Endovascular Mechanical Thrombectomy versus Thrombolysis in Patients With Iliofemoral Deep Vein Thrombosis – a Systematic Review and Meta-Analysis

Michael K. W. Lichtenberg MD, FESC

Arnsberg Vascular Center

Arnsberg, Germany

September 2020

BD

Conflict of Interest - Disclosure

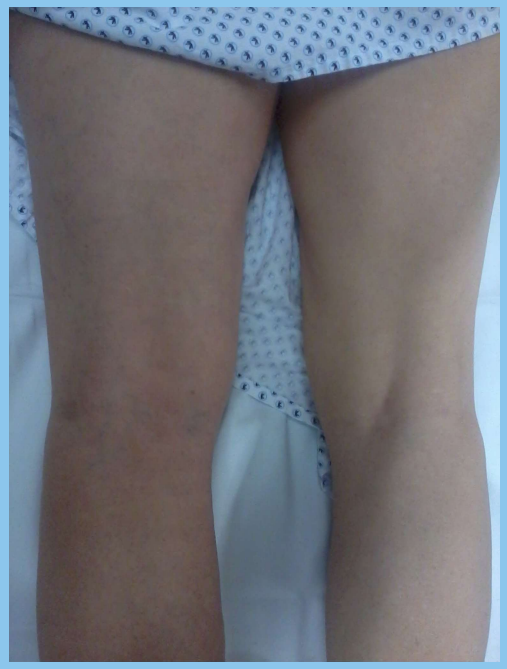
Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

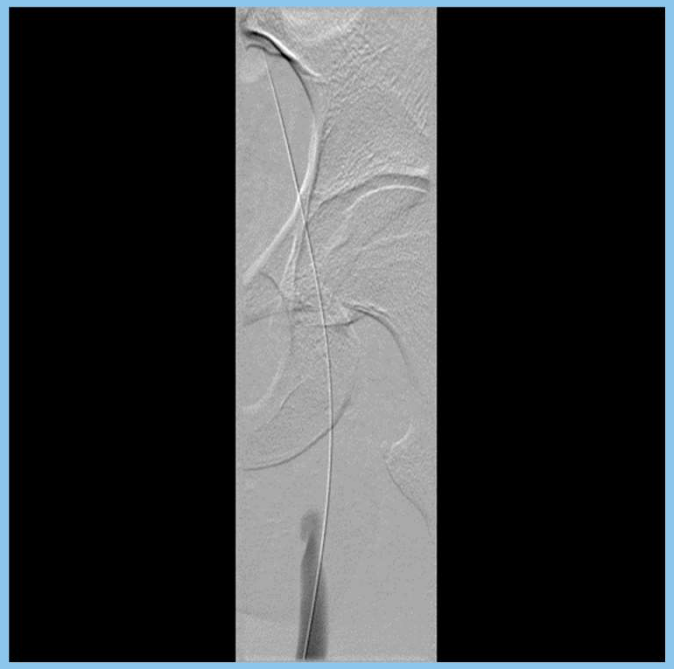
Affiliation/Financial Relationship	**Company**
1. Honoraria for lectures: BD, Boston Scientific GmbH, Straub Medical, Terumo, Biotronik, Veryan	AB Medica, Volcano, Optimed
2. Honoraria for advisory board activities: Veniti, Optimed GmbH, Straub Medical, Biotronik, Veryan, Boston Scientific, Philips	
3. Participation in clinical trials: Biotronik, CR Bard, Veryan, Straub Medical, Veniti, Boston Scientific, LimFlow,Terumo, Philips, Optimed, IPmedical	
4. Research funding: Biotronik, Boston Scientific, Veryan, Veniti, AB Medica, Philips, CRBard, Optimed	

- PTS is a frequent, but underestimated chronic complication after iliofemoral DVT[1]
- 25-50% at risk for developing PTS following an acute iliofemoral DVT (ATTRACT 28%)[2]
- 11% severe PTS[3]

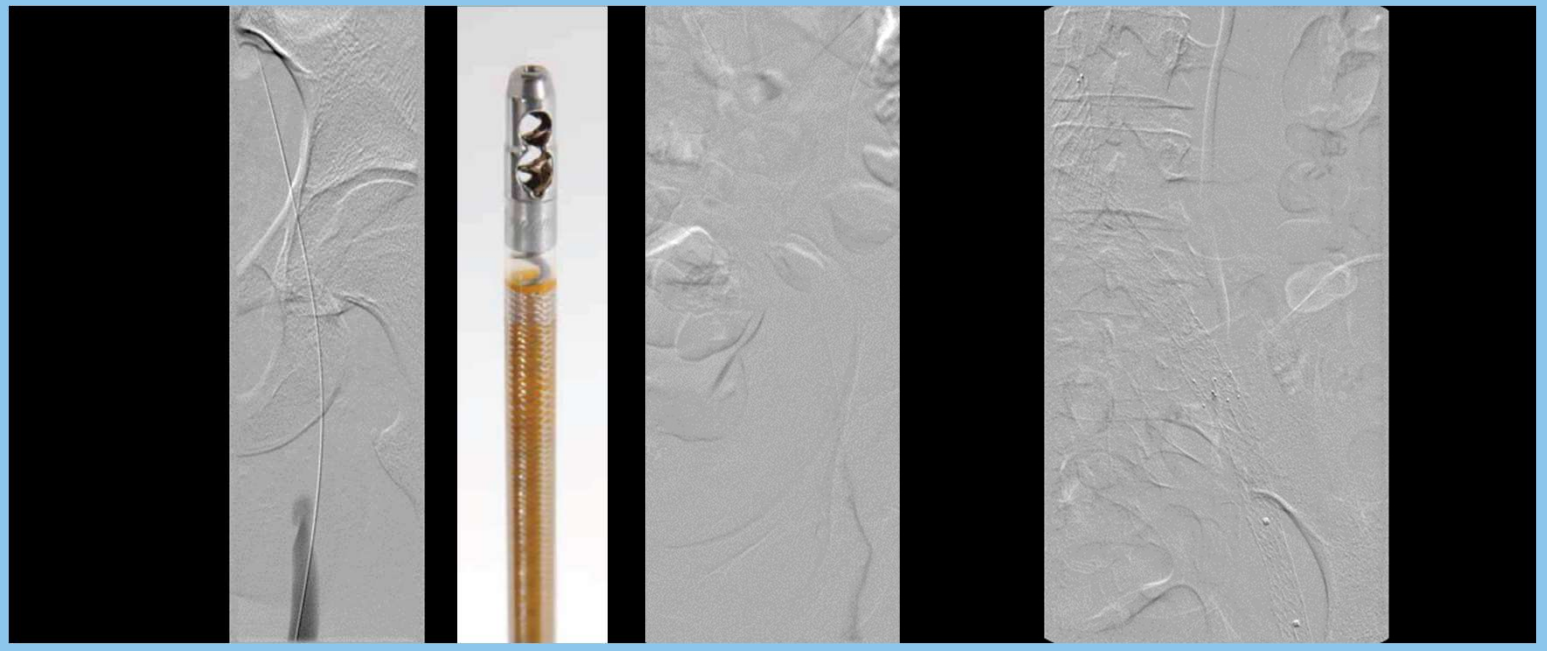
1. White RH. The epidemiology of venous thromboembolism. Circulation 2003;107 (23 Suppl 1): I4-8.
2. Akesson H, Brudin L, Dahlstrom JA, Eklöf B, Ohlin P, Plate G. Venous function assessed during a 5 year period after acute ilio-femoral venous thrombosis treated with anticoagulation. Eur J Vasc Surg 1990;4(1):43-48.
3. Meissner M, Gloviczki P, Comerota A, Dalsing MC, Eklof BG, Gillespie DL et al. Early thrombus removal strategies for acute deep venous thrombosis: Clinical practice guidelines of the society for vascular surgery and the American venous forum. J Vasc Surg 2012; 55:1449-462.

22 y, female, acute onset of symptoms





Descending DVT in May – Thurner syndrome.
Transpopliteal access, 10 F Aspirex® Endovascular System



8 F: blood volume aspiration up to 75 ml/min
10 F: blood volume aspiration up to 130 ml/min

ATTRACT subgroup analysis

Endovascular Thrombus Removal for Acute Iliofemoral Deep Vein Thrombosis: Analysis from a Stratified Multicenter Randomized Trial

What are the clinical implications?

- "The findings support early use of PCDT in patients with acute iliofemoral DVT who have severe symptoms, low bleeding risk, and who attach greater importance to a reduction in early and late symptoms than to the risks, costs, and inconvenience of PCDT."
    - "In patients with acute iliofemoral DVT, PCDT does appear to provide greater reduction in acute leg pain and swelling through 30 days follow-up, as well as reduced PTS severity, reduced moderate-or-severe PTS, and greater improvement in venous disease-specific quality of life through 24 months."

Comorata et al. Endovascular Thrombus Removal for Acute Iliofemoral Deep Vein Thrombosis. Analysis From a Stratified Multicenter Randomized Trial. Circulation. Volume 139, Issue 9, 26 February 2019, Pages 1162-1173

Patient outcomes (efficacy analysis)

Outcome	PCDT N=196		No PCDT N=195		Risk Ratio		P Value
	Events	(%)	Events	(%)	Estimate	95% CI	
PTS*							
Ulcer (any assessment)	9	4.6%	12	6.2%			
Villalta ≥ 5 (without ulcer)	86	44%	88	45%			
Late endovascular procedure only	1	0.5%	0	0%			
Total	**96**	**49%**	**100**	**51%**	**0.95***	**0.78, 1.15**	**0.59**

Villalta 24 months: **PCTD 3.95 vs 5.54 non-PCTD, p = 0.0033**
VCSS 24 months: **PCTD 1.98 vs 2.80 non-PCDT, p = 0.018**
Veines 24 months: **PCTD 28.63 vs 23.02 non-PCDT, p = 0.029**

Moderate- severe PTS (Villalta ≥ 10)	**36**	**18%**	**55**	**28%**	**0.65***	**0.45,0.94**	**0.021**
Severe PTS: Villalta ≥ 15	17	8.7%	30	15%	0.57*	0.32, 1.01	0.048
Severe PTS: VCSS ≥ 8	13	6.6%	28	14%	0.46*	0.24, 0.87	0.013

Comorata et al. Endovascular Thrombus Removal for Acute Iliofemoral Deep Vein Thrombosis. Analysis From a Stratified Multicenter Randomized Trial. Circulation. Volume 139, Issue 9, 26 February 2019, Pages 1162-1173

SAFETY REPORTING

Outcome	PCDT N=196		No PCDT N=195		Risk Ratio		P Value
	Events	(%)	Events	(%)	Estimate	95% CI	
Major non-PTS treatment failure	4	2%	5	2.6%	0.80	0.22, 2.92	0.73
Any treatment failure **	97	49%	103	53%	0.93	0.77, 1.13	0.47
Major bleeding in first 10 days	3	1.5%	1	0.5%	2.98	0.31, 28.4	0.32
Any bleeding in first 10 days	7	3.6%	4	2.1%	1.74	0.52, 5.85	0.36
VTE:							
First 30 days	11	5.8%	6	3.1%	1.82	0.69, 4.83	0.22
Total over 24 months	26	13%	18	9.2%	1.44	0.81, 2.53	0.21
Death	6	3.1%	6	3.1%	0.99	0.33, 3.03	0.99

Bleeding complication

PEARL Registry[1]: 4.5% (minor/major)
Venous Registry[2]: 11% major,16% minor
CAVENT[3] (CDT arm): 22% (minor/major)

1. Leung et al. Rheolytic Pharmacomechanical Thrombectomy for the Management of Acute Limb Ischemia: Results From the PEARL Registry. J Endovasc. Ther. 2015 Aug;22(4):546-57
2. Mewissen et al. Catheter-directed Thrombolysis for Lower Extremity Deep Venous Thrombosis: Report of a National Multicenter Registry. Radiology 1999; 211:39–49
3. Enden et al. Long-term outcome after additional catheter-directed thrombolysis versus standard treatment for acute iliofemoral deep vein thrombosis (the CaVenT study): a randomised controlled trial. Lancet. 2012 Jan 7;379(9810):31-8

Safety, procedural success and outcome of the Aspirex S endovascular thrombectomy system in the treatment of iliofemoral deep vein thrombosis- data from the Arnsberg Aspirex registry

Michael Lichtenberg, Willhelm Friedrich Stahloff, Ahmet Ozkapi, Rick de Graaf and Frank Breuckmann

Inclusion criteria:

Acute thrombotic or thromboembolic occlusion (onset of pain < 14 days)

FU: up to 24 months

Endpoints:

Assessment of the effectiveness and safety of the ASPIREX®S catheter

MAE, QoL, CEAP, VCSS

Lichtenberg et al. Safety, procedural success and outcome of the Aspirex ® S endovascular thrombectomy system in the treatment of iliofemoral deep vein thrombosis - data from the Arnsberg Aspirex registry. Vasa. 2019 Jul;48(4):341-346

Mechanical thrombectomy: Aspirex

Size	Length cm	GW	OD mm	rVD mm	Rotation rpm	MAC ml/min	Head
6 F	110	0,018	2,0	3 – 5	60.000	45	L-shape
	135	0,018	2,0				
8 F	85	0,018	2,6	5 - 8	40.000	75	L-shape
	110	0,018	2,6				
10 F	110	0,025	3,3	7 – 12	40.000	130	8-shape

GW-Guidewire, OD-outer diameter, rVD-recommended Vessel Diameter,
MAC-maximum aspiration capacity

Arnsberg Aspirex registry

Table I. Overview of patients' demographics at baseline.

	N (%)
Total	**56 (100 %)**
Age mean (median [Range]) in years	52 (51 [17–89])
Female N (%)	37 (66 %)
Male N (%)	19 (34 %)
Smoking status	
Current N (%)	9 (16 %)
Former N (%)	4 (7 %)
Hypertension	
Yes	28 (50 %)
Malignancy	
Current active	4 (7 %)
Condition post	5 (5 %)
Oral contraceptive	
Yes	21 (38 %)
No	35 (62 %)

Table II. Lesion characteristics and clinical symptoms.

	N (%)
Type of occlusion	**56 (100 %)**
Acute	40 (71 %)
Subacute	13 (23 %)
Acute on chronic	3 (6 %)
Underlying lesion	**56 (100 %)**
May-Thurner syndrome	30 (53 %)
Not determined	10 (18 %)
Cancer (active/condition post)	5 (9 %)
Post-thrombotic alterations	9 (16 %)
Mechanical (e.g. V. cava clip)	1 (2 %)
Peripartal condition	1 (2 %)
Clinical symptoms	**56 (100 %)**
Swelling, est pain	38 (68 %)
Swelling only	12 (21 %)
Swelling/rest pain/lividity	6 (11 %)

Lichtenberg et al. Safety, procedural success and outcome of the Aspirex ® S endovascular thrombectomy system in the treatment of iliofemoral deep vein thrombosis - data from the Arnsberg Aspirex registry. Vasa. 2019 Jul;48(4):341-346

Table III. Overview of target vessel lesions.

	N (%)
Location of occlusion (vessel)	**56 (100 %)**
Left complete pelvic veins including CVF, left femoral vein (may also include profunda femoral vein and distal part of IVC)	42 (75 %)
Left common iliac vein only	7 (13 %)
Left common iliac vein/Left external iliac vein without CVF	3 (5 %)
Right complete pelvic veins	4 (7 %)
Length of occlusion [mm] N = 56 (100 %)	
Mean (SD)	156.6 (72.0)
Median (Range)	150.0 (60–410)

CVF: common femoral vein; IVC: inferior vena cava; SD: standard deviation.

Table IV. Interventional details for thrombectomy procedure.

	N (%)
Access	56 (100 %)
Left popliteal vein	27 (48 %)
Left femoral vein	12 (21 %)
Bi-femoral	5 (9 %)
Left common femoral vein	3 (5 %)
Right popliteal vein	3 (5 %)
Right femoral vein	3 (5 %)
Right saphena parva vein	3 (6 %)
Aspirex size (French)	
10	47 (84 %)
8	9 (16 %)
Sheath size	
10	31 (55 %)
11	16 (29 %)
8	7 (12 %)
12	2 (4 %)
Heparin [IU]	
5000	50 (89 %)
10,000	6 (11 %)
Thrombolysis	
No	52 (93 %)
Yes	4 (7 %)
Number of implanted stents	
1	24 (43 %)
2	21 (38 %)
3	8 (14 %)
4	3 (5 %)
Mean (SD)	1.9 (1.2)
Treatment duration [min]	
Mean (SD)	94.2

SD: standard deviation.

Lichtenberg et al. Safety, procedural success and outcome of the Aspirex ® S endovascular thrombectomy system in the treatment of iliofemoral deep vein thrombosis - data from the Arnsberg Aspirex registry. Vasa. 2019 Jul;48(4):341-346

Table V. Patency analysis.

	N (%)
Patency on follow-up month 1	**56 (100 %)**
Yes	54 (95 %)
Patency on follow-up month 6	**52 (100 %)**
Yes	49 (94 %)
Patency on follow-up month 12	**45 (100 %)**
Yes	39 (87 %)

Table VI. Clinical outcome and safety analysis.

	N (%)
Time on intensive care unit [days]	**56 (100 %)**
0	53 (95 %)
1	2 (3 %)
2	1 (2 %)
Post-thrombotic syndrome (PTS) analysis after 12 months	**53 (100 %)**
Low PTS (CEAP Score < 3, rVCSS Score < 3)	34 (64 %)
Moderate PTS (CEAP Score > 3, rVCSS > 3)	19 (36 %)
Patients by number of adverse events (non-device related but procedure related)	**56 (100 %)**
No puncture site bleeding complication, hematoma	45 (80 %)
Yes (puncture site bleeding complication, hematoma)	11 (20 %)
Patients by number of serious adverse events (non-device related but procedure related)	**56 (100 %)**
No rehospitalization, re-occlusion of target vein, prolonged hospitalization because of AV-Fistula operation	48 (86 %)
Yes (rehospitalization, re-occlusion of target vein, prolonged hospitalization because of AV-Fistula operation)	8 (14 %)
Device malfunction reported on Aspirex	0 (0 %)

Patency FU 1 month: 95%
Patency FU 6 months: 94%
Patency FU 12 months: 87%

Patency was defined as target lesion restenosis < 50 % in DUS

Lichtenberg et al. Safety, procedural success and outcome of the Aspirex ® S endovascular thrombectomy system in the treatment of iliofemoral deep vein thrombosis - data from the Arnsberg Aspirex registry. Vasa. 2019 Jul;48(4):341-346

Endovascular mechanical thrombectomy versus thrombolysis in patients with iliofemoral deep vein thrombosis – a systematic review and meta-analysis

Database: Reviewers searched MEDLINE and web-based platforms of specialized journals

Keywords:

- deep vein thrombosis, deep venous thrombosis
- Thrombectomy, iliofemoral deep venous thrombosis, thrombolytic therapy, hematuria, hemolysis, post-thrombotic, syndrome, pulmonary embolism

Publication years: Search period was January 2001 to February 2019

Inclusion criteria:

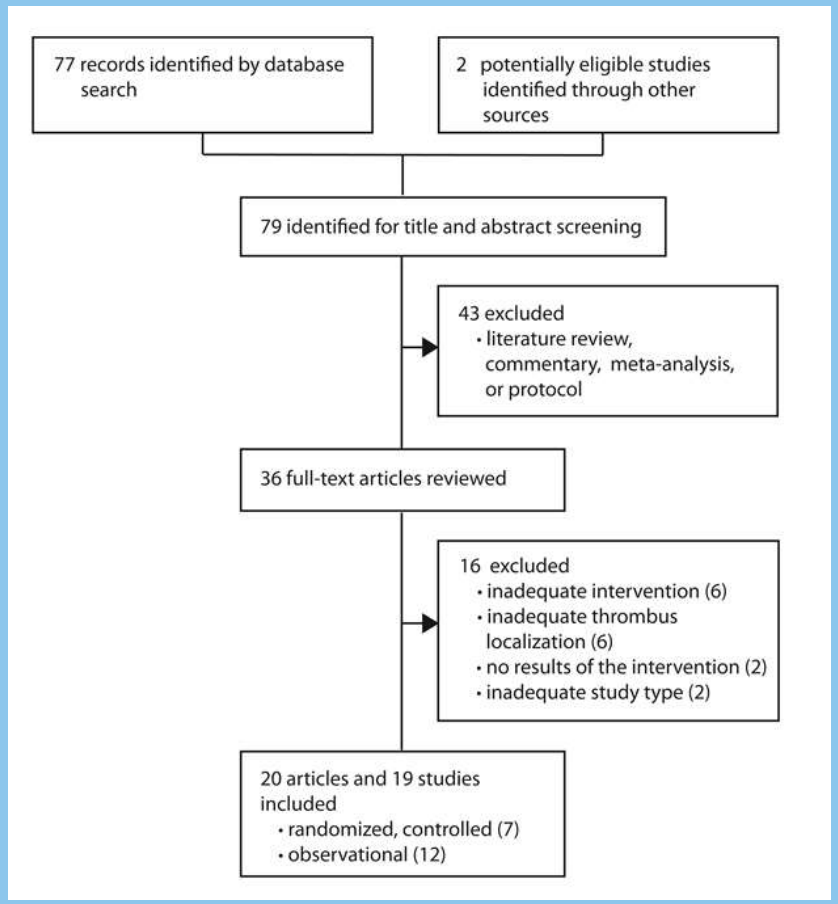
Catheter-directed thrombolysis (CDT), systemic thrombolysis, ultrasound-accelerated CDT

Eligible endovascular thrombectomy systems for PMT were the, AngioJet™ Rheolytic thrombectomy system (Boston Scientific Corporation, Marlborough, MA, USA), the Trellis peripheral infusion system (Covidien Inc., Mansfield, MA, USA), Penumbra's Indigo System (Penumbra, Inc., Alameda, CA, USA), and the AspirexS catheter (Straub Medical, Wangs, Switzerland). Studies on thrombolysis with

Adjunctive PMT (PCDT) were allocated to the PMT-group.

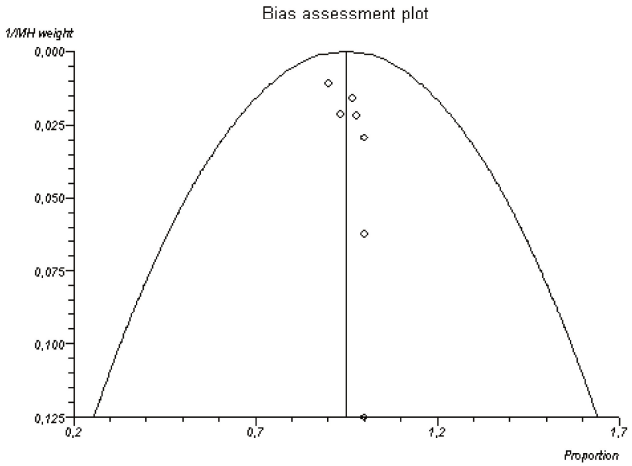
Lichtenberg et al. Endovascular mechanical thrombectomy versus thrombolysis in patients with iliofemoral deep vein thrombosis - a systematic review and meta-analysis. Vasa. 2020 May 25;1-9

Included Literature for Meta-analysis



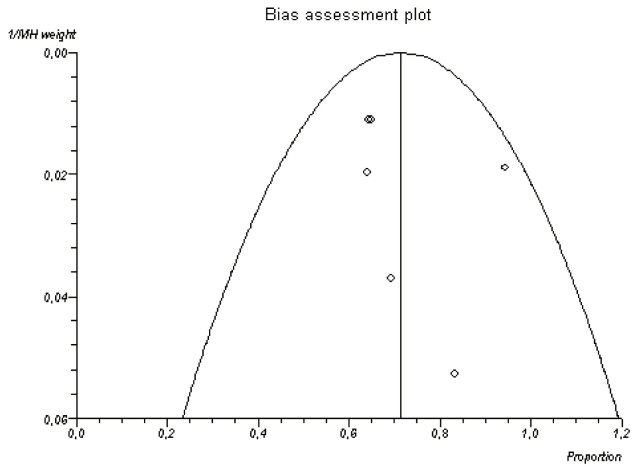
Lichtenberg et al. Endovascular mechanical thrombectomy versus thrombolysis in patients with iliofemoral deep vein thrombosis - a systematic review and meta-analysis. Vasa. 2020 May 25;1-9

A Thrombolysis grade II or III



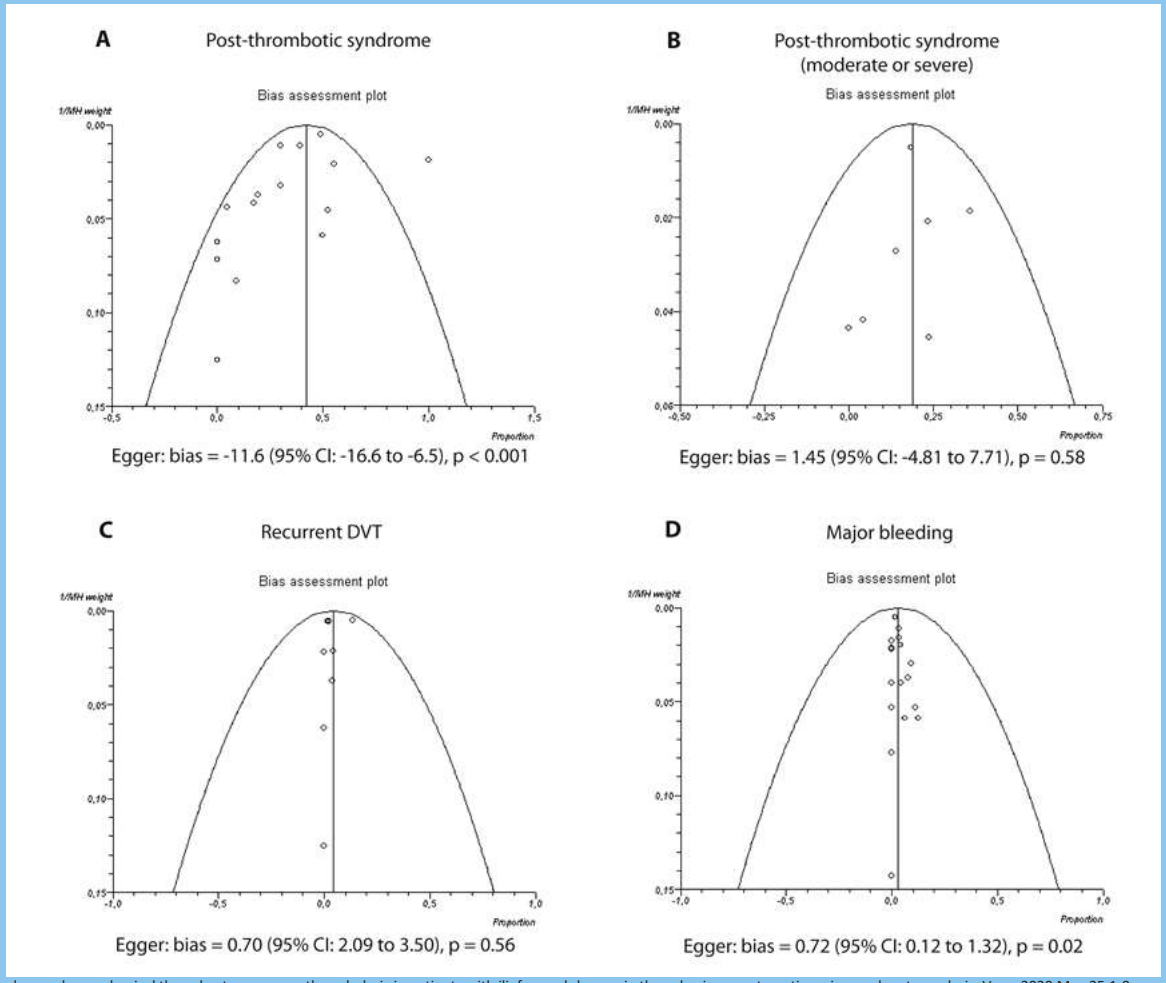
Egger: bias = -0.08 (95% CI: -3.36 to 3.20), p = 0.95

B Primary patency at 6 months

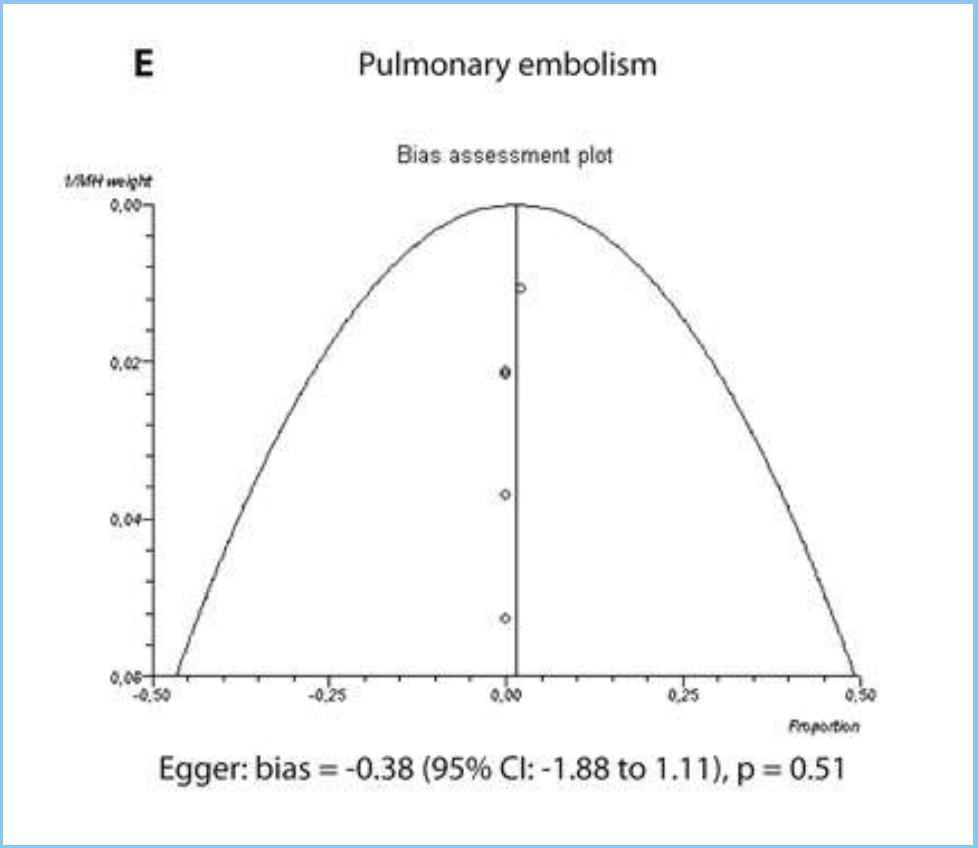


Egger: bias = -3.71 (95% CI: -12.9 to 5.48), p = 0.36

Lichtenberg et al. Endovascular mechanical thrombectomy versus thrombolysis in patients with iliofemoral deep vein thrombosis - a systematic review and meta-analysis. Vasa. 2020 May 25;1-9



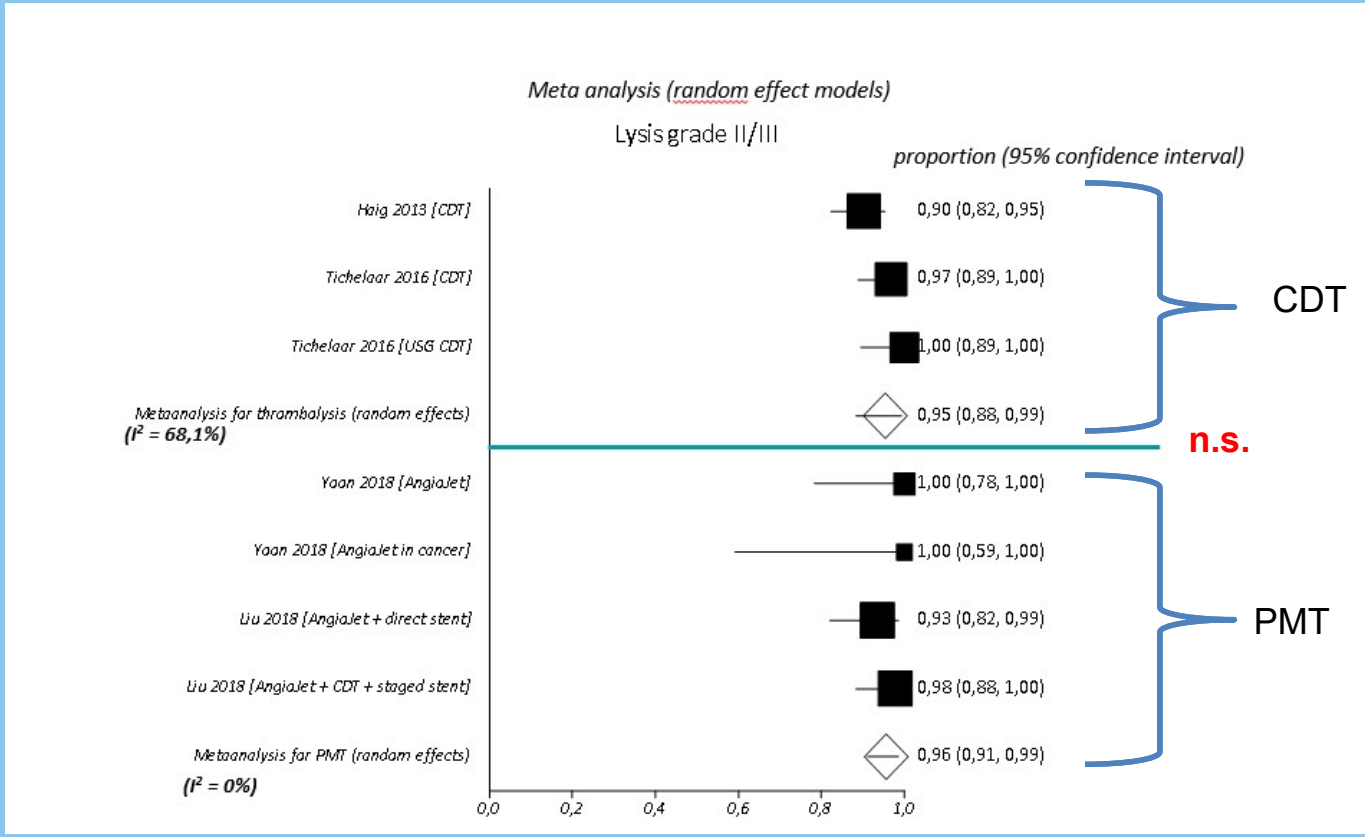
Lichtenberg et al. Endovascular mechanical thrombectomy versus thrombolysis in patients with iliofemoral deep vein thrombosis - a systematic review and meta-analysis. Vasa. 2020 May 25;1-9



Lichtenberg et al. Endovascular mechanical thrombectomy versus thrombolysis in patients with iliofemoral deep vein thrombosis - a systematic review and meta-analysis. Vasa. 2020 May 25;1-9

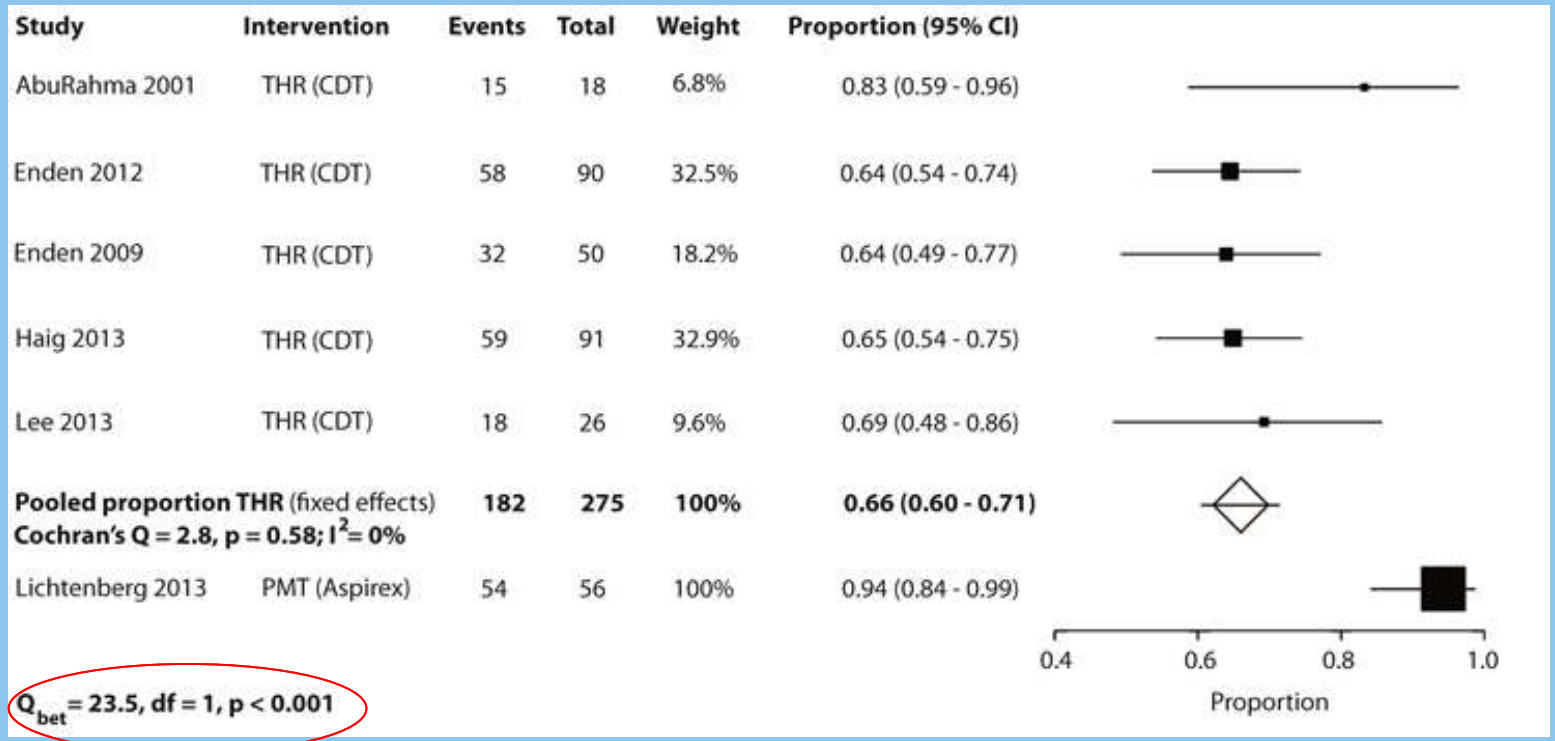
Lysis grade II/III

Klinikum Hochsauerland
Akademisches Lehrkrankenhaus
Westfälische Wilhelms-Universität Münster



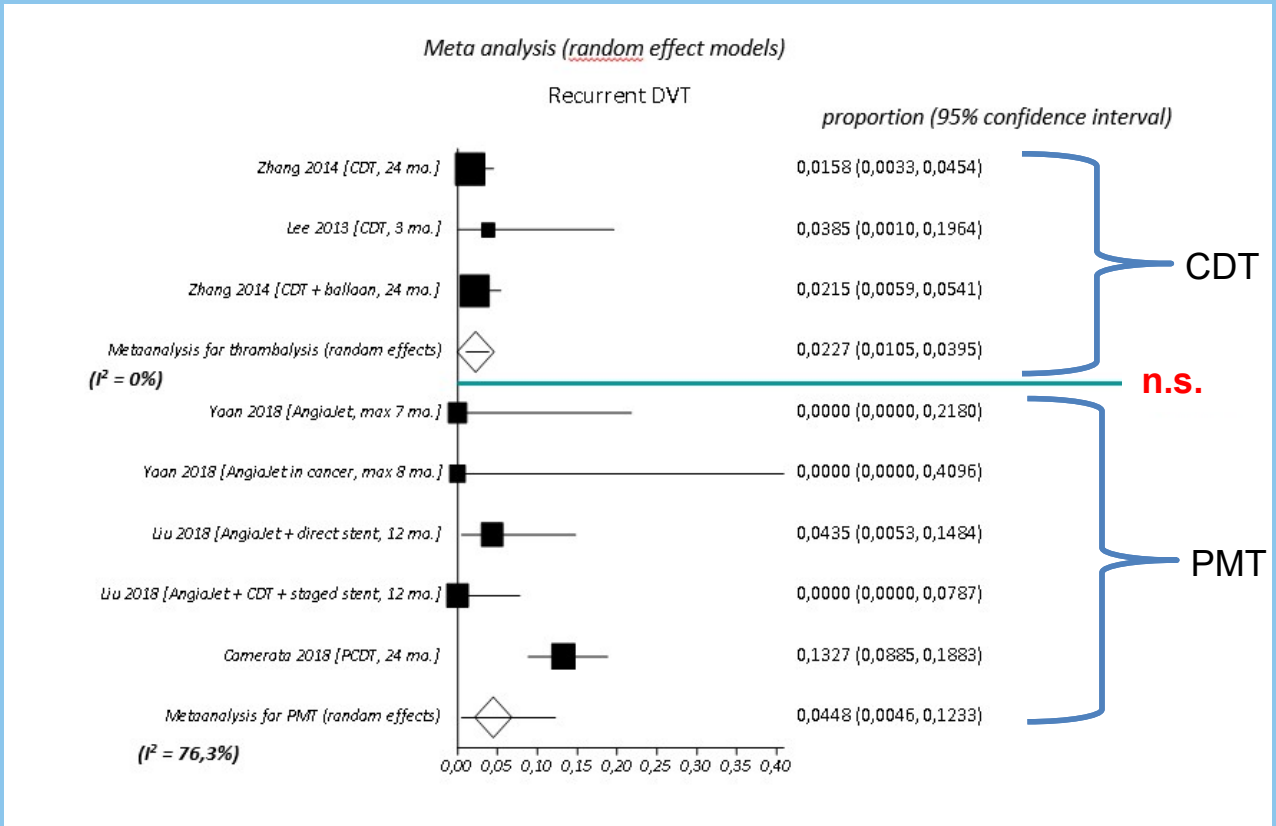
Lichtenberg et al. Endovascular mechanical thrombectomy versus thrombolysis in patients with iliofemoral deep vein thrombosis - a systematic review and meta-analysis. Vasa. 2020 May 25;1-9

6-month primary patency after IfDVT by treatment strategy.



Lichtenberg et al. Endovascular mechanical thrombectomy versus thrombolysis in patients with iliofemoral deep vein thrombosis - a systematic review and meta-analysis. Vasa. 2020 May 25;1-9

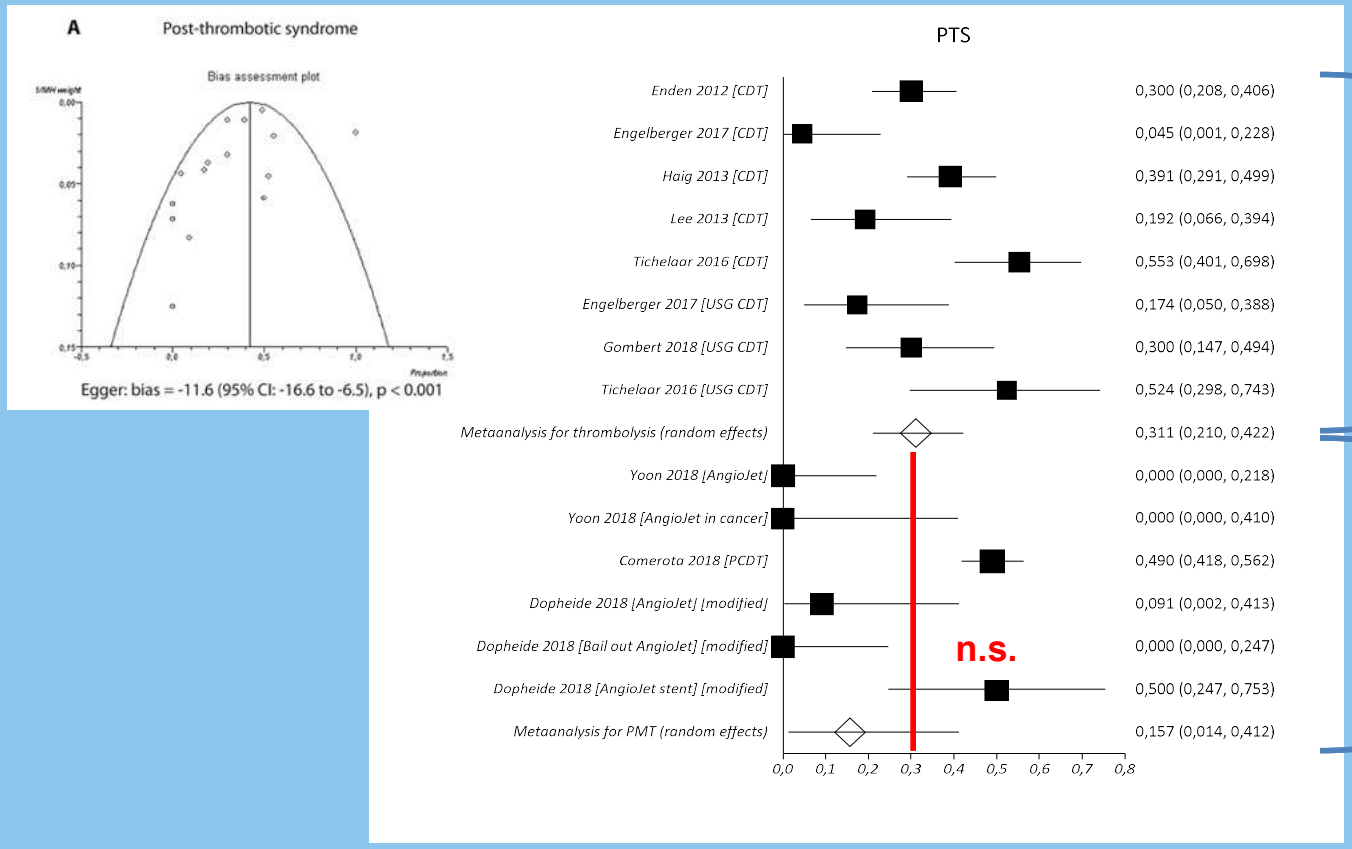
Recurrent DVT



Lichtenberg et al. Endovascular mechanical thrombectomy versus thrombolysis in patients with iliofemoral deep vein thrombosis - a systematic review and meta-analysis. Vasa. 2020 May 25;1-9

Overall PTS rate

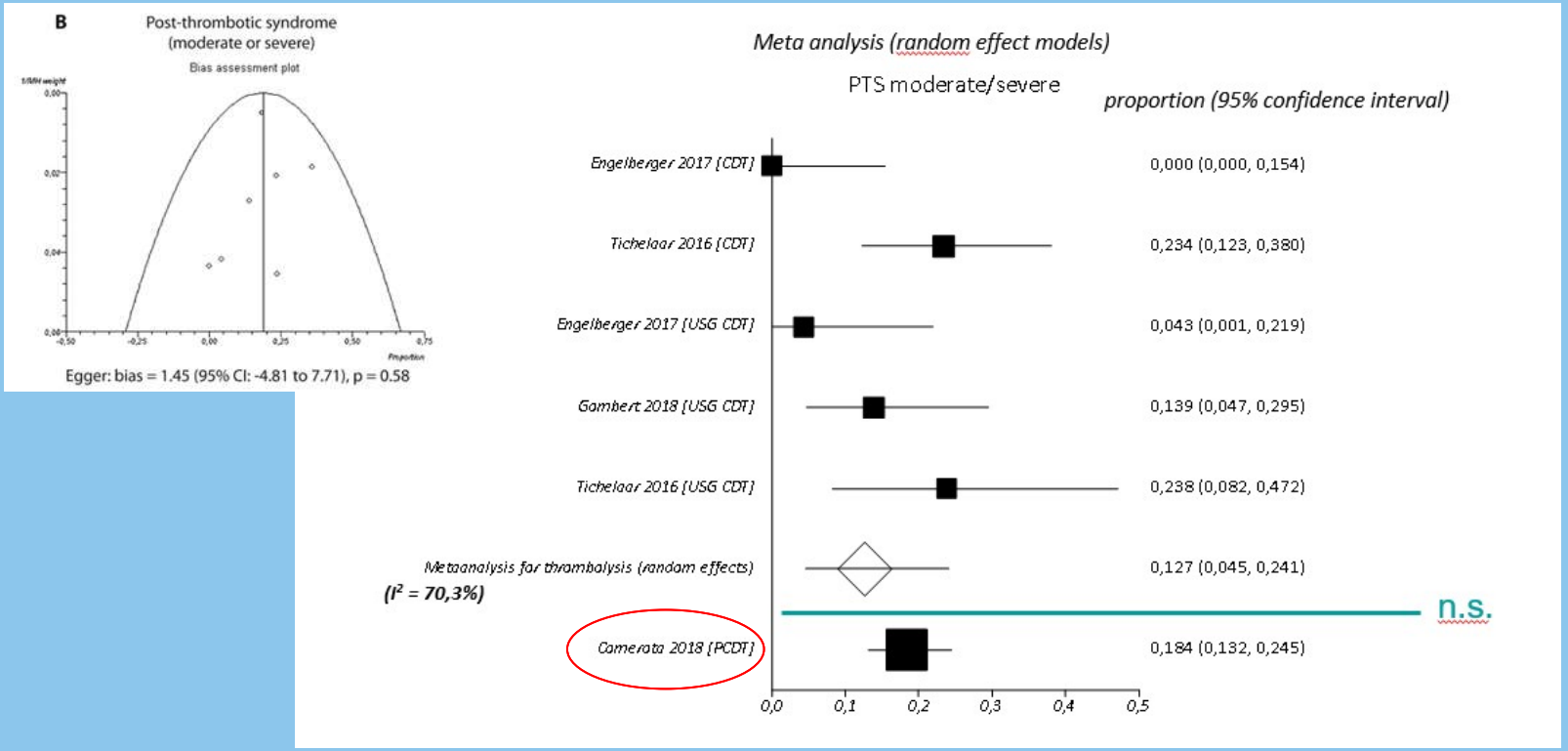
Klinikum Hochsauerland
Akademisches Lehrkrankenhaus
Westfälische Wilhelms-Universität Münster



Lichtenberg et al. Endovascular mechanical thrombectomy versus thrombolysis in patients with iliofemoral deep vein thrombosis - a systematic review and meta-analysis. Vasa. 2020 May 25;1-9

Klinikum Hochsauerland
Akademisches Lehrkrankenhaus
Westfälische Wilhelms-Universität Münster

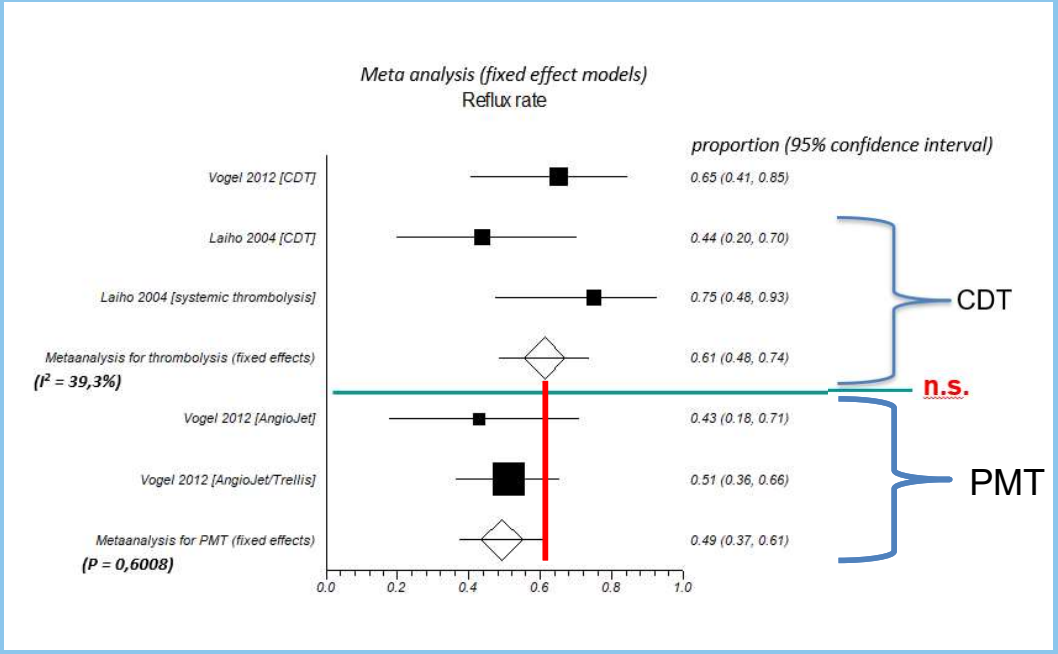
Moderate/Severe PTS



Lichtenberg et al. Endovascular mechanical thrombectomy versus thrombolysis in patients with iliofemoral deep vein thrombosis - a systematic review and meta-analysis. Vasa. 2020 May 25;1-9

Klinikum Hochsauerland
Akademisches Lehrkrankenhaus
Westfälische Wilhelms-Universität Münster

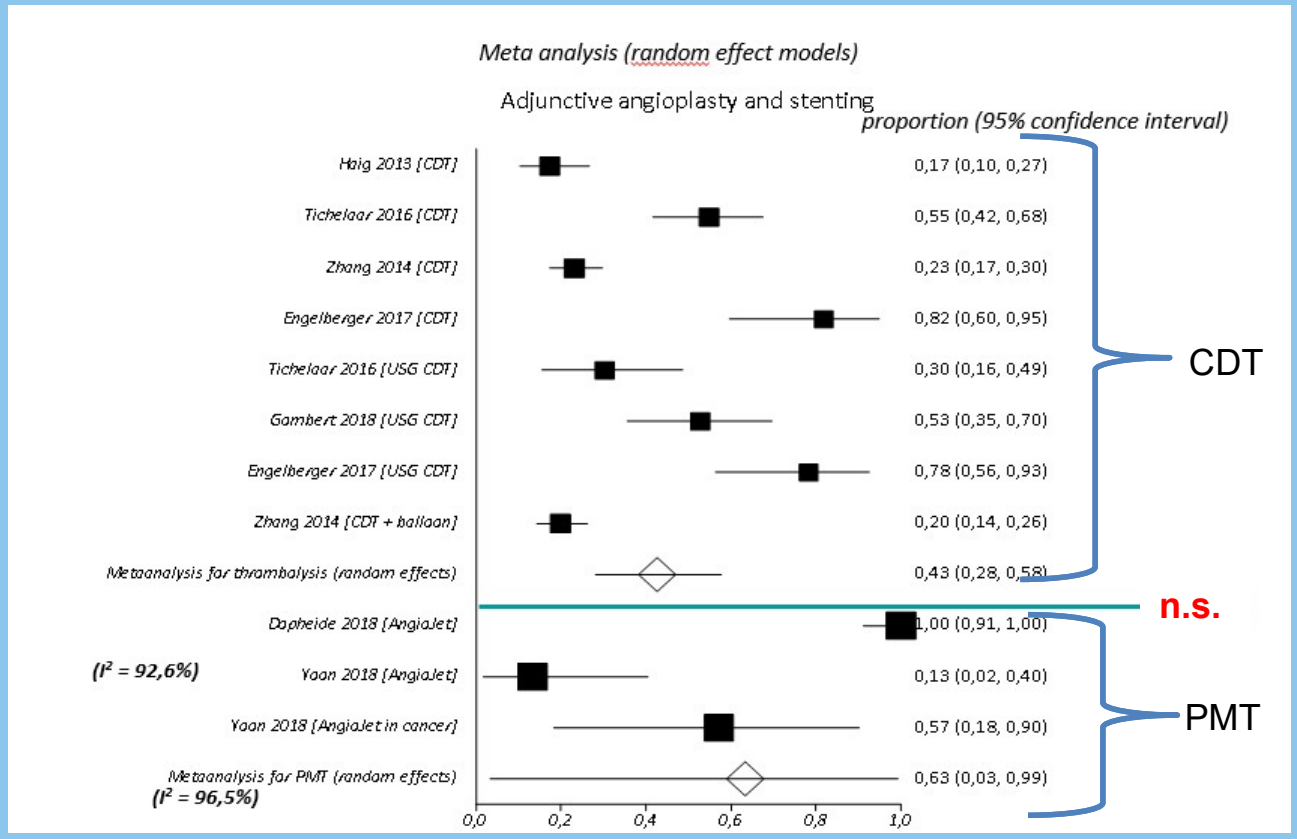
Reflux rate



Lichtenberg et al. Endovascular mechanical thrombectomy versus thrombolysis in patients with iliofemoral deep vein thrombosis - a systematic review and meta-analysis. Vasa. 2020 May 25;1-9

Klinikum Hochsauerland
Akademisches Lehrkrankenhaus
Westfälische Wilhelms-Universität Münster

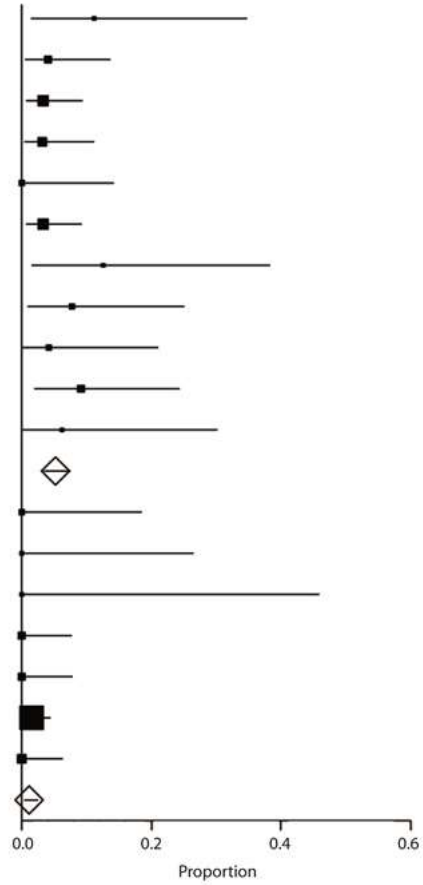
Adjunctive angioplasty and stenting



Lichtenberg et al. Endovascular mechanical thrombectomy versus thrombolysis in patients with iliofemoral deep vein thrombosis - a systematic review and meta-analysis. Vasa. 2020 May 25;1-9

Safety: Major bleeding complications

Study	Intervention	Events	Total	Weight	Proportion (95% CI)
AbuRahma 2001	THR (CDT)	2	18	4.1%	0.11 (0.01 - 0.35)
Enden 2009	THR (CDT)	2	50	11.0%	0.04 (0.01 - 0.14)
Enden 2009	THR (CDT)	3	90	19.7%	0.03 (0.01 - 0.09)
Tichlaar 2016	THR (CDT)	2	62	13.6%	0.03 (0.00 - 0.11)
Engelberger 2015	THR (CDT)	0	24	5.4%	0.00 (0.00 - 0.14)
Haig 2013	THR (CDT)	3	92	20.1%	0.03 (0.01 - 0.09)
Laiho 2004	THR (CDT)	2	16	3.7%	0.13 (0.02 - 0.38)
Lee 2013	THR (CDT)	2	26	5.8%	0.08 (0.01 - 0.25)
Engelberger 2015	THR (UA CDT)	1	24	5.4%	0.04 (0.00 - 0.21)
Tichelaar 2016	THR (UA CDT)	3	33	7.4%	0.09 (0.02 - 0.24)
Laiho 2004	THR (systemic)	1	16	3.7%	0.06 (0.00 - 0.30)
Pooled proportion THR (fixed effects) **Cochran's Q = 8.3, p =0.60; I^2 = 0%**		**21**	**451**	**100%**	**0.05 (0.03 - 0.07)**
Murphy 2010	PMT (AngioJet)	0	18	4.9%	0.00 (0.00 - 0.19)
Yoon 2018	PMT (AngioJet)	0	12	3.4%	0.00 (0.00 - 0.27)
Yoon 2018	PMT (AngioJet in cancer)	0	6	1.8%	0.00 (0.00 - 0.46)
Liu 2018	PMT (AngioJet + direct stent)	0	46	12.2%	0.00 (0.00 - 0.08)
Liu 2018	PMT (AngioJet + CDT + staged stent)	0	45	11.9%	0.00 (0.00 - 0.08)
Comerota 2019	PMT (PCDT)	3	196	51.0%	0.02 (0.00 - 0.04)
Lichtenberg 2019	PMT (Aspirex)	0	56	14.8%	0.00 (0.00 - 0.06)
Pooled proportion PMT (fixed effects) **Cochran's Q = 1.6, p = 0.95; I^2 = 0%**		**3**	**379**	**100%**	**0.01 (0.00 - 0.03)**

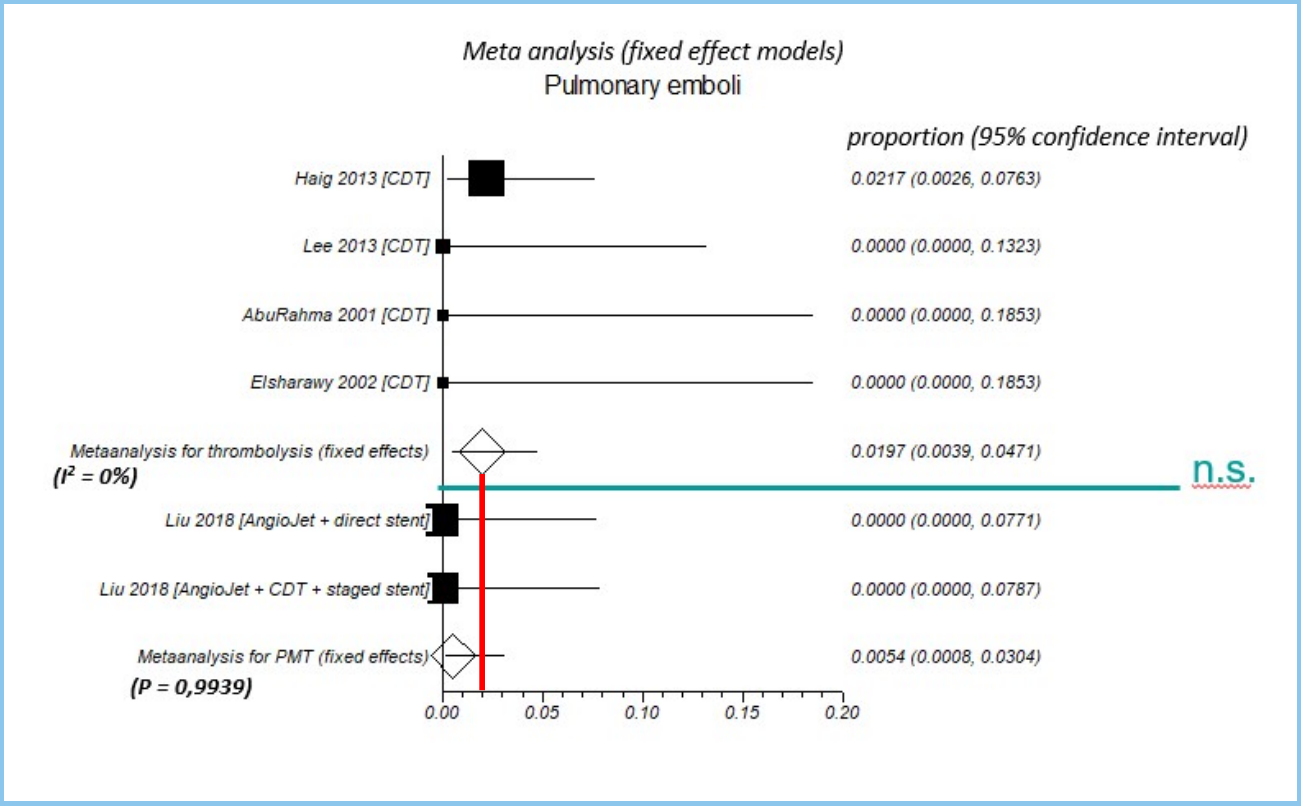


Q_{bet} = 12.4, df = 1, p < 0.001

Lichtenberg et al. Endovascular mechanical thrombectomy versus thrombolysis in patients with iliofemoral deep vein thrombosis - a systematic review and meta-analysis. Vasa. 2020 May 25;1-9

Klinikum Hochsauerland
Akademisches Lehrkrankenhaus
Westfälische Wilhelms-Universität Münster

Pulmonary embolism

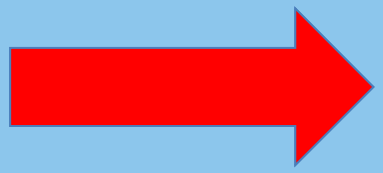


Lichtenberg et al. Endovascular mechanical thrombectomy versus thrombolysis in patients with iliofemoral deep vein thrombosis - a systematic review and meta-analysis. Vasa. 2020 May 25;1-9

Klinikum Hochsauerland
Akademisches Lehrkrankenhaus
Westfälische Wilhelms-Universität Münster

Conclusion

- Possible advantage for PMT is observed lower rate of bleeding complications
  - Trend towards lower pulmonary embolism
- PMT and CDT are quite similar in efficacy
  - Trend towards lower overall PTS and reflux with PMT



According to this meta-analysis, efficacy is similar but there are observational disadvantages CDT

Lichtenberg et al. Endovascular mechanical thrombectomy versus thrombolysis in patients with iliofemoral deep vein thrombosis - a systematic review and meta-analysis. Vasa. 2020 May 25;1-9

Indications, contraindications for Aspirex®S

Intended purpose:
Aspirex®S catheters in combination with the Straub Medical Drive System (REF SRS-Set/80300) are intended for the percutaneous transluminal removal of fresh thrombotic or thromboembolic material from blood vessels outside the cardiopulmonary, coronary and cerebral circulations.

Indicated for:
Native blood vessels or vessels fitted with stents, stent grafts or native or artificial bypasses outside the cardiopulmonary, coronary and cerebral circulations.

Potential adverse effects include, but are not limited to:
- embolisms, especially distal thromboembolisms
- pulmonary embolisms of all degrees of severity
- thromboses, especially recurrent thromboses
- re-occlusion
- vessel wall injury or valve damage
- vessel dissection / perforation / rupture
- perforation as a result of mural calcium being torn out of the vessel wall
- arteriovenous fistula / pseudo-aneurysm
- haematoma, bleeding, haemorrhage
- organ perforation
- implants such as stents / stent grafts / bypass grafts getting damaged, caught or dislodged
- disruption of the catheter and/or guidewire: debris remaining in the body
- allergic reactions to catheter material
- death
- infections or necrosis at the puncture site
- allergic reactions
- catheter-induced sepsis

Use of Aspirex®S catheters is not permitted in the following cases:
- patients not suitable for thrombectomy
- vessels of the cardiopulmonary, coronary or cerebral circulations
- undersized or oversized vessel diameters
- impossibility to pass the lesion completely with the guidewire
- subintimal position of the guidewire – even if only in short segments
- use in stents, stent grafts, or vena cava filters if the guidewire has become threaded at any point in the wire mesh / construction of stent, stent graft, or vena cava filter or the lining of the stent graft
- if the introducer sheath, the guide catheter, the guidewire or the Aspirex®S catheter sustains any damage, especially kinking
- in the fracture area of broken stents
- known or suspected allergy to any of the components of the system or to a medicinal product to be administered in connection with the planned procedure
- persistent vasospasm
- during imaging by Magnetic Resonance Imaging (MRI)
- during use of a defibrillator on the patient
- during use of electrosurgery on the patient
- for veterinary purposes

Thank you!