Risk factors and classification of reintervention following deep venous stenting for acute iliofemoral deep vein thrombosis

Anna L. Pouncey, BA (Hons), BMBCh, MRCS (Eng),^a Taha Kahn, MBBS, MD, FRCS,^a Rachel I. Morris, BSc (Hons), MBChB,^a Prakash Saha, BSc (Hons), MBBS, FRCS, PhD,^a Narayanan Thulasidasan, MBBS, MRCS, FRCR,^b and Stephen A. Black, MD, FEBVS, MBBCM, FRCS (ED),^a London, UK

ABSTRACT

Background: Acute iliofemoral deep vein thrombosis (DVT) is associated with the development of post-thrombotic syndrome (PTS). Thrombolysis and deep venous stenting can restore vessel outflow and can reduce the incidence of PTS. However, for a proportion of patients, subsequent stenosis or reocclusion will necessitate further intervention. In the present study, we aimed to identify the risk factors, examine the outcomes (reintervention success and PTS), and develop a classification system for reintervention.

Methods: A retrospective single-center cohort study of patients who had undergone successful lysis for iliofemoral DVT from 2013 to 2017. The patients' records and imaging studies were examined for demographics, risk factors, extent of thrombus and vessel clearance, stenting, flow, reintervention, anticoagulation compliance, Villalta score, and secondary patency. From our findings, a system of classification for patients for whom procedures have failed was developed, constituting technical, hematologic, flow related, or multiple factors.

Results: Of 143 limbs (133 patients), 48 (33.6%) had required reintervention, of which 25 had presented with reocclusion (17.4%). The median time to reintervention was 45 days. The need for reintervention was associated with inferior vena cava thrombus (risk ratio [RR], 2.16; P < .01), stenting across the inguinal ligament (RR, 2.08; P < .01), and anticoagulation noncompliance (RR, 7.09; P < .01). Successful reintervention was achieved in 31 limbs (64.6%): 23 of 23 (100%) treated before occlusion vs 8 of 25 (36.4%) treated after occlusion (RR, 32.31; P < .01). A greater incidence of any PTS was observed for patients requiring reintervention (median Villalta score, 3 [interquartile range, 1-5]; vs 1 [interquartile range, 1-4]; RR, 2.28; P = .029). Cases without complete vessel occlusion (reintervention and control) had a lower rate of any PTS (14.0% vs 42.9%; RR, 3.06; P < .01) and moderate to severe PTS (3.0% vs 14.3%; RR, 4.76; P = .046) Technical issues were observed in 54.2% of reintervention cases and 6.3% of cases not requiring reintervention (P < .01). Flow-related issues were observed in 43.8% of the reintervention cases and no cases not requiring reintervention (P < .01). Flow-related issues were observed in 43.8% of the reintervention cases and no cases not requiring reintervention (P < .01). Of the reintervention cases, 27.1% were multifactorial and were associated with a lower rate of vessel salvage; however, this did not translate into a significant difference in secondary patency on survival analysis (RR, 1.70; P = .429).

Conclusions: A large proportion of patients required reintervention because of potentially preventable factors. Anticoagulation compliance, thrombus burden, and poor flow are important risk factors to consider in patient selection. Reintervention increased the risk of PTS and was more often successful when achieved before vessel occlusion. (J Vasc Surg Venous Lymphat Disord 2022; :1-8.)

Keywords: Deep vein thrombosis treatment; Deep venous stent; Post-thrombotic syndrome; Surgical reintervention; Thrombolysis

Post-thrombotic syndrome (PTS) causes disability and impaired quality of life, with chronic pain, limb swelling, and ulceration.¹ PTS will develop in \leq 50% of patients after iliofemoral deep vein thrombosis (DVT) if treated with anticoagulation and compression stockings alone, and 15% will develop ulceration.^{2,3} Post-thrombotic morbidity is related to the extent of residual thrombus, and lower quality of life scores have been demonstrated for

patients who have developed reflux or chronic occlusion.^{4,5} Studies have shown that early clot clearance with percutaneous thrombolytic strategies can restore venous patency and potentially reduce PTS severity in those with iliofemoral DVT.⁶⁻⁹

A high rate of stenting following percutaneous thrombolysis is to be expected, with a degree of extrinsic compression demonstrated for \sim 80% of iliofemoral

From the Cardiovascular Division, Academic Department of Vascular Surgery, St. Thomas' Hospital, King's College London^a; and the Department of Interventional Radiology, Guys and St. Thomas Hospital.^b

Author conflict of interest: none.

Additional material for this article may be found online at www.jvsvenous.org. Correspondence: Stephen A. Black, MD, FEBVS, MBBCM, FRCS (ED), Cardiovascular Division, Academic Department of Vascular Surgery, St. Thomas' Hospital, King's College London, UK (e-mail: Stephen.black@kcl.ac.uk).

The editors and reviewers of this article have no relevant financial relationships to disclose per the Journal policy that requires reviewers to decline review of any manuscript for which they may have a conflict of interest. 2213-333X

²²¹³⁻³³³⁷

Crown Copyright © 2022 Published by Elsevier Inc. on behalf of the Society for Vascular Surgery. This is an open access article under the CC BY license (http:// creativecommons.org/licenses/by/4.0/).

https://doi.org/10.1016/j.jvsv.2022.03.006

2 Pouncey et al

DVT cases.¹⁰ Results from the National Venous Registry have demonstrated that iliac patency at 1 year was significantly better in limbs stented (for treatment of narrowing or residual obstruction) compared with limbs treated with lysis alone (74% vs 53%; P < .001).¹¹ However, for a proportion of patients (13%-21%), reocclusion or stenosis will occur, and further intervention will be required.^{12,13} Reintervention has been shown to be associated with a higher risk of PTS and has been postulated as one of the factors that reduces the efficacy of treatment in the large randomized controlled trials reported in this field.^{6,7,14}

Various factors have been purported to increase the risk of reintervention, including suboptimal thrombolysis and poor inflow or outflow.^{12,15} Current evidence supports the use of large-diameter, self-expanding stents, extending distally or proximal, as needed, to ensure coverage of residual disease with sufficient inflow and outflow.^{10,12} However, our understanding of the key technical aspects and our ability to predict failure is still evolving. In the present retrospective study, we evaluated the causes of reocclusion and stenosis after deep venous interventions for acute iliofemoral DVT and developed a classification system to standardize analysis of the technical treatment outcomes for use in clinical practice and further research.

METHODS

Patient selection. Patients presenting to a tertiary vascular center between November 2013 and 2017 with symptomatic acute or subacute iliofemoral DVT of ≤28 days' duration were identified from a prospectively collected database, with a minimum follow-up of 12 months, for which treatment in the acute setting was previously described.⁹ All the patients who had undergone successful lytic treatment (>50% clot clearance) were selected. Patients for whom thrombolysis was contraindicated, those for whom successful lysis was not achieved, and those for whom a congenital inferior vena cava (IVC) abnormality was identified were excluded from the present study (Supplementary Fig 1, online only). All the patients provided written informed consent before they underwent treatment. Institutional review board or ethics approval and patient consent are not required at our institution for retrospective data reviews.

Reintervention: threshold and technical approach.

Reinterventions were performed for patients with symptom recurrence correlating with a >50% reduction in the in stent diameter and for those perceived to have a threatened stent (ie, worsening stenosis on sequential imaging studies), a correctable anatomic issue such as poor inflow or after stent occlusion. Reintervention was also performed for those with an identified mechanical problem (eg, stent fracture or compression) in the presence of symptoms. Percentage of reduction of the in stent diameter was assessed using B-mode ultrasound Journal of Vascular Surgery: Venous and Lymphatic Disorders

ARTICLE HIGHLIGHTS

- **Type of Research:** A single-center, retrospective cohort study
- **Key Findings:** Reintervention for stenosis/occlusion following iliofemoral deep venous thrombolysis was required for in 48 of 143 limbs and was associated with technical (54.2%), flow-related (43.8%), and hematologic (33%) issues, inferior vena cava thrombus (risk ratio, 2.16), and stenting across the inguinal ligament (risk ratio, 2.08). Reocclusion reduced reintervention success (36.4% vs 100%) and increased the risk of post-thrombotic syndrome.
- **Take Home Message:** A large proportion of patients required reintervention because of potentially preventable factors. Anticoagulation compliance, thrombus burden, and poor flow are important risk factors to consider in patient selection. Vessel reocclusion increased the risk of post-thrombotic syndrome. Reintervention was more often successful when performed before complete vessel occlusion.

by comparing the patent nonstenosed stent diameter and the diameter of the stenosed segment.

Reinterventions consisted of one or a combination of the following: venoplasty, acute clot removal (thrombolysis), crossing of chronic occlusions, correction of mechanical stent issues, extension of stenting to cover residual disease, and measures to improve inflow. Stent placement and need for additional stenting were evaluated with intravascular ultrasound (Philip Volcano Corp, Amsterdam, Netherlands). We used standard methods for venoplasty and stent placement.¹⁶ Intermittent pneumatic compression was begun from the start of treatment, which is routine for all deep venous interventions at our institution.^{17,18}

During the procedure, a loading dose of unfractionated heparin was administered before predilation or venoplasty. After completion of the procedure, the activated coagulation time was monitored, and therapeutic lowmolecular-weight heparin was administered within 1 hour. This was continued until the transition to oral anticoagulation therapy after a surveillance duplex ultrasound at 2 weeks. Further decisions regarding alterations to the anticoagulation regimen or the duration of anticoagulation were made in conjunction with the hematology department.

After the procedure, duplex ultrasound surveillance was performed on day 1, at 2, 6, 12, and 26 weeks, and then annually. Primary patency was defined as ongoing vessel patency without reintervention. Primary-assisted patency was defined as ongoing vessel patency after reintervention without occlusion, and secondary patency as ongoing patency after reintervention for vessel occlusion. Journal of Vascular Surgery: Venous and Lymphatic Disorders Volume ■, Number ■

Table I. Classification of etiology of restenosis or occlusionafter lysis and stenting for iliofemoral deep vein throm-bosis (DVT)

Failure classification	Etiology
Type 1, technical	
la, No stent	Residual disease
1b, Missed inflow	Inadequate stenting of existing venous lesions; stent not extended distally
1c, Missed outflow	Inadequate stenting of existing venous lesions; stent not extended proximally
ld, Device failure: fracture (F), compression (C), or migration (M)	Stent failure can be subcategorized as F, C, or M
Type 2, flow	Scarring or occlusion of vessels not amenable to stenting—femoral, profunda, or popliteal vein
Type 3, hematologic	
3a, dose-related	Noncompliance or subtherapeutic anticoagulation
3b, non–dose-related	Thrombosis despite anticoagulation
Type 4, multifactorial	Mixed etiology

Assessment of risk factors, reintervention etiology, and outcomes. Retrospective data were analyzed for patient demographics, risk factors, extent of initial and residual thrombus, stent insertion, anatomic coverage, time to reintervention and in stent stenosis, reintervention performed, and procedural success. The hematologic records and biochemical results were examined for the presence of thrombophilia and issues with anticoagulation.

Postprocedural outcomes were measured using the Villalta score for the severity of PTS and surveillance duplex ultrasound scans for assessment of vessel patency. Two independent consultant experts performed a retrospective assessment of the intraprocedural venographic imaging to establish vessel patency (profunda covered or occluded, femoral and popliteal veins occluded or diseased), quality of inflow and outflow, persistence of collateral flow, and the presence of stent issues (fracture or compression).

Failure classification. Following an analysis of the literature and our tertiary center experience, we developed a system for the classification of failure (restenosis or occlusion requiring reintervention) as follows (Table I).

A technical error was classified as a type 1 and included type 1a, inadequate stenting, defined as failure to stent in the presence of residual disease^{12,15}; type 1b, missed inflow, defined as failure to extend the stent distally

across residual disease; type 1c, missed outflow, defined as failure to extend the stent proximally across residual disease¹⁹; and type 1d, defined as device failure secondary to stent fracture, compression, or migration.¹⁹ Type 2 was defined as flow-related, referring to scarring or occlusion of the femoral, profunda, or popliteal veins, which are not amenable to stenting and, thus, limit inflow.²⁰ Type 3 was defined as hematologic and includes type 3a, dose-related, defined as noncompliance, inadequate dosing, or poor international normalized ratio control; and type 3b, failure of anticoagulation, defined as thrombosis despite anticoagulation.²¹⁻²³ Cases for which more than one cause of failure were identified were classified as type 4, multifactorial.

Statistical analysis. The data are presented as the median and range for nonparametric continuous variables and as percentages for categorical data. To assess the significance of the differences between continuous nonparametric variables, the Mann-Whitney U or Kruskal-Wallis test was used. The χ^2 test or the Fisher exact test (for counts of <5) were used for categorical data, with the risk ratios (RRs) and 95% confidence intervals (CIs) presented for significant variables. No adjustments were made for multiple significance testing and P < .05 was deemed statistically significant. Binary logistic regression was conducted to determine the relationship between the need for reintervention and significant variables, using the finalfit and glm R packages (available at: https://finalfit.org) in RStudio,24 with conversion to RRs using the Orsk package, as previously described by Zhang and Yu.²⁵ Assessment of missing data, collinearity, and model fit were performed using the Akaike information criterion, C-statistic, and Hosmer-Lemeshow test.²⁶ The duration of vessel patency was assessed using Kaplan-Meier survival analysis and the log-rank Mantel-Cox test with Prism, version 9.0.0 (GraphPad, San Diego, CA).

RESULTS

A total of 152 limbs were identified, of which 7 were excluded because of unsuccessful lysis and 2 because of an untreated congenital IVC occlusion. Of the remaining 143 limbs (133 patients), 95 (66.4%; 88 patients) remained patent and required no further intervention (Fig 1) and 48 limbs (33.6%; 45 patients) had required reintervention. Of these 48 limbs, 25 (17.4%) had presented with reocclusion, 6 of which were deemed unsuitable for further endovascular treatment. Overall, the median time to reintervention was 45 days (range 5-773 days): 66 days (range, 5-418 days) for reintervention before occlusion and 19 days (range, 6-773 days) for reinterventions occurring in the first 6 weeks.

Analysis of risk factors. Analysis of the patient risk factors revealed that a younger patient age was associated



Fig 1. An example of a good result without stenting to the common femoral vein.

with the need for reintervention (32 vs 46 years; P < .01), with no other systemic risk factors significant. A strong association between the extent of thrombosis at the index treatment, signified by IVC involvement (RR, 2.16; 95% CI, 1.40-3.31; P < .01), profunda occlusion (RR, 2.78; 95% CI, 1.87-4.11; P < .01), or femoral vein occlusion (RR, 3.11; 95% CI, 2.44-3.96; P = .036) and need for reintervention was found. The presence of nonocclusive disease in an otherwise patent femoral or popliteal vessel was not found to have a significant effect (P = NS). A greater reintervention rate was observed for cases requiring a stent across the inguinal ligament (RR, 2.08; 95% Cl, 1.35-3.21; P < .01), with stent fracture or compression occurring in 4 of 32 cases (12.5%). After the procedure, noncompliance with anticoagulation therapy was also associated with reocclusion (RR, 7.09; 95% CI, 2.18-23.04; P < .01; Table II). Among the reintervention cohort, no significant differences were found in the risk factors between the cases treated before and after occlusion.

Binary logistic regression was conducted to determine the relationship between the need for reintervention

Journal of Vascular Surgery: Venous and Lymphatic Disorders 2022

and significant variables (ie, age, IVC involvement, stent across the inguinal ligament, profunda vein occlusion, femoral vein occlusion, and anticoagulation compliance; Supplementary Table, online only). The model was statistically significant $[\chi^2$ (6) = 15.50; P = .05] and explained 46.4% of the variance in reintervention and correctly classified 83.8% of cases. The need for a stent across the inguinal ligament (RR, 2.65; 95% CI, 1.74-3.27; P < .01) and IVC involvement (RR, 2.37; 95% CI, 1.43-3.09; P < .01) significantly increased the likelihood of reintervention. Anticoagulation noncompliance was also shown to significantly increase the odds of reintervention (RR, 3.26; 95% Cl, 2.40-3.46; P < .01). An increase in age was associated with a small decrease in the risk of reintervention per year (RR, 0.97; 95% Cl, 0.94-1.00; P = .046). Although occlusion of the profunda or femoral vein was strongly associated with the need for reintervention, such occlusion did not significantly contribute to the model.

Reintervention: technical success and patient outcome. Overall, 38 of 48 reintervention cases (79.2%) had received venoplasty, with 22 (45.8%) requiring further stenting and 16 (33.3%) requiring further thrombolysis. Successful reintervention was achieved in 31 of 48 cases (64.6%). This was achieved for all cases managed before complete vessel occlusion (before occlusion) but for only 8 of 25 cases (36.4%) after occlusion (RR, 32.31; 95% CI, 2.05-508.36; P < .01). A significant difference in secondary patency at 3 years was observed between reintervention before occlusion (100%) and reintervention after occlusion (19%; P < .001; Fig 2, a).

A greater incidence of any PTS at 1 year was observed among patients requiring reintervention (reintervention: median Villalta score, 3 [interquartile range, 1-5] vs no reintervention: median Villalta score, 1 [interquartile range, 1-4]; RR, 2.28; 95% CI, 1.00-4.75; P = .029; Fig 3). However, this did not translate into a significant increase in moderate to severe PTS (P = .48). In addition, cases with maintained vessel patency (reintervention before occlusion and controls) had had a lower rate of any PTS (14.0% vs 42.9%; RR, 3.06; 95% CI, 1.53-6.12; P < .01) and moderate to severe PTS (3.0% vs 14.3%; RR, 4.76; 95% CI, 1.03-21.98; P = .049) than those receiving reintervention after occlusion.

Validation of classification system. Technical issues were observed in 54.2% of the reintervention cases compared with 6.3% of the cases not requiring reintervention (P < .01; Supplementary Fig 2, online only). Of these, device failure contributed to only four cases (three open cell stents and one closed cell stent), all within earlier years of the study and with recurrence of patient symptoms. Hematologic issues were identified in 33.3% of the reintervention cases, of which 13 of 16 (81%) were dose related compared with 1.1% of cases

Journal of Vascular Surgery: Venous and Lymphatic Disorders Volume ■, Number ■

Table	II. Demographics,	risk factors,	anticoagulation		
compliance, thrombus extent, and procedural factors					

	Reinter			
Characteristic	No	Yes	P value	
Patients	88 (100)	45 (100)	NA	
Age, years	46 (14-80)	32 (16-77)	.003ª	
Symptoms, days	5 (1-28)	5 (1-21)	.743	
Male sex	42 (47.7)	20 (44.4)	.720	
Predisposing factors				
Smoker	22 (25.0)	11 (24.4)	.944	
Cancer	7 (7.95)	1 (2.2)	.265	
Thrombophilia	25 (28.4)	15 (33.3)	.560	
Anticoagulation factors				
Noncompliance	1 (1.14)	9 (20.0)	<.001 ^a	
Extent of thrombus	n = 95 limbs	n = 48 limbs		
Left side DVT	70 (73.7)	37 (77.1)	.69	
Bilateral DVT	10 (10.5)	6 (12.5)	.781	
IVC	12 (12.6)	17 (35.4)	.002ª	
Popliteal	54 (56.8)	29 (60.4)	.722	
Inflow factors				
Profunda covered or occluded	1 (1.1)	6 (12.5)	.006 ^b	
Femoral vein occluded	0 (0)	3 (6.25)	.036 ^b	
Popliteal vein occluded	0 (0)	2 (4.2)	.111	
Stent across inguinal ligament	14 (14.7)	18 (37.5)	.003 ^b	
DVT, Deep vein thrombosis, IVC, inferior vena cava; NA, not applicable. Data presented as number (%) or median (range). ${}^{a}P < .01$.				

 ${}^{b}P < .01.$ ${}^{b}P < .05.$

not requiring reintervention (a single dose-related case; P < .01). Flow-related issues were observed in 43.8%% of the reintervention cases and none of the controls (P < .01; Supplementary Fig 3, online only). Overall, 27.1% of the reintervention cases were multifactorial (Table III). Cases classified as multifactorial in etiology were associated with a lower rate of vessel savage. However, this did not translate into a statistically significant difference in secondary patency on survival analysis (P = .429; Fig 2, *b*).

Temporal analysis of the proportion of cases with technical errors and those requiring reintervention revealed a learning curve. Although an initial increase in technical errors and reinterventions after service expansion was observed for patients treated between 2014 and 2015, this was followed by a consistent decrease in both the proportion of reintervention cases (–6.96%) and technical errors (–21.47%) for patients treated between 2015 and 2017 (Supplementary Fig 4, online only).

DISCUSSION

In the present study, we have reported the etiology and outcomes of reintervention after interventional treatment of acute iliofemoral DVT. Reintervention was required for 33.5% of cases (48 of 143 limbs). Reintervention was successful in all cases managed before complete vessel occlusion had developed, with subsequent maintenance of secondary patency over 3 years and a low incidence of PTS. Comparatively, patients with complete vessel reocclusion (17.4%) were observed to have worse outcomes, with successful reintervention for only 36.4% and a greater incidence and severity of PTS (any PTS, 42.9% vs 14.0% [P < .01]; moderate to severe PTS, 14.3% vs 3.0% [P = .046]). These adverse patient outcomes were likely related to a lack of inflow and increased severity of deep venous fibrosis after multiple episodes of thrombosis.^{4,5} Because no significant differences in the risk factors or the extent of thrombus between patients who had undergone reintervention before and after occlusion were identified, it is possible that these cases might have been preventable with earlier intervention. This highlights the importance of careful duplex ultrasound surveillance.

The classification system proposed and validated in our report-categorizing failure into technical, flow-related, and hematologic issues (Table I)-presents a paradigm for standardized assessment of treatment failure. This system can be used to enable comparable outcome reporting, develop targeted treatment improvement strategies, mitigate operator learning curves, and optimize patient selection and treatment pathways.²⁷ The classification of reintervention cases in the present study revealed that most had resulted from potentially preventable causes, with technical issues observed in 54.2%. This highlights the need for multidisciplinary review, audit, and training during acquisition of technical expertise. Within our center, a learning curve was observed, with a 6.96% decrease in the overall reintervention requirement since 2015 and a 21.47% decrease in technical errors. The reduction in technical errors might have been secondary to an increased use of intravascular ultrasound, enabling greater precision in the assessment of stenosis and stent placement compared with venography; however, clearly, learning plays a role.²⁸ This finding is important in the context of interpreting data from large randomized controlled trials in which the experience of the treating interventionalist could have a bearing on the outcomes.

Within the present study, flow-related issues were observed in 43.8% of the reintervention cases and in none of the controls (P = .0001). The risk factors for reintervention included IVC involvement and stenting across the inguinal ligament—markers of thrombus burden and inflow. Inflow issues have previously been reported as a key factor contributing to stent reocclusion after

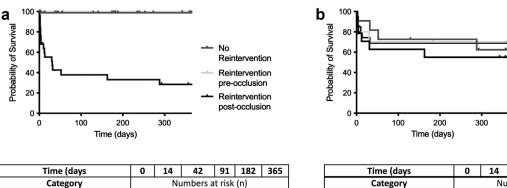
Journal of Vascular Surgery: Venous and Lymphatic Disorders 2022

Technical

Haematological

Multifactorial

Flow



62

20

83 82

23

11 9

78 72

23

9 5

23

92

23

25

23

14

No reintervention

Reintervention pre- occlusion

Reintervention post-occlusion

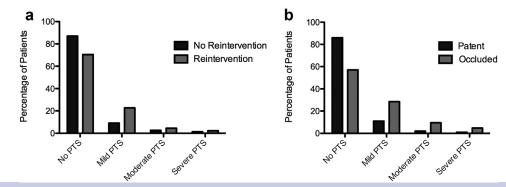
Time (days	0	14	42	91	182	365
Category		Nu	mbers	at risk	(n)	
Technical	20	15	14	14	14	13
Flow	10	9	8	8	8	7
Haematological	11	11	10	9	8	4
Multifactorial	14	10	9	9	8	6

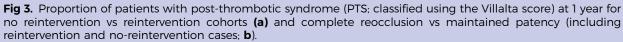
Fig 2. Comparison of secondary patency survival of no reintervention vs reintervention before occlusion vs reintervention after occlusion (**a**) and reintervention cases classified by etiology (technical, flow-related, hematologic, and multifactorial; **b**).

intervention for the treatment of PTS.^{29,30} These results corroborate the importance of the assessment of flow to enable selection of an appropriate treatment strategy.³⁰ This includes dynamic duplex ultrasound assessment of flow before intervention and venographic assessment of flow at the beginning and end of the procedure. In addition, owing to the improvement in the range of dedicated venous stents, with greater radial force and flexibility, it has become more advantageous to stent below the inguinal ligament rather than sacrifice the optimization of inflow.^{10,12} In the present study, device failure contributed to only four cases (three opencell and one closed-cell stent), all within earlier years of the study and with recurrence of patient symptoms.

Appropriate anticoagulation prescription and compliance is essential for maintenance of vessel patency.²⁹ In the setting of acute iliofemoral DVT, this represents a unique challenge owing to heterogeneity in patient age and the etiology of DVT in a cohort of patients most often naive to anticoagulant therapy.⁹ In the present study, noncompliance with anticoagulation was associated with an increased risk of stenosis or reocclusion (RR, 3.26), and 33.3% of reintervention cases were classified as having hematologic issues. This is concordant with literature reporting that >30% of patients were nonadherent with prophylactic anticoagulant therapy.³¹ Improvement in treatment acceptability and, therefore, compliance might be achievable with the prescription of direct oral anticoagulant agents. However, a multidisciplinary team approach with hematologic assessment and consideration of underlying thrombophilia is crucial given the increased risk of rethrombosis associated with direct oral anticoagulant agents in the presence of antiphospholipid syndrome.³²

The present study was limited by its retrospective, nonrandomized design, with a degree of heterogeneity owing to the variation in techniques (ie, catheterdirected thrombolysis, AngioJet), stents used (ie, open cell vs closed cell), and the learning curves for operator expertise. At present, no threshold has been universally





Journal of Vascular Surgery: Venous and Lymphatic Disorders Volume $\blacksquare,$ Number \blacksquare

Table III. Number and proportion of patient limbs stratified by reintervention and failure classification type^a

Category	No reintervention	Reintervention	P value
Technical	6/95 (6.30)	26/48 (54.2)	.0001
Hematologic	1/95 (1.10)	16/48 (33.3)	.0001
Flow	0/95 (0.0)	21/48 (43.8)	.0001
Multifactorial	0/95 (0.0)	13/48 (27.1)	.0001
Technical factors			
No stent	0/95 (0.0)	3/48 (6.3)	.0362
Inflow	3/95 (3.2)	13/48 (27.10)	.0001
Outflow	3/95 (3.2)	6/48 (12.5)	.0608
Device failure	0/95 (0.0)	4/48 (8.3)	.012

Data presented as number/total (%).

^aIdentified on intraprocedural venography at completion of initial treatment; hematologic issues were identified through assessment of patient records and biochemical results.

accepted for reintervention. The standard practice within our institution has been to reintervene for patients with symptom recurrence correlating with a reduction in vessel diameter of >50%, which might represent a more aggressive surveillance approach than practiced elsewhere.

At present, controversy remains regarding the efficacy and cost-effectiveness of thrombolysis and stenting for iliofemoral DVT.³³ Reintervention, or the need thereof, can affect both the clinical outcomes and the longterm cost-effectiveness. Our findings highlight that work should continue to ensure optimization of patient selection, technical accuracy, and postoperative care, with standardized postoperative surveillance protocols and reporting to enable us to accurately assess interventional merit by ensuring we compare effective surgical treatment to effective medical treatment.

CONCLUSIONS

A large proportion of patients required reintervention because of potentially preventable factors. In the present study, we have described and validated a classification system for the assessment of reintervention after deep venous stenting for acute iliofemoral DVT. Understanding and mitigating the learning curve for deep venous intervention could help reduce the reinterventions required as a result of technical concerns, as demonstrated in our study. Anticoagulation compliance, thrombus burden, and poor flow are important risk factors to consider in patient selection and treatment. The need for reintervention and vessel reocclusion increased the risk of PTS. and reintervention was more often successful when performed before complete vessel occlusion. Our results have emphasized the need for three factors to optimize patient outcomes: precision in stenting technique, postprocedural surveillance, and adherence to anticoagulation therapy.

AUTHOR CONTRIBUTIONS

Conception and design: AP, TK, RM, PS, NT, SB Analysis and interpretation: AP, TK, RM, PS, NT, SB Data collection: AP, TK, RM, PS, NT, SB Writing the article: AP, TK, SB Critical revision of the article: AP, TK, RM, PS, NT, SB Final approval of the article: AP, TK, RM, PS, NT, SB Statistical analysis: AP, TK, RM, PS, NT, SB Obtained funding: Not applicable Overall responsibility: SB

REFERENCES

- Kahn SR, Shbaklo H, Lamping DL, Holcroft CA, Shrier I, Miron MJ, et al. Determinants of health-related quality of life during the 2 years following deep vein thrombosis. J Thromb Haemost 2008;6:1105-12.
- Enden T, Haig Y, Kløw NE, Slagsvold CE, Sandvik L, Ghanima W, et al. Long-term outcome after additional catheter-directed thrombolysis versus standard treatment for acute iliofemoral deep vein thrombosis (the CaVenT study): a randomised controlled trial. Lancet 2012;379:31-8.
- Kahn SR, Shapiro S, Wells PS, Rodger MA, Kovacs MJ, Anderson DR, et al. Compression stockings to prevent post-thrombotic syndrome: a randomised placebo-controlled trial. Lancet 2014;383:880-8.
- Comerota AJ, Grewal N, Martinez T, Chen T, Disalle R, Andrews L, et al. Postthrombotic morbidity correlates with residual thrombus following catheter-directed thrombolysis for iliofemoral deep vein thrombosis. J Vasc Surg 2021;55:768-73.
- Broholm R, Sillesen H, Damsgaard MT, Jørgensen M, Just S, Jensen LP, et al. Postthrombotic syndrome and quality of life in patients with iliofemoral venous thrombosis treated with catheterdirected thrombolysis. J Vasc Surg 2011;54(Suppl):18S-25S.
- Enden T, Kløw NE, Sandvik L, Slagsvold CE, Ghanima W, Hafsahl G, et al. Catheter-directed thrombolysis vs. anticoagulant therapy alone in deep vein thrombosis: results of an open randomized, controlled trial reporting on short-term patency. J Thromb Haemost 2009;7: 1268-75.
- Vedantham S, Goldhaber SZ, Julian JA, Kahn SR, Jaff MR, Cohen DJ, et al. Pharmacomechanical catheter-directed thrombolysis for deep-vein thrombosis. N Engl J Med 2017;377:2240-52.
- Comerota AJ, Kearon C, Gu C-S, Julian JA, Coldhaber SZ, Kahn SR, et al. Endovascular thrombus removal for acute iliofemoral deep vein thrombosis. Circulation 2019;139:1162-73.
- Pouncey AL, Gwozdz AM, Johnson OW, Silickas J, Saha P, Thulasidasan N, et al. AngioJet pharmacomechanical thrombectomy and catheter directed thrombolysis vs. catheter directed thrombolysis alone for the treatment of iliofemoral deep vein thrombosis: a single centre retrospective cohort study. Eur J Vasc Endovasc Surg 2020;60:578-85.
- 10. Mahnken AH, Thomson K, de Haan M, O'Sullivan GJ. CIRSE standards of practice guidelines on iliocaval stenting. Cardiovasc Intervent Radiol 2014;37:889-97.
- Mewissen MW, Seabrook GR, Meissner MH, Cynamon J, Labropoulos N, Haughton SH. Catheter-directed thrombolysis for lower extremity deep venous thrombosis: report of a national multicenter registry. Radiology 1999;211:39-49.
- Avgerinos ED, Hager ES, Naddaf A, Dillavou E, Singh M, Chaer RA. Outcomes and predictors of failure of thrombolysis for iliofemoral deep venous thrombosis. J Vasc Surg Venous Lymphat Disord 2015;3: 35-41.
- Razavi MK, Jaff MR, Miller LE. Safety and effectiveness of stent placement for iliofemoral venous outflow obstruction systematic review and meta-analysis. Circ Cardiovasc Interv 2015;8:e002772.
- Notten P, Cate-Hoek AJ, Arnoldussen CWKP, Strijkers RHW, de Smet AAEA, Tick LW, et al. Ultrasound versus anticoagulation for the prevention of post-thrombotic syndrome (CAVA): a single-blind, multicentre, randomised trial. Lancet 2019;7:E40-9.
- Aziz F, Comerota AJ. Quantity of residual thrombus after successful catheter-directed thrombolysis for iliofemoral deep venous thrombosis correlates with recurrence. Eur J Vasc Endovasc Surg 2012;44: 210-3.

8 Pouncey et al

Journal of Vascular Surgery: Venous and Lymphatic Disorders 2022

- Saha P, Karunanithy N, Cohen A, Hunt B, Breen K, Black S. One-year clinical outcomes following deep venous reconstruction using dedicated venous stents. J Vasc Surg Venous Lymphat Disord 2016;4:152.
- Bækgaard N, Broholm R, Just S, Jørgensen M, Jensen LPP. Long-term results using catheter-directed thrombolysis in 103 lower limbs with acute iliofemoral venous thrombosis. Eur J Vasc Endovasc Surg 2009;39:112-7.
- 18. Ogawa T, Hoshino S, Midorikawa H, Sato K. Intermittent pneumatic compression of the foot and calf improves the outcome of catheterdirected thrombolysis using low-dose urokinase in patients with acute proximal venous thrombosis of the leg. J Vasc Surg 2005;42:940-4.
- Raju S, Tackett P, Neglén P. Reinterventions for nonocclusive iliofemoral venous stent malfunctions. J Vasc Surg 2009;49:511-8.
- Grøtta O, Enden T, Sandbæk G, Gjerdalen GF, Slagsvold C, Bay D, et al. Infrainguinal inflow assessment and endovenous stent placement in iliofemoral post-thrombotic obstructions. CVIR Endovasc 2018;1:29.
- Meissner MH, Gloviczki P, Comerota AJ, Dalsing MC, Eklof BG, Gillespie DL, et al. Early thrombus removal strategies for acute deep venous thrombosis: clinical practice guidelines of the Society for Vascular Surgery and the American Venous Forum. J Vasc Surg 2012;55:1449-62.
- 22. Kearon C, Kahn SR, Agnelli G, Goldhaber S, Raskob GE, Comerota AJ. Antithrombotic therapy for venous thromboembolic disease: American College of Chest Physicians evidence-based clinical practice guidelines (8th edition). Chest 2008;133(Suppl 6):454S-545S.
- Trial M, Kang JM, Park K, Ahn S, Cho S, Han A, et al. Rivaroxaban after thrombolysis in acute iliofemoral venous thrombosis: a randomized , open-labeled, multicenter trial. Sci Rep 2019;9:20356.
- RStudio Team. RStudio: Integrated Development Environment for R. RStudio; 2020. Available at: http://www.rstudio.com/. Accessed February 1, 2020.
- 25. Zhang J, Yu KF. What's the relative risk? A method of correcting the odds ratio in cohort studies of common outcomes. JAMA 1998;280:1690-1.

- Harrison E, Pius R. R for Health Data Science, version 1. Chapman & Hall/CRC; 2021. Available at: https://argoshare.is.ed.ac.uk/healthyr_ book/. Accessed January 15, 2021.
- Boney O, Moonesinghe MASR, Myles PS, Grocott MPW. Standardizing endpoints in perioperative research. Can J Anaesth 2016;63: 159-68.
- Montminy ML, Thomasson JD, Tanaka GJ, Lamanilao LM. A comparison between intravascular ultrasound and venography in identifying key parameters essential for iliac vein stenting. J Vasc Surg 2019;7:801-7.
- 29. Sebastian T, Spirk D, Engelberger RP, Dopheide JF, Baumann FA, Barco S, et al. Incidence of stent thrombosis after endovascular treatment of iliofemoral or caval veins in patients with the postthrombotic syndrome. Thromb Haemost 2019;119:2064-73.
- Jalaie H. Interventional treatment of postthrombotic syndrome. Gefässchirurgie 2015;20:490-7.
- Banerjee A, Benedetto V, Gichuru P, Burnell J, Antoniou S, Schilling RJ, et al. Adherence and persistence to direct oral anticoagulants in atrial fibrillation: a population-based study. Heart 2020;106:119-26.
- Pengo V, Denas G, Zoppellaro G, Jose SP, Hoxha A, Ruffatti A, et al. Rivaroxaban vs warfarin in high-risk patients with antiphospholipid syndrome. Blood 2018;132:1365-71.
- Aherne TM, Walsh SR, Sullivan GJO. The ATTRACT trial may seem more attractive than it first looks for the management of acute deep vein thrombosis. Phlebology 2018;34:221-3.

Submitted Dec 28, 2021; accepted Mar 15, 2022.

Additional material for this article may be found online at www.jvsvenous.org.

Journal of Vascular Surgery: Venous and Lymphatic Disorders Volume ∎, Number ∎

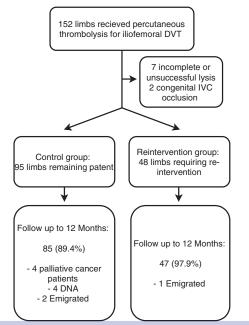
Supplementary Table (online only). Binary logistic regression analysis of risk factors associated with reintervention^a

	Reintervention (limbs)		RR (95% CI); <i>P</i> value		
Variable	No	Yes	Univariable	Multivariable	
Age, years	45.6 ± 15.5	36.7 ± 16.9	0.97 (0.94-0.99); .003	0.97 (0.94-1.00); .046	
IVC thrombus			2.15 (1.39-2.84); .002	2.37 (1.43-3.09); .003	
No	83 (72.8)	31 (27.2)			
Yes	12 (41.4)	17 (58.6)			
Profunda vein occluded			2.77 (1.60-3.21); .018	2.12 (0.63-3.16); .221	
No	94 (69.1)	42 (30.9)			
Yes	1 (14.3)	6 (85.7)			
Femoral vein occluded			3.12 (0-3.12); .990	3.12 (0-3.12); .988	
No	95 (67.9)	45 (32.1)			
Yes	0 (0.0)	3 (100.0)			
Stent below inguinal ligament			2.08 (1.35-2.76); .003	2.65 (1.74-3.27); <.001	
No	81 (73.0)	30 (27.0)			
Yes	14 (43.8)	18 (56.2)			
Anticoagulation noncompliance			3.16 (2.24-3.47); .003	3.26 (2.40-3.46); .002	
No	94 (71.2)	38 (28.8)			
Yes	1 (9.1)	10 ^b (90.9)			

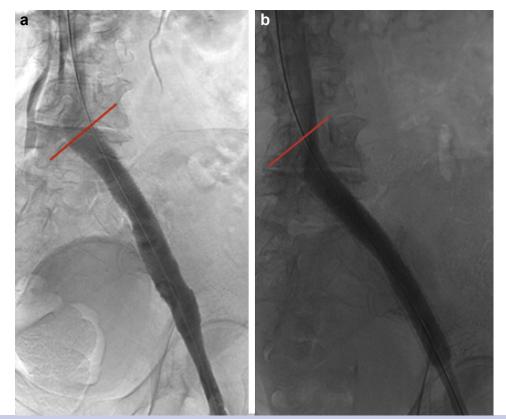
Cl, Confidence interval; IVC, inferior vena cava; RR, risk ratio. ^aNumber in data frame, 143; number in model, 143; missing data, 0; Akaike information criterion, 138.8; C-statistic, 0.838; Hosmer and Lemeshow χ^2 (8); P = .05; Nagelkerke, 0.464. ^bTotal, 10 limbs (9 patients).

8.e2 Pouncey et al

Journal of Vascular Surgery: Venous and Lymphatic Disorders 2022

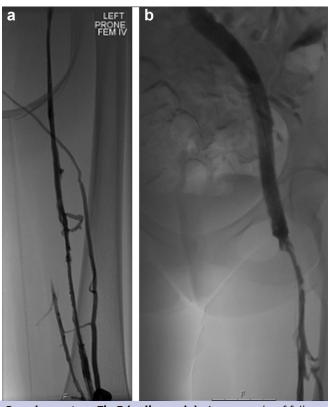


Supplementary Fig 1 (online only). CONSORT (consolidated standards of reporting trials) diagram. *DVT*, Deep vein thrombosis; *IVC*, inferior vena cava.

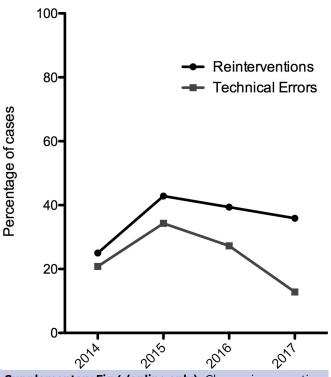


Supplementary Fig 2 (online only). An example of technical failure classification, type lc, missed outflow. **a**, Image showing stent not extended proximally to cover May-Thurner lesion. **b**, Image showing corrective stent extension. Note, crossing of the midline (*red line*) can be used as an indication of appropriate stent extension.

Journal of Vascular Surgery: Venous and Lymphatic Disorders Volume $\blacksquare,$ Number \blacksquare



Supplementary Fig 3 (online only). An example of failure classification type 2, poor flow. **a**, Image before initial placement of iliac stent showing the femoral vein, which looks featureless and has no working valves, with the profunda occluded. The inserted stents became occluded shortly afterward owing to lack of inflow. **b**, Image after thrombolysis showing the profunda vein origin that was open after angioplasty open, with stents now patent for >15 months.



Supplementary Fig 4 (online only). Change in proportion of overall cases requiring reintervention and with identified technical errors over time. A learning curve was demonstrated, with a marked reduction in technical errors after an initial increase associated with service expansion in 2014.