Image Guided Therapy

IVUS Venous Compendium

Philips IGTD Clinical and Medical Affairs

October 2020

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Introduction

Peripheral venous pathology is distinctive from peripheral arterial disease. The basis of the difference in venous and arterial diseases is the complexity of the venous system anatomy and physiology. The anatomy of the lower extremity venous system is dependent on a series of valved flexible conduits and peripheral muscle pumps to return blood against the forces of gravity. The venous system can be divided into three groups – deep, superficial, and perforating veins.[1] Deep veins are located underneath the deep fascia of the lower limb, accompanying the major arteries.[2] Superficial veins are found in the subcutaneous tissue. Perforator veins, which traverse the deep fascia of the leg, connect the deep and superficial venous systems. The venous blood eventually drain into the deep veins. The deep venous system is responsible for 90% of the venous return to the right atrium from the lower extremities.

Diseases of the veins fall into two broad categories: blockage from a blood clot (thrombosis) and inadequate venous drainage (insufficiency) and can further be categorized as acute or chronic. The spectrum of clinical manifestations is broad; they can include asymptomatic telangiectasias, edema, skin changes, and overt ulceration. Abnormalities in venous return can result in chronic venous disease. Regardless of the underlying etiology, ambulatory venous hypertension is the final pathway leading to the more severe manifestations of chronic venous insufficiency such as venous leg ulcers.

Acute and chronic venous disorders are being increasingly recognized as a healthcare priority. Chronic venous disease is known as one of the most common diseases affecting adults with an estimated prevalence >30 million in the United States[4]. However, data suggest its prevalence is still underestimated based on varied presenting manifestations. The prevalence varies for the different venous diseases. The prevalence of varicose veins reported ranged from 1–60%[5,6]. Deep venous thrombosis (DVT) in the lower extremity has an estimated annual incidence of 80 cases per 100,000 and can increase with age; prevalence of lower limb DVT is approximately 1 case per 1000 population.[7] The estimated prevalence of CVI varies, from <1% to 17% in men and <1% to 40% in women.6 The frequency of venous insufficiency is believed to be higher in Westernized and industrialized nations than in developing nations, most likely due to differences in lifestyle and activity7. Estimates show that approximately 1-2% of the adult population presents with lower-limb ulceration, from which 70-90% of these ulcers are attributed to CVI.[8,9]

Chronic venous disease in the lower extremities has a substantial effect on physical health aspects of quality of life. They are associated with a recurrence rate of 60-70% at ten years, resulting in significant morbidity, prolonged disability, and substantial socioeconomic burden. Moreover, the estimated annual direct medical costs for patients with deep venous disease-related venous leg ulcers, managed conservatively, in the Western world totals approximately $9 Billion.[10]

Diagnosis and treatment modalities hinge on a thorough understanding of venous anatomy, hemodynamics, pathophysiology and progression of venous disease. However, the investigation and treatment of venous disease remains incohesive, often focused on narrow, specific aspects of venous disease. This has resulted in a lack of rigorous evidence and consensus on appropriate diagnostic modalities, and in turn, adequate and timely management of the underlying problem.

Background

The CEAP classification provides the framework for investigating patients with chronic venous disease. The system, developed by the American Venous Forum (AVF), provides a mechanism for the uniform diagnosis of venous disease and comparison of populations of patients. The four components of the CEAP classification are a description of the clinical disease class (C) based upon objective signs, the etiology (E), the anatomic (A) distribution of reflux and obstruction, and the underlying pathophysiology (P), whether related to reflux or obstruction.[11]

The CEAP system recognizes seven clinical disease categories as classified below:

Table 1. CEAP classification of chronic venous disease

Class	Clinical manifestation
C0	No visible or palpable signs of venous disease
C1	Telangiectasies or reticular veins
C2	Varicose veins
C3	Edema
C4	Skin changes without ulceration
C5	Healed venous ulcer
C6	Active venous ulcer

Sponsored by the AVF, CEAP underwent a review and revision to improve underlying details in 2004. This included revising terminology, dividing the C4 class into a and b categories and adding several descriptors to the E, A, and P categories.[12] In 2020, AVF again revised the classification by adding details and expanding on each of the four components of the CEAP classification.

Noninvasive testing can identify the pathophysiologic changes (reflux or obstruction) in individual venous segments and, in some cases, defines the underlying "etiology" of CEAP. Several diagnostic tests are available for the evaluation of acute and chronic venous disease. Duplex ultrasonography is the most useful noninvasive test for detecting and localizing chronic venous obstruction and valvular incompetence. However, it provides relatively little quantitative hemodynamic information and is often combined with measurements of hemodynamic severity determined by a number of plethysmographic methods.

Although venous duplex ultrasonography has become the standard for detection of deep venous disease, adjunctive modalities such as contrast, computed tomographic, and magnetic resonance venography have an increasing role.

Both CT-Venography (CT-V) and MR-Venography (MR-V) have evolved significantly in recent years and it is now possible to obtain detailed three-dimensional reconstructions of the venous system so that ilio-caval and pelvic venous pathology can be reliably identified however the effectiveness of both techniques for visualization of the venous vasculature is undetermined given the heterogeneity of the published studies.

Intravascular ultrasound (IVUS) can provide alternative imaging that complements traditional venography. It allows 360-degree two-dimensional gray scale ultrasound image of lumen and vessel wall structures. IVUS imaging of the major axial veins can provide valuable information such as precise location and size of these veins determined from key landmarks and venous branches. More importantly, abnormalities can be visualized including external compression, acute and chronic thrombus, fibrosis, mural wall thickening, and spurs. It provides information about defects within the lumen, degree of stenosis, and structures immediately adjacent to the veins.

While venography is either one dimensional or multiplanar, IVUS gives a full circumferential view of the vein lumen, thus it is adapted better for the elliptical and flattened shape of the vein lumen. IVUS has been shown to be more sensitive than venography[16] and provides additional information such as: assessment of % stenosis, thrombus, real time vessel diameters, length of stenosis, dissection, and location of side branches (without using contrast). This modality helps to accurately determine the dimensions of a vein and appropriate sizing of stents. Additionally, it allows immediate assessment of post-treatment therapy and completeness of treatment. IVUS may also help to minimize the amount of radiation and contrast that the patient is exposed to while determining diagnosis.

Current state of the role of IVUS in the management of deep venous disease

Historically, venography has been considered the standard of care diagnostic method in identifying deep venous disease. CT-V and MR-V still present with difficulties in both feasibility and interpretation. The role of IVUS in the examination of deep veins is emerging, with increasing evidence demonstrating improved accuracy of detection compared to MR-V.[17]

To date, much of the literature on the role of IVUS is specific to certain procedures or venous diseases such as the treatment of venous obstruction and the placement of vena cava filters at the bedside. IVUS has been shown to be significantly more sensitive than multiplanar venography in identifying and characterizing venous stenoses, which has led to changes in treatment plans in 57% of cases most often because of failure of venography to detect a significant lesion (72%; 41/57).[16] An increasing number of studies demonstrate that IVUS is significantly more sensitive than venography in identifying stenotic lesions in the iliac-caval segments. In post-thrombotic syndrome (PTS), the endovenous and parietal fibrotic damage is clearly shown by IVUS so that the full extension of the lesion can be identified and treated.

While IVUS aids in identifying key parameters, including sizing for iliac vein stenting and completeness of therapy, it is unknown whether this translates into improved clinical outcomes, like long-term stent patency. Despite the positive results supporting IVUS use as the new gold-standard diagnostic imaging modality, data demonstrating improved clinical outcomes with the use of this diagnostic application are still required to gain widespread adoption of IVUS as standard of care.

The current clinical recommendations for IVUS and endovascular interventions in peripheral venous disease are located in Appendix 1.

Table 2. Summary of current evidence for ivus use in venous disease

IVUS in iliac/common femoral vein obstruction

- IVUS appears superior to single-plane venography to estimate the degree of a chronic venous obstruction. – **Neglen et al 2002**
- IVUS provides accurate measurements for selection of stent and confirms good wall apposition of the stent after insertion. – **Neglen et al 2002**
- IVUS demonstrated to be superior to single-plane venography for the morphologic diagnosis of iliac venous outflow obstruction and is an invaluable assistance in the accurate placement of venous stents after venoplasty. Venogram results significantly underestimated the degree of stenosis by 30% – **Neglen et al 2002**
- IVUS determination of morphologically significant stenosis appears to be the best available method for the diagnosis of clinically important chronic iliac vein obstruction. – **Neglen et al 2002**
- IVUS has predictive value for symptom improvement and guiding treatment among patients with iliofemoral venous outflow disease (VIDIO trial) – **Gagne et al. 2018**
- Intravascular ultrasound (IVUS) is currently considered the gold standard in diagnosing iliac vein compression; and venography has consistently underappreciated the severity of the compression – **Shammas et al 2018**
- Assessment by IVUS was critical for the stent to cover the entire obstruction in iliofemoral venous obstructions, as opposed to venography, which may underestimate the lesion (VIRTUS trial) – **Razavi et al. 2018**
- IVUS is the current gold standard for the identification of venous obstruction in the lower extremity outflow tract and should be used to ensure the identification of all lesions. – **Lau et al. 2019**

IVUS in non-thrombotic iliac vein lesions

- IVUS identified stenotic lesions in approximately one-third more vein segments than venography and the degree of stenosis was underestimated with venography (VIDIO trial) – **Gagne et al. 2017**
- IVUS diameter and area measurements of baseline stenosis were both statistically significant predictors of clinical improvement at 6 months, whereas venographic diameter measurement of baseline stenosis did not demonstrate significant predictive usefulness (VIDIO trial) – **Gagne et al. 2018**
- IVUS identified 20% more lesions and was more accurate in identifying the location of the iliac-caval confluence and the distal landing zone in the majority of limbs compared with venography – **Montminy et al 2019**

IVUS in chronic venous insufficiency

- IVUS has been found invaluable during stent deployment to accomplish the many necessary technical steps in a more precise fashion than is possible with radiologic guidance alone – **Raju et al. 2008**

- Because of the high diagnostic yield of IVUS in severely symptomatic patients, it should be used routinely even if venography is negative for obstruction– **Raju et al. 2010**

- Venography was poorly sensitive to the presence of obstruction in patients with CEAP C3 limbs and lymphedema who underwent iliac vein stenting – **Raju et al. 2012**

- Venography had 61% sensitivity to the diagnosis of venous obstruction, whereas IVUS had a sensitivity of 88% for significant (>50% area stenosis) venous obstruction – **Raju et al. 2012**

IVUS in deep vein thrombosis

- IVUS was more sensitive than venography in the detection of residual thrombus and underlying venous lesions after percutaneous pharmacomechanical thrombectomy for iliofemoral DVT – **Murphy et al. 2010**

- IVUS was superior in delineating lumen surface morphology for assessing the lytic outcomes of thrombolytic regimens in limbs with DVT and/or iliac vein stent thrombosis – **Raju et al. 2014**

- IVUS should be viewed as complementary to assess residual thrombus – **Raju et al. 2014**

- Both venogram and balloon contouring may miss important lesions, and both not appear to be superior when compared with IVUS - **Ascher et al. 2017**

IVUS in post-thrombotic syndrome

- IVUS is invaluable, both as a diagnostic and therapeutic tool to direct ilio-caval stent placement as treatment for proximal iliofemoral obstruction – **Meissner et al. 2007**

- IVUS is recommended even when venography is negative for obstruction, as the diagnostic yield is very high, especially when combined with the routine "balloon sizing" maneuver. – **Raju et al 2013**

- IVUS planimetry is essential in proper assessment of post-thrombotic iliac veins as it may look deceptively normal due to only a slight diameter reduction on venography. – **Raju et al 2013**

- When stenosis was identified by both IVUS and venography, the degree of stenosis was underestimated with venography (VIDIO trial) – **Gagne et al. 2017**

- IVUS changed the treatment plan in >50% of cases. In 35% of cases, the decision to place a venous stent was based solely on IVUS (VIDIO trial) – **Gagne et al. 2017**

- IVUS diameter and area measurements of baseline stenosis were both statistically significant predictors of clinical improvement at 6 months, whereas venographic diameter measurement of baseline stenosis did not demonstrate significant predictive usefulness (VIDIO trial) – **Gagne et al. 2018**

- IVUS measurement of post-procedural stenotic change (both diameter and area stenosis) was a highly significant predictive model for future improvement, while venogram measurement of stenotic change did not demonstrate a significant correlative relationship with later clinical improvement (VIDIO trial) – **Gagne et al. 2018**

- IVUS is superior to venography for procedural guidance during iliac vein stent placement, including the identification of lesions and the correct location of maximal stenosis – **Montminy et al 2019**

- IVUS examination has a high diagnostic yield as a single intraoperative investigative modality in patients with clinical signs and symptoms of chronic venous disease. – **Saleem et al 2019**

Abstracts

1. Venography versus intravascular ultrasound for diagnosing and treating iliofemoral vein obstruction

Paul J. Gagne, MD, Robert W. Tahara, MD, Carl P. Fastabend, MD, Lukasz Dzieciuchowicz, MD, William Marston, MD, Suresh Vedantham, MD, Windsor Ting, MD, and Mark D. Iafrati, MD
J Vasc Surg Venous Lymphat Disord. 2017 Sep;5(5):678-687.
https://pubmed.ncbi.nlm.nih.gov/28818221/

Objective
The Venogram vs IVUS for Diagnosing Iliac vein Obstruction (VIDIO) trial was designed to compare the diagnostic efficacy of intravascular ultrasound (IVUS) with multiplanar venography for iliofemoral vein obstruction.

Methods
During a 14-month period beginning July 2014, 100 patients with chronic Clinical, Etiologic, Anatomic, and Pathophysiologic clinical class C4 to C6 venous disease and suspected iliofemoral vein obstruction were enrolled at 11 U.S. and 3 European sites. The inferior vena cava and common iliac, external iliac, and common femoral veins were imaged. Venograms were measured for vein diameter; IVUS provided diameter and area measurements. Multiplanar venograms included three views: anteroposterior and 30-degree right and left anterior oblique views. A core laboratory evaluated the deidentified images, determining stenosis severity as the ratio between minimum luminal diameter and reference vessel diameter, minimal luminal area, and reference vessel area. A 50% diameter stenosis by venography and a 50% cross-sectional area reduction by IVUS were considered significant. Analyses assessed change in procedures performed on the basis of imaging method and concordance of measurements between each imaging method.

Results
Venography identified stenotic lesions in 51 of 100 subjects, whereas IVUS identified lesions in 81 of 100 subjects. Compared with IVUS, the diameter reduction was on average 11% less for venography ($P < .001$). The intraclass correlation coefficient was 0.505 for vein diameter stenosis calculated with the two methods. IVUS identified significant lesions not detected with three-view venography in 26.3% of patients. Investigators revised the treatment plan in 57 of 100 cases after IVUS, most often because of failure of venography to detect a significant lesion (41/57 [72%]). IVUS led to an increased number of stents in 13 of 57 subjects (23%) and the avoidance of an endovascular procedure in 3 of 57 subjects (5%). Overall, IVUS imaging changed the treatment plan in 57 patients; 54 patients had stents placed on the basis of IVUS detection of significant iliofemoral vein obstructive lesions not appreciated with venography, whereas 3 patients with significant lesions on venography had no stent placed on the basis of IVUS.

Conclusions
IVUS is more sensitive for assessing treatable iliofemoral vein stenosis compared with multiplanar venography and frequently leads to revised treatment plans and the potential for improved clinical outcome.

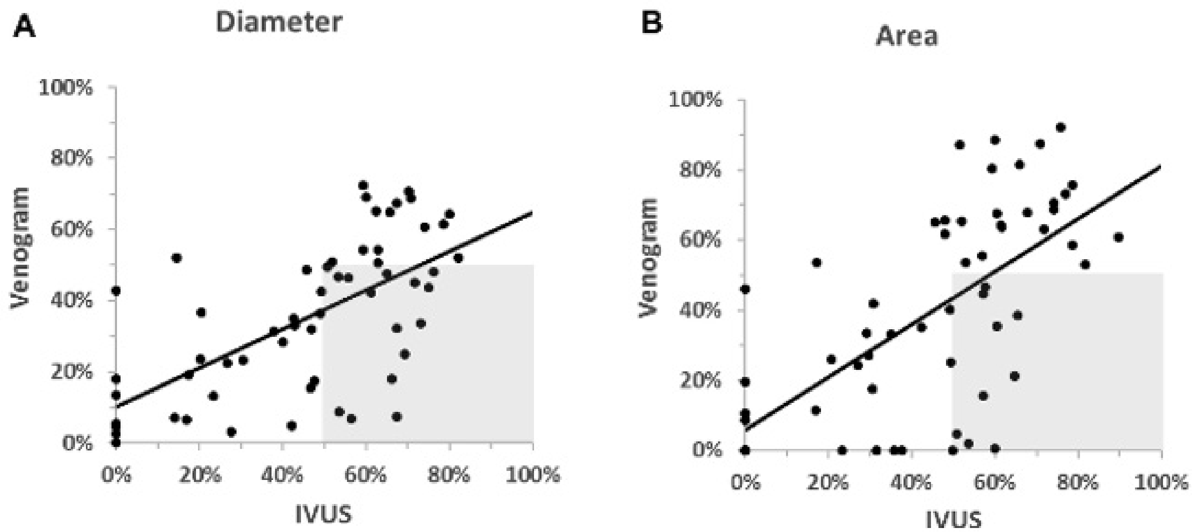

Fig 2. A, Correlation of percentage diameter reduction as determined by venography vs intravascular ultrasound (*IVUS*) on baseline, preintervention imaging studies. The *shaded area* depicts subjects for whom the venogram measurement was ≤50% diameter reduction but the IVUS measurement was >50% diameter reduction. **B,** Correlation of cross-sectional area (CSA) reduction as determined by venography vs IVUS on baseline, pre-intervention imaging studies. The *shaded area* depicts subjects for whom the venogram measurement was ≤50% CSA reduction but the IVUS measurement was >50% CSA reduction.

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2. Analysis of threshold stenosis by multiplanar venogram and intravascular ultrasound examination for predicting clinical improvement after iliofemoral vein stenting in the VIDIO trial

Paul J. Gagne, MD, Antonios Gasparis, MD, Stephen Black, MD, Patricia Thorpe, MD, Marc Passman, MD, Suresh Vedantham, MD, William Marston, MD, Mark Iafrati, MD
J Vasc Surg Venous Lymphat Disord. 2018 Jan;6(1):48-56.e1.
https://pubmed.ncbi.nlm.nih.gov/29033314/

Background
Selecting patients for iliofemoral vein stenting has traditionally relied on the identification and quantification of stenotic lesions with imaging such as multiplanar venography. Recently, intravascular ultrasound (IVUS)imaging has become more available. However, to date, the usefulness of these imaging modalities using the customary >50% treatment threshold for diameter (multiplanar venography) and area (IVUS) stenosis of iliofemoral veins has not been validated prospectively within the context of clinical improvement.

Objective
To assess the diagnostic usefulness of venography and IVUS for prediction of clinical improvement, and to better define a baseline threshold of iliofemoral vein stenosis where interventional treatment is more likely to result in symptom improvement in Clinical Etiologic Anatomic Pathophysiologic (CEAP) classification of 4-6 chronic venous insufficiency patients.

Methods
The multicenter Venogram Versus Intravascular Ultrasound for Diagnosing and Treating Iliofemoral Vein Obstruction (VIDIO) trial prospectively enrolled 100 symptomatic patients (Clinical Etiologic Anatomic Pathophysiologic classification [CEAP] of 4-6) with suspected iliofemoral venous outflow disease. Venous stenting for presumed significant iliofemoral vein stenosis, based on imaging and clinical findings, was performed on 68 patients. Based on imaging, stenosis was characterized as non-thrombotic in 48 patients and post-thrombotic in 20 patients. Each underwent baseline and post-stenting venography and IVUS to compare the diagnostic and clinical usefulness of the tests. The revised Venous Clinical Severity Score was used to assess clinical patient outcome. A >4-point reduction in the revised Venous Clinical Severity Score between baseline and 6 months was used as an indicator of clinically meaningful improvement. Receiver operating characteristic curve analysis was used to determine the optimal diameter and area thresholds for prediction of clinical improvement.

Results
Clinical improvement after stenting was best predicted by IVUS baseline measurement of area stenosis (area under the curve, 0.64; P=0.04), with >54% estimated as the optimal threshold of stenosis indicating interventional treatment. With measurement of lumen gain from baseline to after the procedure, the optimal reduction in vein stenosis correlative of later clinical improvement was >41%; IVUS measurement of area stenosis was most predictive (area under the curve, 0.70; P=0.004). Venographic measurements of baseline stenosis and stenotic change were not predictive of later improvement. In a 48-patient non-thrombotic subset analysis, IVUS diameter rather than area measurements of baseline stenosis were significantly predictive of clinical success, but indicated a higher optimal threshold of stenosis (>61%) may be necessary.

Conclusions
This study suggests that IVUS shows significant usefulness at predicting when stenting iliofemoral vein stenosis in patients clinical-etiologic-anatomic-pathophysiologic classification of 4-6 will result in significant symptom improvement. Our findings corroborate the conventional >50% cross-sectional area threshold by IVUS as defining a clinically significant iliofemoral stenosis that, when stented, has significant predictive value for symptom improvement. In non-thrombotic patients, however, a threshold of >61% diameter stenosis by IVUS may better predict clinical improvement.

Philips key figures/tables

Table IV. Receiver operating characteristic (ROC) analyses of venographic and intravascular ultrasound (*IVUS*) measurements of baseline stenosis in all stented patients (N = 64)

Group	Cutoff value, %	Sensitivity	Specificity	Youden index	AUC (95% CI)	*P*
MPV Dia	>52	0.50	0.71	0.21	0.57 (0.44-0.70)	.33
IVUS Dia	>56	0.80	0.50	0.30	0.64 (0.51-0.76)	.05
IVUS Area	>54	0.83	0.47	0.31	0.64 (0.51-0.76)	.04

AUC, Area under the curve; *CI,* confidence interval; *IVUS Area,* intravascular ultrasound area reduction measurement; *IVUS Dia,* intravascular ultrasound diameter measurement; *MPV Dia,* multiplanar venographic diameter measurement.

3. Defining the utility of anteroposterior venography in the diagnosis of venous iliofemoral obstruction

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J Vasc Surg Venous Lymphat Disord. 2019 Jul;7(4):514-521.e4.
https://pubmed.ncbi.nlm.nih.gov/30926244/

Background
Intravascular ultrasound (IVUS) is the current standard for the diagnosis of obstruction in the iliac and femoral veins. However, multiple venographic findings including collaterals, pancaking, and contrast thinning have been suggested to improve the sensitivity of venography.

Objective
The objective of our study was to further elucidate where and how anteroposterior venography may successfully guide the diagnosis of venous obstruction.

Methods
A retrospective review of patients with chronic venous insufficiency who received iliofemoral stenting by a single practitioner at a tertiary medical center between January 2014 and August 2016 was performed. Patients who had records of anteroposterior venography and IVUS were included. Patients who underwent reoperation, did not have complete records of venography and IVUS, or had preoperative acute deep vein thrombosis were excluded. All patients with a greater than 50% luminal area reduction by IVUS underwent balloon angioplasty and stent placement. The locations of stenosis, collaterals, pancaking, and contrast thinning with venography, the locations of stenosis with IVUS, and the location of each stent placed were recorded.

Results
There were 107 patients who underwent venous stenting guided by venography and IVUS in this study. Six patients who underwent reoperation, 1 patient who had an acute preoperative deep vein thrombosis, and 14 patients who had incomplete records were excluded. Thus, 86 patients with 77 left lower extremity and 68 right lower extremity studies were available for analysis. The sensitivity by stenosis on venography was 4% in the left common iliac vein (CIV), 44% in the left external iliac vein (EIV), and 44% in the common femoral vein (CFV). The sensitivity by stenosis on venography in the right CIV, EIV, and CFV was 21%, 46%, and 40%, respectively. Combined, pancaking and collaterals had a sensitivity of 97% in the left CIV. IVUS resulted in a change in plan in 2%, 32%, and 48% of patients in the left CIV, EIV, and CFV, and in 26%, 35%, and 48% of patients in the right CIV, EIV, and CFV, respectively.

Conclusions
Anteroposterior venography can indirectly diagnose obstruction of the left CIV through the identification of collaterals and pancaking. The combination of low sensitivity and a high rate of change of plan owing to IVUS precludes complete reliance on anteroposterior venography for the diagnosis of lesions in the left EIV and CFV and the right CIV, EIV, and CFV. IVUS must be used to comprehensively identify all venous iliofemoral lesions.

Philips key figures/tables

Table IV. Venographic characterization of obstruction by combinations of stenosis, collaterals, and pancaking

	Left			Right		
Location	**CIV**	**EIV**	**CFV**	**CIV**	**EIV**	**CFV**
Stenosis and collaterals on venography compared with IVUS						
Sensitivity	58.6	55.8	44.4	52.6	53.6	37.0
Specificity	57.1	72.0	100.0	80.0	91.7	100.0
PPV	93.2	80.6	100.0	76.9	96.8	100.0
NPV	12.1	43.9	76.9	57.1	29.7	70.7
Stenosis and pancaking on venography compared with IVUS						
Sensitivity	87.1	46.2	48.1	50.0	48.2	48.1
Specificity	57.1	88.0	76.0	73.3	91.7	78.0
PPV	95.3	88.9	52.0	70.4	96.4	59.1
NPV	30.8	44.0	73.1	53.7	27.5	69.6
Collaterals and pancaking on venography compared with IVUS						
Sensitivity	97.1	36.5	3.7	55.3	19.6	11.1
Specificity	42.9	60.0	88.0	56.7	91.7	95.1
PPV	94.4	65.5	14.3	61.8	91.7	60.0
NPV	60.0	31.3	62.9	50.0	19.6	61.9
Stenosis, collaterals, and pancaking on venography compared with IVUS						
Sensitivity	97.1	57.7	48.1	65.8	55.4	48.1
Specificity	42.9	60.0	76.0	56.7	91.7	80.5
PPV	94.4	75.0	52.0	65.8	96.9	61.9
NPV	60.0	40.5	73.1	56.7	30.6	70.2

CIV, Common iliac vein; *EIV,* external iliac vein; *IVUS,* intravascular ultrasound; *NPV,* negative predictive value; *PPV,* positive predictive value.
Data are presented as percentages.

4. A comparison between intravascular ultrasound and venography in identifying key parameters essential for iliac vein stenting

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J Vasc Surg Venous Lymphat Disord. 2019 Nov;7(6):801-807.
https://pubmed.ncbi.nlm.nih.gov/31196766/

Background

Deep venous stenting has become the primary treatment option for obstructive venous disease. Precise identification and quantification of the disease as well as localization of optimal landing zones are key elements to success. Compared with venography (anteroposterior projection), intravascular ultrasound (IVUS) seems to be more sensitive in determining those parameters.

Objective

This study was a blinded comparison of the relative accuracy of venography compared with IVUS in determining key parameters essential for iliac vein stenting.

Methods

Between October 2013 and November 2015, there were 155 limbs (152 patients) that underwent an endovascular intervention for chronic iliofemoral vein stenosis. Venography and IVUS data were reviewed by vascular surgeons and radiologists, respectively, each blinded to the other to identify location and severity of maximal stenosis, location of iliac-caval confluence, and optimal distal landing zone. Data from venography were compared with data from IVUS. Maximal stenosis was defined as the most severe stenosis found among the four segments-common iliac vein, external iliac vein, common femoral vein, and infrarenal vena cava. IVUS was the «gold standard» for comparisons.

Results

Venography failed to identify lesion existence in 19% of limbs. The median maximal area stenosis was significantly higher with IVUS than with venography (69% vs 52%; $P < .0001$). Furthermore, venographic correlation with IVUS for the anatomic location of maximal stenosis was present in only 32% of the limbs; venography missed the location of maximal stenosis in more than two-thirds of limbs. The iliac-caval confluence location on venography correlated with IVUS findings in only 15% of patients. In 74%, it was located higher with IVUS than with venography. The mean difference was one vertebral body. Agreement between venography and IVUS on location of the distal landing zone was only 26%. The distal landing zone defined with IVUS was lower than with venography in 64% of limbs.

Conclusions

Compared with IVUS, venography substantially and significantly misses stenotic lesions-their location and severity; venography also misidentifies the location of the iliac-caval confluence and the distal landing zone in the majority of limbs. Those differences between IVUS and venography suggest that IVUS is the better diagnostic and procedural tool in iliac-caval stenting.

Philips key figures/tables

Table II. Maximal stenosis[a] on venography vs intravascular ultrasound (*IVUS*; N = 115 limbs[b])

Maximal area stenosis, %			*P* value
Venography	52 (0-100)		<.0001
IVUS	69 (50-90)		
IVUS stenosis invisible on venography			27 (19)
Segment location agreement, venography vs IVUS, for maximal stenosis			46 (32)
Location of stenosis			
	Venography[c]	**IVUS**[c]	***P* value**
CFV	34 (29)	8 (6)	<.0001
EIV	42 (36)	23 (16)	
CIV	40 (34)	112 (78)	
IVC	0	1 (1)	

EIV, External iliac vein; *CFV*, common femoral vein; *CIV*, common iliac vein; *IVC*, inferior vena cava.
Categorical variables are presented as number (%). Continuous variables are presented as median (range).
[a]The most severe of the stenoses present among the four iliac-caval-femoral segments. Only visible venographic stenoses were included for area stenosis calculation.
[b]Of 155 limbs, 40 were excluded from analysis because stenosis detail was poor on venography (17 limbs) or IVUS (23 limbs); see text.
[c]More than one lesion was found per venogram or IVUS image.

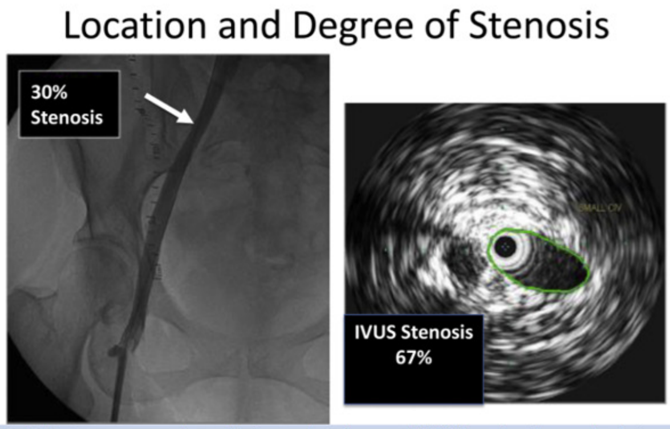

Fig 3. Disparity between venography and intravascular ultrasound (*IVUS*) in estimating maximal stenosis. In the example shown, the common iliac vein (CIV) was identified as the site of maximal location with an estimated diameter stenosis (53% area stenosis) as shown (*left*). IVUS area stenosis at the same location was higher at 67% area stenosis (*right*). The major disparity between the two techniques, however, was in identifying the segment of maximal stenosis. The two techniques identified different segments as the site of maximal stenosis in more than two-thirds of limbs. See text.

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5. Device and imaging-specific volumetric analysis of clot lysis after percutaneous mechanical thrombectomy for iliofemoral DVT

Erin H Murphy, Harshal S Broker, Eric J Johnson, J Gregory Modrall, R James Valentine, Frank R Arko
J Endovasc Ther. 2010 Jun;17(3):423-33. doi: 10.1583/10-3088.1.
https://pubmed.ncbi.nlm.nih.gov/20557187/

Objective
To determine the most accurate method of assessing clot lysis after percutaneous mechanical thrombectomy for iliofemoral deep vein thrombosis (DVT) and to evaluate the effectiveness of two different pharmacomechanical thrombectomy devices.

Methods
Between 2004 and 2009, 33 patients (18 women; mean age 47 years) with iliofemoral DVT underwent pharmacomechanical thrombectomy using the AngioJet (n = 18) or Trellis (n = 15) devices with 10 mg of tenecteplase. Intravascular ultrasound (IVUS) and venography were performed over the iliofemoral segments before and after treatment. Cross-sectional vessel and lumen diameters were measured from the IVUS scans and the post-procedure anteroposterior and lateral venograms at 3 points (proximal, mid-section, and distal) along each iliofemoral vein by 2 independent observers blinded to the treatment method. Volumes of the recanalized segments were calculated and compared to volumes of the original venous segments to assess clot lysis with each PMT device. IVUS scans and venograms were also compared for their ability to identify residual lesions or clot in need of treatment. Repeatability between and among observers was analyzed using the Bland and Altman method.

Results
All procedures were successfully completed; there were only 2 minor bleeding complications. The mean volume of the recanalized segment was 2255+/-66 mm^3 by IVUS, representing 80% lysis of the clot compared to what was perceived as >90% lysis with venography ($p<0.05$). IVUS was able to delineate significant residual thrombus, stenosis, or May-Thurner anatomy requiring ancillary interventions in 100% of patients versus 48% (16/33) on the venograms ($p<0.01$). Quantitative assessments of the diameters of the involved venous segments from the venograms and IVUS were consistent between and among observers. Comparing the similar patient subgroups, AngioJet resulted in greater clot lysis (88%) versus the Trellis device (72%; $p<0.01$), corresponding to recanalized venous segment volumes of 2486+/-74 and 2025+/-57 mm^3 and total venous segment volumes of 2826+/-84 and 2813+/-79 mm^3, respectively.

Conclusions
IVUS is superior to venography for detection of residual thrombus and underlying venous pathology after pharmacomechanical thrombectomy. While greater clot lysis was seen with the AngioJet system, both the AngioJet and Trellis devices resulted in excellent clinical clot lysis.

Philips key figures/tables

TABLE 2
Imaging-Specific Postintervention Assessment of Clot Burden, Degree of Thrombolysis, and Underlying Venous Pathology

	Venography: Perceived Assessment	IVUS: Actual Assessment	p
Venous segment volume, mm^3	N/A	2819±83 (2675–2999)	N/A
Recanalized segment volume, mm^3	2261±56 (1991–2298)	2255±66 (1912–2412)	NS
Post-treatment thrombus volume, mm^3	0	564±32 (74–901)	<0.01
Degree of thrombolysis, %	>90	80	<0.05
Identification of underlying venous lesions requiring intervention	16/33 (48%)	33/33 (100%)	<0.01

Continuous data are presented as means±standard deviation; categorical data are given as counts (percentages). N/A: not available, NS: not significant.

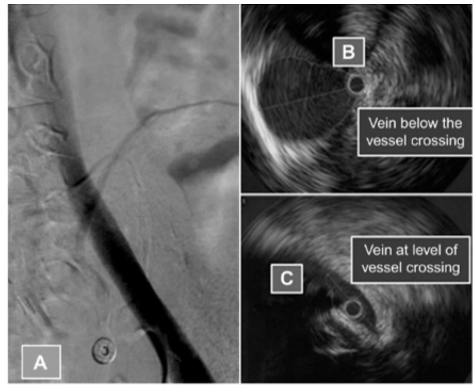


Figure 5 ◆ Comparison of completion IVUS and venography for the detection of underlying venous pathology following PMT. Venography may appear normal (**A**) despite the presence of pervasive venous lesions, such as May-Thurner anatomy, visualized here with IVUS (**B, C**). Failure to recognize and treat these underlying venous lesions may reduce the benefits of intervention and increase the patient's risk of DVT recurrence.

6. Intravascular ultrasound scan evaluation of the obstructed vein

Peter Neglén and Seshadri Raju
J Vasc Surg. 2002 Apr;35(4):694-700. doi: 10.1067/mva.2002.121127.
https://pubmed.ncbi.nlm.nih.gov/11932665/

Objective
The purpose of this study was the comparison of intravascular ultrasound scanning (IVUS) with transfemoral venography in the assessment of chronic iliac vein obstruction.

Methods
IVUS and standard, single-plane, transfemoral venography were performed in 304 consecutive limbs during balloon dilation and stenting of an obstructed iliac venous segment. The appearance of the obstruction was described, and the degree of stenosis (maximal diameter reduction) was estimated with venography and IVUS. The stenotic area was derived with diameter calculations (∏r2) and also was measured with the built-in software of the IVUS apparatus before and after dilation and stenting in 173 limbs. Preoperative hand/foot differential pressure and preoperative dorsal foot venous and intraoperative transfemoral hyperemia-induced pressure elevations after intra-arterial injection of papaverine hydrochloride were measured.

Results
With IVUS, fine intraluminal and mural details were detected (e.g., trabeculation, frozen valves, mural thickness, and outside compression) that were not seen with venography. The median stenosis (with diameter reduction) on venographic results was 50% (range, 0 to 100%) and on IVUS results was 80% (range, 25% to 100%). In a comparison with IVUS as the standard, venography had poor sensitivity (45%) and negative predictive value (49%) in the detection of a venous area stenosis of >70%. The actual stenotic area was more severe when measured directly with IVUS (0.31 cm^2; range, 0 to 1.68 cm^2) versus derived (0.36 cm^2; range, 0 to 3.08 cm^2; P <0.001), probably as a result of the noncircular lumen geometry of the stenosis. No correlation was found between any of the preoperative or intraoperative pressure measurements and degree of stenosis with or without collaterals. When collaterals were present, a more severe stenosis (median, 85%; range, 25% to 100%) was observed (versus a 70% stenosis in the absence of collaterals; range, 30% to 99%; P <.001), along with actual stenotic area (with collaterals: median, 0.24 cm^2; range, 0 to 1.18 cm^2; without collaterals: median, 0.45 cm^2; range, 0.02 to 1.68 cm^2; P <0.01) and a higher rate of hyperemia-induced pressure gradient (> or =2 mm Hg; with collaterals, 34%; without collaterals, 11%; P <0.05).

Conclusions
Venous IVUS appears to be superior to single-plane venography for the morphologic diagnosis of iliac venous outflow obstruction and is an invaluable assistance in the accurate placement of venous stents after venoplasty. No preoperative or intraoperative pressure test appears to adequately measure the hemodynamic significance of the stenosis. In lieu of adequate hemodynamic tests, IVUS determination of morphologically significant stenosis appears to be presently the best available method for the diagnosis of clinically important chronic iliac vein obstruction. Collateral formation should perhaps be looked on as an indicator of a more severe stenosis, although significant obstruction may exist with no collateral formation.

Philips key figures/tables

Table I. Degree of obstruction, diameters, and calculated and actual transverse lumen areas (median [range])

Obstruction (n = 304)		*Before stenting (n = 173)*			*After stenting (n = 173)*		
With venography	*With IVUS*	*Diameter (cm)*	*Calculated area (cm²)*	*Actual area (cm²)*	*Diameter (cm)*	*Calculated area (cm²)*	*Actual area (cm²)*
50% (0 – 100%)	80% (25% – 100%)*	0.67 (0 – 1.98)	0.36 (0 – 3.08)	0.31 (0 – 1.68)†	1.48 (0.85 – 1.91)	1.72 (0.56 – 2.86)	1.67 (0.65 – 2.60)†

*$P < .001$, compared with obstruction on venographic results.
†$P < .001$, comparison of actual area with calculated area.
IVUS, Intravascular ultrasound scanning.

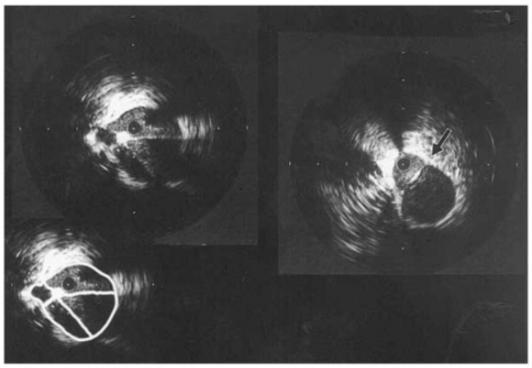


Fig 6. Intraluminal details visualized with intravascular ultrasound scanning. Postthrombotic trabeculation (*left*, trabeculae and vein wall artificially enhanced in *lower image*) and intraluminal web (*right, arrow*).

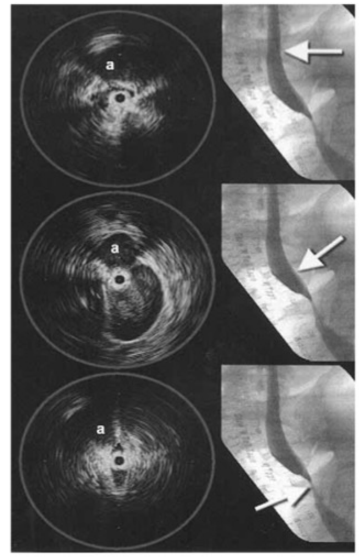


Fig 8. Several iliac venous intravascular ultrasound scan (IVUS) images *(left)* and transfemoral venogram *(right)* obtained in post-thrombotic limb. On IVUS images, iliac artery *(a)* is in similar position and catheter can be seen in vein *(black circle)*. *Arrows* on venogram indicate levels where IVUS images were obtained. With transverse orientation of stenosis with IVUS, venogram appearance may be near normal despite severe stenosis *(top)* as compared with sagital orientation of the stenosis, when findings on IVUS and venogram correspond *(bottom)*. *Middle images* show nonstenotic vein on both investigations.

7. High prevalence of nonthrombotic iliac vein lesions in chronic venous disease: a permissive role in pathogenicity

Seshadri Raju and Peter Neglen
J Vasc Surg. 2006 Jul;44(1):136-43; discussion 144. doi: 10.1016/j.jvs.2006.02.065.
https://pubmed.ncbi.nlm.nih.gov/16828437/

Background
Nonthrombotic iliac vein lesions (NIVL), such as webs and spurs described by May and Thurner, are commonly found in the asymptomatic general population. However, the clinical syndrome, variously known as May-Thurner syndrome, Cockett syndrome, or iliac vein compression syndrome, is thought to be a relatively rare contributor of chronic venous disease (CVD), predominantly affecting the left lower extremity of young women.

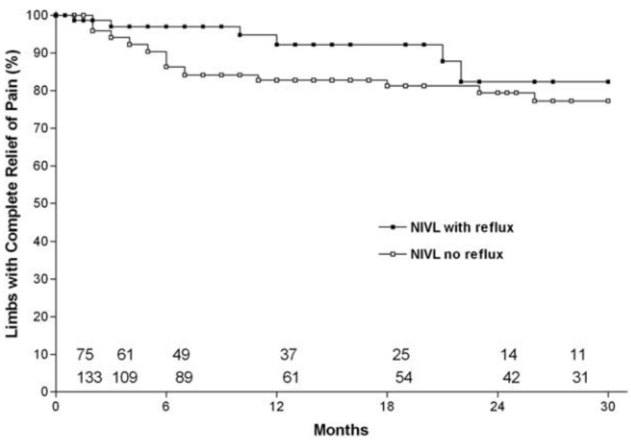
Objective
The present study describes the much broader disease profile that has emerged with the use of intravascular ultrasound (IVUS) scanning for diagnosis and analyzes stent placement outcome in two specific NIVL subsets that may offer clues to their pathogenic role.

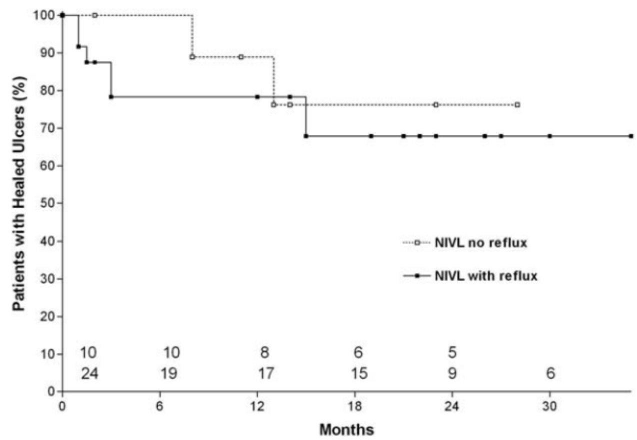
Methods
Among 4026 patients with CVD symptoms spanning the range of CEAP clinical classes, IVUS examinations were selectively done in severely symptomatic patients for indications as described. Iliac vein obstructive lesions were found by IVUS examination in in 938 limbs of 879 patients. 53% of the limbs had NIVL, 40% were post-thrombotic, and 7% were a combination by distinctive IVUS appearance supplemented by ancillary clinical data. Stents were placed in 332 limbs in 319 patients in two NIVL subsets. The subsets, one with and one without associated distal limb reflux, were compared. Reflux was left untreated in the first subset.

Results
The median age was 54 years (range, 18 to 90 years). The female-male ratio was 4:1 and the left-right ratio was 3:1. NIVL lesions in the iliac vein occurred at the iliac artery crossing (proximal lesion) and also at the hypogastric artery crossing (distal lesion), a new IVUS finding. Venography was only 66% sensitive, with 34% of venograms appearing “normal.” IVUS had a diagnostic sensitivity of >90%. The cumulative results observed at 2.5 years after stent placement in the NIVL subsets with reflux and without reflux, respectively, were complete relief of pain 82% and 77%, complete relief of swelling 47% and 53%, complete stasis ulcer healing 67% and 76%, and overall clinical relief outcome 75% and 79%. These results are nearly identical between the two subsets even though distal reflux remained uncorrected in the NIVL plus reflux subset.

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.

Philips key figures/tables





8. Unexpected major role for venous stenting in deep reflux disease

Seshadri Raju, Rikki Darcey, and Peter Neglén
J Vasc Surg. 2010 Feb;51(2):401-8; discussion 408. doi: 10.1016/j.jvs.2009.08.032. Epub 2009 Dec 14.
https://pubmed.ncbi.nlm.nih.gov/20006920/

Background
Treatment of chronic venous insufficiency (CVI) has largely focused on reflux. Minimally-invasive techniques to address superficial and perforator reflux have evolved, but correction of deep reflux continues to be challenging. The advent of intravascular ultrasound (IVUS) scan and minimally invasive venous stent technology have renewed interest in the obstructive component in CVI pathophysiology.

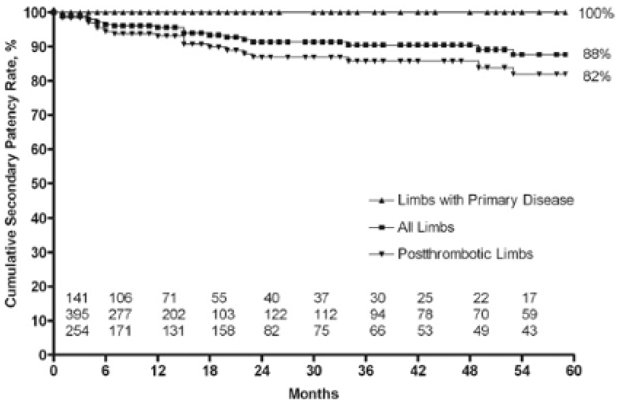
Objective
The aim of this study is to assess stent-related and clinical outcomes following treatment by iliac venous stenting alone in limbs with a combination of iliac vein obstruction and deep venous reflux.

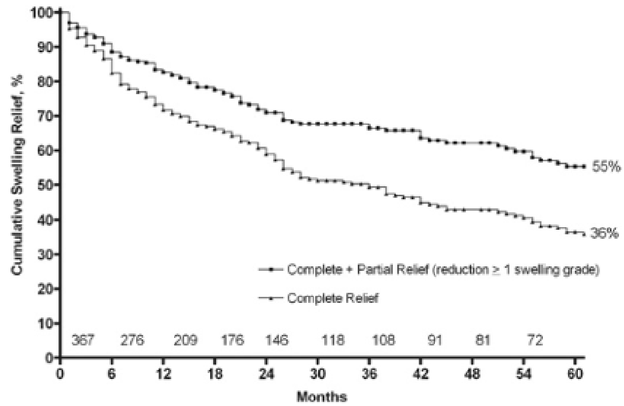
Methods
A total of 528 limbs in 504 patients, ranging in age from 15 to 87, underwent IVUS-guided iliac vein stent placement to correct obstruction over an 11-year period. The etiology of obstruction was nonthrombotic in 196 (37%), post-thrombotic in 285 (54%) limbs, and combined in 47 (9%). Clinical severity class of CEAP was C3 in 44%, C(4,5) in 27%, and C6 in 25% of stented limbs. Deep venous reflux was present in all limbs, associated with superficial and/or perforator reflux in 69%. Reflux was severe in 309/528 (59%) limbs (reflux multi-segment score > or = 3) and 224/528 (42%) limbs had axial reflux. Venography and other functional tests had poor diagnostic sensitivity to detect obstruction, which was ultimately diagnosed by IVUS. The IVUS-guided iliac vein stenting was the only procedure performed and the associated reflux was left uncorrected.

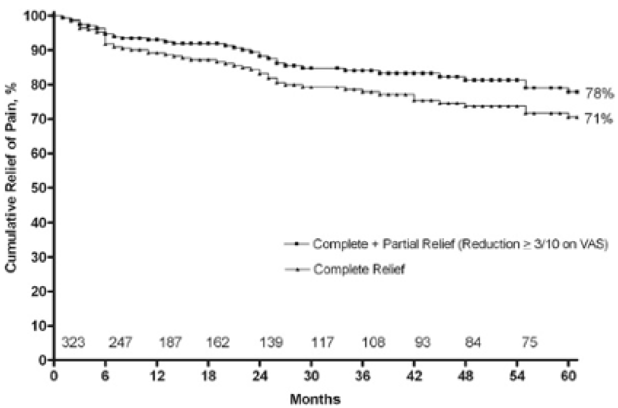
Results
There was no mortality; morbidity was minor. Cumulative secondary stent patency was 88% at 5 years; no stent occlusions occurred in nonthrombotic limbs. Cumulative rates of limbs with healed active ulcers, freedom of ulcer recurrence in legs with healed ulcers (C5), and freedom from leg dermatitis at 5 years were 54%, 88%, and 81%, respectively. Cumulative rate of substantial improvement of pain and swelling at 5 years was 78% and 55%, respectively. Quality of life improved significantly. Reflux parameters did not deteriorate after stenting.

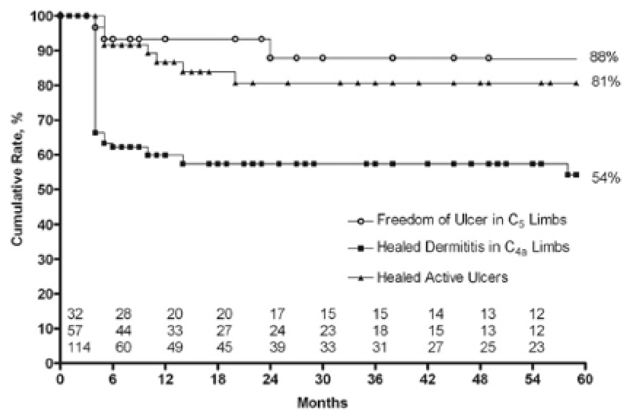
Conclusions
Iliac venous stenting alone is sufficient to control symptoms in the majority of patients with combined outflow obstruction and deep reflux. Partial correction of the pathophysiology in limbs with multisystem or multilevel disease can provide substantial symptom relief. Percutaneous stent technology in concert with other minimally-invasive techniques to address superficial and/or perforator reflux offers such partial correction in limbs with advanced CVI and complex venous pathology. Open correction of obstruction or reflux is now required only infrequently as a “last resort”.

Philips key figures/tables









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9. Diagnosis and treatment of venous lymphedema

Seshadri Raju, James Brooke Furrh, and Peter Neglén
J Vasc Surg. 2012 Jan;55(1):141-9. doi: 10.1016/j.jvs.2011.07.078. Epub 2011 Sep 29.
https://pubmed.ncbi.nlm.nih.gov/21958566/

Background
Chronic venous disease (CVD) is a common cause of secondary lymphedema. Venous lymphedema is sometimes misdiagnosed as primary lymphedema and does not receive optimal treatment. We have routinely used intravascular ultrasound (IVUS) imaging in all cases of limb swelling.

Objective
The aim of this study is to show that (1) routine use of IVUS can detect venous obstruction missed by traditional venous testing, and (2) iliac-caval venous stenting can yield satisfactory clinical relief and can sometimes reverse abnormal lymphangiographic findings.

Methods
The study comprised CVD patients who underwent iliac vein stenting. Lymphangiography was abnormal in 72 of 443 CEAP C(3) limbs, with leg swelling as the primary complaint (abnormal lymphangiography group). Clinical features and stent outcome were compared with a control group of 205 of 443 with normal lymphangiography (normal lymphangiographic group).

Results
Clinical features were a poor guide to the diagnosis of lymphedema. Isotope lymphangiography was not helpful in differentiating primary from secondary lymphedema. Venography had 61% sensitivity to the diagnosis of venous obstruction. IVUS had a sensitivity of 88% for significant (≥50% area stenosis) venous obstruction. At 40 months, cumulative secondary stent patency was similar for the abnormal (100%) and normal lymphangiographic (95%) groups. Swelling improved significantly after stent placement in the abnormal lymphangiographic group (mean [standard deviation] swelling grade improvement 0.8 ± 1.1) but was less ($P < 0.004$) than in the control group (1.4 ± 1.3). Complete swelling relief was 16% and 44% ($P < 0.001$) and partial improvement (≥1 grade of swelling) was 45% and 66% ($P < 0.01$) in the abnormal and normal lymphangiographic groups, respectively. Associated pain was present in 50% and 36% of the swollen limbs in the abnormal and normal lymphangiographic groups. Pain relief (≥3 visual analog scale) at 40 months was 87% and 83%, respectively ($P = 0.3$), with 65% and 71%, experiencing complete pain relief. Quality of life criteria improved after stent placement in both groups but to a better extent in the normal lymphangiographic group. Abnormal lymphangiography improved or normalized in 9 of 36 (25%) of those tested after stent correction.

Conclusions
Prevailing practice patterns and diagnostic deficiencies probably result in the misdiagnosis of many cases of venous lymphedema as “primary” lymphedema. IVUS is recommended to rule out venous obstruction as the associated or initiating cause of lymphedema. Iliac venous stenting to correct the obstruction has excellent long-term patency and good clinical outcome, although results are not as good as in those with normal lymphatic function.

Philips key figures/tables

Fig 3. Venography is poorly sensitive to iliac vein obstruction. **Left,** A venogram appears unremarkable. **Right,** A tight stenosis is present, as shown by the IVUS image. Measured lumen area by IVUS planimetry was 44.3 mm^2. Normal value in adults is ~175 mm^2. A 75% stenosis can therefore be calculated to be present.

10. Endovenous management of venous leg ulcers

Seshadri Raju, Orla K Kirk, Tamekia L Jones
J Vasc Surg Venous Lymphat Disord. 2013 Apr;1(2):165-72. doi: 10.1016/j.jvsv.2012.09.006. Epub 2013 Feb 15.
https://pubmed.ncbi.nlm.nih.gov/26992338/

Background
Compression is the current «standard» in the treatment of venous leg ulcers, and corrective surgery is ancillary. The emergence of safe and effective minimally invasive corrective techniques prompts a reappraisal of this paradigm.

Objective
The aim of the current analysis is to show that most venous leg ulcers resistant to conservative therapy can be successfully managed by endovenous technologies and to describe the related procedure selection protocols.

Methods
Among 192 consecutive limbs with venous leg ulcers, 189 were treated by (1) endovenous laser ablation (n = 30), (2) iliac vein stent placement (n = 89), or (3) both (n = 69). Residual deep reflux was not treated. No specialized wound care was used, and 38% of patients did not use stockings. Outcome measures were time to heal the ulcer and cumulative long-term healing.

Results
Sixty percent of the limbs were post-thrombotic. The median reflux segment score was 3 (range, 0-7). Thirty-seven percent had deep axial reflux. Median intravascular ultrasound-detected stenosis was 70% (range, 0%-100%) in stented patients. Sensitivity of venography to iliac vein obstruction was 52%. Postprocedural mortality was 0%, and 2% had deep venous thrombosis (<30 days). By 14 weeks, 81% of the small ulcers approximately ≤1 inch in diameter had healed. Larger ulcers were slower in healing ($P < 0.001$). Post-thrombotic etiology, presence of uncorrected deep reflux, demographic factors, or stocking use had no bearing on healing time. Long-term cumulative healing at 5 years overall was 75%. Healing was better in nonthrombotic limbs compared with post-thrombotic limbs (87% vs 66% at 5 years; $P < 0.02$) but was similar among the various demographic subsets, procedures, and whether or not patients used compression. Quality-of-life measures improved significantly. Cumulative long-term healing was unaffected by residual axial reflux and was unrelated to hemodynamic severity (air plethysmography, ambulatory venous pressure). However, long-term ulcer healing was inferior in limbs with reflux segment score of ≥3 ($P < 0.03$). Post-thrombotic limbs with a reflux score of ≥3 had the lowest cumulative healing among cohorts, but even in this category, 60% of limbs had durable healing with very few recurrences.

Conclusions
Most venous leg ulcers in this consecutive series achieved long-term healing with the described minimally invasive algorithm. Uncorrected residual reflux was not an impediment to ulcer healing. Ulcers sized ≤1 inch required no specialized or prolonged wound care. Compression was not necessary to achieve or maintain healing after interventional correction.

Philips key figures/tables

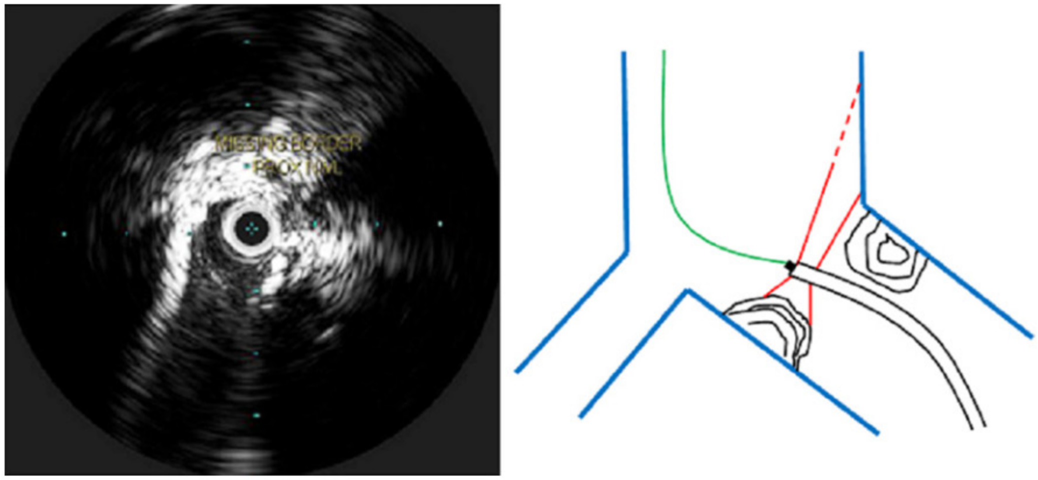

Fig 7. Left, Missing border appearance occurs when the intravascular ultrasound catheter is not coaxial in the center but tilted to the long axis. Only part of the lesion will be visible in the narrow image cross-cut. The lumen in the quadrant opposite from the lesion looks elongated due to the oblique cross-cut. **Right**, The schema illustrates how this might happen. The missing border appearance frequently occurs near the hypogastric or venocaval orifice. The blurred border is likely from image degradation due to distance.

11. Predicting iliac vein compression with computed tomography angiography and venography: correlation with intravascular ultrasound

Nicolas W Shammas, Gail A Shammas, Sue Jones-Miller, Qais Radaideh, Allyson R Winter, Andrew N Shammas, Istvan Z Kovach, Bassel Bou Dargham, Ghassan E Daher, Rayan Jo Rachwan, W John Shammas, Waleed Omar, Aman Manazir, Srikanth Kasula
J Invasive Cardiol. 2018 Dec;30(12):452-455.
https://pubmed.ncbi.nlm.nih.gov/30504513/

Background
Intravascular ultrasound (IVUS) is considered the gold standard in diagnosing common iliac vein (CIV) compression. The presence of >50% surface area reduction by IVUS is considered significant compression by most operators.

Objective
Evaluated the role of computed tomography angiography (CTA) and venography in diagnosing CIV compression when compared to IVUS.

Methods
All patients who underwent CTA of the pelvis with venous filling phase, IVUS, and venography within a few weeks apart to evaluate for symptomatic CIV compression from one cardiovascular practice were retrospectively reviewed. Quantitative vascular analysis was performed on all images obtained to determine (1) percent stenosis (PS) by venogram; and (2) minimal lumen area (MLA) and PS by CTA and IVUS at the compression site (using ipsilateral distal CIV as reference area). Spearman's rank correlation, paired t-tests, or signed rank tests were performed as appropriate to compare between values of MLA and PS among the three different imaging modalities.

Results
A total of 96 patients were included (62.5% females; mean age, 62.3 ± 14.8 years). A significant correlation was found between MLA-CTA and MLA-IVUS (Spearman's rho, 0.27; P=0.01) and PS-CTA and PS-IVUS (Spearman's rho, 0.327; P<0.01). A significant correlation was also found between PS-venogram and PS-IVUS (Spearman's rho, 0.471; P<0.001). MLA-CTA and MLA-IVUS had a median difference of +41 mm^2 (95% CI, 25.0-57.5; P<.001) whereas PS-CTA and PS-IVUS were not statistically different (median difference, -5.6 mm^2; 95% CI, -12.2 to 0.7). Furthermore, PS-IVUS and PS-venogram had a median difference of +15.2% (95% CI, 10.4-20.1; P<.001).

Conclusions
PS-venogram correlates with PS-IVUS, but venogram underestimates the PS by an average of 15.2%. In contrast, PS-CTA and PS-IVUS are not statistically different despite an over-estimation of MLA by CTA when compared to IVUS. Therefore, we conclude that PS-CTA and not PS-venogram can be used to predict PS on IVUS.

Philips key figures/tables

Table 2. Computed tomography angiography and intravascular ultrasound variables.

Variable	n	Value
CT-MLA at lesion (mm^2)	89	129.9 ± 68.1
CT-MLA reference (mm^2)	67	286.7 ± 101.5
CT-percent stenosis (%)	67	50.4 ± 26.3
Venography MLD at lesion (mm)	82	10.9 ± 4.4
Venography MLD reference (mm)	82	18.0 ± 4.2
Venography percent stenosis (%)	82	40.6 ± 19.0
IVUS-MLA at lesion (mm^2)	95	86.1 ± 48.8
IVUS-MLA reference (mm^2)	94	205.6 ± 75.1
IVUS-percent stenosis (%)	94	56.2 ± 22.3
IVUS post stent MLA at lesion (mm^2)	81	198.9 ± 66.1

Data provided as mean ± standard deviation.
CT = computed tomography; IVUS = intravascular ultrasound; MLA = minimal luminal area; MLD = minimal luminal diameter.

Appendix 1

Management of Chronic Venous Disease: Clinical Practice Guidelines of the European Society for Vascular Surgery (ESVS)[19]

- IVUS recommended as complementary to phlebography for determining ilio-caval venous compression
- CT-V and MR-V should be limited to the specific indications, e.g. for planning possible treatment, because of insufficient scientific evidence is stated to judge the true effectiveness of CT-V and MR-V for visualization of the venous vasculature

Guidelines of the Italian Society of Phlebology[20]

- IVUS is useful and a gold standard in the identification and quantification of morphological iliac stenosis and applicable in an intervention phase

Clinical Recommendations for Venous Leg Ulcers of the Society for Vascular Surgery (SVS) and the AVF:[21]

- In patients with clinically significant iliac and caval obstruction combined with infrainguinal reflux or obstruction, percutaneous balloon angioplasty with stenting is suggested as the initial procedure over deep venous valvular reconstructions or open operative bypass procedures because it is much less invasive and presents less risk to the patient
- In a patient with inferior vena cava or iliac vein total vein occlusion or severe stenosis, with or without lower extremity deep venous reflux disease that is associated with skin changes at risk for venous leg ulcer (CEAP C4b), healed ulcer (CEAP C5) or active venous leg ulcer (CEAP C6), venous angioplasty and stent recanalization is recommended in addition to standard compression therapy to aid in venous ulcer healing and to prevent recurrence

Clinical Recommendations for Iliofemoral DVT of the Interdisciplinary Expert Panel on Iliofemoral Deep Vein Thrombosis (InterEPID):[22]

- At the time of clot removal, stenting of the iliac venous system, with self-expanding metallic stents, may be considered in cases of clinically significant stenosis or extrinsic compression

The 2020 appropriate use criteria for chronic lower extremity venous disease of the AVF, the SVS, the American Vein and Lymphatic Society, and the Society of Interventional Radiology[23]

The aim of the criteria is to provide clarity to the application of certain venous procedures, duplex ultrasound imaging, timing, and reimbursements, in the treatment of chronic lower extremity venous disease. The appropriate use criteria are intended to serve as a guide to patient care in areas where high-quality evidence is lacking to aid clinicians in making day-to-day decisions for common venous interventions.

Appropriateness criteria for iliac vein or inferior vena cava (IVC) stenting as first-line treatment:

- Iliac vein or IVC stenting for obstructive disease without superficial truncal reflux as first-line treatment in a symptomatic patient with skin or subcutaneous changes, healed or active ulcers (CEAP classes 4-6) is appropriate
- Iliac vein or IVC stenting for obstructive disease with or without superficial truncal reflux as first-line therapy in a symptomatic patient with edema due to venous disease (CEAP class 3), provided careful clinical judgment is exercised because of the potential for a wide range of coexisting nonvenous causes of edema may be appropriate
- Iliac vein or IVC stenting for obstructive disease in an asymptomatic patient for iliac vein compression, such as May-Thurner compression, for incidental finding by imaging or telangiectasia (CEAP class 1) is never appropriate

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Search methods

A comprehensive literature search strategy comprising 20 unique searches was conducted in PubMed on January 12, 2018. All searches were conducted with a date filter applied (1/1/1995 – 1/12/2018). A total of 713 papers were identified, of which 530 were duplicates and 183 were unique publications. On March 11, 2020, the search was rerun with 7 new operators. A total of 729 papers were identified, of which 308 were duplicates and 421 were unique publications. Full search strategy is detailed in Table 1 - Table 6.

A total of 46 papers and 1 case report underwent full paper review. The literature was surveyed to assess the objectives, study design, power, patient population, and conclusions regarding use of the IVUS device. Level of evidence of each publication was also graded per Oxford Centre for Evidence-based Medicine (http://www.cebm.net/oxford-centre-evidence-based-medicine-levels-evidence-march-2009) and Scottish Intercollegiate Guidelines Network (http://www.sign.ac.uk/guidelines/fulltext/50/annexoldb.html)

For this compendium, the top 11 papers were chosen by committee consensus based on the following criteria: strength of study objectives of IVUS usage, level of evidence, study design and results.

Table 1. Full Search Strategy and Output (conducted in PubMed on January 12, 2018.)

Number	Terms/operators	Search results
1	(("intravascular ultrasound") AND vein) AND iliac	83
2	(("intravascular ultrasound") AND vein) AND femoral	70
3	(("intravascular ultrasound") AND vein) AND peripheral	51
4	(("intravascular ultrasound") AND vein) AND iliofemoral	13
5	(("intravascular ultrasound") AND vein) AND iliocaval	13
6	(("intravascular ultrasound") AND venous) AND iliac	83
7	(("intravascular ultrasound") AND venous) AND femoral	69
8	(("intravascular ultrasound") AND venous) AND peripheral	52
9	(("intravascular ultrasound") AND venous) AND iliofemoral	14
10	(("intravascular ultrasound") AND venous) AND iliocaval	13
11	((IVUS) AND vein) AND iliac	45
12	((IVUS) AND vein) AND femoral	49
13	((IVUS) AND vein) AND peripheral	26
14	((IVUS) AND vein) AND iliofemoral	6
15	((IVUS) AND vein) AND iliocaval	4
16	((IVUS) AND venous) AND iliac	44
17	((IVUS) AND venous) AND femoral	44

Number	Terms/operators	Search results
18	((IVUS) AND venous) AND peripheral	24
19	((IVUS) AND venous) AND iliofemoral	6
20	((IVUS) AND venous) AND iliocaval	4
Abstracts identified		**713**
	Deletion of Duplicates	530
Total abstracts reviewed		**183**
	Exclusions after Review of Abstracts	131
Total publications included		**52**

Table 2. Updated Search Strategy for Search Stratified by Anatomic Location* and Output (conducted in PubMed on March 11, 2020.)

Number	Terms/operators	Results
1	(("intravascular ultrasound") AND vein) AND iliac	45
2	(("intravascular ultrasound") AND vein) AND femoral	23
3	(("intravascular ultrasound") AND vein) AND peripheral	9
4	(("intravascular ultrasound") AND vein) AND iliofemoral	17
5	(("intravascular ultrasound") AND vein) AND iliocaval	7
6	(("intravascular ultrasound") AND venous) AND iliac	43
7	(("intravascular ultrasound") AND venous) AND femoral	23
8	(("intravascular ultrasound") AND venous) AND peripheral	10
9	(("intravascular ultrasound") AND venous) AND iliofemoral	17
10	(("intravascular ultrasound") AND venous) AND iliocaval	7
11	((IVUS) AND vein) AND iliac	21
12	((IVUS) AND vein) AND femoral	10
13	((IVUS) AND vein) AND peripheral	4
14	((IVUS) AND vein) AND iliofemoral	5
15	((IVUS) AND vein) AND iliocaval	2
16	((IVUS) AND venous) AND iliac	21
17	((IVUS) AND venous) AND femoral	11

Number	Terms/operators	Search results
18	((IVUS) AND venous) AND peripheral	5
19	((IVUS) AND venous) AND iliofemoral	5
20	((IVUS) AND venous) AND iliocaval	1

* As this search was completed for the last literature review, the search is filtered to only include articles from January 12th, 2018 till the date of the search.

Table 3. Search Strategy for Search Stratified by Disease State and Outputs

Number	Terms/operators	Results
1	(("intravascular ultrasound" OR "IVUS") AND (Vein OR Venous) AND ("non-thrombotic compression" OR "acute deep vein thrombosis" OR "post-thrombotic syndrome" OR "chronic venous insufficiency"))	35

Table 4. Search Strategy for Search Stratified by Approved Venous Devices or Those Pending Approval and Outputs

Number	Terms/operators	Results
1	("intravascular ultrasound" OR "IVUS") AND (Vein OR Venous) AND (Vici OR "Zilver Vena" OR Venovo OR Abre)	5
2	("intravascular ultrasound" OR "IVUS") AND (Vein OR Venous) AND (VIRTUS OR VIVO OR VERNACULAR OR ABRE)	383

Table 5. Search Strategy for Analyzing Health Economics Associated With Intravascular Ultrasound Use in the Lower Extremity Venous System and Outputs

Number	Terms/operators	Results
1	("intravascular ultrasound" OR "IVUS") AND (Vein OR Venous) AND cost) AND (benefit OR effectiveness OR utilization)	11
2	("intravascular ultrasound" OR "IVUS") AND (Vein OR Venous) AND (health AND economic)	3
3	("intravascular ultrasound" OR "IVUS") AND (Vein OR Venous) AND (expense)	6
4	("intravascular ultrasound" OR "IVUS") AND (Vein OR Venous) AND (reimbursement)	0
Duplicates identified		**2**

Table 6. Updated Search Output

Abstracts identified	**729**
Deletion of duplicates	308
Total abstracts reviewed	**421**
Exclusions after review of abstracts	393
Total publications included	**28**

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