Contralateral limb improvement after unilateral iliac vein stenting argues against simultaneous bilateral stenting

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ABSTRACT

Objective: Symptoms of chronic venous insufficiency secondary to obstructive iliofemoral disease are often bilateral. The impact of iliofemoral stenting of the more symptomatic lower extremity on clinical outcomes in the less affected contralateral extremity is not clear. Such benefit, secondary to offloading of collaterals, may potentially be of the magnitude that the contralateral extremity does not require intervention.

Methods: A retrospective review of contemporaneously entered electronic medical record data of 368 patients/limbs with initial unilateral iliocaval stents (240 left and 128 right) placed during a 3-year period from 2015 to 2017 was performed. Patients who underwent simultaneous bilateral stenting or had occlusive disease were excluded. Of the remainder, the impact of stenting on contralateral leg symptoms was evaluated by analyzing visual analog scale (VAS) pain score (1-10), grade of swelling (1-3), and Venous Clinical Severity Score (VCSS). The duration of any improvement and need for intervention on the contralateral side were also appraised. Kaplan-Meier analysis was used to assess stent patency after intervention, whereas paired *t*-tests were used to examine clinical outcomes.

Results: Of the 368 limbs that underwent stenting with a combination of a Wallstent (Boston Scientific, Marlborough, Mass) with a Z stent (Cook Medical, Bloomington, Ind) for stenotic lesions, 304 patients (89 men and 215 women) had contralateral symptoms (200 left and 104 right). The cause was post-thrombotic syndrome in 229 limbs and May-Thurner syndrome or nonthrombotic iliac vein lesion in 75 limbs. In this contralateral group, at 12 months, the VAS pain score improved from 5 to 0 ($P < .0001$), the grade of swelling went from 3 to 1 ($P < .0001$), and VCSS went from 5 to 3 ($P < .0001$) after stenting of the ipsilateral side. During the median follow-up of 20 months, 15 contralateral limbs underwent stenting. Median time to stenting of the contralateral limb after ipsilateral stenting was 9 months. The median VAS pain score, grade of swelling, and VCSS in this group before stenting were 6.5, 2, and 5 compared with 0 ($P < .0001$), 1 ($P = .27$), and 3 ($P = .0021$), respectively, in those members of the contralateral group who did not require stenting. Primary and primary assisted patencies at 12 months after contralateral stenting were 78% and 100%, respectively. There were no stent occlusions after contralateral stenting.

Conclusions: Patients with bilateral obstructive iliofemoral venous lesions often experience improvement of the contralateral limb symptoms (95%) after stenting of the worse ipsilateral limb. Only 15 of 304 (5%) symptomatic contralateral limbs had to undergo stenting during the follow-up period because of a worsening clinical picture. Based on this, a staged approach to iliofemoral stenting in patients with bilateral symptoms focusing initially on the more symptomatic limb is suggested. (J Vasc Surg: Venous and Lym Dis 2020;8:565-71.)

Keywords: Iliac vein obstruction; May-Thurner syndrome; Nonthrombotic iliac vein lesion; Iliac vein stenting; Deep venous intervention

There has been an increasing focus on diagnosis and treatment of chronic iliac vein obstruction (CIVO) during the last several years.[1-8] This period has seen the emergence of iliofemoral venous stenting as the first line of treatment of symptomatic CIVO patients. A number of such patients have bilateral disease, often with one extremity more symptomatic than the other. The treatment approach to such patients is not clear, with some practices pursuing simultaneous treatment of bilateral extremities. The role of a staged approach initially stenting the more symptomatic extremity and evaluating the response on the contralateral extremity before stenting of the contralateral extremity is pursued, if needed, has not been explored.

METHODS

Study design. Single-center retrospective analysis of prospectively collected data during a 3-year period from 2015 to 2017 was performed. Patient consent and

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hospital Institutional Review Board approval were obtained for the study.

Setting. The center is a tertiary center for management of venous and lymphatic disorders.

Participants. Patients who underwent unilateral intravascular ultrasound (IVUS) interrogation and iliofemoral venous stenting for CIVO compose the study cohort. Patients who underwent simultaneous bilateral stenting after recanalization for chronic total occlusions or those who underwent stenting after thrombolysis for acute deep venous thrombosis were excluded.

Stenting and follow-up. Patients presenting with disabling symptoms including swelling, pain, hyperpigmentation, and lipodermatosclerosis suggestive of CIVO underwent unilateral IVUS interrogation of the more symptomatic lower extremity to confirm diagnosis before stenting. Stenting used a composite stent configuration of a Wallstent (Boston Scientific, Marlborough, Mass) with a Z stent (Cook Medical, Bloomington, Ind) top. This technique of stenting, stent sizing, and perioperative management have been described in previous publications.[1,9-11] Stent sizes typically ranged from 16 to 20 mm in diameter for the Wallstent and 25 to 30 mm for the Z stent. Antithrombotic therapy was started in the perioperative period and continued for at least 6 months. Currently, such therapy uses a combination of anticoagulation (direct oral anticoagulant or warfarin), cilostazol, and aspirin 81 mg as long as no contraindications exist. Longer term anticoagulation is required in patients with thrombophilia or those who have stent complications (occlusion) after discontinuation of anticoagulation. Aspirin 81 mg is generally continued lifelong. Routine follow-up included duplex ultrasound on day 1 and at 2 and 4 weeks, 3 months, 6 months, and 1 year after intervention and yearly thereafter if patients remained asymptomatic without any evidence of stent malfunction. Clinical assessment was carried out at every follow-up visit starting at 6 weeks.

Measurements. The visual analog scale (VAS) pain score, grade of swelling, and Venous Clinical Severity Score (VCSS) instruments were used at every clinic follow-up to assess the status of the patient. These instruments were used to evaluate both ipsilateral and contralateral limbs.

Contralateral intervention and reintervention. During the course of follow-up, if patients developed disabling symptoms on the contralateral side, they underwent IVUS interrogation and stenting as dictated by IVUS findings. The initial stenting, as noted previously, and subsequent contralateral stenting were performed using a Wallstent-Z stent combination. This composite stent configuration uses a Z stent cap at the top of the Wallstent to provide additional radial resistive force, at the same time preventing jailing of the contralateral side. At the time of contralateral stenting, the Z stent is allowed to flower by cutting the cranial nylon suture after partially unsheathing the stent and resheathing it again, in the process allowing easy interdigitation of the Z stents on both sides (Fig 1). Details of this technique of composite iliac vein stenting have been described previously.[12] In addition, if patients experienced recurrence of symptoms on either the ipsilateral or contralateral side, they underwent repeated IVUS interrogation and correction of the cause of stent malfunction. The causes of stent malfunction included in-stent restenosis, stent compression, combination of in-stent restenosis and stent compression, and stent occlusion.

Statistical analysis. Statistical analysis was performed using SPSS statistics version 24 software (IBM Corp, Armonk, NY). Paired/unpaired *t*-test was used to examine preintervention and postintervention outcomes within and between ipsilateral and contralateral limbs. Kaplan-Meier analysis was used to assess stent patency after intervention. *P* value $<.05$ was considered significant.

ARTICLE HIGHLIGHTS

- **Type of Research:** Single-center, retrospective analysis of prospectively collected data
- **Key Findings:** In 304 patients who underwent initial iliofemoral venous stenting of the more symptomatic side for bilateral chronic iliac vein obstruction, at 12 months there was contralateral improvement in visual analog scale pain score, grade of swelling, and Venous Clinical Severity Score after stenting of the ipsilateral side. During a median follow-up of 20 months, only 15 (5%) contralateral limbs required stenting.
- **Take Home Message:** A staged approach to iliofemoral stenting in patients presenting with bilateral chronic iliac vein obstruction focusing initially on the more symptomatic limb is suggested.

RESULTS

Of the 368 limbs that underwent stenting (Wallstent-Z stent combination) for stenotic lesions, 304 had contralateral symptoms. Mean age of this contralateral group (215 women and 89 men) was 63 years. The contralateral limb was the left in 200 and the right in 104 patients. The cause of symptoms was post-thrombotic syndrome in 229 limbs and nonthrombotic iliac vein lesions in 75 limbs. Preoperative duplex ultrasound revealed that in 234 of 304 patients for whom all the iliofemoral segments (common femoral, external iliac, and common iliac) were visible, 227 (97%) had stenosis in one or more segments. Stenosis was most common and most severe in the common iliac segment, followed by the

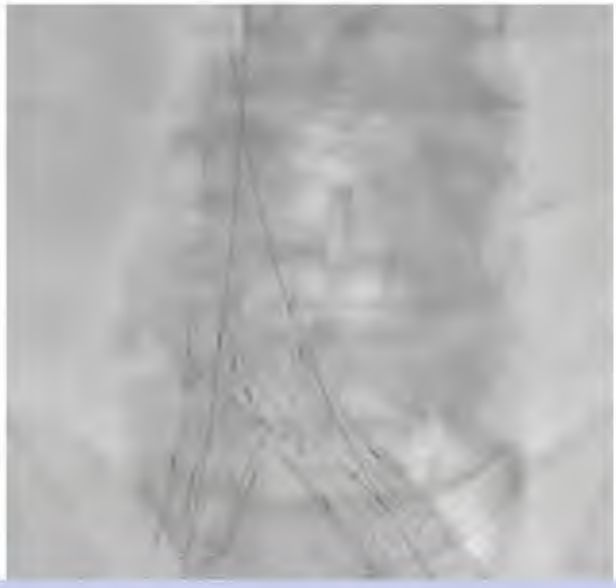

Fig 1. Bilateral iliac vein stenting using a composite (Wallstent-Z stent) stent configuration. Note the interdigitation of the right and left Z stents.

external iliac segment and finally the common femoral segment. Median follow-up in the study was 20 months.

Impact on contralateral side after ipsilateral stenting. In the contralateral group, at 12 months, the VAS pain score improved from 5 to 0 ($P < .0001$), the grade of swelling went from 3 to 1 ($P < .0001$), and VCSS went from 5 to 3 ($P < .0001$) after stenting of the ipsilateral side.

Intervention on the contralateral side. Of the 304 contralateral limbs, 15 required stenting during the follow-up period because of persistent (9/15 [60%]) or worsening (6/15 [40%]) symptoms after initial improvement. The median VAS pain score, grade of swelling, and VCSS in the contralateral limb group before stenting were 6.5, 2, and 5 compared with 0 ($P < .0001$), 1 ($P = .27$), and 3 ($P = .0021$), respectively, in those members of the contralateral group who did not require stenting. Median time to stenting of the contralateral limb after ipsilateral stenting was 9 months.

Clinical outcomes after contralateral stenting. After stenting of the contralateral side, the median VAS pain score, grade of swelling, and VCSS on that side improved to 5, 1, and 4 at 12 months. In addition, on the ipsilateral side, at 24 months, there was no significant difference in VAS pain score, grade of swelling, or VCSS between those who underwent contralateral stenting and those who did not (Table I).

Stent patency after contralateral stenting. Primary and primary assisted patencies at 12 months after contralateral stenting were 78% and 100%, respectively (Fig 2). There were no stent occlusions after contralateral stenting.

Table I. Comparison of clinical findings at 24 months in the ipsilateral limb with and without contralateral stenting

	With contralateral stent (n = 15)	Without contralateral stent (n = 289)	*P* value
Pain	4	3.5	.74
Swelling	1	1	.33
VCSS	4	4	.76

VCSS, Venous Clinical Severity Score.

Clinical characteristics: ipsilateral vs contralateral stenting. Before stenting, there was no difference in the baseline VCSS, VAS score, and grade of swelling between those who underwent just ipsilateral stenting (ipsilateral group) and those who underwent contralateral stenting (contralateral group) as well (Table II). At 12 months after stenting, there was no difference in clinical outcomes of VCSS, VAS score, and grade of swelling between the ipsilateral and contralateral groups (Table III). There was also no statistically significant difference in stent patencies between the groups (Table IV).

DISCUSSION

An overwhelming number of patients undergoing stenting for CIVO in this study had bilateral symptoms (83%). The current paradigm of management of such patients is not well defined. Many practices pursue simultaneous bilateral stenting in patients presenting with symptoms of CIVO in both legs. Whereas bilateral stenting may still be necessary, our study demonstrated that this is the case in only a small fraction of patients presenting with bilateral symptoms. Use of a staged approach focusing initially on the more symptomatic lower extremity helps identify the contralateral limbs with persistent symptoms or worsening symptoms that require stenting.

Contralateral improvement with ipsilateral stenting. Of the 304 patients with bilateral symptoms, only 5% merited stenting of the less symptomatic contralateral side because of worsening clinical condition. This highlights the role of offloading of collateral channels on the contralateral side by virtue of relief of the more severe ipsilateral obstruction (Fig 3). This is of importance because only 9 of 315 (3%) contralateral limbs did not experience improvement and went on to require contralateral stenting as well. Another 6 of 15 experienced worsening after initial improvement, probably because of progressive worsening of obstruction overcoming the benefit from offloading of collaterals. This resulted in a total of 15 patients (5%) who required contralateral limb stenting.

Outcomes after contralateral stenting. Clinical improvement was noted in the contralateral limbs after stenting. In addition, for the 15 limbs that underwent

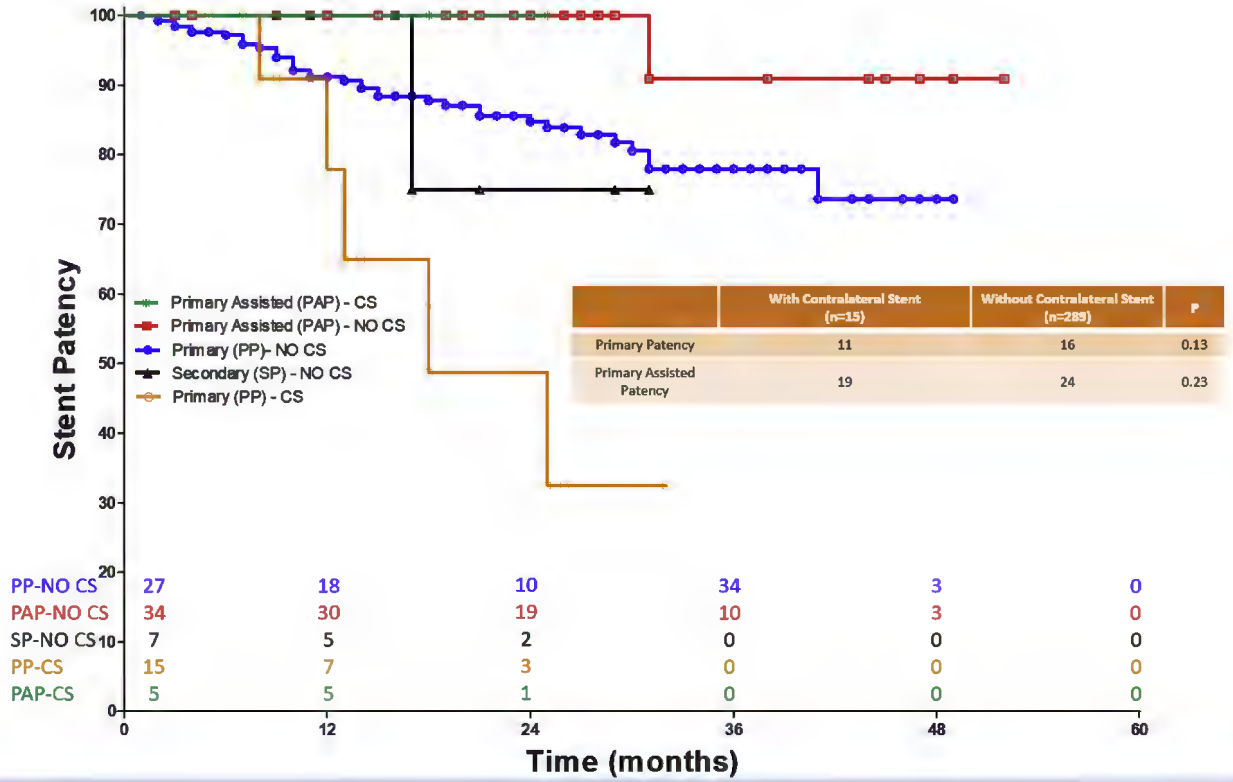

Fig 2. Patencies after ipsilateral and contralateral stent placement. *CS,* Contralateral stenting; *PAP,* primary assisted patency; *PP,* primary patency; *SP,* secondary patency.

Table II. Baseline clinical parameters before stenting of patients who underwent contralateral stenting as well vs those patients who underwent just ipsilateral stenting

	Contralateral group (n = 15)	Ipsilateral group (n = 289)	*P* value
Pain	6	5	.30
Swelling	2	3	.59
VCSS	5	5	.97

VCSS, Venous Clinical Severity Score.

Table III. Comparison of clinical findings at 12 months after stenting between the ipsilateral limb and the contralateral limb

	With contralateral stent (n = 15)	Without contralateral stent (n = 289)	*P* value
Pain	5	6	.56
Swelling	1	1.5	.30
VCSS	4	4	.58

VCSS, Venous Clinical Severity Score.

contralateral stenting, such stenting did not adversely affect clinical or stent-related outcomes on the ipsilateral side. From a stent perspective, good patencies were noted after both ipsilateral and contralateral stenting.

Table IV. Stent patencies of the contralateral stent vs the ipsilateral stent

	With contralateral stent (n = 15), months (range)	Without contralateral stent (n = 289), months (range)	*P* value
Primary patency	11 (1-32)	16 (0-49)	.13
Primary assisted patency	6 (4-10)	10.5 (0-45)	.40

Another finding we noted was that use of the Wallstent-Z stent combination appears to result in decreased incidence of contralateral stenting compared with use of the Wallstent alone. The Wallstent has a contralateral stent rate of 13%.[13] This decreased requirement of contralateral stenting from use of a composite stent configuration (Wallstent-Z stent) is likely to be a result of the lack of need of significant stent extension into the cava that is required with use of Wallstents alone. This can potentially lead to partial or complete contralateral jailing and subsequent symptom development.

Technique of contralateral stenting. For the 5% of patients who required bilateral stenting, as noted previously, contralateral stenting occurred about 9 months after ipsilateral stenting. The stent configuration that

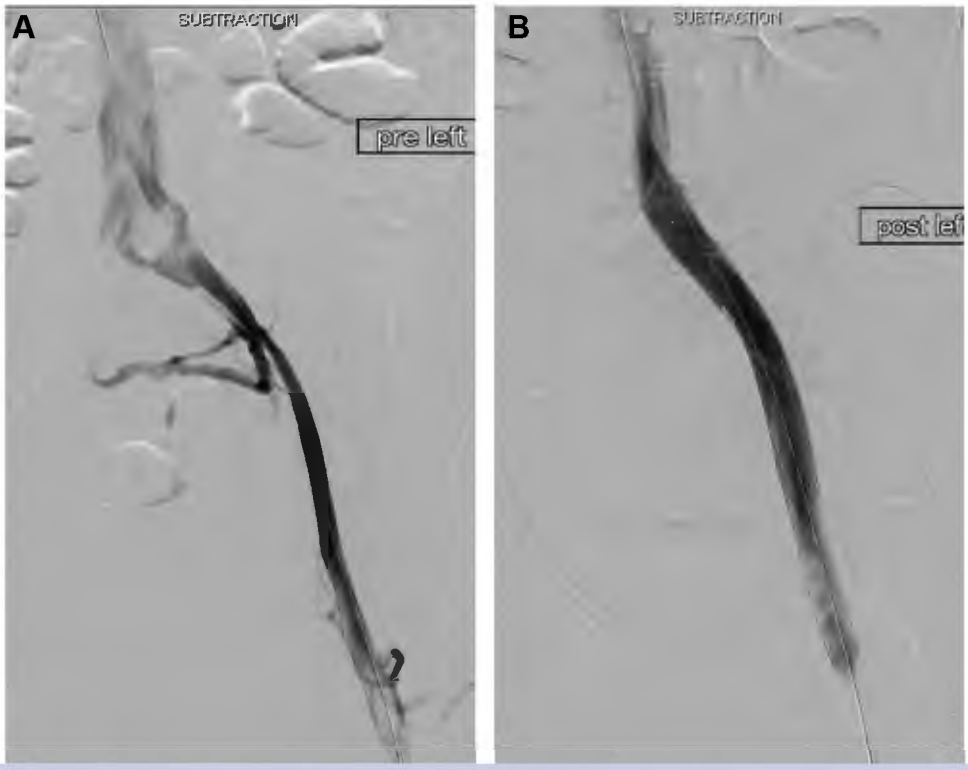

Fig 3. Venogram before **(A)** and after **(B)** stenting demonstrates the disappearance of collateral cross-pelvic channels (that cause overloading) after stenting.

we have found to work best is the Wallstent-Z stent combination (Fig 4). Use of other techniques, including double barrel (Fig 5), inverted Y fenestration (Fig 6), and apposition (Fig 7), is fraught with problems. The double-barrel stenting, when it is performed in a staged manner, results in luminal compromise of the more recently placed stent from extrinsic compression. In addition, endothelialization of the stents occurred both within and outside, resulting in reduction of luminal area. As we know from Poiseuille's equation, flow is related to the fourth power of the radius.

$$\text{Flow (F)} = \frac{\text{Pressure gradient } (\Delta P)}{\text{Resistance (R)}}$$

$$F = \frac{\Delta p \Pi r^4}{8 L \eta}$$

where L is length of vein, η is viscosity of blood, and r is radius of vein.

Given that flow is related to r^4, one 24-mm stent allows eight times as much flow as two 12-mm-diameter double-barreled stents. Adding endothelialization, which has more of an impact with two stents as opposed to one, the flow advantage for a single stent increases even further. These reasons make the double-barrel technique a not so favorable option.

Inverted Y fenestration is a bilateral stent technique used when the previously placed Wallstent covers the contralateral outflow tract. It works by creation of a fenestra through the jailed stent and then stenting through the fenestra (Fig 6). Recent data have shown that the risk of contralateral deep venous thrombosis with jailing can be as high as 10%.[14] This represents a problematic way to stent the confluence to begin with. In addition, unpublished data from our practice noted a higher reintervention rate after inverted Y fenestra confluence stenting. Jailing of the contralateral limb outflow should therefore be avoided to begin with. The apposition technique has the same problems as the inverted Y because the outflow channel is still jailed by the ipsilateral stent with the additional concern for further progression of disease in the unstented portion of the common iliac vein leading up to the confluence. In light of this, the best technique of bilateral stenting is the use of a Wallstent-Z stent combination to construct the iliocaval confluence (Fig 1). In our practice, simultaneous bilateral iliofemoral venous stenting is pursued only in the setting of bilateral recanalization procedures for chronic total occlusions.

Fig 4. Composite femoroiliocaval venous stenting with Wallstent-Z stent combination. The Z stent acts as a top and provides additional chronic outward force across the iliocaval choke point.

Fig 5. Double-barrel stent configuration across the iliocaval confluence. In this patient, the right stent extends beyond the left stent.

Fig 6. Creation of a left to right fenestra with balloon angioplasty of the interstice after wire access across and subsequent stenting (Wallstent-Z stent combination) through that fenestra.

Suggested protocol. Based on these findings, we suggest a protocol of stenting of the worse limb initially, reserving contralateral stenting for those limbs that continue to remain symptomatic or worsen over time after initial improvement.

Limitations of the study include its inherent retrospective nature and relatively short median follow-up time of 20 months.

CONCLUSIONS

Patients with bilateral obstructive iliofemoral venous lesions often experience improvement of the contralateral limb symptoms (95%) after stenting of the worse ipsilateral limb. Only 5% of symptomatic contralateral limbs had to undergo stenting during the follow-up period because of a worsening clinical picture. This represents an improvement (from 13%) compared with use

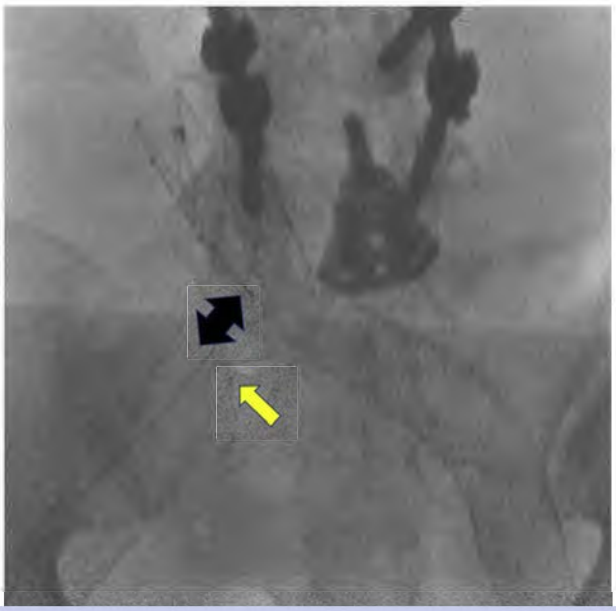

Fig 7. Apposition stenting with a gap (*black arrow*) between the end of the common iliac vein stent on the right (*yellow arrow*) and the left Wallstent that has jailed the right iliac vein outflow. If progression of disease occurs in this gap, it will require conversion to an inverted Y fenestra. This patient had a Z stent placed after apposition stenting many years ago to fix stent compression on the left side.

of Wallstents alone. Based on this, a staged approach to iliofemoral stenting in patients with bilateral symptoms focusing initially on the more symptomatic limb is suggested.

AUTHOR CONTRIBUTIONS

Conception and design: AJ, SR
Analysis and interpretation: AJ, CN, SR
Data collection: AJ, CN
Writing the article: AJ, CN, SR
Critical revision of the article: AJ, SR
Final approval of the article: AJ, CN, SR
Statistical analysis: CN
Obtained funding: Not applicable
Overall responsibility: AJ

REFERENCES

1. 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.
2. Knipp BS, Ferguson E, Williams DM, Dasika NJ, Cwikiel W, Henke PK, et al. Factors associated with outcome after interventional treatment of symptomatic iliac vein compression syndrome. J Vasc Surg 2007;46:743-9.
3. Hartung O, Loundou AD, Barthelemy P, Arnoux D, Boufi M, Alimi YS. Endovascular management of chronic disabling ilio-caval obstructive lesions: long-term results. Eur J Vasc Endovasc Surg 2009;38:118-24.
4. Kolbel T, Lindh M, Akesson M, Wasselius J, Gottsater A, Ivancev K. Chronic iliac vein occlusion: midterm results of endovascular recanalization. J Endovasc Ther 2009;16:483-91.
5. Raju S, Neglen P. Percutaneous recanalization of total occlusions of the iliac vein. J Vasc Surg 2009;50:360-8.
6. Rosales A, Sandbaek G, Jorgensen JJ. Stenting for chronic post-thrombotic vena cava and iliofemoral venous occlusions: mid-term patency and clinical outcome. Eur J Vasc Endovasc Surg 2010;40:234-40.
7. Meng QY, Li XQ, Qian AM, Sang HF, Rong JJ, Zhu LW. Endovascular treatment of iliac vein compression syndrome. Chin Med J 2011;124:3281-4.
8. Ye K, Lu X, Li W, Huang Y, Huang X, Lu M, et al. Long-term outcomes of stent placement for symptomatic non-thrombotic iliac vein compression lesions in chronic venous disease. J Vasc Interv Radiol 2012;23:497-502.
9. Raju S, Buck WJ, Crim W, Jayaraj A. Optimal sizing of iliac vein stents. Phlebology 2018;33:451-7.
10. Jayaraj A, Buck W, Knight A, Johns B, Raju S. Impact of degree of stenosis in May-Thurner syndrome on iliac vein stenting. J Vasc Surg Venous Lymphat Disord 2019;7:195-202.
11. Jayaraj A, Crim W, Knight A, Raju S. Characteristics and outcomes of stent occlusion after iliocaval stenting. J Vasc Surg Venous Lymphat Disord 2019;7:56-64.
12. Raju S, Ward M Jr, Kirk O. A modification of iliac vein stent technique. Ann Vasc Surg 2014;28:1485-92.
13. Neglen P, Darcey R, Olivier J, Raju S. Bilateral stenting at the iliocaval confluence. J Vasc Surg 2010;51:1457-66.
14. 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.

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