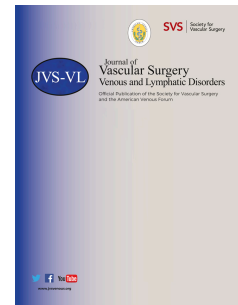


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Criteria to predict mid-term outcome after stenting of chronic iliac vein obstructions (PROMISE trial)

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**Criteria to predict mid-term outcome after stenting of chronic iliac vein obstructions  
(PROMISE trial)**

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**Type of Research:** Single center, retrospective analysis of prospectively collected registry data

**Key Findings:** Endovenous stenting was performed in 108 patients. Of those, 90 patients had chronic post-thrombotic obstruction, while 18 patients had non-thrombotic iliac vein lesion. Loss of patency occurred in 20 patients, all were treated for post-thrombotic obstruction. In addition to indication for stenting, stent occlusion is predicted by low peak flow velocity and post thrombotic changes in inflow veins.

**Take home message:** Endovascular venous stenting for chronic venous outflow obstructions is an efficacious and safe treatment in selected patients. Failure may be predicted by low peak flow velocity and post thrombotic changes in inflow veins.

**Table of Contents Summary:** Patients with post-thrombotic changes displayed significantly higher occlusion rates than patients with non-thrombotic venous lesions in this retrospective, single-center analysis of 108 patients undergoing endovenous stenting. Predictive for stent occlusion were low peak flow velocity and postthrombotic changes within inflow veins.

## **Abstract**

**Background:** Endovenous stent placement has become a first-line approach to prevent post-thrombotic syndrome in patients with chronic post-thrombotic obstruction (PTO) or non-thrombotic iliac vein lesions (NIVL) if conservative management fails. This study aims to identify factors associated with loss of patency to facilitate patient selection for endovenous stenting.

**Methods:** We retrospectively analyzed 108 consecutive patients following successful endovenous stenting for chronic vein obstruction performed at a single institution from January 2008 to July 2020. Using multivariable logistic regression, we explored potential predictive factors for loss of stent patency, including baseline demographics, postthrombotic changes as

well as peak flow velocities measured in the common femoral vein (CFV), deep femoral vein (DFV) and femoral vein (FV) using duplex ultrasound.

**Results:** Mean follow-up duration was  $41 \pm 26$  months and participants had a mean age of  $47.4 \pm 15.4$  years with 46.3% women. Ninety (83.3%) patients had PTO and 18 (16.7%) had NIVL, predominantly due to May Thurner syndrome. Loss of patency occurred in 20 (18,5%) patients, all treated for PTO. Comorbidities, side of intervention and sex did not differ between patients with occluded and patent stents. Stent occlusion was more common with increasing number of stents implanted ( $p < 0.001$ ) and with distal stent extension into and beyond the CFV ( $p < 0.001$ ). Preinterventional predictive factors for stent occlusion were lower duplex ultrasound peak velocity in the CFV (OR 7.52 95% CI 2.54 – 22.28;  $p < 0.001$ ) and FV (OR 10.75 95% CI 2.07 – 55.82;  $p < 0.005$ ), as well as post-thrombotic changes in the DFV (OR 4.51 95% CI 1.53 – 13.25;  $p = 0.006$ ) and FV (OR 3.62 95% CI 1.11 – 11.84;  $p = 0.033$ ). Peak velocities of  $\leq 7$  cm/s (IQR 0-20) in the CVF and  $\leq 8$  cm/s (IQR 5-10) in the FV were significantly associated with loss of patency

**Conclusions:** Insufficient venous inflow as assessed by low peak velocities in the CFV and FV as well as postthrombotic findings represent reliable risk predictors for stent occlusions, warranting their inclusion into the decision-making process for invasive treatment of PTO.

**Keywords:** postthrombotic syndrome; postthrombotic obstruction, non-thrombotic iliac vein lesion; vascular patency; duplex ultrasound, venous stenting, iliac vein stenting

## Introduction

The incidence of deep vein thrombosis is estimated at around 1/1000 persons per year in Western Europe [1]. Depending on thrombosis location, 20-83% of patients develop postthrombotic syndrome (PTS) despite adherence to optimal anticoagulation regimes [1,2]. Overall, iliac veins are involved in about 40% of proximal vein thromboses [3]. Anticoagulation and compression therapy fail to achieve sufficient recanalization in approximately 70% of these patients, resulting in persistent outflow obstruction which plays an essential role in the development of PTS [4,5]. Endovenous stent placement, initially introduced in the 1990s, has become the first-line revascularization approach to prevent PTS in patients with chronic non-thrombotic iliac vein lesions (NIVL) or chronic post-thrombotic vein obstruction (PTO) in iliofemoral veins [6, 7, 8, 9], thereby surpassing surgical management as the primary treatment strategy due to suboptimal clinical outcomes and low to moderate patency rates [10,11]. In a meta-analysis of 14 studies comprising 1987 patients, primary patency rates following stenting of chronic obstructive venous disease varied between 67.0% to 98.7% for follow-up durations ranging from 6 months to 120 months [12]. However inability of the randomized ATTRACT trial [13] to confirm the "open vein hypothesis" in patients with acute deep vein thrombosis and unclear evidence for endovascular treatment of chronic iliac vein obstruction, suggests that patient selection needs rigorous reconsideration. One reason for the disappointing results of the ATTRACT trial may have been the inclusion of patients with femoropopliteal thrombosis, in addition to the low technical success rate (60%) and small proportion of patients undergoing iliac vein stenting (28%).

In this retrospective, single-center study we explored potential factors to Predict Mid-term outcome after endovenous Stenting in patients with chronic PTO or NIVL (PROMISE trial). Improved understanding of factors associated with increased risk of stent occlusion may

facilitate patient selection in order to avoid disadvantageous interventions and treatment failure. We hypothesized that, prior to revascularization, inguinal vein inflow at the level of the femoral bifurcation before revascularization is an important determinant of stent patency.

## Methods

### Study design

We retrospectively analyzed a series of prospectively enrolled, consecutive patients that underwent venous stent placement for chronic vein obstructions due to PTO or NIVL at the Division of Angiology, University Hospital of Bern, Switzerland, between January 1<sup>st</sup> 2008 and July 1<sup>st</sup> 2020. Patient data were collected using the clinical information system ClinicWinData (CWD, Erlangen, Germany), paper-based patient records, and the electronic data systems PACS-IDS7, i-pdos Prod and ixserv.4 (ixmid software, Cologne, Germany). Inclusion criteria comprised the availability of a readable duplex ultrasound scan and ascending contrast phlebography, magnetic resonance venography (MRV) or computer tomographic venography (CTV) at baseline. Images were reviewed with focus on postthrombotic changes in the common femoral vein (CFV), deep femoral vein (DFV) and femoral vein (FV). We did not record the length of the primary lesions. All duplex ultrasound examinations were performed by trained examiners in our department and with patient in the supine position. We measured the maximum amplitude of antegrade spontaneous flow of the Doppler frequency curve (Fig. 1). Venous segments were defined as post-thrombotic if one of the following criteria were present: i) thickened venous wall, ii) presence of intraluminal septa, or iii) reduced venous caliber and incomplete compressibility. Results for tibial and peroneal veins were not included in the present analysis, due to sample size restrictions. Venous inflow, defined as peak flow velocity in cm/s,

was determined prior to stent placement using duplex ultrasound measurements in the CFV at the level of the inguinal ligament and 2 cm below the femoral vein confluence (DFV and FV, respectively).

### Study population

From January 1<sup>st</sup> 2008 through July 1<sup>st</sup> 2020 (150 months), 452 patients with iliofemoral venous disease underwent endovenous interventions in our institution. Overall, 241 patients were treated for acute vein thrombosis and 211 patients for chronic vein obstruction. Patients with acute thrombosis or malignancy-induced venous compression were excluded from analysis. Patients with chronic venous disorders were eligible for endovenous treatment if their clinical symptoms could be attributed to venous hypertension with a CEAP clinical stage of  $\geq 3$ , or if venous claudication was present. Out of 211 patients undergoing endovenous iliofemoral stenting for chronic vein obstruction, a total of 108 patients fulfilled the prespecified criteria (readable imaging/duplex ultrasound, chronic PTO or NIVL) and were included in the present analysis (Figure 2). Baseline demographic information (age, gender) and comorbidities (renal impairment, arterial vascular disease, diabetes mellitus, arterial hypertension, smoking history, obesity, history of thrombophilia) were recorded for all included patients. Thrombophilia testing was performed in selected patients with family history and/or suggestive history and included antithrombin, protein C, protein S, factor VIII, fibrinogen, activated protein C resistance, genetic test for the Factor V Leiden gene mutation, genetic test for the Prothrombin gene mutation, lupus anticoagulant, antiphospholipid antibodies, beta 2 glycoprotein 1 antibodies. Previous use of anticoagulation and number of VTE events preceding the intervention were not recorded. Skin changes and subjective clinical symptoms were documented and quantified using the Villalta

score [14]. Renal failure was defined as a glomerular filtration rate < 30 ml/min, while arterial vascular disease was defined as the presence of established cerebrovascular disease, coronary artery disease or peripheral artery disease. We recorded obesity as a binary variable, defined as a BMI above 30. Thrombophilia was defined as laboratory proven. The study was approved by the Swiss Ethics Committee on research involving humans (ID 2020-00825), and all enrolled patients provided written informed consent to participate in the study.

### Stenting procedure

In patients with NIVL endovenous stent implantation was undertaken using intravenous remifentanyl for analgesia and propofol for light sedation. In view of higher pain levels, associated with dilatation of postthrombotic changes, stenting for PTO was treated under general anesthesia. After ultrasound-guided access had been established via popliteal or femoral veins using 10-French sheaths, biplane venograms were obtained by digital subtraction angiography with a frame rate of two images per second. Subsequently crossing of venous lesions was attempted with stiff, angled 0.035-inch hydrophilic wires (Terumo Corporation, Tokyo Japan) or with 0.018-inch wires (Astato 30, Asahi-intecc, USA). In the event of failure to pass the target lesion using this approach, additional right jugular vein access was obtained and bidirectional wire access was attempted. Pre-dilation of all obstructions was conducted using high-pressure balloons and stent implantation was performed in a cranial to caudal direction. If more than one stent was implanted, overlap by at least 1cm was ensured. The following stents were used depending on target lesion location: i) in the common iliac vein (CIV), Sinus XL stent (Optimed, Ettlingen, Germany), Venovo Venous stent (Bard Medical, Georgia, USA), Sinus obliquus stent (Optimed, Ettlingen, Germany) and Vici Venous Stent (Boston Scientific, Maple Grove,



Minnesota, USA), ii) in the external iliac vein (EIV) or CFV, Sinus XL Flex stent (Optimed) or Zilver Vena stent (Cook, Bloomington, Indiana, USA), iii) for extension into the DFV or FV, Sinus Superflex stent (Optimed). Post-dilatation was performed to achieve complete stent expansion and satisfactory alignment. Subsequently, a venogram was obtained to confirm stent patency, adequate adaption to the vessel wall, and coverage of the entire lesion. Patients received 5.000 IU of unfractionated heparin intraprocedurally with repeated administration every 2 hours. All procedures were performed by interventionalists with several years of experience. We ensured complete coverage of postthrombotic venous segments in the iliofemoral veins, while avoiding jailing of the contralateral side by using the Sinus obliquus stent (Optimed, Ettlingen, Germany) in common iliac veins. Anticoagulation was initiated after completion of the procedure using full-dose low-molecular heparin for 24 hours followed by vitamin K antagonists or direct oral anticoagulants. The choice of specific anticoagulant was at the discretion of the interventionalist. Oral anticoagulation was continued for a minimum of six months in patients with NIVL and for at least 12 months or indefinitely in patients with post-thrombotic lesions. Compression therapy in use was continued after the intervention. Requirement for long-term compression therapy was determined during follow-up visits.

### **Follow-up procedure**

Duration of follow-up was defined as the time from the index intervention until the most recent follow-up appointment or until first stent occlusion. Time intervals between additional rescue procedures such as venoplasty for in-stent restenosis or thrombolysis for stent occlusion were not measured and hence secondary patency rates were not analyzed. Clinical follow-up visits were conducted by vascular specialists in our outpatient department at 2 weeks, 3 months and 12

months postintervention, and annually thereafter. Clinical symptoms and lower limb skin changes were recorded using the Villalta score. PTS was defined as a total score of  $\geq 5$  points or the presence of a venous ulcer. During follow-up visits each treated venous segment was examined by duplex ultrasound focusing on thrombotic or postthrombotic changes as well as flow patterns. Patency was defined as the presence of cranial flow in the absence of  $> 50\%$  lumen reduction.

## Statistical analysis

Continuous variables following a normal distribution are presented as means and standard deviations, while continuous variables with skewed distributions (Villalta score, stent number, and US velocity) are displayed as medians with interquartile ranges. Categorical variables are summarized as frequencies and percentages. Differences in baseline characteristics between patients with patent and occluded stents were assessed using the Independent Sample T Test, Mann Whitney U test, Chi-squared or Fisher's exact test, where appropriate. For the purpose of additional analyses, non-normally distributed variables (US velocity of CFV, DFV and FV) were log transformed to achieve a normal distribution. Cumulative patencies for stented limbs in patients with NIVL and PTO were compared using Kaplan-Meier survival curves and log-rank tests. Multivariate logistic regression models were used to explore the proportional contribution of flow velocity and postthrombotic lesions of the inflow veins (CFV, DFV and FV) to development of stent occlusion.

All analyses were adjusted for age and sex (model 1), in addition to smoking status and comorbidities (renal failure, arterial vascular diseases, hypertension, obesity, thrombophilia) (model 2). Sensitivity analysis was performed adjusting for covariates in model 2 as well as for

stent location (model 3). We explored variance inflation factors (VIF) for this multivariable model, detecting no collinearity ( $VIF < 2$ ). Receiver operating characteristic (ROC) curves were modelled to determine optimal threshold values for preintervention flow velocities in predicting stent patency as well as their sensitivity, specificity, positive predictive value (PPV) and negative predictive values (NPV). We also calculated the sensitivity, specificity, PPV and NPV using both flow velocities and postthrombotic changes in model 1 and model 2. The Youden index was used to identify optimal velocity cut-off values to predict future stent patency. P-values  $< 0.05$  were considered statistically significant. All statistical analyses were performed using IBM SPSS software, version 27.0 and Stata version 17.

## Results

Participants were predominantly men (53,7%) with a mean age of  $47.4 \pm 15.4$  years. The left side was affected more frequently (64,8%) than the right side. Involvement of the inferior vena cava (IVC) was present in 37 patients (34.3%), while the CFV and femoropopliteal segments were affected in 75 (69%) and 52 patients (48 %). PTO was the indication for stent placement in 90 (83,3%) and NIVL in 18 (16.7%) patients, respectively. Sixteen patients with NIVL had May-Thurner syndrome, one patient suffered from retroperitoneal fibrosis and one patient had an arterial aneurysm causing venous compression. Nearly half of the patients treated were obese (49.1%). Arterial hypertension was present in a third of participants (33.3%), yet only 6 patients (5.6%) had concomitant arterial vascular disease. The median Villalta score was 7.5 (IQR 5-13) at baseline. Fourteen patients had known thrombophilia (8 heterozygous APC resistance (factor V Leiden mutation), 2 antiphospholipid syndrome, 3 protein S deficiencies and one patient with an increased factor VIII level). Baseline patient characteristics and comorbidities are displayed in

Table I. The technical success of stenting in our cohort was 100%. No stent migration, acute target limb deep vein thrombosis, pulmonary embolism, major bleeding or death occurred during the study. One stent fracture was observed, however this patient was excluded from the trial following withdrawal of consent. Twelve of the 20 patients with stent occlusions underwent more than one reintervention, of which one third (4 patients) finally ended with definitive reocclusion.

### **Predictors for loss of stent patency**

During a mean follow-up of  $41 \pm 26$  months, stent occlusion occurred in 20 (18.5%) patients, all of whom had been treated for PTO. No occlusion occurred in patients treated for NIVL. Figure 3 shows cumulative patency rates for patients with NIVL as compared to patients with PTO. During follow-ups we did not detect any stenosis  $> 50\%$  preceding subsequent stent occlusion. All patients experiencing stent occlusions developed symptoms, 14 patients suffered from leg swelling, one patient had a non-healing leg ulcer, four patients complained of venous claudication and one patient reported sensation of heaviness. Eleven patients presented outside the scheduled follow-up visits. All 20 patients with stent occlusion reported compliance with anticoagulation therapy and 9 (45.0%) were taking additional antiplatelet therapy at the time of the event (Table I). Ten occlusions (50%) occurred within the first year. In 16 (17.8%) patients with PTO, anticoagulation was discontinued due to various reasons without stent occlusion occurring during follow-up. If thrombotic deposits were observed on ultrasound during follow-up, anticoagulation was resumed in patients that had previously discontinued it. In continuously anticoagulated patients, the quality of anticoagulation was monitored by means of INR or anti-factor Xa activity and dosage adjustments were performed if levels were outside the target range.

Characteristics of patients with patent and occluded stents are shown in Table I. Prevalence of renal failure, arterial vascular disease, hypertension, obesity and thrombophilia did not differ between patients with or without stent occlusion. Moreover there were no differences regarding the side of intervention and patient sex. Thrombophilia was more frequent in limbs with PTO, yet the presence of thrombophilia was not statistically associated with stent occlusion. In patients with loss of patency, the number of stents implanted was significantly higher ( $p < 0.001$ ) and distal stent extension into the CFV ( $n = 66$ ; 61.1% or DFV and FV ( $n = 8$ ; 7.4%) was significantly more common ( $p < 0.001$ ) compared to patients with patent stents. Additionally peak velocities of  $\leq 7$  cm/s (IQR 0-20) in the CFV and  $\leq 8$  cm/s (IQR 5-10) in the FV, as well as postthrombotic changes in the CFV, DFV and FV prior to stent placement were all significantly associated with stent occlusion (Table I and II). Following log transformation and adjustment for sex and age, lower preinterventional flow velocity in the CFV (OR 7.52, 95% CI 2.54 – 22.28;  $p < 0.001$ ) and FV (OR 10.75, 95% CI 2.07-55.82;  $p = 0.005$ ), but not DFV, were associated with higher odds of stent occlusion. Similarly, the presence of postthrombotic changes of the DFV (OR 4.51, 95% CI 1.53 - 13.25;  $p = 0.006$ ) and FV (OR 3.62, 95% CI 1.11 - 11.84;  $p = 0.033$ ) were associated with higher risk of occlusion (Table II). Findings remained consistent following adjustment for smoking status and comorbidities (renal failure, arterial vascular disease, hypertension, obesity and thrombophilia). Additional adjustment for stent location attenuated the results, yet the association between lower duplex ultrasound velocity in the CFV and stent occlusion remained highly significant (OR 7.42, 95% CI 1.99 - 27.68;  $p = 0.003$ , Table III).

Acknowledging the unique features of the different etiologies, we excluded patients with NIVL in model 3. Restriction of the analysis to patients with a PTO provided similar results to the main analysis, but the association between postthrombotic signs in the FV and stent occlusion was

attenuated (OR 1.3, 95% CI 0.30 - 5.31;  $p = 0.74$ ). A sensitivity analysis was performed adjusting for covariates in model 2, as well for stent location (model 3) and number of stents implanted (model 4). We observed a higher risk of occlusion with increasing number of stents (data not shown), and further adjustment for stent number did not materially change findings (Supp Table 1).

We performed ROC curve analysis to assess the performance of flow velocity in predicting stent occlusion.

Threshold values of 6.5 cm/s and 9 cm/s in CFV and FV, respectively, were identified as cut-offs with the best overall predictive performance. Peak velocity of 6.5 cm/s in the CFV was associated with a sensitivity of 92%, specificity of 50%, PPV of 89% and NPV of 58.8% in predicting primary stent patency. A velocity of 9 cm/s in the FV demonstrated a sensitivity, specificity, PPV and NPV of 72%, 65%, 90% and 34% for primary stent patency, respectively.

Seven out of 17 patients (41.2%) with velocities below 6.5 cm/s in the CFV achieved stent patency, while 10 patients (11.1%) with velocities above 6.5 cm/s experienced stent occlusions.

Sensitivity, specificity, PPV and NPV using both inflow velocity and postthrombotic changes of inflow veins (model 2) were 40%, 95.4, 66.7% and 87.5%, respectively. The finding that lower preinterventional peak flow velocities are associated with higher risk of stent occlusion remained consistent among all three inflow veins.

## Discussion

Endovenous stent placement has emerged as the method of choice in the treatment of chronic femoro-ilio-caval venous outflow obstructions since the late 1990s [6,7,8,9]. Stenting of outflow obstructions in the lower extremities can be performed with high technical success and low

periprocedural morbidity, yet patency rates can vary widely [12,15,16,17]. Our findings are consistent with previous studies regarding technical success, safety and patency rates of endovenous stent placement. We observed an overall technical success rate of 100% without occurrence of major adverse events. In accordance to the study by Neglén et al. [6], neither the side of the intervention nor patient sex significantly influenced stent patency in our cohort. Similar to previous studies we also found patency rates to be lower in patients with PTO compared to patients with NIVL (79.5% vs. 100%) [6,12,18,19]. The comparatively poor outcomes in PTO reflects the more distal extension of venous changes in these patients in contrast to patients with chronic non-thrombotic venous lesions, which are characterized by short-segment stenosis or occlusion in the pelvic axis. Previous studies have emphasized that adequate inflow into stented segments from femoral veins is a prerequisite to maintaining patency [6,20,21]. However, the definition of adequate inflow has remained unclear, with no further details given by previously published studies. In the present study, we retrospectively explored predictors for mid-term patency loss after stenting for PTO or NIVL, specifically examining the influence of venous inflow, defined as peak velocity, and the presence of postthrombotic changes in the CFV, DFV and FV prior to intervention. After a mean follow-up duration of  $41 \pm 26$  months the patency rate was 100% in patients with NIVL, compared to 79.5% in patients with PTO. In addition to the etiology of venous obstruction, lower peak velocity in the CFV and FV were associated with increased risk of stent occlusion, demonstrating the importance of femoral inflow for durable revascularization success. Postthrombotic changes of inguinal inflow veins were associated with significantly higher rates of stent occlusion, reflecting the comparatively poor prognosis conferred by PTO as the underlying etiology of venous outflow obstruction. As such, the presence of postthrombotic changes in the DFV and FV was

associated with a 4 to 5-fold increased risk of patency loss. Our findings demonstrate that low venous inflow velocity may be a risk factor for subsequent stent occlusion, warranting the inclusion of this parameter into the patient selection process for endovenous stenting. Once stent occlusion occurs clinical deterioration may be exacerbated even further, particular in patients with PTS. Additional therapeutic options are limited in this situation, meaning that decision-making aids are of central importance. Flow velocities in the CFV demonstrated the greatest sensitivity for predicting primary stent patency, while inflow via DFV performed better in identifying those patients at risk of stent occlusion. Adding both inflow velocity and postthrombotic change to prognostic models did not substantially improve performance, suggesting that inflow velocity alone may provide satisfactory discriminatory ability. These results suggest that inflow via both CFV and DFV can aid in risk stratification, yet our findings remain to be replicated and elucidated in future prospective studies. On multivariate analysis also including stent location as well, low peak velocity in the CFV remained as the singular significant, independent predictor for stent occlusion that can be easily evaluated and incorporated into the decision-making process before the procedure.

This study is the first to systematically explore predictors of venous stent occlusion which can be incorporated into the decision-making process prior to an intervention. As depicted in the ROC curves, measurement of venous inflow velocities in inguinal veins represents a single and robust method to better delineate risks and benefits of iliac stenting in PTO. Peak velocity of 6.5 cm/s in the CFV was associated with a sensitivity of 92% for stent patency, indicating that this value might be a useful single pre-interventional threshold to be considered when selecting patients for endovenous stenting.



1 There are several limitations to this study. The sample size was moderate, particularly for NIVL  
2 patients for which no stent occlusion was observed. Furthermore, the generalizability of results is  
3 limited by the retrospective, single center design and mid-term follow-up duration, necessitating  
4 the prospective replication of our findings to confirm the clinical utility of CFV imaging and  
5 ultrasound assessment for risk stratification of stent occlusion. The study focused on the  
6 exploration of preinterventional parameters for risk prediction, and it remains to be determined  
7 whether postinterventional characteristics could further improve predictive power. Due to the  
8 broad range of stents used, we cannot exclude that stent choice is a relevant confounder for  
9 patency loss, as certain stents may outperform others. The postinterventional Villalta score was  
10 not collected in every patient and thus could not be evaluated statistically. Only 51% of eligible  
11 patients were included in our analysis raising the possibility of selection bias. Lastly, while  
12 different clinical cut-offs of velocity would be important to be explored in predicting primary  
13 stent patency, our study had a small sample size and precluded our opportunity to explore  
14 further.

15  
16 In summary, endovascular venous stenting appears to be an efficacious and safe method for  
17 treatment of chronic venous outflow obstructions. However, patient selection for intervention  
18 remains essential with regard to patency rates. Patients with non-thrombotic venous lesions and  
19 sufficient inflow into stent system are likely to profit from interventional therapy. In contrast risk  
20 of stent occlusion and clinical deterioration must be weighed against potential benefits in patients  
21 with PTO. Our findings show that insufficient venous inflow by means of low peak velocity in  
22 the FV and CFV as well as the presence of postthrombotic changes are associated with higher

1 risk of stent occlusion and might facilitate patient selection for endovenous stenting. We plan to  
2 evaluate this predictive model in a future prospective clinical trial.

#### 3 4 **Conflict of interest**

5 None.

#### 6 7 **Funding**

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Table I. Baseline patient characteristics and comorbidities

Demographics	Total (n= 108)	occluded (n= 20)	open (n= 88)	p-value
Age, years	47.4±15.4	47.1±15.8	47.5±15.4	0.785
Sex (female)	50 (46.3%)	7 (35%)	43 (48.9%)	0.262
Smoking	22 (20.4%)	3 (15%)	19 (21.6%)	0.759*
Renal failure	12 (11.1%)	2 (10%)	10 (11.4%)	0.611*
Arterial vascular disease	6 (5.6%)	1 (5%)	5 (5.7%)	0.693*
Hypertension	36 (33.3%)	4 (20%)	32 (36.4%)	0.161
Obesity	53 (49.1%)	11 (55%)	42 (47.7%)	0.557
Thrombophilia	14 (13%)	2 (10%)	12 (13.6%)	0.497*
Intervention side (left)	70 (64.8%)	10 (50%)	60 (68.2%)	0.124
<b>Etiology:</b>				
NIVL	18 (16.7%)	0	18 (20.5%)	<b>0.022*</b>
PTO	90 (83.3%)	20 (100%)	70 (79.5%)	
Anticoagulation at last F/U, yes	80 (74.1%)	18 (90%)	62 (70.5%)	0.072
Anti-platelet agents at last F/U, yes	9 (8.3%)	4 (20%)	5 (5.7%)	0.059*
stents (number)	2 (1-2)	2 (2- 3)	2 (1- 2)	<b>&lt;0.001</b>
<b>stent localization:</b>				
CIV and EIV	34 (31.5%)	0	34 (38.6%)	<b>&lt; 0.001</b>
Additional stent in CFV	66 (61.1%)	14 (70%)	52 (59.1%)	
Additional stent in DFV and FV	8 (7.4%)	6 (30%)	2 (2.3%)	
US velocity, CFV (cm/s)	20 (10- 30)	7 (0- 20)	20 (10- 30)	<b>0.001</b>
US velocity, DFV (cm/s)	11 (8- 20)	10 (5.75- 15)	12 (10- 20)	0.177
US velocity, FV (cm/s)	10 (5- 15)	8 (5- 10)	10 (8- 15)	<b>0.001</b>
US postthrombotic signs, CFV	73 (67.6%)	20 (100%)	53 (60.2%)	<b>0.001</b>
US postthrombotic signs, DFV	25 (23.1%)	10 (50%)	15 (17%)	<b>0.003*</b>
US postthrombotic signs, FV	61 (56.5%)	16(80%)	45 (51.1%)	<b>0.019</b>

\*Fisher's Exact Test

Abbreviations: SD, standard deviation; NIVL, non-thrombotic iliac vein lesions; PTO, post-thrombotic obstruction; F/U, follow-up; CIV, common iliac vein; EIV, external iliac vein; CFV, common femoral vein; FV, femoral vein; US, ultrasound

Definitions: renal failure GFR < 30 ml/min; arterial vascular disease established cerebrovascular disease, coronary artery disease or peripheral artery disease; obesity BMI > 30.0 kg/m<sup>2</sup>.

Table II. Odds ratios for stent occlusion defined for logarithmic ultrasound velocity measurements and post-thrombotic signs defined for inflow veins in the groin

	Model 1		Model 2	
	p-value	OR (95% CI)	p-value	OR (95% CI)
Log US velocity, CFV (cm/s)	<0.001	7.52 (2.54, 22.28)	<0.001	9.49 (2.74, 32.83)
Log US velocity, DFV	0.081	6.79 (0.79, 58.20)	0.097	6.22 (0.72, 54.06)
Log US velocity, FV	0.005	10.75 (2.07, 55.82)	0.012	10.23, (1.68, 62.32)
US postthrombotic signs, DFV	0.006	4.51 (1.53, 13.25)	0.008	5.02 (1.53, 16.42)
US postthrombotic signs, FV	0.033	3.62 (1.11, 11.84)	0.042	3.64 (1.05, 12.70)

Model 1: adjusted for age and sex

Model 2: adjusted for age and sex smoking, comorbidities (renal failure, vascular diseases, hypertension, obesity, thrombophilia)

Log transformation was performed for US velocities due to skewed distribution.

Abbreviations: CFV, common femoral vein; DFV, deep femoral vein; FV, femoral vein; US, ultrasound; OR, odds ratio

Table III. Odds ratios for peak flow velocity and post-thrombotic lesions contributing to stent occlusion using model 3

Model 3		
	p-value	OR (95% CI)
Log US velocity, CFV (cm/s)	0.003	7.42 (1.99, 27.68)
Log US velocity, DFV (cm/s)	0.23	6.58 (0.31, 139.54)

Log US velocity, FV (cm/s)	0.13	5.05 (0.62, 41.31)
US postthrombotic signs, DFV	0.13	2.81 (0.73, 10.74)
US postthrombotic signs, FV	0.74	1.3 (0.30, 5.31)

Model 3: adjusted for age, sex, smoking, comorbidities (renal impairment, vascular diseases, hypertension, obesity (yes, no), thrombophilia) and stent localization

Log transformation was performed for US velocities due to skewed distribution.

US postthrombotic signs, CFV was excluded from analysis due to all occluded patients had signs

Abbreviations: CFV, common femoral vein; DFV, deep femoral vein; FV, femoral vein; US, ultrasound; OR, odds ratio

Supp Tabl 1. Odds ratios for velocity and postthrombotic lesions contributing to stent occlusion in model 3 and model 4

	Model 3		Model 4	
	p-value	OR (95% CI)	p-value	OR (95% CI)
Log US velocity, CFV (cm/s)	<b>0.003</b>	<b>7.42 (1.99, 27.68)</b>	<b>0.002</b>	<b>0.065 (0.01, 0.35)</b>
Log US velocity, DFV	0.23	6.58 (0.31, 139.54)	0.122	0.06 (0.002, 2.15)
Log US velocity, FV	0.13	5.05 (0.62, 41.31)	0.33	0.33 (0.04, 3.02)
US postthrombotic signs, DFV	0.13	2.81 (0.73- 10.74)	0.051	3.95 (0.99, 15.66)
US postthrombotic signs, FV	0.74	1.3 (0.30-5.31)	0.82	0.83 (0.17, 4.17)

Model 3: adjusted for age, sex, smoking, comorbidities (renal impairment, vascular diseases, hypertension, obesity (yes, no), thrombophilia) and stent localization

Model 4: adjusted for age, sex, smoking, comorbidities (renal impairment, vascular diseases, hypertension, obesity (yes, no), thrombophilia) and stent localization, stent number

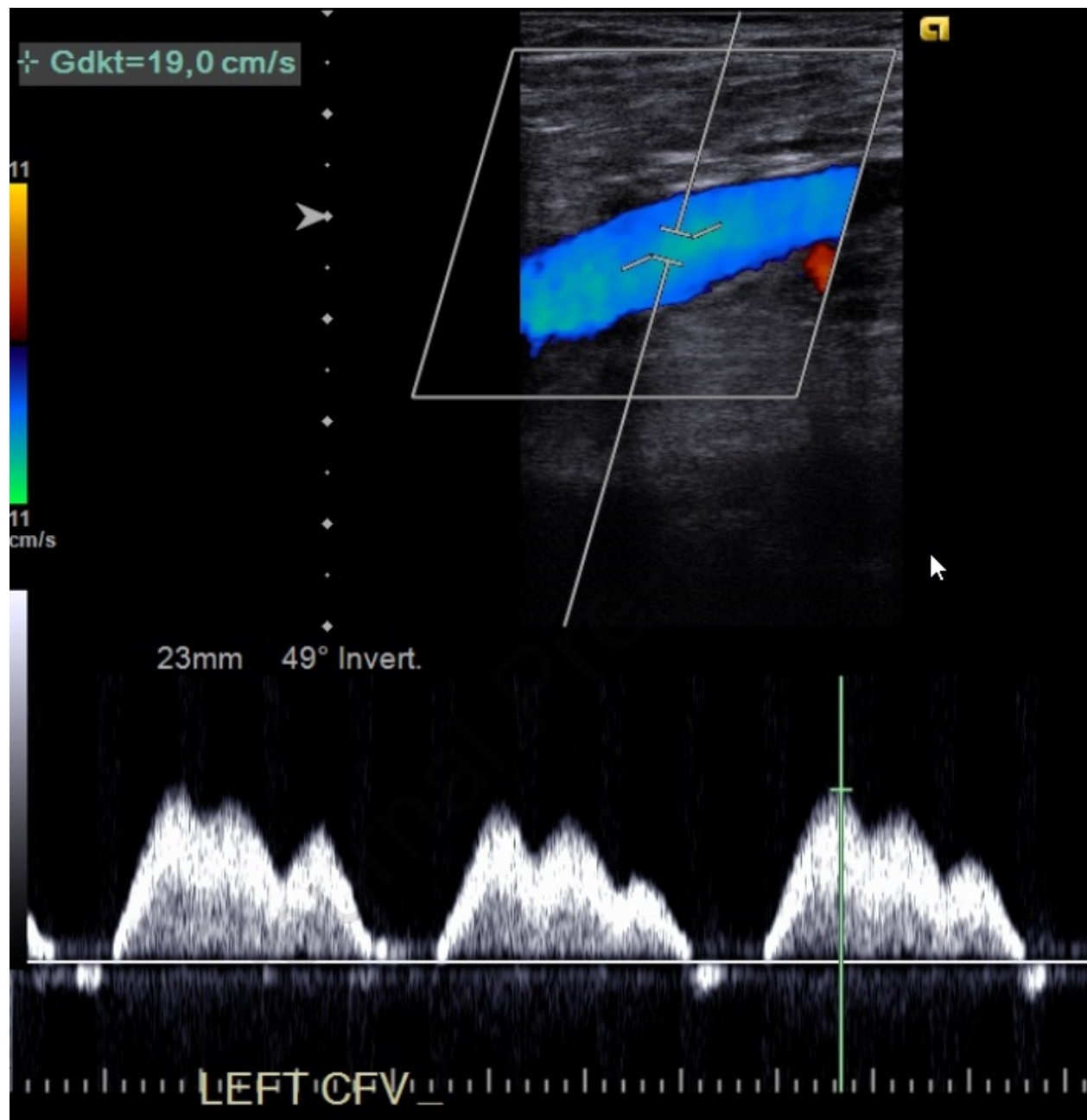
Log transformation was performed for US velocities due to skewed distribution.

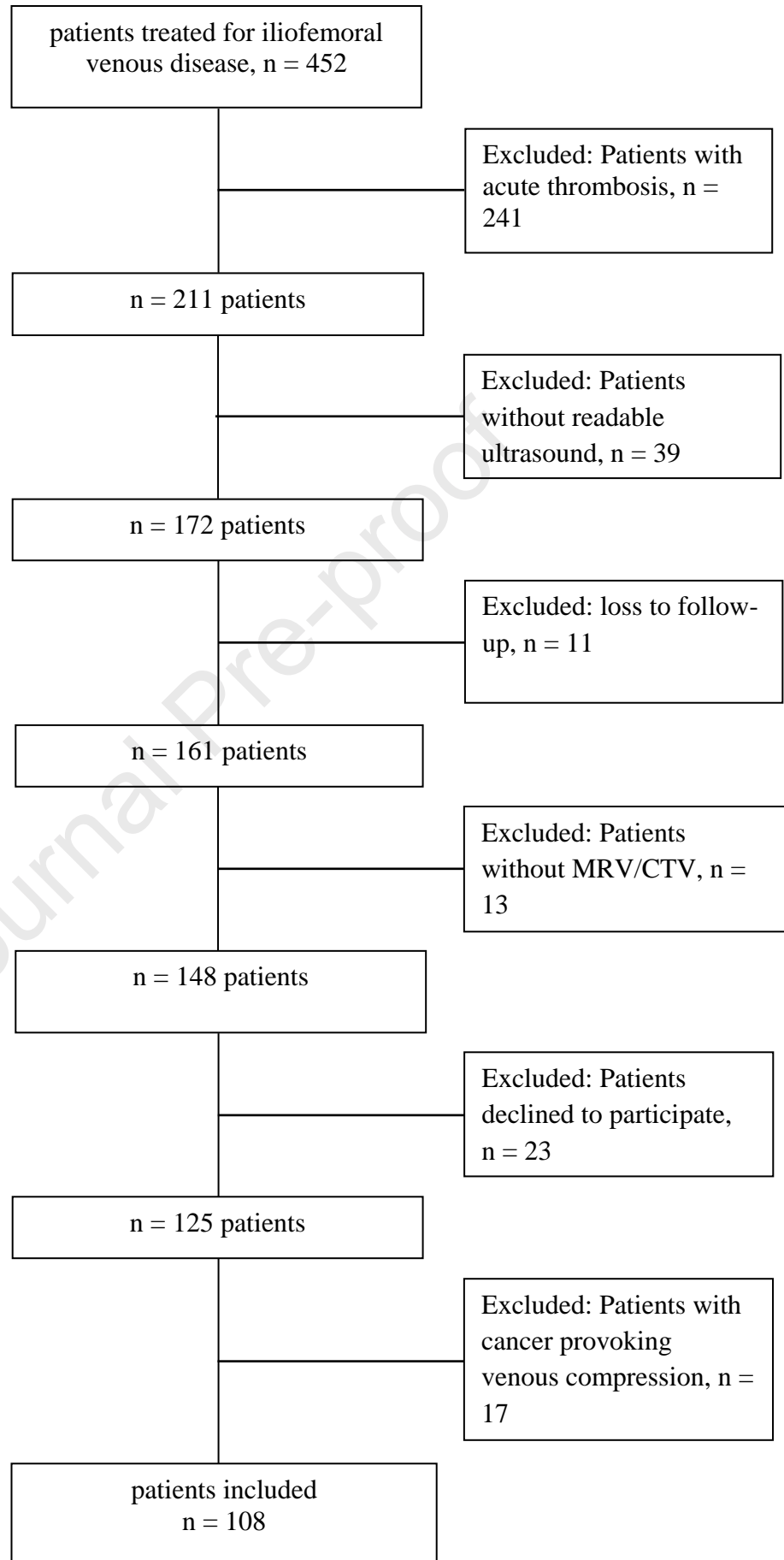


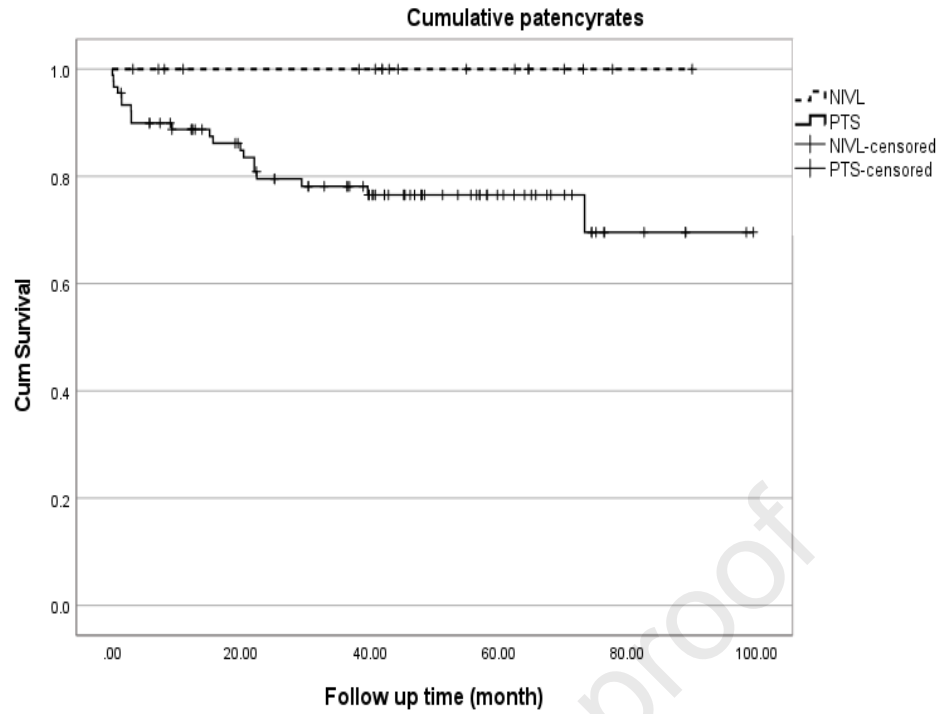
US postthrombotic signs, CFV was excluded from analysis due to all occluded patients had sign

Abbreviations: CFV, common femoral vein; DFV, deep femoral vein; FV, femoral vein; US,

Ultrasound; OR, odd's ration







Follow up time of patients	Patients at risk (number)	Censored due to loss of follow-up	
		Events	
1 <sup>st</sup> year	108	10	10
2 <sup>nd</sup> year	88	7	8
3 <sup>rd</sup> year	73	1	5
4 <sup>th</sup> year	67	1	26
5 <sup>th</sup> year	40	0	12
6 <sup>th</sup> year	28	0	14
7 <sup>th</sup> year	28	1	8
8 <sup>th</sup> year	19	0	3
9 <sup>th</sup> year	16	0	2
10 <sup>th</sup> year	14		

Total number of patients 108.

Figure 1: Measurement of peak flow velocity in the left CVF. The insonation angle was set  $\leq 60^\circ$  and aligned to the direction of flow.

Figure 2. Study algorithm for selection of patients.

Figure 3. Kaplan-Meier curves of univariate cumulative patency rates for stented limbs with non-thrombotic iliac vein lesions (NIVL) and post-thrombotic vein obstruction (PTO).