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Outcomes and predictors of failure of iliac vein stenting after catheter-directed thrombolysis for acute iliofemoral thrombosis



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ABSTRACT

Objective: Iliac vein stenting is recommended to treat venous outflow obstruction after catheter-directed thrombolysis for acute iliofemoral deep venous thrombosis (DVT). Data on the outcome of proximal and distal stent extension are limited. Proximal stent extension to the vena cava may obstruct the contralateral iliac vein, whereas distal extension below the inguinal ligament contradicts common practice for arterial stents. The aim of this retrospective study was to assess outcomes and predictors of failure of iliac vein stents and contralateral iliac vein thrombosis, taking into consideration stent positioning.

Methods: Consecutive patients who underwent thrombolysis and stenting for DVT between May 2007 and September 2017 were identified from a prospectively maintained database. The intraoperative venograms were reviewed for proximal stent placement (covering >50% contralateral iliac vein orifice) and distal placement across the inguinal ligament. End points were ipsilateral DVT recurrence, post-thrombotic syndrome (PTS; Villalta score ≥ 5), and contralateral DVT. Patients with chronic contralateral DVT or contralateral iliac vein stenting at baseline were excluded from the contralateral DVT outcome evaluation. Survival analysis and Cox regression models were used to determine outcomes.

Results: Of 142 patients lysed, 73 patients (12 bilateral DVTs; mean age, 45.8 ± 17.2 years; 46 female patients) were treated with various combinations of thrombolytic techniques and at least one self-expanding iliac stent (77 stented limbs). Thirty-day recurrence developed in nine (12.3%) patients. The 3-year primary patency and secondary patency rates were 75.2% and 82.2%, respectively. The single predictor for loss of primary patency was incomplete thrombolysis ($\leq 50\%$; hazard ratio [HR], 7.41; $P = .002$). Overall, 3 of 12 (25%) stents extending below the inguinal ligament occluded at 1 month, 2 months, and 9 months, respectively. The overall rate of PTS (Villalta score ≥ 5) in the stented cohort was 14.4% at 5 years. This was predicted by incomplete lysis ($< 50\%$; HR, 7.09; $P = .040$), stent extension below the inguinal ligament (HR, 6.68; $P = .026$), and male sex (HR, 6.02; $P = .041$). Of the 17 stents that extended into the contralateral common iliac vein and 58 stents that did not, there were 1 (5.9%) and 5 (8.6%) contralateral DVTs ($P = .588$) at an average follow-up of 27.4 ± 33.7 and 22.2 ± 22.3 months ($P = .552$), respectively.

Conclusions: Iliac stenting after thrombolysis for acute DVT guarantees high patency and low PTS rates, provided adequate thrombus resolution has been achieved before stent placement. Stent placement below the inguinal ligament does not affect the patency but may be associated with a higher PTS rate. Stenting proximal to the ilio caval confluence, although a precipitating factor, may not independently increase the likelihood of contralateral DVT. (J Vasc Surg: Venous and Lym Dis 2019;7:153-61.)

Keywords: Iliac vein stenting; Catheter thrombolysis; Deep venous thrombosis; Post-thrombotic syndrome

Catheter-directed thrombolysis (CDT) for acute iliofemoral deep venous thrombosis (DVT) has been increasingly used during the past decade, targeting severe

acute symptoms and potentially prevention of post-thrombotic syndrome (PTS).¹ The results of various retrospective and prospective randomized studies have been inconsistent, but there is little doubt that CDT will remain in the treatment armamentarium for patients with symptomatic iliofemoral DVT with good life expectancy and low bleeding risk.¹⁻⁵ Still, our knowledge of technical aspects and our ability to predict failures are evolving.

Stenting of iliac vein narrowing or obstruction noted to be present after thrombolysis seems to be a critically important component of a successful procedure.^{2,6} Accumulated experience favors liberal stenting, as a general rule using flexible, large-diameter, self-expanding stents, extending into the inferior vena cava (IVC) and,

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if needed, into the common femoral vein to ensure sufficient inflow and outflow of the stent.⁶⁻⁹

However, both concepts of stent extension have been challenged. Distal stent extension below the inguinal ligament contradicts usual practice with arterial stents and may be associated with higher stenosis and thrombosis rates, whereas proximal stent extension to the IVC may jail and obstruct the contralateral iliac vein, leading to thrombosis.¹⁰⁻¹⁵

For ipsilateral stent failure, other than suboptimal inflow and outflow, studies have also demonstrated male sex, prior DVTs, and thrombotic lesions as predictors of failure.⁶⁻¹⁰ When acute DVT is treated, suboptimal thrombolysis is the most powerful predictor of failure.^{6,11,12} Contralateral thrombosis has been associated with neointimal formation in the small interstices of the traditionally used Wallstent (Boston Scientific, Natick, Mass) or Protégé (Covidien, Plymouth, Minn), which may assume the properties of a covered stent, resulting in increased flow resistance and possible occlusion or thrombosis of the contralateral iliac vein. Despite these concerns, current studies have demonstrated a relatively low rate of contralateral thrombosis, although they lack a comparison with those patients who did not have a stent placed across the contralateral iliac vein orifice.¹³⁻¹⁵

This retrospective study aimed to assess outcomes of iliac vein stenting and predictors of failure and contralateral iliac vein thrombosis while taking into account stent positioning.

METHODS

The study protocol was reviewed and approved by the Institutional Review Board of the University of Pittsburgh.

Study design. Consecutive patients who underwent CDT for iliofemoral DVT between May 2007 and September 2017 were identified from a prospectively maintained institutional database. Patients who received at least one stent were selected for analysis. Medical records were reviewed for patients' demographics, baseline characteristics and risk factors, venous imaging studies, indications, intraprocedural notes, periprocedural complications, and long-term outcomes. The intraoperative venograms were also reviewed to assess the degree of proximal and distal stent projection into the IVC lumen and across the inguinal ligament, respectively. The contralateral venous outflow was considered jailed when it was covered by the protruding stent by >50%, and distal extension was considered below the inguinal ligament when the tip of the stent was visualized below the cranial border of the femoral head (in anteroposterior view).

Primary end points were ipsilateral DVT recurrence and contralateral iliofemoral DVT; PTS (Villalta score ≥ 5) was the secondary end point. Two patients with baseline

ARTICLE HIGHLIGHTS

- **Type of Research:** Retrospective cohort study of a prospectively maintained database
- **Key Findings:** In 77 stented limbs of 73 patients with acute iliofemoral deep venous thrombosis (DVT), 3-year primary patency and secondary patency were 75% and 82%, respectively; incomplete thrombolysis (<50%) predicted loss of primary patency (hazard ratio [HR], 7.41; $P = .002$). Twelve stents extended below the inguinal ligament; three (25%) thrombosed. Post-thrombotic syndrome (Villalta score ≥ 5) was 14% at 5 years and was predicted by incomplete lysis (HR, 7.09; $P = .04$), stent extension below the inguinal ligament (HR, 6.68; $P = .026$), and male sex (HR, 6.02; $P = .041$). Stent extension over the contralateral iliac vein was not an independent predictor of contralateral DVT ($P = .588$).
- **Take Home Message:** A strategy of complete thrombus removal for acute iliofemoral DVT is recommended. Stent extension into the contralateral iliac vein or below the inguinal ligament appears to be an acceptable adjunct to thrombolysis and iliac vein stenting for DVT.

chronic contralateral DVT and contralateral iliac vein stenting were excluded from the contralateral DVT outcome.

Definitions. Indications for thrombolysis as an alternative to anticoagulation alone were limited to symptomatic patients with acute iliofemoral DVT and no absolute contraindication to lysis per the Society for Vascular Surgery guidelines.⁶ The rate of clot lysis was determined on the basis of the estimated amount of residual clot on venography completion compared with the pretreatment venogram.² The physicians reviewing the venograms (E.D.A., Y.P.) were blinded to the clinical outcomes of the patients.

PTS was assessed using the Villalta score. The Villalta score is calculated on the basis of five patient-related venous symptoms (pain, heaviness, cramps, pruritus, and paresthesia) and six clinician-assessed physical signs (skin induration, redness, hyperpigmentation, pretibial edema, venous ectasia, and pain during calf compression), which are rated on a 4-point scale: 0, none; 1, mild; 2, moderate; and 3, severe. Points can sum to a total score ranging between 0 and 33. Patients with a sum score of ≥ 5 are classified as having PTS.

A major complication was defined as any event requiring an intervention, rehospitalization, or persisting kidney function deterioration with the need for hemodialysis within 30 days of the procedure. Freedom from

rethrombosis was defined as maintained patency of the treated iliofemoral or caval segment, irrespective of the popliteal or distal vein segments.

Periprocedural protocol. Based on a DVT protocol to maintain therapeutic partial thromboplastin times, heparin was intravenously administered to the patients before the procedure. All patients underwent lower extremity duplex ultrasound imaging before intervention. In addition, patients were selectively (inconclusive findings on duplex ultrasound examination or multiple prior DVTs) evaluated with computed tomography venography of the abdomen and pelvis with intravenous administration of contrast material. All interventions were performed by vascular surgeons in endovascular suites equipped with fixed imaging capability. All patients were discharged on therapeutic oral anticoagulation or low-molecular-weight heparin, with graduated elastic compression stockings (20-30 mm Hg). The duration of anticoagulation treatment was determined on the basis of the underlying cause and the presence of a hypercoagulable state per the American College of Chest Physicians guidelines.¹⁶ Patients' compliance and socioeconomic background were limiting factors in fully maintaining the goals and recommendations relayed to patients on discharge and follow-up. Antiplatelet therapy with aspirin and clopidogrel (for at least 3 months) was initiated in all patients after iliac vein stent placement.

Thrombolysis technique. Our technique has been thoroughly described elsewhere.¹⁷⁻²⁰ Treatment was done under conscious sedation and local anesthesia in all patients. Although it was initially routine early in our experience out of concern for pulmonary embolism, use of temporary IVC filters has since become more selective. Ultrasound-guided popliteal vein access was obtained in most patients (prone position) regardless of whether the thrombus had involved the popliteal or tibial veins. In six patients, access was obtained through the femoral or small saphenous vein. Unfractionated heparin was routinely administered intravenously (100 units/kg) but not monitored. Ascending venography was performed through a 6F or 8F sheath. In patients with thrombosis at the popliteal access site, 2 mg of tissue plasminogen activator (tPA [Alteplase]; Genentech, San Francisco, Calif) was provided at the start of the procedure through the sheath. With the intent to provide a single-session treatment, pharmacomechanical thrombolysis (PMT) was used in patients with acute DVT (<14 days). PMT was performed with either the AngioJet catheter (Bayer HealthCare, Medrad Inc, Indianola, Pa) or the Trellis device (Covidien Vascular, Mansfield, Mass), which was eventually removed from the market. Device use was at the discretion of the operator. The power-pulse mode was initially used with the AngioJet catheter, administering 6 to 8 mg of tPA into the thrombus. The catheter

was then switched to thrombectomy mode after a dwell time of 20 minutes. Similar tPA doses were administered with the Trellis device for every 30-cm segment treated. Catheter-directed lysis was used selectively, as either a primary or secondary intervention, using a standard multi-side hole catheter or the EKOS catheter (EKOS Corporation, Bothell, Wash; ultrasound-assisted thrombolysis) at the discretion of the operator. This was reserved for residual thrombus after PMT, for patients with subacute DVT (>14 days old), or for those in whom the age of the clot was ill-defined. Usually, patients undergoing thrombolysis in multiple sessions required scheduled lysis checks at 12- to 24-hour intervals. Iliac vein stenosis seen on completion venography was routinely treated with self-expanding stents (Wallstent or Protégé). The common iliac vein and the external iliac vein were typically stented with a 14- to 18-mm stent and a 12- to 14-mm stent, respectively. The chosen length was tailored to cover the diseased segment. Early in our experience (<2012), there was a hesitance for stent deployment below the inguinal ligament, whereas proximal deployment would typically extend to the vena cava if the iliac lesion was within 2 cm of the caval confluence.

All patients continued systemic anticoagulation after the lysis intervention, and baby aspirin was initiated when a stent was placed. IVC filters were retrieved either on completion of the lysis procedure or at a later scheduled time in the presence of any residual thrombus because of perceived risk of embolization. The length of anticoagulation was decided on the basis of the nature of the DVT and the underlying risk factors.

Follow-up. Duplex ultrasound imaging was performed to assess for vessel patency and to evaluate for venous reflux and valvular competence. Reflux was determined at the femoral and popliteal levels and was considered significant if >1 second. Additional imaging (venography, computed tomography venography, or magnetic resonance venography) was performed for clinically suspected recurrence or with a nondiagnostic duplex ultrasound evaluation. Clinical, Etiology, Anatomy, and Pathophysiology (CEAP) and Villalta scores were obtained during follow-up visits at 1 month, 3 months, 6 months, and 12 months and annually thereafter. In consultation with a hematologist, a hypercoagulable workup, if not previously done, was also obtained during follow-up.

Statistical analysis. Descriptive characteristics are reported as mean \pm standard deviation or as number of cases and percentages. Preoperative baseline characteristics and perioperative complications were studied at the patient level; DVT recurrence or stent thrombosis and PTS were analyzed at the limb level. Kaplan-Meier analysis was used to assess survival functions. The effect of baseline and operative predictors on study end points

was assessed using Cox regression models. Significant associations were expressed as hazard ratios (HRs). Results were considered statistically significant when P value was $<.05$. Data were analyzed using Statistical Package for the Social Sciences, version 17 (SPSS Inc, Chicago, Ill).

RESULTS

Of 142 patients treated with various combinations of thrombolytic techniques, 73 patients (12 bilateral DVTs) had received at least one self-expanding iliac stent during the study period, and this represents our study group (77 stented limbs). The mean age was 45.8 ± 17.2 years, and 46 patients (63.0%) were female (Table I); 37 patients (50.7%) were treated in two sessions (mean number, 2.2 ± 0.7). PMT alone was used in 12 (16.4%) patients, CDT alone in 8 (11.0%); the remaining 53 (72.6%) were treated with a combination of CDT and PMT in different sequences, with either CDT following suboptimal PMT or PMT for residual thrombus following CDT. Around one to four stents were used for a median diameter of 16 mm (range, 14-20 mm) in the common iliac vein and 14 mm (range, 12-16 mm) in the external iliac vein. The stents extended proximally covering the contralateral iliac vein in 18 (21.2%) limbs and distally below the inguinal ligament in 12 (14.1%) limbs. Four of the 12 (33.3%) patients with bilateral DVT received bilateral iliac stents. One patient had chronic contralateral iliac vein thrombosis, and one had contralateral iliac vein stent on presentation.

Perioperative outcomes. DVT recurred perioperatively in nine (12.3%) patients (two bilateral DVTs). Four of them (six limbs) had incomplete thrombolysis ($\leq 50\%$); the rest recurred despite successful lysis ($>50\%$; Table II). None of these recurrences had progressed to phlegmasia or limb-threatening venous congestion, so surgical thrombectomy was not required in any. In three of these, a reintervention was performed, and an additional stent was placed; two were successful.

Two major complications occurred: one access site hematoma in the popliteal fossa that required surgical evacuation, with no further events; and one epidural hematoma compressing the spinal canal, causing progressive neurologic deficits that also required surgical evacuation. Eight other patients had minor complications, including 5 (6.8%) cases of remote bleeding that required blood transfusion, 2 (2.7%) arrhythmias, and 1 (1.4%) transient acute-on-chronic renal failure. The 5 systemic bleeds included 1 case of minor gastrointestinal bleeding, 3 cases of severe hemoglobin drop with no apparent source, and 1 rectus sheath hematoma extending into the retroperitoneum.

Ipsilateral recurrence and PTS. The mean imaging and clinical follow-up of the patients was 14 ± 15 months (range, 1-65 months) and 32 ± 32 months (range, 1-110 months), respectively. During the follow-up period,

Table I. Baseline characteristics and technical aspects of study cohort

Patients/limbs	73/85
Age, years	45.8 ± 17.2
Female sex	46 (63)
Left-sided DVT	50 (69)
Presenting symptom (indication)	
Pain or swelling	62 (84.9)
Phlegmasia	11 (15.1)
Duration of symptoms, days	
≤ 14 days	57 (78.1)
>14 days	16 (21.9)
Risk factors	
Malignant disease	10 (13.7)
Hypercoagulable disorder	24 (32.9)
Recent surgery	16 (21.9)
Previous DVT	30 (41.1)
Immobility	7 (9.6)
Medication (eg, contraceptives)	3 (4.1)
Trauma	3 (4.1)
Clinically significant PE (on admission)	3 (4.1)
DVT involving the vena cava	30 (41.1)
Technique	
CDT only	8 (11.0)
PMT only	12 (16.4)
Combined	53 (72.6)
Stent data	
Common iliac vein	19 (22.4)
Extending to the IVC covering $>50\%$	18 (21.2)
Diameter, mm	15.4 ± 1.8
External iliac vein	5 (5.9)
Extending to the CFV below the inguinal ligament	12 (14.1)
Diameter, mm	13.5 ± 3.0

CDT, Catheter-directed thrombolysis; CFV, common femoral vein; DVT, deep venous thrombosis; IVC, inferior vena cava; PE, pulmonary embolism; PMT, pharmacomechanical thrombolysis. Categorical variables are presented as number (%). Continuous variables are presented as mean \pm standard deviation.

five more patients developed stent thrombosis (Table II), accounting for overall 1-, 2-, and 3-year primary patency rates for the stented limbs of 83.1%, 79.9%, and 75.2%, respectively (Fig. a). In addition to the three reinterventions performed during the postoperative period, one additional reintervention was performed at 30 months. The 3-year secondary patency rate was 82.2% (Fig. b).

Multivariate analysis (Table III) showed that the single predictor for primary patency loss was incomplete thrombolysis ($\leq 50\%$; HR, 7.4; $P = .002$). Of stents extending below the inguinal ligament, 25% (3/12) failed at 1 month, 2 months, and 9 months; stenting below the inguinal ligament or into the IVC was not a predictor of failure.

Table II. Patient, deep venous thrombosis (DVT), and technical characteristics of stent failures

No.	Sex/age	DVT location/ duration	Etiology or risk factor	Treatment	Time at failure, months	Comment
10	F/54	Iliocaval Bilateral/30 days	Ovarian cancer Recent surgery (biopsy)	PMT only 1 session	1	Inability to continue lysis ≤50% lysis 30-day recurrence
24	F/68	Iliocaval Bilateral/31 days	NSCLC T2N2 2 sessions	CDT and PMT	1.8	>50% lysis
29	M/56	Iliocaval Bilateral/2 days	Previous DVT Hypercoagulable Thrombosed indwelling IVC filter	CDT and PMT 2 sessions	1	Chronic RLE DVT ≤50% lysis 30-day recurrence
55	M/53	Iliofemoral Left/2 days	Recent surgery Previous DVT May-Thurner	CDT and PMT 2 sessions	1.0	>50% lysis 30-day recurrence Successful reintervention within 8 days with stent extension; patent on follow-up
72	M/16	Iliofemoral Left/17 days	Previous DVT Hypercoagulable (MTHFR) May-Thurner	CDT and PMT 3 sessions	1	Chronic DVT lesions ≤50% lysis 30-day recurrence
75	M/22	Iliofemoral Right/15 days	Immobility Recent surgery (spinal)	CDT and PMT 2 sessions	1	≤50% lysis 30-day recurrence
80	F/28	Iliofemoral Left/7 days	Recent delivery Rethrombosis	3 sessions	1	>50% lysis 30-day recurrence Reintervention after 72 hours with proximal stent extension, immediate failure within 30 days
82	M/38	Iliofemoral Left/2 days	Previous DVT	CDT and PMT 2 sessions	15.5	>50% lysis
117	F/36	Iliofemoral Left/2 days	May-Thurner	CDT only 2 sessions	30	>50% lysis
126	F/23	Iliofemoral Left/30 days	History of right adnexal mass compressing IVC Previous DVT Recent surgery History of immobility	CDT only 3 sessions	1	>50% lysis 30-day recurrence
137	M/36	Iliofemoral Left/10 days	Previous DVT with left iliac vein stent May-Thurner	CDT and PMT 4 sessions	9	>50% lysis
143	F/35	Iliofemoral Right/9 days	Trauma-provoked DVT Hypercoagulable	PMT only 2 sessions	2	>50% lysis
148	F/23	Iliofemoral Left/14 days	Previous DVT Hypercoagulable (antithrombin III deficiency)	CDT and PMT 3 sessions	0	Subclinical PE >50% lysis 30-day recurrence
149	F/39	Iliofemoral Left/10 days	Previous DVT	CDT and PMT 2 sessions	1	>50% lysis 30-day recurrence Reintervention after 30 days with stenting; patent on follow-up

CDT, Catheter-directed thrombolysis; IVC, inferior vena cava; NSCLC, non-small cell lung cancer; PE, pulmonary embolism; PMT, pharmacomechanical thrombolysis; RLE, right lower extremity.

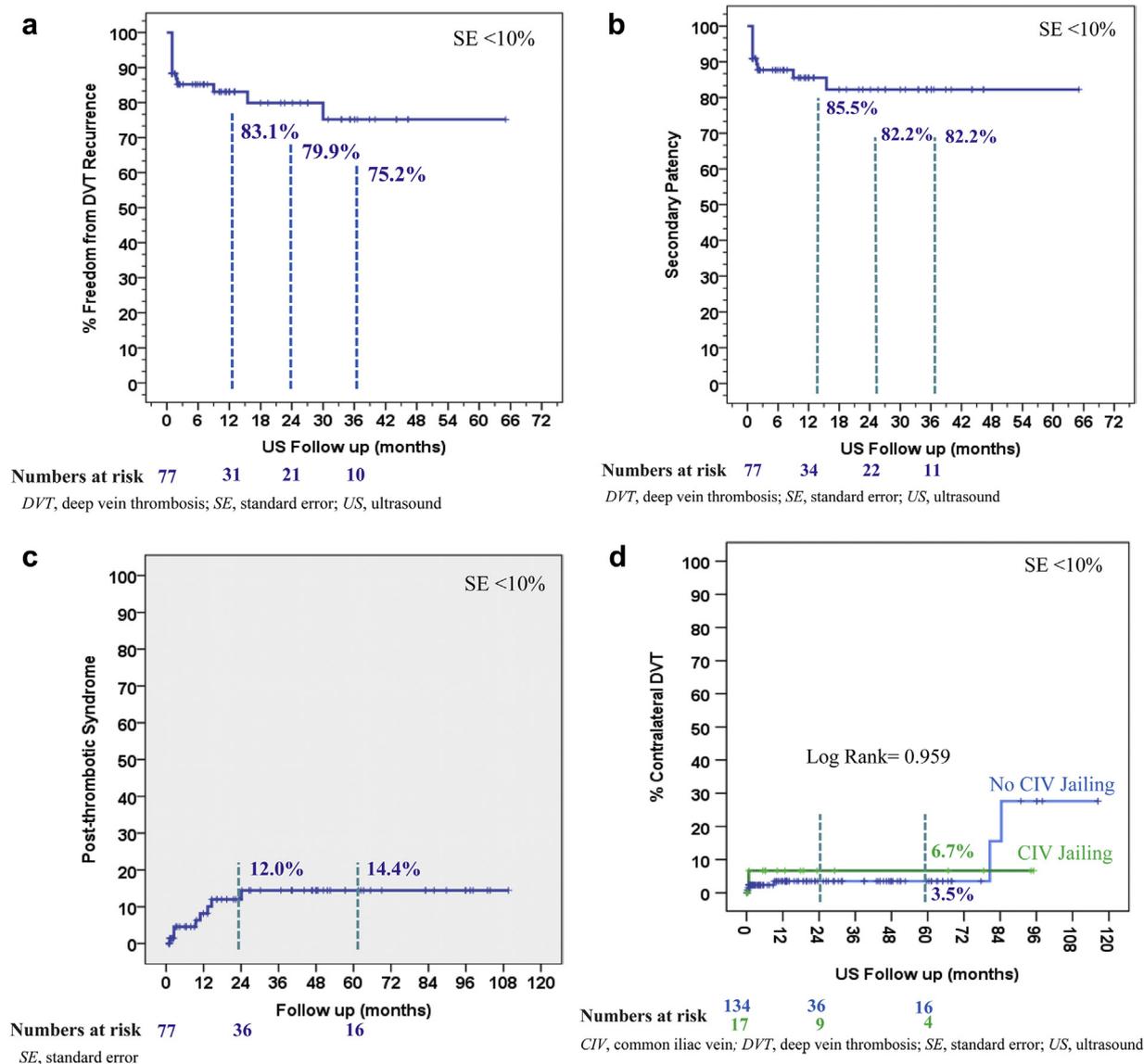


Fig. a, Kaplan-Meier curve for primary deep vein thrombosis (DVT) stent patency. **b**, Kaplan-Meier curve for secondary DVT stent patency. **c**, Kaplan-Meier curve for post-thrombotic syndrome (PTS) in the stented cohort. **d**, Kaplan-Meier curves for cumulative contralateral DVT incidence comparing patients with and without contralateral common iliac vein (CIV) jailing. SE, Standard error; US, ultrasound.

The overall rate of PTS (Villalta score ≥ 5) in the stented cohort at 2 and 5 years was 12.0% and 14.4% (Fig. c). The development of PTS was predicted by being male (HR, 6.02; $P = .041$), incomplete lysis ($<50\%$; HR, 7.09; $P = .040$), and stenting below the inguinal ligament (HR, 6.68; $P = .026$; Table III).

Contralateral thrombosis. Excluding the two patients with contralateral chronic DVT or contralateral iliac vein stent at baseline, there were 75 stented limbs for analysis. Of those, 17 stents covered the common iliac vein on the contralateral side and 58 stents did not. One (5.9%) and five (8.6%) contralateral DVTs ($P = .588$) occurred at an average follow-up of 27.4 ± 33.7 and 22.2 ± 22.3 months ($P = .552$), respectively.

In another analysis combining the ipsilateral stented patients without jailing of the contralateral common iliac vein (58 limbs) and our DVT patients who underwent thrombolysis without any stent deployment (76 limbs—not included in our previous analysis), there were six contralateral DVTs (4.5%). Comparing this group with the 17 patients in the jailed common iliac vein group (Fig. d), the cumulative contralateral DVT incidence was 3.5% and 6.7% at 5 years, respectively ($P = .959$).

DISCUSSION

For acute iliofemoral DVT, iliac vein stenting after thrombolysis is associated with high anatomic and clinical success, provided thrombus has been sufficiently removed before stenting. Stent extension below the

Table III. Cox regression model for predictors of primary deep venous thrombosis (DVT) stent patency and post-thrombotic syndrome (PTS)

	HR	P value
Primary patency		
Lysis \leq 50%	7.41	.002
Stent below the inguinal ligament	2.22	.277
Side (left)	1.71	.486
Symptom duration	1.03	.279
PTS		
Lysis \leq 50%	7.09	.040
Stent below the inguinal ligament	6.68	.026
Sex (male)	6.02	.041
Previous DVT	0.65	.614
Symptom duration	1.03	.525

HR, Hazard ratio.

inguinal ligament and proximally into the vena cava is not independently associated with ipsilateral recurrence or contralateral DVT.

Catheter-based intervention for iliofemoral DVT is being increasingly performed, and despite conflicting results, accumulating data support its use in symptomatic patients with good life expectancy and low bleeding risk.^{1,21} The main advantages of catheter-based interventions are re-establishment of iliofemoral inline flow, faster symptom resolution, valve function preservation, and reduction of PTS severity. Interventional success rates are high, with reported 2- and 5-year patency rates between 65% and 90%, even as technical considerations are evolving.^{11,22-26} Among those, liberal use of stents to treat an underlying chronic lesion or external compression (eg, May-Thurner syndrome) is vital to maintain vessel patency and is currently recommended by both the American Venous Forum and Cardiovascular and Interventional Radiological Society of Europe guidelines.^{6,7} Indicative of this is the national venous registry-reported 1-year venous patency that was significantly better in limbs treated with iliac stents (74%) than in limbs without stent placement (53%; $P < .001$).² Still, the major randomized trials Catheter-directed Venous Thrombolysis (CaVenT) and Acute Venous Thrombosis: Thrombus Removal with Adjunctive Catheter-Directed Thrombolysis (ATTRACT) did not have a high stent use rate after thrombolysis, and this has been criticized as a limiting factor to show superiority of catheter interventions.^{3-5,21,27,28}

Our estimated 3-year primary patency was 75.2%, and incomplete lysis ($<50\%$ lysis) was predictive of its loss. Complete $\geq 50\%$ lysis and low postlysis thrombus score, known as the open vein hypothesis, are now established predictors of long-term, durable patency and PTS.^{2,12,23} In broader terms, incomplete vessel lysis resulting in poor inflow or outflow will inevitably lead to vessel

rethrombosis. This correlation has long been suggested. Mewissen et al² quantified the degree of clot lysis in patients entered into the national venous registry and showed that increased lysis correlated with improved 1-year patency. Similarly, Comerota et al have repeatedly demonstrated that quality of life and post-thrombotic morbidity correlate with residual thrombus after CDT.²⁹⁻³¹ Therefore, physicians who embark on a strategy of thrombus removal to treat patients with extensive DVT should persist to completely resolve the thrombus burden. Our study further emphasizes that any residual thrombus should be considered chronic, necessitating stent placement. Most of the stent failures in our series and other studies occurred within 30 days; thus, the first postoperative follow-up visit should occur within 2 to 4 weeks of the procedure, which will help identify and possibly correct these potential problems. Most patients who achieved 30-day primary patency remained patent in the long term.

The decision as to when to stent based on two-dimensional venography after successful thrombolysis can be challenging. If intravascular ultrasound is not used, multiple angled projections and a low threshold for stenting should be employed. Self-expanding nitinol or stainless steel large-diameter stents have traditionally been used, but novel dedicated “venous” stents will soon enter the U.S. market. Appropriate stenting of the iliac vein can be challenging for various reasons: lesions may extend distally to the common femoral vein; traditional stent deployment technology has accuracy limitations; and locating the ilio caval confluence may be difficult (unless intravascular ultrasound is being used). These challenges have been previously addressed. Regarding infrainguinal extension of stents, it has previously been shown to potentially reduce stent patency, even though overall patency rates remain relatively high. A recent series of chronic DVT stenting demonstrated no difference in primary patency at 12 months between those who underwent stenting confined to the suprainguinal location and those who required infrainguinal stent extension (68% vs 65%; $P = .7$). On the contrary, the authors have found that failure to land stents in healthy vein contributed to early reocclusion and was corrected with infrainguinal extension.³² Our results confirmed this finding. Interestingly, stent extension below the inguinal seems to be independently associated with higher rates of PTS, mirroring the extent of the disease and the loss of both iliac and common femoral valve function. Our PTS rates (14% at 5 years) were otherwise much lower than those reported in the large randomized trials CaVenT (43% at 5 years) and ATTRACT (47% at 2 years), and this may reflect the fact that we are studying a “stented” population, or there may be potential bias related to our small sample.^{4,5} In our previously published analysis of the entire lysed cohort, the PTS rate was 28% at 3 years.¹²

Regarding proximal landing, the initial recommendation was to deploy and to extend Wallstents 3 to 5 cm cephalad into the IVC to avoid caudal migration or restenosis as the peripheral stent ends have lower outward radial force compared with the central body of the stent.¹³ This concept was later challenged as it was observed that patients after iliac stenting with caval extension might develop contralateral DVT. The hypothesis is that the small stent interstices gradually become lined with neointima and eventually the stent assumes the properties of a covered stent, obstructing the contralateral iliac vein outflow. Murphy et al suggested the use of a proximal Z stent (Cook Medical, Bloomington, Ind), which has larger interstices, to maintain contralateral blood flow. In their more recent analysis of chronic DVT cases, they compared 755 limbs with consecutive Wallstent caval extensions (2006-2010) and 982 limbs with Z stent extensions (2011-2015) and analyzed for subsequent contralateral DVT incidence. Cumulative contralateral DVT was 1% and 10% at 54 months in the Z stent and Wallstent groups, respectively ($P < .001$) or 0.3% vs 2.1% in absolute (not time-related) rates.¹³ Along the same lines, Caliste et al reviewed 41 iliac stents jailing the contralateral iliac vein and reported a 9.7% incidence of contralateral DVT. Interestingly, three of four contralateral DVTs were identified in patients who were not compliant with anticoagulation.¹⁴ Nevertheless, the limitation of both studies is the lack of a control group, thus underestimating intrinsic factors (eg, hypercoagulable disorders, malignant disease) that may lead to a contralateral DVT. Our comparison between jailed and nonjailed common iliac veins shows no difference in the incidence of contralateral DVTs. Expanding our analysis to include the nonstented DVTs (134 total limbs), the incidence of DVT was 3.5% in nonjailed iliac veins and 6.7% in jailed (17 limbs) iliac veins at 5 years ($P = .959$). Similarly, in a European study, only 2.7% (10/376) developed contralateral iliac DVT after initial ipsilateral iliac stenting that occurred with complete coverage of the contralateral iliac vein. The cumulative incidence of contralateral DVT after 6 years was 4%. Acute DVT, preoperative contralateral internal iliac vein thrombosis, pre-existing IVC filters, and anticoagulation noncompliance were predictive factors.¹⁵ It appears that the need to completely cover the contralateral common iliac vein may not be that frequent, but if it needs to be done, it is reasonably safe and durable.

Some limitations of our study include its retrospective nature, which might bias the results. Complete data regarding compliance with compression stockings and intensity and duration of anticoagulation therapy, which could potentially affect the results, were missing. It could also be argued that in our contralateral DVT and PTS analysis, patients with follow-up of <6 months were included, although the expected effect may be manifested well beyond 2 years. In an attempt to eliminate

this effect, the Kaplan-Meier estimation was used. Regarding PTS, the 1-month Villalta score was shown to be a strong independent predictor of PTS over time, which supports our findings despite the lack of long-term follow-up data for some patients.³³ Nevertheless, this study reflects the results of contemporary thrombolysis and stenting practice for acute DVT.

CONCLUSIONS

Our study identified the success of obtaining complete venous lysis as the dominant predictor of iliac vein stent patency and PTS, whereas stent positioning below the inguinal ligament did not affect outcomes, provided it extended into a nondiseased vein segment. Stent placement across the ilio caval confluence does not appear to be independently associated with contralateral iliac DVT.

AUTHOR CONTRIBUTIONS

Conception and design: EA, EH, MS, GA, RC
 Analysis and interpretation: EA, ZS, MM, RC
 Data collection: EA, ZS, AAA, YP
 Writing the article: EA, ZS, AAA, YP, EH, MS, GA, RC
 Critical revision of the article: EA, MS, GA, MM, RC
 Final approval of the article: EA, ZS, AAA, YP, EH, MS, GA, MM, RC
 Statistical analysis: EA, ZS, AAA
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