Lower Extremity Venous Stent Placement: A Large Retrospective Single-Center Analysis

Tarub S. Mabud, MD, MSc, David M. Cohn, MS, Victoria A. Arendt, MD, Gyeong-Sik Jeon, MD, Xiao An, MD, PhD, Jinxin Fu, MD, Andre D. Souffrant, BS, Anna M. Sailer, MD, PhD, Rajesh Shah, MD, David Wang, MD, Daniel Y. Sze, MD, PhD, William T. Kuo, MD, Daniel L. Rubin, MD, MS, and Lawrence V. Hofmann, MD

ABSTRACT

Purpose: To study short-term and long-term outcomes of lower extremity venous stents placed at a single center and to characterize changes in vein diameter achieved by stent placement.

Materials and Methods: A database of all patients who received lower extremity venous stents between 1996 and 2018 revealed 1,094 stents were placed in 406 patients (172 men, 234 women; median age, 49 y) in 513 limbs, including patients with iliocaval stents (9.4% acute thrombosis, 65.3% chronic thrombosis, 25.3% nonthrombotic lesions). Primary, primary assisted, and secondary patency rates were assessed for lower extremity venous stents at 1, 3, and 5 years using Kaplan-Meier analyses and summary statistics. Subset analyses and Cox regression were performed to identify risk factors for patency loss. Vein diameters and Villalta scores before and up to 12 months after stent placement were compared. Complication and mortality rates were calculated.

Results: Primary, primary assisted, and secondary patency rates at 5 years were 57.3%, 77.2%, and 80.9% by Kaplan-Meier methods and 78.6%, 90.3%, and 92.8% by summary statistics. Median follow-up was 199 days (interquartile range, 35.2–712.0 d). Patency rates for the subset of patients (n = 46) with ≥ 5 years of follow-up (mean ± SD 9.1 y ± 3.4) were nearly identical to cohort patency rates at 5 years. Patients with inferior vena cava stent placement (hazard ratio 2.11, $P < .0001$) or acute thrombosis (hazard ratio 3.65, $P < .0001$) during the index procedure had significantly increased risk of losing primary patency status. Vein diameters were significantly greater after stent placement. There were no instances of stent fracture, migration, or structural deformities. In patients with chronic deep vein thrombosis, Villalta scores significantly decreased after stent placement (from 15.7 to 7.4, $P < .0001$). Perioperative mortality was < 1%, and major perioperative complication rate was 3.7%.

Conclusions: Cavo-ilio-femoral stent placement for venous occlusive disease achieves improvement of vein disease severity scores, increase in treated vein diameters, and satisfactory long-term patency rates.

ABBREVIATIONS

DVT = deep vein thrombosis, IVC = inferior vena cava, LCIV = left common iliac vein, LEIV = left external iliac vein, RCIV = right common iliac vein

From the Department of Radiology, Stanford University School of Medicine (T.S.M., D.M.C., V.A.A., A.D.S., A.M.S., D.W., D.Y.S., W.T.K., D.L.R., L.V.H.), 291 Campus Drive, Stanford, CA 94305; Department of Radiology, CHA University Bundang Medical Center (G.-S.J.), Seongnam, South Korea; Department of Radiology, Shanghai General Hospital (X.A.), Shanghai, China; Department of Radiology, Chinese PLA General Hospital (J.F.), Beijing, China; and Department of Radiology, Palo Alto Veterans Administration Health Care System (R.S.), Palo Alto, California. Received February 6, 2019; final revision received June 2, 2019; accepted June 17, 2019. Address correspondence to T.S.M.; E-mail: tmabud@stanford.edu

L.V.H. is a paid consultant for Cook, Inc (Bloomington, Indiana) and W.L. Gore & Associates (Flagstaff, Arizona); is a shareholder in Cook, Inc; owns equity in Confluent Medical (Scottsdale, Arizona), Boston Scientific (Marlborough, Massachusetts), and Medtronic (Minneapolis, Minnesota); and is the founder of, on the board of directors for, and owns equity in Grand Rounds (San Francisco, California). D.Y.S. is a paid consultant for Boston Scientific, Koli Inc (Fremont, California), RadiAction Medical (Tel Aviv, Israel), Astra-Zeneca (Wilmington, Delaware), BlackSwan Vascular (Hayward, California), Bristol-Myers Squibb (New York, New York), BTG (West Conshohocken, Pennsylvania), Eisai (Woodcliff Lake, New Jersey), Embolx, Inc (Sunnyvale, California), W.L. Gore & Associates, and Terumo Medical Corporation (Somerset, New Jersey); receives institutional support from BTG, W.L. Gore & Associates, Merit Medical Systems, Inc (South Jordan, Utah), and Sirtex Medical Inc (Woburn, Massachusetts); and owns equity in Confluent Medical and Proteus Digital Health, Inc (Redwood City, California). None of the other authors have identified a conflict of interest.

Table E1 can be found by accessing the online version of this article on *www.jvir.org* and clicking on the Supplemental Material tab.

J Vasc Interv Radiol 2020; 31:251–259

https://doi.org/10.1016/j.jvir.2019.06.011

EDITORS' RESEARCH HIGHLIGHTS

- This single-institution study assessed long-term patency of venous stent placement (N = 1,094) in 513 limbs for thrombotic (n = 383) and nonthrombotic (n = 130) indications.
- Overall 30-d complication rate was 6.4% (26/406), including 15 major (3.7%) and 11 minor (2.7%) complications. Primary assisted and secondary patency rates at 5-y follow-up approached 90%. In patients with chronic venous thrombosis (n = 56), Villalta scores significantly improved after stent placement.
- Caval stent placement and acute thrombosis at the time of the index procedure are associated with increased risk of losing primary patency.
- Although implanted stents were not specifically designed or approved by the US Food and Drug Administration for venous intervention, structural integrity was maintained in the cases, and no reported stent fractures were identified.

Endovascular treatment of lower extremity venous stenosis and occlusion with stent placement has been performed for decades with favorable safety and efficacy profiles and excellent clinical outcomes compared with invasive surgical techniques (1–3). Despite this, at the present time, no venous stents have been approved by the US Food and Drug Administration. Instead, physicians use arterial or biliary stents, which were not specifically engineered for the biomechanical requirements of venous interventions. Data supporting the long-term safety and effectiveness of endovenous stent placement in the lower extremities and iliocaval region are scarce. To date, only 1 research group has enrolled at least 100 patients (from an outpatient private practice center) to capture long-term follow-up of such stents (4). Currently, the American Heart Association only conditionally recommends that balloon angioplasty—with or without stent placement—"be considered" after thrombolysis as a means to prevent recurrent thrombosis and subsequent chronic venous insufficiency for patients with acute thrombotic occlusions (Level B, Class IIB evidence) (5). The recent ATTRACT trial concluded that for acute femoropopliteal deep vein thrombosis (DVT), the combination of anticoagulation and pharmacomechanical catheter-directed thrombolysis, with or without stent placement, did not show decreased incidence of post-thrombotic syndrome over anticoagulation alone (6). However, further analysis of ATTRACT data revealed that for patients with acute iliofemoral DVT, combined therapy reduced long-term incidence and severity of post-thrombotic syndrome, with concurrent improvement in quality of life (7). For chronic DVT and for nonthrombotic lesions (eg, external venous compression), there are no consensus guidelines on appropriate endovascular management. The present study evaluated the safety and patency of lower extremity venous stents for both thrombotic and nonthrombotic venous disease through retrospective analysis of a single center. This study additionally assessed the increase in vein diameter achieved after stent placement through analysis of images obtained before and after stent placement.

MATERIALS AND METHODS

Cohort Identification and Data Collection

With institutional review board approval, the electronic health records were queried at a single center for all consecutive adult patients who underwent iliac, femoral, or iliofemoral venous stent placement, with or without inferior vena cava (IVC) stent placement, for the first time between July 1996 and April 2018; a cohort selection tool that identifies patients based on procedural codes related to venous stent placement was used (8). Written informed consent was waived. A total of 1,094 stents were placed in 406 patients (172 men and 234 women; median age, 49 y), across 513 limbs, including patients with iliocaval stents (9.4% acute thrombosis, 65.3% chronic thrombosis, 25.3% nonthrombotic lesions). Concurrent IVC filter retrieval was performed in 18.5% (75 of 406) of the cohort. A database entitled VITAL (Venous InTerventionAL) was constructed using REDCap for the collection of patient demographic, clinical, procedural, and follow-up data (9). Manual electronic chart review was performed to populate the database.

Image Analysis and DVT Status

Two interventional radiology (IR) physicians, each with > 10 years of experience (G.J., X.A.), reviewed all ultrasound, computed tomography venography, magnetic resonance venography, and conventional venography imaging studies for each patient on the institutional picture archiving and communication system. Vein segment measurements (minimum and maximum cross-sectional diameter for each iliofemoral vein segment and for the long axis of the suprarenal and infrarenal IVC) before and after stent placement were obtained from axial images from computed tomography and magnetic resonance venography studies using the picture archiving and communication system electronic measurement tool. Completely occluded vessels, which were identifiable on radiologist review, were considered to have a luminal diameter measurement of 0 mm. Studies before and after stent placement were identified as studies closest in date to the index stent placement (both before and after) and constrained to within 1 year before or after the procedure. Follow-up duration of imaging studies was calculated using summary statistics. Characterization of the stents (presence, minimum and maximum cross-sectional diameter, location) and DVT characteristics (presence, chronicity, location) were also captured in the database based on review of imaging. The chronicity of DVT was defined as acute, subacute, or chronic if symptoms in the medical record or radiologist imaging review suggested that thrombosis had occurred within the past 14 days (acute), 15–28 days (subacute), or >

28 days (chronic) (10). Acute-on-chronic DVT was defined as acute DVT superimposed on pre-existing chronic DVT. Patients who had a venous stenosis but did not have clinical or imaging evidence of prior DVT were placed into a nonthrombotic category (4). At the study institution, guidelines for stent placement for nonthrombotic iliac vein compression included patient-reported leg swelling involving the thigh and calf coupled with the imaging finding of at least 70% stenosis or < 4 mm short-axis venous axial diameter in iliofemoral vein segments, confirmed with catheter-based venography (11). Imaging data, such as vein diameter measurements, were validated by independent review by a second IR physician, and by a data science team.

Procedural Details and Complications

All procedure notes were reviewed to identify the nominal stent diameters used for each patient at the vein level. Data regarding stent location from both procedure notes and imaging review were compared to ensure data cleanliness and validity. Stent selection and sizing varied by physician preference and vessel segment. Generally, empirical stent diameter selection was employed, with 20–24 mm in the IVC, 12–16 mm in the common iliac vein, 12–14 mm in the external iliac vein, and 10–12 mm below the inguinal ligament used. Additional caudal stents were typically the same diameter or 2 mm larger than the patent inflow vessel. Venoplasty of all stents in this study was performed to either the nominal diameter of the stent or 2 mm less than the nominal diameter. For stents placed in the IVC, institutional practice was to use a single stent rather than the double-barrel technique. Details regarding stent brands, stent sizes, and angioplasty balloons used after stent placement are summarized in **Table E1** (available online on the article's Supplemental Material page at *www.jvir.org*). Review of all follow-up imaging reports was performed to assess the occurrence of stent fracture, migration, kinking, or other structural deformity. Complications occurring during or after the procedure, including mortality, were documented through full chart review and classified as major or minor according to Society of Interventional Radiology (SIR) guidelines (10).

Patency Rates

Longitudinal outcomes of venous stent placement were evaluated as primary, primary assisted, and secondary patency rates. Per convention, primary patency is defined as the time from initial venous stent placement until either the reocclusion of a leg with prior stent placement or a reintervention to maintain patency. Primary assisted patency is the time from initial stent placement to the first occurrence of an occlusion, while allowing for intervening endovascular interventions (eg, angioplasty, stent placement, catheter-directed thrombolysis) to maintain stent patency. Secondary patency is the time from initial stent placement until the permanent occlusion of a vein (10). Patency rates are calculated at the limb level, as multiple stents can be placed within a single limb; loss of patency of any of the stents within the limb is counted as a loss of limb patency.

Clinical Venous Disease Severity Assessment

To characterize venous disease severity for patients with postthrombotic syndrome, all clinic notes before and after the stent procedure were retrospectively reviewed for Villalta scores recorded by the physician provider during the clinic visit. Venous disease before stent placement was further assessed and characterized using CEAP (Clinical-Etiology-Anatomy-Pathophysiology) classification for chronic venous disorders scores. Values before stent placement were obtained from the clinic note that described preparation for the stent placement procedure. Values after stent placement were obtained from the clinic note that described the clinic visit immediately following the stent procedure. Owing to the evolving clinical practice at the study institution and in IR, follow-up procedures varied across the study period. Follow-up at the study institution was generally tailored to each patient based on the extent of disease, if DVT was provoked or unprovoked, completion venography, and patient travel distance, among other factors; patients typically received 1 month of follow-up, and additional imaging or clinical follow-up was determined at that time based on the aforementioned factors. Villalta scores after stent placement were constrained to scores within 12 months of the stent procedure and before any reintervention.

Statistical Analyses

Baseline characteristics for the total study population and subgroups are described as absolute numbers and percentages for categorical variables, with mean ± SD or median and interquartile range reported for continuous variables. Summary statistics were calculated to characterize stent diameters, vein diameters, and Villalta scores. Paired *t* tests were performed to determine statistically significant differences in vein diameters before and after stent placement and Villalta scores for patients with both before and after stent values available. Both summary statistics and Kaplan-Meier methods were used to calculate limb-level patency rates. Summary statistics express counts of limbs that had lost patency divided by the total number of limbs with at least 1 stent placed at risk. Kaplan-Meier methods were used to analyze time until patency loss. For Kaplan-Meier analyses, follow-up was initiated at the time of a patient's first stent placement. Patients were censored at the time of their last known follow-up encounter or death.

Both summary statistics and Kaplan-Meier results are presented because of their differing assumptions regarding patients who are lost to follow-up. As this study is from a referral institution with patients traveling long distances (often out of state or overseas) for venous interventions, it is difficult to have all patients return for follow-up.

Summary statistics implicitly assume that patients who are lost to follow-up do not subsequently lose patency (overestimating treatment success). Alternatively, Kaplan-Meier methods implicitly assume that patients are truly lost to follow-up, rather than patients with good outcomes for whom a clinician has deemed further follow-up unnecessary (underestimating treatment success). As such, the true patency rate will be lower than the summary statistic result, but higher than the Kaplan-Meier result. Kaplan-Meier methods have the advantages of allowing for the construction of confidence intervals and multivariate regression.

Outcomes were assessed at 1 year, 3 years, and 5 years after stent placement for both methods. Subset analysis was performed to examine summary statistic patency rates based on indication for stent placement (acute DVT, chronic DVT, or nonthrombotic occlusion). To assess long-term outcomes, patency rates were calculated using summary statistics for the subcohort of patients who had > 5 years of follow-up. All statistical analyses were performed using R software (12). Kaplan-Meier analyses were performed using the R package "survival" (13).

Multivariate Cox regression was performed to identify any significant differences in patency rates based on several variables; binary variables were constructed for IVC stent placement status (whether the IVC received a stent during the intervention), thrombophilia status (antiphospholipid syndrome, prothrombin deficiency, protein C or S deficiency, antithrombin deficiency, hyperhomocysteinemia, elevated factor VIII, fibrinogen defects, prothrombin gene G20210A mutation, and factor V Leiden mutation), and limb laterality. Owing to the low incidence of thrombophilia and the current recommendations against testing patients for such, individuals not tested were assumed to not have a thrombophilic disorder (14). Categorical variables were derived for indication for stent intervention (acute DVT, subacute DVT, acute-on-chronic DVT, chronic DVT, nonthrombotic lesion), and anticoagulation regimen (any anticoagulant prescribed after stent placement). In this retrospective study, physicians could use anticoagulation regimens and antiplatelets of choice, including dose and duration. At the study institution, general practice has been to follow the American Academy of Chest Physicians anticoagulation guidelines for DVT (15). For the purposes of statistical analysis, these regimens have been categorized as enoxaparin only, enoxaparin with bridge to warfarin, enoxaparin with bridge to rivaroxaban, and enoxaparin with a bridge to another anticoagulant (eg, fondaparinux, dabigatran).

RESULTS

Patient Cohort

Demographic and clinical characteristics of the final patient cohort and a clinical assessment of the affected limbs before intervention as CEAP and Villalta scores are presented in Table 1. Median follow-up was 199 days (interquartile range, 35.2–712.0 d). Most venous stent placement procedures (approximately 99%) were performed by 19 fellowship-trained IR physicians, and < 1% were performed by 3 vascular surgeons during the early portion of the study period.

Table 1. Patient Demographics and Limb Characteristics

Characteristic	Value
Patient demographics (n = 406)	
Age, y, median (IQR)	48.9 (36.0–62.1)
Female sex, n (%)	234 (57.6)
White race, n (%)	274 (67.5)
IVC stent, n (%)	154 (37.9)
Concurrent complex IVC filter removal, n (%)	75 (18.5)
Thrombophilia, n (%)	81 (20.0)
Limb characteristics (n = 513)	
Stent indication, n (%)	
DVT, acute and chronic	383 (74.7)
Nonthrombotic	130 (25.3)
Affected limb, n (%)	
Left	365 (71.2)
Right	148 (28.8)
Iliofemoral stent distribution, n (%)	
Iliac only	379 (73.9)
Femoral only	10 (1.9)
Iliofemoral	124 (24.2)
Preintervention Villalta score, mean ± SD	
Left limb (n = 87)	15.2 ± 8.8
Right limb (n = 57)	16.8 ± 8.2
Preintervention CEAP class, mean ± SD	
Left limb (n = 35)	2.9 ± 1.4
Right limb (n = 10)	3.4 ± 1.4

DVT = deep vein thrombosis; IQR = interquartile range; IVC = inferior vena cava.

Patency Rates

Kaplan-Meier plots of limb-level stent patency are presented in the Figure. Table 2 provides 1-, 3-, and 5-year patency rates (via Kaplan-Meier and summary statistics methods), along with 95% confidence intervals for Kaplan-Meier analyses. A subset analysis of patency rates based on thrombotic disease status is presented in Table 3. Patients with chronic DVT and nonthrombotic occlusions had higher patency rates than patients with acute DVT. Follow-up ≥ 5 years (9.1 y ± 3.4) was available for 46 patients (11.3%) comprising 53 limbs (34 chronic DVT, 8 acute DVT, 11 nonthrombotic). Beyond 5 years, only 1 of these 53 limbs had loss of patency status (1 left limb, initially manifesting with acute DVT, with loss of secondary patency); otherwise, the patency rates for this long-term follow-up subcohort did not change after 5 years of follow-up.

Multivariate Cox Regression

In a multivariate model of limb-level primary patency, patients with IVC stent placement during their index procedures

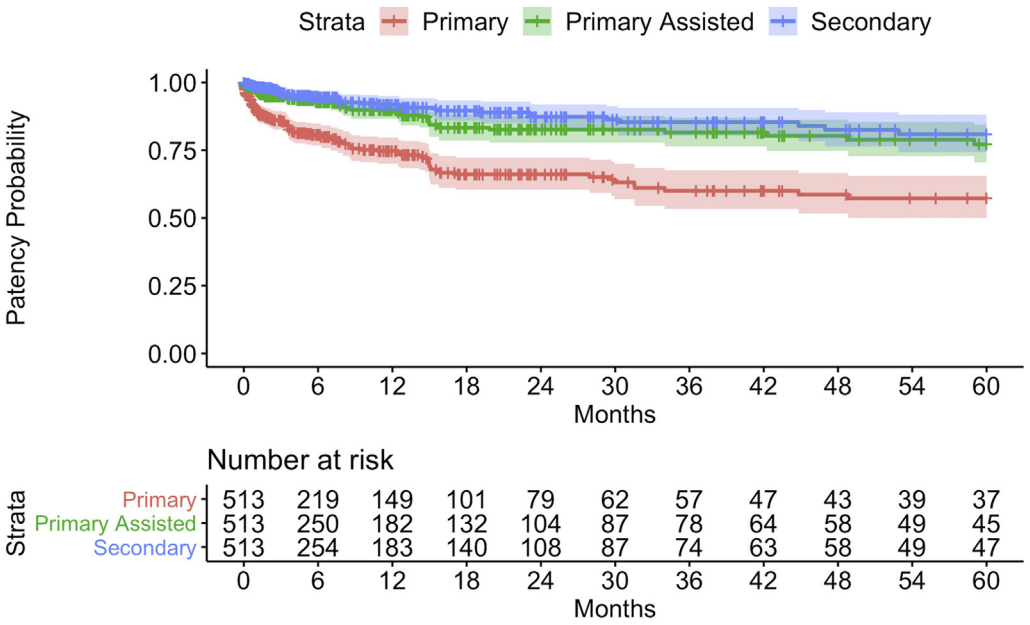

Figure. Kaplan-Meier analysis. Longitudinal probability of primary, primary assisted, and secondary patency following lower extremity venous stent placement, with 95% confidence intervals (shaded).

Table 2. Comparison of Cohort Limb-Level Patency Rates Based on Calculation Method

	Kaplan-Meier			Summary Statistics		
	1-y (95% CI)	3-y (95% CI)	5-y (95% CI)	1-y	3-y	5-y
Primary patency, %	74.7 (70.1–79.7)	60.0 (53.3–67.6)	57.3 (50.0–65.6)	83.0	78.9	78.6
Primary assisted patency, %	90.0 (86.6–93.4)	81.6 (76.5–87.0)	77.2 (70.5–84.5)	93.6	90.8	90.3
Secondary patency, %	91.8 (88.7–95.0)	85.4 (80.4–90.7)	80.9 (74.3–88.1)	95.1	93.4	92.8

CI = confidence interval.

Table 3. Summary Statistic Limb-Level Patency Rates Based on Thrombotic Status of Initial Stent Indication

	Acute Thrombosis (n = 48)			Chronic Thrombosis (n = 335)			Nonthrombotic Lesion (n = 130)		
	1-y	3-y	5-y	1-y	3-y	5-y	1-y	3-y	5-y
Primary patency, %	66.7	64.6	62.5	83.0	77.9	77.6	89.2	86.9	86.9
Primary assisted patency, %	87.5	85.4	81.2	93.7	93.5	90.4	95.4	93.1	93.1
Secondary patency, %	89.6	89.6	89.6	94.0	97.7	97.7	100	97.7	97.7

Note–Acute-on-chronic deep vein thrombosis was considered to be chronic thrombosis, whereas subacute deep vein thrombosis was considered to be acute thrombosis.

had a significantly increased risk of losing primary patency status (hazard ratio 2.11, 95% confidence interval [1.38, 3.22], $P < .0001$). Patients with acute DVT at the time of stent placement were also more likely to lose primary patency (hazard ratio 3.65, 95% confidence interval [1.74, 7.64], $P < .0001$). Thrombophilia status, limb laterality, and anticoagulation regimen were not associated with patency loss.

Stent and Vein Diameters

A total of 1,094 vein segments with stents were analyzed. All vein segments that received stent placement were, on average, larger in diameter after stent placement. The mean nominal diameters of stents placed in each vein segment were 19.8 mm ± 1.5 in the suprarenal IVC, 17.9 mm ± 0.5 in the infrarenal IVC, 13.7 mm ± 0.3 in the left common iliac vein (LCIV), 12.6 mm ± 0.6 in the right common iliac vein (RCIV), 12.9 mm ± 0.5 in the left external iliac vein (LEIV), 12.3 mm ± 0.8 in the right external iliac vein, 11.9 mm ± 0.7 in the left common femoral vein, 11.9 mm ± 0.6 in the right common femoral vein, 11.3 mm ± 1.7 in the left femoral vein, and 11.5 mm ± 2.5 in the right femoral vein. The mean maximum diameters before stent placement for each vein segment were: 24.7 mm ± 5.0 in the

Table 4. Stent Characteristics, Vein Diameters, and Vein Diameter Comparison before and after Stent Placement

Vein Segment	Total Stents (N = 1,094) (%)	Mean Nominal Stent Diameter, mm (SD)	Mean Maximum Prestent Vein Diameter, mm (SD)	Mean Maximum Poststent Vein Diameter, mm (SD)	Mean Minimum Prestent Vein Diameter, mm (SD)	Mean Minimum Poststent Vein Diameter, mm (SD)	Vein Diameter Paired *t* Test *P* Value (n)*
Suprarenal IVC (long axis)	15 (1.4)	19.8 (1.5)	24.7 (5.0)	25.2 (5.7)	17.0 (6.8)	19.8 (3.1)	NA (≤ 15)
Infrarenal IVC (long axis)	153 (14.0)	17.9 (0.5)	16.3 (10.4)	18.9 (6.1)	11.4 (7.8)	16.2 (5.2)	.057 (38)
LCIV	344 (31.4)	13.7 (0.3)	5.6 (5.8)	10.8 (3.7)	2.5 (3.4)	8.5 (3.3)	< .001 (80)
RCIV	140 (12.8)	12.6 (0.6)	4.5 (5.4)	9.5 (4.5)	2.8 (4.4)	7.9 (4.0)	< .001 (35)
LEIV	193 (17.6)	12.9 (0.5)	6.2 (5.8)	10.2 (3.8)	3.9 (4.5)	8.2 (3.5)	< .001 (50)
REIV	85 (7.8)	12.3 (0.8)	6.2 (5.7)	8.7 (4.2)	3.0 (4.3)	7.3 (3.7)	.39 (21)
LCFV	96 (8.8)	11.9 (0.7)	7.6 (5.3)	9.2 (3.9)	5.1 (4.3)	6.8 (3.8)	.11 (25)
RCFV	33 (3.0)	11.9 (0.6)	8.1 (4.7)	11.5 (2.8)	4.9 (4.4)	9.3 (2.0)	NA (≤ 15)
LFV	22 (2.0)	11.3 (1.7)	6.9 (3.4)	7.9 (2.0)	4.4 (3.4)	4.3 (2.3)	NA (≤ 15)
RFV	9 (0.8)	11.5 (2.5)	7.3 (1.2)	9.5 (0.7)	4.0 (4.0)	2.0 (2.8)	NA (≤ 15)
Other†	4 (0.4)						

IVC = inferior vena cava; LCFV = left common femoral vein; LCIV = left common iliac vein; LEIV = left external iliac vein; LFV = left femoral vein; RCFV = right common femoral vein; RCIV = right common iliac vein; REIV = right external iliac vein; RFV = right femoral vein.

*NA indicates that sample size was deemed insufficient (n ≤ 15) to provide a meaningful comparison of prestent vs poststent maximum vein diameter.

†Other veins include left popliteal femoral vein, left profunda femoris, right popliteal vein, and superior vena cava. NA individuals were included in paired *t* tests comparing prestent and poststent vein diameters only if both values were available; no *t* tests were performed for veins with insufficient sample sizes.

suprarenal IVC, 16.3 mm ± 10.4 in the infrarenal IVC, 5.6 mm ± 5.8 in the LCIV, 4.5 mm ± 5.4 in the RCIV, 6.2 mm ± 5.8 in the LEIV, 6.2 mm ± 5.7 in the right external iliac vein, 7.6 mm ± 5.3 in the left common femoral vein, 8.1 mm ± 4.7 in the right common femoral vein, 6.9 mm ± 3.4 in the left femoral vein, and 7.3 mm ± 1.2 in the right femoral vein. The mean maximum diameters after stent placement for each vein segment were 25.2 mm ± 5.7 in the suprarenal IVC, 18.9 mm ± 6.1 in the infrarenal IVC, 10.8 mm ± 3.7 in the LCIV, 9.5 mm ± 4.5 in the RCIV, 10.2 mm ± 3.8 in the LEIV, 8.7 mm ± 4.2 in the right external iliac vein, 9.2 mm ± 3.9 in the left common femoral vein, 11.5 mm ± 2.8 in the right common femoral vein, 7.9 mm ± 2.0 in the left femoral vein, and 9.5 mm ± 0.7 in the right femoral vein. The LCIV, LEIV, and RCIV had statistically significant ($P < .001$) increases in maximum vein diameter after stent placement. The distribution of veins with stents, nominal stent diameters used, and maximum and minimum stent vein diameters before and after stent placement are summarized in Table 4. Measurements before stent placement were obtained a mean 67 days ± 71 before the index stent procedure; measurements after stent placement were obtained a mean 91 days ± 86 after the procedure.

Clinical Assessment

Villalta scores decreased significantly, from 15.7 ± 8.6 before stent placement to 7.4 ± 6.5 after stent placement (paired *t* test: n = 56, $P < .0001$). Measurements before stent placement were obtained a mean 27 days ± 33 before the index stent procedure, and measurements after stent placement were obtained a mean 80 days ± 78 after the procedure. Data for comparison of Villalta scores before and after stent placement were available only for individuals with chronic DVT.

Complications

Overall 30-day complication rate was 6.4% (26 of 406); there were 15 major (3.7%) and 11 minor (2.7%) complications. Of the 26 complications, 69.2% (16 of 26) occurred after intervention for chronic DVT, and 26.9% (10 of 26) occurred after intervention for acute DVT. No complications occurred after intervention for nonthrombotic disease. Filter retrieval procedures were involved in 34.6% (9 of 26) of complications, all of which were chronic DVT cases. Complications are summarized in Table 5. The intraprocedural complication rate was 0.5% (2 of 406, 1 major, 1 minor; 2 of 2 chronic DVT cases). The rate of bleeding complications (at any site) within 30 days of the index procedure was 2.0% (8 of 406, 4 major, 4 minor; 8 of 8 chronic DVT cases). The rate of thrombotic complications within 30 days of the index procedure was 2.2% (9 of 406, 9 major; 9 of 9 acute DVT cases), and the rate of other complications was 1.7% (7 of 406, 1 major, 6 minor; 6 of 7 chronic DVT cases, 1 of 7 acute DVT case). Perioperative mortality was 1.0% (4 of 406; 4 of 4 nonthrombotic cases); all 4 patients who died had

Table 5. Complications (N = 406)

	n (%)	Descriptions of Major Complications
Intraprocedural complications		1) IVC pseudoaneurysm and associated retroperitoneal bleeding requiring IVC stent graft placement, hematoma aspiration, and percutaneous drain placement
Major	1 (0.3)	
Minor	1 (0.3)	
Bleeding complications		1) Active extravasation of internal iliac artery branch requiring readmission for embolization; 2) Access site hematoma requiring embolization of femoral artery branch; 3) GI bleed requiring transfusion; 4) Jugular access site bleed requiring transfusion
Major	4 (1.0)	
Minor	4 (1.0)	
Thrombotic complications		1–9) Lower extremity DVT following intervention
Major	9 (2.2)	
Minor	0 (0.0)	
Other complications		1) Suspected duodenal perforation following IVC catheterization requiring diagnostic laparotomy, later diagnosed as a duodenal diverticulum without perforation
Major	1 (0.3)	
Minor	6 (1.5)	
Mortality	4 (1.0)	1–4) Complications of metastatic cancer, unrelated to stent placement procedure

Note–Major and minor complications categorized according to Society for Interventional Radiology (SIR) guidelines (10).
DVT = deep vein thrombosis; GI, gastrointestinal; IVC = inferior vena cava.

advanced metastatic cancer, and none of the deaths were directly attributable to the stent procedure. There were no reported instances of stent fracture, migration, or structural deformities on follow-up imaging.

DISCUSSION

This study describes a broad experience with stent placement for lower extremity venous obstructions from a referral hospital over a large cohort. Patency rates were comparable to rates from past retrospective cohorts (4). Patency rates were additionally found to be lower in patients with acute thrombosis and patients with IVC stent placement. Stent placement resulted in significant decreases in Villalta scores after intervention, accompanied by increased vein diameters. This retrospective study supports the current practice of arterial or biliary stent placement for both thrombotic and nonthrombotic venous disease, while demonstrating a favorable safety profile. A number of dedicated venous stents specifically indicated for iliofemoral venous pathology have been under development (16). The results of this study may help characterize a comparative baseline by which to assess the safety and efficacy of such products.

In the only other study of a large cohort with long-term follow-up, Neglén et al (4) found 6-year primary, primary assisted, and secondary patency rates of 79%, 100%, and 100% in nonthrombotic disease and 57%, 80%, and 86% in thrombotic disease. In comparison, the 5-year patency rates presented in this study are higher for thrombotic disease (both acute and chronic). For nonthrombotic disease, the 5-year primary patency rate is higher, but the primary assisted and secondary patency rates are slightly lower. Direct comparisons between studies of stent patency are difficult owing to differences in cohort composition. Most notably, 38% of this study's cohort had IVC stent placement owing to thrombotic disease, in contrast to other studies, in which < 10% had stent placement owing to thrombotic disease (3,4). Moreover, 18.5% of this study's cohort had concurrent complex IVC retrieval performed. These differences are likely due to the fact that the study institution is a referral hospital, rather than an exclusive outpatient center as in the cohort reported by Neglén et al (4). In the multivariate model, patients who received IVC stents during their index procedure were more than twice as likely to lose primary patency than patients who did not require IVC stents. Past studies of stent patency have typically excluded patients with malignancy (3,4), whereas 12.3% of this cohort had a malignancy at the time of stent placement, potentially affecting patency rates.

This study aligns with previous findings that thrombotic occlusions—particularly acute DVT—have lower rates of long-term patency than nonthrombotic occlusions (4), possibly owing to persistent venous wall or valvular damage and dysfunction after thrombosis. Theoretically, the higher incidence of thrombophilic disorders among patients with thrombotic occlusions should also predispose this cohort to reocclusion, but thrombophilia has been inconclusively linked to risk of patency loss (4). Cox regression analysis did not find a significant association between thrombophilia

and patency loss. Anticoagulation regimen was also not associated with risk of patency loss. However, there was considerable heterogeneity among regimens in this 20-year retrospective study, and owing to data constraints, only a coarse categorization scheme that excluded dose and duration could be applied. Further investigation is warranted into the effects of anticoagulation on stent patency.

There was a marked difference in the 5-year secondary patency rates between patients with acute and chronic DVT. This discrepancy may be due to the proinflammatory nature of acute thrombosis, which could predispose these patients to a more aggressive foreign body response to stent placement compared with chronic thrombosis or nonthrombotic pathology. However, patients with acute DVT may benefit from initial treatment with anticoagulation and subsequent stent therapy if symptoms persist. The superior patency rates in the chronic DVT group in this study suggest a potential new treatment paradigm that involves stent placement after an initial "calming" period in which the thrombus matures from acute DVT to chronic DVT. However, for this new paradigm to be fully supported, stent patency rates would need to be proven to be directly correlated with clinical outcomes in further study.

This study describes a surrogate metric for mechanical performance of stents, used in an off-label fashion in the venous system, by detailing the venous diameters before and after stent placement correlated with the nominal diameter of the implanted stent. For example, the mean LCIV nominal stent diameter was 13.7 mm, with minimum and maximum mean diameters after stent placement of 8.5 mm and 10.8 mm, respectively. Venoplasty of all stents in this study was performed to either the nominal diameter of the stent or 2 mm less than the nominal diameter. This suggests that currently used stents, which generally have an iliac artery and biliary indication, have insufficient radial strength to maintain their nominal diameter when used for venous pathology. Such data may be useful in designing and developing new stents tailored for the mechanical forces of veins.

Villalta scores correlate closely with clinical, physiologic, and quality-of-life measures in patients with thrombotic lesions (17). Villalta scores after stent placement were statistically significantly lower compared with scores before stent placement, further supporting the use of venous stents for chronic thrombotic lower extremity venous outflow occlusions. The overall complication rate was low. Notably, there were no recorded instances of stent migration or fracture in > 1,000 stent placement procedures, and there were no recognized instances of pulmonary embolism. Perioperative mortality was low and was due to malignancy rather than stent placement. Nine patients developed lower extremity DVT within 30 days of stent procedures; 6 had underlying thrombophilia, and the remaining 3 had DVT provoked by trauma or prolonged immobility following a surgical procedure. These 9 patients all initially had stent placement following acute DVT.

The primary limitations of this study relate to its retrospective nature and the evolving medical record over the past 20 years at the study institution. In 2008, an institution-wide electronic medical record (Epic Systems, Verona, Wisconsin) was installed for all inpatient, outpatient, and procedural documentation. Before this, the study institution had a combination of paper and rudimentary electronic information systems. Therefore, the highest fidelity clinical information in this study is limited to patients treated over the past decade, but nearly 70% of the cohort is from 2008 onward. Owing to the protracted study period, some aspects of clinical practice, such as stent device or anticoagulant choice, have changed over time. However, > 90% of iliocavofemoral stents placed at the study institution since 1996 have been either WALLSTENT (Boston Scientific, Marlborough, Massachusetts) or S.M.A.R.T. (Cordis Corp, Milpitas, California) stents, and the patency analysis was designed to control for variables such as anticoagulation regimen using Cox regression. The rate of minor complications is likely underestimated in this retrospective study, as they are less likely to be clearly recorded in the medical record. Additionally, the rate of stent damage, migration, or deformity may be underreported, as these issues may not have been fully captured in follow-up imaging reports.

Manual chart review, image review, and data entry are inherently error prone, particularly on a large scale. To mitigate data entry error, routine training sessions for data curators and automated data validation systems within the REDCap database (eg, flagging of nonnumerical data entered into a numerical data field) were employed. Additionally, after data entry, a data science team systematically screened, validated, and cleaned the data in conjunction with clinicians to generate the final, analyzable dataset. Data were incomplete for vein diameters or Villalta scores, as not all patients in the study had follow-up imaging or clinic visits. Therefore, whereas average Villalta scores before and after stent placement use all available measurements, the sample sizes for statistical analysis comparing scores before and after intervention are limited to only patients who had scores measured both before and after an intervention. This limits the analysis of Villalta scores before and after intervention to patients with chronic DVT; patients with acute DVT typically presented to the emergency department rather than to the IR clinic for visits before intervention during which Villalta measurements would have been taken. Villalta scores were also not routinely obtained for patients with nonthrombotic venous pathology. Additionally, systematic collection of vein disease severity scores during IR clinic visits did not begin until 2015. Nevertheless, the institution's indications for endovenous stent treatment have not significantly changed over the study period, so the subset analyses for patients with Villalta values before and after stent placement are likely representative.

In conclusion, this study presents an assessment of longitudinal outcome measures for a large retrospective cohort of patients who received lower extremity venous stents at a referral hospital. Specifically, this analysis provides probabilities of stent patency, risk factors for a multivariate model of stent occlusion, stent and vein diameters, Villalta scores, and complication rates from a referral hospital setting, in

contrast to previously reported outpatient private practice cohorts. Stent placement is safe and effective for both thrombotic and nonthrombotic lower extremity venous occlusions. Further study is necessary to more comprehensively link clinical outcomes to stent patency and changes in vein diameter and to evaluate a wider range of variables that may have an effect on stent patency.

ACKNOWLEDGMENTS

This research was funded by the Stanford Medical Scholars Program and the Stanford University Department of Radiology.

REFERENCES

1. O'Sullivan GJ, Semba CP, Bittner CA, et al. Endovascular management of iliac vein compression (May-Thurner) syndrome. J Vasc Interv Radiol 2000; 11:823–836.
2. Jost CJ, Gloviczki P, Cherry KJ, et al. Surgical reconstruction of iliofemoral veins and the inferior vena cava for nonmalignant occlusive disease. J Vasc Surg 2001; 33:320–328.
3. Hartung O, Otero A, Boufi M, et al. Mid-term results of endovascular treatment for symptomatic chronic nonmalignant iliocaval venous occlusive disease. J Vasc Surg 2005; 42:1138–1143.
4. Neglén P, Hollis KC, Olivier J, Raju S. Stenting of the venous outflow in chronic venous disease: long-term stent-related outcome, clinical, and hemodynamic result. J Vasc Surg 2007; 46:979–990.e1.
5. Kahn SR, Comerota AJ, Cushman M, et al. The postthrombotic syndrome: evidence-based prevention, diagnosis, and treatment strategies. A Scientific Statement from the American Heart Association. Circulation 2014; 130:1636–1661.
6. Vedantham S, Goldhaber SZ, Julian JA, et al. Pharmacomechanical catheter-directed thrombolysis for deep-vein thrombosis. N Engl J Med 2017; 377:2240–2252.
7. Comerota A, Kearon C, Gu C, et al. Endovascular thrombus removal for acute iliofemoral deep vein thrombosis: analysis from a stratified multicenter randomized trial. Circulation 2019; 139:1162–1173.
8. Lowe HJ, Ferris TA, Hernandez PM, Weber SC. STRIDE—an integrated standards-based translational research informatics platform. AMIA Annu Symp Proc 2009; 2009:391–395.
9. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform 2009; 42:377–381.
10. Vedantham S, Grassi CJ, Ferral H, et al. Reporting standards for endovascular treatment of lower extremity deep vein thrombosis. J Vasc Interv Radiol 2009; 20:S391–S408.
11. Carr S, Chan K, Rosenberg J, et al. Correlation of the diameter of the left common iliac vein with the risk of lower-extremity deep venous thrombosis. J Vasc Interv Radiol 2012; 23:1467–1472.
12. R Core Team. *R: A Language and Environment for Statistical Computing*. Vienna, Austria: R Foundation for Statistical Computing; 2014.
13. Therneau T, Lumley T. Package "survival". 2015. Available at: ftp://164.41.45.44/pub/plan/R/web/packages/survival/survival.pdf. Accessed November 23, 2018.
14. Bates SM, Greer A, Middeldorp S, Veenstra DL, Prabulos AM, Vandvik PO. VTE, Thrombophilia, Antithrombotic Therapy, and Pregnancy—Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest 2012; 141:e691S–e736S.
15. Kearon C, Akl EA, Comerota AJ, et al. Antithrombotic Therapy for VTE Disease: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest 2012; 141:e419S–e496S.
16. Jayaraj A, Raju S. The venous stent: is it primetime yet? In: Chaar C, editor. *Current Management of Venous Diseases*. Cham: Springer International Publishing; 2018. p. 489–496.
17. Soosainathan A, Moore HM, Gohel MS, Davies AH. Scoring systems for the post-thrombotic syndrome. J Vasc Surg 2013; 57:254–261.

Table E1. Characteristics of Stent and Angioplasty Devices Used

Stent brand (N = 1,094), n (%)	
S.M.A.R.T.	690 (63.1)
WALLSTENT	288 (26.3)
Palmaz (Cordis Corp)	34 (3.1)
VIABAHN (W. L. Gore & Associates, Inc, Newark, Delaware)	21 (1.9)
Zilver (Cook, Inc, Bloomington, Indiana)	15 (1.4)
Protege (Medtronic, Minneapolis, Minnesota)	4 (0.4)
WallFlex (Boston Scientific)	13 (1.2)
Other	35 (3.2)
Stent brand distribution (%)	
Suprarenal IVC (n = 15)	WALLSTENT (66.7%), WallFlex (13.3%), Palmaz (13.3%), S.M.A.R.T. (6.7%)
Infrarenal IVC (n = 153)	WALLSTENT (52.3%), S.M.A.R.T. (36.6%), Palmaz (5.2%), WallFlex (3.3%), other (2.6%)
LCIV (n = 344)	S.M.A.R.T. (57.5%), WALLSTENT (27.0%), Palmaz (6.4%), Zilver (3.2%), other (5.8%)
LEIV (n = 193)	S.M.A.R.T. (75.6%), WALLSTENT (19.2%), VIABAHN (2.6%), other (2.6%)
LCFV (n = 96)	S.M.A.R.T. (77.1%), WALLSTENT (15.6%), VIABAHN (3.1%), Zilver (1.0%), other (3.1%)
LFV (n = 22)	S.M.A.R.T. (81.8%), WALLSTENT (9.1%), VIABAHN (9.1%)
RCIV (n = 140)	S.M.A.R.T. (69.3%), WALLSTENT (25.0%), VIABAHN (1.4%), Palmaz (1.4%), Zilver (1.4%), other (1.4%)
REIV (n = 85)	S.M.A.R.T. (75.3%), WALLSTENT (12.9%), VIABAHN (7.1%), Protégé (4.7%)
RCFV (n = 33)	S.M.A.R.T. (75.8%), WALLSTENT (12.1%), VIABAHN (6.1%), Zilver (3.0%), other (3.0%)
RFV (n = 9)	S.M.A.R.T. (77.8%), WALLSTENT (11.1%), VIABAHN (11.1%)
Stent diameter, mm, mean ± SD	
Suprarenal IVC	19.8 ± 1.5
Infrarenal IVC	17.9 ± 0.5
LCIV	13.7 ± 0.3
LEIV	12.9 ± 0.5
LCFV	11.9 ± 0.7
LFV	11.3 ± 1.7
RCIV	12.6 ± 0.6
REIV	12.3 ± 0.8
RCFV	11.9 ± 0.6
RFV	11.5 ± 2.5
Stent length, mm, mean ± SD	
Suprarenal IVC	76.3 ± 20.4
Infrarenal IVC	70.3 ± 66.3
LCIV	76.9 ± 75.2
LEIV	75.6 ± 62.4
LCFV	75.2 ± 43.6
LFEMV	80.0 ± 25.6
RCIV	75.9 ± 44.9
REIV	75.7 ± 42.2
RCFV	74.1 ± 30.1
RFV	76.3 ± 15.1

continued

Table E1. Characteristics of Stent and Angioplasty Devices Used *(continued)*

Stent angioplasty balloon brand (N = 912), n (%)	
ATLAS (Bard Peripheral Vascular, Inc, Tempe, Arizona)	393 (43.1)
CONQUEST (Bard Peripheral Vascular, Inc)	63 (6.9)
Armada (Abbott Cardiovascular, St. Paul, Minnesota)	16 (1.8)
Mustang (Boston Scientific)	14 (1.5)
OPTA (Cordis Corp)	13 (1.4)
Maxi (Medtronic, Minneapolis, Minnesota)	11 (1.2)
Other	36 (4.3)
Stent angioplasty balloon diameter, mm, mean ± SD	
ATLAS	13.9 ± 3.2
CONQUEST	11.7 ± 2.1
Armada	13.0 ± 1.7
Mustang	10.4 ± 0.9
OPTA	12.6 ± 1.9
Maxi	16.0 ± 1.7
Other	11.1 ± 3.8

IVC = inferior vena cava; LCFV = left common femoral vein; LCIV = left common iliac vein; LEIV = left external iliac vein; LFV = left femoral vein; RCFV = right common femoral vein; RCIV = right common iliac vein; REIV = right external iliac vein; RFV = right femoral vein.