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LING

Pharmacomechanical Thrombolysis

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Disclosure

Speaker name:

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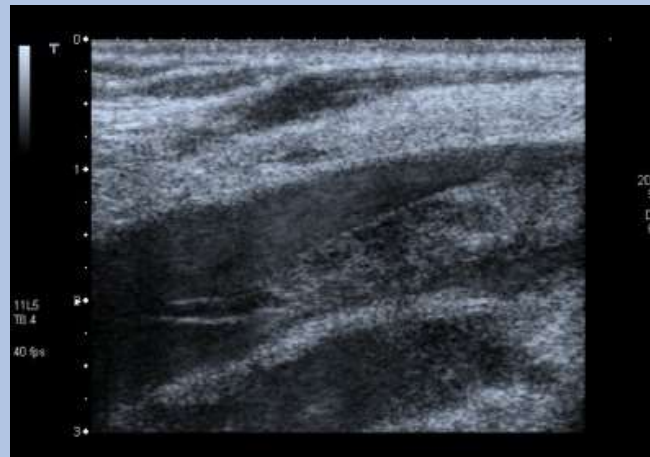
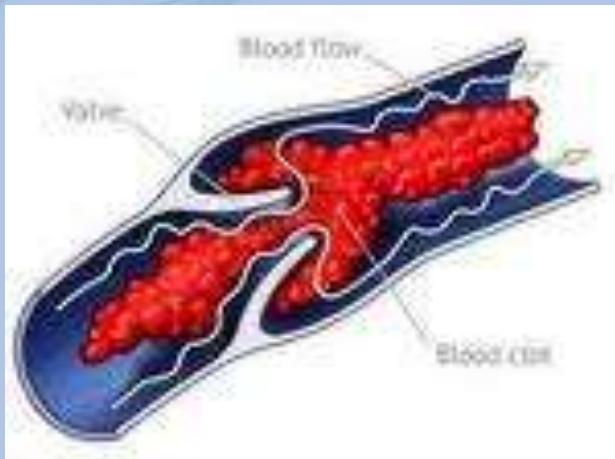
I have the following potential conflicts of interest to report:

- Consulting
- Employment in industry
- Stockholder of a healthcare company
- Owner of a healthcare company
- Other(s)

- I do not have any potential conflict of interest

Deep Vein Thrombosis (DVT)

- Third leading vascular disease after MI and stroke
- Incidence 100 -180/ 100.000 person-years
- Incidence rates increase with age in both genders
- Expected to double between 2006 – 2050



Deep Vein Thrombosis (DVT)

- Consequences of DVT are:
 - Pulmonary embolism
 - Phlegmasia cerulea dolens
 - Postthrombotic syndrome (PTS)



Post thrombotic syndrome (PTS)

- Most common chronic complication after DVT
- develops in 25-50% after DVT within 3 – 6 months up to 2 years
- increased morbidity and
- impaired quality of life
 - correlates with severity of PTS
- increased health care costs up to 50%



Post thrombotic syndrome (PTS)

- independent predictors:
 - recurrent ipsilateral DVT (2 to 6-fold increase) (Kahn S.R., Ann Intern Med 2008; Prandoni P, Ann Intern Med 1996)
 - insufficient anticoagulation (2.5-fold increase) (Van Dongen CJJ, J Thromb Haemost 2005)
 - Age, BMI, female gender (Kahn SR, Thromb Res 2011)
- Proximal DVT has a higher risk for PTS than infrapopliteal distal DVT

«Open vein» hypothesis

- Involvement of common femoral or iliac vein independent predictor of PTS (Tick LW, J Thromb Haemost 2010), independent of other DVT localisations (Kahn SR, Ann Intern Med 2008)
 - >50% risk in 2 years
 - ≈ 30% are severe PTS (claudication, ulceration)

Treatment of acute DVT

- prevention of aggravation (i.e. pulmonary embolism and PTS)
- Anticoagulation
 - LMWH, VKA, DOAC
- Elastic compression stockings
 - 30-40 mmHg
- Interventional Treatment
 - Catheter directed thrombolysis (CDT)
 - Pharmacomechanical thrombolysis (PMT)
- (surgical approach)

Pharmacomechanical Thrombolysis (PMT)

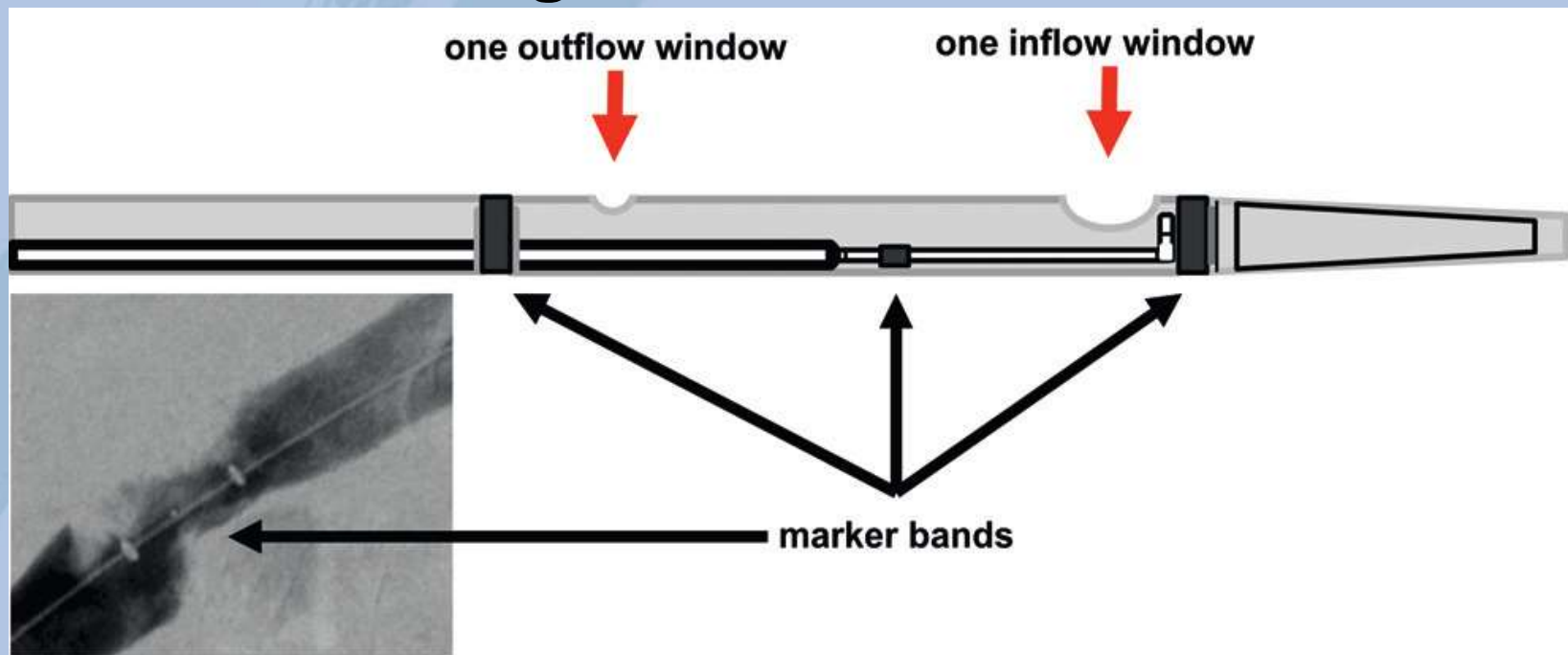
- catheter-mounted thrombectomy devices with
- **intrathrombus** delivery of fibrinolytic drugs
 - to improve drug dispersion and maceration/ aspiration of venous thrombi
- Compared to CDT alone:
 - Major bleeding rate 3-5 %
 - 50% reduction of fibrinolytic drug dose
 - 50% reduction of hospitalisation time

PMT Devices

Device	Manufacturer	Notes
AngioJet ZelanteDVT	Boston Scientific	High Velocity saline jets (Venturi) with break up and aspiration of clots, PowerPulse option
AngioJet Solent Omni/ Proxi		
Cleaner XT / 15	Argon	Obligational IVC filter, rotating wire macerating clot
Trellis-8	Covidien	Recalled by FDA 2015; rotational wire and infusion/ aspiration



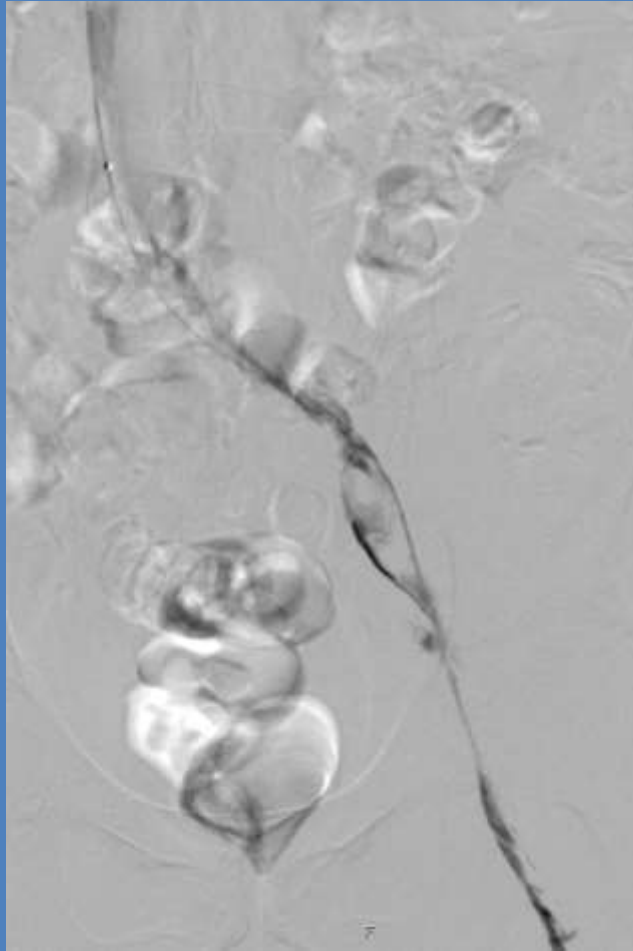
Rotational Rheolytic Thrombectomy AngioJet Zelante DVT®



Schematic drawing of the tip of the 8 French AngioJet ZelanteDVT® catheter (Boston Scientific, Maple Grove, MN. USA).

- isovolumetric, directional, hydrodynamic thrombectomy device using accelerated reversed fluid running through the inside of the catheter and provides a strong **-600** mmHg suction (Venturi) effect at the catheter tip.
- treatment segment with one larger proximal suction window and one smaller distal outflow window (arrows) identifiable under fluoroscopy through two marker bands.
- inbetween eccentric middle marker indicating the (opposite) direction of the in- and outflow windows.

PMT Procedure



Baseline

+/- preceding CDT



PMT



After PMT

PMT Procedure



Venography +/- IVUS

Ballooning and Stenting

End Result

PMT Complications

- Embolisation
- Hemolysis of red blood cells
- Hemoglobinuria
- Elevated potassium level
- Brady- / Tachyarrhythmia

PEARL Registry

(Peripheral Use of AngioJet Rheolytic Thrombectomy with a Variety of Catheter Lengths)

- Evaluation of safety and outcome of proximal DVT treated with AngioJet® devices
- 329 DVT patients undergoing
 - Rheolytic thrombectomy (RT) without lytic agent (4%)
 - 1.4 h procedure time
 - PMT (35%)
 - 2 h procedure time
 - PMT and CDT (52%)
 - 22 h procedure time
 - RT and CDT (9%)
 - 41 h procedure time

PEARL Registry

(Peripheral Use of AngioJet Rheolytic Thrombectomy with a Variety of Catheter Lengths)

- Freedom of rethrombosis
 - 3 months 94% (95% CI, 91%–96)
 - 6 months 87 % (95% CI, 82%–91%)
 - 12 months 83 % (95% CI, 77%–88%)
- Overall bleeding 4.5%
 - Major bleeding in 3.6 %
 - None related to AngioJet® devices
- PE 0.3%
- Renal insufficiency 0.3%

Present recommendations

- Extensive, i.e. iliofemoral thrombosis with
 - Recent onset of symptoms (i.e. ≤ 14 days)
 - Low risk of bleeding
 - Life expectancy of at least 1 year
 - Treated at an experienced vascular center
- CDT/ **PMT** and balloon angioplasty \pm stenting might be considered (Grade B) (AHA)
- anticoagulant alone acceptable alternative to CDT in all patients with acute DVT (Grade 2C) (ACCP)

Kahn S.R et al. Circulation; 2014 Oct 28;130(18):1636-61.

Kearon C. et al. Chest; 2016 Feb;149(2):315-352.

RCTs on prevention of PTS

NCT number	Study Name	Study Objective
NCT 00143598	The SOX Trial	Knee-length elastic compression therapy to prevent PTS
NCT 00426075	Full leg vs below knee stockings	Non-inferiority of knee length compression to prevent PTS
NCT 01578122	CELEST	Elastic compression 25 mmHg vs 35 mmHg
NCT 01429714	The Ideal DVT Study	Individual tailored elastic compression
NCT 02148029	EFFORT2	Excercise Training to prevent PTS
NCT 02553720	ATLANTIS	Additional Aqua Therapy to reduce PTS rates
NCT 02679664	SAVER	Statins in preventing recurrent DVT and PTS
NCT 00251771	CaVenT	CDT in acute DVT
NCT 00790335	ATTRACT	PMT in acute DVT to prevent PTS

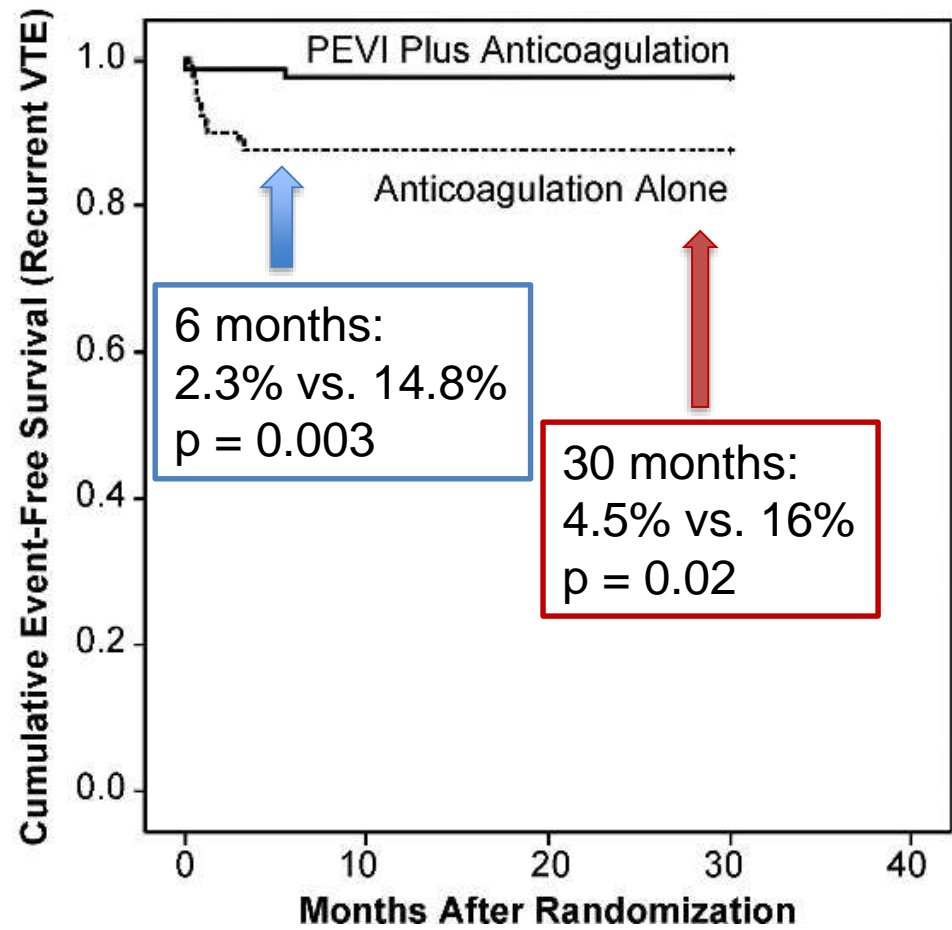
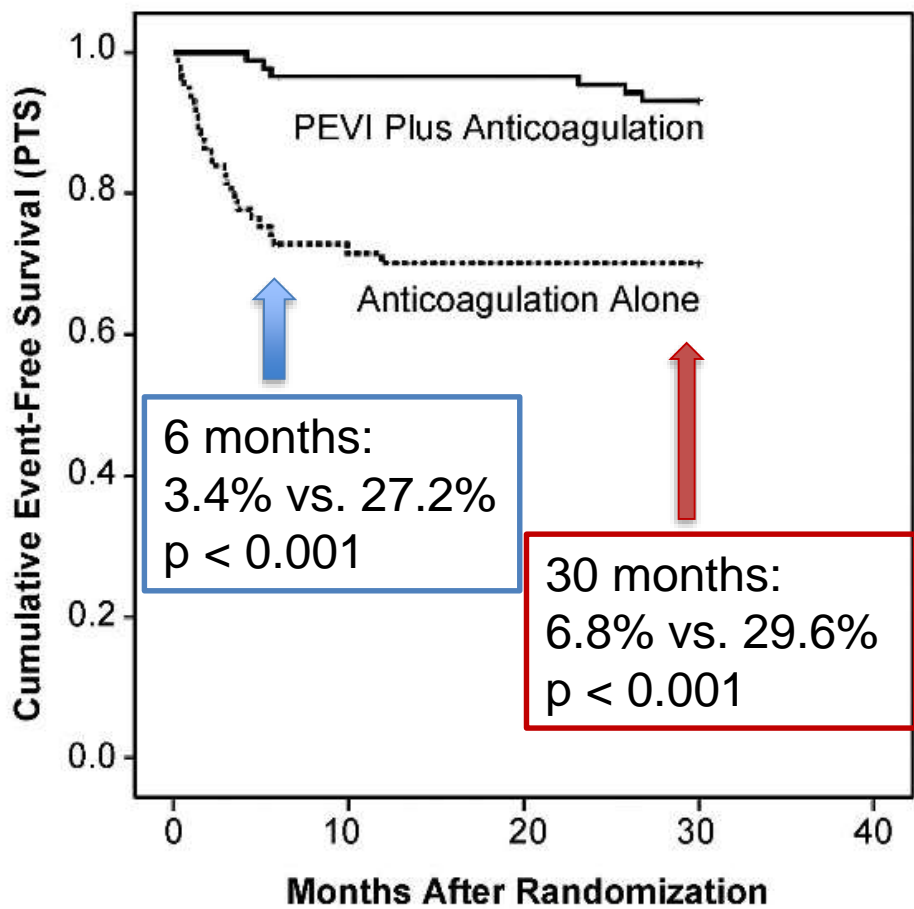
Torpedo Trial

(Thrombus Obliteration by Rapid Percutaneous Endovenous Intervention in Deep Venous Occlusion)

- RCT comparing endovenous intervention + anticoagulation (n= 91) vs. anticoagulation alone (n=92) in acute DVT
- objective: superiority of intervention in reduction of venous thromboembolism (VTE) and PTS at 6 months
- Follow up of 30 ± 5 months
- PMT with AngioJet DVX® (26%, [PP 78%]) and Trellis® (12%)
 - Thrombusaspiration (52%)
 - add. CDT postinterventional (37%)

Torpedo Trial

(Thrombus Obliteration by Rapid Percutaneous Endovenous Intervention in Deep Venous Occlusion)



ATTRACT Trial

(Acute venous thrombosis: thrombus removal with adjunctive Catheter-Directed Thrombolysis)

- Multicenter, randomized, open-label, assessor-blinded, two-arm, controlled clinical trial
- 692 patients with acute proximal DVT (iliac, common femoral and/ or femoral vein) randomized to
 1. PMT (AngioJet® or Trellis®) with rTPA+ standard therapy
 2. Standard therapy
- Primary outcome was development of PTS between 6 and 24 months

ATTRACT Trial

(Acute venous thrombosis: thrombus removal with adjunctive Catheter-Directed Thrombolysis)

Outcome	Pharmacomechanical- Thrombolysis Group (N=336)	Control Group (N=355)	Risk Ratio (95% CI)	P Value
	<i>number of patients (percent)</i>			
Post-thrombotic syndrome between 6 and 24 mo*				
Ulcer at any follow-up assessment	12 (4)	17 (5)		
Villalta score ≥ 5 without ulcer	144 (43)	154 (43)		
Late endovascular procedure only	1 (<1)	0		
Total	157 (47)	171 (48)	0.96 (0.82–1.11)[†]	0.56
Post-thrombotic syndrome according to follow-up visit [‡]				
At 6 mo	78/291 (27)	113/285 (40)	0.68 (0.53–0.86)	
At 12 mo	92/272 (34)	88/258 (34)	0.99 (0.78–1.26)	
At 18 mo	85/245 (35)	76/222 (34)	1.01 (0.79–1.30)	
At 24 mo	79/258 (31)	86/239 (36)	0.85 (0.66–1.09)	
Major non–post-thrombotic syndrome treatment failure	4 (1)	7 (2)	0.58 (0.17–1.98) [§]	0.38 [¶]
Any treatment failure	158 (47)	176 (50)	0.94 (0.80–1.09) [†]	0.39 [¶]
Moderate-to-severe post-thrombotic syndrome**	60 (18)	84 (24)	0.73 (0.54–0.98)[†]	0.04[¶]

Summary

- Interventional strategies offer rapid thrombus removal and pot. faster relief of symptoms
- Despite the two disputed recommendations (AHA/ ACCP) on interventional strategies in DVT:
- PMT is a safe and effective strategy to treat acute proximal DVT and prevent severe acute (i.e. PE) as well as chronic aggravation (i.e. PTS)
- Careful patient selection is necessary
- Further RCTs are needed

Thank you for your attention!



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