Update on Venous Thromboembolic Disease Interventions

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Annual Incidence

- 1.6 per 1000 people
- up to 10 per 1000 in elderly
- Cumulative risk of VTE by age 80 is 11%
- 600,000 – 900,000 cases annually
- >500,000 hospital admissions annually

Disease	Incidence per 100,000
Venous Thromboembolism	168
Prostate Cancer	142
Breast Cancer	125

Often missed/undiagnosed

- 1st symptom of DVT is often fatal PE
- PE can mimic or accompany
  - Pneumonia
  - CHF
  - NSTEMI
  - Asthma
  - Anxiety
- 10 – 30% of VTE patients die within 30 days
- 30% risk of another VTE within 10 years

Clinical Characteristics of patients with PE: "EMPEROR" Study

Feature	PE Confirmed (n=1880)	PE not confirmed (n=528)
Dyspnea	50%	51%
Pleuritic chest pain	39%	28%
Cough	23%	23%
Substernal chest pain	15%	17%
Fever	10%	10%
Hemoptysis	8%	4%
Syncope	6%	6%
Unilateral leg pain	6%	5%
Unilateral leg swelling	24%	18%

Pollack CV, Schreiber D, Goldhaber SZ, Slattery D, Fanikos J, O'Neil BJ, Thompson JR, Hiestand B, Briese BA, Pendleton RC, Miller CD, Kline JA. Clinical characteristics, management, and outcomes of patients diagnosed with acute pulmonary embolism in the emergency department: initial report of EMPEROR (Multi- center Emergency Medicine Pulmonary Embolism in the Real World Registry). J Am Coll Cardiol 2011;57(6):700 – 706.

Serum D-Dimer

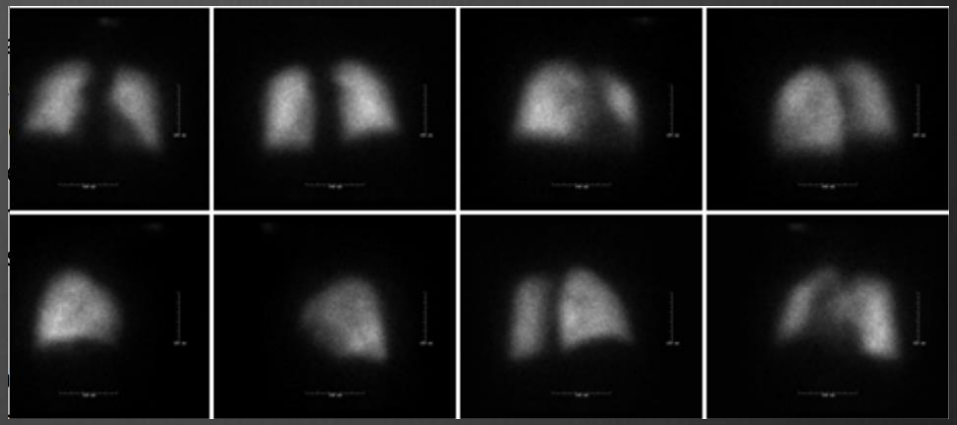
- Degradation product of fibrinolysis
- Sensitivity for DVT/PE can be as high as 95%
- Negative predictive value is high
- With Negative result, 3 month Thromboembolic Risk <1%
- Low Specificity for DVT/PE
- Conditions that can produce fibrin:
  - Cancer
  - Inflammation
  - Bleeding
  - Trauma
  - Surgery
- Positive predictive value is low

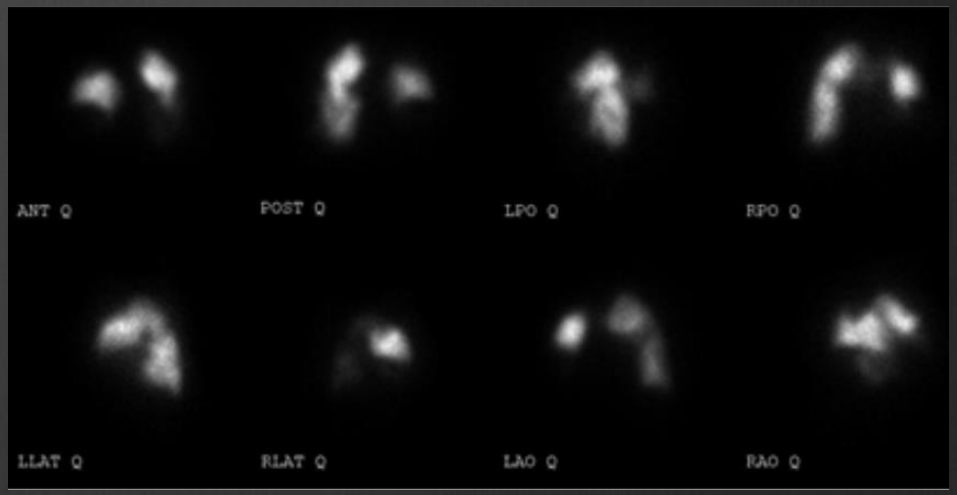
Multi-detector CT

- High spatial and temporal resolution
- Visualize pulmonary arteries at least to segmental level
- Negative predictive value 89 – 96%
- Positive predictive value 92 – 96%

Ventilation Perfusion Scan

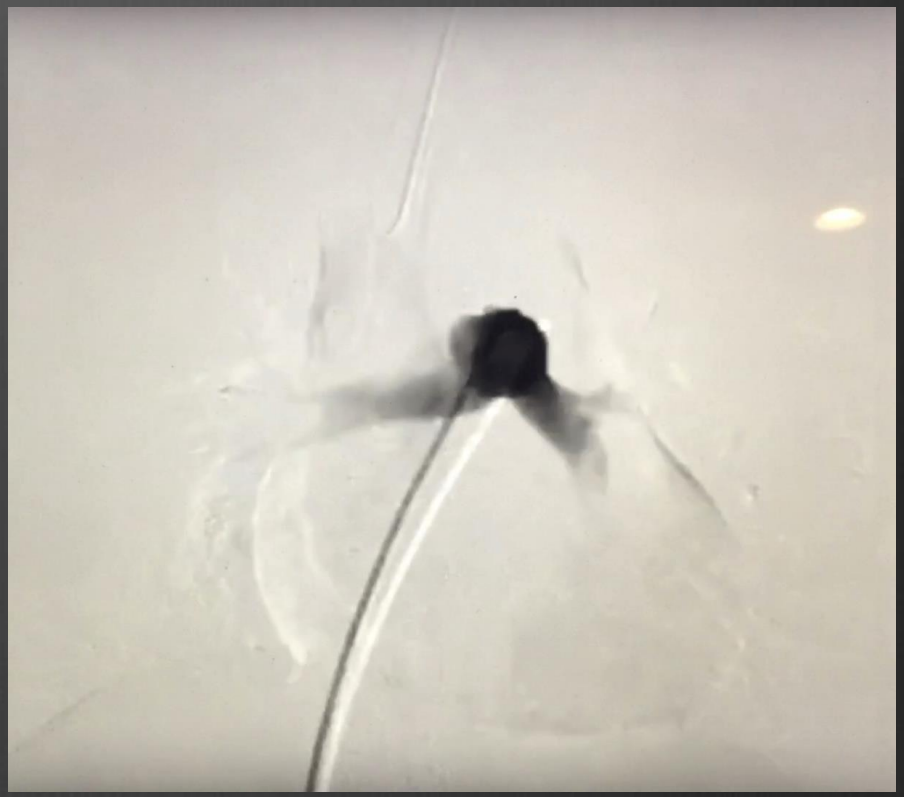
- PIOPED classification
  - High probability
  - Intermediate
  - Low probability
  - Normal
- Modified
  - High probability (diagnostic for PE)
  - Normal (excludes PE)
  - Non-diagnostic





Pulmonary Angiography

- Old “gold standard”
- Can visualize 1-2mm thrombi
- Complications
  - Minor 5%
  - Major 1%
  - Death 0.5%

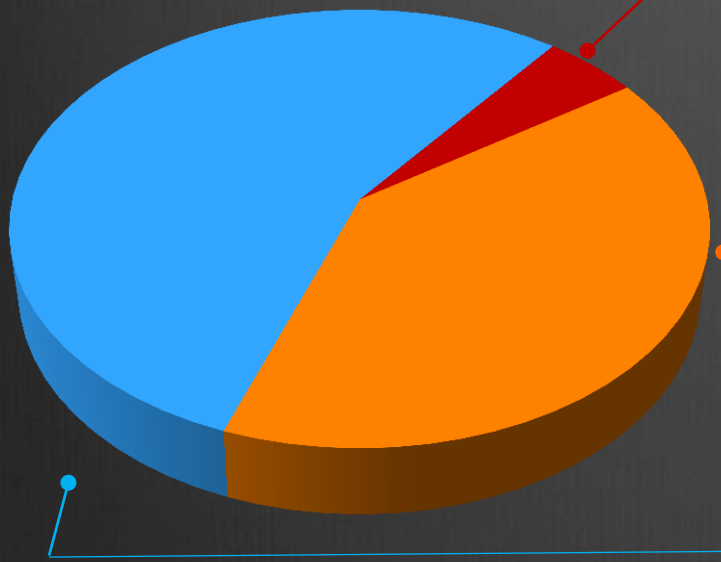


Echocardiography

- Negative predictive value 40%
- RV Strain (RV/LV)
- Tricuspid Regurgitation
- PA Pressure
  - Bernoulli equation

$$P_1 + \frac{1}{2}\rho V_1^{\,2} + \rho g h_1 = P_2 + \frac{1}{2}\rho V_2^{\,2} + \rho g h_2$$

PE patient population profile



MASSIVE PE
[High risk]
5% PE population
58%[1] **mortality** @ 3 months

SUBMASSIVE PE
[Moderate/Intermediate risk]
40% PE population
2-3%[2,3] **mortality** to
21%[1] **mortality** @ 3 months

MINOR PE
[Low risk]
55% PE population
Good prognosis
Low mortality rate

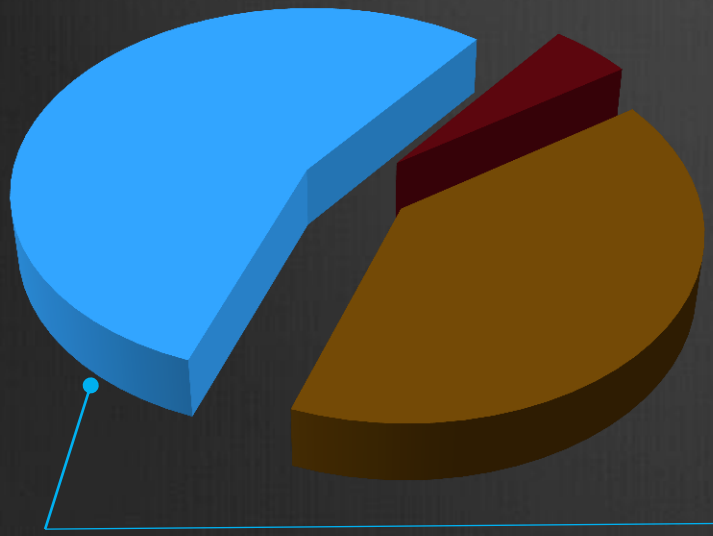
Risk Stratification of Pulmonary Embolism Patients

Risk Assignment	Severity	% PE Population	% Mortality	Characteristics
Massive (High)	Severe	5	>50	Hypotension, circulatory collapse hemodynamic instability
Submassive Intermediate-High risk	High	10	21	RVD without hypotension; elevated troponin and elevated BNP
Submassive Intermediate-Low risk	Medium	15		RVD without hypotension and either elevated troponin or elevated BNP, but not both
Minor	Minor	45 to 70	15	Dyspnea; chest pain

BTG

Minor/Low Risk Pulmonary Embolism

- Unfractionated Heparin or LMWH
- Transition to Oral AC
- Treat for 3 months if provoking event is no longer present
- Treat for as long as the provoking event persists, possibly indefinitely (e.g. cancer)
- Treat for longer if unprovoked (6 months)
  - 20% risk of recurrence



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Good prognosis
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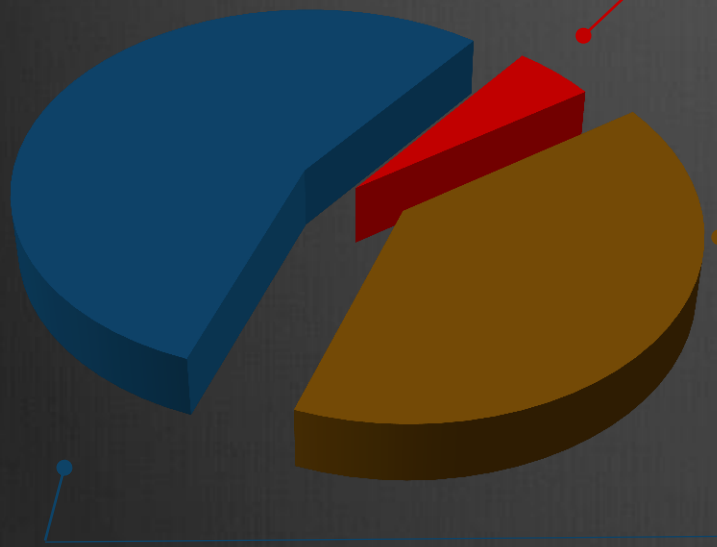
But …

- AC alone doesn't dissolve clot
- Patient's own fibrinolytic pathway
- May take weeks/months



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BTG

IV Thrombolysis
in Hemodynamically Unstable Patients

- Restores pulmonary perfusion more rapidly than AC alone
- Early resolution of obstruction leads to
  - prompt reduction in PA pressure
  - Improvement in RV function
- >90% response rate
- Associated with reduction in mortality or recurrent PE in high risk patients

IV Thrombolysis
in Hemodynamically Unstable Patients

- Major Bleeding Risk 0.8 % to 22%
- Intracranial Hemorrhage ~2%
- Bleeding risk is increased with age > 65
- Bleeding risk is decreased when concomitant Heparin dose modified with a PTT 1.5 to 2 x baseline

Meta-analysis of Randomized Clinical Trials comparing Thrombolytics with Hepartin

- 11 Trials, 748 patients
- Included all PE and Massive PE

	Trials That Included Patients with Major PE		
Outcome	**Thrombolysis n/N(%)**	**Heparin n/N(%)**	**OR (95% CI)**
Recurrent PE or death	12/128 (9.4)	24/126 (19.0)	0.45 (0.22–0.92)
Recurrent PE	5/128 (3.9)	9/126 (7.1)	0.61 (0.23–1.62)
Death	8/128 (6.2)	16/126 (12.7)	0.47 (0.20–1.10)
Major bleeding	28/128 (21.9)	15/126 (11.9)	1.98 (1.00–3.92)

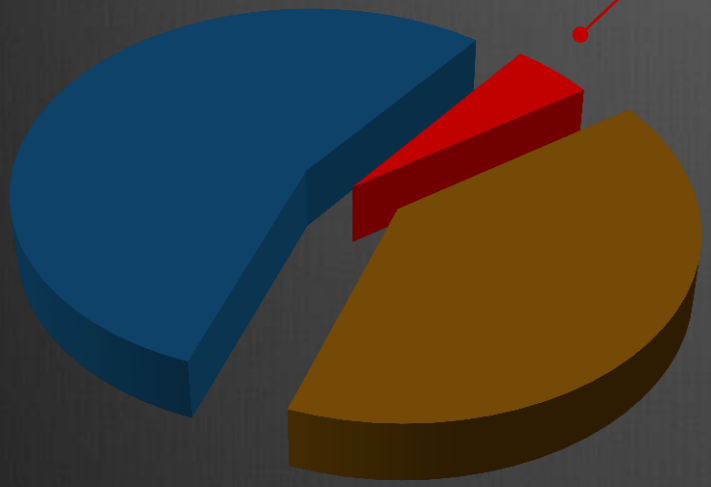
PE Indicated Pulmonary embolism

Wan S et al. Thrombolysis compared with heparin for the initial treatment of pulmonary embolism. Circulation. 2004 Aug. 10;110(6):744-9.

Meta-analysis of Randomized Clinical Trials comparing Thrombolytics with Heparin

- "Compared with heparin, thrombolytic therapy was associated with a significant reduction in pulmonary embolism or death in the 5 trials that included patients with **major (hemodynamically unstable) pulmonary embolism** (9.4% versus 19.0% OR 0.45, 95% CI 0.22 to 0.92, number needed to treat=10)"
- "no evidence for a benefit of thrombolytic therapy compared with heparin for the initial treatment of unselected patients with acute pulmonary embolism."
- "… a clear benefit is suggested among those at highest risk of recurrence or death, in particular, patients with major pulmonary embolus who present with hemodynamic instability."

Wan S et al. Thrombolysis compared with heparin for the initial treatment of pulmonary embolism. Circulation. 2004 Aug. 10;110(6):744-9.



MASSIVE PE
[High risk]
58%[1] **mortality** @ 3 months

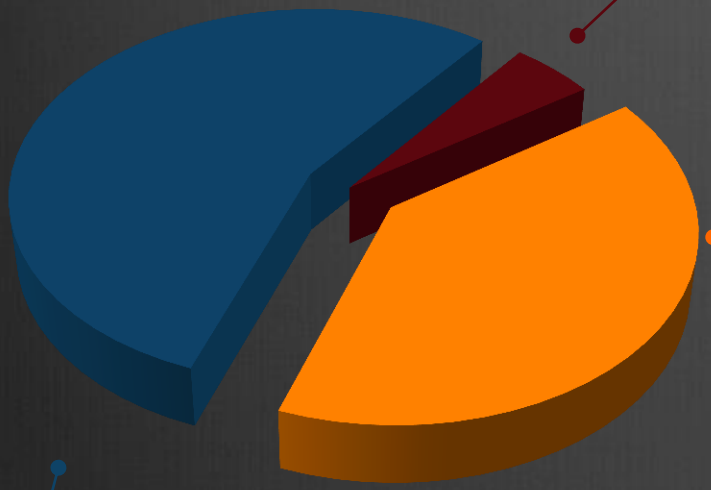
- **Hypotension**
- **Hemodynamic Instability**
- **Circulatory Collapse**

IV Thrombolytics

IV TPA

- 100 mg TPA
- Accelerated infusion regiment over 2 hours preferred
- Heparin: target PTT 1.5 to 2 x control

What about sub-massive PE?



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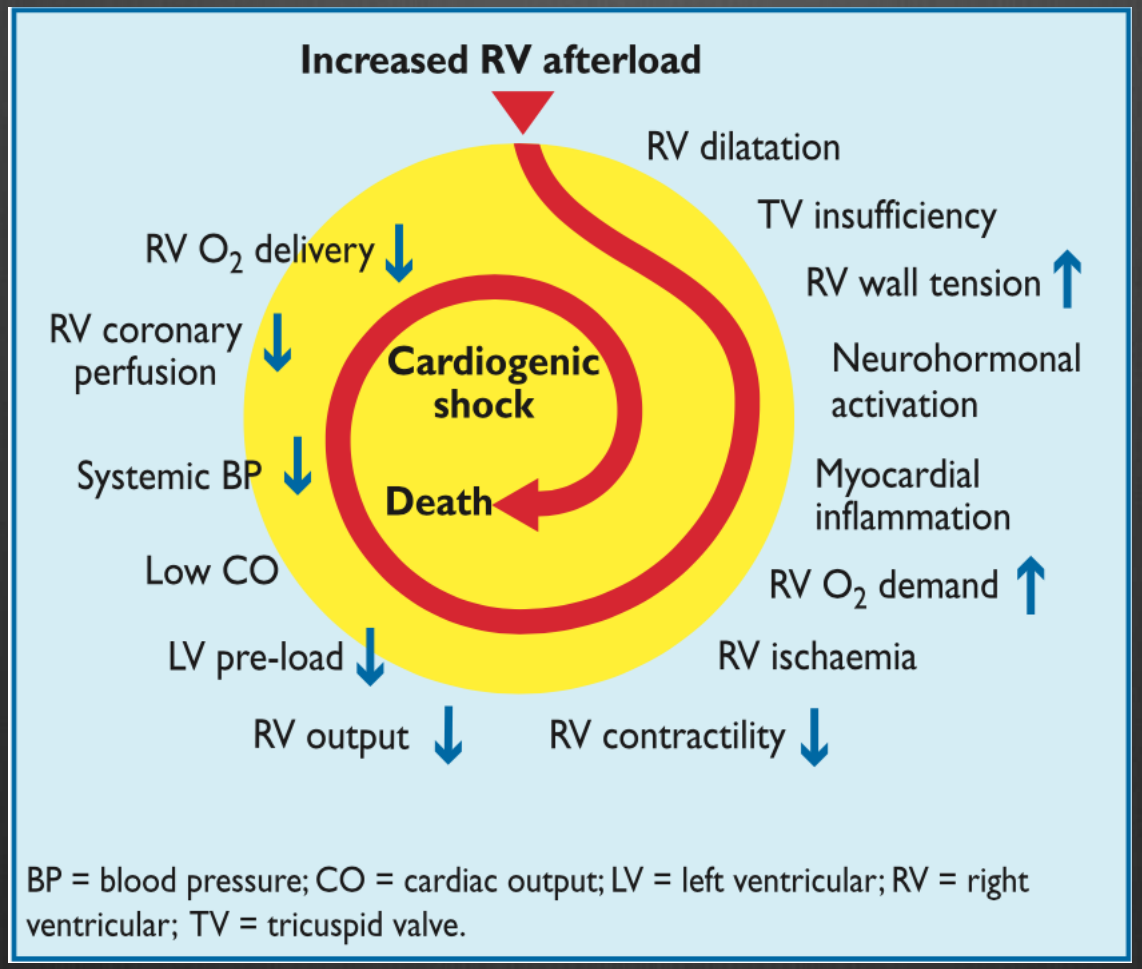
Key factors contributing to hemodynamic collapse in acute PE



* 2014 ESC Guidelines on the diagnosis and management of acute pulmonary embolism:
The Task Force for the Diagnosis and Management of Acute Pulmonary Embolism of the European Society of Cardiology (ESC)

Rational for more aggressive therapy

- Reduce Thrombus Burden
- Improve pulmonary reperfusion/capillary blood flow/gas exchange
- Decrease RV afterload
- Prevent RV failure and hemodynamic collapse
- Decrease risk of developing Chronic Pulmonary Hypertension

In Hemodynamically Stable PE

RV/LV Ratio	In Hospital Mortality	Adverse event Rate at 30 days:
≤ 0.9	1.9%	51.3%
> 0.9	6.6%	80.3%

Fremont B et al. Prognostic value of echocardiographic right/left ventricular end-diastolic diameter ratio in patients with acute pulmonary embolism. CHEST 2008;133:358-362

Quiroz R et. al. Right ventricular enlargement on chest computed tomography. Circulation. 2004;109:2401-2404

RV/LV Ratio	3 Months Mortality
< 1.0	0%
> 1.0 and ≤ 1.5	8%
> 1.5	17%

Van der Meer RW et al. Right ventribular dysfunction and pulmonary obstruction index at helical CT: prediction of clinical outcome during 3-month follow-up in patients with acute pulmonary embolism. Radiology 2005; 235:798-803.

International Cooperative Pulmonary Embolus Registry (ICOPER)

- Prospective study of 2,454 consecutive PE patients at 52 hospitals in 7 countries
- Presence of RV hypokinesis associated with 57% increase in mortality rate at 3 months

Mortality rate at 3 months

21% with R.V. **hypokinesis**

15% with no R.V. **hypokinesis**

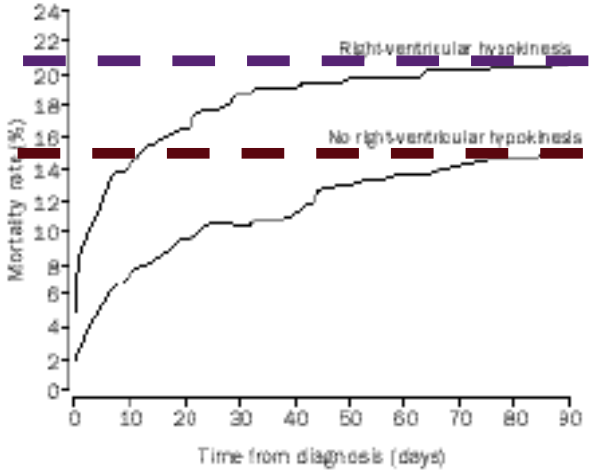
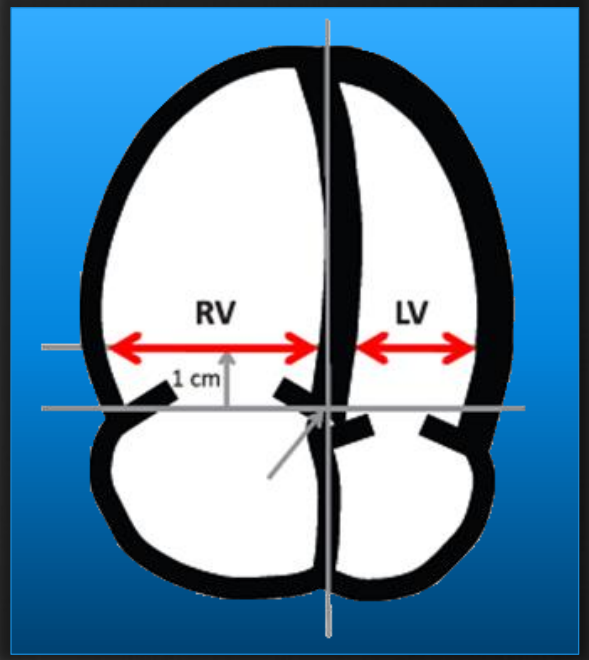


Figure 3: **Cumulative mortality according to status of right-ventricular function on baseline echocardiogram**

Goldhaber, SZ et al, Acute pulmonary embolism: clinical outcomes in the International Cooperative Pulmonary Embolism Registry (ICOPER), Lancet 1999; 353: 1386-89.

Measuring RV/LV Ratio

- Apical 4 Chamber View
- End Diastolic Image
- Center line through Interventricular Septum
- Obtain tricuspid annular line
- Obtain subannular line 1cm above annular line
- Obtain RV and LV dimensions using endocardial borders



Pulmonary Embolism Thrombolysis (PEITHO) trial

- Multicenter, Randomized, Double Blind
- IV bolus of Tenecteplase + Heparin vs. Placebo + Heparin
- 1006 patients
- RV dysfunction (Echo or CT) & Myocardial injury confirmed by positive troponin
- Primary endpoint: Composite all-cause death or hemodynamic decompensation/collapse

Pulmonary Embolism Thrombolysis (PEITHO) trial

Good

- All-cause death or hemodynamic decompensation/collapse significantly reduced
  - 2.6% vs. 5.6%, p=0.015
- Significant Reduction in Hemodynamic collapse
  - 1.6% vs. 5%, p=0.002

Bad

- Major Bleeding
  - 6.3% vs. 1.5
- Hemorrhagic Stroke
  - 2% vs. 0.2%
- Bleeding risk increases for age >65

Can we decrease risk of bleeding by using a lower dose of IV TPA and still achieve good results?

Moderate Pulmonary Embolism Treated With Thrombolysis (from the "MOPETT" Trial)

- 121 Patients
- "Moderate" PE
- > 95 SBP < 200
- ½ dose TPA
- 1º Endpoint: Reduction in Pulmonary artery pressure

Exclusion Criteria

- Eligibility for full dose Lytic
- Onset > 10 days
- Contraindication to heparin or lytics

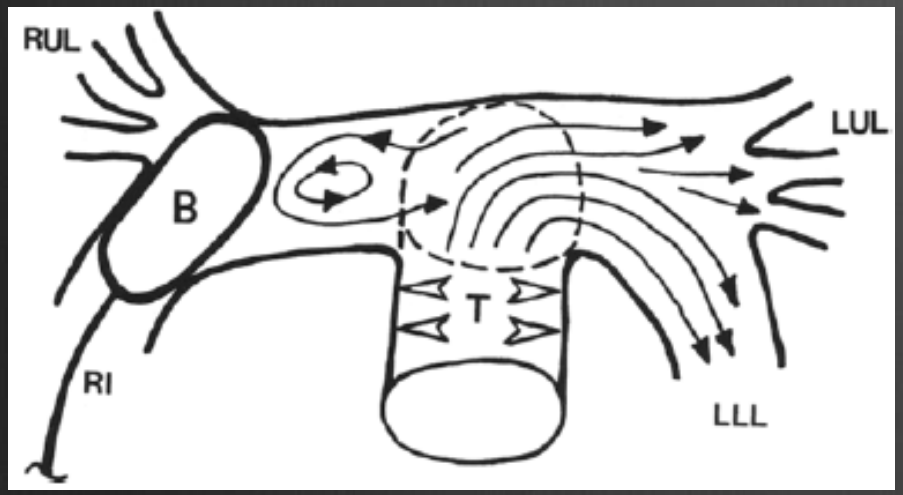
Moderate Pulmonary Embolism Treated With Thrombolysis (from the "MOPETT" Trial)

Pulmonary Artery Systolic Pressure (mmHg)			
	TG (n=61)	CG (n=60)	p Value
On Admission	50 ± 6	51 ±7	0.4
Within 48h	34 ± 7	41 ± 4	<0.001
6 months	31 ± 6	49 ± 8	<0.001
28 ± 5 months	28 ± 7	43 ± 6	>0.001

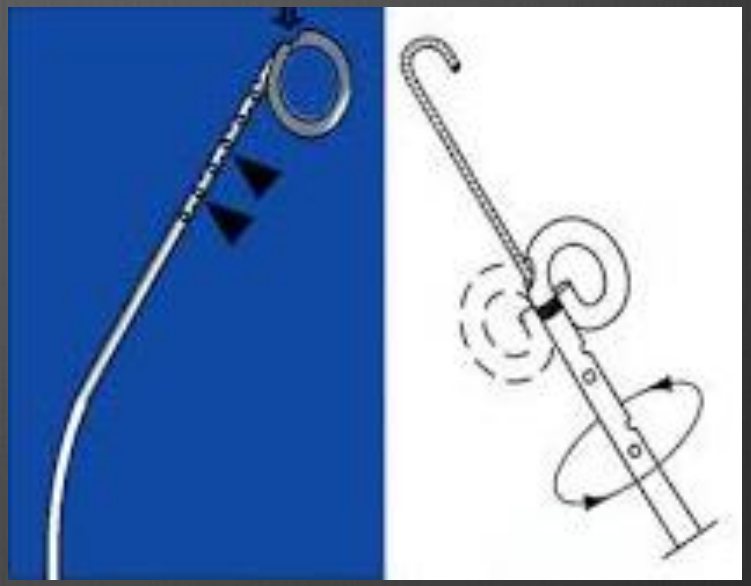
Secondary Endpoints			
	TG (n=61)	CG (n=60)	p Value
Recurrent PE	0	3 (5%)	0.08
Total mortality	1 (1.6%)	3 (5%)	0.30
Hospital Stay	2.2 ± 0.5	4.9 ± 0.8	<0.001
Bleeding	0	0	-

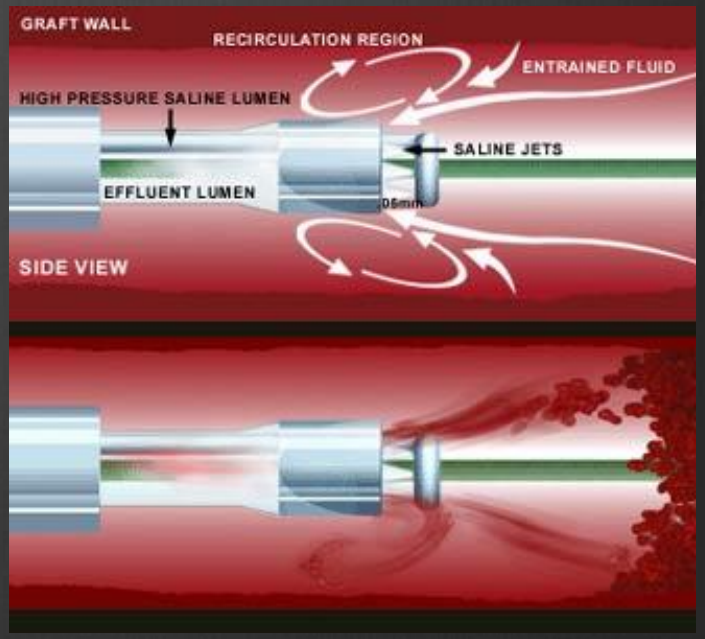
Can we lower the dose of Thrombolytic even more?

Catheter Directed Therapy



- Local administration of Lytic
- Higher drug concentration results in more rapid thrombolysis
- Even distribution results in faster treatment of thrombus
- Can use even lower t-PA dose!

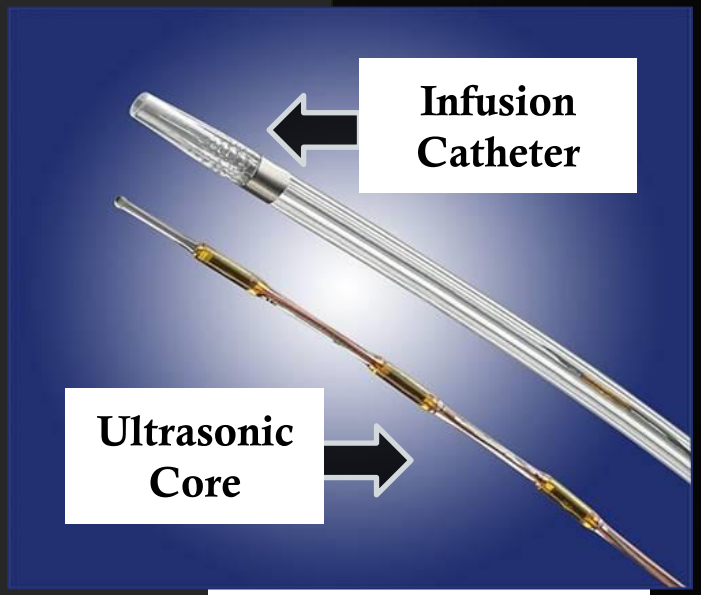


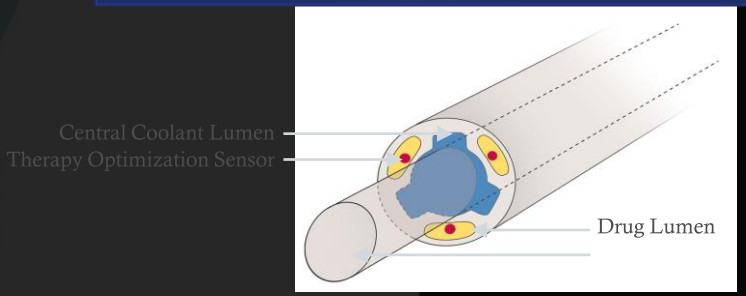

GRAFT WALL
RECIRCULATION REGION
ENTRAINED FLUID
HIGH PRESSURE SALINE LUMEN
SALINE JETS
EFFLUENT LUMEN
SIDE VIEW

EKOS

(Ultrasound Assisted Thrombolysis/Acoustic Pulse Thrombolysis™)

- 5.4 Fr catheter
- 106 and 135 cm working length
- 6, 12, 18, 24, 30, 40 and 50 cm treatment zones





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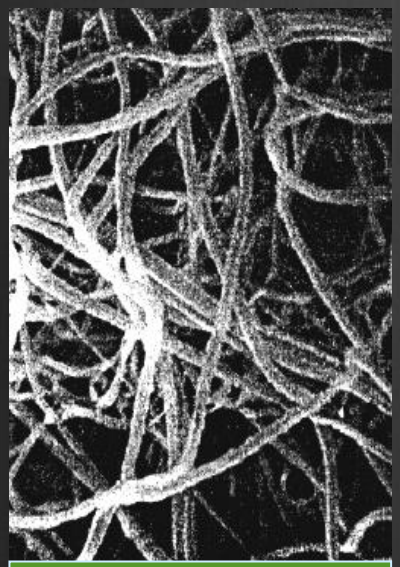
EKOS

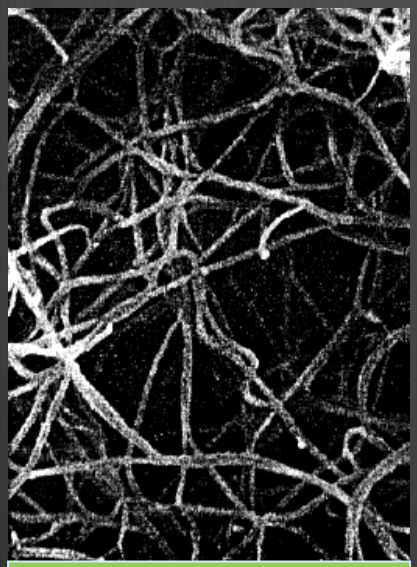
(Ultrasound Assisted Thrombolysis/Acoustic Pulse Thrombolysis™)

Fibrin Separation

Ultrasound separates fibrin without fragmentation of emboli



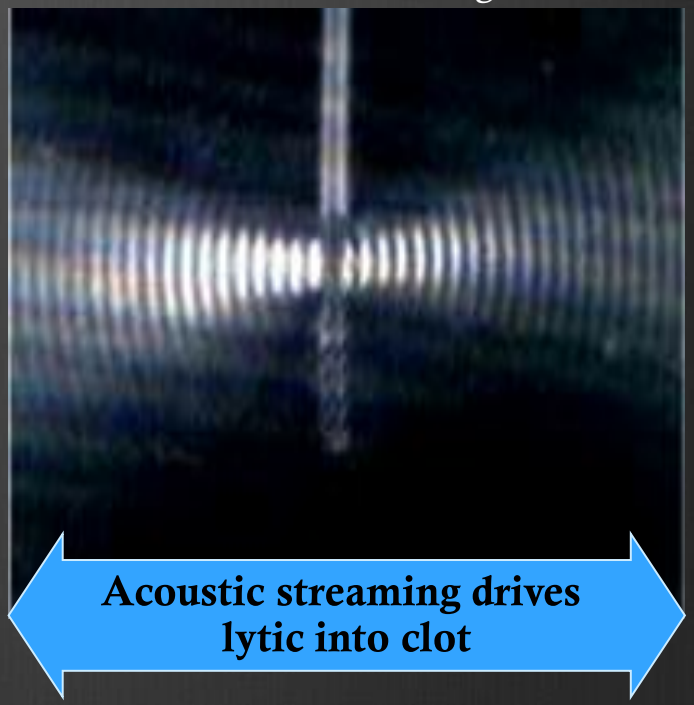
Fibrin without Ultrasound



Fibrin With Ultrasound

Active Drug Delivery

Drug is actively driven into clot by "Acoustic Streaming"



BTG

Evidence for CDT

- Single Center Studies
- Meta-analysis of historic published data
- ULTIMA trial
- SEATTLE II trial

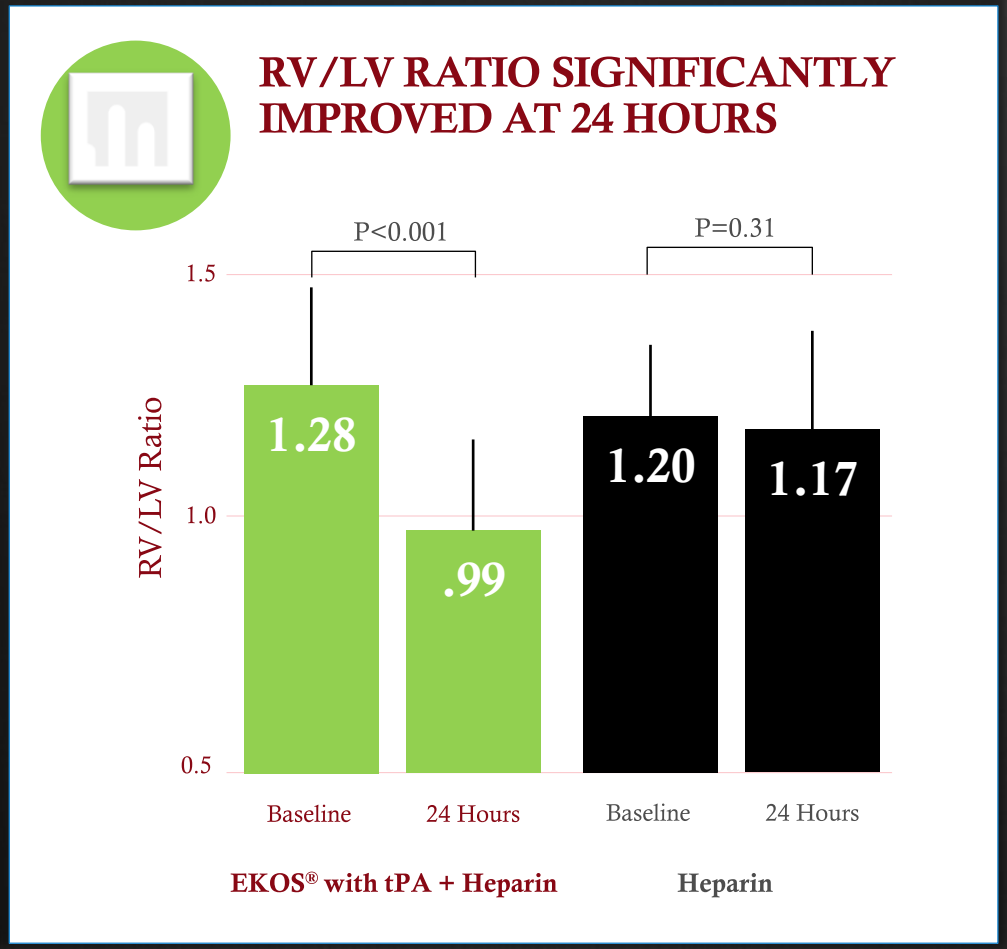
ULTIMA trial

- Determine whether fixed low-dose catheter-directed ultrasound accelerated thrombolysis is superior to heparin alone in reversal of RV dilatation in submassive/intermediate risk PE

ULTIMA trial

- 59 patients with acute PE
- Hemodynamically stable / Intermediate category
- RV/LV $\geq$ 1.0
- Randomized
  - Heparin + US Assisted CDT (n=30)
  - Heparin (n=29)

ULTIMA trial



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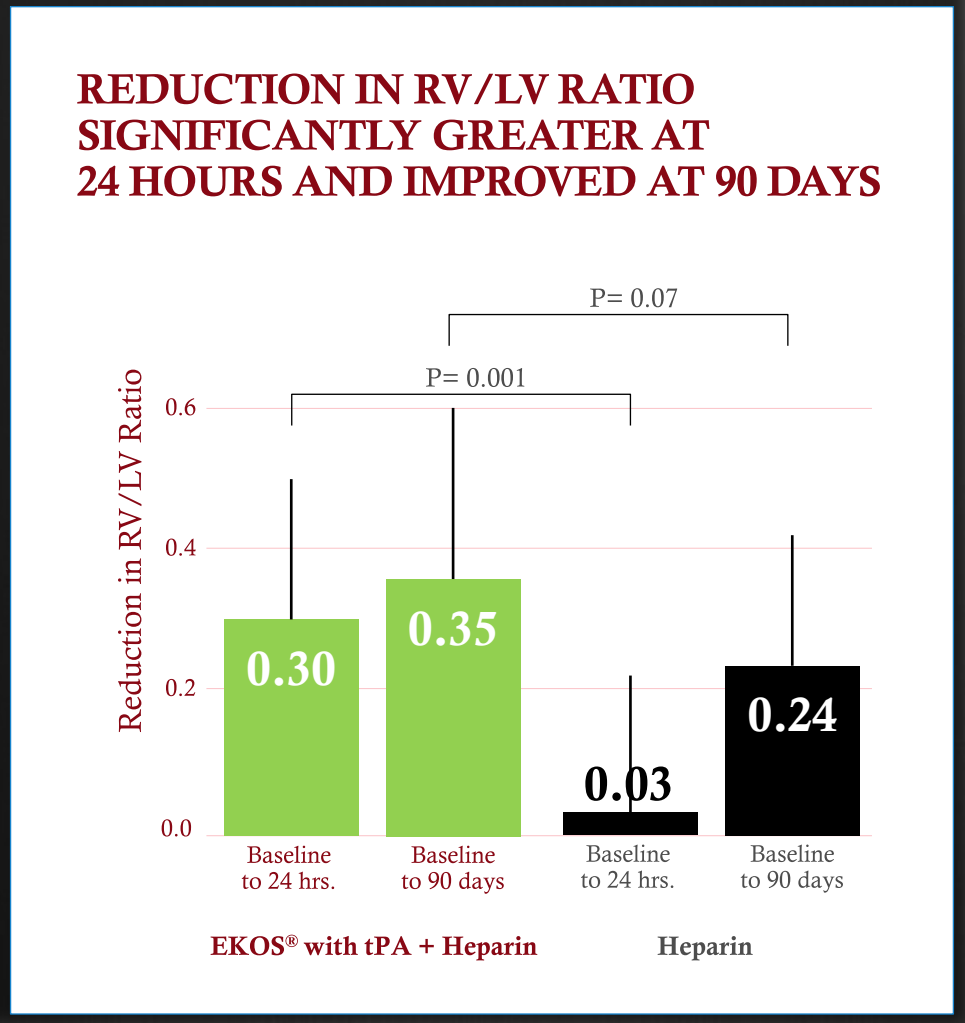


ULTIMA trial

- RV Dysfunction significantly improved with Ultrasound Assisted Thrombolysis vs. Heparin alone ($p=0.003$)

No statistical difference in safety outcomes with EKOS® with tPA + Heparin than Heparin alone

Clinical Outcome at 90 days					
	EKOS with tPA + Heparin		Heparin (n=29)		p Value
Death	0	0%	1*	0%	0.49
Recurrent VTE	0	0%	0	0%	1.00
Major Bleeding	0	0%	0	0%	1.00
Minor Bleeding	3**	10%	1***	3%	0.61

*Rehospitalization and death from advanced pancreatic cancer
**Two patients with transient mild hemoptysis without medical intervention, one patient with groin hematoma requiring manual compression
***One patient with transient bleeding following endoscopic removal of colon polyp
Kucher N et al. Randomized, controlled trial of ultrasound-assisted catheter-directed thrombolysis for acute intermediate-risk pulmonary embolism.
Circulation. 2014;129:479-486

ULTIMA Trial Conclusion

- **Fixed-dose, ultrasound-assisted catheter-directed thrombolysis EKOS® regimen was superior to anticoagulation alone in improving RV dysfunction at 24 hours without an increase in bleeding complications.**

SEATTLE II Trial

- Prospective, Single-Arm, Multicenter Trial of US Facilitated, Low Dose, Fibrinolysis for Acute Massive & Submassive PE
- 150 Patients
- 22 Centers

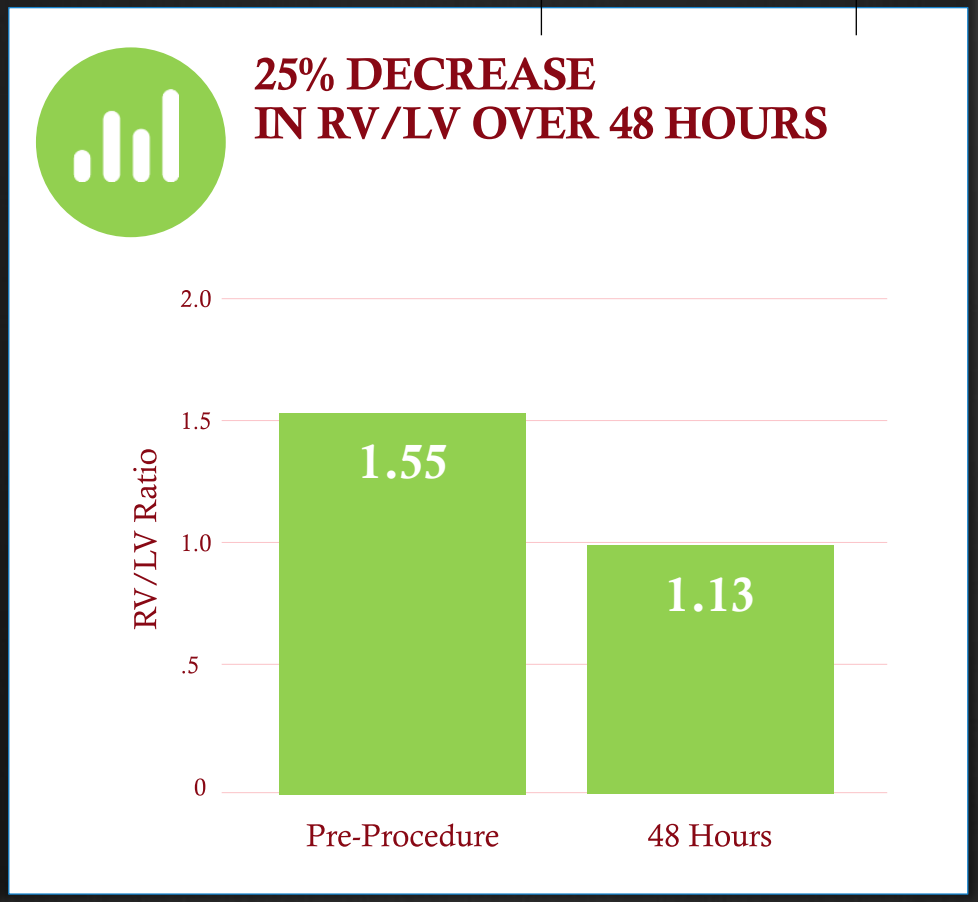
SEATTLE II Trial

- Primary Efficacy
  - Change in RV/LV ratio from baseline to 48 hours
- Secondary Efficacy
  - Change in invasively measured PA systolic pressure from baseline to device removal and as estimated on 48-hour echocardiogram
- Primary Safety
  - Major bleeding within 72 hours of start of procedure

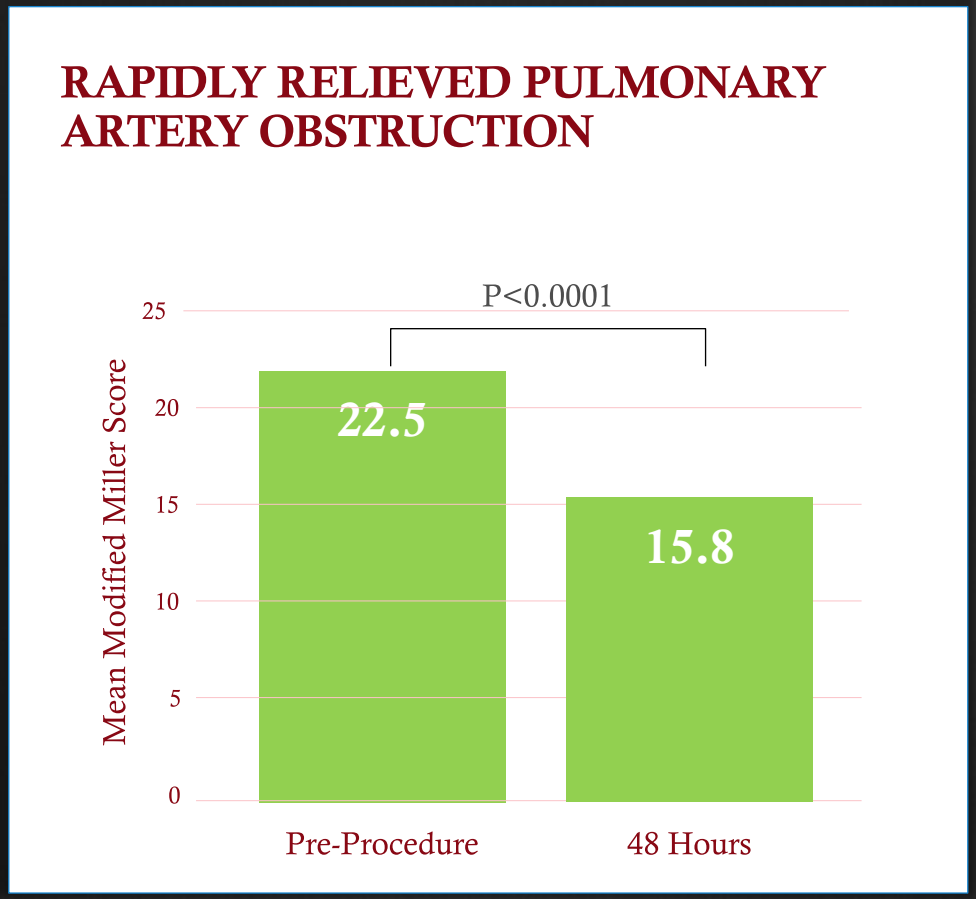
SEATTLE II Trial

Enrolled Patient Characteristics	N	%
Total enrollment	150	100%
Massive/Submassive PE	31/119	21%/79%
Unilateral/Bilateral PE	20/130	13%/87%
Concomitant use of antiplatelet agents	51	34%
Total rtPA dose	23.7 $\pm$ 2.9 mg	

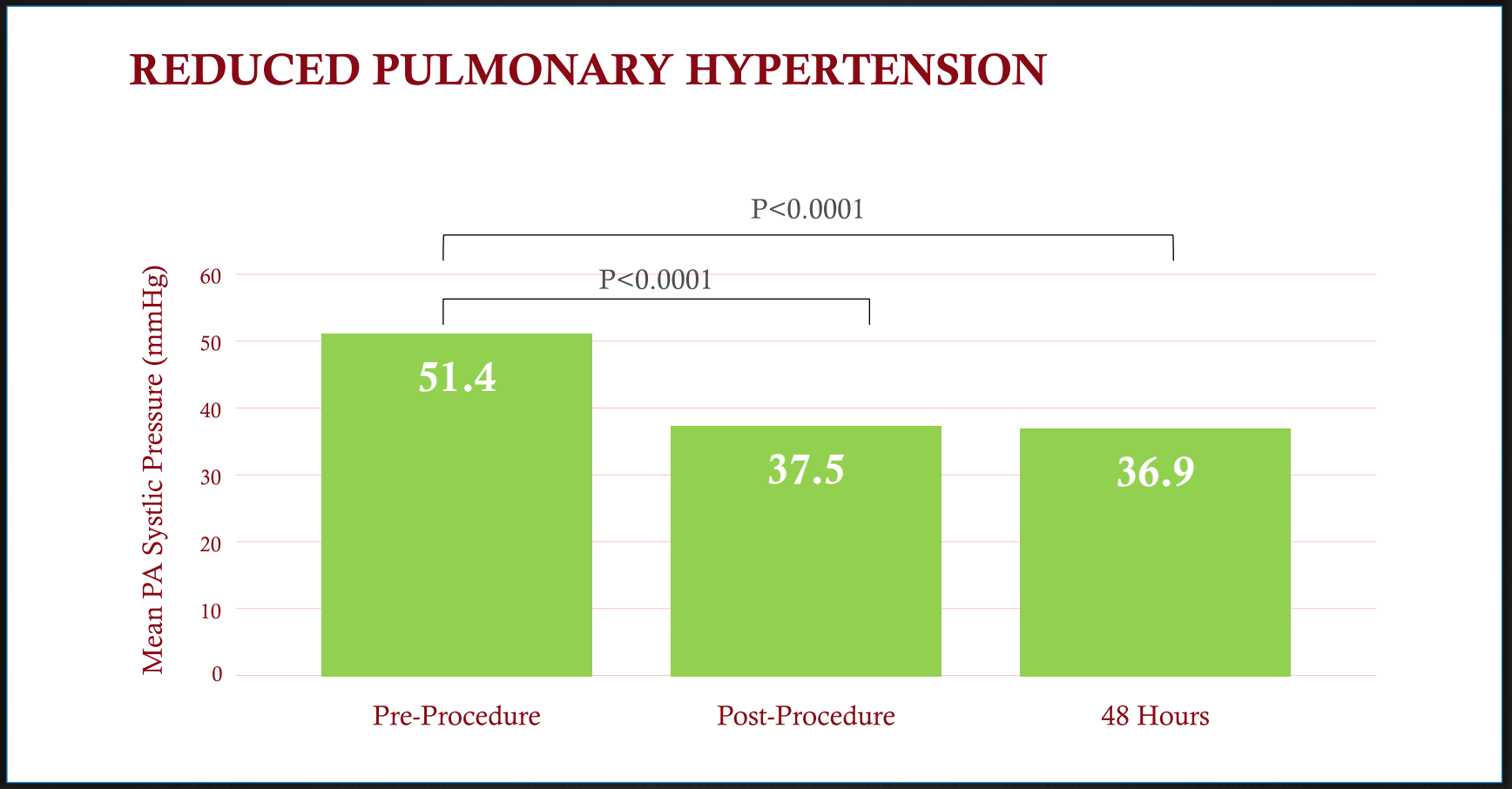
SEATTLE II Trial



SEATTLE II Trial



SEATTLE II Trial



SEATTLE II Trial

Clinical Outcomes	N=150
Length of stay	8.8 ± 5
In-hospital death, n (%)	3 (2)
30-day mortality	4 (2.7)
Serious adverse events due to device, n (%)	2 (1.3)
Serious adverse events due to t-PA, n (%)	2 (1.3)
Major Bleeding	17 (11.4)
Moderate (GUSTO)	16 (10.7)
Severe (GUSTO)	1 (0.7)
Intracranial Hemorrhage, n (%)	0 (0)

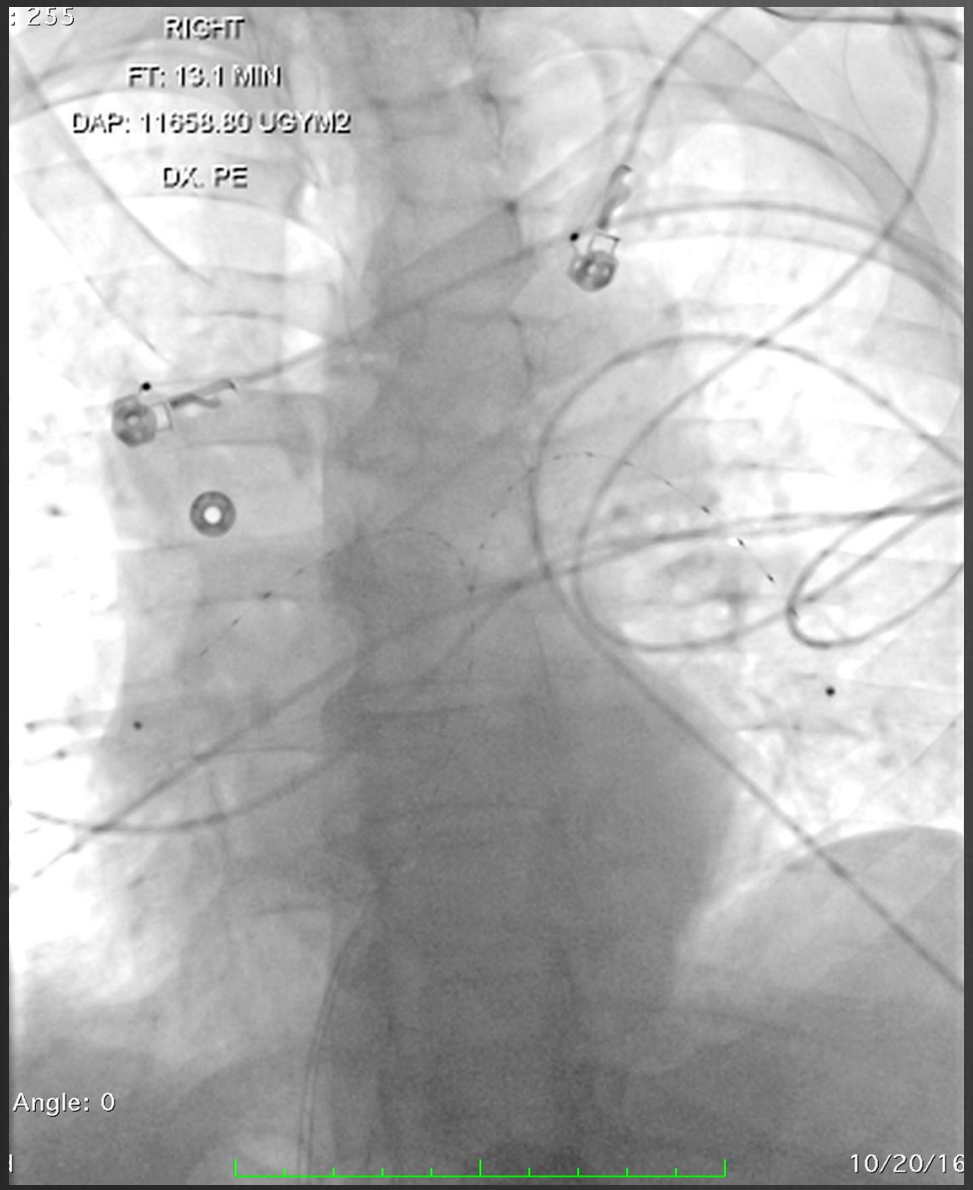
SEATTLE II Trial

Study	Intracranial Hemorrhage (Fibrinolysis Group)
ICOPER	9/304 (3%)
PEITHO	10/506 (2%)
SEATTLE II	0/150 (0%)

SEATTLE II Trial

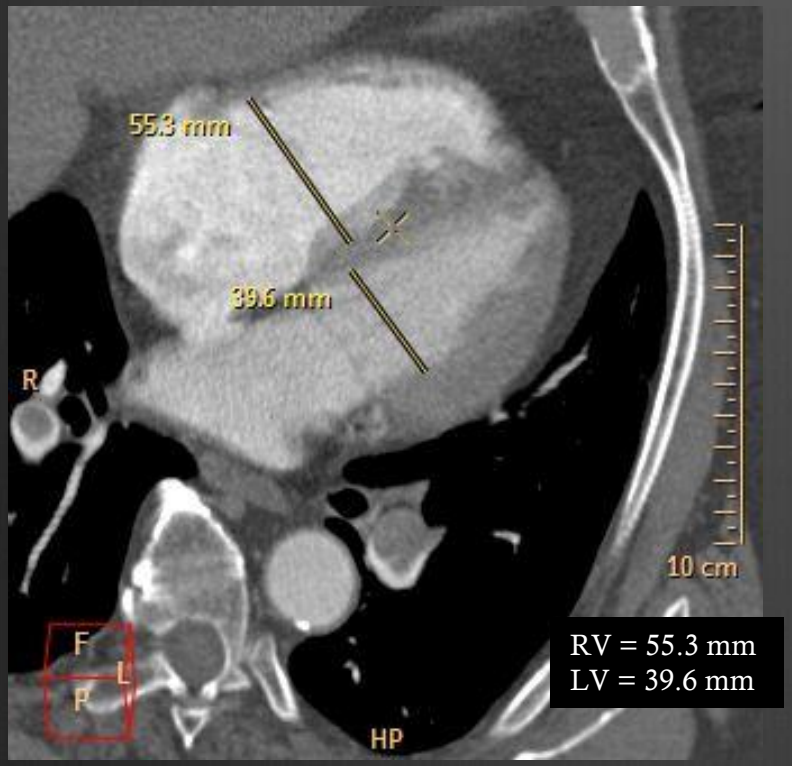
Conclusion:

- Ultrasound-facilitated, catheter directed, low-dose fibrinolysis for acute PE:
  - Improves RV function and decreases pulmonary hypertension
  - Minimizes risk of Intracranial Bleed

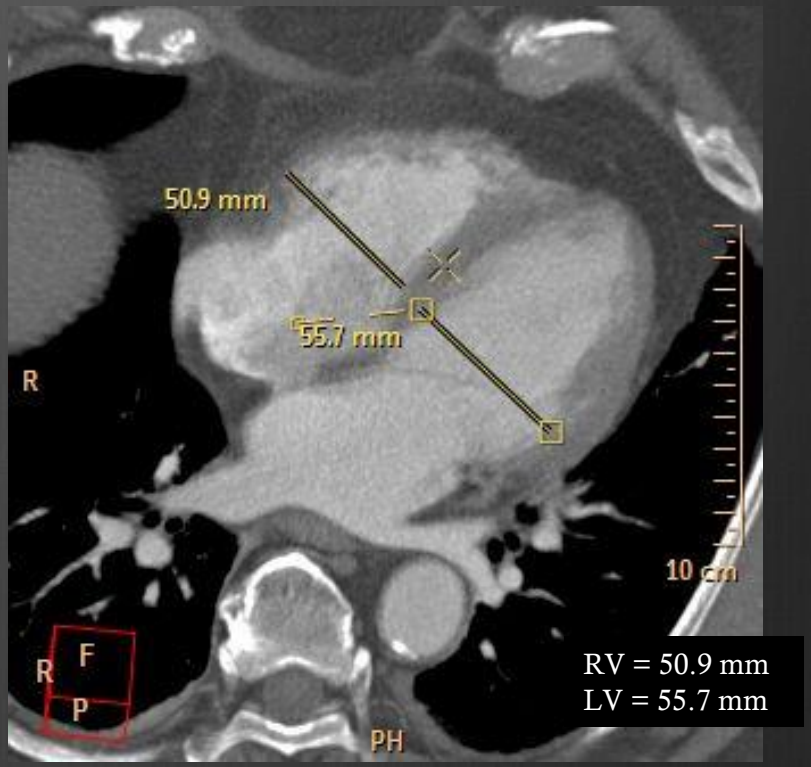


US Assisted CDT Protocol:

- Unilateral
  - t-PA 1mg/hr for 24 hours
- Bilateral
  - t-PA 1mg/hr per device for 12 hours
- Coolant through secondary channel
- Heparin at 1.5 to 2x control
- Saline through catheters after t-PA dose is completed



Pre-treatment
RV/LV = 1.40



Post-treatment
RV/LV = 0.91

Pulmonary Embolectomy

- Friedrich Trendelenburg in early 1900's
- First successful embolectomy 1924
  - Martin Kirschner
- High Mortality (between 30% and 59%)
  - Recent articles as low as 6%
- Rarely performed
- Considered/advocated in Hemodynamically Unstable patient with contraindication to or have failed thrombolytics

Acute Pulmonary Embolus

Minor (Low Risk)
Dyspnea, chest pain

→ Unfractionated Heparin or LMWH
Transition to Oral AC

Submassive (Intermediate Risk)
Hemodynamically stable / No hypotension
RV Dysfunction/Increased RV/LV ratio

→ Consider Ultrasound Assisted, Catheter Directed Thrombolysis
Concomitant Heparin with PTT 1.5 to 2x baseline

Massive (High Risk)
Hypotension /
Hemodynamic Instability

→ 100 mg TPA
Accelerated infusion regiment over 2 hours preferred
Heparin: target PTT 1.5 to 2 x control

↓

Remains Hemodynamically Unstable
Failed Thrombolysis or Unable to undergo Thrombolysis
Consider Surgical Embolectomy

Lower Extremity VTE Disease

How well do we diagnose DVT?

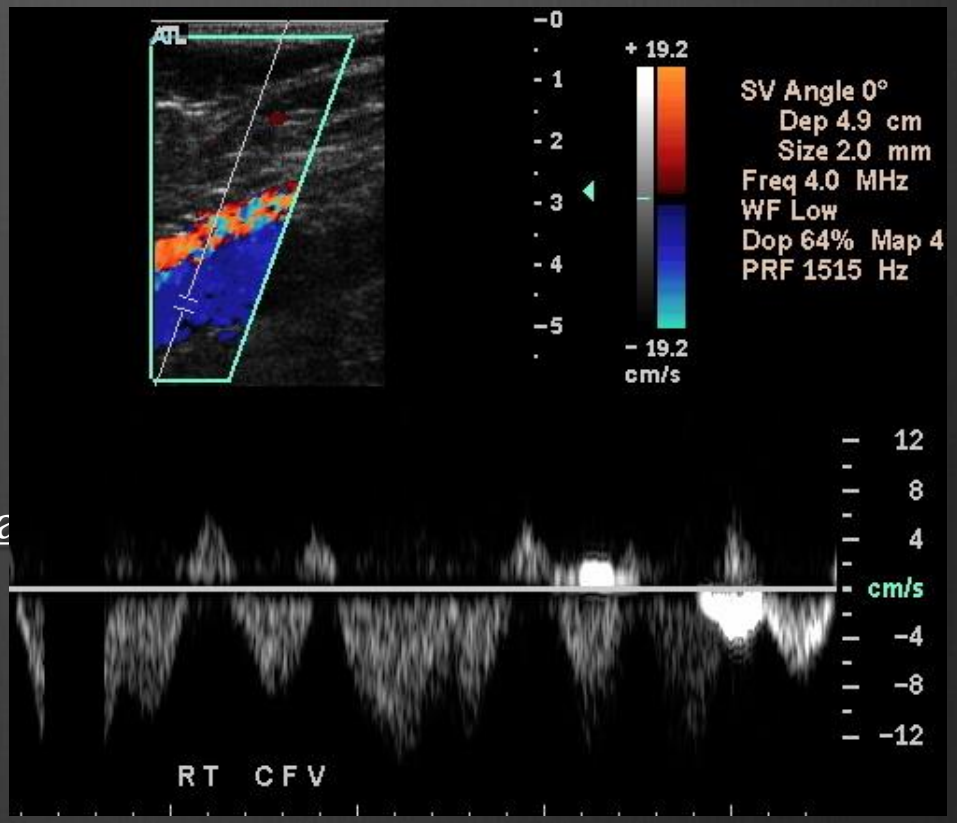
- Clinical Dx suggested by symptoms:
  - Leg swelling
  - Leg pain
  - Tenderness on deep palpation
  - Erythema
  - Pain on dorsiflexion of foot (Homan's Sign)
- Accuracy of these clinical findings as independent indicators of DVT is ~50%
- Although assessment of patient risk factors improves Positive Predictive Value, physical exam is still not good enough.

Serum D-Dimer

- High negative predictive value
- Low Specificity for DVT/PE

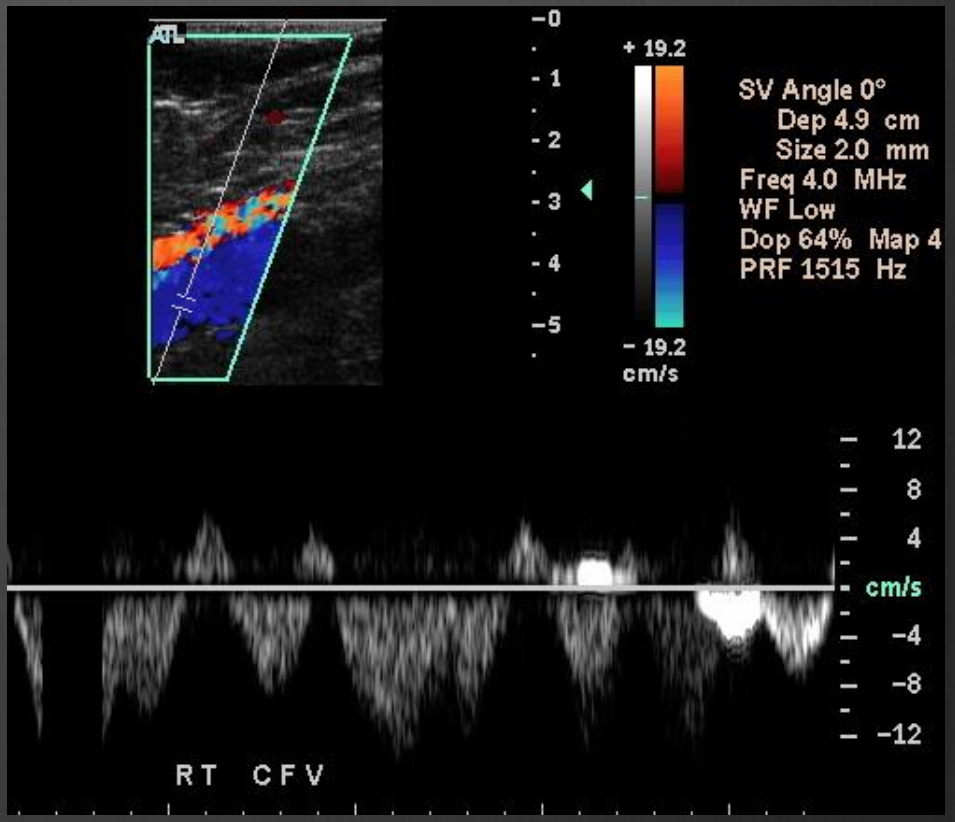
Ultrasound

- Mainstay of DVT imaging
  - Low risk
  - Low cost
  - High specificity
  - High sensitivity 95%
    - (From CFV to popliteal vein!)



Ultrasound

- Sensitivity calf veins ~80%
- Not great for imaging:
  - Pelvic veins
  - IVC



Venography

- "Gold Standard"
- Used rarely in U.S.
  - Not readily available
  - Higher cost
  - Patient discomfort
  - Small risk of complications

MR Venography

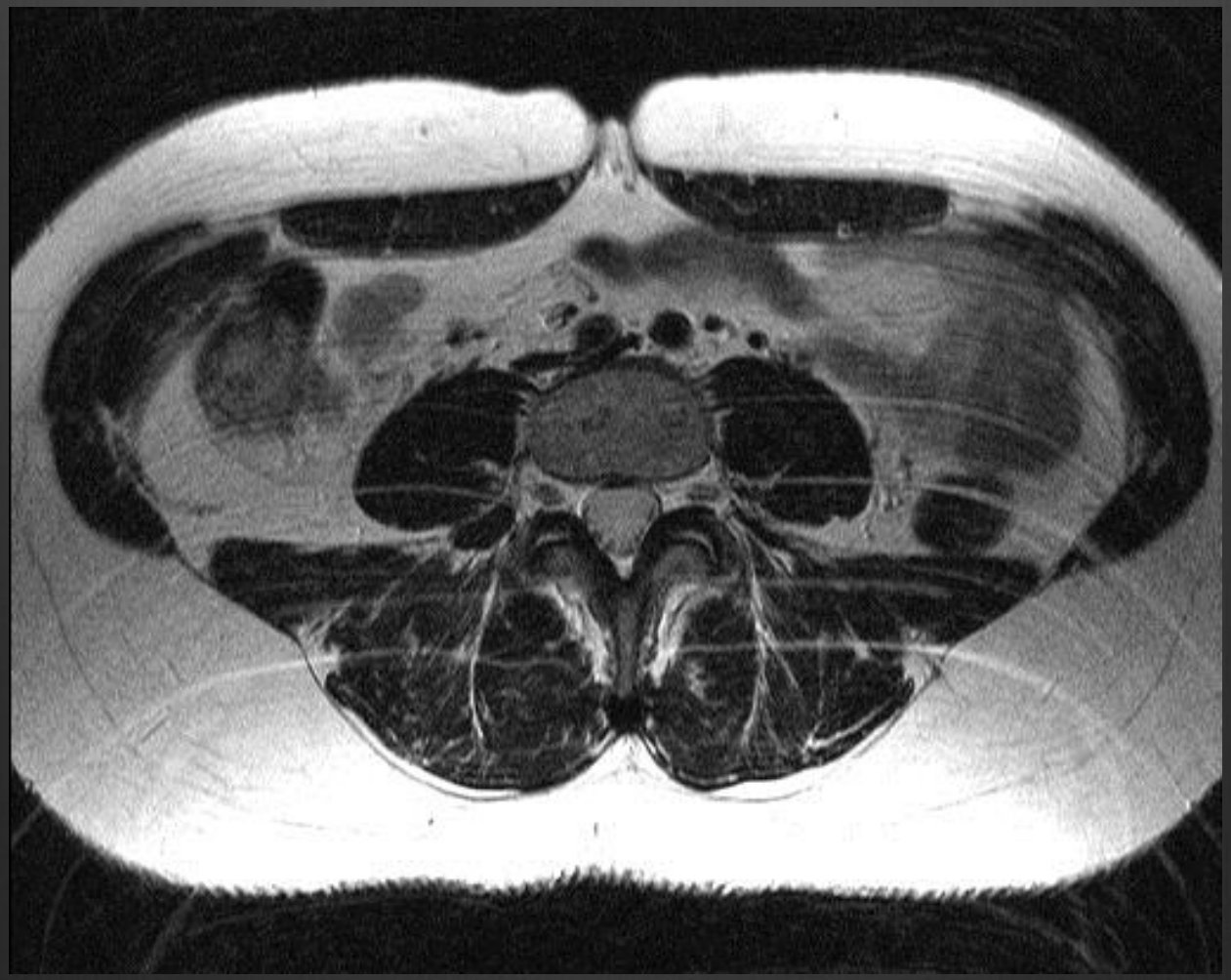
- Excellent sensitivity and specificity
- Not practical as screening due to:
  - Expense
  - Length of exam

MRV in iliac veins	
Sensitivity	100%
Specificity	96%
Positive Predictive Value	90%
Negative Predictive Value	100%

May Thurner Syndrome
(iliac vein compression syndrome)

- Compression of Left Common iliac vein between right common iliac artery and Spine
- Can cause Left LE DVT
- Often unrecognized
- ~5% DVT
- Women : Men = 3:1

May Thurner Syndrome



CT / CT Venography

Pros

- Good for visualization of Pelvic Veins & IVC
- Can often diagnose cause of DVT
  - Mass/Tumor
- DVT often detected incidentally on routine CT

Cons

- If contrast bolus not tailored to venous phase, DVT can be easily missed
- “flow” phenomena can mimic DVT

We diagnosed VTE; now what?

Clinical Spectrum of Lower Extremity VTE

- Superficial Phlebitis
- Deep Venous Thrombosis
- Phlegmasia Alba Dolens
- Phlegmasia Cerulea Dolens

Superficial Thrombo-phlebitis

- Greater Saphenous
- Lesser Saphenous
- Other superficial veins

Superficial Phlebitis

Symptoms

- Palpable cord in Saphenous or other superficial vein
- Erythema
- Limited edema

Standard Treatment

- Analgesics
- Support stockings
- Elevation
- Warm compresses
- Anticoagulants ***not*** indicated

Deep Venous Thrombosis

- Common Femoral Vein
- Superficial Femoral Vein
- Popliteal Vein
- Tibial Veins
- Iliac Veins
- IVC

Deep Venous Thrombosis

Symptoms

- Edema
- Pain
- Distended Superficial Veins
- Warm Extremity

Standard Treatment

- Anticoagulation
- Systemic Lytics?
- CDT?

Deep Venous Thrombosis

Symptoms

- Edema
- Pain
- Distended Superficial Veins
- Warm Extremity

Standard Treatment

- Anticoagulation
- ~~Systemic Lytics~~
- CDT?

Phlegmasia Alba Dolens

- Symptoms
  - Pale, cool extremity
  - Weak or absent pulses
    - Arterial insufficiency believed due to arterial spasm (usually transient)
- Treatment
  - Anticoagulation
  - Consider CDT

Phlegmasia Cerulea Dolens

- Symptoms
  - Cyanotic, Cool, Painful, Pulseless extremity
  - Arterial collapse due to tense edema in presence of extensive DVT (compartment syndrome)
  - Complicated by Gangrene/Amputation ~50%
  - Limb loss likely

Phlegmasia Cerulea Dolens

- Treatment
  - Surgical thrombectomy
  - Fasciotomy

What about Catheter Directed Therapy for average run of the mill DVT?

When should we consider it?
What's the evidence?

Answers

Catheter Directed Therapy/Pharmacomechanical Thrombolysis/Thrombectomy

Techniques / Devices

- Infusion catheter
- Fogarty balloons
- Angiojet
- Angiovac
- Treratolla
- Trellis
- EKOS

Lytics

- Streptokinase
- Urokinase
- Alteplase
- Reteplase
- Tenecteplase

Guidelines

- ACCP 2008: “In selected patients with extensive acute proximal DVT (e.g. iliofemoral DVT), symptoms <14 days, good functional status, life expectancy > 1 year, lower risk of bleeding, we suggest that catheter directed thrombolysis may be used to reduce acute symptoms and post-thrombotic morbidity if appropriate expertise and resources are available (Grade 2B).

Guidelines

- ACCP 2012, 2016: “In patients with acute proximal DVT of leg, we suggest anticoagulation therapy alone over CDT (Grade 2C).
- “Remarks: Patients who are most likely to benefit from CDT, who attach a high value to prevention of post-thrombotic syndrome (PTS), and a lower value to the initial complexity, cost and risk of bleeding with CDT, are likely to choose CDT over anticoagulation alone.”

Guidelines

- American Heart Association
- Society of Interventional Radiology
- American College of Radiology
- European Society of Cardiology
- Society of Vascular Surgery

"CDT is reasonable as first-line treatment of patients with acute IFDVT to prevent PTS in selected patients at low risk of bleeding (Class IIa, Level of Evidence B)"

Why not just Anticoagulate?

- Prevents formation of new clots
- Prevents propagation of existing clots
- Reduces risk of PE
- Some degree of patency is restored in ~80% of patients by 6 weeks
- Complete Resolution of DVT ~50%

Why not just Anticoagulate?

- Does not dissolve existing clot; Relies on patient's own fibrinolytic mechanism (may take weeks to months)
- Reduces, but does not eliminate, risk of PE (5%)
- Failure of therapy / clot propagation 6-10%
- DVT recurrence 3-10%
- 50% of patients may be sub-therapeutic
- Risk of Bleeding 3-5%
- *High rates of Post Thrombotic Syndrome (PTS)*

Post-Thrombotic Syndrome

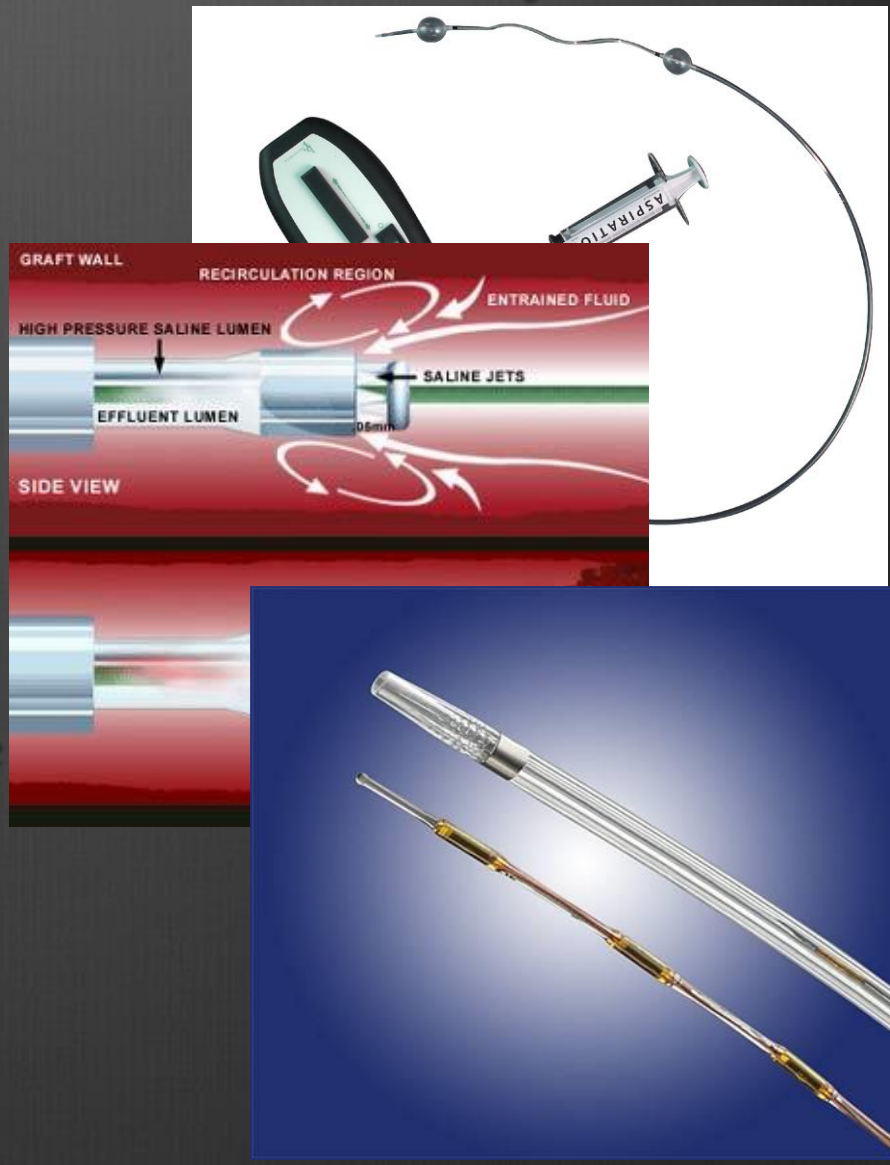
- 20 – 50% of patients with proximal DVT
- Symptoms
  - Chronic Pain
  - Swelling
  - Discoloration
  - Skin ulceration
- Lower QoL at 2 years than patients with Arthritis, Chronic Lung Disease, Diabetes

Long-term outcome after additional catheter-directed thrombolysis versus standard treatment for acute iliofemoral deep vein thrombosis (the **CaVenT study**): a randomized controlled trial (Lancet 2012)

- 209 Patients with Acute IFDVT
- 89 Anticoagulation / 87 Anticoagulation + CDT
- Higher patency at 6 months
- Post Thrombotic Syndrome
  - 37 patients in CDT group vs. 63 Control ($p<0.0001$)
  - Absolute Risk Reduction of 28%
- 3 Major Bleeds in CDT group

Pharmacomechanical Thrombolysis

- Trellis
- AngioJet
- EKOS
- Accelerated Thrombolysis
  - Decrease infusion time
  - Decreased thrombolytic dose



EKOS – Multicenter Registry

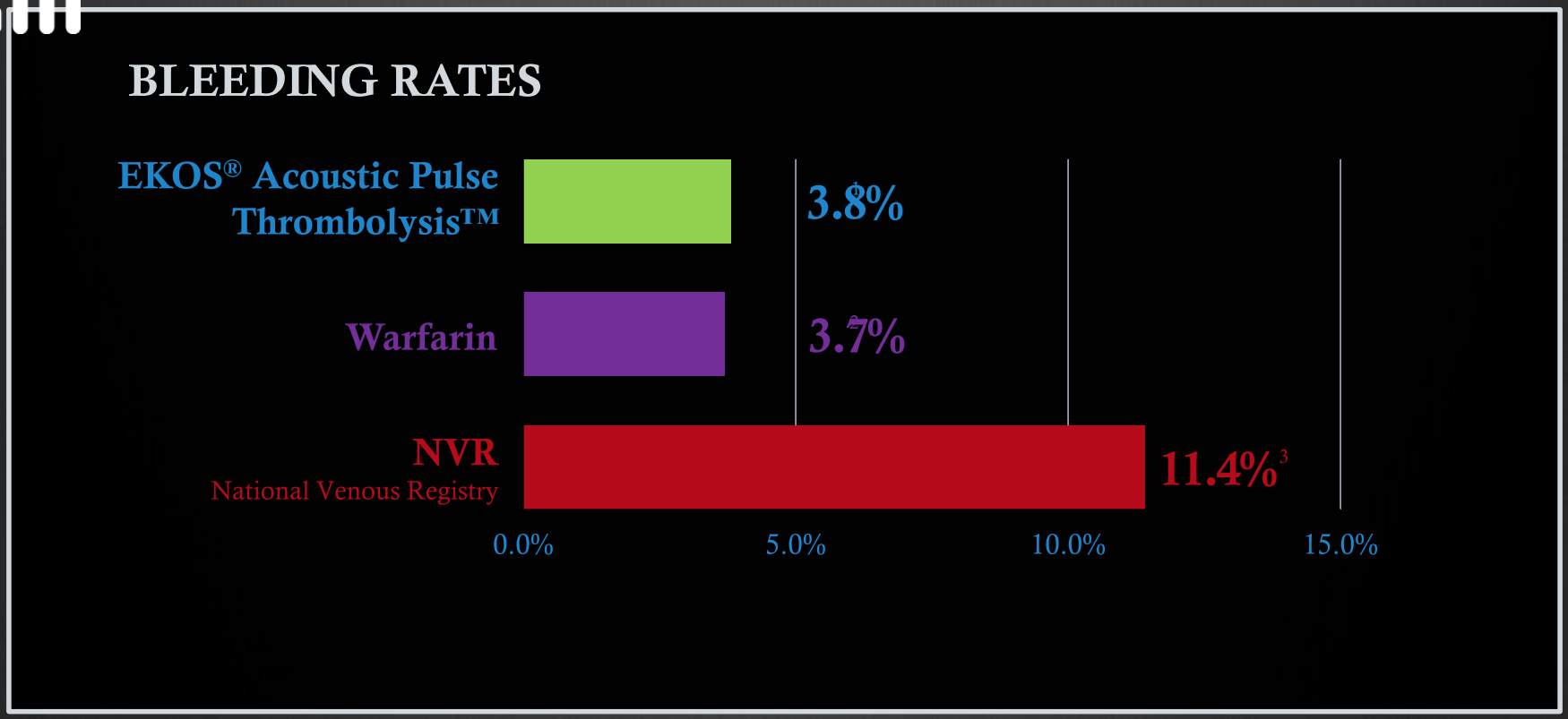
- 8 Sites
- 53 cases (acute, subacute, chronic, acute-on-chronic)
- Compared to standard CDT

EKOS – Multicenter Registry

	Urokinase		Alteplase (t-PA)		Reteplase (r-PA)	
	EKOS®[1] (n=14)	CDT[2] (n=38)	EKOS®[1] (n=9)	CDT[2] (n=32)	EKOS®[1] (n=22)	CDT[2] (n=12)
Median Drug Dose	2.02 MU	4.36 MU	14.0 mg	21.6 mg	6.9 U	21.4 U
Median Infusion Time	19.3 hr.	40.6 hr.	18.0 hr.	30.8 hr.	24.0 hr.	24.3 hr.

BTG

EKOS – Multicenter Registry



Engelberger et al. Fixed Low-dose ***ultrasound-assisted catheter-directed thrombolysis*** followed by routine stenting or residual stenosis for acute ilio-femoral deep-vein thrombosis; Thrombosis and Haemostasis 111.6/2014.

- Prospective study of 87 consecutive iliofemoral DVT patients treated with US assisted CDT
- 20mg TPA over 15 hours
- Follow up at 3, 6, and 12 months measuring primary treatment success
- 1 major bleeding (1%), 6 minor bleedings (7%)

	3 months	6 months	12 months
No PTS	88%	92%	94%
No visible signs of venous disease	51%	53%	61%

BTG

Baylor Experience:

Lin et al. Catheter-Directed Thrombectomy and Thrombolysis for Symptomatic Lower-Extremity Deep Vein Thrombosis: Review of Current Interventional Treatment Strategies. Perspect Vasc Surg Endovasc Ther. 2010 Sep;22(3):152-63.

- 178 Patients
- Acute (≤14 days)
- Chronic DVT (>14 days)

Chronic DVT	PMT only AngioJet	PMT only Trellis	APT only EKOS®
100% angiographic clearance	39%	0%	64%
Decrease in pain and/or swelling	28%	33%	64%

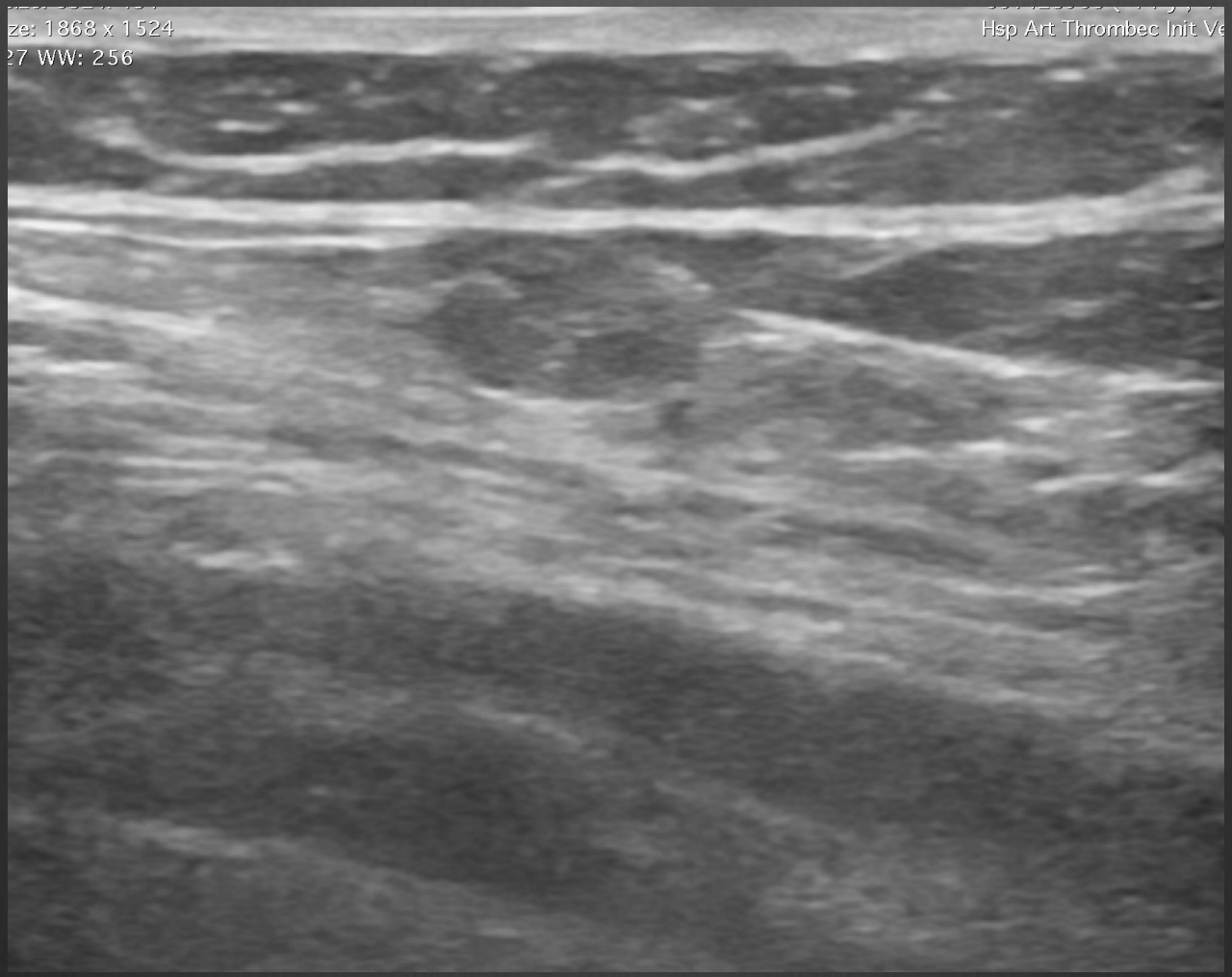
BTG

Multicenter Registry and published data conclusion:

- Ultrasound Assisted Catheter Directed Thrombolysis
  - Safe & Effective in treating DVT
  - Ultrasound reduces total infusion time, provides more complete thrombolysis
  - Reduced bleeding rates

Case: Iliac DVT

- 71 y.o.f.
- 6 back surgeries
- Multiple DVT's
- On Coumadin
- IVC Filter placed in 2008
- Presented with Severe RLE Swelling
- 10/10 Pain
- Unable to ambulate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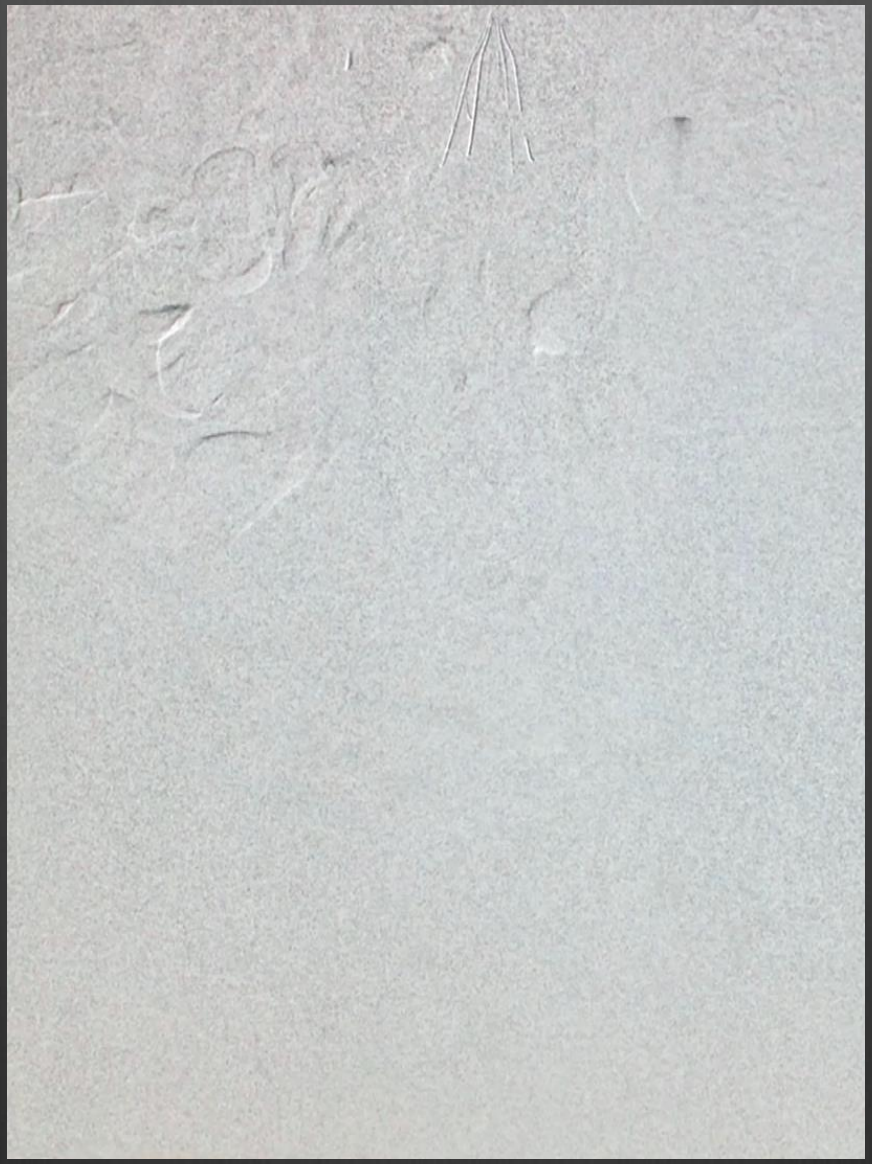

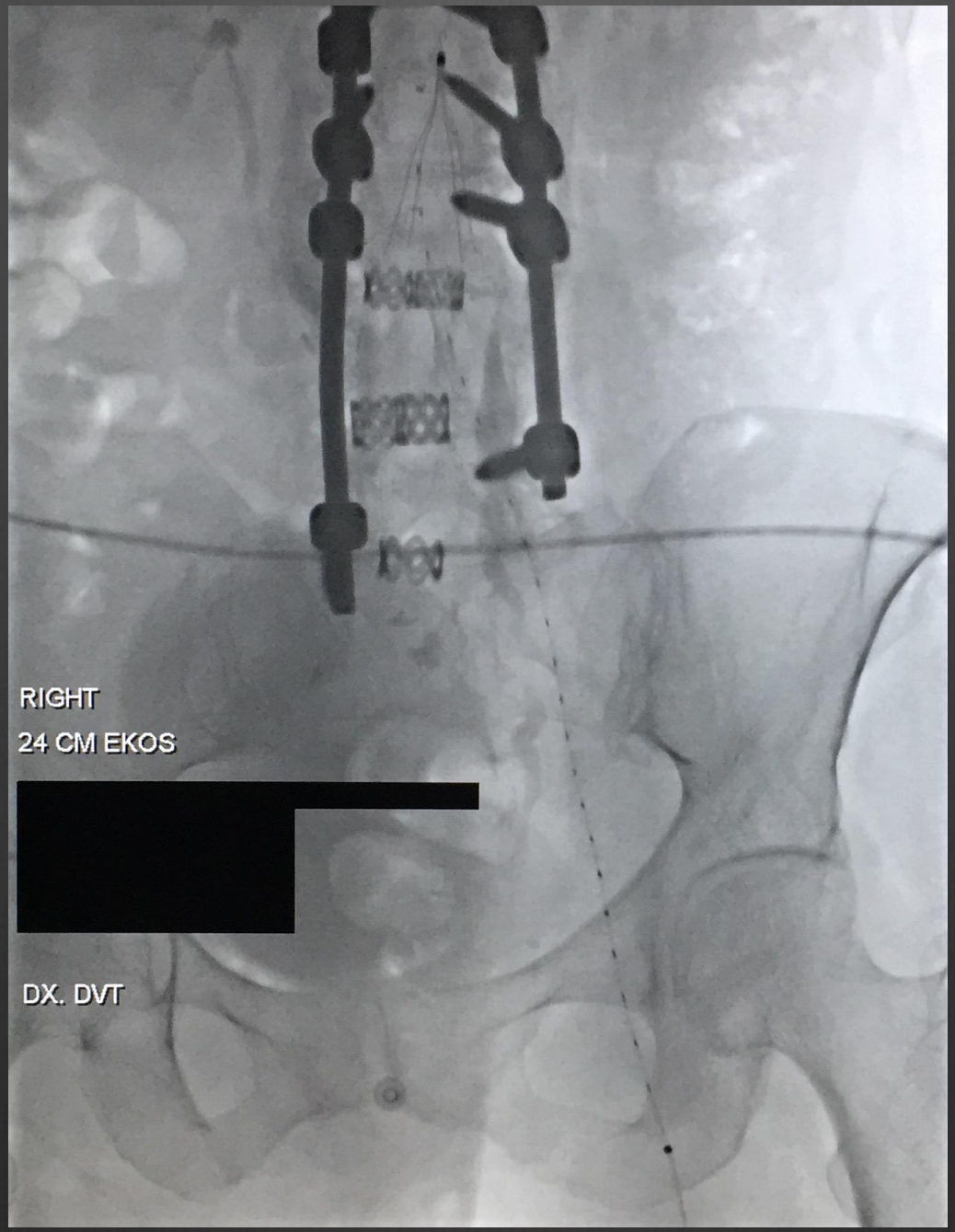
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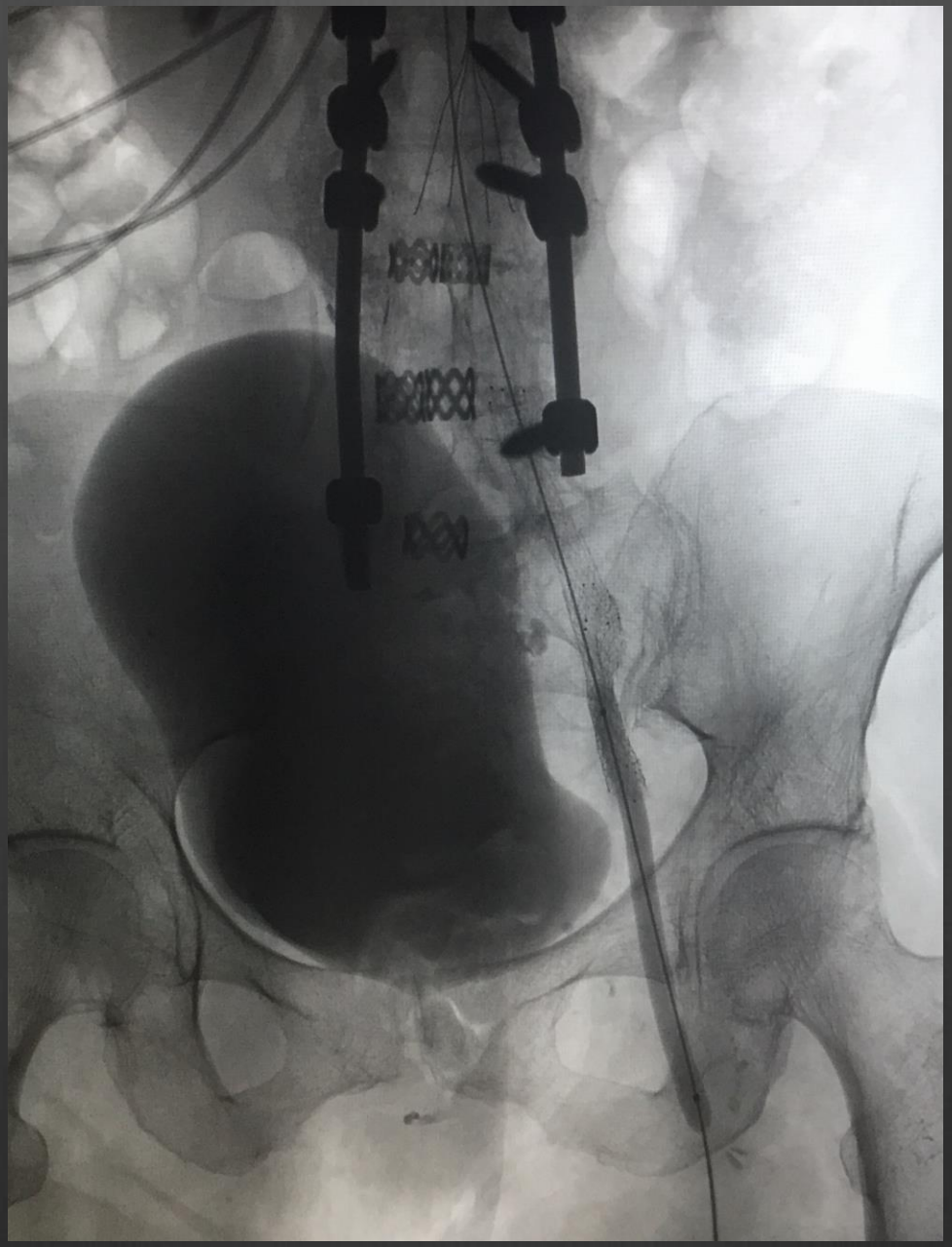

Follow up

- 1 month and 6 months
- Swelling down
- No recurrent DVT
- States: “I feel great!”

Criteria for Catheter Directed Therapy in DVT

- Documented *Proximal* DVT (Ilio-femoral)
- No absolute contraindication to lytics
- Reasonable life expectancy

- Acute DVT (<14 days) have greater potential for success

Contraindications to CDT

(contraindications to thrombolytics)

Absolute

- Active bleeding
- Recent Neurologic surgery
- Trauma or CVA <2month
- Brain Tumor
- Severe HTN
- Coagulopathy
- Allergy to Thrombolytic

Relative

- Surgery < 10 days prior
- Recent Trauma or GI bleed
- Subacute bacterial endocarditis
- Pregnancy
- Pancreatitis
- Anything that can increase bleeding risk

Treatment Algorithm for LE VTE

Superficial Thrombophlebitis	Analgesics Support stockings Elevation Warm compresses
SFV – Popliteal – Calf DVT	Anticoagulation Treat Underlying Lesion
Proximal / ilio-femoral DVT Phlegmasia Cerulia Alba	Anticoagulation Catheter Directed Therapy Treat Underlying Lesion
Phlegmasia Cerulia Dolens	Surgical Embolectomy Faciotomy

Fin