Iliofemoral outflow obstruction

- Acute and chronic DVT -

Awareness, Diagnostic approach, Treatment strategies

Michael K.W. Lichtenberg, MD

Venous Center Arnsberg

Klinikum Hochsauerland
Akademisches Lehrkrankenhaus
Westfälische Wilhelms-Universität Münster

EVIDENCE / GUIDELINES „General“

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association

Management of Massive and Submassive Pulmonary Embolism, Iliofemoral Deep Vein Thrombosis, and Chronic Thromboembolic Pulmonary Hypertension: A Scientific Statement From the American Heart Association

Michael R. Jaff, M. Sean McMurtry, Stephen L. Archer, Mary Cushman, Neil Goldenberg, Samuel Z. Goldhaber, J. Stephen Jenkins, Jeffrey A. Kline, Andrew D. Michaels, Patricia Thistlethwaite, Suresh Vedantham, R. James White, Brenda K. Zierler and on behalf of the American Heart Association Council on Cardiopulmonary, Critical Care, Perioperative and Resuscitation, Council on Peripheral Vascular Disease, and Council on Arteriosclerosis, Thrombosis and Vascular Biology

European Heart Journal Advance Access published August 29, 2014

European Heart Journal
doi:10.1093/eurheartj/ehu283

ESC GUIDELINES

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)

Endorsed by the European Respiratory Society (ERS)

CHEST™ JOURNAL
Official Publication of the American College of Chest Physicians

Antithrombotic Therapy for VTE Disease Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines Clive Kearon , MD , PhD ; Elie A. Akl , MD , MPH , PhD ; Anthony J. Comerota , MD ; Paolo Prandoni , MD , PhD ; Henri Bounameaux , MD ; Samuel Z. Goldhaber , MD , FCCP ; Michael E. Nelson , MD , FCCP ; Philip S. Wells , MD ; Michael K. Gould , MD , FCCP ; Francesco Dentali , MD ; Mark Crowther, MD ; and Susan R. Kahn , MD

DGA
Deutsche Gesellschaft für Angiologie
Gesellschaft für Gefäßmedizin e.V.

Diagnostik und Therapie
der Venenthrombose
und der Lungenembolie

Datum der Verabschiedung: 10. Oktober 2015
Gültigkeitsdatum: 09. Oktober 2020

Federführende Fachgesellschaft:
Dt. Gesellschaft für Angiologie – Gesellschaft für Gefäßmedizin

Dedicated treatment recommendations

American College of PHLEBOLOGY
advancing vein care

PRACTICE GUIDELINES
Chronic Deep Venous Obstruction

Cardiovasc Intervent Radiol (2014) 37:889–897
DOI 10.1007/s00270-014-0875-4

CIRSE

CIRSE STANDARDS OF PRACTICE GUIDELINES

CIRSE Standards of Practice Guidelines on Iliocaval Stenting

Andreas H. Mahnken · Ken Thomson ·
Michiel de Haan · Gerard J. O'Sullivan

DGA
Deutsche Gesellschaft für Angiologie
Gesellschaft für Gefäßmedizin e.V.

Lichtenberg et al: **Standards for Recanalization of Chronic Venous Outflow Obstructions. VASA accepted**

Agenda

- Epidemiology
- Venous Anatomy
- Venous Disease
- Patient Selection
- Stent Placement

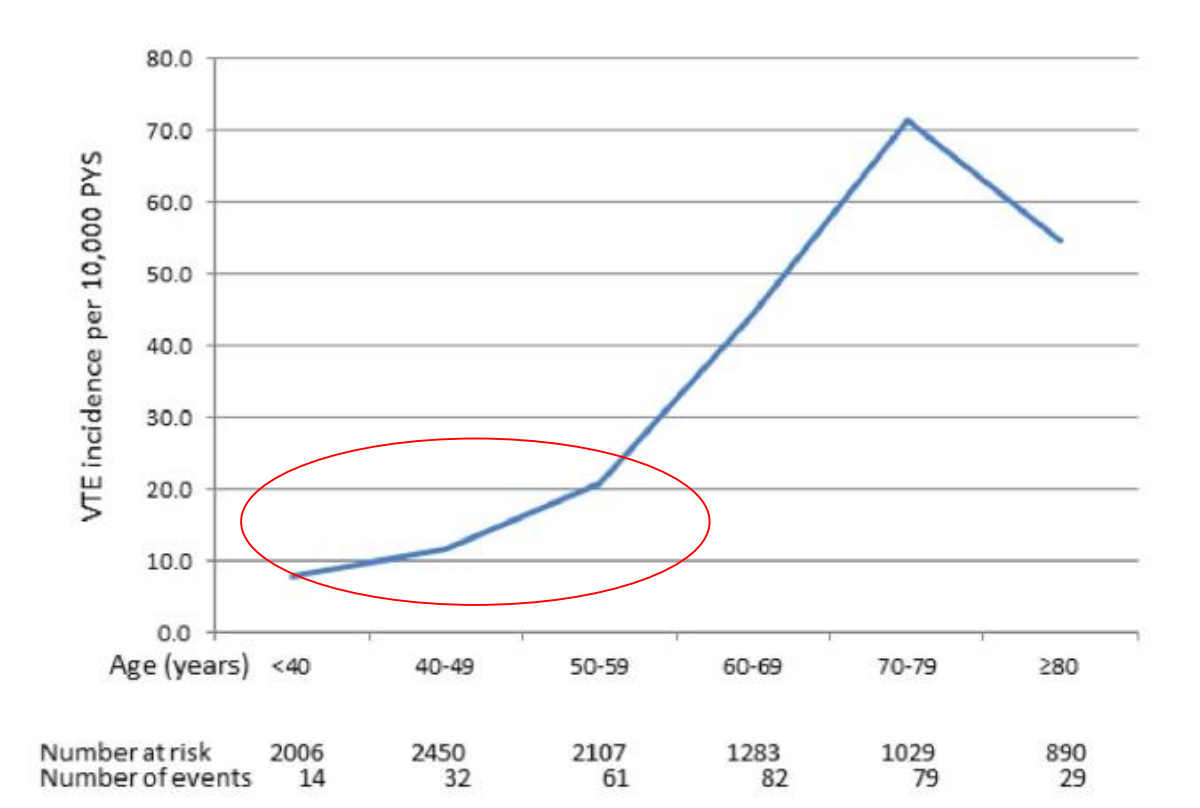
Venous thromboembolism (VTE) in Europe. The number of VTE events and associated morbidity and mortality

Thromb Haemost. 2007 Oct;98(4):756-64

	Outpatient	During hospital stay	Total
VTE			
Deep vein thrombosis	200.482	265.233	465.715
Pulmonary embolism	86.511	209.471	295.982
VTE associated death	108.535	261.477	370.012
Patient on anticoagulation	8.124	18.349	26.473
Patient not on anticoag.	63.541	153.853	217.394
Sudden death	36.870	89.275	126.145
Chronic complications			
Postthrombotic Syndrome[b]	177.236	218.437	395.673
Pulm. Hypertension	1.173	2.961	4.135

Ereignisse pro Jahr in 6 europäischen Ländern

VTE Incidence Framingham cohort



1995-2014:

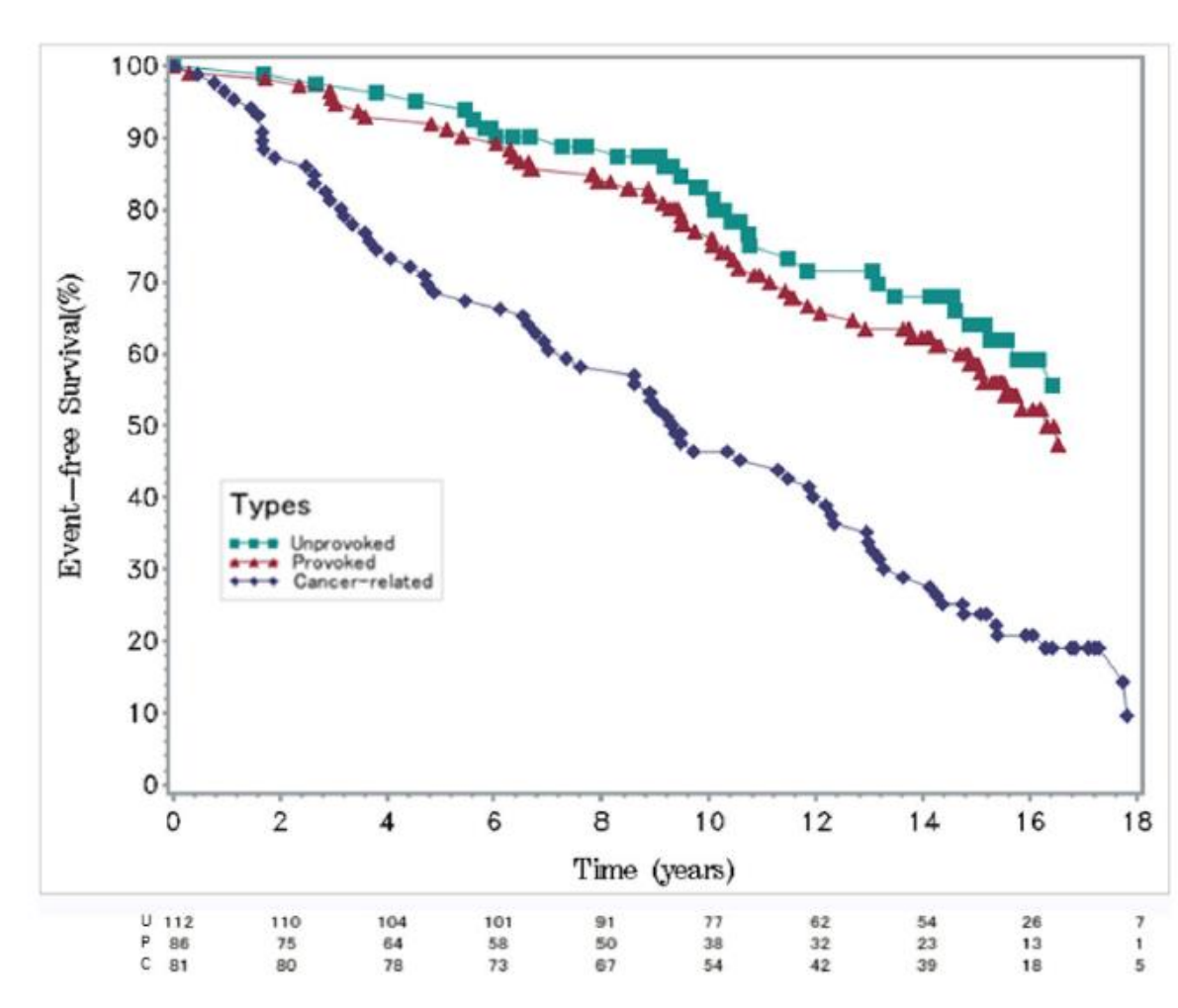
104,091 person-years

297 incident VTE (PE+DVT)

IR: 20.3/10,000

Thromb Res. 2016 September ; 145: 27–33. doi:10.1016/j.thromres.2016.06.033.

Mortality rates



Thromb Res. 2016 September ; 145: 27–33. doi:10.1016/j.thromres.2016.06.033.

Conservative Therapy

Study	Pts	Type	Follow Up (yr)	Treatment	PTS/ ALL	PTS/ SEVERE
Prandoni 1996	355	Outpatients	8	Elastic Compression Stockings (ECS)	29%	9%
Brandjes 1997	194	Outpatients	6	ECS/ No ECS	31%/70%	11%/23%
Franzeck 1996	39	Low Risk Pts	12	ECS (54% compliance)	36%	8%
Stain 2005	34	Pts treated with warfarin after VTE	5	ECS	43%	1.4%
Schulman 2006	897	Consecutive patients (no cancer)	10	Warfarin	56%	6%

J Thromb Thrombolysis (2009) 28:465–476

Study	Population	Mean follow-up	PTS, % (n)				PTS ulcer, %
			Overall	Mild	Moderate	Severe	(n)
Reverse Galanaud (2012)	367 1st unprovoked proximal DVT	6 months	31.6 (116)	79.3 (92)	15.5 (18)	5.2 (6)	1.7 (2)
Ten Cate-Hoek (2010)	125 Proximal DVT	2 years	29.6 (37)			7.5 (3)	~ 0.8 (1)
SOX trial Kahn (2014)	806 First proximal DVT	2 years	51.3 (185)	67.6 (119)	17.0 (30)	15.3 (27)	4.4 (17)
		ECS arm	51.4 (178)	66.1 (111)	22.0 (37)	11.9 (20)	4.1 (16)
ELATE Kahn (2005)	145 unprovoked proximal DVT	2.2 years	37 (55)			11 (4)	~ 1.4 (n = 2)
CANANO	1st proximal DVT	3 years	35.6 (47)			6.4 (3)	
Prandoni (2004)	First proximal DVT	2 years up to 5 years	25.7 (23) 49.1 (44)			13.0 (3) 22.7 (10)	2.2 (2) 6.7 (6)
EINSTEIN trial	Proximal DVT	5 years	29 (45)	89 (40)		11 (5)	2 (1)
Cheung (2016)			40 (66)	91 (60)		9 (6)	6 (4)

Kahn S. et al. Determinants of health-related quality of life during the 2 years following deep vein thrombosis. Journal of Thrombosis and Haemostasis 2009, 6: 1105-1112

QOL measure	Variable*	Parameter estimate	*P*-value
SF-36 PCS	Post-thrombotic syndrome	− 7.1	< 0.0001
	Age (per year)	− 0.14	0.0009
	Proximal (vs. distal) DVT	− 2.9	0.01
	Inpatient (vs. outpatient) at time of DVT diagnosis	− 2.6	0.04
SF-36 MCS	Post-thrombotic syndrome	− 1.8	0.11
	Age (per year)	0.10	0.008
VEINES-QOL	Post-thrombotic syndrome	− 4.4	< 0.0001
VEINES-Sym	Post-thrombotic syndrome	− 5.2	< 0.0001

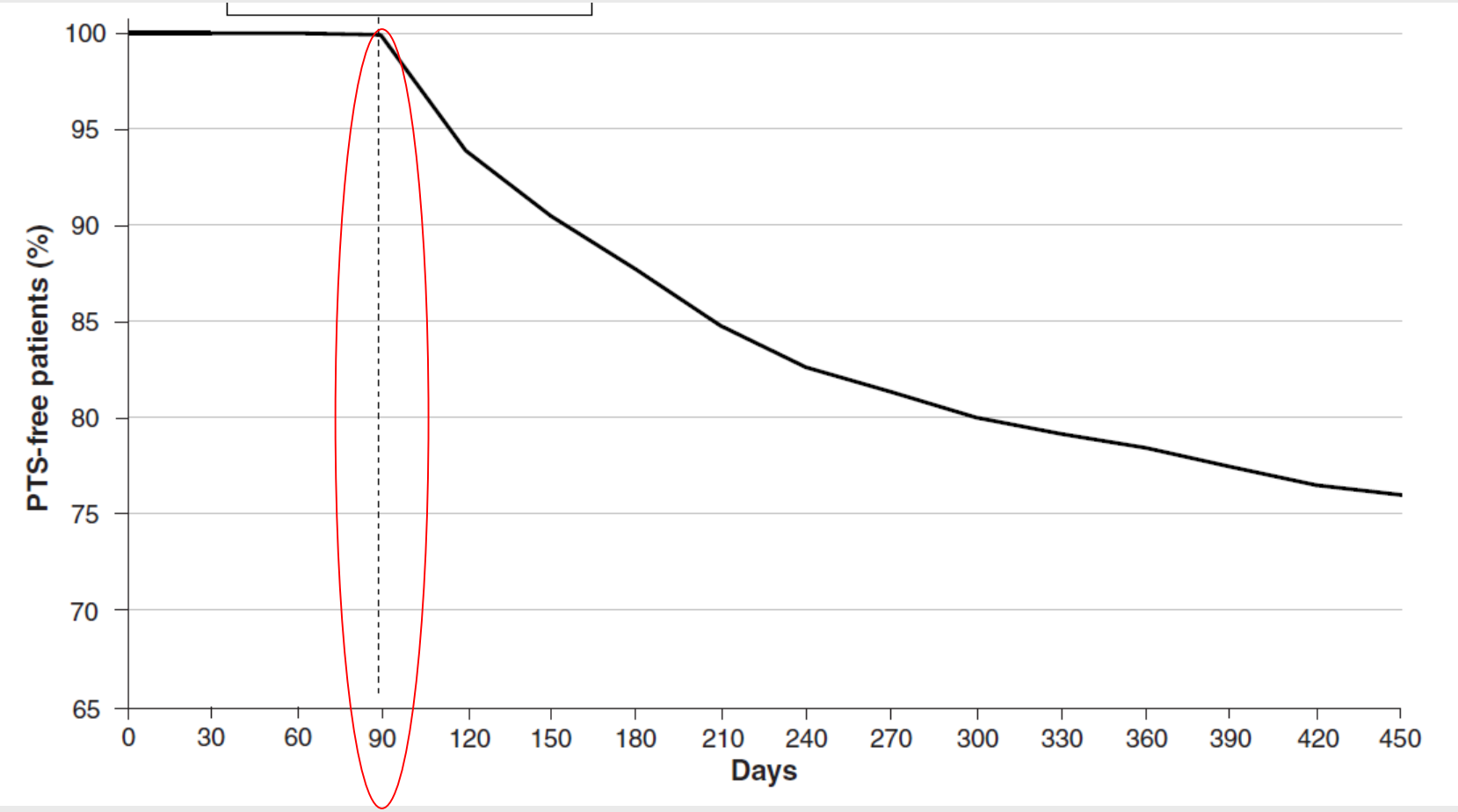
Economic burden of deep-vein thrombosis, pulmonary embolism, and post-thrombotic syndrome

Annualized Resource Utilization and Costs for Patients in Post-Thrombotic Syndrome Subanalysis[a]

Group	PTS (n = 624) Mean	PTS (n = 624) S.D.	PTS (n = 624) Median	No PTS (n = 1781) Mean	No PTS (n = 1781) S.D.	No PTS (n = 1781) Median
Resource utilization (number)						
Pharmacy claims	49.4	54.2	33.8	40.4	43.2	27.0
Related outpatient claims	30.3	27.6	26.5	22.4	24.8	16.0
Other outpatient claims	107.4	128.7	70.4	71.7	88.7	45.9
Hospital admissions						
Index event						1.0
Other admissions						0.0
Length of stay (days)						
Index event						5
Other admissions						0
Health care costs (U.S. $ × 1000)						
Pharmacy costs	3.7	8.4	1.5	3.3	8.2	1.0
Related outpatient costs	1.4	2.9	0.9	0.9	2.1	0.4
Other outpatient costs	10.1	18.7	4.8	6.5	13.3	2.6
Inpatient costs						
Index event	16.6	40.5	5.5	14.7	37.4	6.3
Other admissions	24.0	69.2	0.0	12.0	36.1	0.0
Total costs	55.8	101.1	20.6	37.4	66.1	15.8
Total costs (adjusted)	47.6			35.9		

Anually costs
PTS: 20.569 $
No PTS: 15.834 $

Am J Health-Syst Pharm—Vol 63 Oct 15, 2006 Suppl 6



Am J Health-Syst Pharm—Vol 63 Oct 15, 2006 Suppl 6

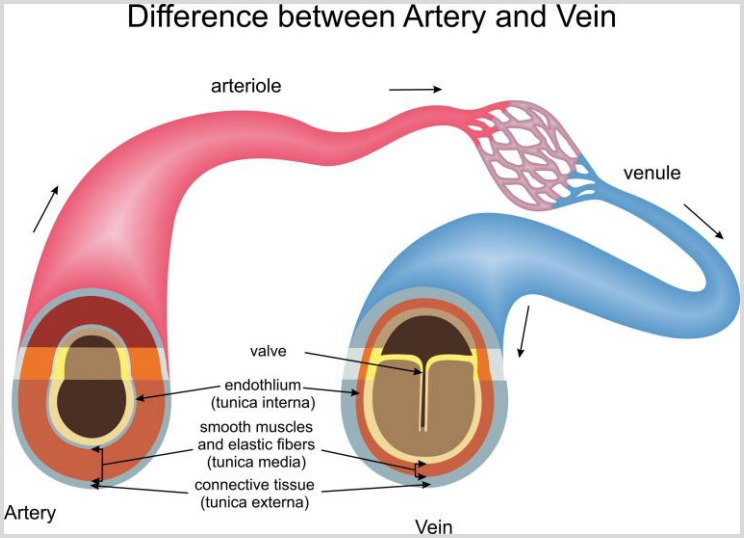
Venous Anatomy

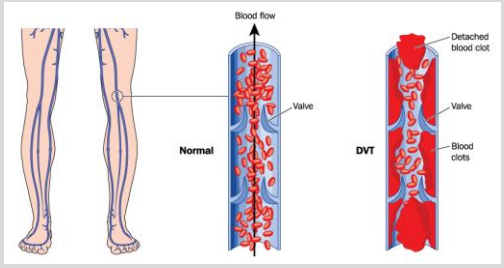
Venous Versus Arterial Anatomy

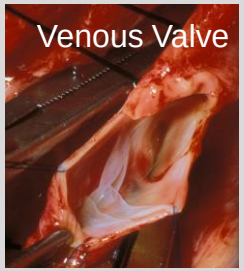
"These are not arteries." – Peter Neglen, MD

Arteries

- Low volume
- High pressure
- Pulsatile flow
- Stiffer vessel walls
- Thick muscle layer
- No Valves





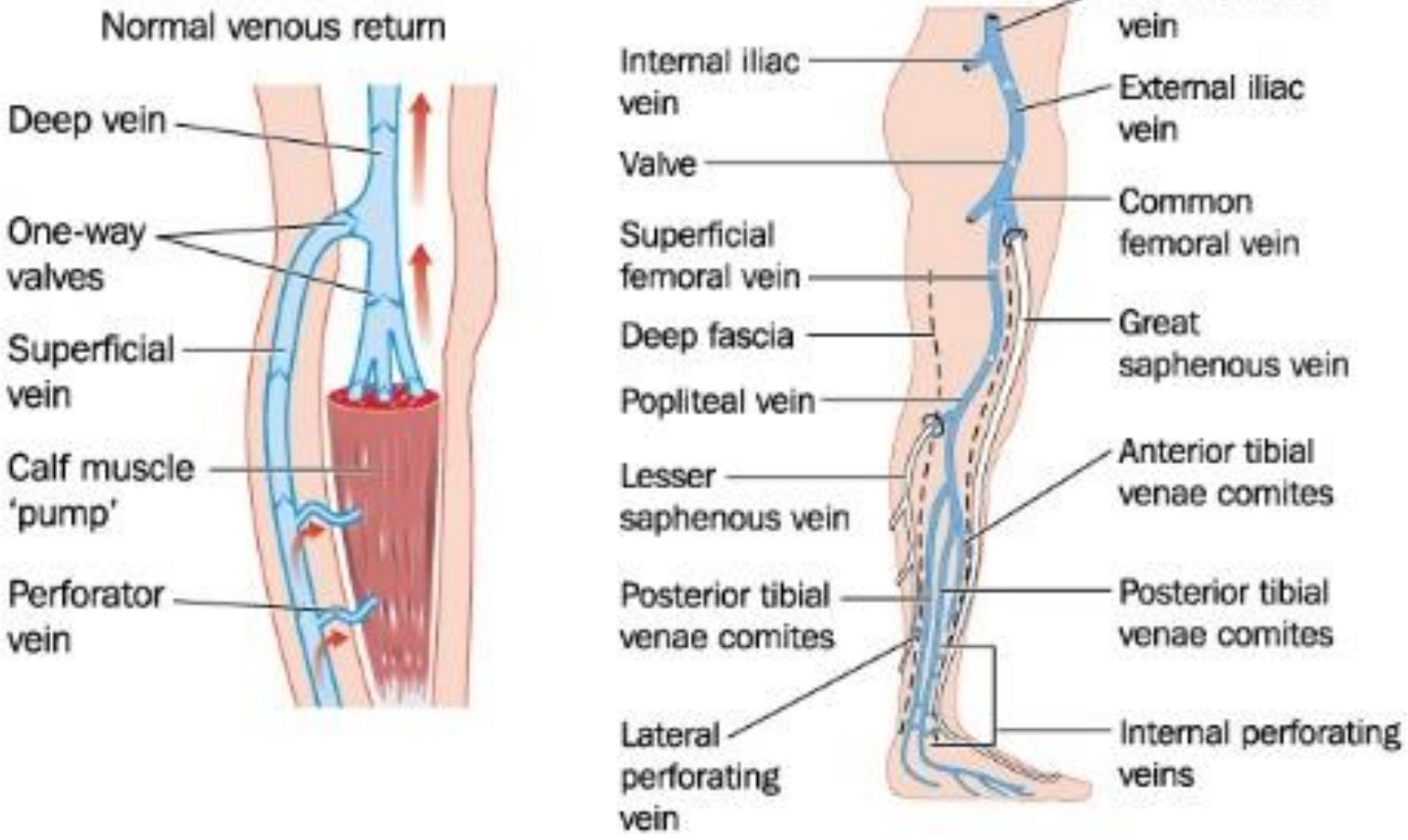


Images courtesy P. Neglen MD

Veins

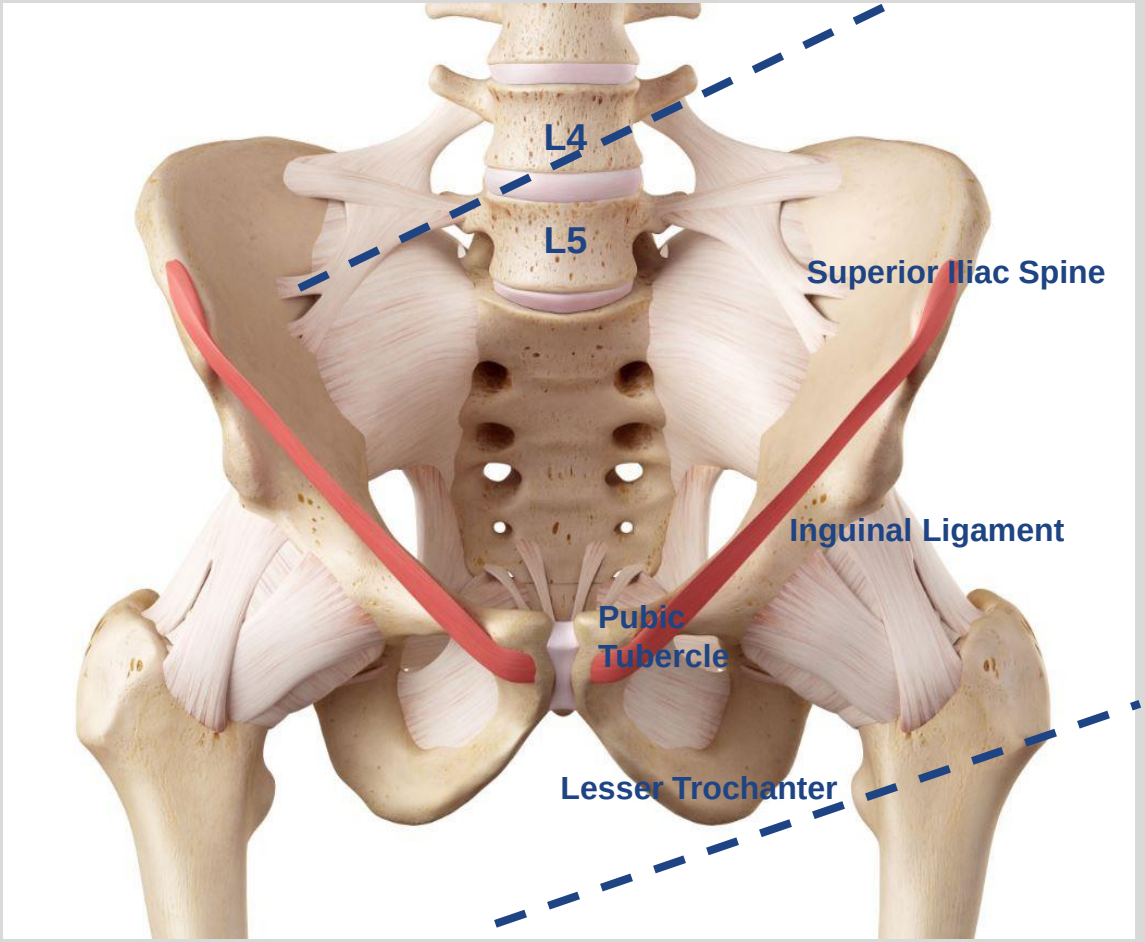
- High volume
- Low pressure
- Phasic flow
- High compliance
- Thin muscle layer
- Valves

Venous Anatomy



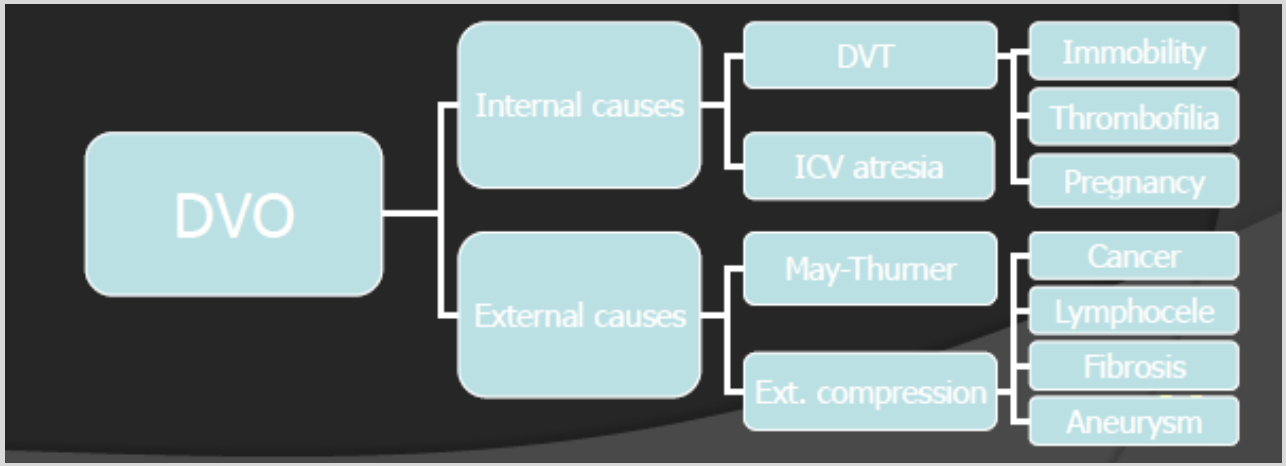
Pelvic Landmarks

- Iliofemoral veins extend from confluence of iliac veins at IVC (L4-L5) to lesser trochanter
- Bony landmarks are useful for access, wire guidance and stent placement



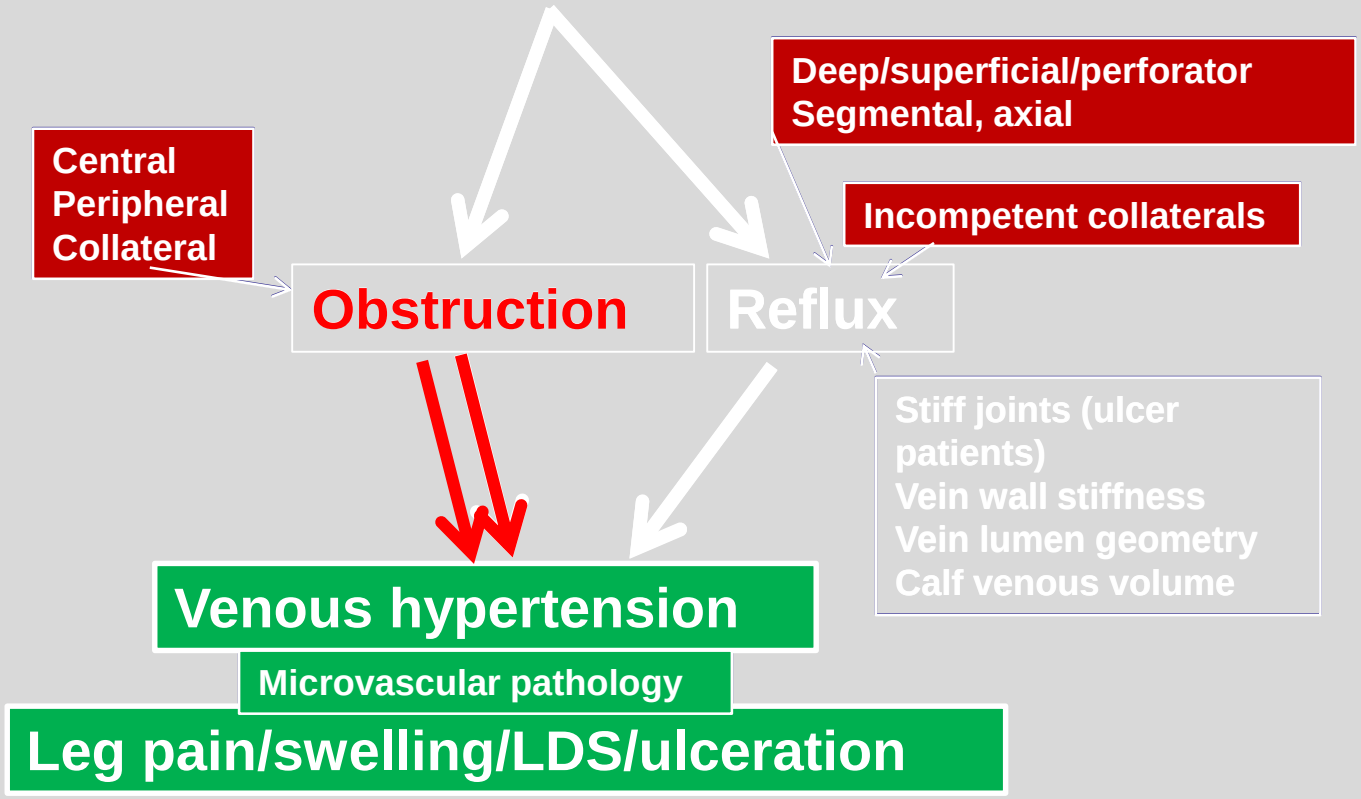
Venous Disease

- Pathophysiology
- Etiology



- Venous hypertension:
  - Deep venous insufficiency (< 90 mmHg)
  - Deep venous obstruction !! (> 200 mmHg)

Iliofemoral Venous Disease



Post Thrombotic Syndrome

Ambulatory Venous Pressures & Symptoms

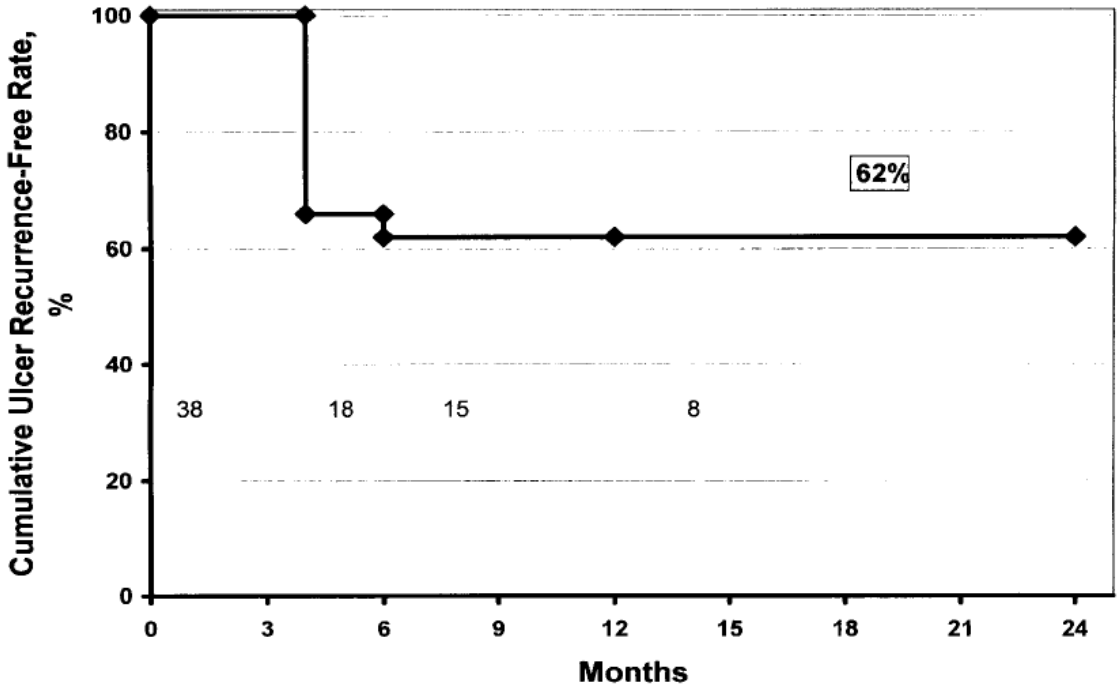
- 28 mmHg – Asymptomatic
- 36 mmHg – Varicosities
- 41 mmHg – Edema
- 47 mmHg – Hyperpigmentation
- 60 mmHg – Ulceration

Greater pressure associated with worse PTS symptoms

Linder et al: J Vasc Surg 1986

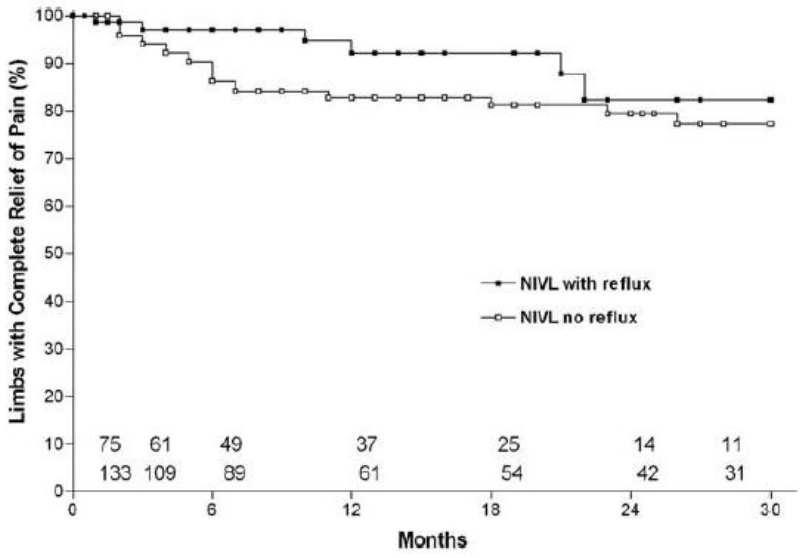
(J Vasc Surg 2002;35:8-15.)

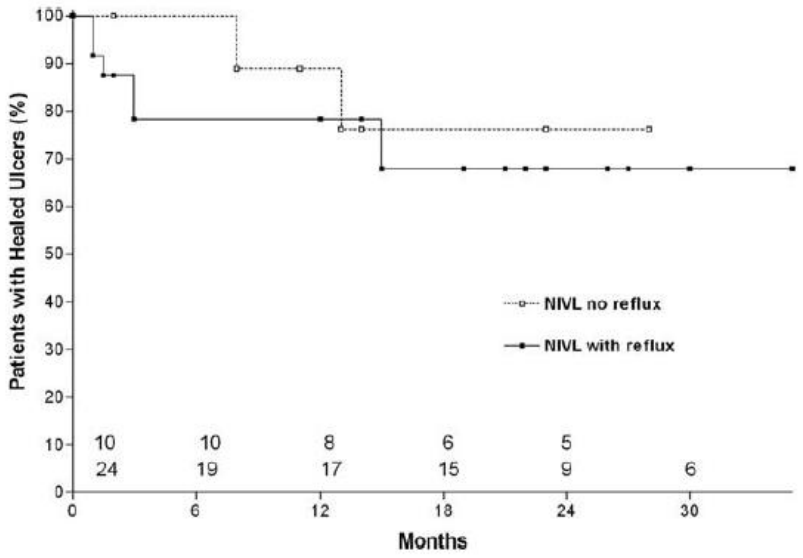
Ulcer Healing



Purpose: The purpose of this study was the presentation of the results of iliac venous stent placement in the management of chronic venous insufficiency (CVI).

NIVL treatment better than reflux treatment





High prevalence of nonthrombotic iliac vein lesions in chronic venous disease: A permissive role in pathogenicity

Seshadri Raju, MD, and Peter Neglen, MD, PhD, *Flowood, Miss*

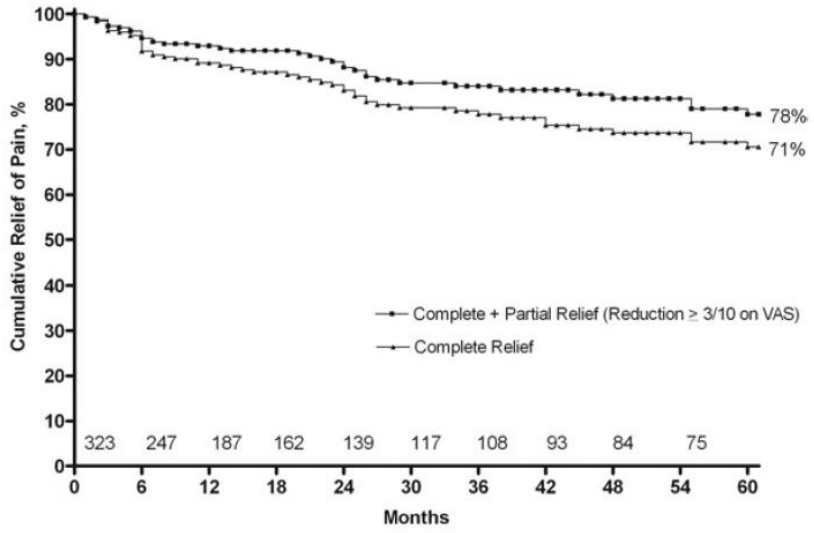
Conclusions: NIVL has high prevalence and a broad demographic spectrum in patients with CVD. Similar lesions in the asymptomatic general population may be permissive of future development of CVD. Stent placement alone, without correction of associated reflux, often provides relief. (J Vasc Surg 2006;44:136-44.)

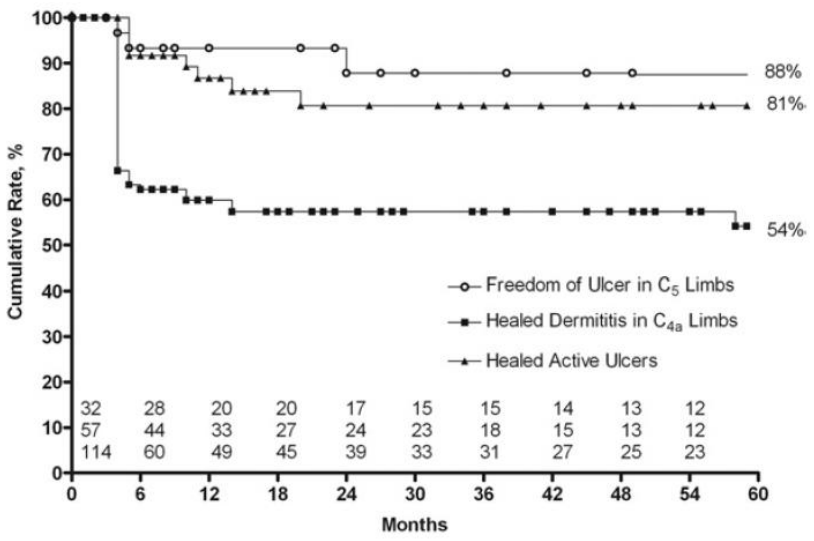
From the Society for Vascular Surgery

(J Vasc Surg 2010;51:401-9.)

Unexpected major role for venous stenting in deep reflux disease

Seshadri Raju, MD,[a] Rikki Darcey, BS,[b] and Peter Neglén, MD, PhD,[b] *Jackson and Flowood, Miss*



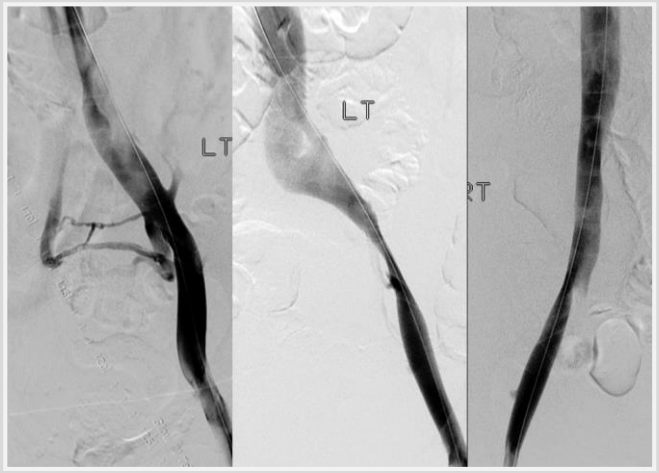


Conclusion: Iliac venous stenting alone is sufficient to control symptoms in the majority of patients with combined outflow obstruction and deep reflux. Partial correction of the pathophysiology in limbs with multisystem or multilevel

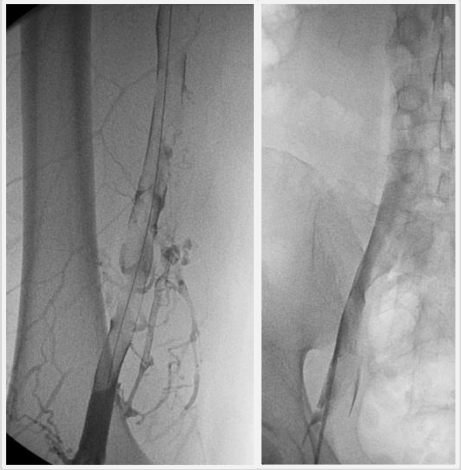
Venous Disease

- ☑ Pathophysiology
- ☐ Etiology

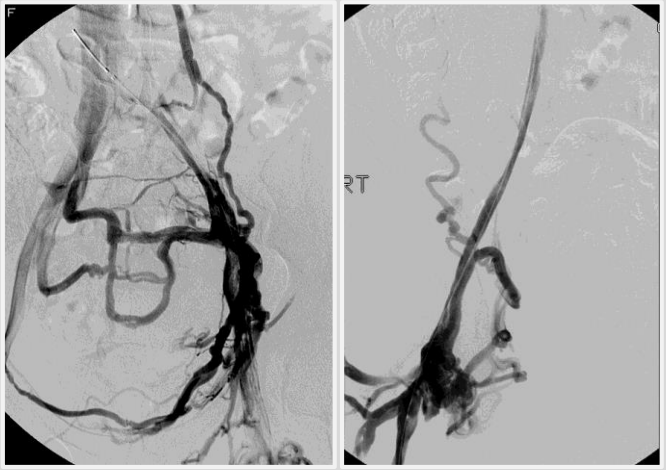
Three Primary Etiologies



NIVL
Non-thrombotic iliac vein lesions



Acute DVT



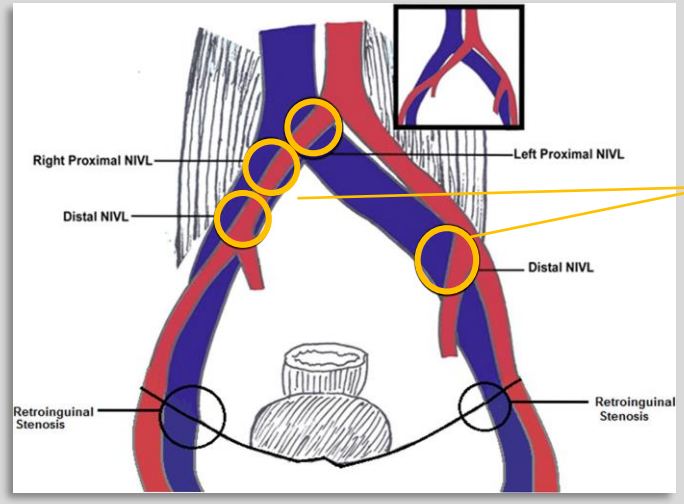
Postthrombotic iliac vein lesions

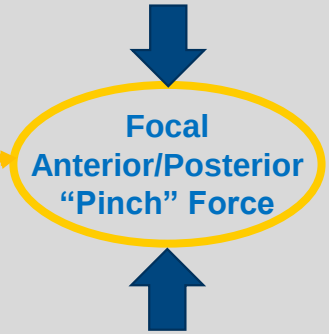
Other Etiologies

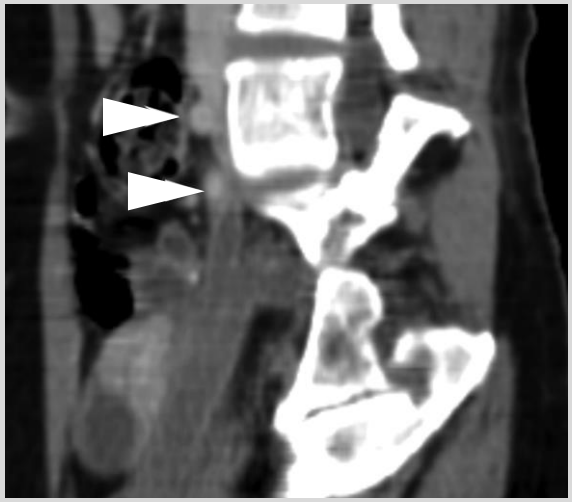
- Benign or malignant tumors
- Retroperitoneal fibrosis
- Atresia of the IVC
- Miscellaneous
  - iatrogenic injury, irradiation, cysts and aneurysms

Non-Thrombotic Iliac Vein Lesion (NIVL)

- NIVL is where veins are impinged, compressed, or damaged by a neighboring artery or structure
- NIVL's may precipitate iliofemoral DVT
- 24% of NIVL's thought to be clinically significant[1]
- NIVL's are highly under appreciated due to lack of accurate diagnosis by standard venography imaging. Venography was only 66% sensitive, with 34% of venograms appearing "normal." IVUS had a diagnostic sensitivity of > 90%[2]



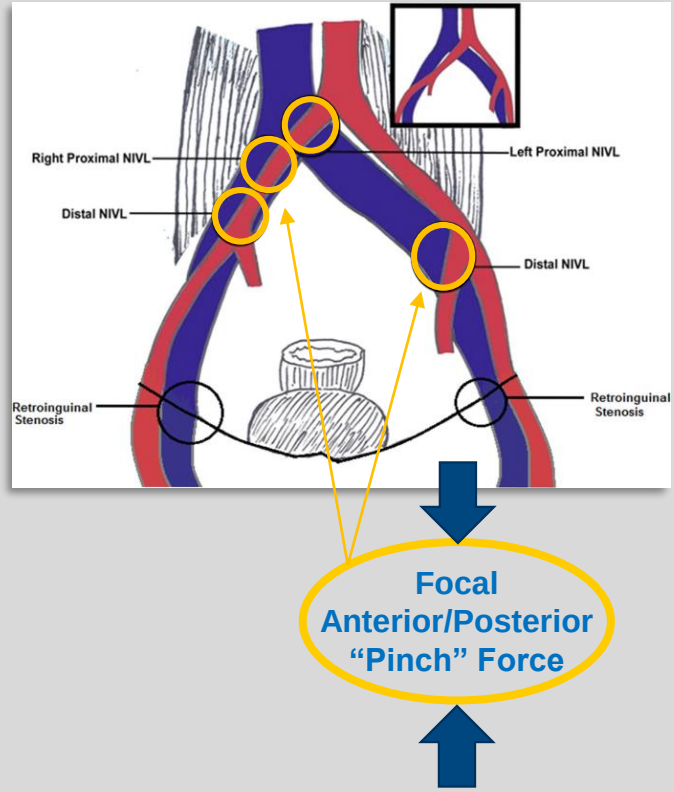




1. Marston W, Fish D, Incidence of and risk factors for iliocaval venous obstruction in patients with active or healed venous leg ulcers. *J Vasc Surg* 2011;54:1303-8
2. Raju S, Neglén P. High prevalence of nonthrombotic iliac vein lesions in chronic venous disease: A permissive role in pathogenicity, *J Vasc Surg* 2006;44:136-44

Non-Thrombotic Iliac Vein Lesion (NIVL)

- NIVL's present as:
  - Left-right ratio = 3:1
  - Female-male ratio = 4:1
  - Proximal (iliac artery crossing) and distal lesion (hypogastric artery crossing)
  - Median age 54 years (range: 18-90)

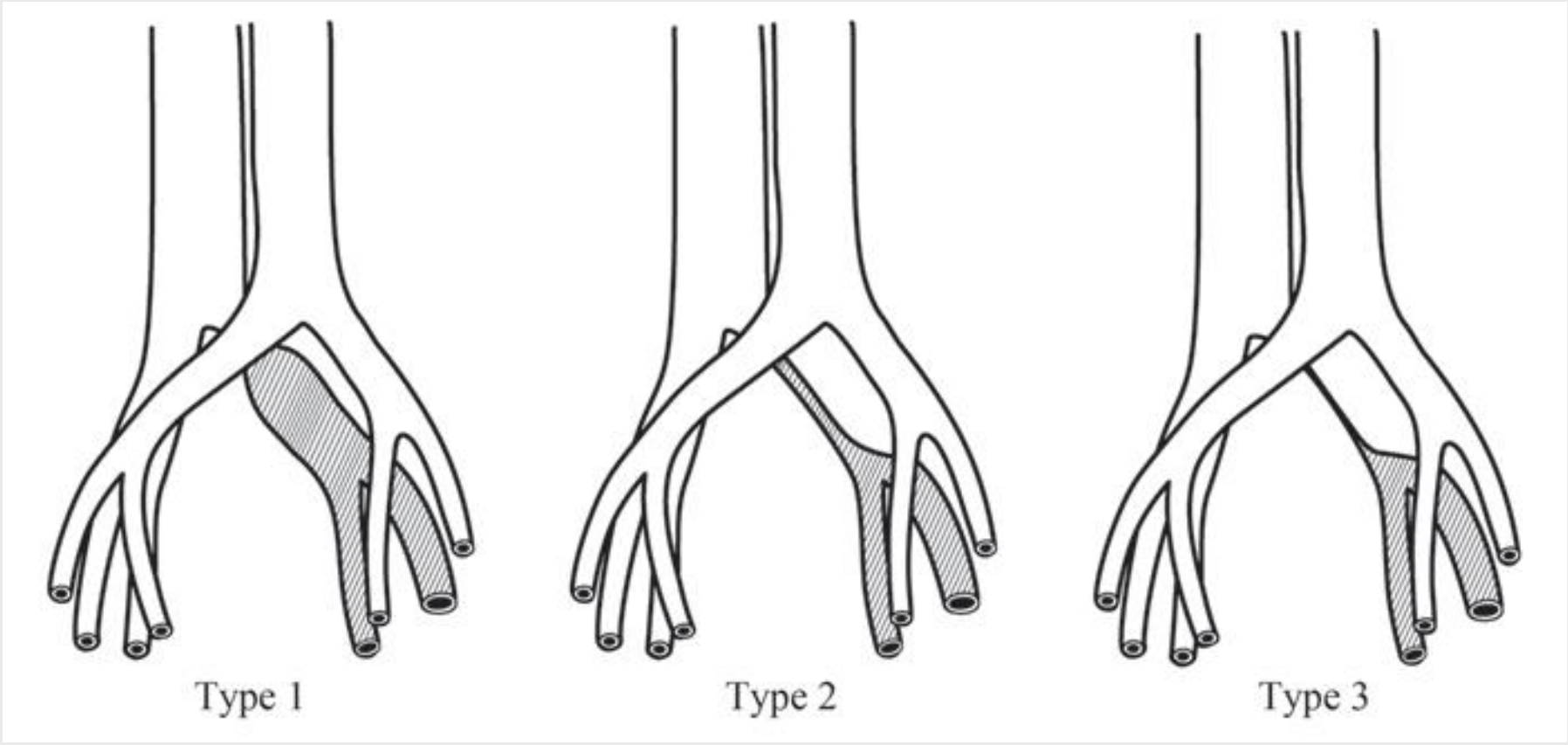


- NIVL: underlies May-Thurner or Cockett's Syndrome
  - A syndrome is a set of signs and symptoms that appear together and characterize a medical condition.

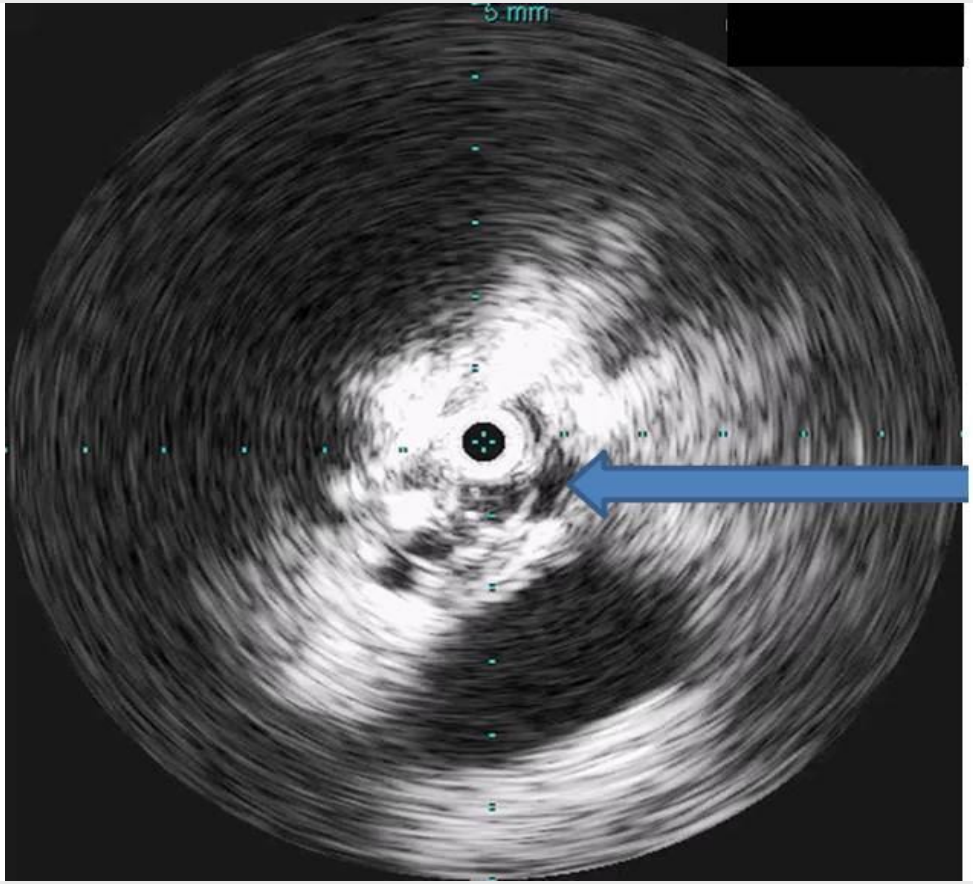
- NIVL clinical impact without previous DVT
  - May be permissive of future development of chronic venous disease CVD
  - May lead to venous valve reflux

Raju S, Neglén P. High prevalence of nonthrombotic iliac vein lesions in chronic venous disease: A permissive role in pathogenicity, *J Vasc Surg* 2006;44:136-44.

May Thurner Syndrom



Ung BJ et al. May-Thurner Syndrome Complicated by Acute Iliofemoral Vein Thrombosis: Helical CT Venography for Evaluation of Long-Term Stent Patency and Changes in the Iliac Vein, AJR 2010; 195:751–757)



Venenwandverdickung,
Fibrosebildung, Trabekel,
lokale Thromben

Non-Thrombotic Iliac Vein Lesion (NIVL)

The impact of non-thrombotic iliac vein lesion (NIVL) on acute DVT and postthrombotic obstruction

- Often underlying NIVLs found (left 84%, right 66%)

Chung JW, Yoon CJ. Acute iliofemoral deep vein thrombosis: evaluation of underlying anatomic abnormalities by spiral CT venography. *J Vasc Interv Radiol.* 2004;15:249-56.

- Stenting of the stenosis after early clot removal improves patency from 27-44% to 86-93%

Juhan CM, Alimi YS. Late results of iliofemoral venous thrombectomy. *J Vasc Surg* 1997;25:417-22.
Mickley V, Schwagierek R. Left iliac venous thrombosis caused by venous spur: treatment with thrombectomy and stent implantation. *J Vasc Surg* 1998;28:492-7.
Wohlgemuth,WA, Weber H. PTA and stenting of benign venous stenoses in the pelvis: long-term results. *Cardiovasc Intervent Radiol*. 2000; 23: 9–16.

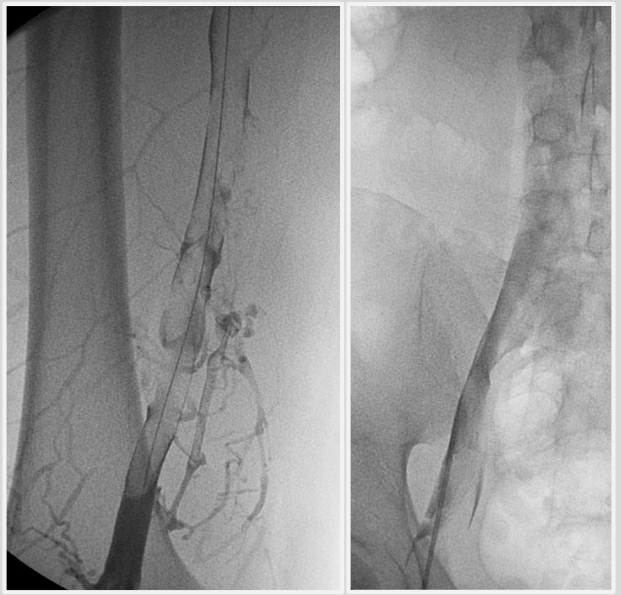
- Poor recanalization with external compression of the iliac vein (70-80% remains obstructed)

Fraser D, Moody A. Iliac compression syndrome and recanalization of femoropopliteal and iliac venous thrombosis: A prospective study with magnetic resonance venography. *J Vasc Surg.* 2004;40:612-19.

Acute DVT

Treatment Goal is to Reduce DVT Recurrence and Postthrombotic Syndrome

- Treatment window = **two weeks**
- Patients with iliofemoral DVT (IFDVT) have a twofold increased risk of developing PTS
- Venous stenting in conjunction with thrombus removal is safe and effective and has low incidence of PTS



Images courtesy P. Neglen MD

Foegh P, Jensen LP. Factors associated with long-term outcome in 191 patients with ilio-femoral DVT treated with catheter-directed thrombolysis. *Eur J Vasc Endovasc Surg*. 2017;53(3):419-24.

Engelberger RP, Fahrni J, Willenberg T, et al. Fixed low-dose ultrasound-assisted catheter-directed thrombolysis followed by routine stenting of residual stenosis for acute ilio-femoral deep-vein thrombosis. *Thromb Haemost*. 2014;111(6):1153-60.

ten Cate-Hoek AJ, Henke PK. The post thrombotic syndrome: Ignore it and it will come back to bite you. *Blood Rev*. 2016;30(2):131-7.

Recurrent DVT Rate

Clinical course of DVT after the first episode of symptomatic deep venous thrombosis following **traditional systemic anticoagulant therapy**.

Study Design: Prospective Study of 355 Patients with First Episode of DVT

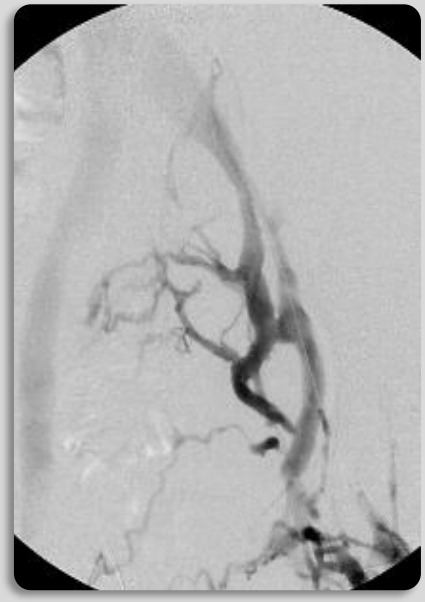


Image courtesy P. Neglen MD

Follow-up Period	Recurrent DVT Rate
2 years	17.5%
5 years	24.6%
8 years	30.3%

Prandoni P, Lensing AW, Cogo A, et al. The long-term clinical course of acute deep venous thrombosis. *Ann Intern Med*. 1996;125(1):1-7.

American College of PHLEBOLOGY
advancing vein care

PRACTICE GUIDELINES
Chronic Deep Venous Obstruction

American Venous Forum
Promoting venous and lymphatic health

SOCIETY FOR CLINICAL VASCULAR SURGERY

the IVC. Eighty percent of iliofemoral DVTs, DVTs that involve the iliocaval segment in addition to the veins below the inguinal ligament, have an underlying iliac vein compression. This compression is thought to be a lesion which increases the risk of iliofemoral DVT, especially in individuals who have other risks for thrombosis including oral contraceptive use.[22] For

American Venous Forum
Promoting venous and lymphatic health

Society for Clinical Vascular Surgery

SOCIETY FOR VASCULAR SURGERY® DOCUMENTS

Early thrombus removal strategies for acute deep venous thrombosis: Clinical Practice Guidelines of the Society for Vascular Surgery and the American Venous Forum

Mark H. Meissner, MD,[a] Peter Gloviczki, MD,[b] Anthony J. Comerota, MD,[c] Michael C. Dalsing, MD,[d] Bo G. Eklof, MD,[e] David L. Gillespie, MD,[f] Joann M. Lohr, MD,[g] Robert B. McLafferty, MD,[h] M. Hassan Murad, MD,[i] Frank Padberg, MD,[j] Peter Pappas, MD,[k] Joseph D. Raffetto, MD,[l] and Thomas W. Wakefield, MD,[m] *Seattle, Wash; Rochester, Minn; Toledo, Ohio; Indianapolis, Ind; Helsingborg, Sweden; Rochester and New York, NY; Cincinnati, Ohio; Springfield, Ill; Newark, NJ; West Roxbury, Mass; Ann Arbor, Mich*

- **2. Indications for early thrombus removal**
  - **2.1. We suggest a strategy of early thrombus removal in selected patients meeting the following criteria:**
    - **(a) a first episode of acute iliofemoral deep venous thrombosis**
    - **(b) symptoms <14 days in duration**
    - **(c) a low risk of bleeding**
    - **(d) ambulatory with good functional capacity and an acceptable life expectancy (Grade 2C)**

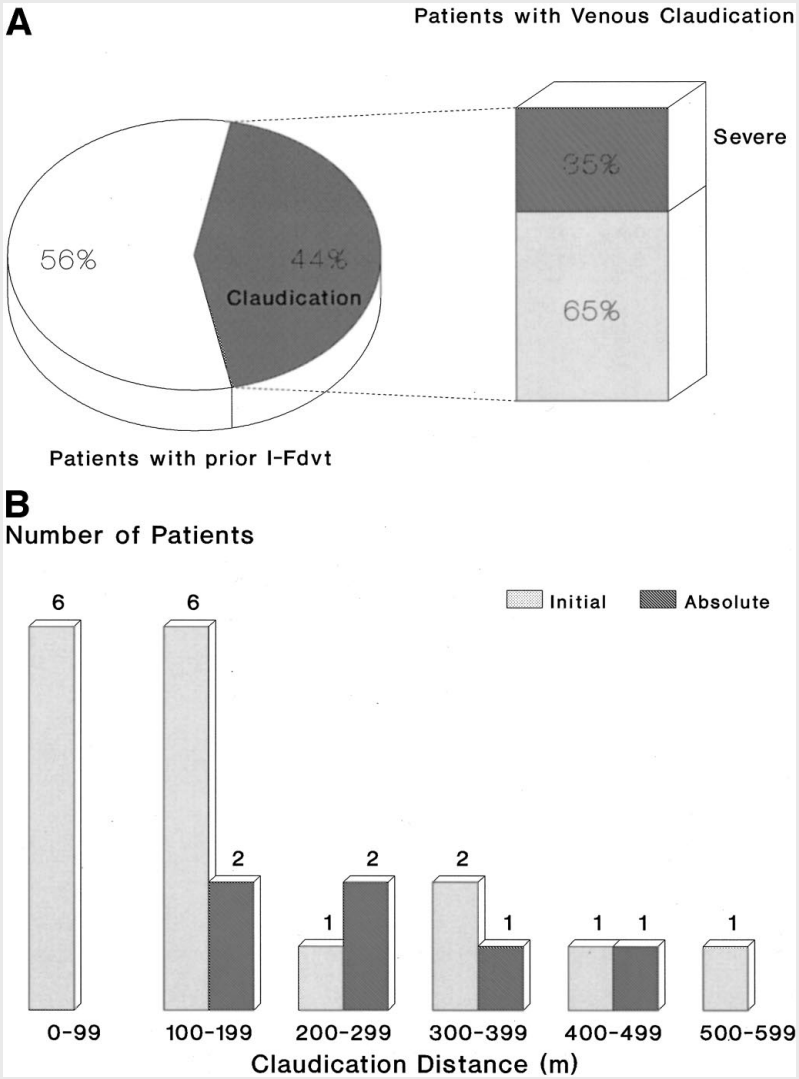
5.1. We recommend the use of self-expanding metallic stents for treatment of chronic iliocaval compressive or obstructive lesions that are uncovered by any of the thrombus removal strategies (Grade 1C). and

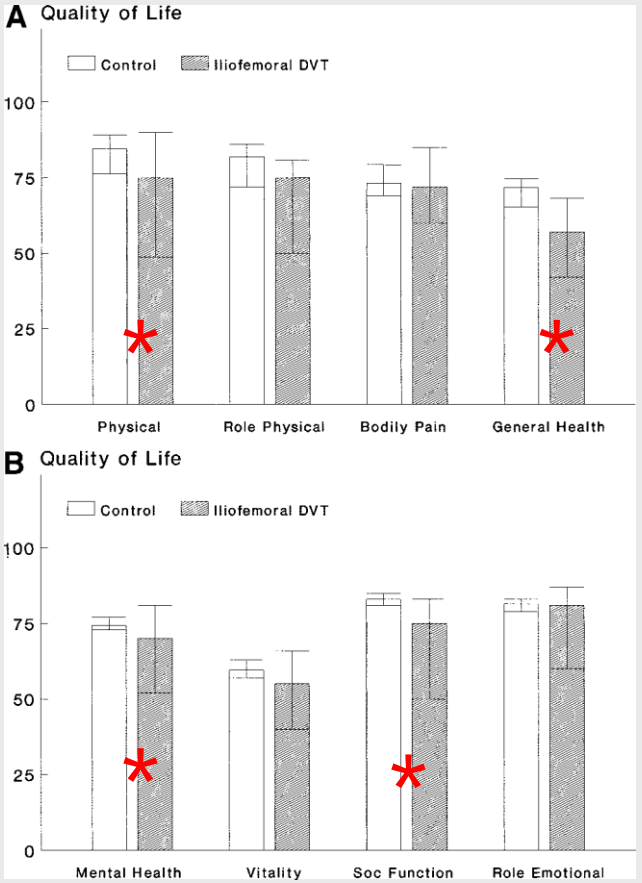
Venous Claudication in Iliofemoral Thrombosis

Long-term Effects on Venous Hemodynamics, Clinical Status, and Quality of Life

(*Ann Surg* 2004;239: 118 –126)

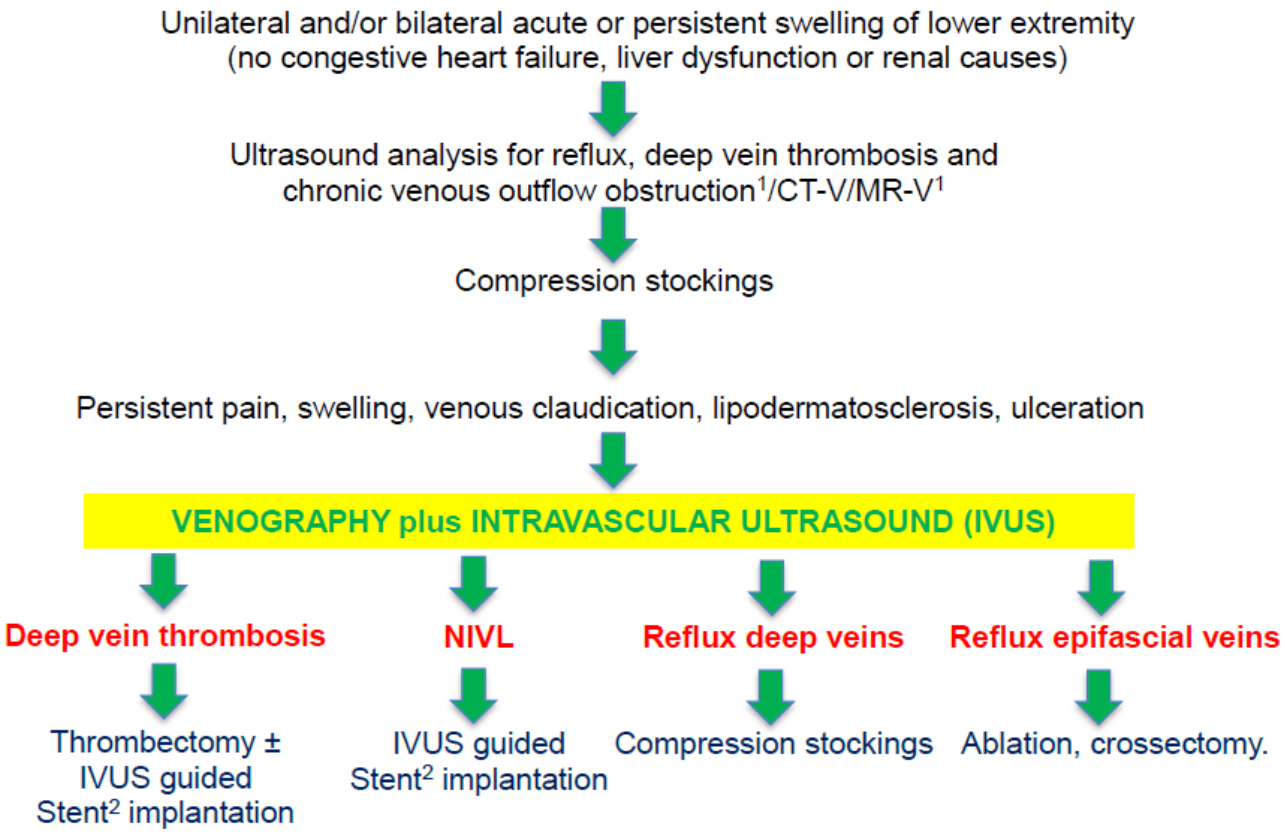
39 patients with prior iliofemoral DVT (22-86 years)
Follow up 5 years





Patient Selection

Lichtenberg et al: **Standards for Recanalization of Chronic Venous Outflow Obstructions. VASA accepted**



1) Consider further diagnostic to rule out compression by abdominal mass.
2) Only dedicated venous stents are recommended.

CT-V: CT Venography; MR-V: MR Venography

Clinical assessment

http://www.veinforum.org/uploadDocs/1/Revised-VCSS---June-2010.pdf

NAME:

		LEFT						RIGHT					
	Initial	Pre-Op	3-4 Days	3-4 Weeks	3-4 Months	1 Year	Initial	Pre-Op	3-4 Days	3-4 Weeks	3-4 Months	1 Year
DATE:												
CEAP (0-6)												
Fatigue: (Y/N)												
VCSS (0-3 Each)												
Pain												
Varicose Vein												
Venous Edema												
Pigmentation												
Inflammation												
Induration												
Active Ulcers												
Ulceration Duration												
Active Ulcer Size												
Compressive Therapy												
Total												
Complications: Blank (none) to 3 (severe)												
Hyperpigmentation												
Phlebitis												
Paresthesia												
Erythema												
Ecchymosis												
Infection												
Thermal Injury												
Other												
Patient Satisfaction: (None/Partly/Very)												
Varicose Veins:(None/ Residual/New/Recur)												
Outcome:(Not successful/ Successful/N/A)												

Patient Selection for Successful Venous Stenting

- Clinical severity of the disease
  - Don’t treat the lesion, treat the patient
- Findings on Investigations
- Treatment Considerations
  - Can the patient be stented?
    - Assess landing zones
    - Sufficient inflow to the CFV?
    - Need for endophlebectomy?

Clinical Severity of the Disease
CEAP Classification

Clinical*
- C_0 - No clinical signs
- C_1 - Small varicose veins
- C_2 - Large varicose veins
- C_3 - Edema
- C_4 - Skin changes without ulceration
- C_5 - Skin changes with healed ulceration
- C_6 - Skin changes with active ulceration

Etiology*
- E_C - Congenital
- E_P - Primary
- E_S - Secondary
  (usually due to prior DVT)

Anatomy*
- A_S - Superficial veins
- A_D - Deep veins
- A_P - Perforating veins

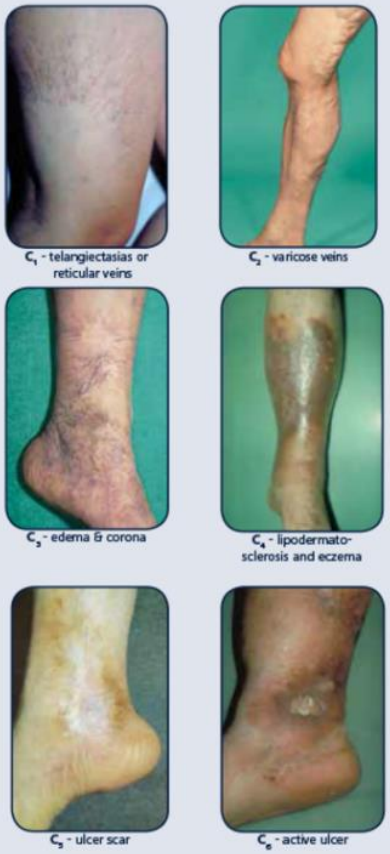
Pathophysiology*
- P_R - Reflux
- P_O - Obstruction

"Early application of compression should be performed to correct swelling and progressive scarring and to initiate the healing process by improving the venous microcirculation."

Kistner R. Specific Steps to Effective Management of Venous Ulceration. Supplement to Wounds June 2010.

*Fronek HS, Bergan JJ, et al. The Fundamentals of Phlebology: Venous Disease for Clinicians. 2004. pg 151.

Clinical Classifications with examples



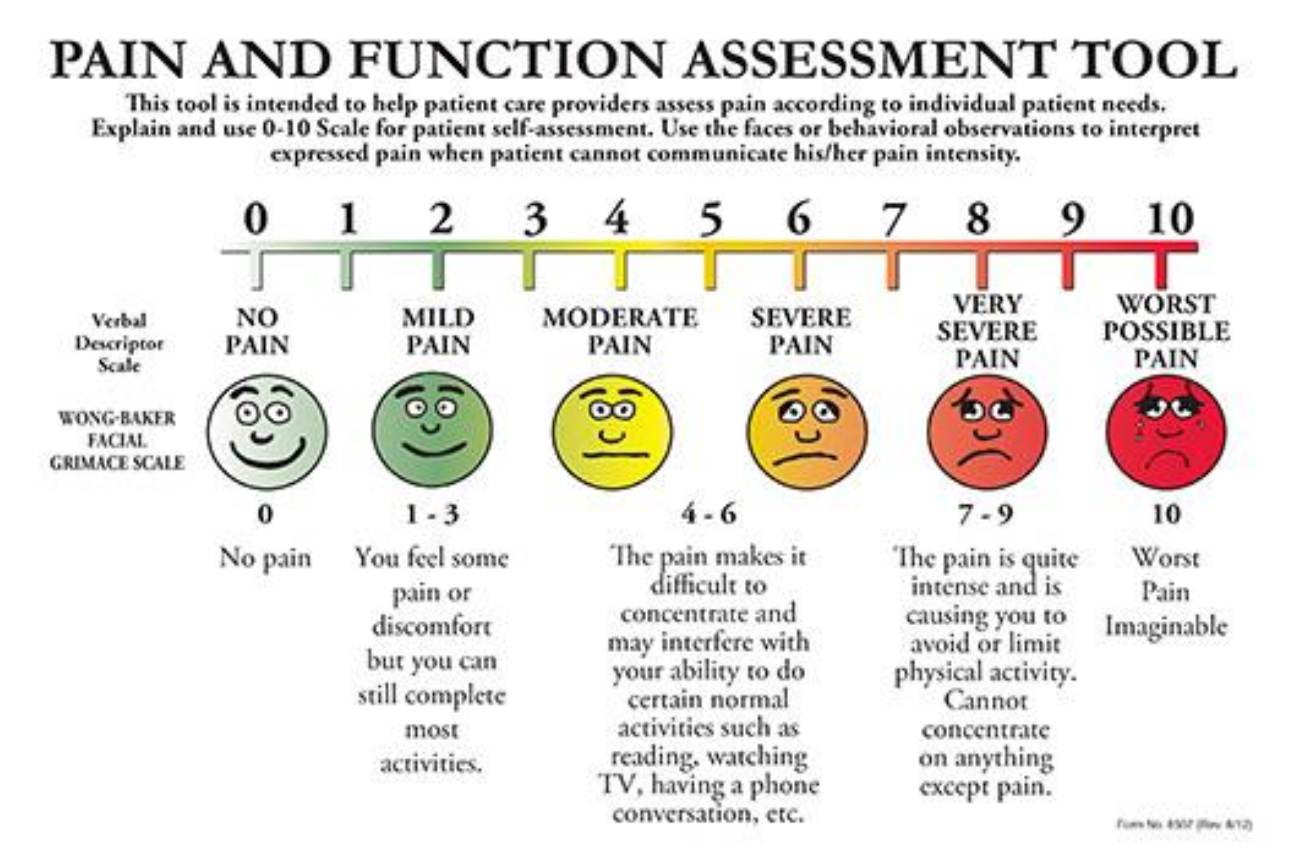
Clinical*
- C_0 - No clinical signs
- C_1 - Small varicose veins
- C_2 - Large varicose veins
- C_3 - Edema
- C_4 - Skin changes without ulceration
- C_5 - Skin changes with healed ulceration
- C_6 - Skin changes with active ulceration

Visual Indications for Treatment

https://www.sigvaris.com/usa/en-us/knowledge/ceap-classification. Accessed July 23, 2017

VAS Pain Scale

Visual Analog Scale



/www.cedars-sinai.edu/Patients/Programs-and-Services/Pediatric-Surgery/Patient-Guide/Managing-your-childs-pain.asp. Accessed August 2, 2017

Clinical Severity of the Disease

Specific clinical signs and symptoms

Severe C_3, C_{4-6} (CEAP) and/or pain >5 (VAS)

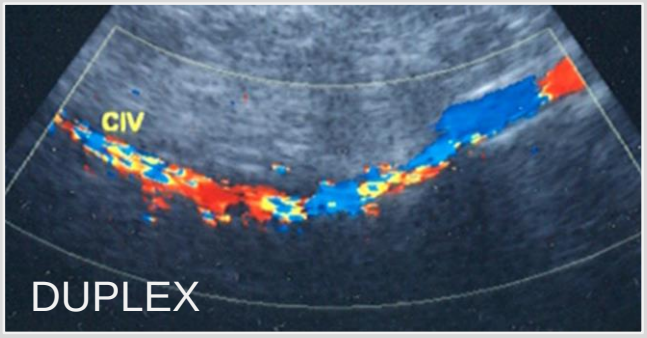
Additional indications for treatment

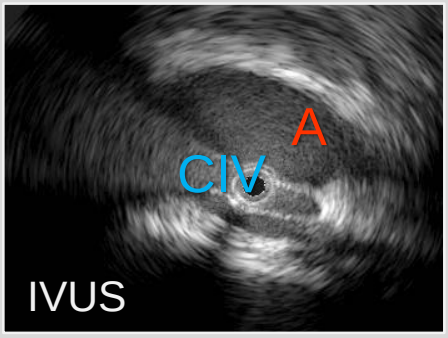
- abdominal collaterals, atypical varicose veins, early varicose vein recurrence
- venous claudication
- postthrombotic disease
- pain out of proportion to lesion
- no detectable lesion explaining symptoms

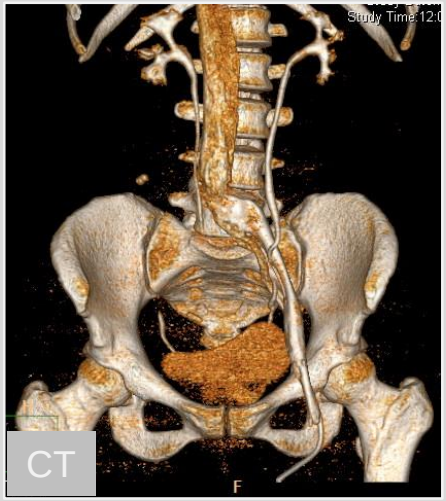
Initial Investigation and Imaging Modalities

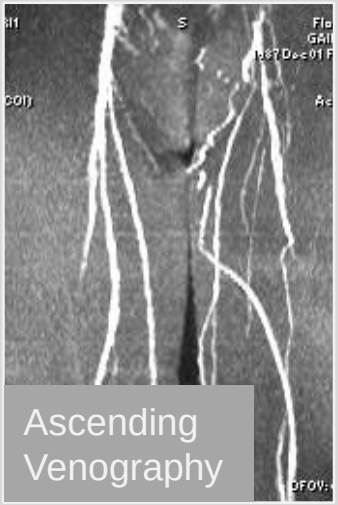
Initial Patient Investigations

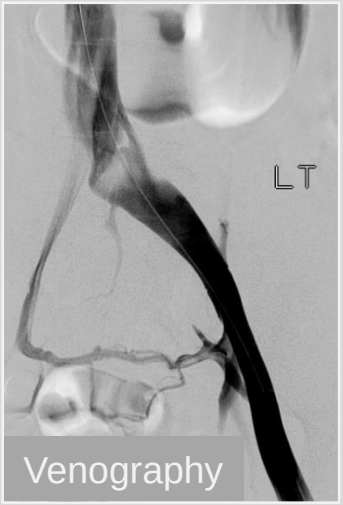
- Duplex Doppler scanning (incl. pelvic outflow)
- Transfemoral antegrade and descending venogram
- MRV, CT-V or IVUS
- Ascending venography











Images courtesy P. Neglen MD

Positive Indicators of Obstruction on Tests

- Stenosis/occlusion on DUS, venogram, MR-V, CT-V or IVUS
- Presence of collaterals
- Positive pressure test
- Absence of respiratory variations in the groin

…but the absence of collaterals, no pressure gradient and phasic variations in the groin does <u>not</u> exclude significant obstruction

Evaluating Findings to Determine if Clinically Significant

Easy to measure a hemodynamically significant arterial obstruction, while impossible in the venous system

- Unknown at what degree an obstruction is hemodynamically significant
- No test to assess hemodynamically significant stenosis is available
- **Morphological area/diameter stenosis >50% is considered significant**

Neglén P, Hollis KC, Olivier J, and Raju S. Stenting of the venous outflow in chronic venous disease: long-term stent-related outcome, clinical, and hemodynamic result. *J Vasc Surg* 2007;46:979-90.
Hartung, Otero A, Boufi M et al. Mid-term result of endovascular treatment for symptomatic chronic nonmalignant iliocaval venous occlusive disease. *J Vasc Surg* 2005;42:1138-44.
Neglén P, Raju S. Proximal lower extremity chronic venous outflow obstruction: Recognition and treatment. *Seminars in Vascular Surgery* 2002; 15:57-64.

Can the patient be stented?

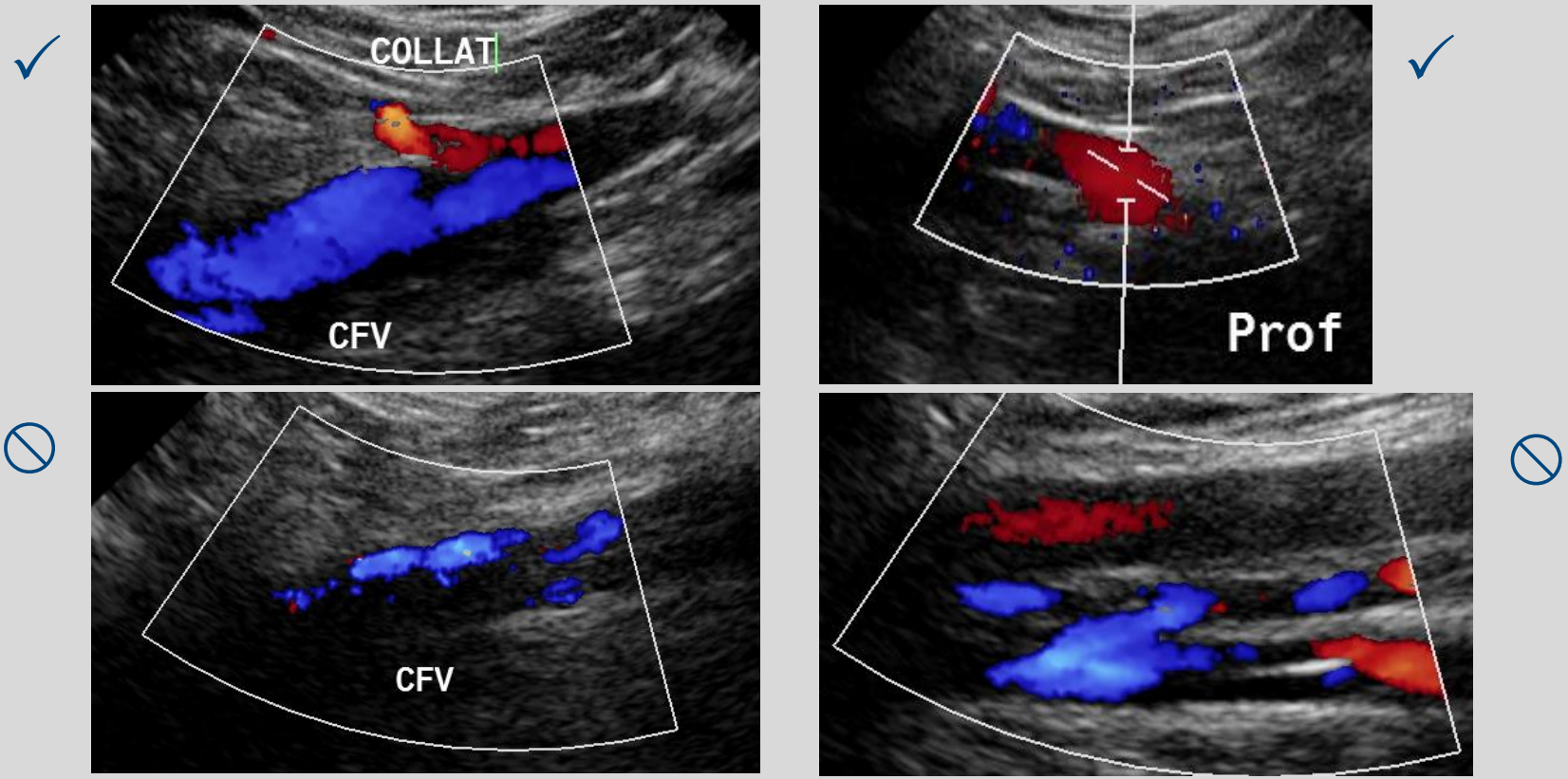
Attempt to assess the central and peripheral extent of the disease before the intervention is scheduled using DUS, venogram, CTV, MRV etc.

1. Central “landing zone” – single lumen
    a. Is the IVC patent?
    b. Does the disease involve the IVC?
    c. Is the potential outflow of the stent system appropriate?
    d. Is the contralateral venous outflow compromised?

2. Peripheral “landing zone” – single lumen
    a. Is the CFV involved?
    b. Is there a potential landing zone in the CFV above the profunda-femoral vein confluence?
    c. Is there a sufficient inflow from the periphery to sustain patency of a stent placed in the pelvic outflow?

Identifying the “Landing Zones”

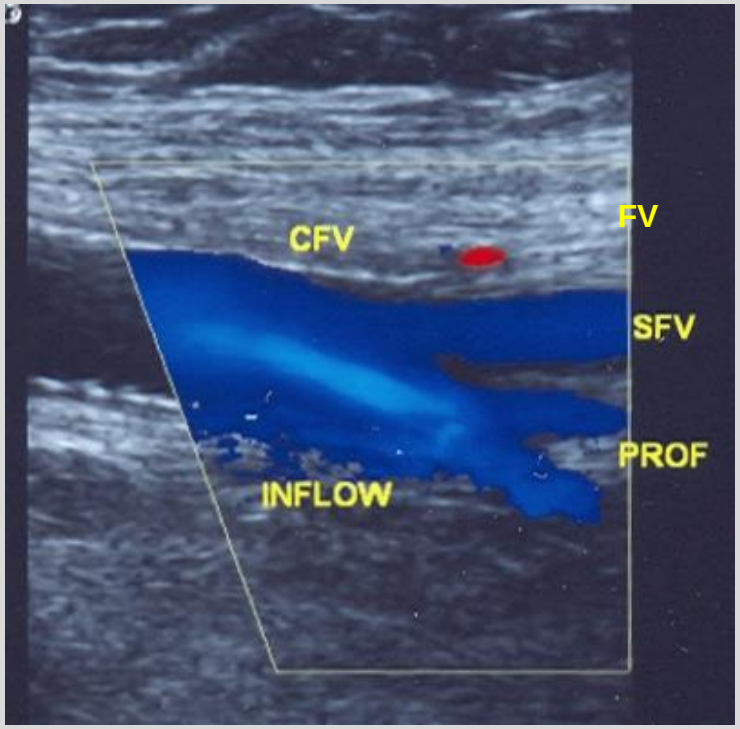
Outflow of the stent system is usually not an issue, but inflow to the CFV segment is. A one-lumen segment of the CFV vein is preferable with a “reasonable” inflow from the profunda and/or the femoral veins.

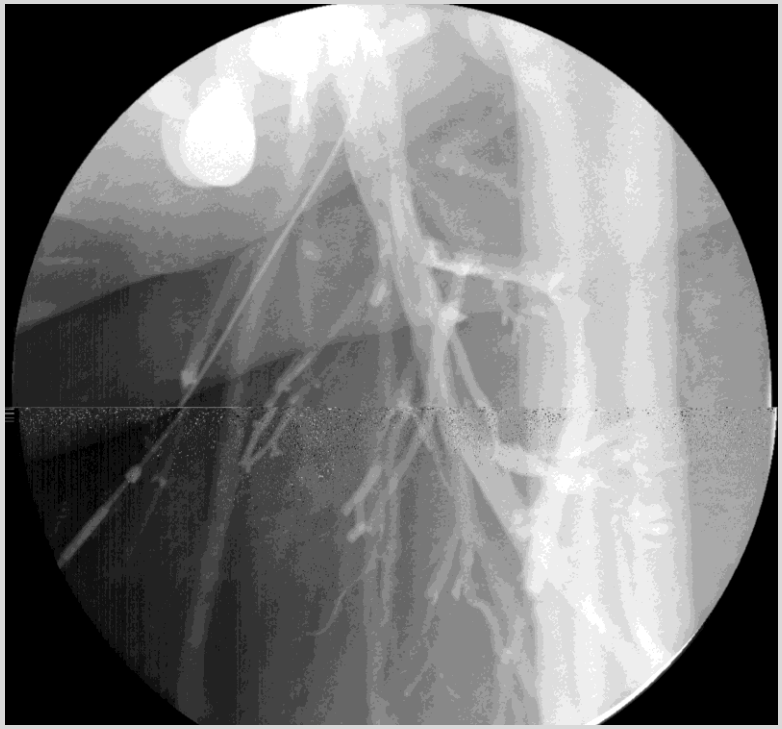


Images courtesy of Prof. A. Comerota

Assessment of the Inflow

Inflow is Vital for Patency



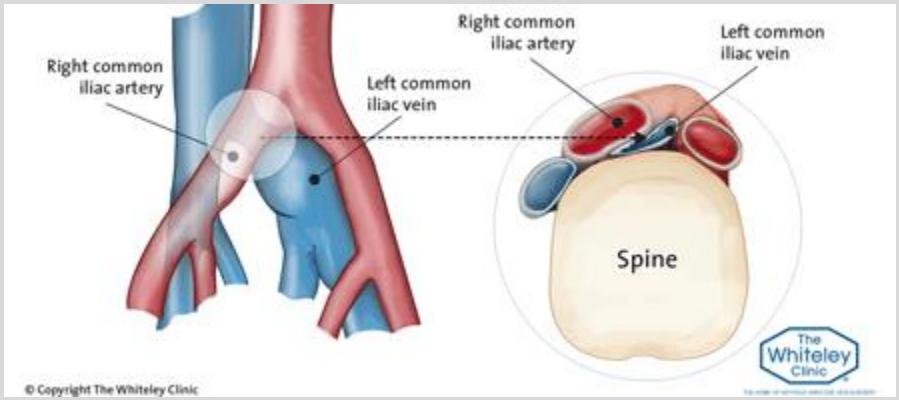


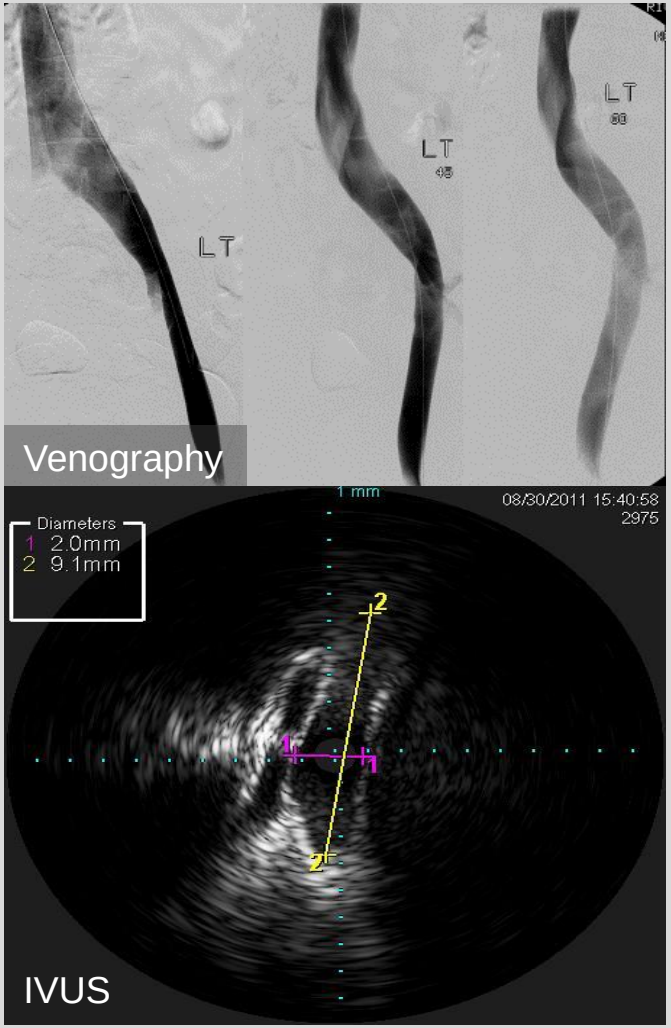
Profunda vein inflow

Images courtesy of Prof. A. Comerota

Non-Thrombotic Iliac Vein Lesion (NIVL)

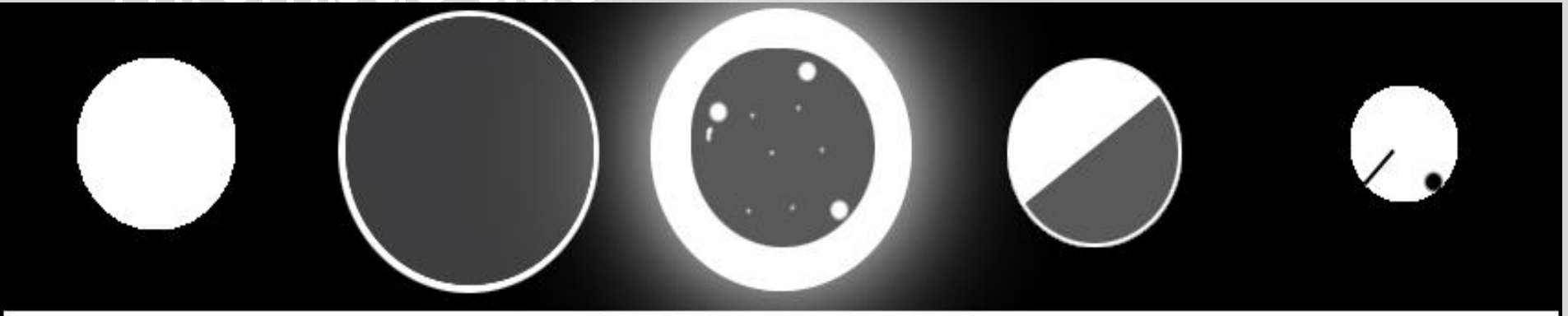
- **NIVL's can be challenging to visualize using venography alone.**
- **IVUS is often used to characterize the lesion.**





Images courtesy P. Neglen MD

Thrombus age



Normal vein

Homogeneously opacified vein lumen with no thrombus

*) It is important to distinguish a collapsed, healthy vein from a post-thrombotic diseased vein with a diminished lumen diameter

Average diameter common femoral vein: 8 - 12 mm

Acutely thrombosed vein

Dilated low-intensity vein lumen with small enhanced rim of vein wall and enhancing halo (edema)

Average diameter common femoral vein 15 - 20 mm

Subacutely thrombosed vein

Dilated low intensity vein lumen with thick enhancing rim of contrast (vein wall) Usually there are some small hyperintense areas within the thrombus as sign of recanalization

"Old" thrombosed vein

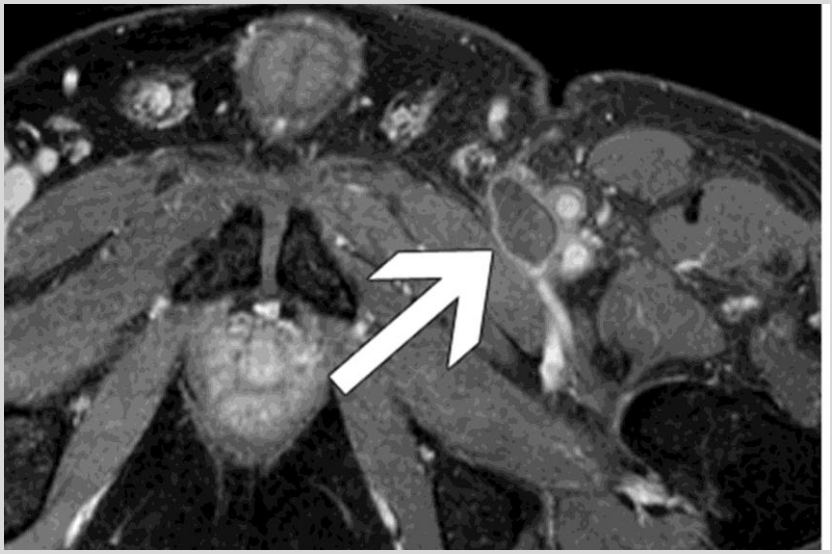
Normalisation of vein lumen in size with an opacified part (open lumen) and a low intensity part that still is filled with thrombus

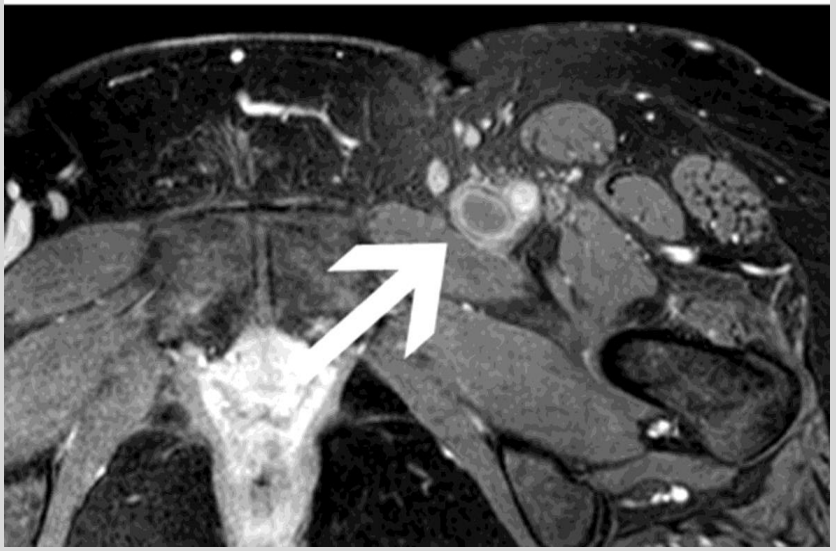
*) It is important to distinguish this from a proximal thrombus extension that does not completely obstruct the lumen

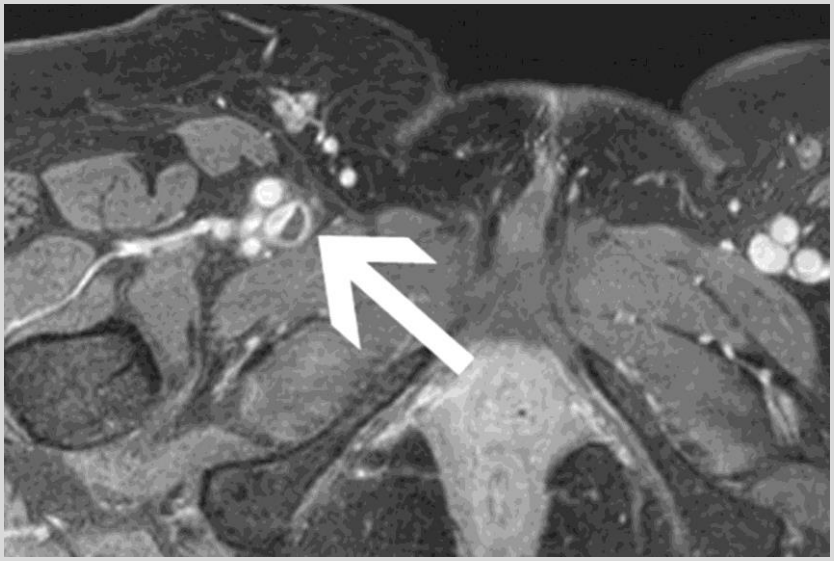
Post-thrombotic vein

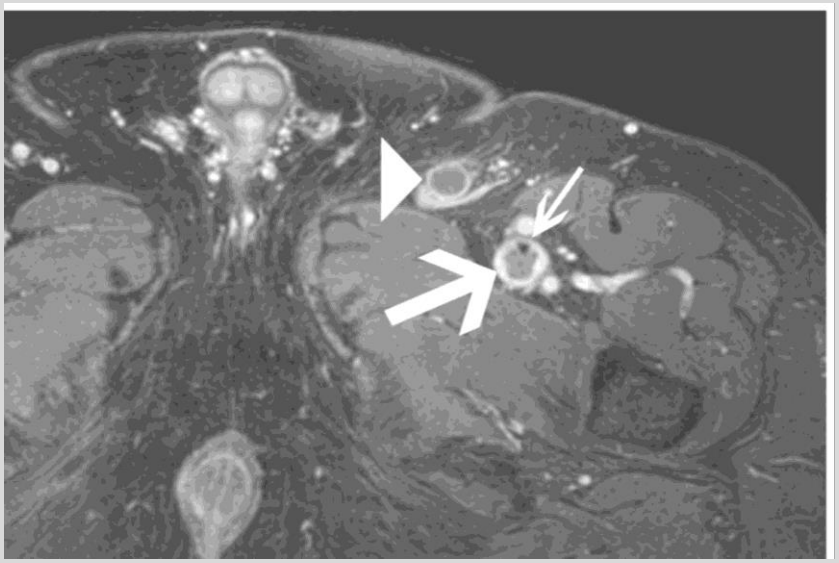
Reduced size vein lumen in comparison with normal vein which is homogeneously opacified with 1 or more sharply demarcatable very low intensity black 'dots' or lines adhered to the vein wall

Thrombus age









Lichtenberg et al: **Standards for Recanalization of Chronic Venous Outflow Obstructions. VASA accepted**

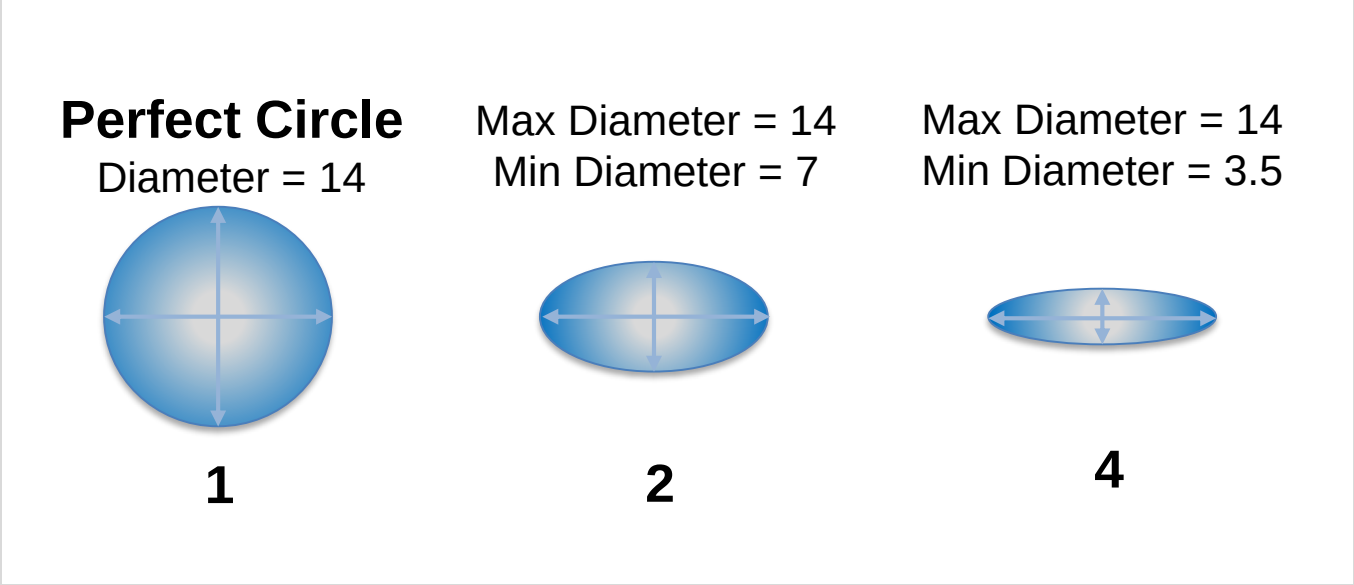
- **Advantages of IVUS**
- Dynamic measurement of area and the degree of stenosis
- Analysis of morphological changes in the vein (the formation of fibrosis, scars, thrombi)
- Dynamic evaluation of compression, such as in the presence of the May-Thurner syndrome
- No need for contrast medium in patients with kidney failure
- Exact determination of the diameter and length of the required vein stent
- Exact placement of the vein stent
- Stent analysis after implantation

Stents decrease flow resistance with a circular shape

Shape defined by Aspect Ratio

Aspect Ratio = Maximum Diameter to Minimum Diameter

Aspect Ratio



- Smaller Aspect Ratio = Better Lumen Quality

Summary

- Intervention should be considered after thorough patient diagnosis and investigation
- Combine conservative treatment (anticoagulation therapy) with invasive procedures
- Stenting should be considered if patient has a lesion >50%, is symptomatic, has good inflow and good landing zones, and a guidewire can cross the lesion

Endovascular intervention

- Optimal Interventional Setting
- Access
- Identifying Obstructive Lesion
- Stent Sizing
- Planning Stent Stack

Optimal Interventional Setting

- Appropriate operating table with C-arm:
  - Power injector
  - Subtraction
  - Image magnifier

- External ultrasound for cannulation guidance

- Consider general anesthesia in all, but especially, cases of with occlusion, bilateral disease, and IVC involvement

- Consider positioning of arms, IV lines, cables, etc. to limit interference with the C-arm With venography, multi-planar (45°, 60°, 90°) views are, generally, required

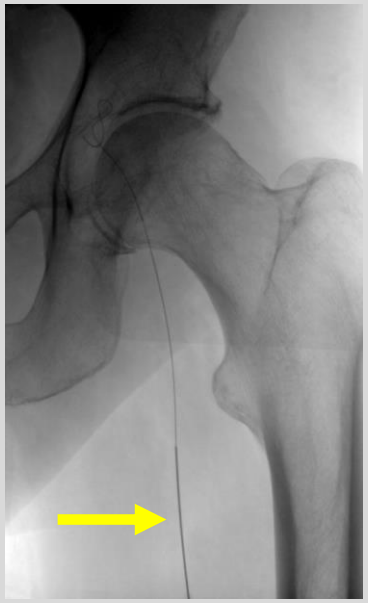
- Availability of intravascular ultrasound (IVUS)

Access Options

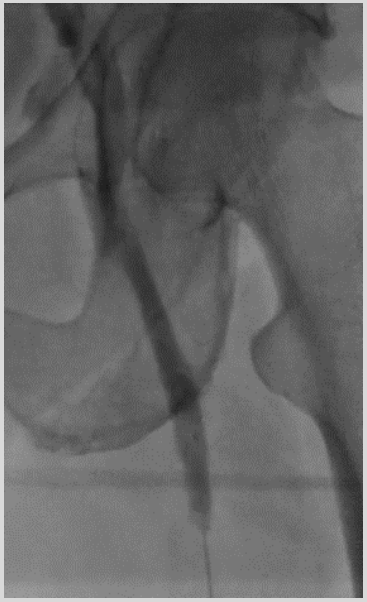
- Ipsilateral versus contralateral access
- Femoral vein
  - Facilitates recanalization of occlusions from below (“pushability”)
  - Evaluation of the inflow to the stent
  - Placement of the stent in relationship to distal tributaries
- Popliteal vein
  - Cases of catheter-directed thrombectomy
  - Access for inflow to femoral/common femoral vein
- Jugular vein – *Ensure a sterile back table is provided to support stent deployment*
- Profunda vein – When a large profunda vein is the main inflow to iliofemoral veins

Ipsilateral Mid-femoral Access

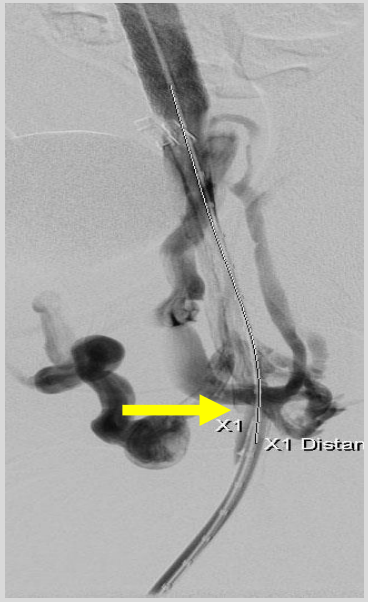
The tip of the inserted sheath needs to be ***below*** the confluence of the profunda and femoral veins (anatomical landmark - trochanter minor)



Mid-thigh access



Entire CFV visualized



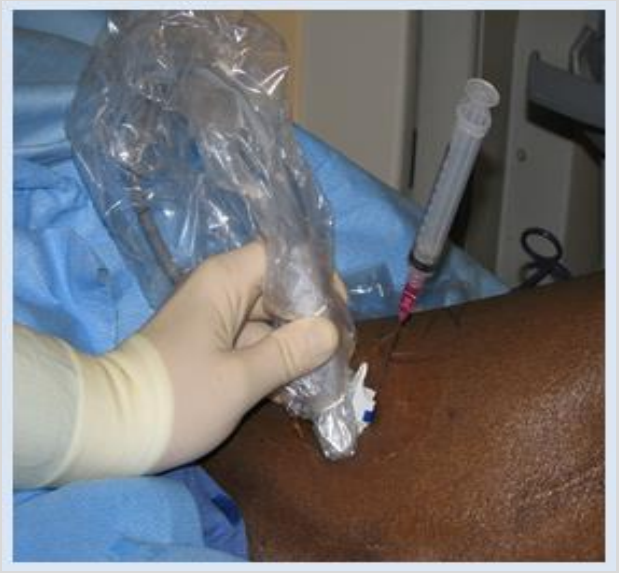
Too high a stick

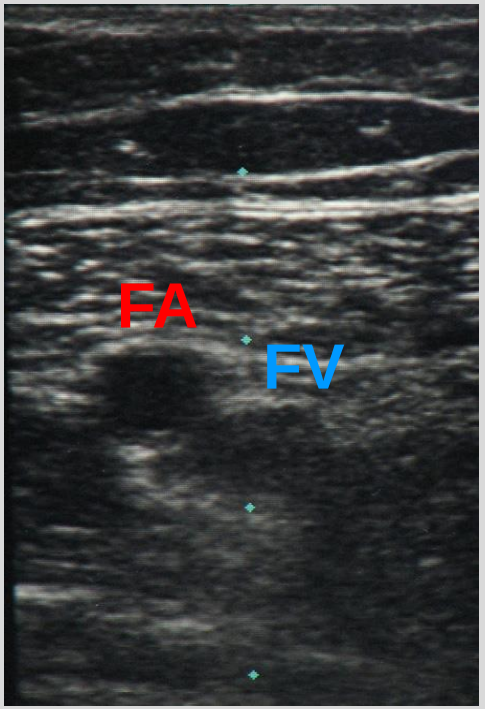
This is to allow:

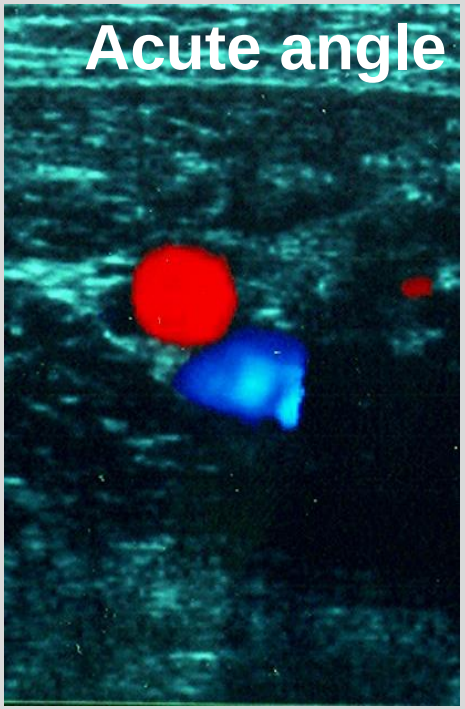
- The entire common femoral vein (CFV) to be visualized
- Assessment of the flow into the stent system

Identifying the Femoral Vein

Slide the U/S probe distally from the CFV and identify the profunda-femoral vein confluence…



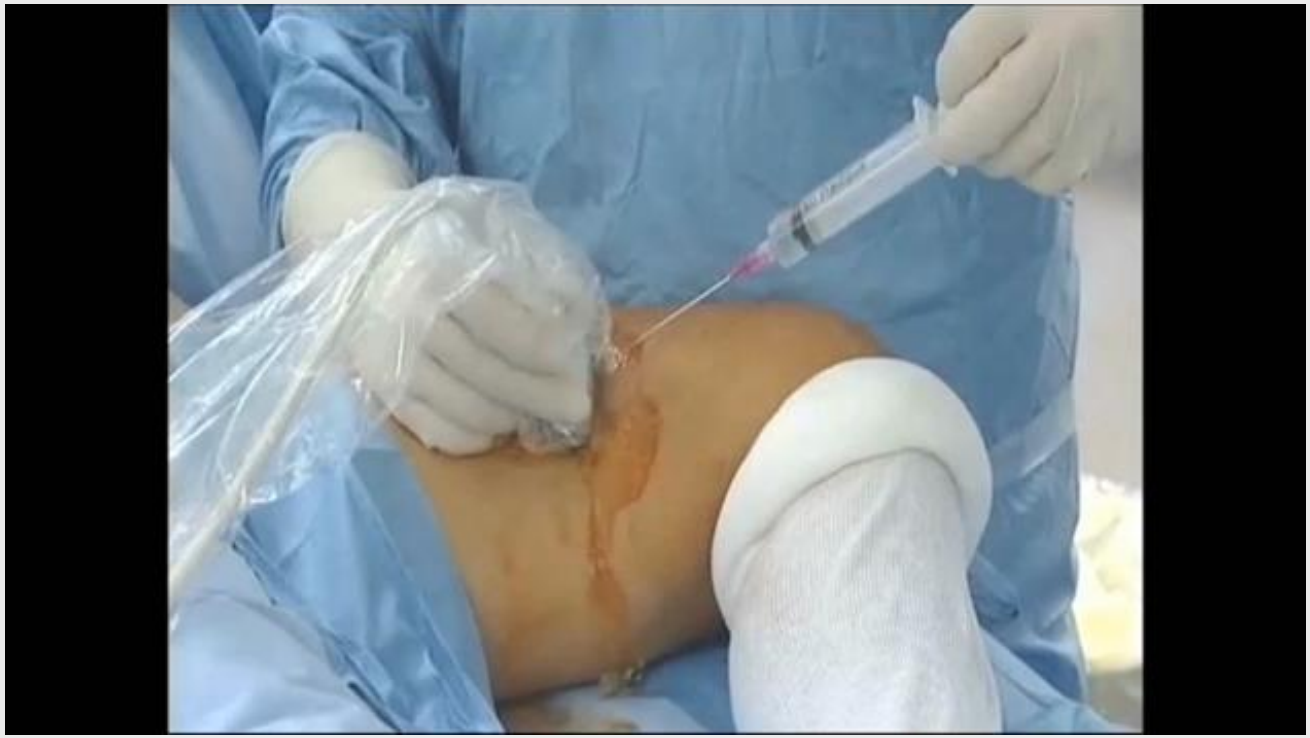




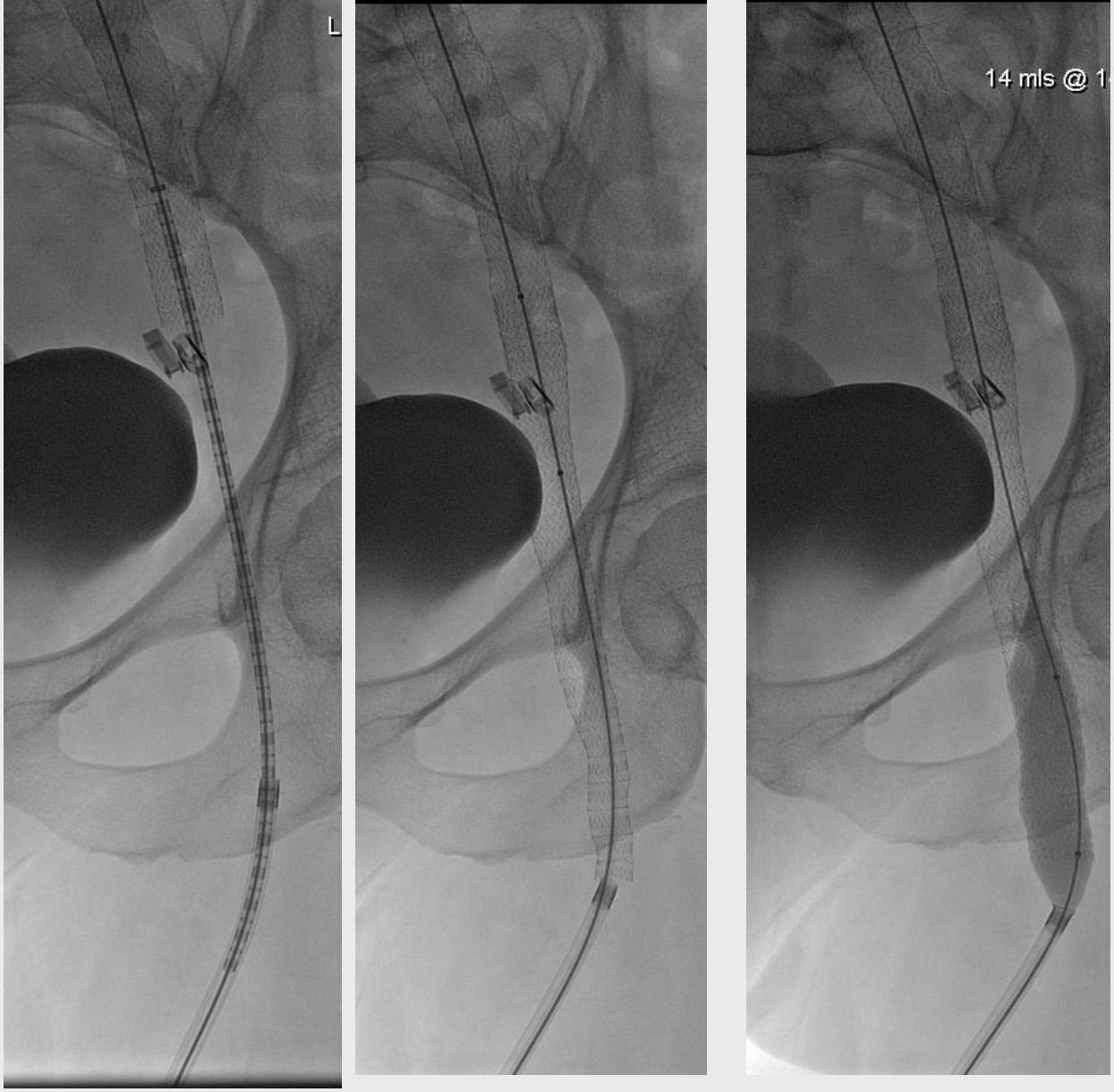
(Transverse image shown)

- At the mid-thigh, the femoral vein will stay separated from the artery
- Note: Acute, rather than obtuse, angle of the needle track

Images courtesy P. Neglen MD



- Patient in “frog leg” position on table
- Use ultrasound to identify femoral vein
  - U/S gel facilitates imaging
  - Transverse (shown above) or longitudinal approaches
- Initial venipuncture with 20- to 22-ga needle on a 10-mL syringe
- Introduce guide wire
- Replace needle with introducer sheath
- Return patient’s legs to supine position



Watch out for foreshortening-
This is a definite potential disadvantage of this site of access
Brite Tip Sheath is key

Stent Placement

- ☑ Optimal Interventional Setting
- ☑ Access
- ❑ Identifying Obstructive Lesion
- ❑ Stent Sizing
- ❑ Planning Stent Stack

Identifying the Obstructive Lesion

- Venography
  - Ideally, power injector with subtraction
  - Multi-planar views (45°, 60°, 90°) to identify location of stenosis and extent
  - Shows collaterals and inflow/outflow

- *However:*
  - Underestimates stenosis by 30%
  - Inaccurate location or extent on venogram in 41%
  - Normal venogram findings in 17-25%

Hingorani A, Alhabouni S, Ascher E, et al. Role of IVUS versus venograms in assessment of iliac-femoral vein stenosis. *J Vasc Surg*. 2010;52:804.
Raju S, Neglen P. High prevalence of nonthrombotic iliac vein lesions in chronic venous disease: a permissive role in pathogenicity. *J Vasc Surg*. 2006;44:136–144.
Neglen P, Raju S. Intravascular ultrasound scan evaluation of the obstructed vein. *J Vasc Surg*. 2002;35:694–700.
Forauer AR, Gemmete JJ Intravascular ultrasound in the diagnosis and treatment of iliac vein compression (May-Thurner) syndrome. *J Vasc Interv Radiol*. 2002;13(5):523-7.

Reference Vein Diameter (RVD)

Each Target Vein Segment (TVS) has an RVD:

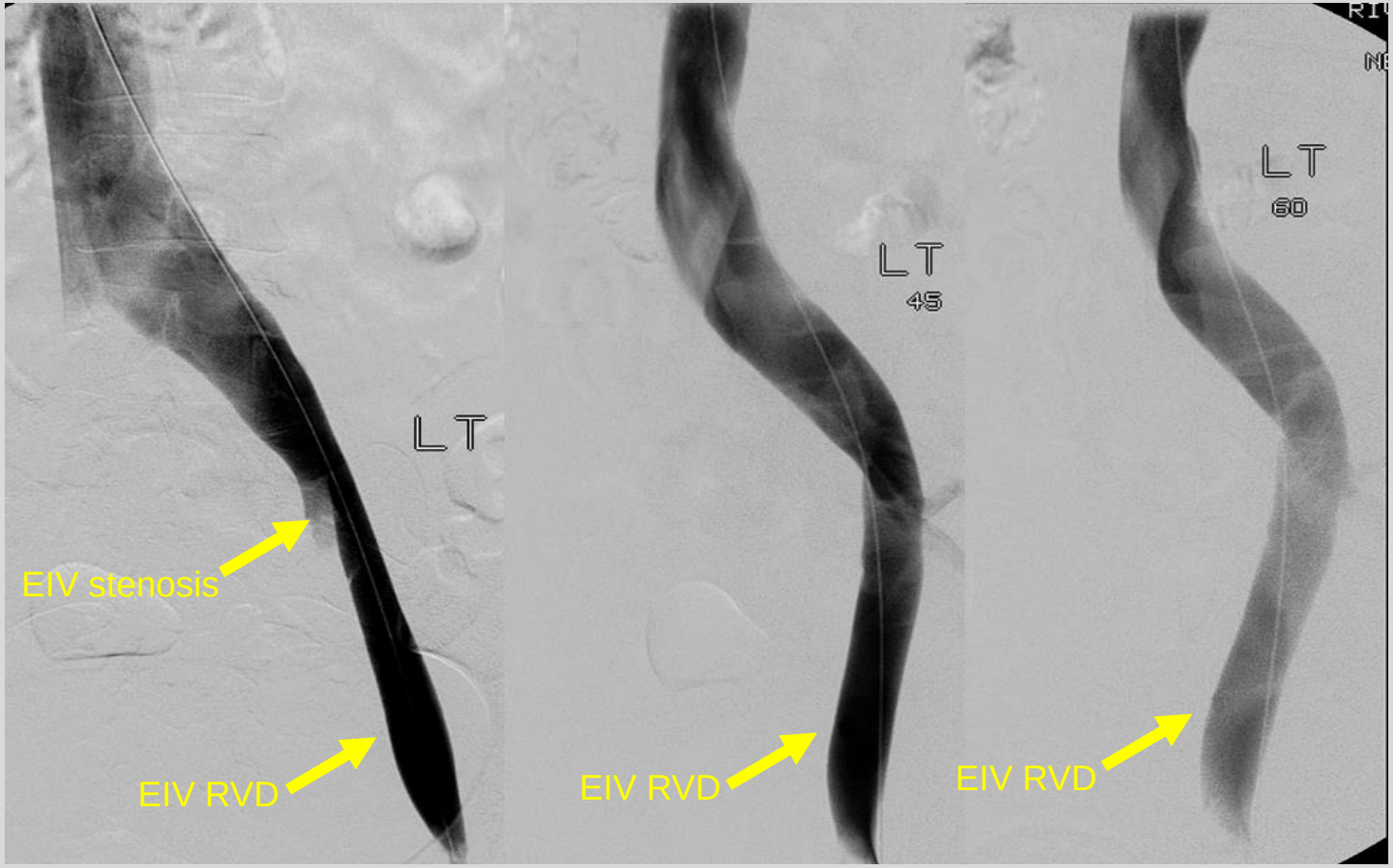
- Will be measured in normal healthy vein
- Must accurately assess lesion and landing zones
- Appropriate stent diameter estimated (in order of preference):
  - The venous segment immediately peripheral to the TVS.
  - The venous segment immediately central to the TVS.
  - The contralateral venous segment at the same level as the TVS.
  - The literature-reported vein diameter of the CIV (16 mm), EIV (14 mm), and CFV (12 mm).

Gasparis A. Labropuolous N. (2011, February) Venous Outflow Obstruction, Managing Intervention After Iliofemoral Thrombolysis. *Endovascular Today.*.

Identifying Lesion and RVD - NIVL

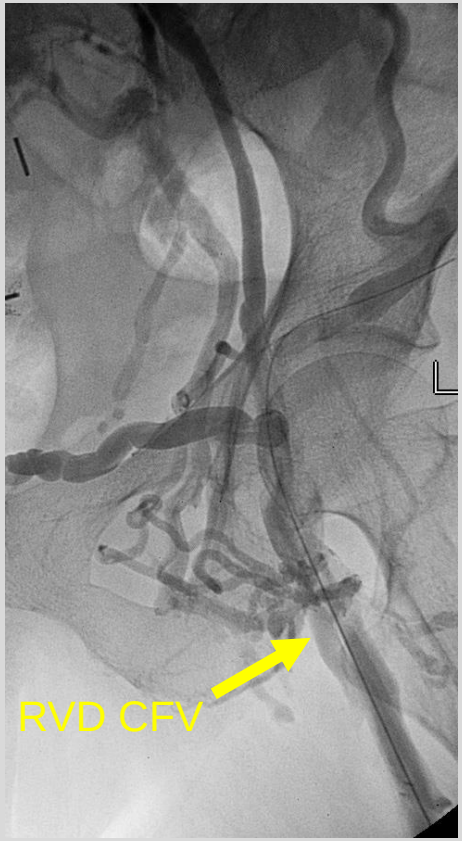
Use the tightest stenosis in any projection

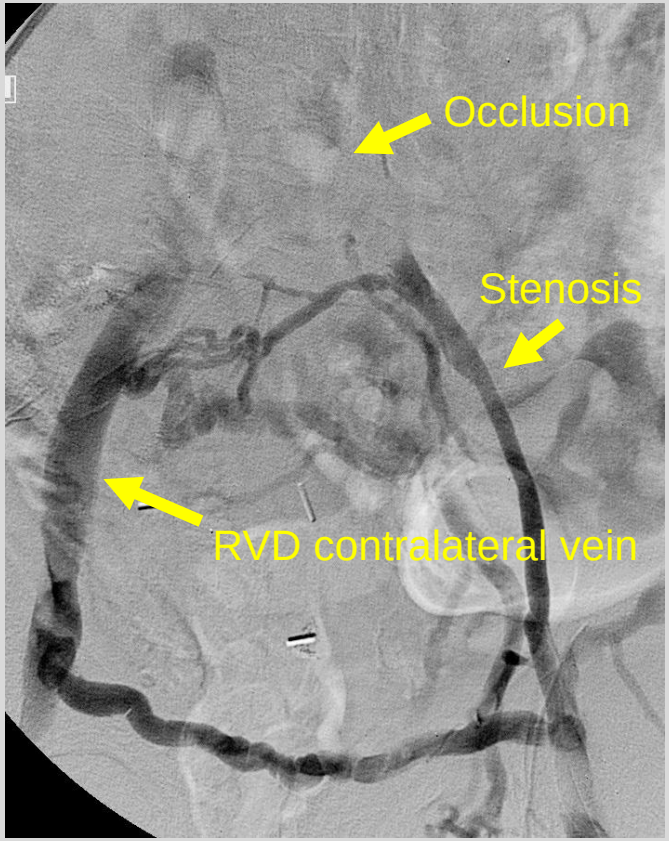
RVD for EIV is the peripheral EIV above the inguinal ligament



Images courtesy P. Neglen MD

Identifying Lesion and RVD - PTS





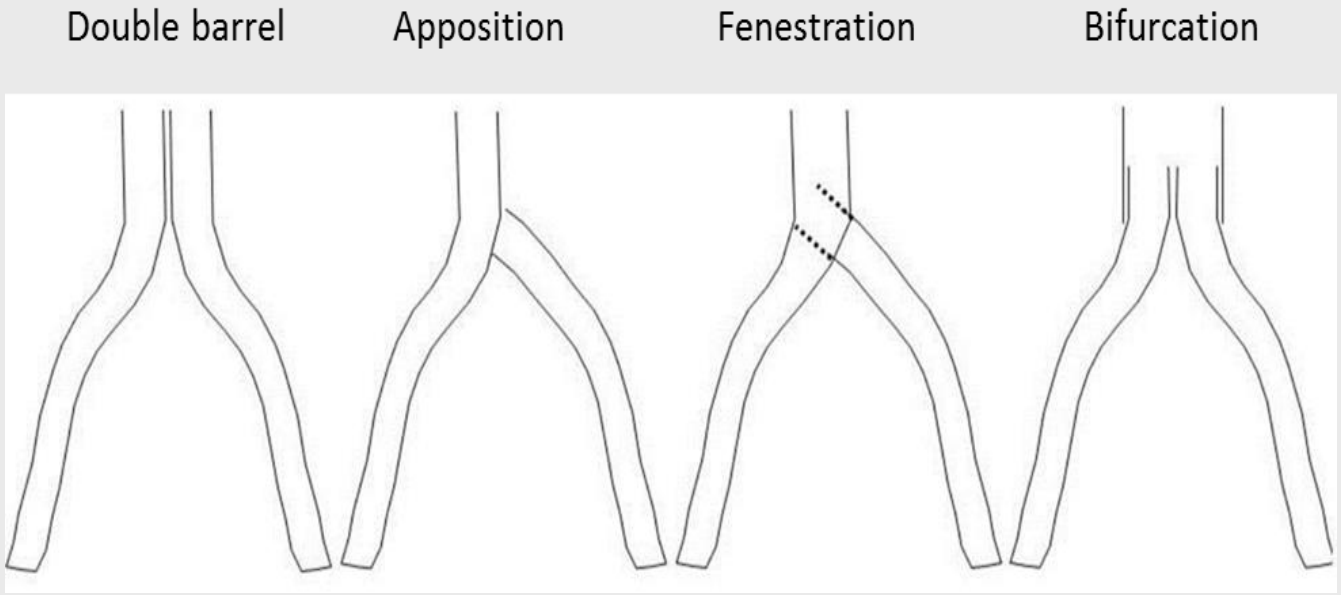
The last option being the literature-reported vein diameter

Images courtesy P. Neglen MD

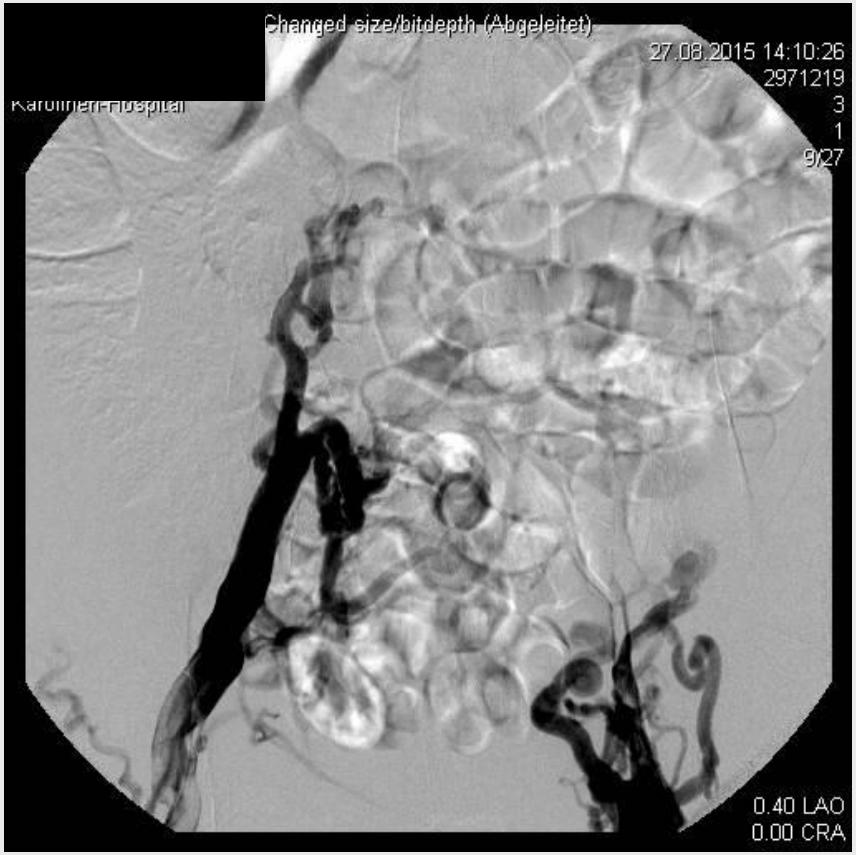
Stent Placement

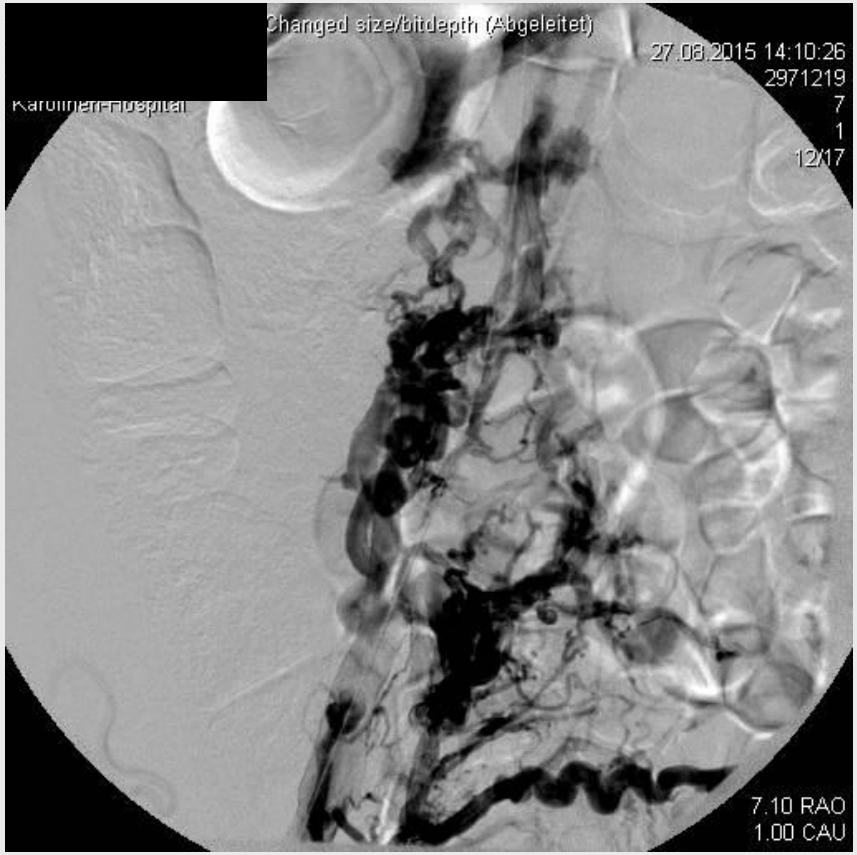
- ☑ Optimal Interventional Setting
- ☑ Access
- ☑ Identifying Obstructive Lesion
- ☑ Stent Sizing
- ☐ Planning Stent Stack

Graaf et al., Cardiovasc Intervent Radiol. 2015;38:1198-204 (30).

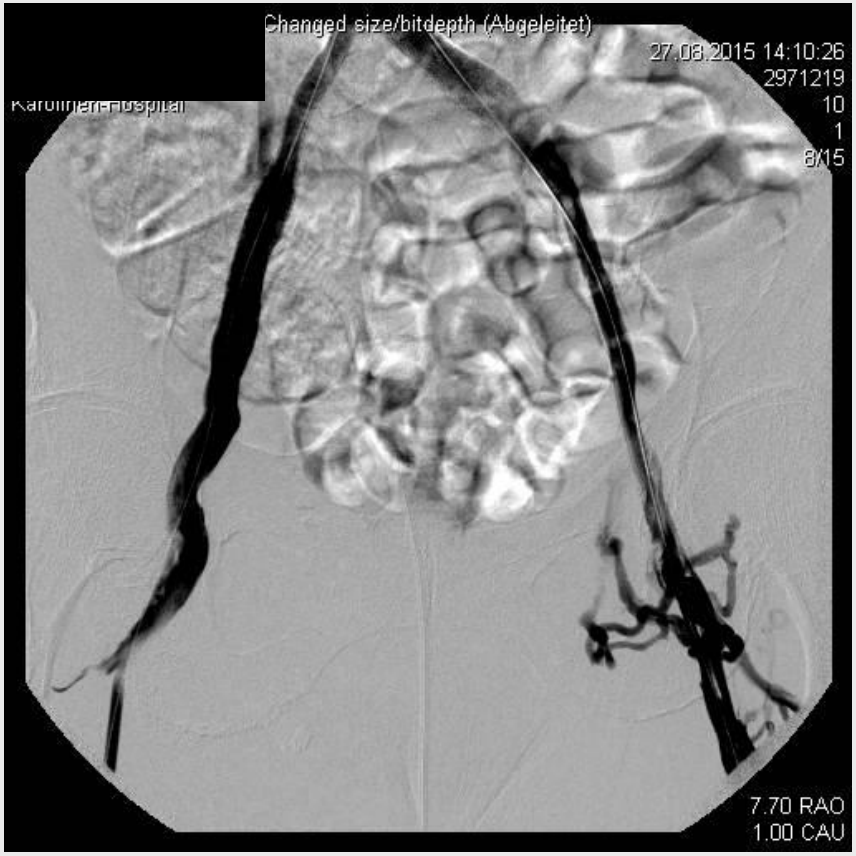


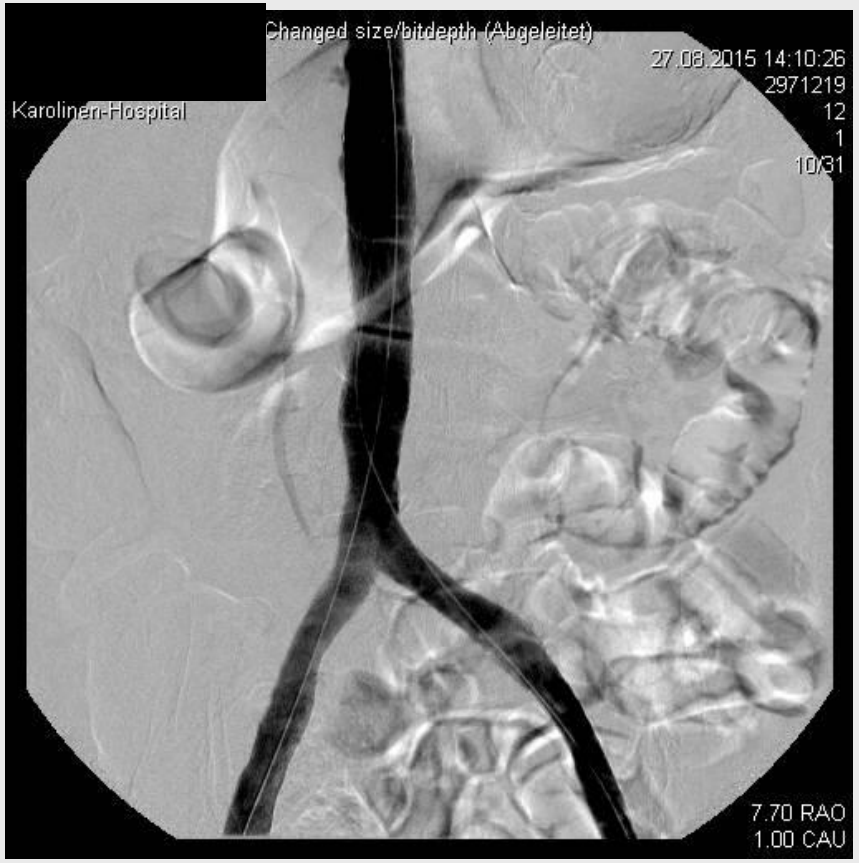
C6 Stadium, 58 Jahre, Z.n. peripartaler Thrombose vor 30 Jahren



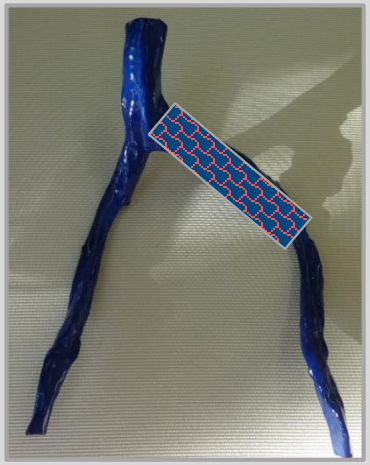


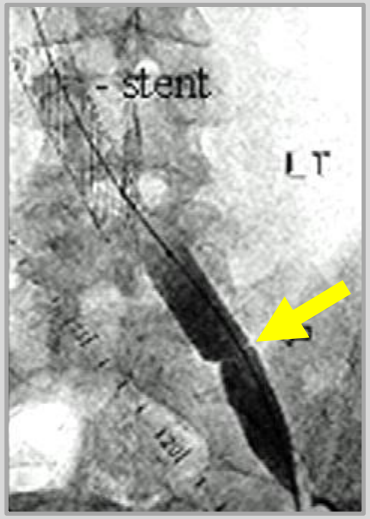
Sinus XL Stent (22 x 80 mm)
4 x Veniti Stent (16 x 120 mm + 14 x 60 mm)





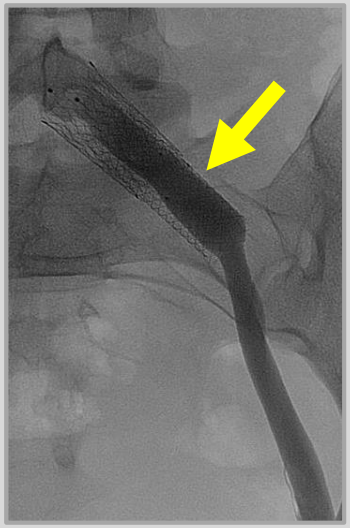
Special Considerations:
Confluence of Internal and External Iliac Veins

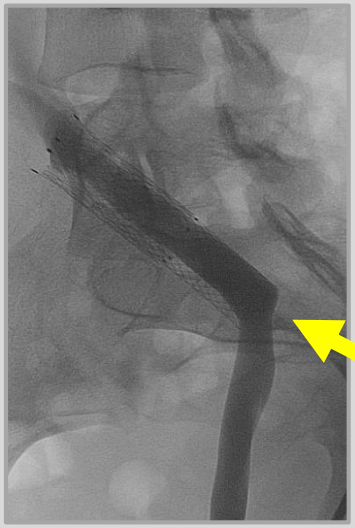




"De novo" stenosis: Stents landing at confluence of two veins, in different planes, with change in inflow rate

"De novo" stenosis

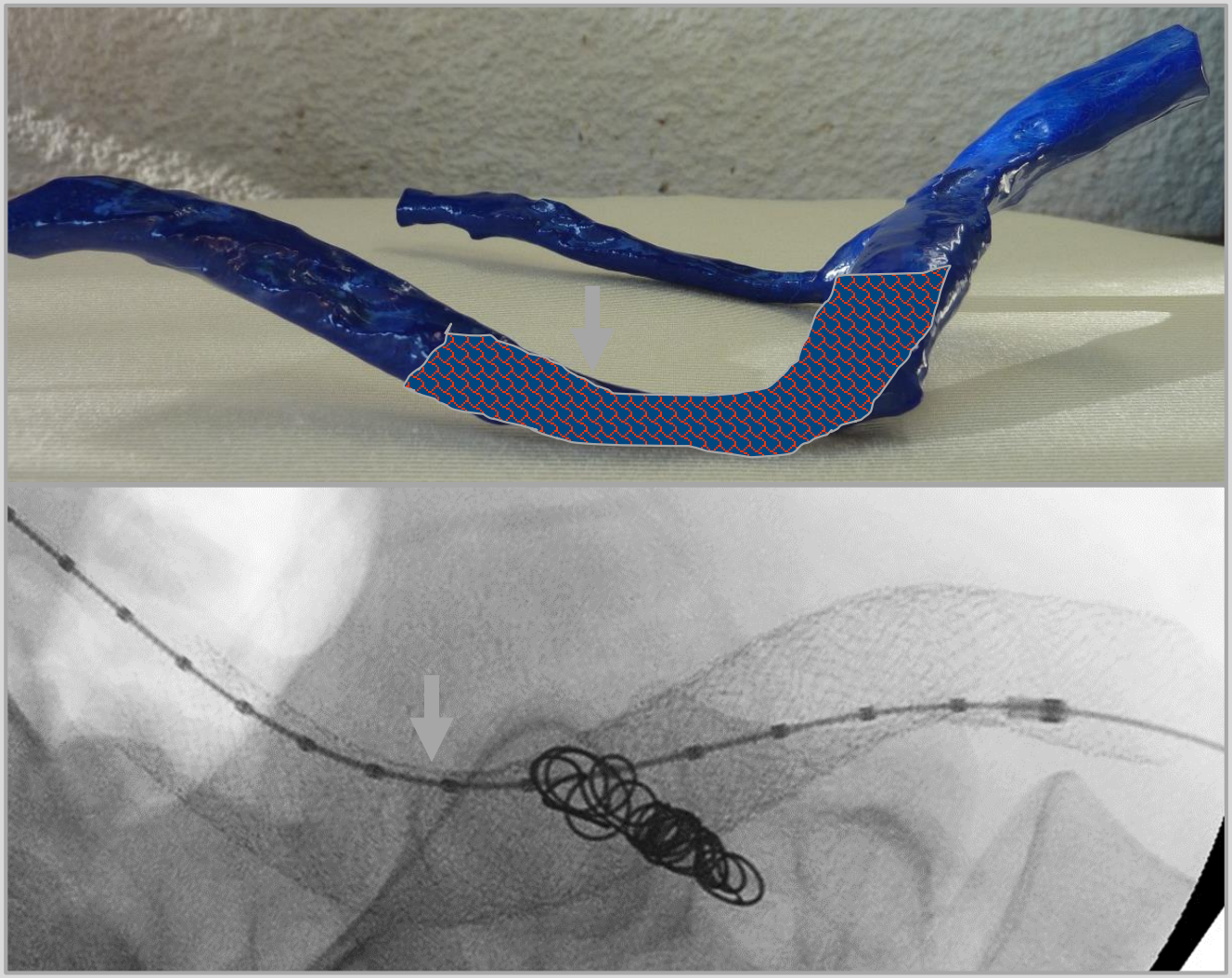




Straightening and "tenting" of vein

Images courtesy P. Neglen MD

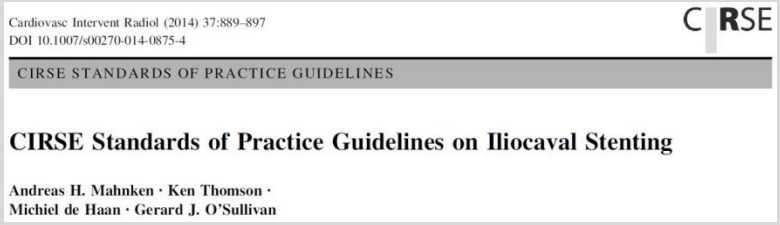
“Going around the curve” – 120 mm stent



Images courtesy P. Neglen MD

Special Considerations:
Inguinal Ligament – A concern?

Lichtenberg et al: **Standards for Recanalization of Chronic Venous Outflow Obstructions. VASA accepted**

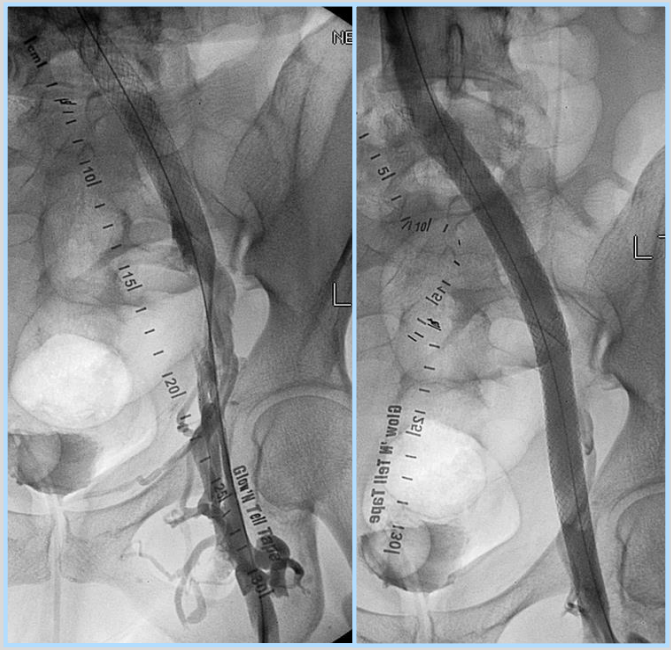

Cardiovasc Intervent Radiol (2014) 37:889–897
DOI 10.1007/s00270-014-0875-4

CIRSE

CIRSE STANDARDS OF PRACTICE GUIDELINES

CIRSE Standards of Practice Guidelines on Iliocaval Stenting

Andreas H. Mahnken · Ken Thomson ·
Michiel de Haan · Gerard J. O'Sullivan



"Stenting across the inguinal ligament should be avoided."

- Guidelines present risk/benefits:

  Risks
  - No data on venous stent fracture
  - Increased risk of early in-stent stenosis

  Benefits
  - ***"Stenting down to a normal flow segment is more important than avoiding crossing the inguinal ligament."***

- Stents should not overlap at the inguinal ligament.

Mahnken A, Thompson K, de Haan M, O'Sullivan G. CIRSE Practice Guidelines on Iliocaval Stenting. *Cardiovasc Intervent Radiol* 2014;37:889–897.

Successful Venous Stenting

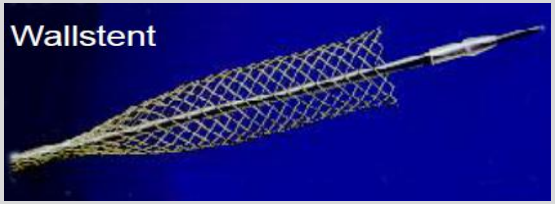
- Understand the venous disease and the obstructive lesion
- Careful selection of patients
- Use optimal setting and techniques
- Adequate anticoagulation therapy and surveillance

ANTICOAGULATION peri-procedure and long-term after a femoro-ilio-caval stent procedure			
Acute IF DVT following early clot removal and stenting	**Non-thrombotic iliac vein lesion** (May-Turner's Syndrome without any concomitant DVT)	**Chronic postthrombotic obstruction**	
		Non-occlusive Obstruction with adequate inflow	Occlusion and/or suboptimal inflow
Stenting performed in one stage after termination of lysis • 3-5000 U heparin i.v. during procedure • Immediate full dose LMWH s.c. at the end of the procedure • SCD compression/early ambulation post-procedure • Start conversion to warfarin same day	Peri-procedure • Prophylactic dose of LMWH before and after procedure • 3-5000 U heparin i.v. during the procedure • SCD compression/early ambulation post-procedure	Peri-procedure • Prophylactic dose of LMWH before procedure • 3-5000 U heparin i.v. during procedure • Immediate full dose LMWH s.c. at the end of the procedure • SCD compression/early ambulation post-procedure • Start conversion to warfarin same day (Non-occlusive obstruction)	
Long-term • Continue standardized conservative treatment as per guidelines incl. BK 20-30mmHg stockings and exercise. Give full dose anticoagulation with LMWH for at least 5 days after intervention and stop LMWH when INR is therapeutic (INR 2.0-3.0).	Long-term • low dose aspirin daily (75-100mg orally) • The stent procedure per se does not require extended (life-long) anticoagulation (warfarin) as a routine 6 months anticoagulation	Long-term • Oral anticoagulation for 6-12 months • Extended (life-long) in patients who is on AC prior to the procedure • Consider extended (life-long) coagulation depending on the VTE disease as per guidelines (e.g. in patients with recurrent DVT, family history, unprovoked first DVT, type of thrombophilia etc.) • The stent procedure per se does not require extended (life-long) anticoagulation (warfarin) as a routine	Long-term • Full dose LMWH alone for at least 14 days • Then start warfarin after stent patency verified by DUS • Oral anticoagulation for 6-12 months • Consider extended (life-long) anticoagulation (warfarin) in all patients with chronic occlusive disease, especially those with a sub-optimal inflow, regardless of guidelines.

Venous Stent Options (CE)

Klinikum Arnsberg
Akademisches Lehrkrankenhaus
Westfälische Wilhelms-Universität Münster

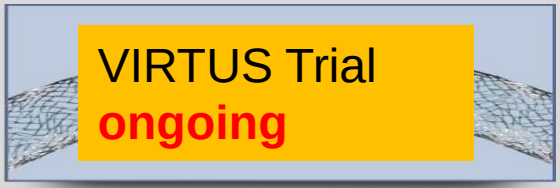
Boston Wallstent



Optimed

Cook Zilver Vena

Veniti Vici



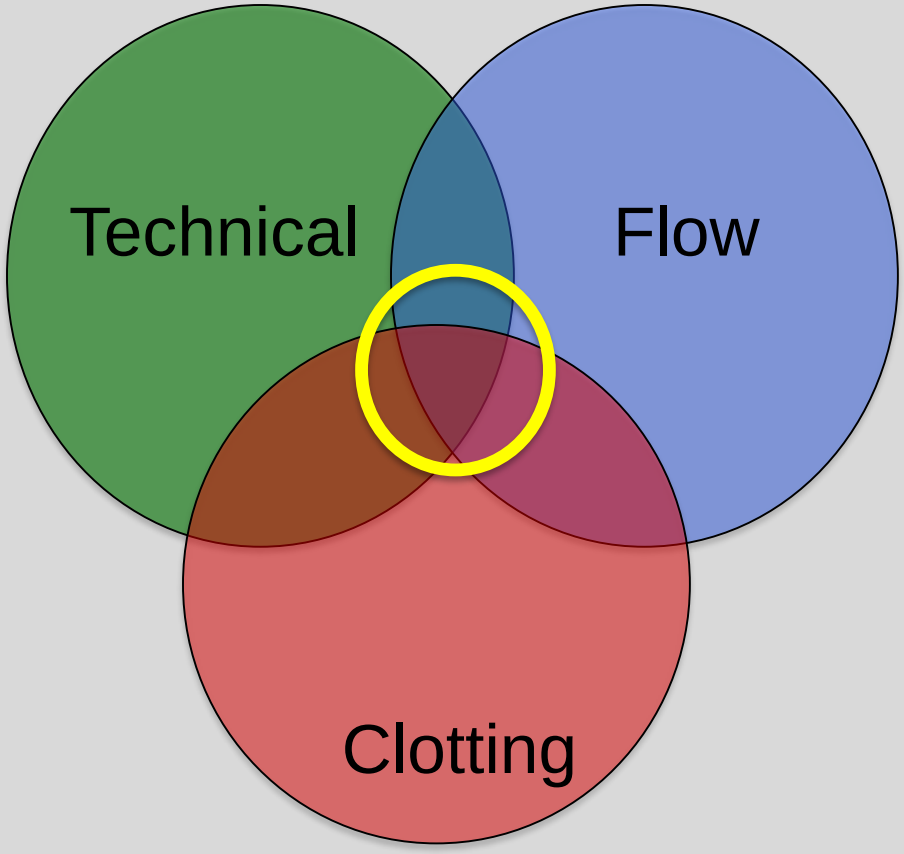
Optimed Sinus obliquus

Bard Venovo

Medtronic ABRE

Stent patency

Stent Choice
Force/
Flexibility
Placement



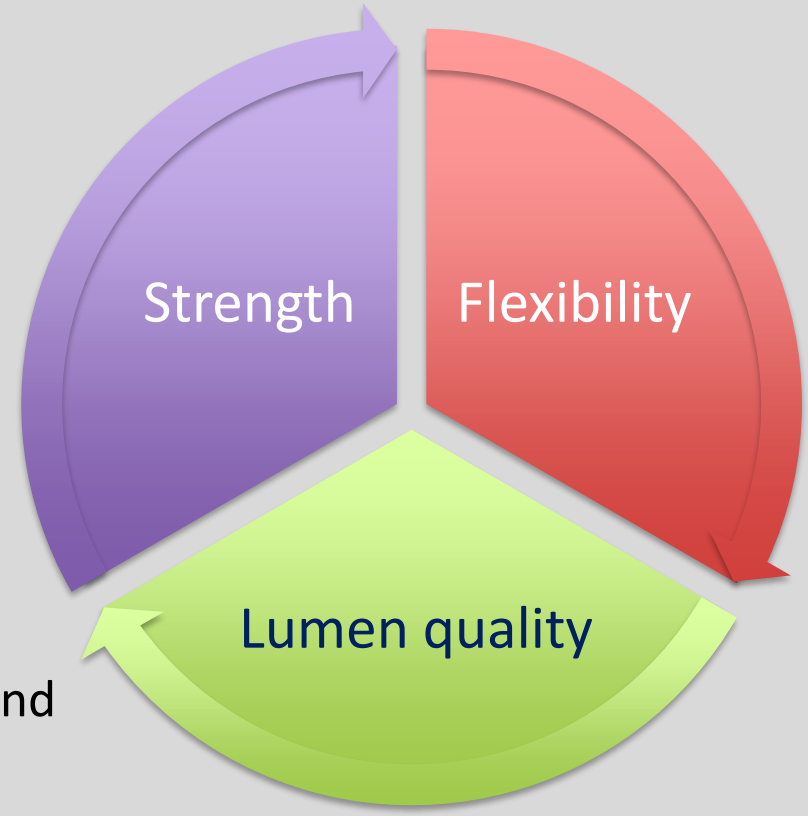
Inflow
Outflow

Anti-coagulation

Venous Stent Attributes

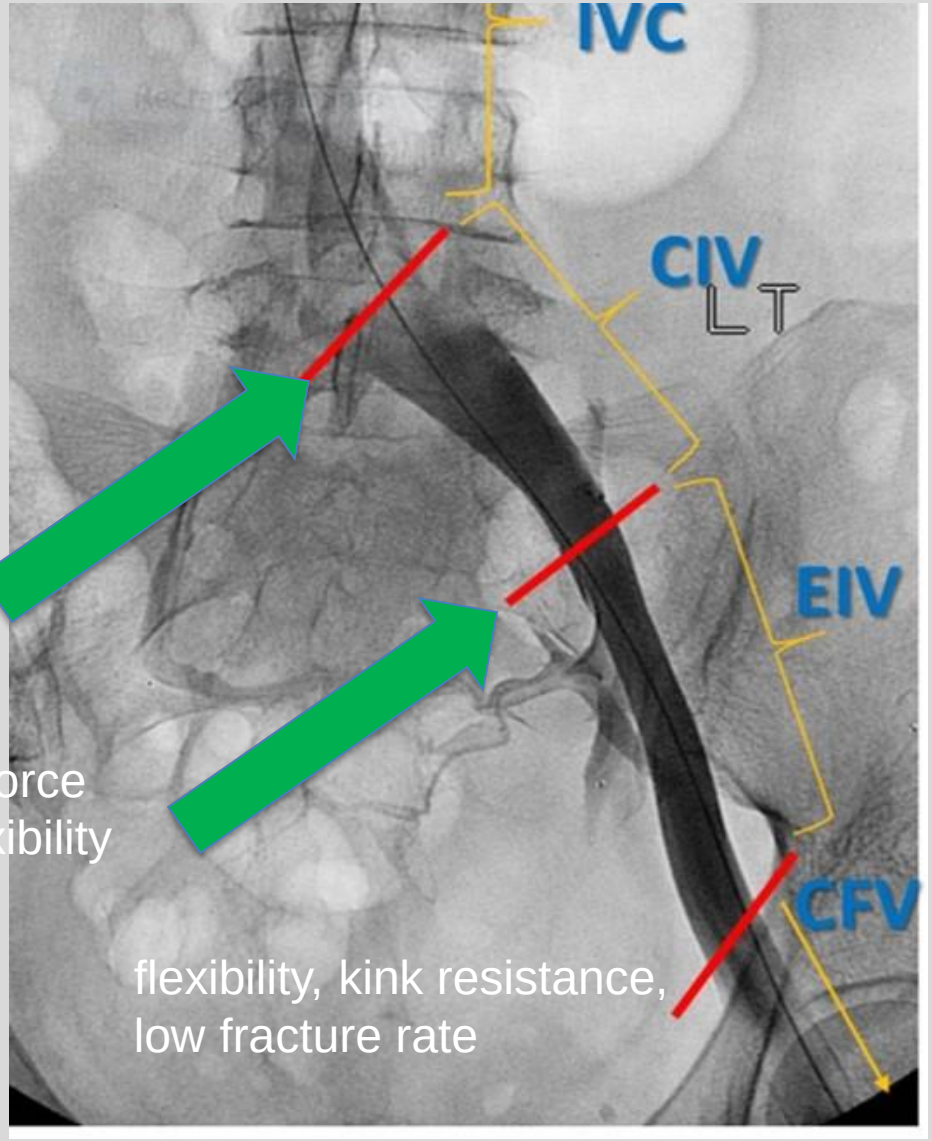
Klinikum Arnsberg
Akademisches Lehrkrankenhaus
Westfälische Wilhelms-Universität Münster

- Self-expandable
- Crush resistant across length of stent
- Sufficient chronic outward force
- Sufficient wall coverage
- Flexibility sufficient to resist kink at physiological angles
- Durability allowing repeated shortening, twisting, and bending at the groin
- Minimal foreshortening on deployment and balloon dilation
- Predictable, consistent deployment



…there is not a perfect venous stent for the whole system..

Different venous stents for different locations

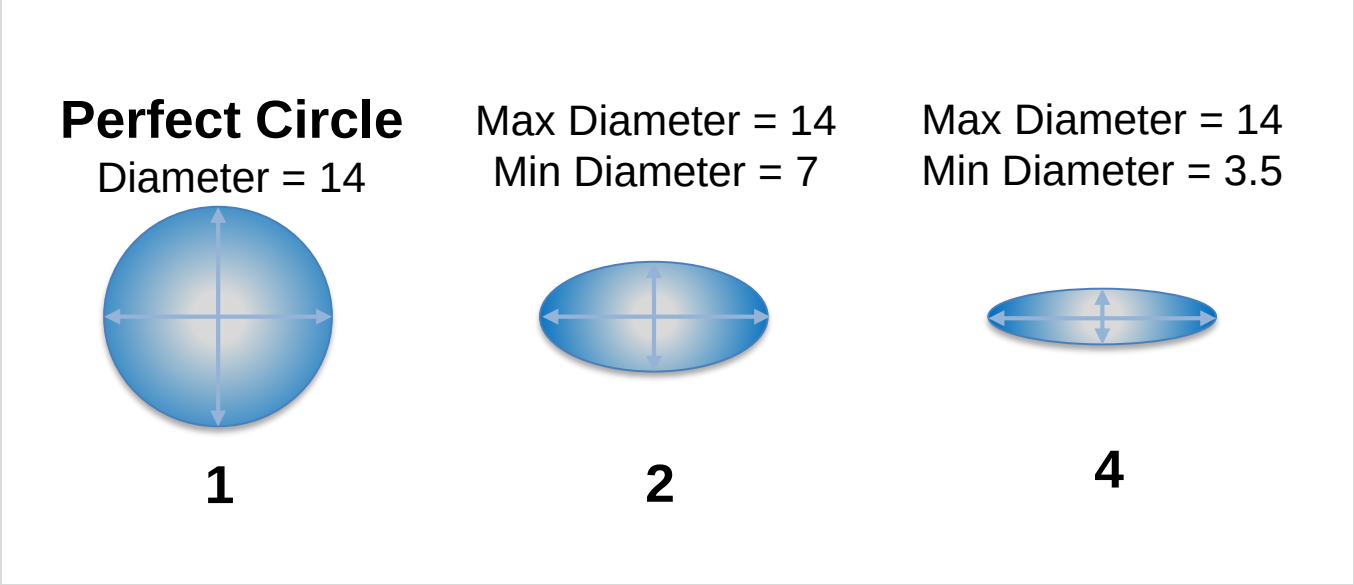


Stents decrease flow resistance with a circular shape

Shape defined by Aspect Ratio

Aspect Ratio = Maximum Diameter to Minimum Diameter

Aspect Ratio



- Smaller Aspect Ratio = Better Lumen Quality

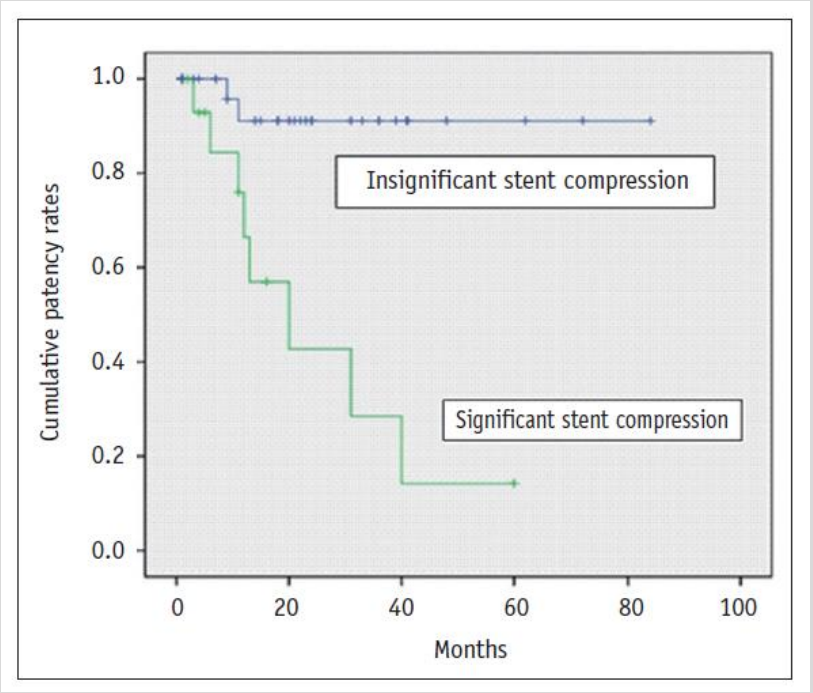
Stent Compression in Iliac Vein Compression Syndrome Associated with Acute Ilio-Femoral Deep Vein Thrombosis

Hun Cho, MD[1], Jin Woo Kim, MD[1], You Sun Hong, MD[2], Sang Hyun Lim, MD[2], Je Hwan Won, MD[1]

Departments of [1]Radiology and [2]Thoracic & Cardiovascular Surgery, Ajou University School of Medicine, Suwon 443-380, Korea

Klinikum Arnsberg
Akademisches Lehrkrankenhaus
Westfälische Wilhelms-Universität Münster

- 48 patients with iliac compression and acute DVT followed for average of 20 months
- Follow-up was performed with CT venography
- Stent compression considered significant if lumen compression was greater that 50% (Aspect Ratio 1:2, or 2)
- Significant stent compression was inversely correlated with stent patency ($p < 0.001$)



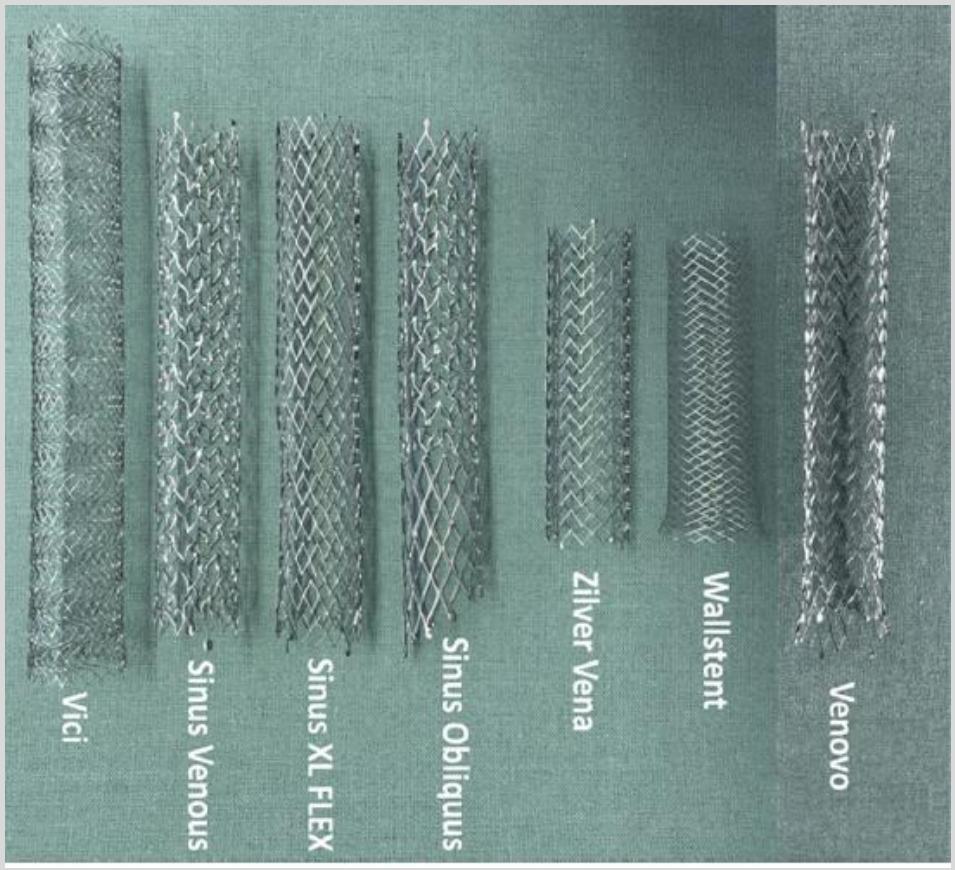
Cho H, Kim JK. Stent Compression in IVCS Associated with Acute Ilio-Femoral DVT. *Korean J Radiol.* 2015;16(4):723-728.

Cardiovasc Intervent Radiol
https://doi.org/10.1007/s00270-018-1916-1

LABORATORY INVESTIGATION

Physical Properties of Venous Stents: An Experimental Comparison

Darius Dabir[1] · Andreas Feisst[1] · Daniel Thomas[1] · Julian A. Luetkens[1] · Carsten Meyer[1] · Ana Kardulovic[2] · Matthias Menne[2] · Ulrich Steinseifer[2] · Hans H. Schild[1] · Daniel L. R. Kuetting[1]



Cardiovasc Intervent Radiol
https://doi.org/10.1007/s00270-018-1916-1

LABORATORY INVESTIGATION

Physical Properties of Venous Stents: An Experimental Comparison

Darius Dabir[1] · Andreas Feisst[1] · Daniel Thomas[1] · Julian A. Luetkens[1] · Carsten Meyer[1] · Ana Kardulovic[2] · Matthias Menne[2] · Ulrich Steinseifer[2] · Hans H. Schild[1] · Daniel L. R. Kuetting[1]

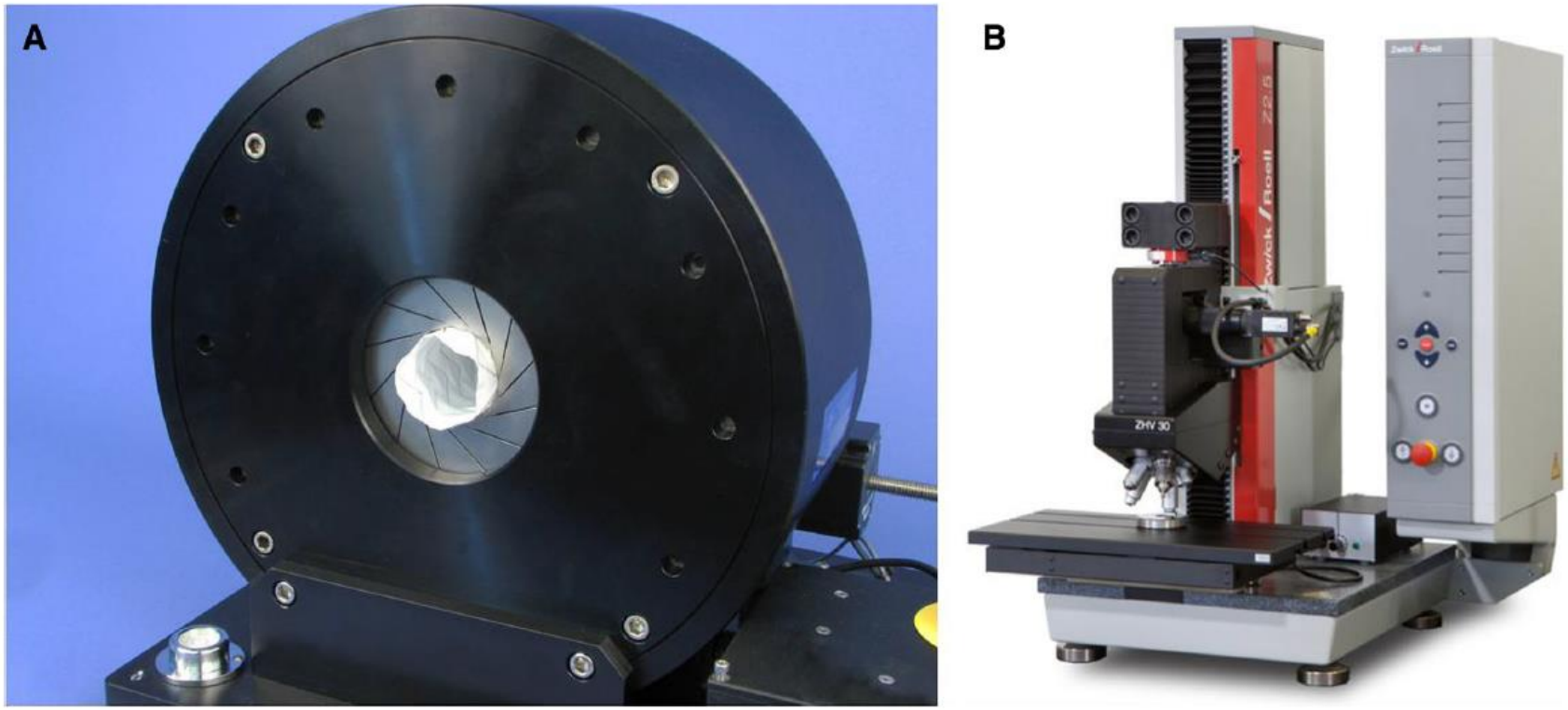
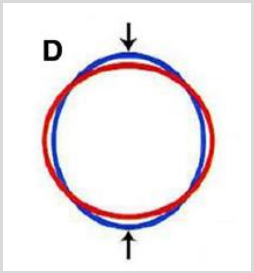
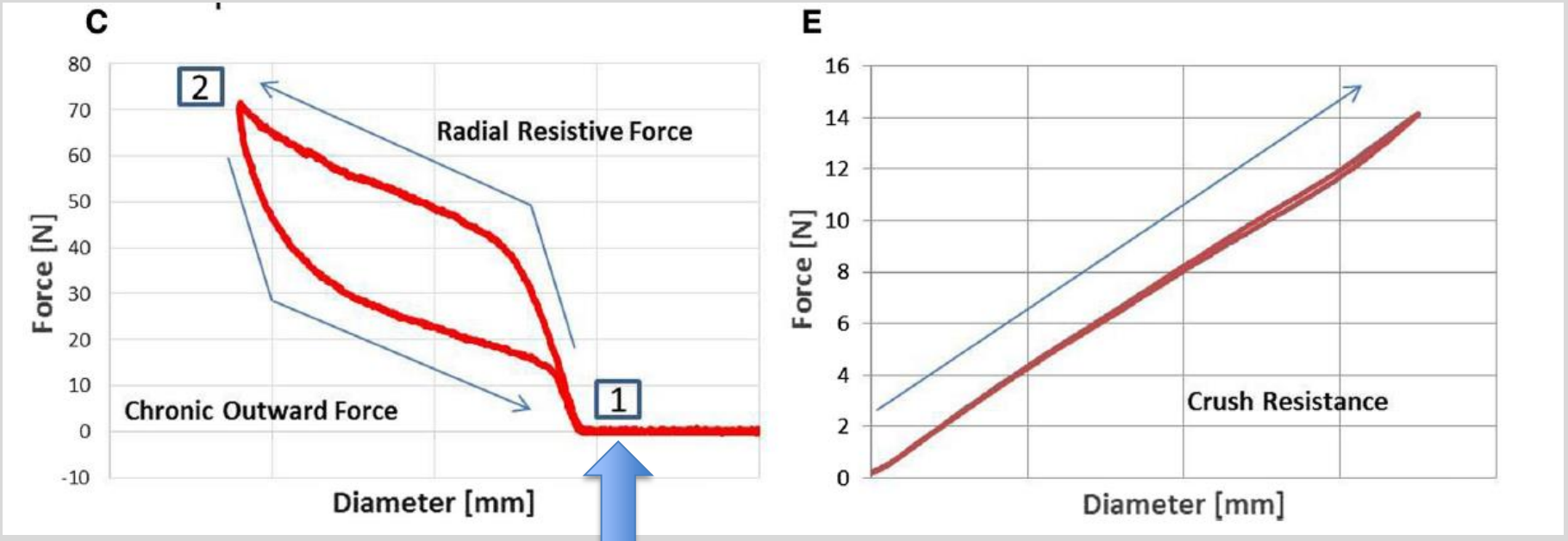


Fig. 2 Force testing machines: **A** radial RX-650 (Machine Solutions Inc., Flagstaff, AZ, USA) with stent, **B** zwickiLine (Zwick Roell, Ulm, Germany)



Radial resistive force: Force during loading
Chronic outward force: Force during unloading



Tests start here fully deployed, then loaded to an outer diameter to 4 mm (2)

Cardiovasc Intervent Radiol
https://doi.org/10.1007/s00270-018-1916-1

LABORATORY INVESTIGATION

Physical Properties of Venous Stents: An Experimental Comparison

Darius Dabir[1] · Andreas Feisst[1] · Daniel Thomas[1] · Julian A. Luetkens[1] · Carsten Meyer[1] · Ana Kardulovic[2] · Matthias Menne[2] · Ulrich Steinseifer[2] · Hans H. Schild[1] · Daniel L. R. Kuetting[1]

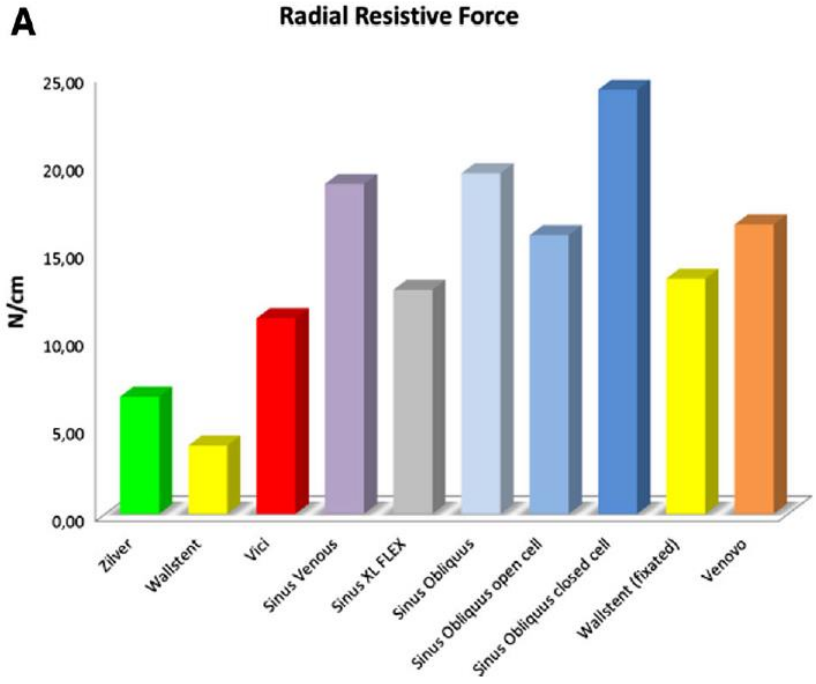
Name	Maximal radial resistive force (N/cm)	Chronic outward force at 90% diameter (N/cm)	Chronic outward force at 80% diameter (N/cm)	Chronic outward force at 50% diameter (N/cm)	Chronic outward force at 30% diameter (N/cm)
Zilver Vena	6.68	2.02	2.26	3.44	6.04
Wallstent	3.89	0.45	0.90	2.10	2.94
Vici	11.14	1.39	1.72	3.34	9.15
Sinus Venous	18.79	4.26	4.80	7.56	16.13
Sinus XL FLEX	12.76	3.00	3.50	5.40	10.68
Sinus Obliquus	19.41	4.35	5.00	7.93	16.97
Venovo	16.49	4.83	5.37	7.35	13.19
Sinus Obliquus (open-cell segment)	15.88	3.87	4.58	7.18	13.96
Sinus Obliquus (closed-cell segment)	24.16	5.67	6.70	10.60	20.14
Wallstent (fixated)	13.40	0.85	1.41	4.72	5.40

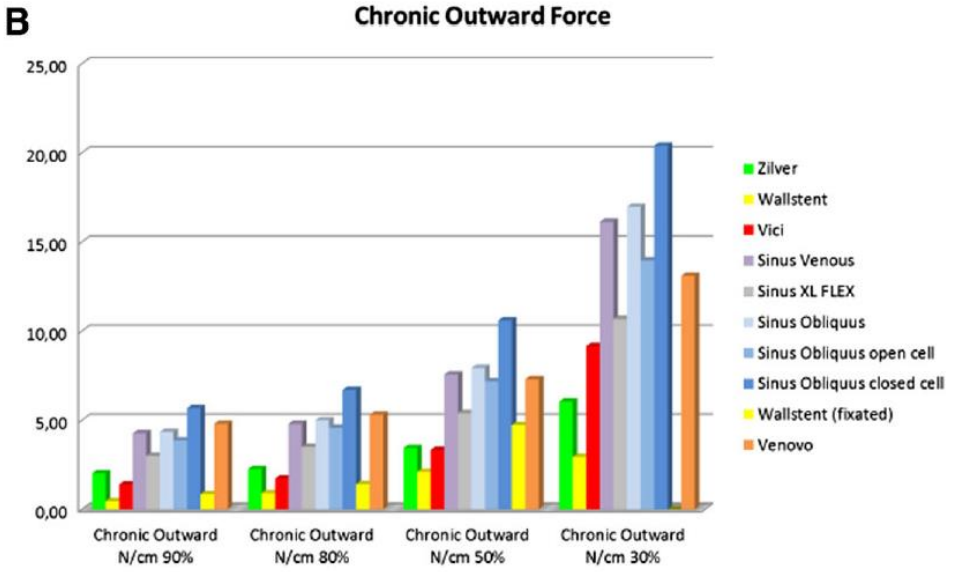
Cardiovasc Intervent Radiol
https://doi.org/10.1007/s00270-018-1916-1

LABORATORY INVESTIGATION

Physical Properties of Venous Stents: An Experimental Comparison

Darius Dabir[1] · Andreas Feisst[1] · Daniel Thomas[1] · Julian A. Luetkens[1] · Carsten Meyer[1] · Ana Kardulovic[2] · Matthias Menne[2] · Ulrich Steinseifer[2] · Hans H. Schild[1] · Daniel L. R. Kuetting[1]



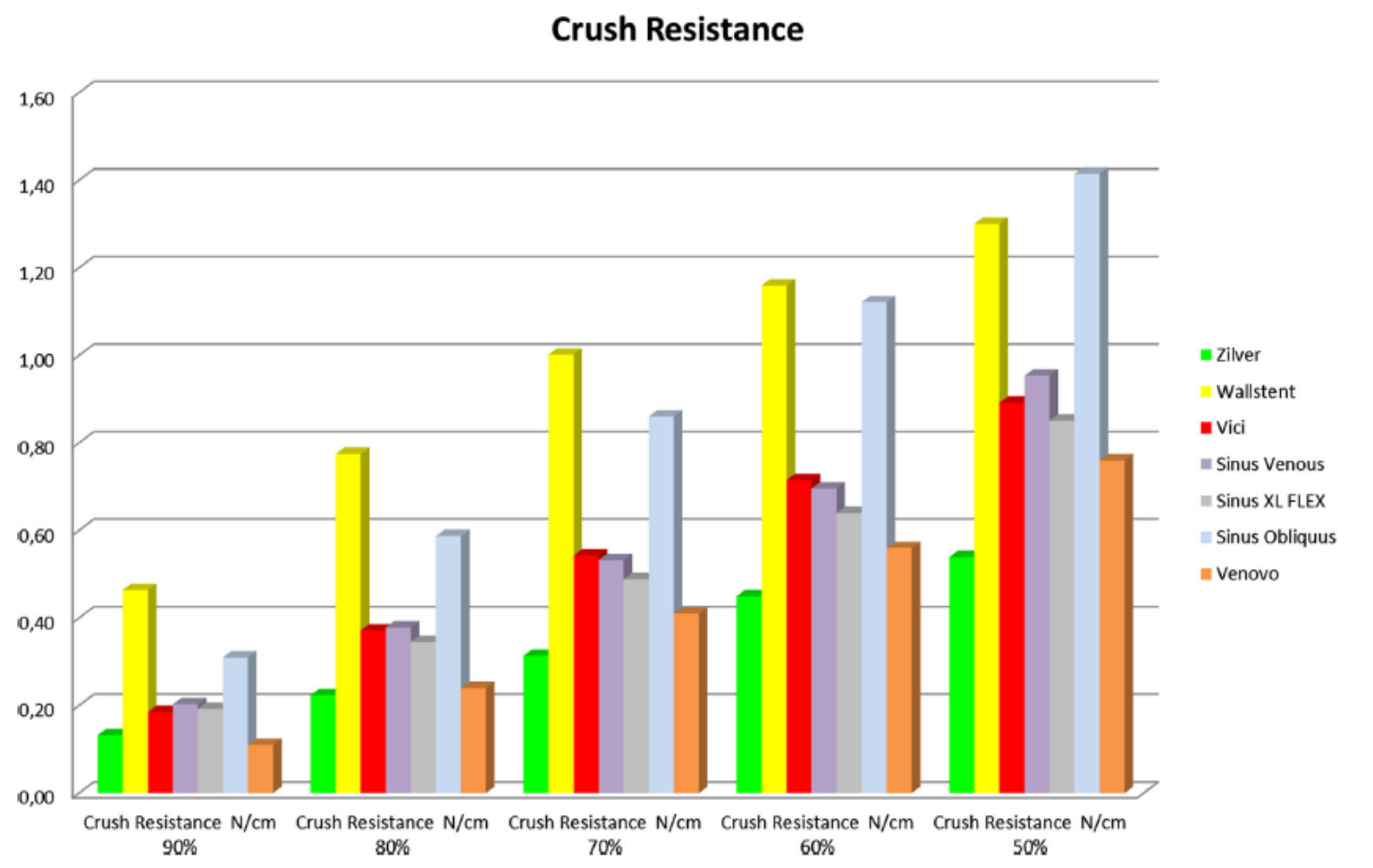


Cardiovasc Intervent Radiol
https://doi.org/10.1007/s00270-018-1916-1

LABORATORY INVESTIGATION

Physical Properties of Venous Stents: An Experimental Comparison

Darius Dabir[1] · Andreas Feisst[1] · Daniel Thomas[1] · Julian A. Luetkens[1] · Carsten Meyer[1] · Ana Kardulovic[2] · Matthias Menne[2] · Ulrich Steinseifer[2] · Hans H. Schild[1] · Daniel L. R. Kuetting[1]



Venous Stenting is Safe and Efficacious

37 Studies, 2,869 Patients, technical success ranged from 94%-96%

American Heart Association.

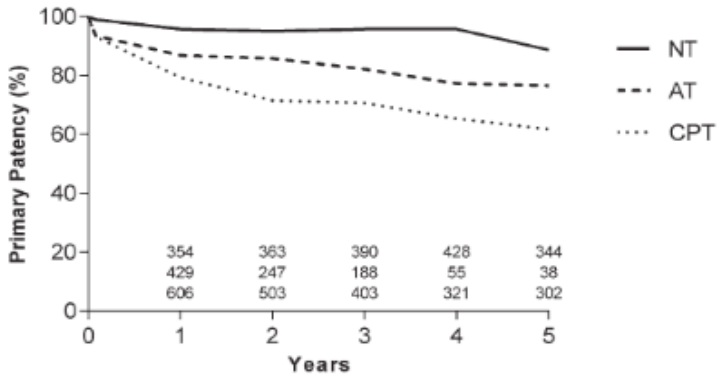
Peripheral Vascular Disease

Safety and Effectiveness of Stent Placement for Iliofemoral Venous Outflow Obstruction

Systematic Review and Meta-Analysis

Mahmood K. Razavi, MD; Michael R. Jaff, DO; Larry E. Miller, PhD

Conclusions—Stent placement for iliofemoral venous outflow obstruction results in high technical success and acceptable complication rates regardless of cause of obstruction. (*Circ Cardiovasc Interv*. 2015;8:e002772. DOI: 10.1161/CIRCINTERVENTIONS.115.002772.)

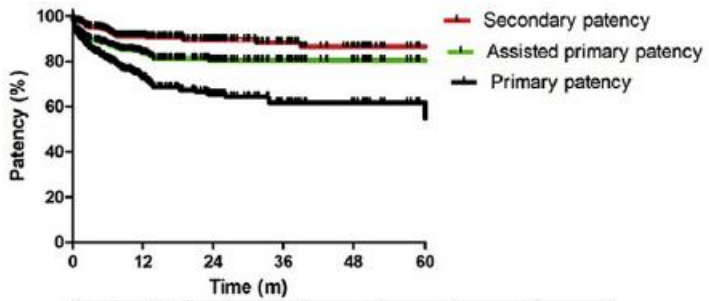


AT = Acute Thrombotic, CPT=Chronic Post Thrombotic
NT=Nonthrombotic

Eur J Vasc Endovasc Surg (2017) 54, 495—503

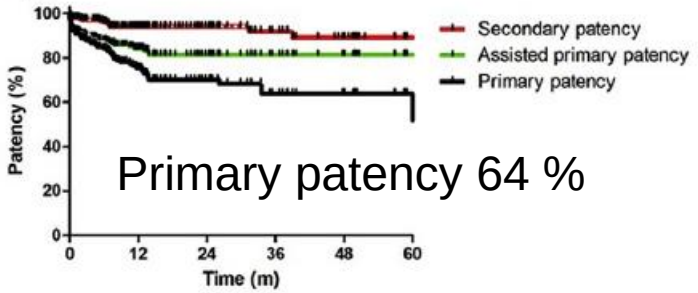
Editor's Choice — Reconstruction of the femoro-ilio-caval outflow by percutaneous and hybrid interventions in symptomatic deep venous obstruction

A Patency rates total population



Total	At risk	0	12	24	36	48
	Secondary	425	219	108	59	35
	A-Primary	425	202	94	49	28
	Primary	425	190	87	43	27

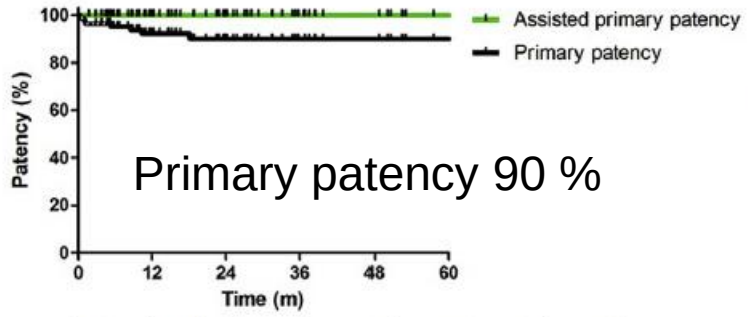
C Patency rates P-PTS



Primary patency 64 %

P-PTS	At risk	0	12	24	36	48
	Secondary	229	114	61	37	22
	A-Primary	229	106	52	30	18
	Primary	229	101	49	27	17

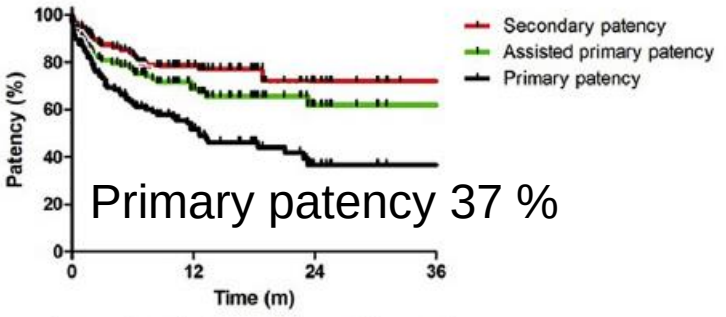
B Patency rates IVCS



Primary patency 90 %

IVCS	At risk	0	12	24	36	48
	A-Primary	87	50	30	15	10
	Primary	87	50	29	14	10

D Patency rates H-PTS Hybrid intervention

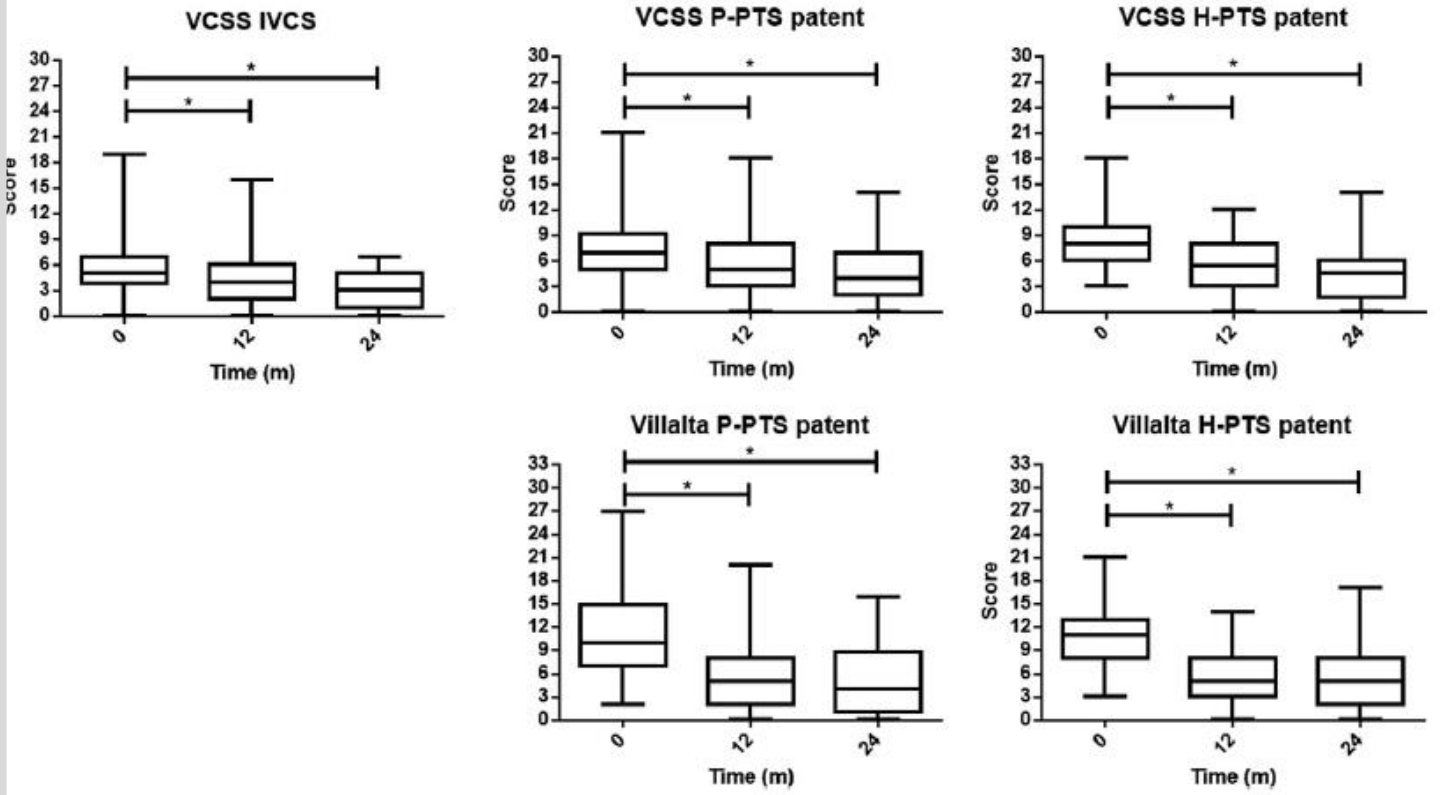


Primary patency 37 %

H-PTS	At risk	0	12	24
	Secondary	109	57	19
	A-Primary	109	49	14
	Primary	109	42	11

Eur J Vasc Endovasc Surg (2017) 54, 495—503

Editor's Choice — Reconstruction of the femoro-ilio-caval outflow by percutaneous and hybrid interventions in symptomatic deep venous obstruction



VIRTUS Feasibility Trial Design

Objective	Assess safety & effectiveness in achieving patency of target venous lesion through 12-M post stent placement
Safety	MAEs @ 30 days
Effectiveness	Primary Patency @ 12-M
Principal Investigators	▪ Dr. William Marston ▪ Dr. Mahmood Razavi
Study Design	Prospective, multicenter, single arm non-randomized, up to 45 sites worldwide
Patient Population	200 subjects with clinically significant chronic non-malignant obstruction of the iliofemoral venous segment – first 30 were feasibility.
Etiologies:	Post Thrombotic (75%); Non Thrombotic (25%)
Core Labs	Venography: Syntactx IVUS: St. Lukes DUS: VasCore/MGH X-Ray: Syntactx

Post-thrombotic

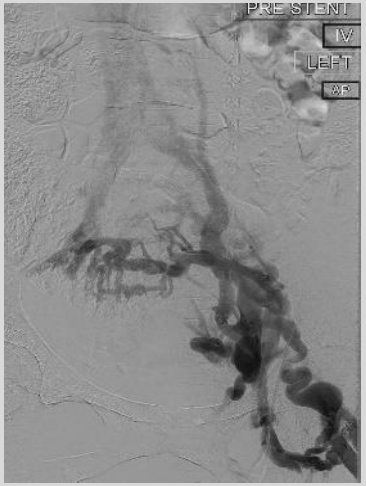


Image Courtesy of Mr. Stephen Black

Non-thrombotic

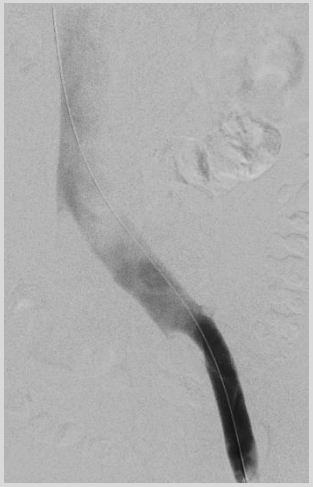
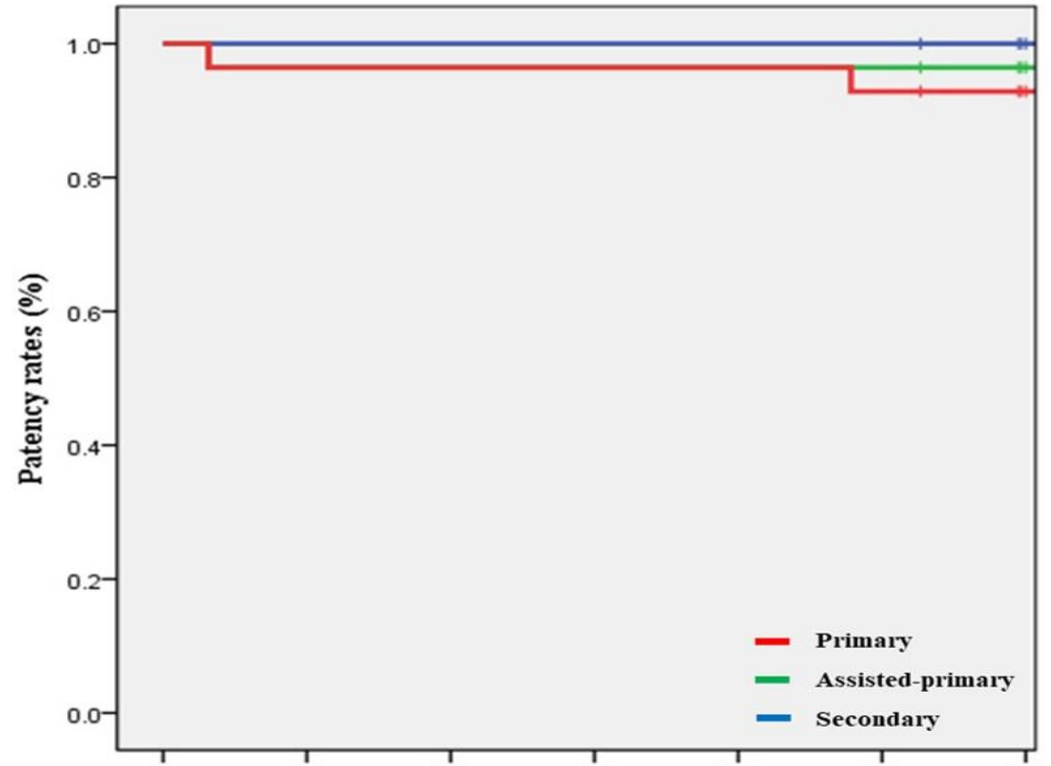


Image Courtesy of Mr. Mahmood Razavi

12-month Patency Data



Primary	28	27	27	27	27	26	22
Asst-Prim	28	27	27	27	27	27	23
2ndary	28	28	28	28	28	28	24

Secondary	100%
Assisted-primary	96%
Primary	93%

Razavi M, et al. J Vasc Surg Venous Lymphat Disord. 2017 Dec 28. pii: S2213-333X(17)30509-7.

Patient Outcome Measures

- 63% of patients had ≥ 50% VCSS score reduction
- 81% of patients with pain reduction at 12 months
- 78% of patients considered QOL improved

	Baseline N=30	6 months N=26*	P value	12 months N=27	P value
VCSS[1]	10 (2-25)	5 (0-30)	<.001	4 (0-23)	<.001
VAS[2]	60 (6-98)	23 (0-84)	.002	21 (0-94)	.001
CIVIQ-20[3]	48 (24-97)	28 (20-91)	.001	33 (20-89)	<.001

* At 6 months, 27 patients had VCSS scores. The 1 patient with 6-month VCSS data (and no VAS or CIVIQ-20 data) at 6 months only had completed form responses for 3 of 10 VCSS domains (all 0's).

1. VCSS – venous clinical severity score
2. VAS – visual analogue scale
3. CIVIQ-20 – chronic venous insufficiency quality of life questionnaire

Razavi M, et al. J Vasc Surg Venous Lymphat Disord. 2017 Dec 28. pii: S2213-333X(17)30509-7.

Arnsberg Venous Registry

> 300 patients included since 2013

Objective	Assess safety & effectiveness in achieving patency of target venous lesion through 36 months post **venous stent** placement in patients with non thrombotic iliac vein lesions and post thrombotic iliac vein lesions.
Effectiveness	Primary Patency @ 12-M // Clincal outcome @ 12 -M
Principle Investigators	▪ Dr. Michael Lichtenberg ▪ Dr. Rick de Graaf
Study Design	Ongoing prospective, single arm, single center non-randomized registry **FU 1 (4 weeks), FU 2 (6 months), FU 3 (12 months),** FU 4 (24 months), FU 5 (36 months)
Patient Population	Subjects with clinically significant chronic non-malignant obstruction of the iliofemoral venous segment

Study is sponsored by German Venous Center Arnsberg

Klinikum Arnsberg
Akademisches Lehrkrankenhaus
Westfälische Wilhelms-Universität Münster

Arnsberg Venous Registry

Venovo – Venous Stent

Objective	Assess safety & effectiveness in achieving patency of target venous lesion through 36 months post **venous stent** placement in patients with non thrombotic iliac vein lesions and post thrombotic iliac vein lesions.
Effectiveness	Primary Patency @ 12-M // Clincal outcome @ 12 -M
Principle Investigators	▪ Dr. Michael Lichtenberg ▪ Dr. Rick de Graaf
Study Design	Ongoing prospective, single arm, single center non-randomized registry **FU 1 (4 weeks), FU 2 (6 months), FU 3 (12 months),** FU 4 (24 months), FU 5 (36 months)
Patient Population	Subjects with clinically significant chronic non-malignant obstruction of the iliofemoral venous segment

Study is sponsored by German Venous Center Arnsberg

Klinikum Arnsberg
Akademisches Lehrkrankenhaus
Westfälische Wilhelms-Universität Münster

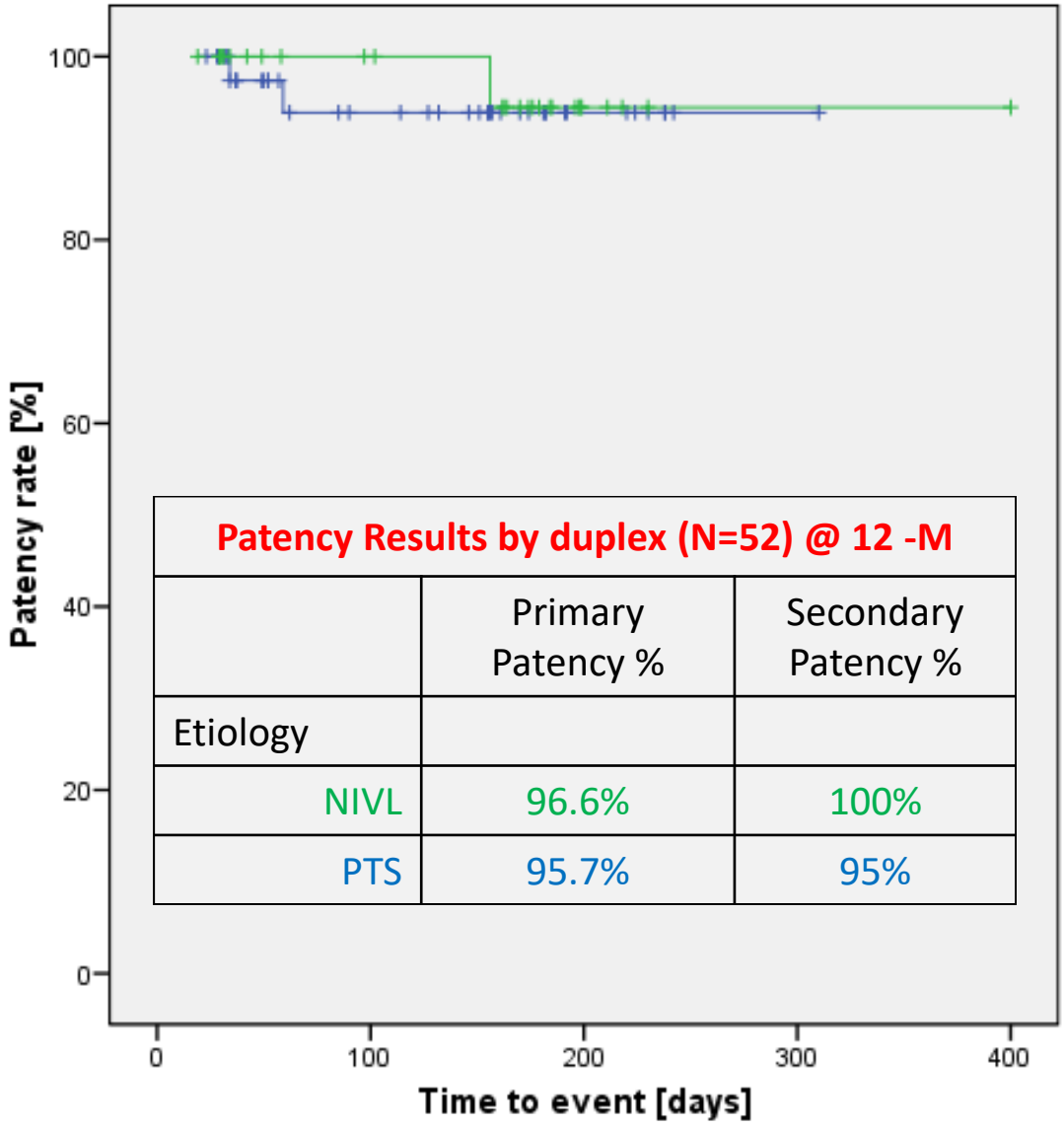
Demographics/Medical History

Demographics/ Comorbidity	No. (%)
Age	57 (19-89)
Male	35 (44%)
Female	45 (56%)
Post-thrombotic	**50 (63%)**
Non-thrombotic	**30 (37%)**
Prev. PE	8 (10%)
Prev. DVT	43 (48%)
High Blood Pressure	40 (50%)
Renal Disease	6 (8%)
Stroke	3 (3%)
Cancer	9 (11%)
Diabetes	11 (14%)
Smoker	13 (16%)

CEAP Score, prior stent	No. (%)
1	0 (0%)
2	1 (1%)
3	41 (51%)
4	28 (36%)
5	8 (10%)
6	2 (2%)
Signs/Symptoms prior stent	**No. (%)**
Pain (incl. venous claudication)	78 (98%)
Varicose Veins	63 (79%)
Edema	62 (78%)
Pigment Changes	41 (51%)
Ulcers	10 (8%)
Use Compression Stockings	68 (85%)

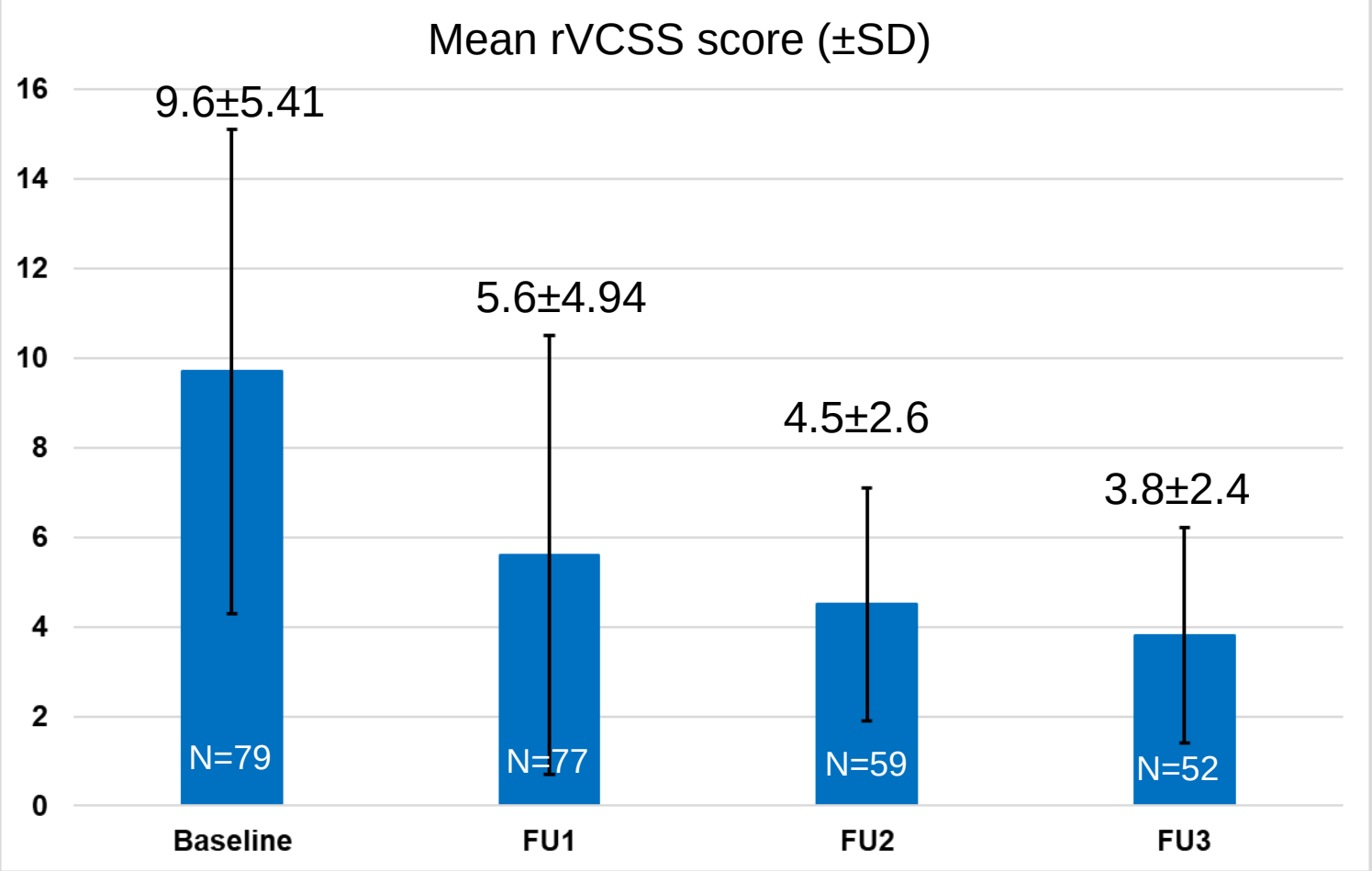
48% > CEAP C4

Patency analysis NIVL vs. PTS



--- NIVL
--- PTS

Patency Results by duplex (N=52) @ 12 -M		
	Primary Patency %	Secondary Patency %
Etiology		
NIVL	96.6%	100%
PTS	95.7%	95%



- 51% had “substantial clinical improvement” (rVCSS ≥2) @12-M
- Venous claudication and persistent swelling improved
- 8/10 venous ulceration were healed @ 12 - M

Klinikum Arnsberg
Akademisches Lehrkrankenhaus
Westfälische Wilhelms-Universität Münster

Arnsberg Venous Registry

VENITI VICI VENOUS STENT® System

Objective	Assess safety & effectiveness in achieving patency of target venous lesion through 36 months post stent placement (VENITI VICI Stent)
Effectiveness	Primary Patency @ 12-M // Clincal outcome @ 12 -M
Principle Investigators	▪ Dr. Michael Lichtenberg ▪ Dr. Rick de Graaf
Study Design	Ongoing prospective, single arm, single center non-randomized registry FU 1 (4 weeks), FU 2 (6 months), FU 3 (12 months), FU 4 (24 months), FU 5 (36 months)
Patient Population	Subjects with clinically significant chronic non-malignant obstruction of the iliofemoral venous segment

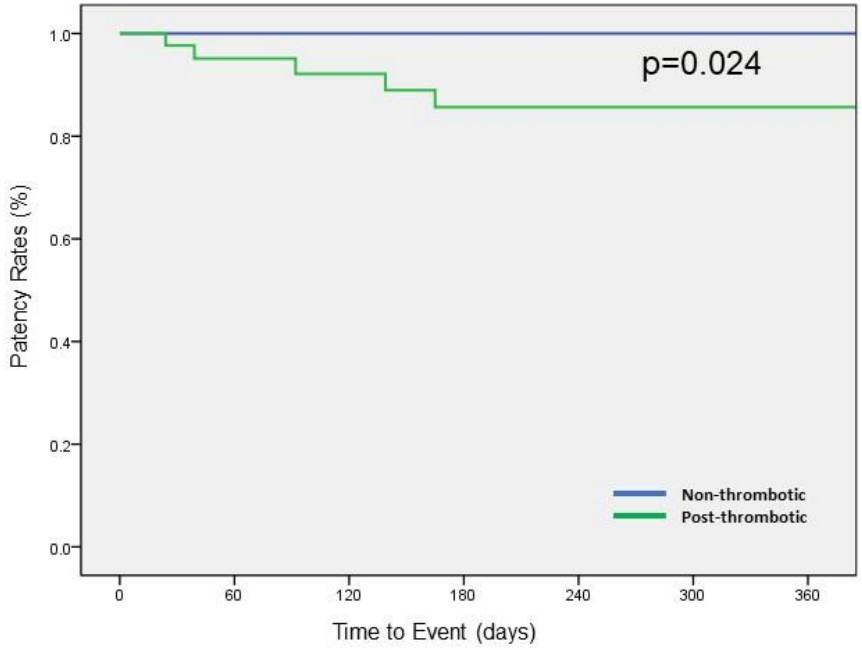
Klinikum Arnsberg
Akademisches Lehrkrankenhaus
Westfälische Wilhelms-Universität Münster

Demographic / Clinical data 90 patients

Demographic/comorbidity	No. (%)
Age	57.4±16.4
Male	43 (48%)
Female	47 (52%)
Post-thrombotic Syndrome	49 (54%)
Non-thrombotic	41 (46%)
History of venous thromboembolic disease	81 (90%)
Pulmonary embolism	22 (24%)
Deep vein thrombosis	43 (48%)
Coronary Artery Disease	6 (7%)
Myocardial Infarction	1 (1%)
Congestive Heart Failure	7 (8%)
High Blood Pressure	48 (55%)
Renal Disease	6 (7%)
Stroke	3 (3%)
Cancer	13 (14%)
Diabetes	13 (14%)
Smoker (current or previous)[a]	15 (17%)

CEAP score, prior to stenting	
1	0 (0%)
2	1 (1%)
3	56 (62%)
4	20 (22%)
5	8 (9%)
6	4 (4%)
Signs and symptoms, prior to stenting[b]	
Pain (inc. venous claudication)	89 (99%)
Varicose veins	83 (92%)
Edema	89 (99%)
Pigment Changes	41 (46%)
Ulcers	10 (11%)
Use of compression stockings	88 (98%)

Patency rates
non-thrombotic vs. post-thrombotic



Non-thrombotic	41	30	29	21	15	13	9
Post-Thrombotic	48	33	30	25	17	15	12

100% @ 12 months

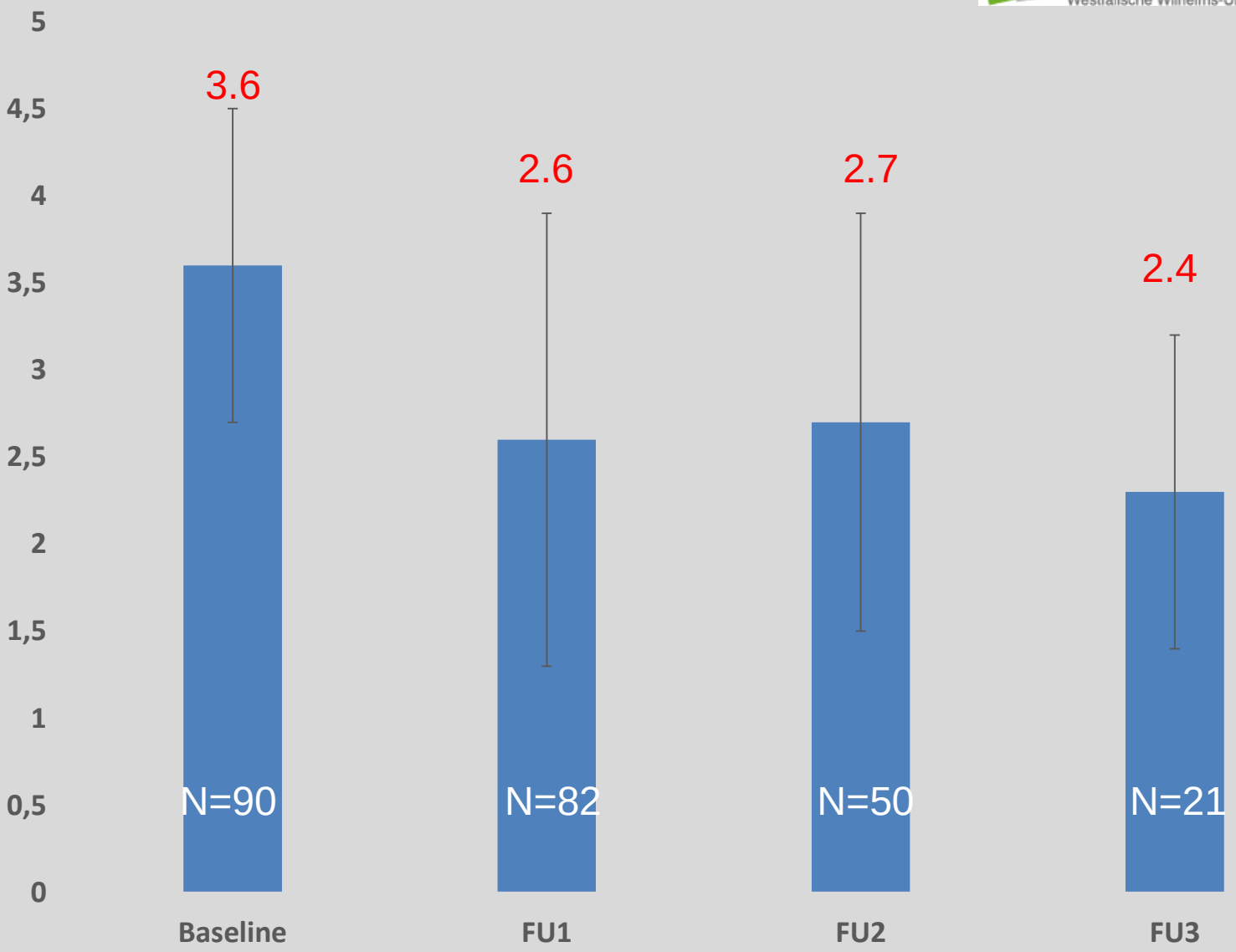
85.7% @ 12 months

Clinical efficacy: rVCSS analysis

	Baseline N=90	1 month N=56	P value	6 months N=29	P value	12 months N=13	P value
All Patients	8 (4, 27)	4 (1, 15)	<.0001	4 (0, 12)	<.0001	4 (0, 15)	.008

Mean CEAP score (±SD)

Klinikum Arnsberg
Akademisches Lehrkrankenhaus
Westfälische Wilhelms-Universität Münster

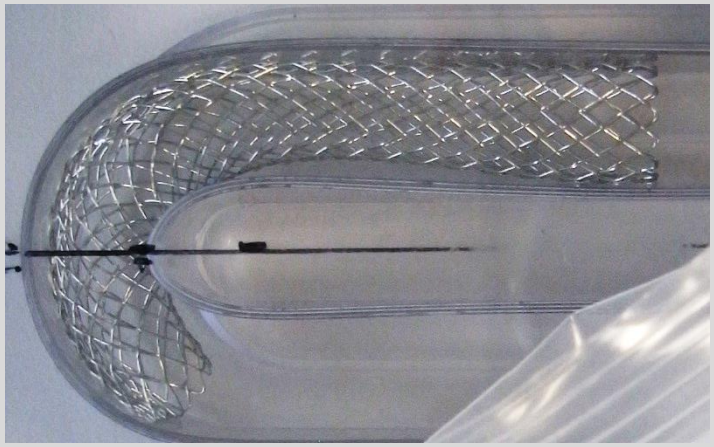


Physical Characteristics

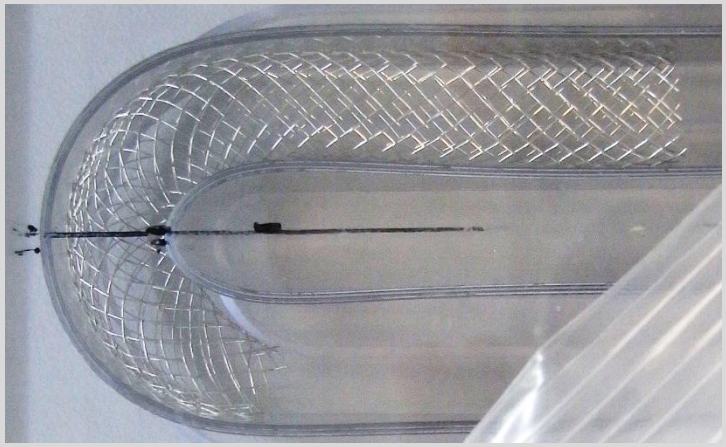
Bending Test

- 12 x 60 mm Stents tested
- 10mm Vessel diameter

Position	Centerline Radius	blueflow Venous stent	Boston Scientific Wallstent
		Minimum open diameter	Minimum open diameter
Stent end 45mm away from peak	10mm	6,0mm	5,5mm



Blueflow Venouse Stent
Position Stent end 45mm away from Peak
Centerline Radius 10mm



Boston Scientific Wallstent
Position Stent end 45mm away from Peak
Centerline Radius 10mm

Take home message

- Use dedicated venous stents !
- Choose wisely - based on lesion morphology
- Choose wisely – based on stent technology

Venous Thrombectomy

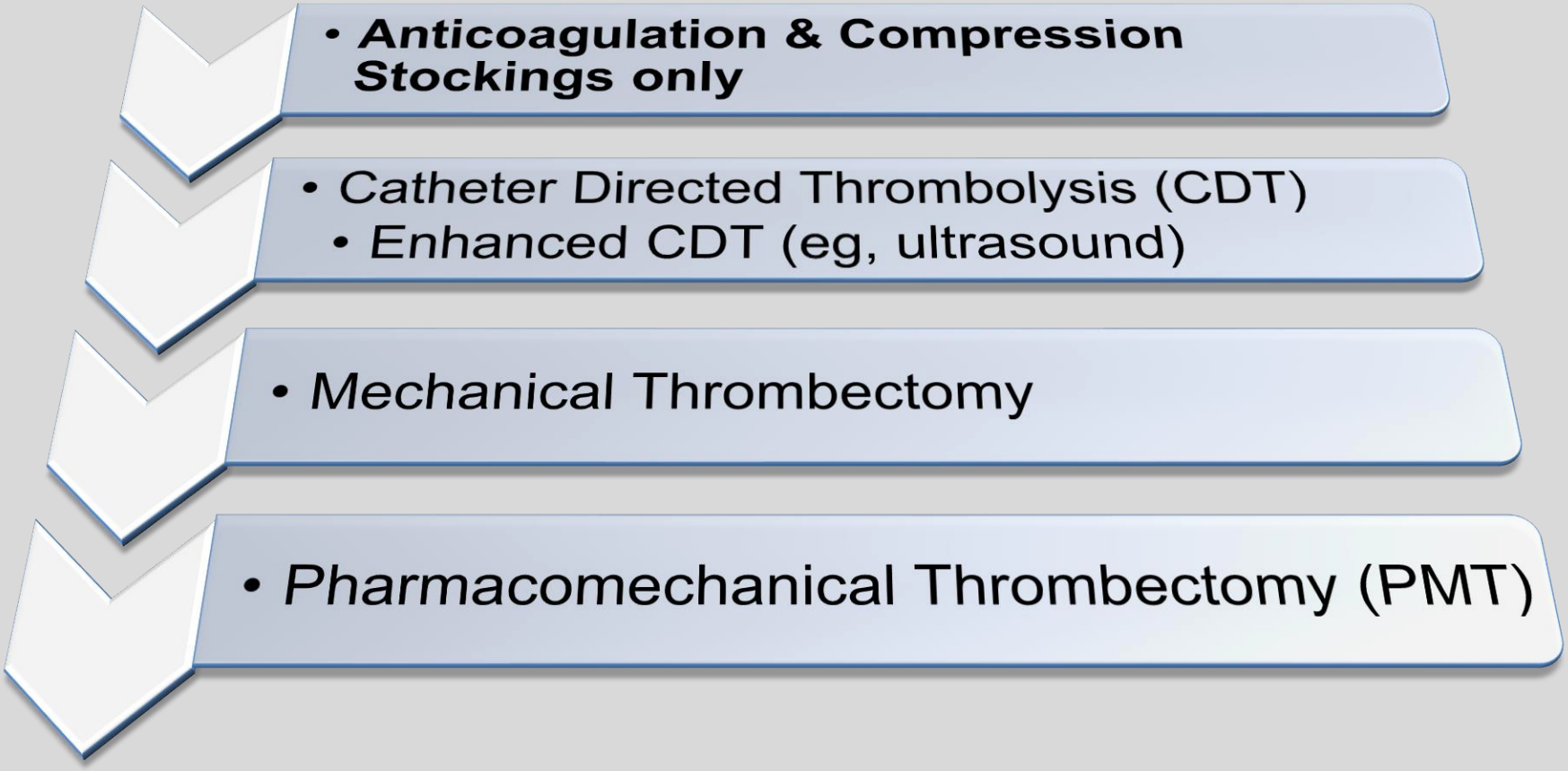
Benefits of an Endovascular Approach for Rapid Flow Restoration in DVT

DVT / VT - what do we need to know?

- Who ist the patient?
  (KI lysis, KI post.int.med., Preg., Tumor, MTS, coag.Dis., Age, etc.)
- Who is the enemy?
  (acute, chronic, acute on chronic)
- What are our arms?
  (recanalisation devices, IVC-Filter, IVUS, Stent)
- What are our opportunities?
  (time, ICU/IMC, capacity for reintervention/control, post interv. surveillance)
- Reimbursement

Venous Thrombus Treatment Options:

Traditional Therapy



Traditional Therapy

- Initial therapy of LMW heparin or unfractionated heparin
- Long term oral anticoagulants (3-6 months)
- Compression stockings to reduce swellin

Comerota et al; “Iliofemoral Venous Thrombosis”; J Vasc Surg 2007; 46:1065-1076

Traditional Therapy

- Prevents clot propagation
- Reduces risk of pulmonary embolism
- May provide moderate symptomatic relief
- **Advantages**
  - Easily administered without specialized skills
  - Low cost of medications / appliances
  - Accepted as standard of care

- **Anticoagulation does NOT:**
  - Resolve clot
  - Reduce risk of venous valvular damage
  - Prevent venous hypertension
  - Prevent or reduce severity of Post Thrombotic Syndrome (PTS)
  - Rapidly resolve symptoms

https://ash.confex.com/ash/2012/webprogram/Paper46479.html

SOX Trial

Elastic Compression Stockings vs Placebo Control

Compression stockings to prevent post-thrombotic syndrome: a randomised placebo-controlled trial

Susan R Kahn, Stan Shapiro, Philip S Wells, Marc A Rodger, Michael J Kovacs, David R Anderson, Vicky Tagalakis, Adrielle H Houweling, Thierry Ducruet, Christina Holcroft, Mira Johri, Susan Solymoss, Marie-José Miron, Erik Yeo, Reginald Smith, Sam Schulman, Jeannine Kassis, Clive Kearon, Isabelle Chagnon, Turnly Wong, Christine Demers, Rajendar Hanmiah, Scott Kaatz, Rita Selby, Suman Rathbun, Sylvie Desmarais, Lucie Opatrny, Thomas L Ortel, Jeffrey S Ginsberg, for the SOX trial investigators

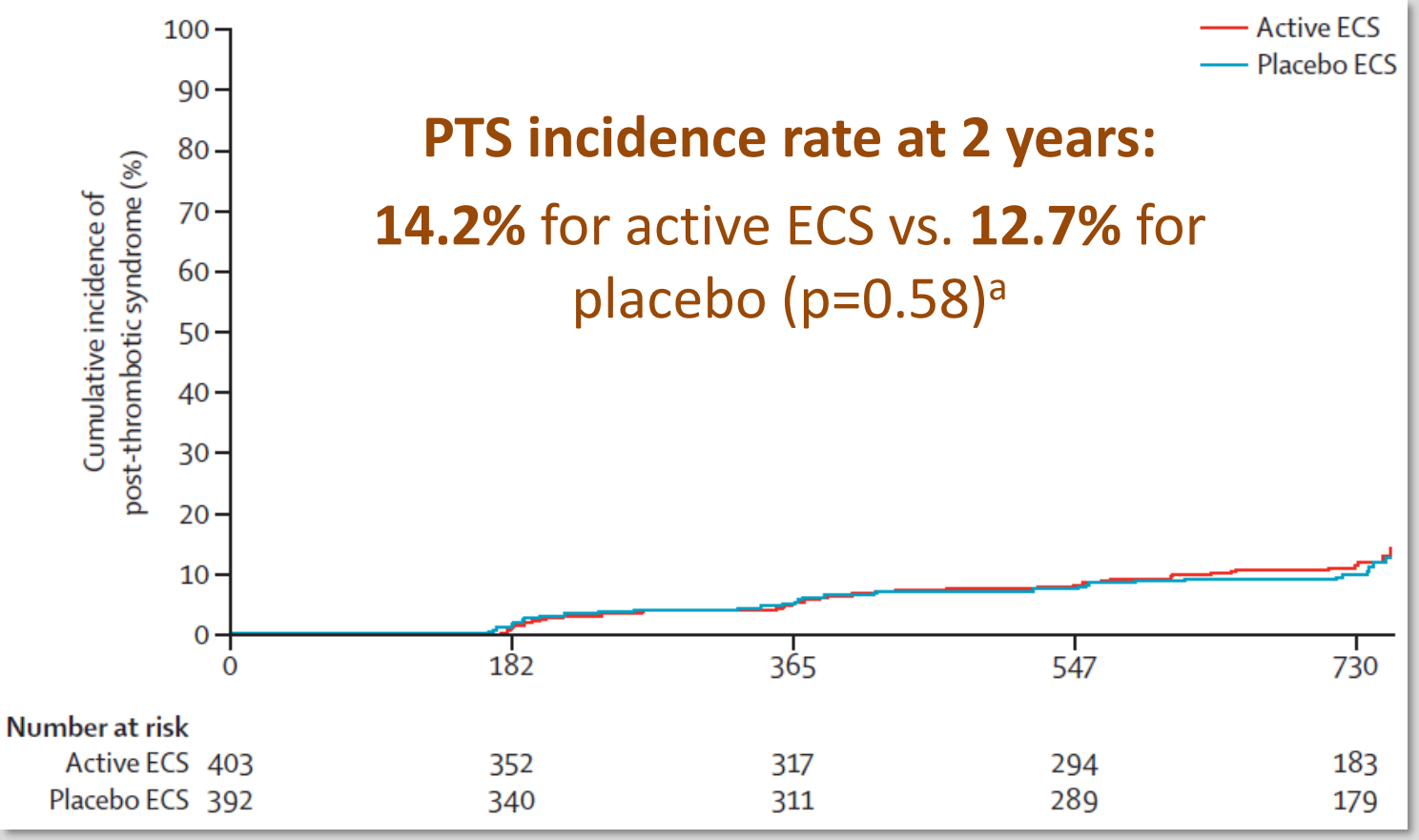
- **Objective:** To evaluate the effectiveness of elastic compression stockings (ECS), compared with placebo stockings to prevent post-thrombotic syndrome (PTS)
- **Design:** Multicenter, randomized, placebo-controlled trial of active (N=410) vs placebo (N=396) ECS
- **Key Inclusion Criteria:** First indicative, proximal DVT (with or without coexisting pulmonary embolism or distal DVT)
- **Primary Endpoint:** PTS diagnosed at 6 months or later using Ginsberg's criteria (ie, leg pain and swelling of ≥1 month)

Kahn SR, Shapiro S, Wells PS, et al SOX trial investigators. Lancet. 2014 Mar 8;383(9920):880-8

SOX Trial Results

Elastic Compression Stockings vs Placebo Control

"ECS did not prevent PTS after a first proximal DVT, hence our findings do not support routine wearing of ECS after DVT"



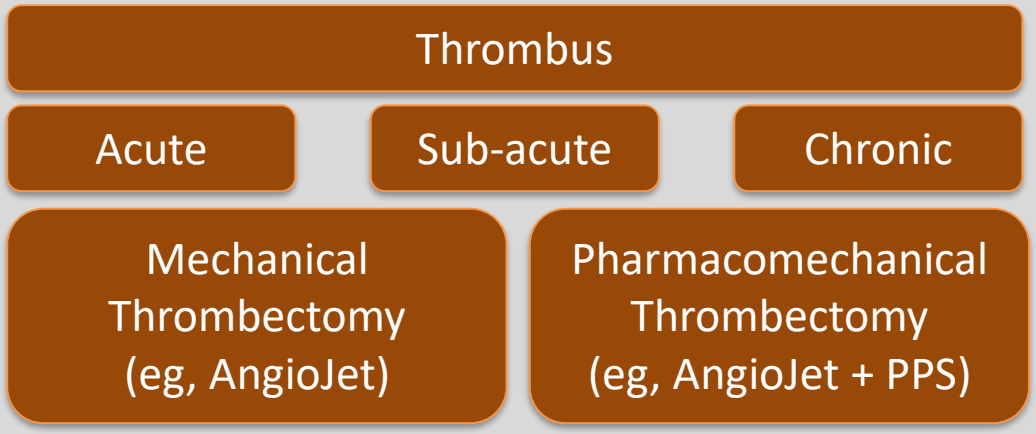
[a]HR adjusted for center 1.13, 95% CI 0.73–1.76; p=0.58

PTS, post-thrombotic syndrome

Kahn SR, Shapiro S, Wells PS, et al SOX trial investigators. Lancet. 2014 Mar 8;383(9920):880-8

Considerations for Endovascular Intervention

- Thrombus age/extent
  - Acute ≤ 14 days (fresh thrombus, easier to remove)
  - Sub-acute ≤ 6 months (fibrin-bound, more stable clot increases difficulty)
  - Chronic ≥ 6 months (organized thrombus, fibrin-rich stable and difficult to remove)
  - Mixed morphology
- Symptoms
  - Pain, leg swelling, difficulty walking
  - Life-style limiting
- Anatomy
  - Common femoral or higher
  - Iliofemoral DVT are typically most symptomatic



PPS, Power Pulse™ Spray

Pharmacomechanical Thrombectomy (PMT)

- Combination of drug and mechanical thrombectomy to remove thrombus
- Allows medication to soften the clot, followed by mechanical action to remove the clot

Advantages

- Minimally invasive
- Removes thrombus
- Can reduce procedure time/length of ICU stay
- May provide rapid symptomatic relief
- Potential for reduced lytic dosage

Limitations

- Specialized skills required
- Higher cost of disposables
- Effectiveness may be reduced in long-standing chronic thrombus

Postthrombotic Syndrome; Patricia E. Thorpe, MD, FSIR; October 2007; Endovascular Today

BERNUTIFUL Trial:

Ultrasound-Assisted CDT vs Conventional CDT

Ultrasound-Assisted Versus Conventional Catheter-Directed Thrombolysis for Acute Iliofemoral Deep Vein Thrombosis

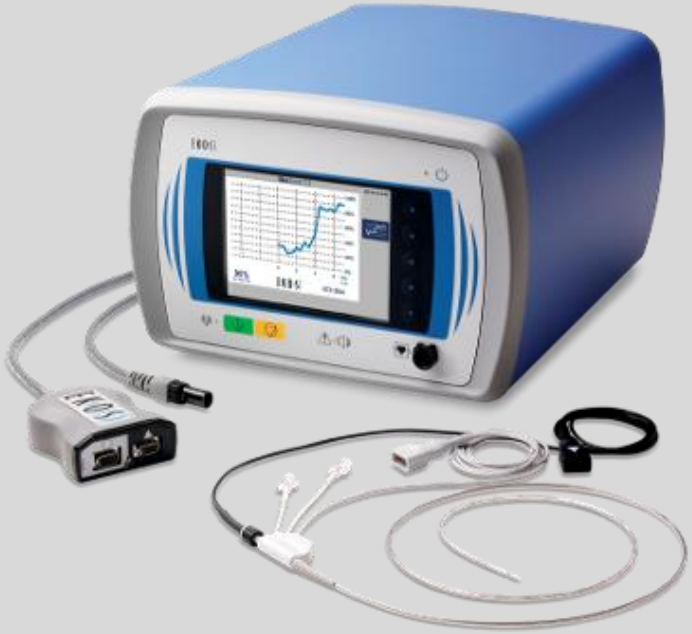
Rolf P. Engelberger, MD; David Spirk, MD; Torsten Willenberg, MD; Adriano Alatri, MD; Dai-Do Do, MD; Iris Baumgartner, MD; Nils Kucher, MD

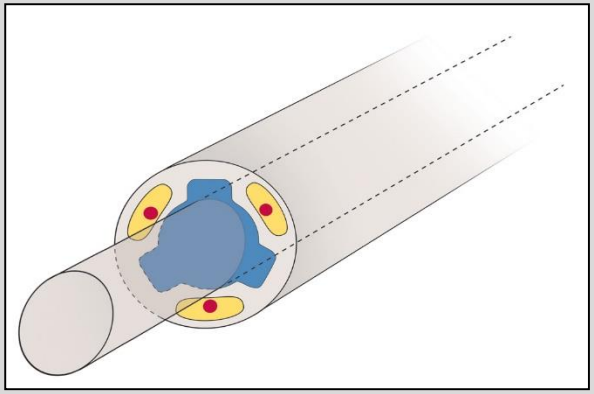
- Objective: Assess whether the addition of intravascular high-frequency, low-power ultrasound energy facilitates the resolution of thrombosis during catheter-directed thrombolysis (CDT)
- Controlled, randomized trial of ultrasound-assisted CDT (N=24) vs conventional CDT (N=24)
  - Thrombolysis regimen for both groups: 20 mg r-tPA over 15 hours
- Patients with acute (<2 weeks) iliofemoral DVT
- Primary efficacy endpoint was the percentage of thrombus load reduction from baseline to 15 hours

Engelberger R, et al. Circ Cardiovasc Interv. 2015 Jan;8(1). pii: e002027.

pharmacomechanical thrombus fragmentation

ultrasound accelerated thrombolysis: EKOS





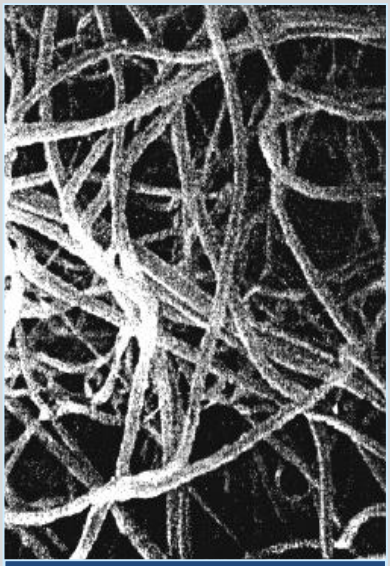
- **5.4 Fr catheter**
- **106 and 135 cm working length**
- **6, 12, 18, 24, 30, 40 and 50 cm treatment zones**

pharmacomechanical thrombus fragmentation

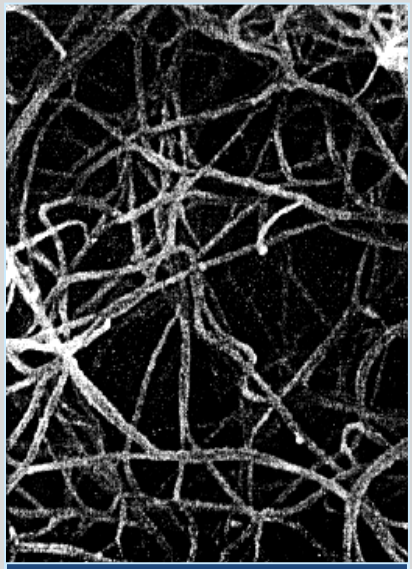
ultrasound accelerated thrombolysis: EKOS

Fibrin Separation

Non-cavitational ultrasound separates fibrin without fragmentation of emboli



Fibrin without Ultrasound

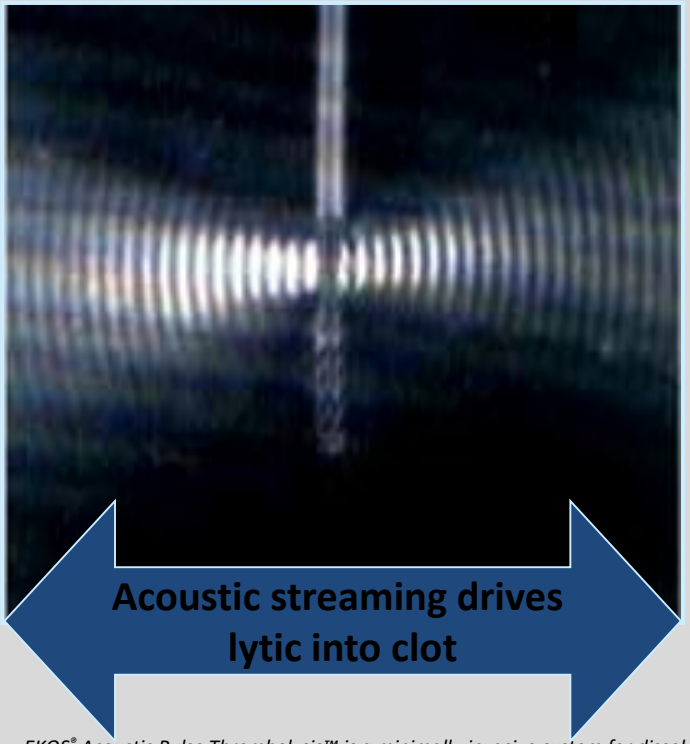


Fibrin With Ultrasound

Braatan et al. Thrmob Haemost 1997;78:1063-8.
Francis et al. Ultrasound in Medicine and Biology, 1995;21(5):419-24.
Soltani et al. Physics in Medicine and Biology, 2008; 53:6837-47.

Active Drug Delivery

Drug is actively driven into clot by "Acoustic Streaming"



EKOS® Acoustic Pulse Thrombolysis™ is a minimally invasive system for dissolving thrombus.

BERNUTIFUL Trial Results:

Ultrasound-Assisted CDT vs Conventional CDT

"The addition of intravascular ultrasound did not facilitate thrombus resolution"

		CDT (N=24)	CDT + Ultrasound (N=24)	*P*
Post-CDT	Thrombus Load Reduction	54%±27%	55%±27%	0.91
	Bleeding Complication Rate	8.3%	12.5%	>0.99
3 Months	Primary Venous Patency	96%	100%	0.33
	PTS Severity (Villalta score)	3.0±3.9	1.9±1.9	0.21

CDT regimen: 20 mg r-tPA over 15 hours
Length-Adjusted Thrombus score was based on venographic filling defects in segments along the indwelling CDT catheter

- Thrombus load and complication rates were similar after CDT or ultrasound-assisted CDT
- 3-month outcomes did not differ significantly between groups
  - Rates of adjunctive therapy use were similar between groups (angioplasty and stenting 83% vs 80%, P>.99; adjunctive thrombus removal 46% vs 29%, P=.37)

Engelberger R, et al. Circ Cardiovasc Interv. 2015 Jan;8(1). pii: e002027.

Mechanical Thrombectomy

- Minimally invasive thrombectomy method
- Allows for rapid thrombus removal
- Supports less dose and duration of lytic agents
  - Decreased bleeding
- Potential for vessel (endothelial) trauma
- Can be used for both arterial and venous clots

Therapeutic options in the treatment of DVT

Conservative medical treatment (eg. LMWH, OAC, DOAC)

OP / Fogarty

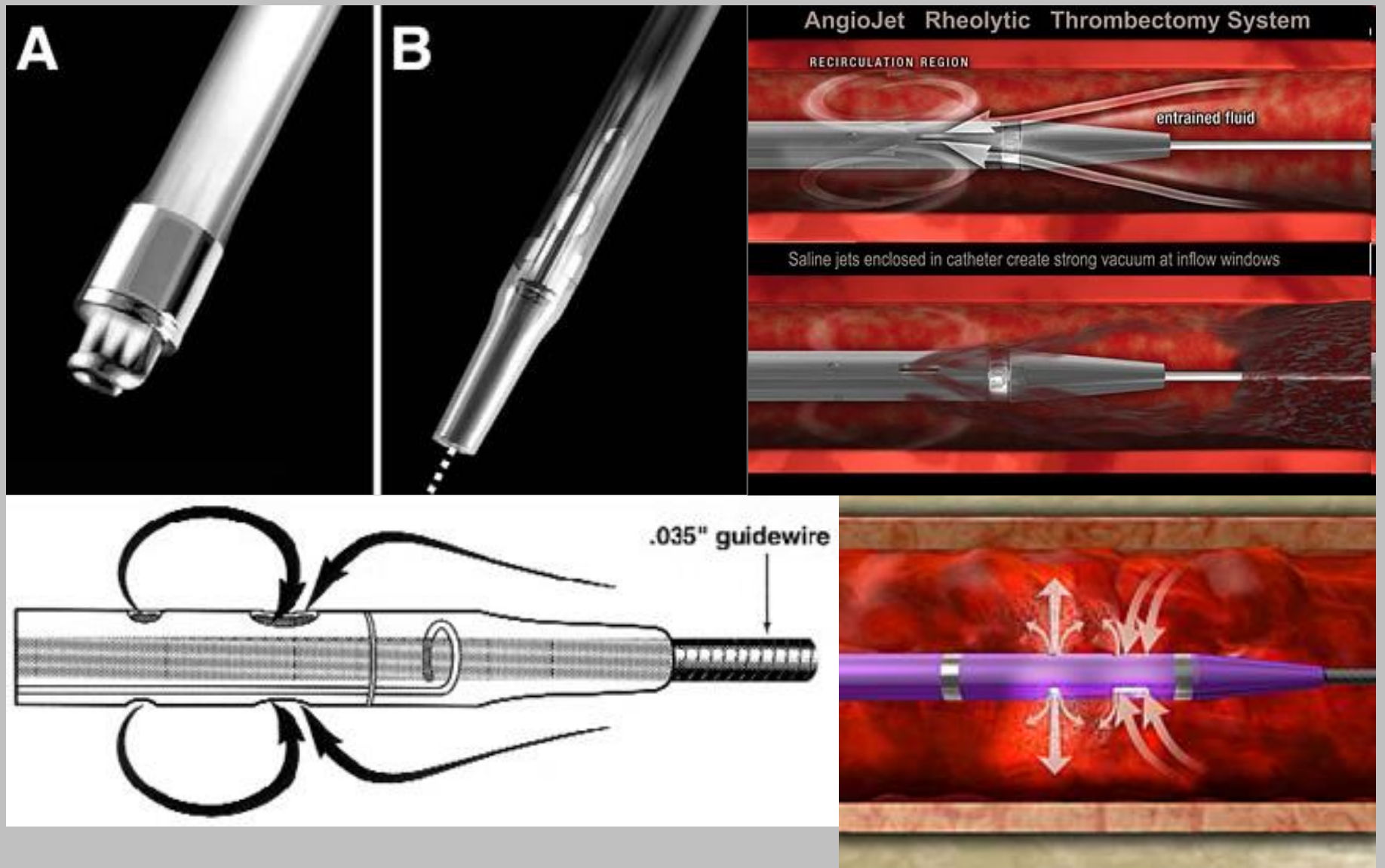
Systemic thrombolysis

Endovascular approaches

- local thrombolysis
- thrombus fragmentation and removal by
  Ballon-PTA, Basket, Aspiration
- thrombus fragmentation
  Tretorola (Teleflex)
  Cleaner 15 / XT (Argon)
  Mantis (Invamed)
- pharmacomechanical thrombolysis
  AngioJet (Boston Sc.)
  EkoSonic (BTG)
- mechanical thrombectomy devices
  Aspirex (Straub)
  Indigo (Penumbra)
  Angiovac (Argon)
  ClearLumen (Walkvascular)

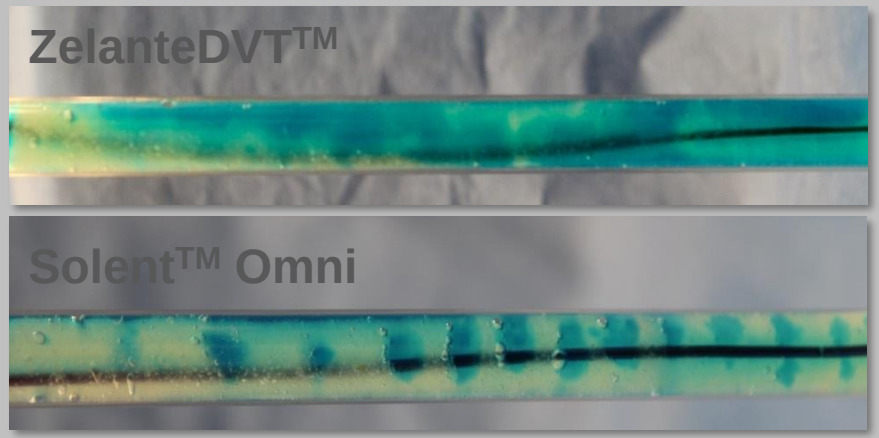
pharmacomechanical thrombus fragmentation

AngioJet



Bench Simulations

Power Pulse™ Delivery

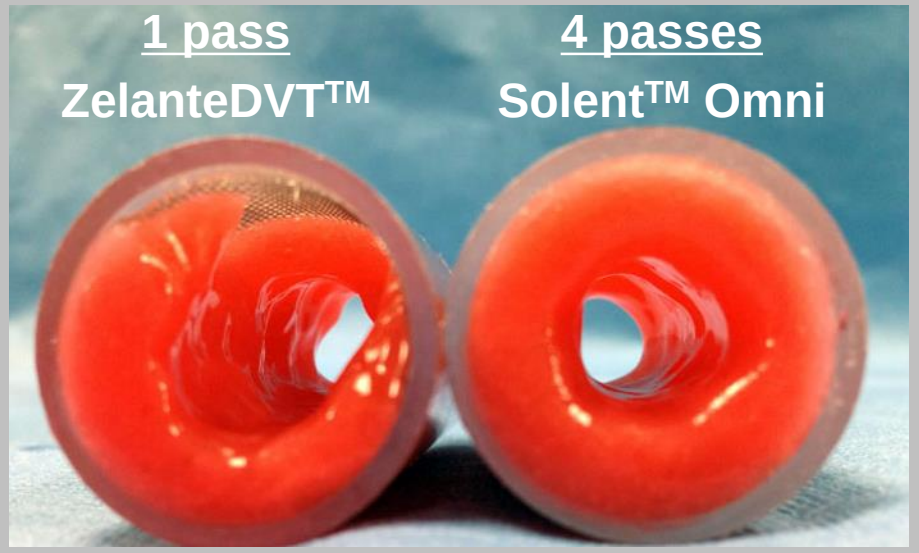


Clot tube model. Catheter advanced at 1mm/sec with Power Pulse (foot pedal) delivery of fluid

Fluid delivered with ZelanteDVT disperses within the clot

Simulated Clot Model of Thrombus Removal

~4x more thrombus removal with ZelanteDVT



BSC fiber clot 100 in a 22 mm tube

BSC data on file. Bench test results may not necessarily be indicative of clinical performance.

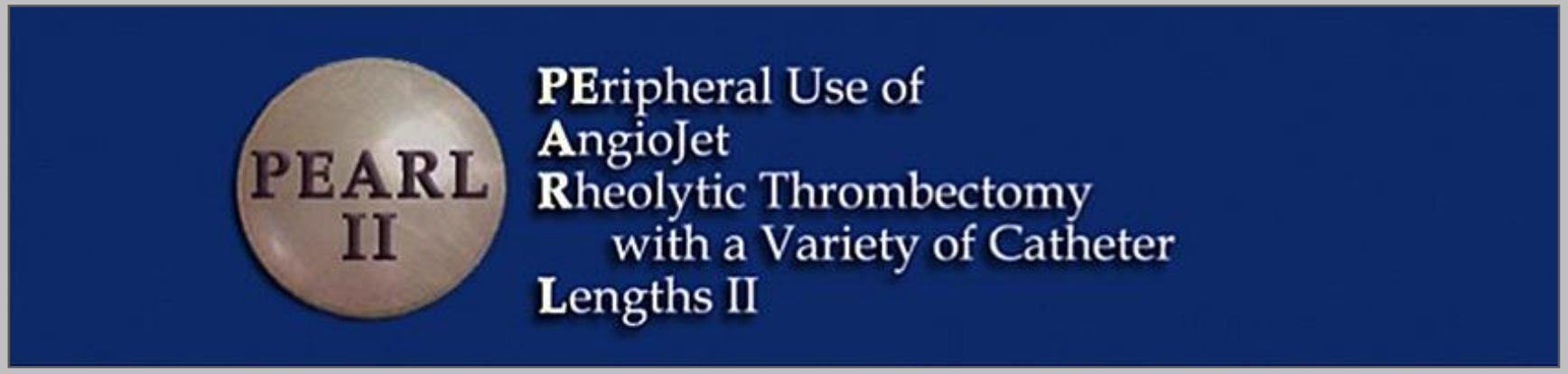
PEARL and PEARL II Clinical Registries

PEripheral Use of

AngioJet™

Rheolytic Thrombectomy With Mid

Length Catheters



PEARL Registry Objectives

- Determine efficacy of thrombus removal from baseline to final angiogram
- Evaluate clinical outcomes of treated patients at defined intervals of 3, 6, and 12 months
- Characterize clinical events
- Characterize treatment options used with the AngioJet® System
- Estimate rate of AngioJet Thrombectomy-related adverse events

PEARL Registry: Venous Cohort

329 patients

73% of cases completed in **<24 hours**

Treatment	Frequency
AngioJet Thrombectomy alone (Rheolytic)	13 (4%)
AngioJet + Lytic by AngioJet (PMT)	115 (35%)
AngioJet Rheolytic + CDT	29 (9%)
AngioJet PMT + CDT	172 (52%)

- **96% of patients had Grade II/III (50%-100%) clot reduction**
  - Clot reduction grade distribution not affected by symptom duration or treatment group
- Significant improvements over baseline in both physical & mental component scores of the SF-12 (P<.0001)
- 83% freedom from rethrombosis at 12 months
- 78% with continued clinical benefit (no recurrent thrombosis or worsened condition in the treated limb) at 12 months

PEARL Comparison
Treatment of Lower Extremity DVT

Patient Characteristics

	PEARL*	Venous Registry†	CaVenT‡	
			CDT	Standard
# of Patients	329	287	90	99
# of Sites	32	63	20	
Prior DVT	40%	31%	10%	9%
Primary Treatment	**AngioJet Thrombectomy With or Without PMT**	**CDT**	**CDT**	**LMWH**
Stent Placement	35%	33%	17%	NA
Primary access	Popliteal	Popliteal	Popliteal	NA
Male	57%	48%	64%	62%
Age (mean)	52.2 yrs	47.5 yrs	53.3 yrs	50.0 yrs
Treatment Location	Iliofemoral – femoral pop	Iliofemoral – femoral pop	CFV or iliofemoral	
Limbs Involved	Left=62%; Right=38%	Left=61%; Right=39%	Left=60%; Right=40%	Left=62%; Right=38%

CDT, catheter-directed thrombolysis; CFV, common femoral vein; LMWH, low molecular weight heparin; PMT, pharmacomechanical thrombolysis

*Garcia,MJ, et al. J Vasc Interv Radiol 2015; 26:777-785
†Mewissen MW, Seabrook GR. Radiology 1999:211:39-49
‡Enden , Haig Y. Lancet 2012:379:31-38

Results from different clinical investigations are not directly comparable.

Treatment Characteristics

		PEARL*	Venous Registry†	CaVenT‡	
				CDT	Standard
Onset of DVT Symptoms	Acute	67% (≤14 days)	66% (≤10 Days)	100% ≤21 days	
	Chronic	33% (>14 days)	16% (>10 Days)	NA	
	Acute & Chronic	NA	19%	NA	
Primary Lytic		TPA	Urokinase	TPA	NA
CDT Drip Times (mean)		**17 hrs**	**48 hrs**	**57.6 hrs (2.4 days)**	NA
Procedure Times	**CDT (N=29)**	**40.9 hrs**	NA	NA	NA
	CDT+PPS/RL (N=172)	**22.0 hrs**	NA	NA	NA
	PPS/RL (N=115)	**2.0 hrs**	NA	NA	NA
Bleeding Complications		**4.5% (major & minor combined)**	**11% (major); 16% (minor)**	**22% (major & minor combined)**	0%

CDT, catheter-directed thrombolysis; PCDT, pharmacomechanical thrombolysis; PPS, power-pulse spray; RL, rheolytic; TPA, tissue plasminogen activator

*Garcia,MJ, et al. J Vasc Interv Radiol 2015; 26:777-785
†Mewissen MW, Seabrook GR. Radiology 1999:211:39-49
‡Enden , Haig Y. Lancet 2012:379:31-38

Results from different clinical investigations are not directly comparable.

PEARL Comparison

Treatment of Lower Extremity DVT

Treatment Effectiveness

		PEARL*	Venous Registry†	CaVenT‡	
				CDT	Standard
Overall % Thrombus Removal		**96%**	**83%**	**89%**	NA
By Lytic Groups: % thrombus removal	**CDT (N=28)**	**93%**	NA	NA	
	CDT+PPS/RL (N=167)	**97%**	NA	NA	
	PPS/RL (N=113)	**95%**	NA	NA	
Acute: % Thrombus Removal		**97%**	**86%**	**89%**	
Chronic: % Thrombus Removal		**95%**	**68%**	NA	
Primary Patency		NA	**6 Mon=65%; 12 Mon=60%**	**6 Mon = 65.9%**	**6 Mon = 47.4%**
Freedom from Rethrombosis		**6 Mon= 87%; 12 Mon=83%**	NA	NA	NA

CDT, catheter-directed thrombolysis; PPS, power-pulse spray; RL, rheolytic

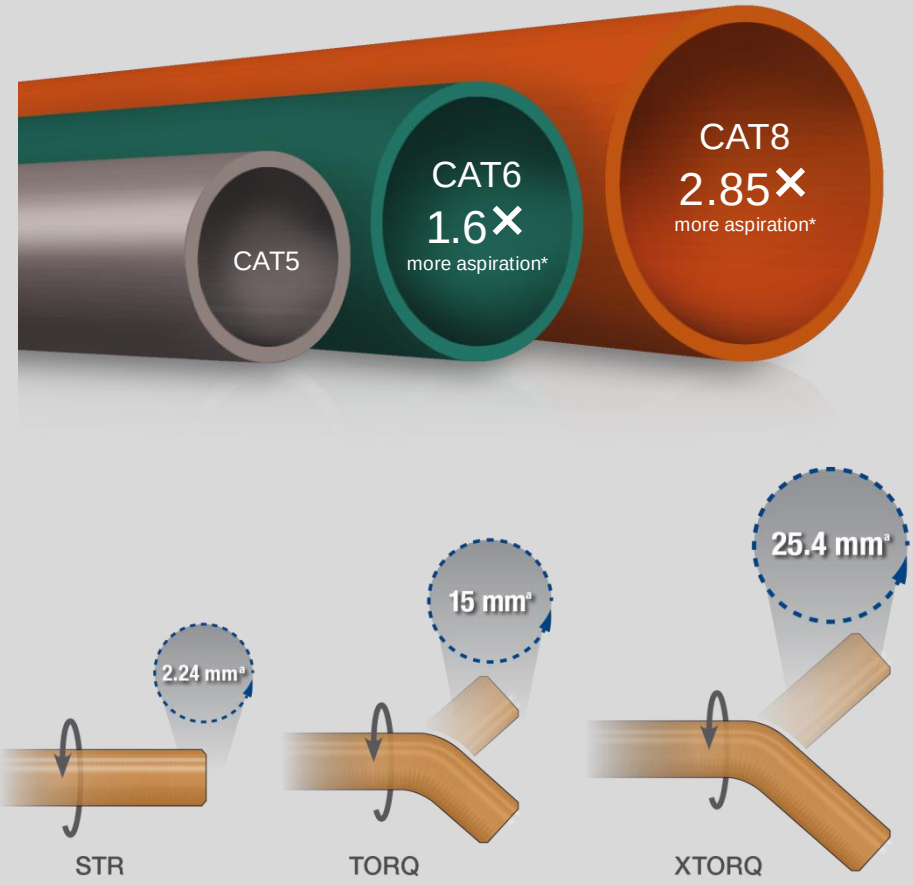
*Garcia,MJ, et al. J Vasc Interv Radiol 2015; 26:777-785
†Mewissen MW, Seabrook GR. Radiology 1999:211:39-49
‡Enden , Haig Y. Lancet 2012:379:31-38

Results from different clinical investigations are not directly comparable.

Mechanical thrombectomy devices

AngioVac	**Indigo**	**Aspirex**
Argon	Penumbra	Straub
no GW	no GW	0,018 GW
	Separator	0,025 GW
		OTW
22F	3,4F, 5F, 6F, 8F	6F, 8F, 10F
75, 120 cm	85,115, 135, 150 cm	85, 95, 110 cm
Aspiration	Aspiration	Aspiration

mechanical thrombectomy: Indigo



Size	3,4F	5F	6F	8F
MAC	42 ml/min	168 ml/min	270 ml/min	**480 ml/min**

mechanical thrombectomy: Angiovac

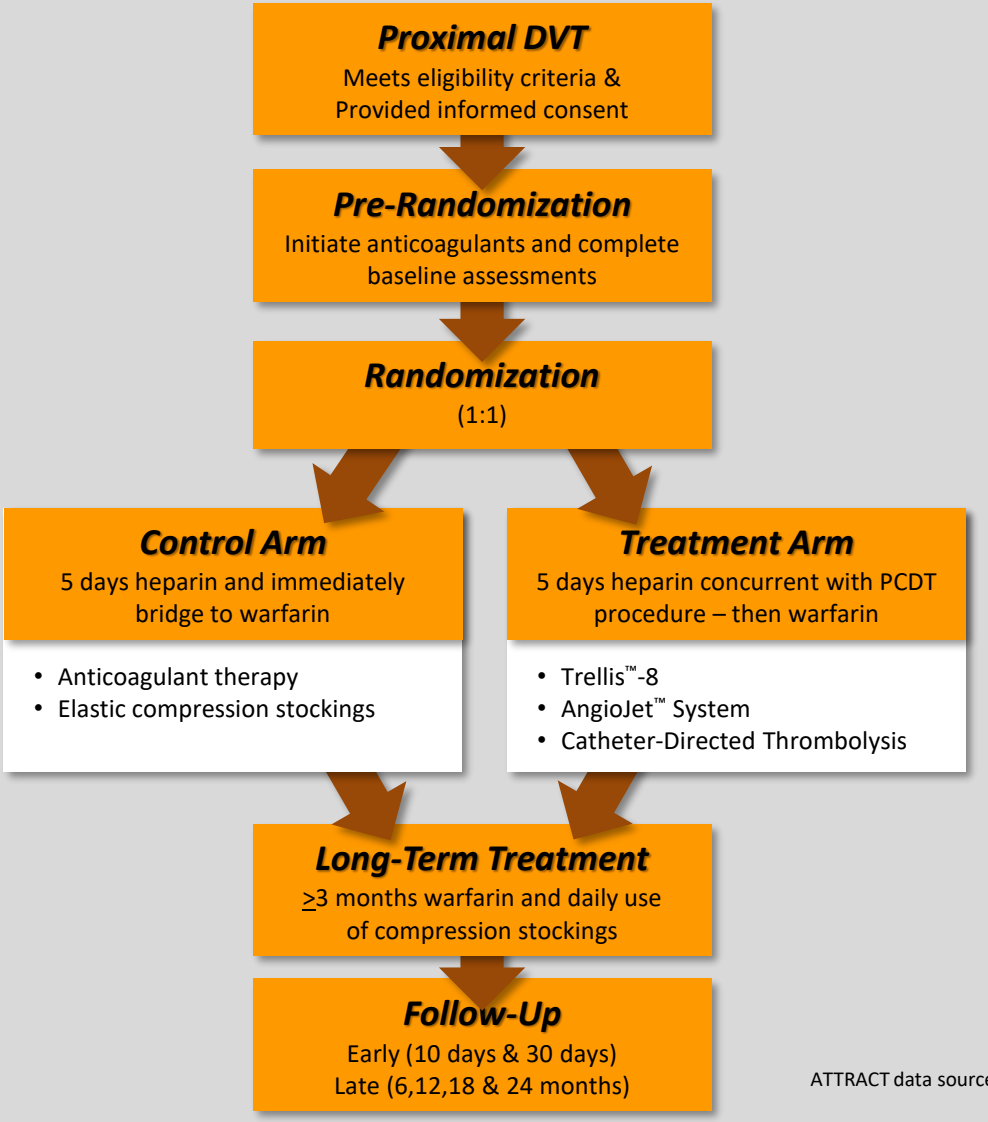
mechanical thrombectomy: Aspirex

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

ATTRACT Trial

Boston Scientific



the Attract STUDY

- 692 patients at 56 U.S. centers
- Determining if the use of PCDT and /or CDT in acute DVT reduces occurrence of post thrombotic syndrome (PTS) over 24 months

ATTRACT data source: Dr. Suresh Vedantham, Washington University Hospital, St. Louis, MO

PCDT Treatment

Treatment Arm
5 days heparin concurrent with PCDT procedure – then warfarin

- Trellis™-8
- AngioJet™ System
- Catheter-Directed Thrombolysis

Initial Treatment
Maximum 25 mg rt-PA

If **good** inflow to popliteal[a]

If **poor** inflow to popliteal

- **AngioJet™ System** (PowerPulse Thrombolysis), **or**
- **Trellis™-8** (Isolated Thrombolysis)

Catheter-Directed Thrombolysis

Adjunctive Options

- **Additional rt-PA** (total max 35 mg)
- **Balloon maceration**
- **Aspiration/mechanical thrombectomy**

Treatment Discontinuation

- **≥90% thrombus removed and flow restored, or**
- **Maximum rt-PA dose or infusion time reached, or**
- **Overt bleeding or complication requiring cessation of therapy**

[a]Lower half of the popliteal vein and ≥1 major calf vein tributary are free of occlusive thrombus.
rt-PA, recombinant tissue plasminogen activator; PCDT, pharmacomechanical catheter-directed thrombolysis

Vedantham S, et al. Rationale and design of the ATTRACT Study: a multicenter randomized trial to evaluate pharmacomechanical catheter-directed thrombolysis for the prevention of postthrombotic syndrome in patients with proximal deep vein thrombosis. Am Heart J. 2013;165(4):523-530.e3

ATTRACT Outcomes

- Primary Outcome : cumulative occurrence of PTS between 6-24 months using the Villalta Scale
  - Villalta Score> 5 or presence of an ulcer
  - The question the study was designed to answer
- PTS Severity: Villalta, VCSS, CEAP Class
- QOL: SF-36, VEINES-QOL/Sym measures
- Symptoms: Likert pain scale, calf circumference
- Costs: Bleeds, VTE, deaths, US/economic

ATTRACT Cohort Characteristics

- 692 patients randomized: 337 PCDT, 355 No-PCDT
  - 62% mean, median age 53 years, 25% previous VTE
  - 57% had IFDVT, median 6 days from DVT diagnosis
- Baseline medical factors & use of anticoagulation, compression, anti-platelet therapy did not differ
- PCDT performance = consistent with past studies
  - Median dose 21mg TPA; median 17 hours treatment
  - Venography: mean thrombus removal 74% ($p < 0.001$)
  - 94% of patients had ≥ 50% of their thrombus removed

Performance of PCDT

INITIAL PCDT METHOD

- Trellis (Technique A)
  - 50 Patients (15%)
- Angiojet (Technique B)
  - 75 Patients (23%)
- Infuse-First (Technique C)
  - 194 Patients (59%)

ADJUNCTIVE PROCEDURE

- Balloon maceration (56%)
- Balloon angioplasty (56%)
- Angiojet (55%)
- Aspiration (19%)
- Trellis (14%)
- Stent placement (30%)

ATTRACT trial

Outcome (24 mo)	PCDT (n=336)	no PCDT (n=335)	P value
Any PTS	**46,7 %**	**48,2%**	**0.56**
Recurrent VTE	12,5%	8,5%	0.09
Generic QOL (SF-36 PCS)	11,8	10,1	0.37
VENOUS QOL (VEINES)	27,7	23,5	0.08
Moderate or Severe PTS	17,9%	23,7%	0.035
MS-PTS IFDVT	18,4%	28,2%	
MS-PTS FPDVT	17,1%	18,1%	
Major bleed	1,7%	0,3%	0.049
Any bleed	4,5%	1,7%	0.049

PTCD less effective in patients ≥65 years (p = 0.038)

SIR, Washington 6.3.2017

Study Outcomes
Short-Term Effects of PCDT

Outcome	PCDT N=336	No-PCDT N=355	P Value
Major Bleeding (10 days)	1.7%	0.3%	0.049
Any Bleeding (10 days)	4.5%	1.7%	0.034
Leg Pain (10 days)	- 1.62	- 1.29	0.019
Leg Pain (30 days)	- 2.17	- 1.83	0.026
Leg Swelling (10 days)	- 0.26	+ 0.27	0.024
Leg Swelling (30 days)	- 0.74	- 0.28	0.051

No fatal or intracranial bleeds in either arm (10 day) PCDT Arm: ¾ transfusions & 2 embolization's

Study Outcomes
Long-Term Effects of PCDT

Outcome (24 Months)	PCDT N=336	No-PCDT N=355	P Value
Any PTS	**46.7%**	**48.2%**	**0.56**
Recurrent VTE	12.5%	8.5%	0.09
Generic QOL (SF-36 PCS)	11.8	10.1	0.37
Venous QOL (VEINES)	27.7	23.5	0.08
Moderate to Severe PTS	17.9%	23.7%	0.035
MS – PTS: IFDVT	18.4%	28.2%	
MS – PTS: FPDVT	17.1%	18.1%	

PCDT less effective in patients ≥ 65 years old (P = 0.038)

Conclusion

- PCDT does not prevent PTS, does increase bleeding
  - Most DVT patients can avoid unhelpful procedure
  - Need better understanding of pathogenesis of PTS
- PCDT reduces early DVT symptoms and PTS severity
  - Open vein hypothesis likely relevant to PTS progression
  - Suggest targeting to IFDVT based on higher risk of PTS

	CaVenT	ATTRACT	Arnsberg
N	90	337	56
Control group without treatment	YES	YES	No
Age, years	53	53	52
Symptom duration, days	<21	<14	< - 4 weeks
Ascending femoropopliteal DVT	**52 %**	**43%**	**25%**
Descending iliofemoral DVT	**48%**	**57%**	**75%**
Mean tPA dose, mg	55 (variable)	21 (max 35 mg)	0
Major bleeding	9.0%	1.7%	0
Definition of criteria for stenting	**NO**	**NO**	**Yes (stenosis > 50%)**
IVUS	**0**	**0**	**100%**
Dedicated venous stents	NO	NO	YES
Stenting rate	**17%**	**30%**	**100%**
Overall PTS 12-24 mts	**41%**	**47%**	**36%**
Patency rate	**75% (2y)**	**Not evaluated**	**92%**

One word on ATTRACT „Reality“

Table 2. (Continued.)

Treatment	Pharmacomechanical-Thrombolysis Group (N=336)	Control Group (N=355)
Type of additional method — no./total no. (%)‡		
Balloon venoplasty	184/297 (62)	—
Balloon maceration	183/297 (62)	—
Rheolytic thrombectomy with AngioJet	180/297 (61)	—
Stent placement	82/297 (28)	—
Large-bore catheter aspiration	63/297 (21)	—
Isolated thrombolysis with Trellis	14/297 (5)	—
Type of stent placed — no./total no. (%)‡		
Wallstent (Boston Scientific)	34/82 (41)	—
SMART (Cordis)	12/82 (15)	—
Protégé (Covidien [now Medtronic])	10/82 (12)	—
Zilver (Cook Medical)	6/82 (7)	—
Luminexx (C.R. Bard)	5/82 (6)	—
Lifestar (C.R. Bard)	2/82 (2)	—
EPIC (Boston Scientific)	2/82 (2)	—
Viabahn (Gore)	1/82 (1)	—
Multiple types	7/82 (9)	—
Not specified	3/82 (4)	—

In 59 % of cases no dedicated venous stent was used

Vedantham S, et al. Pharmacomechanical Catheter-Directed Thrombolysis for Deep-Vein Thrombosis. N Engl J Med. 2017 Dec 7;377(23):2240-2252.

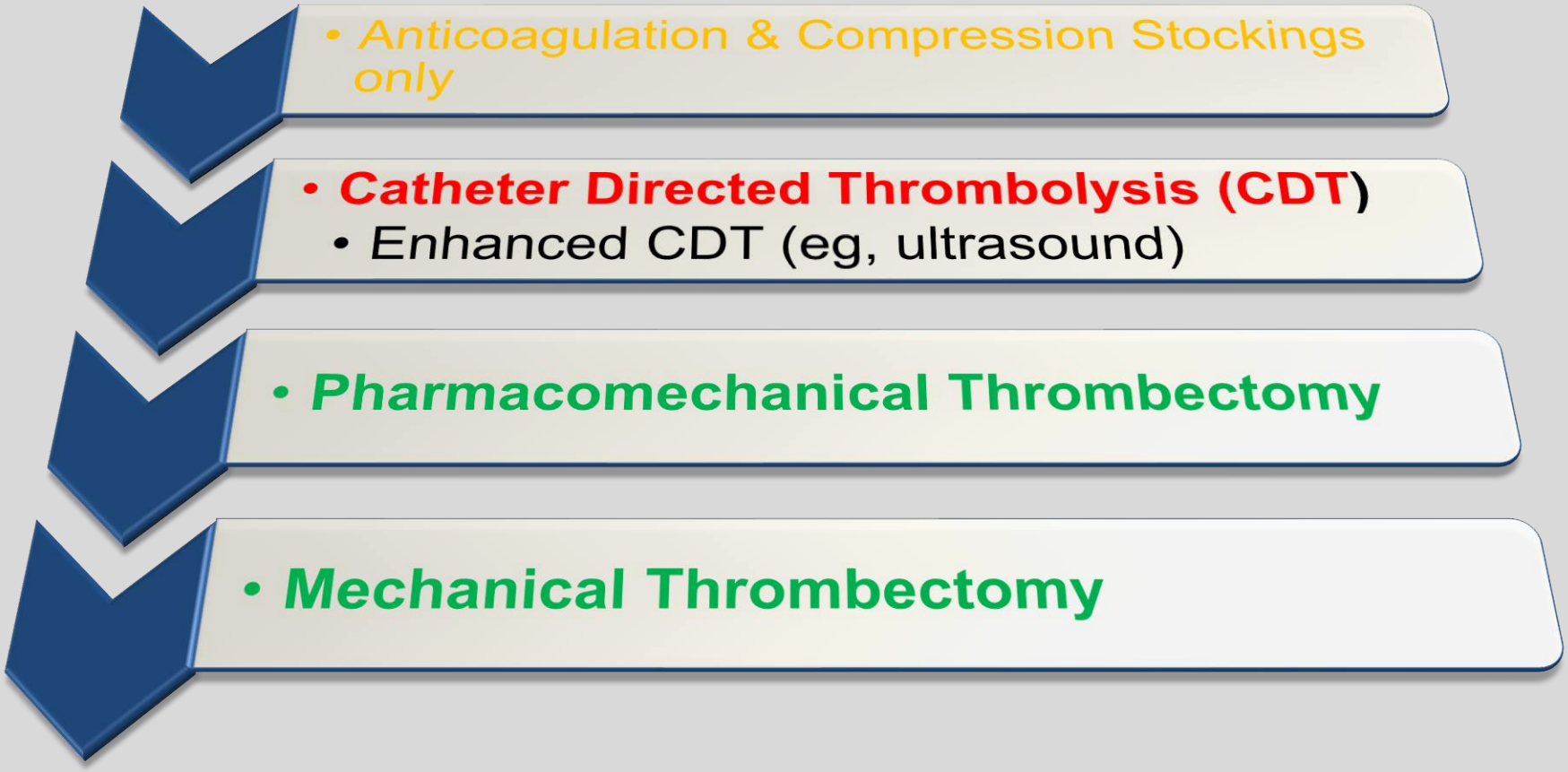
The „ATTRACT“ failures

- Inclusion of femoropopliteal DVT (43%)
- No definition of criteria for stenting
- No IVUS
- No dedicated venous stents (59%)

Outcome 24 months	PCDT (n=336)	No-PCDT (n=355)	P Value
Recurrent DVT	12.5%	8.5%	0.087

- Placebo around 10% recurrent DVT
- ASA 6% recurrent DVT
- NOACS 1% recurrent DVT

Venous Thrombus Treatment Options:
Proactive Endovascular Treatment



Clinical follow-up study with the ASPIREX®S Endovascular System to investigate safety and effectiveness in treatment of iliofemoral DVT patients

- ARNSBERG ASPIREX REGISTRY -

Responsible principal investigator (PI): M. Lichtenberg, R. de Graaf

Study sponsored by Vascular Clinical Research Department, Arnsberg

Klinikum Arnsberg
Akademisches Lehrkrankenhaus
Westfälische Wilhelms-Universität Münster

Patient Demographics

Total N (%)	**56 (100 %)**
Age Mean (Median [Range]) in years	52 (51 [17 - 89])
Female N (%)	**37 (66 %)**
Male N (%)	**19 (34 %)**
General Medical History	**N (%)**
Smoking status (valid observations)	**55 (100 %)**
Current	9 (16 %)
Former	4 (7 %)
Hypertension	**56 (100%)**
Yes	28 (50 %)
Immobilisation (valid observations)	**55 (100 %)**
Yes	4 (7 %)
Malignancy	**56 (100 %)**
Current active	4 (7 %)
Condition post	5 (5 %)
Oral contraceptive	**56 (100 %)**
Yes	21 (38 %)
No	35 (62%)

Study is sponsored by Klinikum Arnsberg

Diagnostic details (contd.)

	N (%)
Type of occlusion	**56 (100 %)**
Acute (< 14 days)	**40 (71 %)**
Subacute (> 14 days)	**13 (23 %)**
Chronic	2 (4 %)
Acute / Chronic	1 (2 %)

	N (%)
Location of occlusion (vessel)	**56 (100 %)**
Left complete pelvic veins including com. femoral vein, left sup. 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 com. femoral vein	3 (5 %)
Right complete pelvic veins	4 (7 %)
Length of occlusion [mm] N=56 (100 %)	**Statistics**
Mean (SD)	156.6 (72.0)
Median (Range)	150.0 (60 – 410)

Study is sponsored by Klinikum Arnsberg

Aspirex treatment (contd.)

		N (%)
Heparin [IU]		**56 (100)**
5,000		50 (89 %)
10,000		3 (5 %)
7,000 **OR** 7,500 **OR** 9,000 (1 patient each)		3 (5 %)
Thrombolysis		**56 (100 %)**
No		52 (93 %)
Yes (bolus)		4 (7%)
Technical success	Yes	**56 (100 %)**
Stent rate		**100 %**
Mean (SD)		**1.9 (1.2)**
Median (Range)		**2 (0 – 6)**
Treatment duration [min]		
Mean (SD)		**94.2 (44.8)**
Median (Range)		81.5 (27.0 – 238.0)

Study is sponsored by Klinikum Arnsberg

Patency analysis: DUS with restenosis < 50%

	N (%)
Patency on FU month 1	53/56 (95%)
Patency on FU month 6 (valid observations)	51/56 (91%)
Patency on FU month 12 (valid observations)	47/56 (84%)

Risk for re-thrombosis:

- Symptoms > 10 days
- CFV and PV involved
- > 1 DVT in past

Study is sponsored by Klinikum Arnsberg

Outcome: Post thrombotic syndrome after 12 months

	N (%)
CEAP Score < 3, rVCSS Score < 3)	43 (77 %)
CEAP Score > 3, rVCSS Score > 3)	13 (23 %)

Study is sponsored by Klinikum Arnsberg