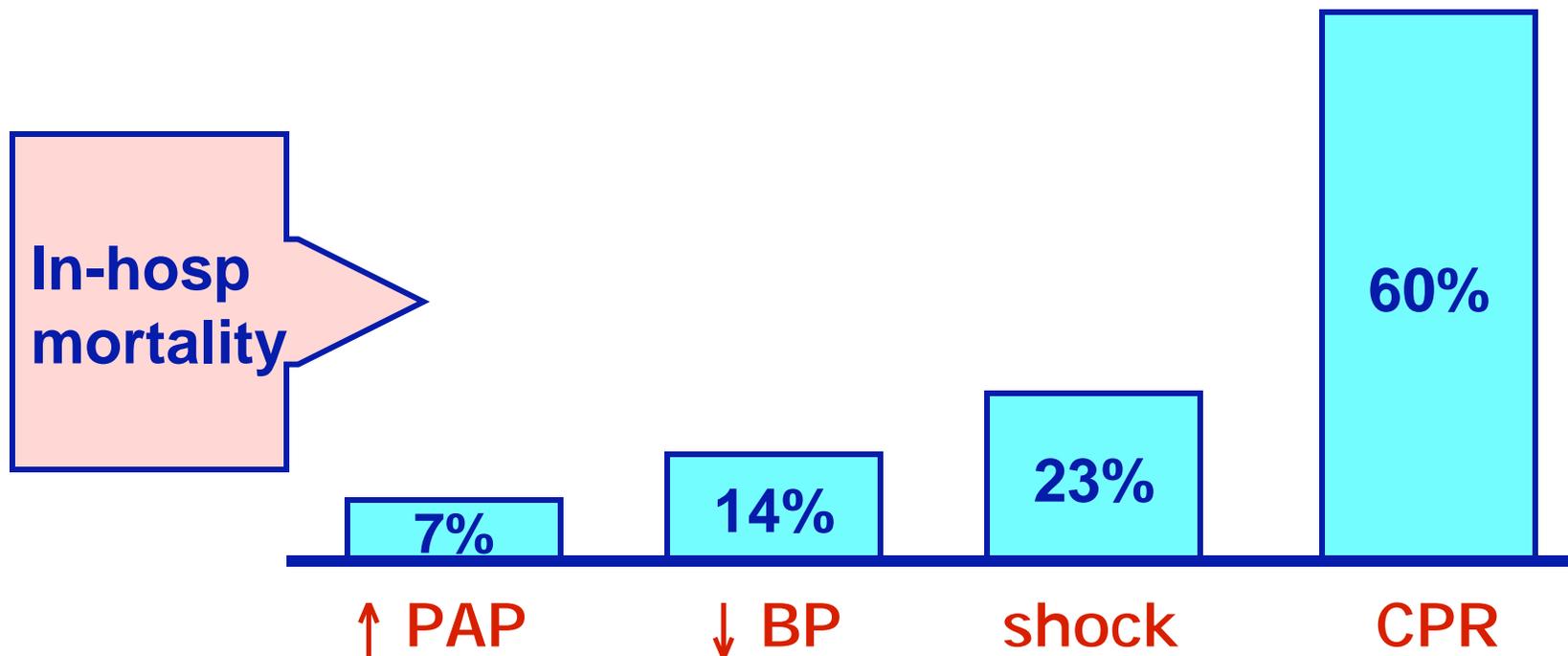
- ❖ Heparin – IV
- ❖ Low molecular weight heparin
- ❖ warfarin
- ❖ NOAC – rivaroxaban

Embolus reduction therapy

- ❖ Thrombolytic therapy – IV
- ❖ Catheter-directed therapy
- ❖ Surgical embolectomy

Mortality from Major PE

- ❖ Prospective study of 1,001 patients with major PE
- ❖ ↓ BP, shock, and/or echo changes



Kasper - JACC 1997;30:1165

Prognosis after Acute PE

Parameter	Worsens prognosis
Clinical	RHF → ↓ BP → shock → arrest High PESI score
Lab	↑ Troponin, ↑ BNP, ↑ D-dimer
Echo	RV dysfunction
CT scan	RV/LV, septal bowing, embolus burden

PE Severity Index (PESI)

Factor at diagnosis	score
Age	1/yr
Male	10
History of heart failure	10
Chronic lung disease	10
History of cancer	30
Temperature $<36^{\circ}\text{C}$	20
Pulse ≥ 110	20
Resp rate ≥ 30	20
Systolic BP <100	30
Altered mental status	60
SaO ₂ $<90\%$	20

Score	30-day mortality
<65	0
66-85	1%
86-105	3%
106-125	10%
>125	24%

Jimenez – Chest 2007;132:24

PE Severity Index (Simplified PESI)

❖ Short-term mortality

Factor at diagnosis	score
Age >80	1
Chronic cardiopul dis	1
History of cancer	1
Pulse \geq 110	1
Systolic BP <100	1
SaO2 <90%	1

Death risk	score
Low (<2%)	0
Higher	1-6

Echocardiogram in PE

- ❖ **Some prognostic value**
 - ❖ **May find RA/RV clots**
- ❖ **RV dysfunction in $\geq 40\%$ of PE**
 - ❖ **CT can show RV dysfunction**
 - ❖ **No evidence of benefit**
 - ❖ **Rarely changes management**
 - ❖ **May worry the patient, doctor**

How is Massive PE Defined?

(confusing term)

Anatomically extensive PE plus:

- ❖ **Cardiac arrest**
- ❖ **Shock**
- ❖ **Overt right heart failure**
- ❖ **Non-transient hypotension**

How is Massive PE Defined?

(confusing term)

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- ❖ **Non-transient hypotension**

Concomitant features:

- ❖ Syncope
- ❖ ↑ myocardial stress biomarkers – troponin, BNP
- ❖ ECG: S₁Q₃T₃, T_{inv} V1-3
- ❖ Echocardiogram: RV dysfunction

Adjunctive Therapy in Massive PE

- 1. +/- small fluid bolus**
- 2. Vasopressor - norepinephrine**
- dopamine, vasopressin
- 3. Inhaled nitric oxide**
- 4. Try to avoid intubation, mech vent**
- 5. CPR**
- 6. ECMO**
- 7. Calm reassurance** “don’t scare the hell out of an already terrified patient”

Anticoagulation in Massive PE

IV heparin

- ❖ **Bolus** = 5,000 U (70 U/kg)
- ❖ **Initial infusion** = 20 U/kg/hr

Importance of Early Anticoagulation

- ❖ 400 consecutive patients with PE Dx'd in ER

Received heparin	30-day mortality	<i>p</i>
In ER	4.4%	<i><0.001</i>
After adm	15.3%	

aPTT therapeutic	30-day mortality	<i>p</i>
<24 hrs	5.6%	<i>0.04</i>
After 24 hrs	14.8%	

Smith – Chest 2010;137:1382

Treatment of Massive PE

(should options other than
anticoagulation be
considered?)

In-hospital PE Mortality

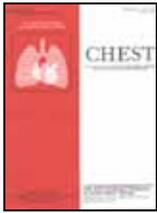
- ❖ Nationwide Inpatient Sample, 1999-2008
- ❖ Unstable = shock or ventilator dependent (3.4% of all PE)

PE	No.	In-hospital mortality
All	2,110,320	8.9%
Stable	2,038,090	7.9%
Unstable	72,230	37.3%

Systemic (IV) Thrombolytic Therapy

Proven benefits:

- ❖ ↓ PAP
 - ❖ ↓ PVR
 - ❖ ↓ angiographic score
 - ❖ ↓ perfusion scan defects
 - ❖ ↑ RV function on echocardiogram
- 1st
24-48
hrs
- ❖ No proven long-term benefits



Therapy of VTE

IV Thrombolytic Therapy vs Anticoagulation for Acute PE

Outcome	Patients / studies	IV TT	Anticoag	Rel effect (TT vs anticoag)
Mortality @ 30 D	847 / 12	3.5%	6.1%	0.7 [0.4-1.3]
Recurrent PE @ 30 D	801 / 9	4.5%	7.4%	0.7 [0.4-1.2]
Major bleeding @ 10 D	847 / 12	9.0%	5.7%	1.63 [1.0-2.7]

Kearon - Chest 2012;141(Suppl 1):e419S

Thrombolytic Therapy for PE

❖ Meta-analysis of 11 RCTs, 748 patients

Heparin Thrombolysis OR

Trials excluding patients with major PE (n=494)

Recurrent PE	2.8%	2.0%	0.8 [0.3-2.1]
Death	2.4%	3.3%	1.2 [0.4-3.1]
Major bleeding	3.2%	2.4%	0.7 [0.2-1.9]

Trials including patients with major PE (n=254)

Recurrent PE	7.1%	3.9%	0.6 [0.2-1.6]
Death	12.4% >	6.2%	0.5 [0.2-1.1]
Major bleeding	11.9% <<	21.4%	2.0 [1.0-3.9]

Wan – Circulation 2004;110:744

Does thrombolytic therapy reduce mortality in massive PE?

Of course it does

(even through no single study has shown this)

IV Thrombolytic Therapy vs Anticoagulation for Acute PE

- ❖ Meta-analysis of 5 RCTs in 154 unstable patients

Outcome	Anticoagulation	Thrombolytic therapy	Rel effect
Death or PE recurrence	19.0%	9.4%	0.45 [0.2-0.9]

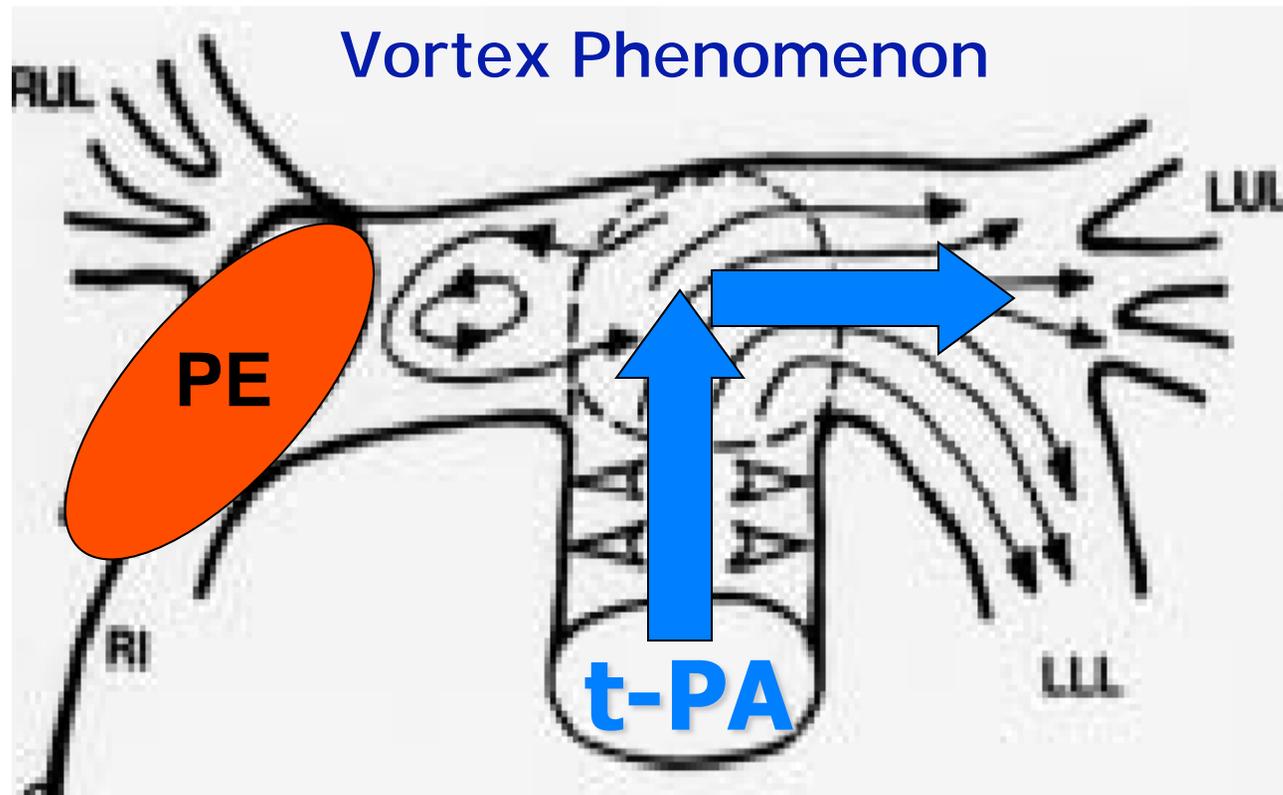
Systemic (IV) Thrombolytic Therapy

Proven benefits: 1. More rapid resolution of PE

Unproven benefits: 1. ↓ mortality
2. ↓ recurrent DVT/PE
3. ↓ pulmonary hypertension

Proven complic'ns: 1. ↑ major bleeding
2. ↑ intracranial bleeding
3. ↑ costs: drugs, ICU, LOS, S/Es
4. Complexity, hassles, time

Why Does IV Lytic Therapy Work so Poorly in PE?



Little t-PA comes into direct contact with an occluding embolus

Schmitz-Rode – Cardiovasc Intervent Radiol 1998;21:199

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>50% have a contraindication to systemic lytic therapy!

Contraindications to Systemic TT

- ❖ **Active, clinically-important bleeding**
- ❖ **Recent* clinically-important bleeding**
- ❖ **Recent* major surgery / trauma / ICH**
- ❖ **Mucosal lesion – lung, GI, GU**
- ❖ **Intracranial lesion**
- ❖ **Bleeding disorder, +/- antiplatelet agent**

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- ❖ Intracranial lesion
- ❖ Bleeding disorder, +/- antiplatelet agent

***Contraindication depends on:**

- 1. how sick the patient is**
- 2. the specifics of the contraindication**
- 3. availability of catheter-directed therapy**

Intravenous Thrombolytic Therapy

- ❖ **No superiority of any agent**
- ❖ **Short infusion/boluses** are more effective and safer than prolonged infusions (≥ 12 hrs)
- ❖ **Bolus infusion** of r-PA (~ 50 mg in ≤ 15 min) is as effective and safe as a 2-hr infusion of 100 mg
- ❖ **Direct PA infusion** of rt-PA is no better than a peripheral IV infusion and \rightarrow more bleeding

Intravenous Thrombolytic Therapy

- ❖ Contra-indicated in ~75%
- ❖ ICU bed required
- ❖ Often not impressive efficacy
- ❖ Major bleeding 10-20%
- ❖ Intracranial hemorrhage 1-3%

t-PA 100 mg/2 hrs
0.6 mg/kg/15 min
50 mg bolus

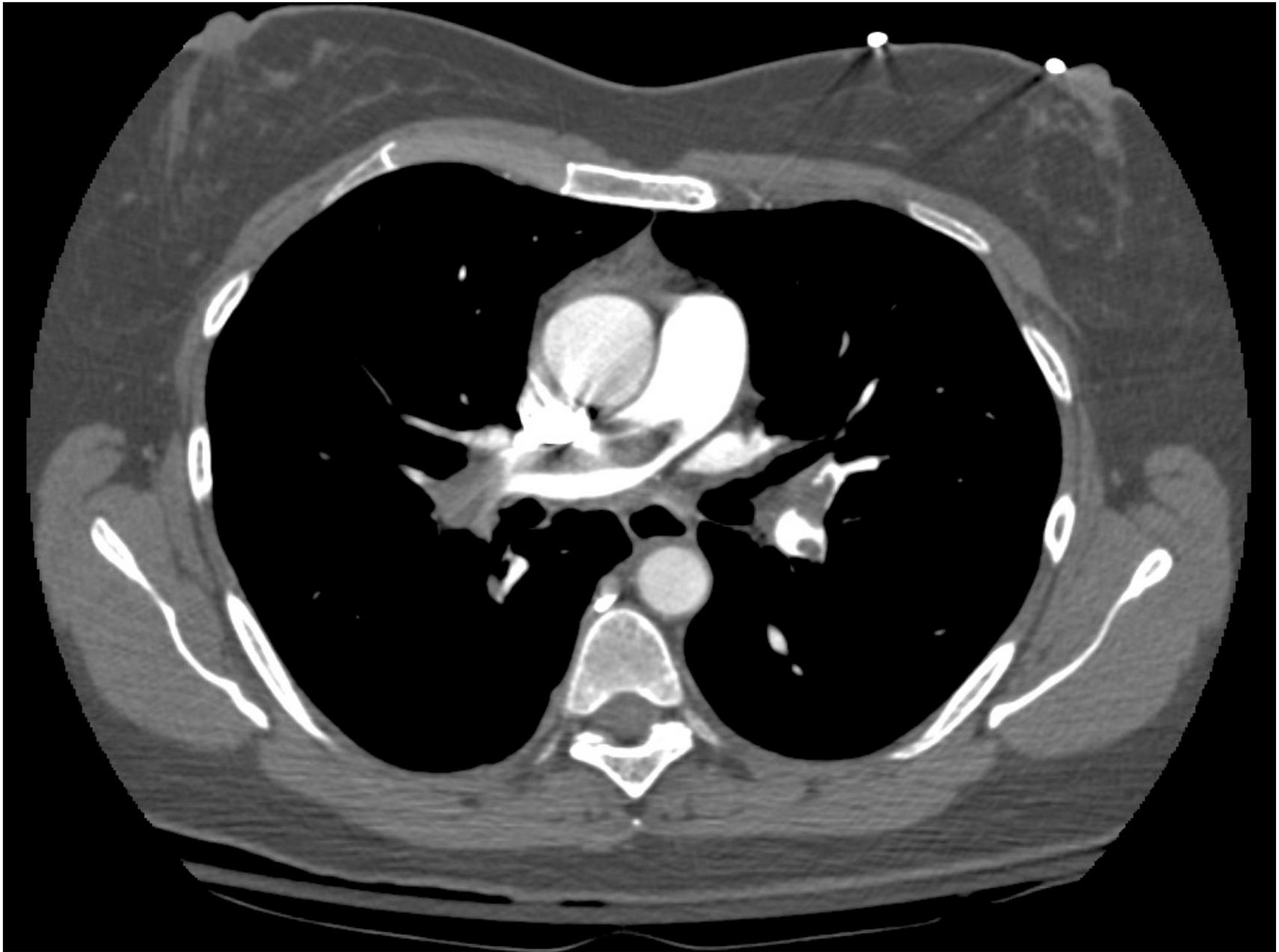
urgency



TNK 30-50 mg bolus

Retepase 10 U boluses x 2
30 min apart

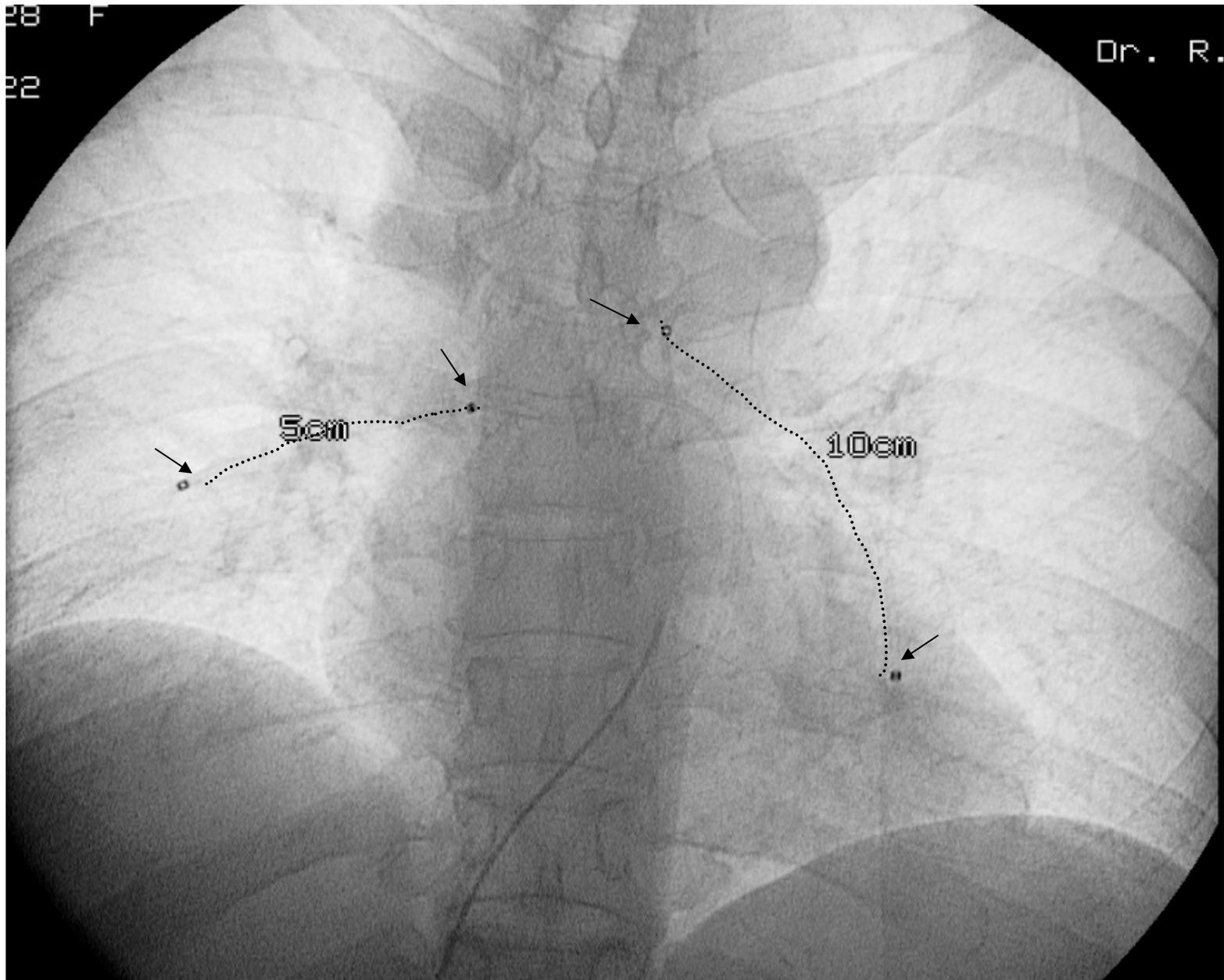
53 yo woman with massive PE after ankle #



Mrs. C.R.

- ▶▶ IV heparin
- ▶▶ Interventional radiology:
 - mechanical fragmentation central emboli
 - catheters inserted into both PAs
 - bilateral pulse spray - total of 42 mg t-PA
- ▶▶ Overnight t-PA 1 mg/hr each PA line

Multi side-hole catheter into each PA



Mrs. C.R.

- ▶▶ Next day → asymptomatic HR = 80
RR = 17 BP = 130/80 SaO₂ = 97% RA
- ▶▶ Repeat angio → >95% resolution
- ▶▶ Lab: no fall in Fg
- ▶▶ Bilateral femoral lines removed
- ▶▶ Next day → discharged on patient-administered SC LMWH + warfarin

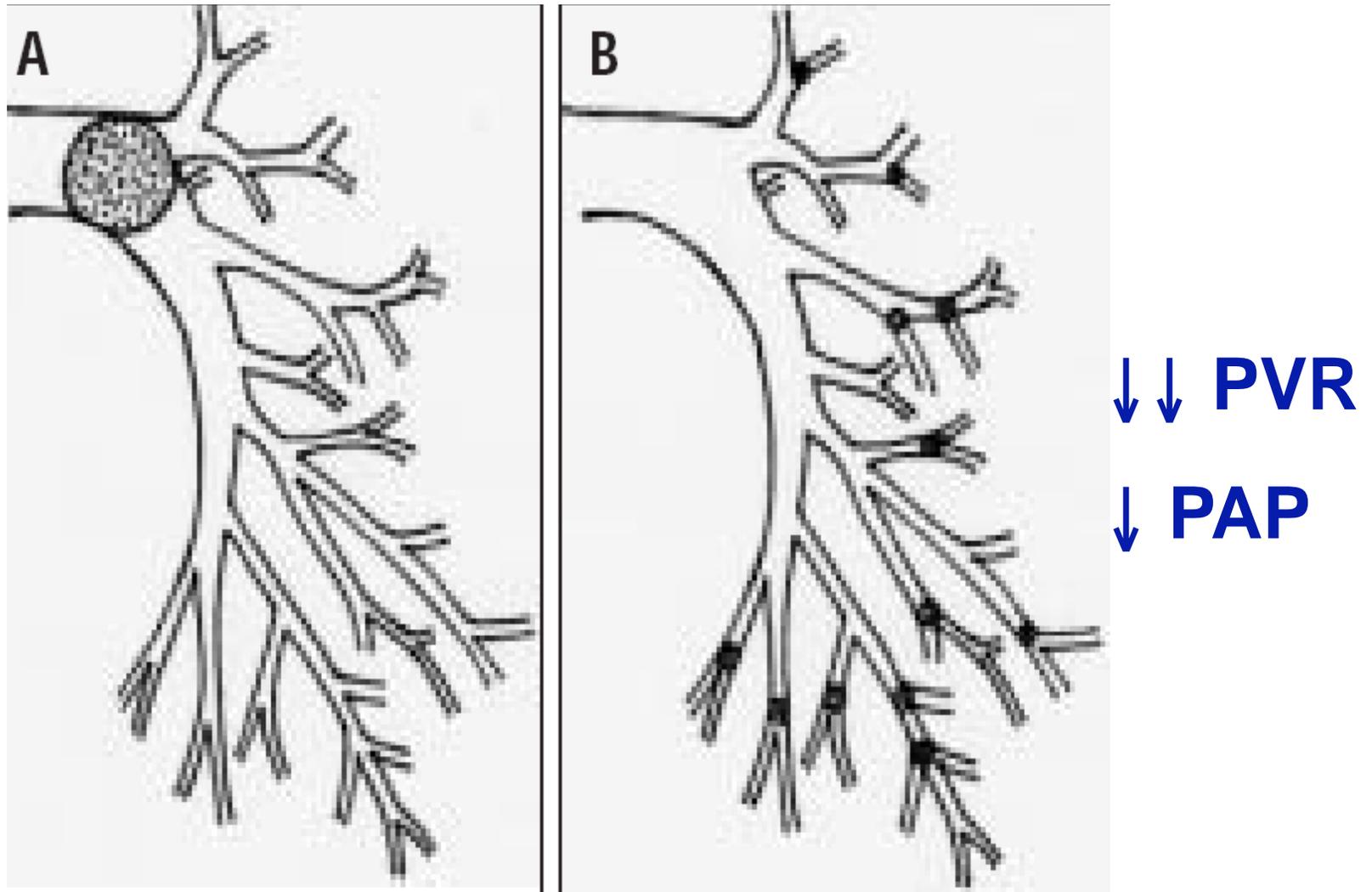
Day after presentation with massive PE



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 - catheter-directed interventions**
- 4. Management of submassive PE**

Effect of Mechanical Fragmentation



Brady – Lancet 1991;338:1186

Systematic Review of CDT

- ❖ 594 patients in 35 studies (no RCTs, 6 prospective)
- ❖ Fragmentation in 70%, local thrombolytic drug infusion in 65%

Clinical success 87%

(stabilization of hemodynamics + resolution of hypoxemia + discharged alive)

Major procedure complications 2.4%

- ❖ Highest complication rate with Angiojet → 28% had major complications; 5/68 deaths

Catheter-Directed Rx of Massive PE

Indications: Main or lobar PE PLUS
Hypotension, clinical RHF
Not based on scary CT, echo, Tp

Contraindic: Too unstable
Not bleeding concerns

Procedure: Mechanical fragmentation
Pulse-spray, intra-embolus t-PA
± t-PA infusion of 1-2 mg/hr

Anticoagulant: IV heparin

Complications of CDT

- 1. Death** – patient was too sick, process takes too long
- 2. Bleeding** – access site, hemoptysis, remote
- 3. Contrast** – allergy, renal dysfunction
- 4. Bradycardia, tachyarrhythmia**
- 5. Cardiac or PA perforation, PA dissection**
- 6. Hemolysis**
- 7. *Radiology staff hide when they see you coming***

Advantages of CDT

- 1. Many fewer contraindications** – patient too unstable
- 2. Likely more effective**
- 3. Safer** – much lower dose of thrombolytic drug (or none)
- 4. Multiple options, tailored to the patient** – fragmentation, aspiration of clot, intra-embolus thrombolysis, angioplasty
- 5. Can continue therapy with infusion**

CDT: *practical points*

- ❖ **Careful patient selection** – not too well, not too sick
- ❖ **Rapid decision**
- ❖ **Be there or send a non-imaging doctor**
- ❖ **Don't mandate an ICU bed**
- ❖ **Treatment success = clinical improvement NOT imaging**

Future Developments

- ❖ **Better prognostication in submassive PE (clinical, echo, biomarker combinations)**
- ❖ **More effective catheter-directed therapies**
 - ultrasound accelerated thrombolysis
 - shortened procedure time (↓ PVR and get out)
- ❖ **Ongoing RCTs**

Treatment Options for Massive PE

Surgical embolectomy

- ❖ Available in very few centers (and when needed)
- ❖ High morbidity, mortality (>10%)

IV thrombolysis

- ❖ Contraindicated in ~70%
- ❖ Often small benefit
- ❖ Increased bleeding risk

Catheter-directed thrombus reduction

- ❖ One contraindication
 - ❖ Highly effective (but no RCTs yet)
 - ❖ Safe
- = treatment of choice for massive PE**

Treatment of Massive PE

Arrest or pre-arrest:

- ❖ IV t-PA 50 mg bolus

Everyone else:

- ❖ catheter-directed therapy
- or
- ❖ IV t-PA 100 mg/2 hrs or 0.6 mg/kg bolus

Fibrinolytic Therapy in *Stable* PE

- ❖ Registry of 1,740 normotensive ER patients with PE

Fibrinolytic therapy	No.	Death \leq 30 days
No	1,699	4.3%
Yes	41	9.7%*

*all 4 died of PE

Pollack – J Am Coll Cardiol 2011;57:700

- ❖ 434 normotensive patients with PE

Fibrinolytic therapy	No.	PE-related mortality at 90 days
No	217	0
Yes	217	12 (5.5%)

Jimenez – J Thromb Haemost 2012;10:1974

Management of *Submassive* PE

= **Big PE but stable patient** (probable RVD)

- ❖ **Treatment controversial**
- ❖ **Aggressive anticoagulation**
- ❖ **Supportive therapy**
- ❖ **Hospital observation until starts to improve**
- ❖ **Echocardiogram – NO**
“widow (la veuve) sign”

Acute PE

Is patient hemodynamically stable?

- 1. Non-transient hypotension
- 2. Clinical Rt heart failure

YES

No

❖ Anticoagulate

❖ Anticoagulate + Embolus reduction procedure

Surgical embolectomy

IV thrombolysis

Catheter-directed thrombus reduction

TEAMS (ThromboEmbolism and Anticoagulant Management at Sunnybrook)

MASSIVE PULMONARY EMBOLISM

***NOTE: This brief document is not intended to be a comprehensive discussion of massive PE but a quick reference guide*

DEFINITION

DIAGNOSTIC APPROACH

SUPPORTIVE THERAPY

ANTICOAGULATION ALONE

SURGICAL EMBOLECTOMY (rarely done)

INTRAVENOUS THROMBOLYTIC THERAPY

CATHETER-DIRECTED EMBOLUS REDUCTION

|

Massive PE: Conclusions -1

1. Do not use thrombolytic therapy in hemodynamically stable patients with PE (la veuve)
2. Do not waste time and resources on blood tests or echo that won't change management
3. **Massive PE** = lots of PE + arrest or shock or sustained hypotension or overt right heart failure
 - 5% of all PE
 - mortality 10→>60% (versus ≤3%)

Massive PE: Conclusions -2

4. **Indication for embolus reduction therapy = to reduce mortality**
5. **IV lytic therapy if:**
 - arrest, pre-arrest
 - CDT not available
 - and if no strong contraindication

} 50 bolus or
100 mg/2 hrs
6. **Catheter-directed therapy = treatment of choice (unless not available or patient pre-arrest)**
7. **Develop local expertise**

Indications for Catheter-Directed Thrombectomy/Thrombolysis

1. In **PE**, with hypotension, overt right heart failure (*increased risk of early death*)
2. In **DVT**, with extensive clot and severe symptoms (*“big clot, can’t walk”*)

References

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