Secondary interventions after iliac vein stenting for chronic proximal venous outflow obstruction

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ABSTRACT

Objective: Iliac vein stent placement is an increasingly common procedure in the treatment of chronic proximal venous outflow obstruction (PVOO), but secondary interventions after vein stent placement remain poorly characterized. Our goal was to identify the incidence, indications, operative findings, and outcomes of secondary interventions after the primary iliac vein stent procedure at a single institution.

Methods: We retrospectively reviewed the clinical history of 490 patients (57.6% female, 42.4% male; mean age, 60.77 years [range, 18-92 years]; 93.28% follow-up, with a mean follow-up of 308.59 days) who underwent iliac vein stent placement for PVOO between October 2013 and January 2016. We evaluated the clinical presentation, intraoperative findings, and outcomes of those patients requiring a secondary intervention after an initial iliac vein stent procedure.

Results: Secondary interventions after an initial stent placement were identified in 50 of 490 patients (10.2%; mean age, 61.54 years [range, 19-92 years]; 58% female [n = 29]). At the time of each individual intervention, 1, 18, 17, 1, and 13 patients had Clinical, Etiology, Anatomy, and Pathophysiology class 2, 3, 4, 5, and 6 disease, respectively. Of these 50 patients, 58% (n = 29) of secondary interventions were due to recurrence of symptoms after the initial stent surgery, 18% (n = 9) were due to the development of new symptoms, and 24% (n = 12) were due to persistence of symptoms. The primary cause of PVOO in the patient cohort was 52% (n = 26) extrinsic iliac vein compression, 28% post-thrombotic, and 20% mixed. Intraoperative findings during the secondary intervention included malposition or angulation of the stent (6% [n = 3]); acute deep venous thrombosis/thrombosis (14% [n = 7]); an additional lesion, that is, stenosis in a native iliac vein proximal or distal to the original lesion (68% [n = 34]); stenosis within the stent, that is, stent stenosis without finding of thrombus or isolated, focal intrastent thrombosis (38% [n = 19]); and impairment of flow of the contralateral vessel from the previously placed stent (6% [n = 3]). The types of secondary interventions included placement of a new stent (86% [n = 43]), isolated balloon angioplasty alone (10% [n = 5]), and catheter pharmacomechanical thrombectomy (14% [n = 7]). Symptomatic improvement was observed after the secondary intervention in 90% of patients (n = 45), whereas only 2% (n = 1) of patients experienced only a transient improvement, and 8% of patients (n = 4) reported no improvement in their symptoms after the secondary interventions.

Conclusions: This study establishes a secondary intervention rate of 10.2% after iliac vein stent placement for chronic PVOO and identifies discrete and definable intraoperative findings as targets for quality improvement. The very good results strongly suggest that an aggressive approach to treatment of these complications is warranted. (J Vasc Surg: Venous and Lym Dis 2019;7:670-6.)

Keywords: Venous insufficiency; Iliac vein stenting; Reintervention; Deep vein thrombosis; May-Thurner syndrome; Venoplasty

The placement of stents in the iliac veins for chronic proximal venous outflow obstruction (PVOO) is increasingly being used in the treatment of venous disease in the lower extremities.[1-3] Whereas generally salutary outcomes have been reported after stent placements in the iliac veins for chronic PVOO,[4-7] very few reports have addressed the complications that may be encountered after a venous stent procedure.[8-12] Characterization of complications specific to venous stents appears incomplete, and the incidence of venous stent complications has not been fully determined. The secondary treatment options are not well described, and the outcomes of these patients who underwent a secondary intervention are unclear. Our experience with venous stents has grown during many years, and we have observed among our venous stent patients discrete types of stent-related complications, different causes of these complications, and various secondary treatment options. We have also observed outcomes of these secondary interventions that seem reproducible. We therefore undertook this preliminary study to begin quantifying

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these complications and characterizing the secondary interventions after placement of venous stents in the iliac veins with the goal of improving the outcomes of venous stent placement.

METHODS

This study was approved by the Institutional Review Board of the Icahn School of Medicine at Mount Sinai and conducted in compliance with the current guidelines of clinical research, as outlined in the Declaration of Helsinki. Informed consent was waived because of the study's low risk and retrospective methodology. The principal investigator (W.T.) and the Icahn School of Medicine at Mount Sinai have an investigator device exemption certificate from the Food and Drug Administration to establish a venous stent registry and to evaluate the outcomes of venous stents.

For this study, we selected only patients who had undergone a major secondary intervention after an initial iliac vein stent placement for chronic PVOO during a 24-month period at our institution. A major secondary intervention is defined as any venography, intravascular ultrasound (IVUS), balloon angioplasty, stent placement, or catheter-based thrombectomy or thrombolysis procedure. Study participants were drawn from a registry of 490 consecutive patients who had undergone vein stent placement for chronic PVOO at the Mount Sinai Hospital. This registry is composed of a retrospective database beginning in October 2013 and has been supplemented with prospective data collection beginning in January 2016. The registry has several categories of information collected from the patients' electronic medical records. The demographic section includes patient name, medical record number, date of birth, date of surgery, age at surgery, sex, and ethnicity. The preoperative data include the clinical scenario of each patient, any deep venous thrombosis (DVT) or pulmonary embolism history, clinical class (Clinical, Etiology, Anatomy, and Pathophysiology classification), and prior history of any superficial venous procedure. Intraoperative data include intraoperative findings of postphlebitic vascular changes, presence of a bilateral or unilateral stent, and number of stents. Postoperative data have outcomes at 30 days, 90 days, 180 days, 1 year, and >1 year. These include any acute DVT, any postoperative reintervention, date of reintervention, minor vs major reoperation, number of days from initial intervention to reoperation, date of last follow-up visit, and additional comments. The medical records, intraoperative venography images, and IVUS images of study patients were individually reviewed.

During the initial venous stent placement, bilateral introducer sheaths were placed in the common femoral veins under ultrasound guidance. Digital subtraction venography was performed with full-strength contrast material, followed by evaluation with IVUS (Visions PV .035; Philips Volcano, San Diego, Calif). The decision for stent placement was guided by a measured reduction in lumen area >50% on IVUS compared with a referenced vessel. Wallstents (Boston Scientific, Marlborough, Mass) of 16-mm and 18-mm diameters and 60-mm or 90-mm lengths, either unilaterally or bilaterally, were placed in the distal inferior vena cava (IVC) and iliac veins guided by the specifics of intraoperative findings. Stent placement was followed by poststent balloon angioplasty using 16-mm or 18-mm balloon catheters when clinically indicated (Charger XXL; Boston Scientific). Procedures were performed in the operating room under intravenous sedation. All patients were discharged on the day of the procedure. Every patient was managed similarly, prescribed postoperative antithrombotic therapy that included a temporary course of rivaroxaban at 10 mg daily followed by long-term aspirin 81 mg daily, except for those patients already receiving anticoagulation or with a sensitivity to one of these medications or when it was declined by the patient. After secondary intervention, all patients were prescribed this anticoagulation and antiplatelet protocol, except those with acute DVT. For these patients, rivaroxaban was given daily at 20 mg, with duration guided by the patient's specific clinical course. Patients were observed postoperatively at 1 month, 3 months, and then every 6 months thereafter with clinical examination and transcutaneous duplex ultrasound. Follow-up data are included in the Table. The decision for reintervention was based primarily on symptoms (eg, persistent symptoms, recurrence of symptoms, or, in a few cases, presentation of new symptoms). Among these patients, venous duplex ultrasound scan was performed to rule out superficial venous disease and DVT. Computed tomography venography or magnetic resonance venography was performed selectively in situations in which physical examination and ultrasound were deemed inadequate.

The secondary interventions were performed in a fashion similar to the initial venous stent procedure.

ARTICLE HIGHLIGHTS

- **Type of Research:** Single-center retrospective cohort study
- **Key Findings:** Of 490 patients who underwent iliac vein stenting, 10.2% had reintervention for persistence, recurrence, or worsening of symptoms. Symptoms improved in 90% of patients who underwent reintervention.
- **Take Home Message:** One of 10 patients needs reintervention after stenting for chronic iliofemoral vein obstruction, and 9 of 10 who undergo reintervention will have symptom improvement. The study identified intraoperative findings as targets for quality improvement.

Table. Clinical characteristics of primary and secondary interventions

Clinical characteristic	
Age, years	62 (±16)
Female	58%
CEAP class at reintervention	
0	0 (0)
1	0 (0)
2	1 (2)
3	18 (36)
4	17 (34)
5	1 (2)
6	13 (26)
Primary intervention	
Unilateral stent placement	36 (72)
Left	29 (58)
Right	7 (14)
Bilateral stent placement	13 (26)
IVC stent placement	1 (2)
Reintervention indication	
Symptom persistence	
Edema only	9 (18)
Ulceration	2 (4)
Pelvic varicosities	1 (2)
Edema of contralateral limb	10 (20)
Symptom recurrence	19 (38)
Edema only	13 (26)
Ulceration	6 (12)
New symptoms	9 (18)
DVT	7 (14)
Reintervention intraoperative findings	
Additional lesion in native vein	34 (68)
In-stent restenosis	19 (38)
Partial stent thrombosis	15 (30)
Acute DVT	7 (14)
Contralateral outflow obstruction	3 (6)
Stent malposition or angulation	3 (6)
Follow-up	
Follow-up time, days	309
Patients lost to follow-up	3 (6)

CEAP, Clinical, Etiology, Anatomy, and Pathophysiology; *DVT*, deep venous thrombosis; *IVC*, inferior vena cava.
Categorical variables are presented as number (%). Continuous variables are presented as mean (standard deviation).

Bilateral introducer sheaths were placed in the common femoral veins or, if indicated clinically, in the femoral veins under ultrasound guidance. Digital subtraction venography and IVUS were used to diagnose any underlying disease. Balloon angioplasty, stent placement, and catheter-based thrombectomy or thrombolysis procedures were performed as clinically indicated.

RESULTS

The vein stent registry at Mount Sinai Hospital was composed of 490 patients who underwent vein stent placement for chronic PVOO at the time of this study. These 490 patients were characterized by a mean age of 60 years (standard deviation, 13.4 years), and 57% were female. Preoperative Clinical, Etiology, Anatomy, and Pathophysiology class for the patient cohort is included in the Table. A history of DVT was present in seven patients. Through the use of venography and IVUS intraoperatively, the cause of PVOO was identified as pure iliac vein compression syndrome in 26 patients, post-thrombotic syndrome in 14 patients, and a combination of iliac vein compression syndrome and post-thrombotic syndrome in 10 patients. Primary interventions included 36 unilateral stent placements (29 left and 7 right), 13 bilateral stents, and 1 stent in the IVC.

Indications for reintervention included 19 patients with recurrence of symptoms, 13 with edema, and 6 who experienced an ulcer recurrence. Ten patients experienced recurrence of symptoms in the contralateral limb after unilateral iliac vein stent placement, and all of these patients received subsequent stent placement in the newly affected limb. Twelve patients experienced persistent symptoms after initial vein stent placement, two of whom had recalcitrant venous stasis ulceration and one with persistent pelvic varicosities. Nine patients suffered from new symptoms, seven of which were DVTs; one patient had severe pain, and one patient had marked edema without evidence of DVT. The mean time to reintervention was 311 days (range, 6-1364 days; standard deviation, ±292.7 days).

Secondary interventions after an initial stent placement were identified in 50 of 490 patients (10.2%; mean age, 61.54 years [range, 19-92 years]; 58% female [n = 29]). Among these 50 patients, 58% (n = 289) of secondary interventions were due to recurrence of symptoms after the initial stent surgery, 18% (n = 9) were due to the development of new symptoms, and 24% (n = 12) were due to persistence of symptoms. Clinical characteristics of the patient cohort can be found in the Table.

Intraoperative findings during the secondary intervention included malposition or angulation of the stent (6% [n = 3]); acute DVT (14% [n = 7]); an additional lesion, that is, stenosis in a native iliac vein proximal or distal to the original lesion (68% [n = 34]); stenosis within the stent, that is, stent stenosis without finding of thrombus or isolated, focal intrastent thrombosis (38% [n = 19]); partial stent thrombosis (30% [n = 15]); and impairment of flow of the contralateral vessel from the previous stent (6% [n = 3]).

The types of secondary intervention included placement of a new stent (86% [n = 43]), isolated balloon angioplasty alone (10% [n = 5]), and catheter pharmacomechanical thrombectomy (14% [n = 7]). A full breakdown of results can be found in the Table.

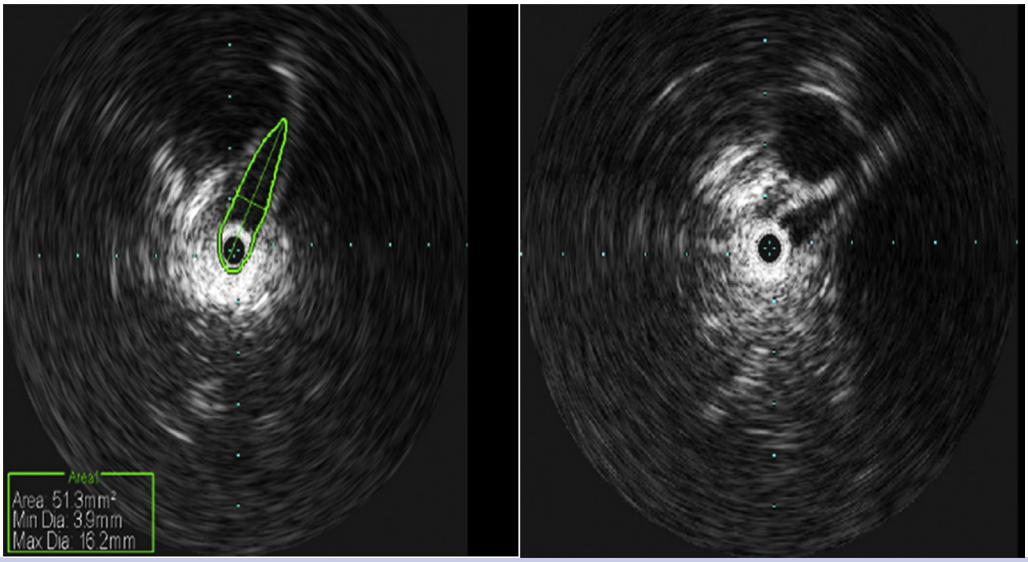

Fig 1. *Left*, Intravascular ultrasound (IVUS) shows a moderate stenosis in the left external iliac vein. *Right*, IVUS shows that the same stenosis has become more severe after placement of a more proximal stent.

Symptomatic improvement was observed after the secondary intervention in 90% of patients (n = 45), whereas only 2% (n = 1) of patients experienced only a transient improvement, and 8% of patients (n = 4) reported no improvement in their symptoms after the secondary interventions.

DISCUSSION

This study establishes that secondary interventions occurred at an incidence of 10% during a 2-year period among a cohort of 490 patients with chronic PVOO who underwent iliac vein stent placement. The incidence of secondary interventions as shown in this study appears accurate as only 7% of our patients have been lost to follow-up, and the mean follow-up of these patients has reached >300 days at the time of this study. This 10% incidence also matches our clinical observation: about 1 in 10 patients after venous stent placement will undergo a secondary intervention within 2 years of the initial procedure.

Patients in this study who underwent a secondary intervention had three distinct clinical presentations. The most common, in approximately 38% (n = 19), was the recurrence of similar symptoms in the same limb that had been stented in the past. Of note, 20% (n = 10) had reinterventions because of symptoms in the contralateral limb. It is unclear whether these patients had worsening symptoms because of an increase in relative stenosis of the untreated limb or whether the improvement of the stented limb led to a greater focus on symptoms of the contralateral leg. In 24% (n = 12), the reintervention was undertaken because of persistent symptoms after the initial venous stent procedure, including two patients with recalcitrant ulceration. In 18% (n = 9) of patients, the patient presented with new symptoms, either in the same extremity or in a previously asymptomatic extremity, and most of these (n = 7) were due to DVT. We found that these different presentations suggest possible causes of the symptoms.

In our experience, symptoms and the severity of symptoms were the most important determinants in the decision of whether to reintervene. Whereas venous duplex ultrasound scan is helpful in ruling out superficial venous disease or DVT as the cause of the presenting symptoms, we found that magnetic resonance venography and computed tomography venography provided less important information than these same scans before the initial venous interventions.

Intraoperatively, venography and IVUS showed several distinct types of pathologic change during these secondary interventions, each warranting a different treatment plan. Among our patients, the most common finding was a new stenosis in the native vein, either distal or proximal to the previous stent. It is difficult to determine whether a new stenosis in the native vein is truly new or whether it is in fact a missed lesion from the initial venous stent procedure. After placement of a proximal stent, we have observed on numerous occasions the appearance of a new stenosis more distally and the transformation of a mild or moderate stenosis to a much more severe one (Fig 1). We suspect that the relief of the distal venous distention after a proximal stent unmasked a pre-existing stenosis as the vessel became unengorged. These observations underscore the importance of completion venography and IVUS after a proximal intervention. A native vein stenosis, new or missed, is best treated with venous stenting.

We have observed several common stent-related findings, including nonocclusive thrombus within the stent, stent angulation due to inadequate overlap of two

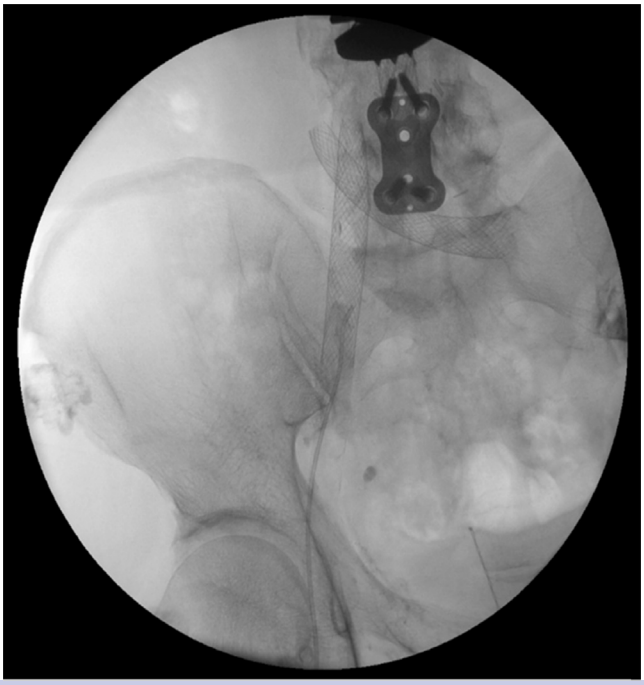

Fig 2. Fluoroscopy shows that both proximal stents are not fully expanded (which, in this case, is more severe on the right side).

stents, and stents that were not fully expanded (Fig 2). Nonocclusive thrombi within the stent and any stents that were not fully expanded were treated with balloon angioplasty. Excessive angulation of two stents was

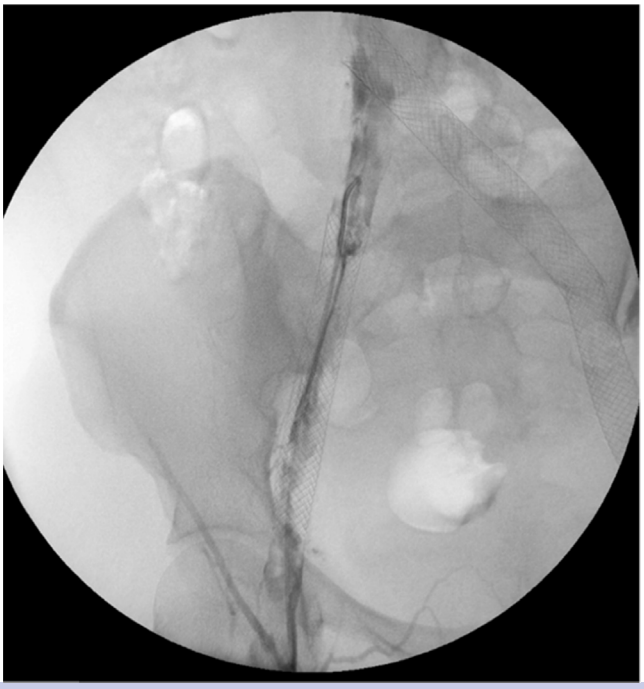

Fig 3. Venogram shows acute stent thrombosis in the right iliac venous stents, probably due to outflow obstruction from the contralateral stent. There is also angulation of the two left iliac stents due to inadequate overlap.

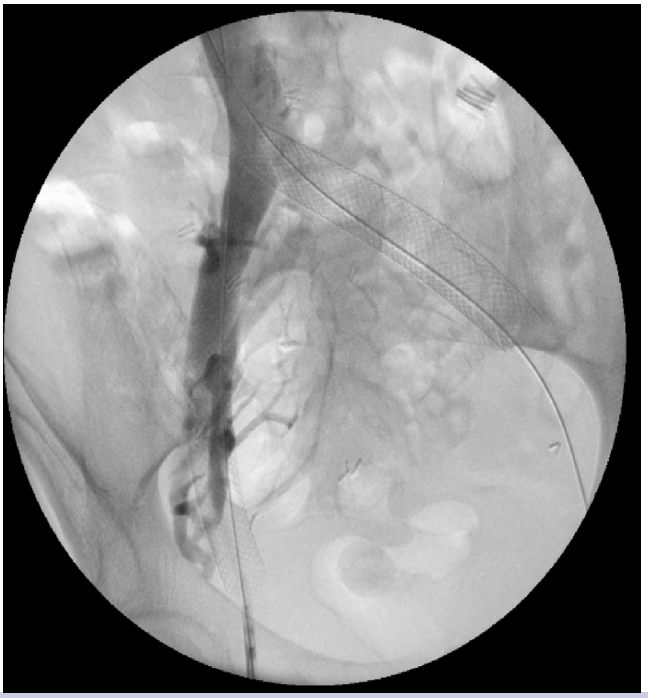

Fig 4. Venogram shows an inferior vena cava (IVC)-left common iliac vein stent, a right external iliac vein stent, and collaterals from the right. With intravascular ultrasound (IVUS) showing no stenosis in the right iliac vein or stent, these findings suggest right iliac outflow obstruction from the left iliac stent.

corrected with the placement of a new stent overlapping the two previous stents.

Acute stent thrombosis was an infrequent complication, occurring in six patients in this study (Fig 3). These patients presented with acute pain or edema. Even though these patients had lower extremity pain and edema in their past medical history, we considered these symptoms novel because of the severity of the pain and the acuteness of the edema. The presentation of acute stent thrombosis bears little resemblance to that of chronic PVOO. The primary goals of intervention are to establish vessel patency and to reduce the thrombus load. This is achieved with catheter-based pharmacomechanical thrombectomy, selective infusion of tissue plasminogen activator during several hours, and balloon angioplasty guided by the specifics of each case. Stent placement is frequently indicated to correct an underlying stenosis that is likely to be the cause of the acute stent thrombosis.

Impairment of outflow from the contralateral iliac vein due to a common iliac venous stent that extended into the distal IVC complicated the clinical course of three patients in this study (Fig 4). The low incidence of this complication suggests that stents extending into the distal IVC, "jailing" the contralateral iliac vein, infrequently result in a complication during the initial few years. This is an interesting finding as May-Thurner syndrome is

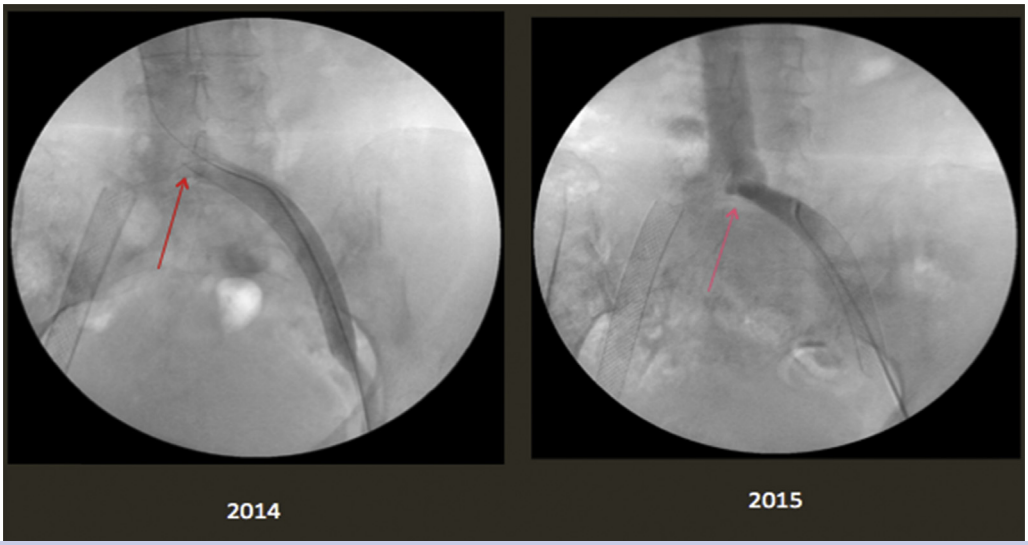

Fig 5. Venogram shows that the inferior vena cava (IVC)-left common iliac vein stent has "melon seeded" distally because of inadequate length of the stent in the IVC.

the most common cause of PVOO, and many stents placed for May-Thurner syndrome potentially jail the contralateral common iliac vein. When impairment of the contralateral iliac vein did occur, these patients presented with new symptoms in a contralateral limb that was previously asymptomatic. The management of this stent complication can be difficult; we have managed this successfully, however, with the delayed transformation of a unilateral iliac venous stent into bilateral iliac kissing stents.

In our study, three stents became malpositioned, but these were not proximal stent migrations to the IVC or the heart. Rather, these phenomena were instead distal stent angulation and malalignments in which the stent "melon seeded" beyond the stenosis (Fig 5). We defined stent migration as any stent movement ≥1.0 cm or any stent movement causing symptoms or requiring reintervention. Stents may foreshorten as they expand in diameter, and this can occur either during balloon dilation immediately after stent deployment or more gradually as the stent expands against the stenosis within the vessel. Because of this variability, the eventual length of some stents is more difficult to determine precisely at deployment. Our technique mandated that the stent be placed at least 2 cm into the distal IVC for a stenosis at the proximal common iliac vein. In addition, we also routinely balloon dilate every stent after placement.

The outcomes of secondary reinterventions have been very good, with >90% of these patients reporting symptomatic improvement. Such outcomes have prompted us to intervene earlier whenever a patient presents with persistent symptoms, recurrent symptoms, or new symptoms.

CONCLUSIONS

Secondary interventions occurred at an incidence of 10% during the first 2 years after the initial venous stent procedure for chronic PVOO. These patients have distinct clinical presentations and several distinct intraoperative findings by venography and IVUS. Treatment options are available for these stent-related complications, and the outcomes after secondary interventions are satisfactory, with 90% of patients reporting symptomatic improvement.

It will be interesting to continue monitoring the secondary interventions of these 490 patients for even longer time intervals. The observed trends and patterns will elucidate the durability of venous stents and the clinical course of patients with chronic PVOO treated with these venous stents.

AUTHOR CONTRIBUTIONS

Conception and design: AA, HS, MM, PF, WT
Analysis and interpretation: AA, JC, JL, WT
Data collection: AA, JC, WT
Writing the article: AA, JC, JL, WT
Critical revision of the article: AA, JC, JL, HS, MM, PF, WT
Final approval of the article: AA, JC, JL, HS, MM, PF, WT
Statistical analysis: Not applicable
Obtained funding: Not applicable
Overall responsibility: WT

REFERENCES

1. Neglen P, Raju S. Balloon dilation and stenting of chronic iliac vein obstruction: technical aspects and early clinical outcome. J Endovasc Ther 2000;7:79-91.

2. Raju S, Owen S, Neglen P. The clinical impact of iliac venous stents in the management of chronic venous insufficiency. J Vasc Surg 2002;35:8-15.
3. Negus D, Fletcher EW, Cockett FB, Thomas ML. Compression and bank formation at the mouth of the left common iliac vein. Br J Surg 1968;55:369-74.
4. Neglen 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;46:979-90.
5. Sharifi M, Javadpoor SA, Bay C, Mehdipour M, Emrani F, Sharifi J. Outcome of stenting in the lower-extremity venous circulation for the treatment of deep venous thrombosis. Vasc Dis Manage 2010;7:e233-9.
6. Raju S, Owen SJ, Neglen P. Recanalization of totally occluded iliac and adjacent venous segments. J Vasc Surg 2002;35:8-15.
7. Raju S, Ward M, Kirk O. A modification of iliac vein stent technique. Ann Vasc Surg 2014;28:1485-92.
8. Heckenkamp J, Gawenda M, Brunkwall J. Vascular restenosis: basic science and clinical implications. J Cardiovasc Surg 2002;43:349-57.
9. Raju S, Tachett P Jr, Neglen P. Reinterventions for non-occlusive iliofemoral venous stent malfunctions. J Vasc Surg 2009;49:511-8.
10. Murphy EH, Johns B, Varney E, Buck W, Jayaraj A, Raju S. Deep venous thrombosis associated with caval extension of iliac stents. J Vasc Surg Venous Lymphat Disord 2017;5:8-17.
11. Neglen P, Raju S. In-stent recurrent stenosis in stents placed in the lower extremity venous outflow tract. J Vasc Surg 2004;39:181-7.
12. Raju S, Johns B, Alias M, Murphy E. Hyperdilatation for iliac vein stent compression and in-stent restenosis. J Vasc Surg Venous Lymphatic Disord 2016;4:138.

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