

# The efficacy of stenting in the iliofemoral vein of patients with venous obstruction and secondary lymphedema from malignancy

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## ABSTRACT

**Objective:** To investigate the safety and effectiveness of venous stenting in patients with chronic iliofemoral venous obstruction and secondary lymphedema from malignancy.

**Methods:** From July 2012 to December 2020, patients with iliofemoral venous obstruction and secondary lymphedema who underwent venous stenting in our institution were reviewed retrospectively. Clinical characteristics, surgical complications, and symptom relief were assessed. Stent patency was evaluated with duplex ultrasound or computed tomographic venography. Twelve-month outcomes were reported.

**Results:** Fifty-three patients with concurrent secondary lymphedema who had stents placed for iliofemoral venous obstruction were included. There were 42 females, and the mean age was 56.9 years. Nonthrombotic iliac vein lesions were identified in 16 patients (30.1%). Immediate technical success was 100%, with an average of two stents implanted. The median Villalta score, and Chronic Venous Disease Quality of Life quality of life questionnaire scores decreased from 12 (IQR, 10-15) and 58 (IQR, 50-66) at baseline, respectively, to 5 (interquartile range [IQR], 4-6) and 28 (IQR, 22-45) at 12 months after the procedure ( $P < .05$ ), showing significant improvement in the quality of life. At the end of a median follow-up of 12 months (range, 3-25 months), the cumulative primary, assisted primary, and secondary patency rates were 70.8%, 76.9%, and 90.1%, respectively.

**Conclusions:** In patients with secondary lymphedema from malignancy, venous stent placement is safe and effective for iliofemoral venous obstruction. (*J Vasc Surg Venous Lymphat Disord* 2023;11:626-33.)

**Keywords:** Venous stent; Ilio-femoral venous obstruction; Secondary lymphedema

Chronic venous obstruction is a common condition that impacts a person's ability to perform daily activities and has a clinical manifestation of edema, heaviness, and skin abnormalities in the lower limbs. Post-thrombotic syndrome (PTS) and nonthrombotic iliac vein lesions (NIVLs) have attracted substantial attention in recent years and are the most frequent causes of chronic iliofemoral venous obstruction. PTS is an unfortunate consequence of acute deep venous thrombosis, and NIVLs are indicative of the nonthrombotic state of the iliac vein compressed by the vertebra and iliac artery, which is Cockett's or May-Thurner syndrome. Patients

with asymptomatic NIVLs do not require stenting. However, symptomatic patients with lymphedema and NIVLs may benefit from the relief of venous hypertension. According to the current literature, endovenous stent implantation has proven to be a viable method of revascularizing iliofemoral venous obstruction in patients with failed conservative treatment.<sup>1</sup> Previous studies have shown that stenting for obstructive venous lesions is safe and effective, with a high patency rate at the 5-year follow-up.<sup>2,3</sup>

Secondary lymphedema of the lower extremities is the excess accumulation of interstitial fluid, which is usually a consequence of cancer-related treatment, such as lymph node dissection and radiotherapy. Similar to symptoms of venous obstruction, secondary lymphatic dysfunction could also result in lower limb swelling, heaviness, and skin changes.<sup>4</sup> Chronic iliofemoral venous obstruction may be present in patients with secondary lymphedema, which is difficult to differentiate on physical examination alone. Leaving venous lesions unresolved, lymphaticovenular anastomosis for lymphedema is not adequate to improve the quality of life in patients with iliofemoral venous obstruction concomitant with secondary lymphedema. To date, there are few studies on the efficacy of stent

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implantation in the iliofemoral vein of patients with venous obstruction and lymphatic impairment. The purpose of this study was to investigate retrospectively the outcome of stent placement in the iliofemoral vein in patients with secondary lymphedema from malignancy.

## METHODS

**Patient selection.** The Institutional Review Board (IRB) reviewed the study protocol and waived informed consent. Patients who underwent stent implantation for chronic iliofemoral venous obstruction in our vascular center between July 2012 and December 2020 were reviewed. Patients at our institution were admitted to decrease edema and heaviness in their lower extremities. Only those patients who concurrently developed lymphedema secondary to cancer treatment (radiotherapy or lymph node dissection) were eligible for our study. Patients with a life expectancy of less than one year, acute venous thrombosis, lesions of the inferior vena cava requiring stent implantation, previous surgical or endovascular intervention in the target vessel, poor venous inflow, or sepsis were excluded. Overall, 332 patients with venous stent implantation were reviewed for eligibility. Patients lost to follow-up or who met the exclusion criteria were excluded. Finally, 53 consecutive patients with secondary lymphedema and chronic iliofemoral venous obstruction were included in the cohort study. The medical records were examined to collect demographic data, procedure details, and surgical complications. Nucleotide lymphangiography was performed to confirm lymphedema. Duplex ultrasound (DUS) examination was performed to screen for iliofemoral venous stenosis of more than 50% after a Valsalva maneuver. Computed tomography venography (CTV) was used to determine the characteristics of the disease. Disease severity can be objectively categorized on the Clinical, Etiology, Anatomy, Pathophysiology (CEAP) classification.

Stenting is indicated for symptomatic patients who are refractory to compression therapy (a Villalta score of >4), iliofemoral vein stenosis of greater than 50%, and extensive formation of collateral veins. PTS and NIVLs comprise the majority of lesions that are treated with iliofemoral vein stenting.

Patients with secondary lymphedema developed symptoms, such as pain, discomfort, or heaviness of the lower limbs, which were similar to venous dysfunction. A definitive diagnosis of secondary lymphedema was based on factors including clinical manifestations, history of pelvic malignancy-related treatment and positive lymphoscintigram. A lymphoscintigram was performed by subcutaneous injection of  $^{99}\text{Tc}^{\text{m}}$ -dextran between the first and second toes. The progression of  $^{99}\text{Tc}^{\text{m}}$ -dextran was monitored by gamma camera imaging at 10 minutes, 20 minutes, 40 minutes, 1 hour, and 2 hours after injection. The diagnosis of lymphedema based on

## ARTICLE HIGHLIGHTS

- **Type of Research:** Single-center retrospective cohort study
- **Key Findings:** A total of 53 patients who had chronic iliofemoral venous obstruction and secondary lymphedema from malignancy underwent stent placement. A good stent patency and symptom relief were found at the 12-month follow-up.
- **Take Home Message:** In patients with secondary lymphedema from malignancy, venous stent placement is safe and effective for iliofemoral venous obstruction.

lymphoscintigram is determined with at least one parameter, including delay in transit time, dermal backflow, a decreased number of visible lymph nodes, the presence of collateral circulation, and visibility of popliteal lymph nodes. Lymphedema is usually classified into three stages according to the International Society of Lymphology.<sup>5</sup> Stage I is a condition in which early accumulation of fluid subsides with limb elevation. Tissue swelling and pitting were not decreased with limb elevation in patients with stage II disease. Trophic skin changes develop in stage III disease. The demographic data are listed in [Table I](#). Most patients were initially prescribed compression treatment for at least 3 months before the venous intervention.

**Endovascular procedure.** All procedures were performed by vascular surgeons with 10 years of experience managing patients with iliofemoral venous obstruction in our hybrid operation room (GE Medical Systems, Chicago, IL). In the supine position, the patient was under local anesthesia. For occlusion of the common iliac vein (CIV) and the upper segment of the external iliac vein (EIV), an ipsilateral femoral vein (or mid-thigh femoral vein) puncture approach was preferred, whereas an ipsilateral popliteal approach was recommended for occlusions involving the inferior segment of the EIC, the common femoral vein (CFV), and the femoral vein. The right jugular vein or the contralateral femoral vein access was needed if single antegrade cannulation was not accessible during the entire procedure. Venous access was performed via ultrasound-guided percutaneous puncture. All patients were injected with 100 IU/kg heparin intravenously after venous catheterization was performed successfully.

Multiplanar venography of the iliofemoral vein was performed to determine the lesion characteristics. An antegrade revascularization approach was usually attempted initially with different kinds of hydrophilic guidewires in our institution. The other vascular approach would be required to pass through the occluded vein from

**Table I.** Baseline data of patients

Demographics	Mean $\pm$ SD, No. (%), or median (IQR)
Age, years	56.9 $\pm$ 10.1
Women	40 (75.5)
BMI, cm/kg <sup>2</sup>	25.1 $\pm$ 3.1
Hypertension	10 (18.9)
Heart disease	8 (15.1)
Diabetes	8 (15.1)
Smoking	7 (13.2)
CEAP	
C2	9 (16.9)
C3	21 (39.6)
C4a	8 (15.1)
C4b	12 (22.6)
C5	1 (1.9)
C6	2 (3.7)
Villalta score	12 (10-15)
CIVIQ-20	58 (50-66)
Radiotherapy history	12 (22.6)
Left leg lesion	48 (90.6)
Lymphedema stage	
I	25 (47.1)
II	20 (37.7)
III	8 (15.1)
Etiology of lymphedema	
Ovarian cancer	18 (33.9)
Cervical cancer	21 (39.6)
Prostate cancer	5 (9.4)
Bladder cancer	4 (7.5)
Other malignancy	5 (9.4) <sup>a</sup>

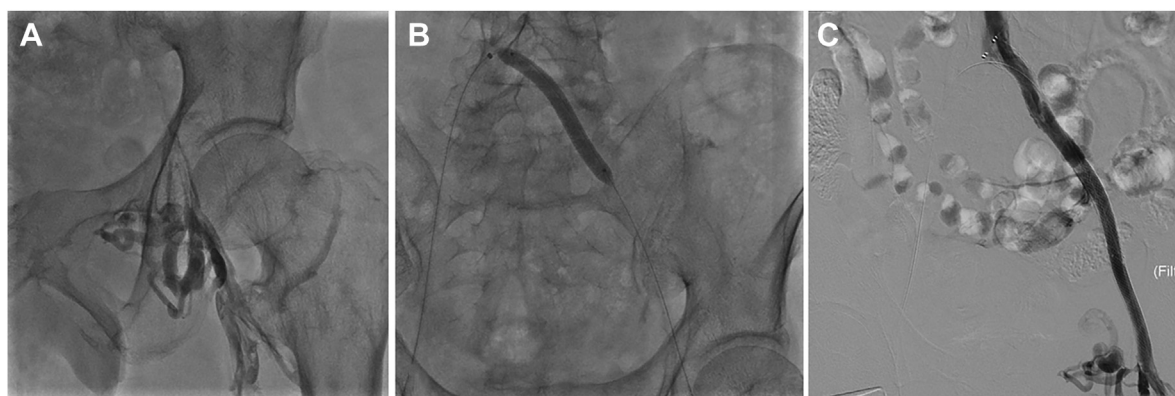
CEAP, Clinical Etiologic Anatomic Pathophysiologic; CIVIQ, Chronic Venous Insufficiency Questionnaire; IQR, interquartile range; SD, standard deviation.  
<sup>a</sup>Other cancers included penile, testicular, retroperitoneal liposarcoma, and metastatic of unknown primary origin.

different directions (antegrade and retrograde) if one single access was difficult to establish. The percutaneous venous procedure was performed one month later when the guidewire failed to pass through the occluded lesion with vascular perforation. Because of the low venous pressure and dense fibrous cover over chronic total occlusion lesions, free hemorrhage is rare. Once the entire chronic total occlusion lesion was passed through, proper reentry into the lumen of the inferior vena cava was confirmed by venography. Gradual predilation with balloons was performed during angioplasty to establish the guidewire pathway. Stenting the entire lesion in continuity with landing sites of the normal segment is essential, although the distal stent end should remain above the orifice of the deep femoral vein to guarantee adequate inflow if extension below the inguinal

ligament into the common femoral vein is needed. Iliocaval confluence was marked with a bilateral iliac venogram, and an extension of the iliac stent of at least 1 cm into the inferior vena cava was needed but did not touch the contralateral vessel wall. We often use a 10- to 16-mm self-expanding stent based on the diameter of the contralateral or the adjacent normal segment. Wallstents (Boston Scientific, Natick MA) are usually deployed in EIV and CFV, and E-Luminexx stents (Bard Peripheral Vascular, Inc, Tempe, AZ) are fit for CIV. Postdilation was performed after stent deployment (Fig 1). After the procedure, the puncture points were closed with ProGlide (Abbott, Chicago, IL) or compressed manually until hemostasis was achieved. Compression stockings and permanent oral anticoagulation were recommended after venous stent placement in all patients.

**Follow-up and outcomes.** All patients were required to complete follow-up visits at 1, 3, 6, and 12 months of follow-up and then annually. At each visit, patients returned to undergo DUS imaging, CTV, physical examination, assessment of lymphedema classification, and to complete the disease-specific questionnaire. Moreover, Villalta and CIVIQ-20 scores were calculated based on preoperative data. Calf circumference was measured at 10 cm below the tibial tuberosity. The primary outcome of the study was primary patency at the 1-year follow-up. The secondary outcomes included the Villalta score, CIVIQ-20, edema relief with lymphedema classification, calf circumference and primary-assisted and secondary patency. Procedural complications included minor and major adverse events based on the Society of Interventional Radiology standards.<sup>6</sup> Primary patency was the target vessel that maintained patency without any additional procedure. Primary assisted patency was defined as patency after treatment for restenosis, and secondary patency was defined as overall patency after restenosis or occlusion. In-stent restenosis was defined as an occlusion or 50% stenosis on DUS imaging, CTV, or venography. Reintervention was reserved for patients with recurrent symptoms and stenosis of the target vessel on DUS imaging or CTV. Early in-stent thrombosis was defined as thrombosis within 1 month after stent placement.

**Statistical analyses.** Continuous variables are presented as the mean  $\pm$  standard deviation (SD) or median (with interquartile range [IQR]), and categorical data are presented as frequencies and percentages. The Villalta and CIVIQ-20 scores from baseline to postoperative scores were analyzed using the Wilcoxon paired rank test. An analysis of the association between baseline variables and primary patency was conducted using logistic regression. Cumulative primary, assisted primary, and secondary patency rates were calculated using the Kaplan-Meier survival curve method. For all data, a *P*



**Fig 1.** Endovascular recanalization for PTS in a 56-year-old male patient. **A**, Venography shows the occlusion of the iliofemoral vein and the appearance of collateral veins. **B**, Successfully retrograde crossing the occlusive lesion from contralateral femoral vein access after the failure of antegrade crossing; through-and-through access is created via loop snare over the guidewire and retrieval from the popliteal vein; revascularization and balloon dilation in the iliofemoral vein, then two stents were placed. **C**, Final venography shows stent patency and disappear of collateral veins.

value of less than .05 was recognized as statistically significant, and SPSS version 25.0 (IBM Corp., Armonk, NY) was used for statistical analysis.

## RESULTS

**Baseline patient data.** Fifty-three patients had a venous stent placed to treat iliofemoral venous occlusive disease. The average patient age was 56.9 years, 42 (75.5%) were female, and most patients were C3 (39.6%) and C4 (37.7%) according to the CEAP classification (Table 1). Nine patients with C2 were included because of severe symptoms, such as heaviness, cramps, pain, or itching, and the requirement for subsequent lymphaticovenular anastomosis. The gender-specific nature of ovarian and cervical cancer (70.9%) resulted in a predominance of women in our study. The median baseline score of the patients was 12 (IQR, 10-15) in Villalta and 58 (IQR, 50-66) in CIVIQ-20. All patients had secondary lymphedema of the lower extremities. Surgical treatment of cervical (39.6%) or ovarian cancer (33.9%) was the common etiology of secondary lymphedema in our study. All patients developed obvious edema, and no patients had stage 0 lymphedema. Stage I lymphedema was most common, occurring in 25 patients (47.1%). Twenty-two patients (37.7%) had stage II lesions, and stage III lesions were present in 8 patients (15.1%). It was more severe in patients with stage III disease, with a median Villalta score of 17.5 and CIVIQ-20 score of 67. The baseline circumference of leg was  $39.5 \pm 4.1$  cm. Five patients with bilateral lymphedema secondary to cancer treatment received compression treatment or lymphaticovenular anastomosis for the contralateral limb.

**Lesion characteristics and procedural data.** Angiographic and procedural details are listed in Table 2. Forty-nine patients (92.4%) underwent endovascular

surgery under local anesthesia. Femoral vein access is usually used in treating iliac venous lesions, and the popliteal vein access site is chosen when the distal EIV and CFV are involved. Thirty-five patients had a history of deep vein thrombosis. Two patients have a venous obstruction owing to compression of lymph nodes. Six patients (11.3%) were implanted with retrievable filters (Denali, Bard Peripheral Vascular, Inc., Tempe, AZ) through the contralateral femoral vein before the crossing of the obstructive lesion; all filters were removed within 3 months. With the previous failure of attempts, the current attempt of recanalization succeeded in five patients. Of 12 patients with a history of radiotherapy, 8 patients were NIVLs, and 4 patients developed PTS. A median of two stents were placed in patients with CIV, EIV, and CIV involvement. Wallstents accounted for 22.5% of 82 stents, and the rest were E-Luminexx stents. For a venous segment with 40% residual stenosis, a repeat stent was placed in one patient to correct stent collapse because of obvious radial force, despite adequate predilation of the venous wall. Five patients developed CFV occlusion and received stenting for obtaining inflow from the femoris vein. Eight of the 53 patients (15.1%) complained of lower back pain after iliac venous stent implantation, which disappeared within four weeks. No minor or major complications immediately occurred. After the procedure, 41 of the 53 patients (77.3%) were prescribed rivaroxaban, and the remaining patients took warfarin for anticoagulation. All patients received concurrent compression therapy.

**Clinical outcomes.** The Villalta score significantly decreased from baseline compared with 12 months after the procedure (12 [IQR, 10-15] and 5 [IQR, 4-6]), respectively;  $P = .013$ ). Similarly, CIVIQ-20 scores at 12 months were significantly lower than pre-stent levels (58 [IQR, 50-

**Table II.** Angiographic and procedural details

Variables	Total (n = 53)
Involved vessel	
CIV only	15 (28.3)
CIV and EIV	16 (30.1)
EIV only	2 (3.7)
EIV and CFV	4 (7.5)
CIV, EIV, and CFV	17 (32.1)
NIVLs	16 (30.1)
Total occlusion	32 (60.3)
Post-thrombotic stenosis	5 (9.4)
Filter deployment	6 (11.3)
Coagulation regime	
Warfarin	12 (22.6)
Rivaroxaban	41 (77.3)
Access site	
Femoral	33 (62.2)
Popliteal	17 (32.1)
Jugular <sup>a</sup>	3 (5.6)
Stent length, mm	127.4. (60-200)
Technical success	53 (100)
Follow-up	12 (3-25)

CFV, Common femoral vein; CIV, common iliac vein; EIV, external iliac vein; NIVL, nonthrombotic iliac vein lesions; PTS, post-thrombotic syndrome.  
Values are number (%) or mean (range).  
<sup>a</sup>Jugular access was used in addition to one other access site (femoral or popliteal).

66] and 28 [IQR, 22-45], respectively;  $P < .001$ ) (Fig. 2). The mean postoperative circumference was  $36.9 \pm 4.3$  cm. According to the circumference measurement, patients in stage I and II decreased significantly (stage I,  $37.0 \pm 2.2$  cm to  $34.0 \pm 1.6$  cm; stage II,  $39.6 \pm 2.3$  cm to  $37.0 \pm 1.5$  cm;  $P < .01$ ), whereas patients in stage III did not have significant change ( $46.8 \pm 1.9$  cm to  $45.7 \pm 1.8$  cm;  $P > .05$ ). However, clinical outcomes improved differently based on the classification of secondary lymphedema (Table III). In patients with stage I lesions at baseline, 20 of 25 patients (80%) improved to stage 0. Twelve of 20 patients (60%) with stage II lesions had at least one stage of improvement. All the patients in stage III did not improve according to the lymphedema classification. One of the 25 patients (4%) patient in stage I, 3 of 20 patients (15%) in stage II, and 6 of 8 patients (75%) in stage III underwent liposuction and lymphaticovenular anastomosis during follow-up. Among 16 patients with NIVLs, 11 patients with stage I and 4 patients with stage II had improvement. However, one patient with stage III lymphedema did not improve their stage.

**Stent patency.** The median follow-up was 12 months (range, 3-25 months). The cumulative primary, assisted primary, and secondary patency rates were 70.8%, 76.9%, and 90.1%, respectively (Fig 3). The primary patency of 16

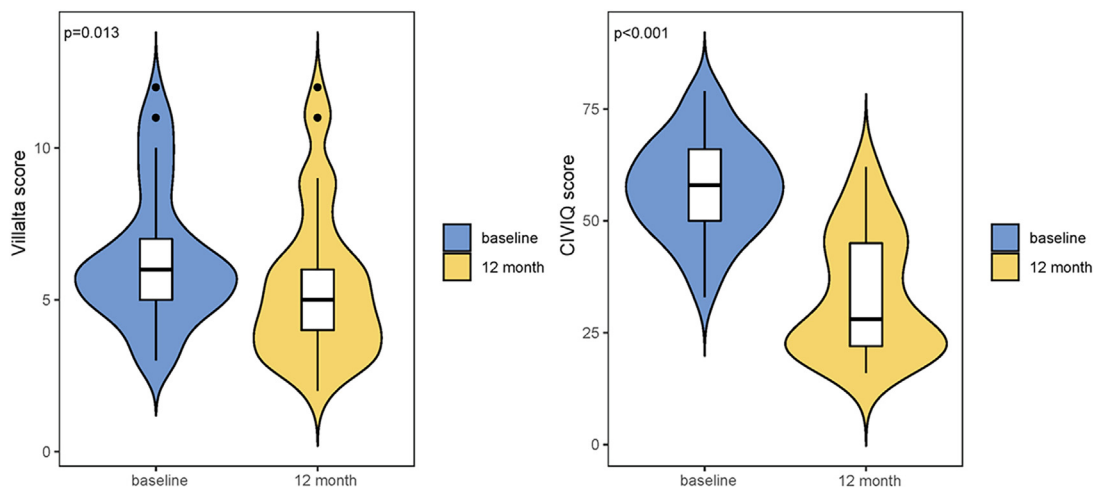
patients with NIVLs is 100% at 12 months. Thirteen patients underwent reintervention during follow-up. The median time to loss of primary patency was 5 months (range, 1-11 months). Four of these 13 patients had a pre-existing coagulation disorder. One patient had early in-stent thrombosis, which was treated with AngioJet pharmacomechanical thrombectomy (Boston Scientific, Marlborough, MA) and stent placement. In-stent restenosis developed in eight patients. Among them, two patients (3.7%;  $n = 2/53$ ) were observed to have stent fractures on venography at the inguinal ligament during follow-up, which were overcome by angioplasty and relining with an E-Luminexx stent. Four patients developed recurrent chronic occlusion. Among them, two patients with occluded stents compressed or invaded by tumors had failed reintervention and were treated with elastic compression stockings without clinical deterioration during the follow-up period. No stent migrations were observed. Two patients died owing to tumor progression and other reasons not related to the stenting procedure.

Multiple logistic regression was conducted to analyze the relationship between different variables and primary patency. Stent extending to CFV (95% CI, 0.051-0.75;  $P = .02$ ), lesions involving the CIV, EIV, and CFV (95% CI, 0.044-0.65;  $P = .01$ ) and thrombophilia (95% CI, 0.032-0.92;  $P = .04$ ) were significantly related to stent patency. The stage of lymphedema, CEAP classification, and anticoagulation regimen were not associated significantly with primary patency at 12 months.

## DISCUSSION

Secondary lymphedema is congestion of lymphatic vessels, usually resulting from surgery, radiotherapy, parasites, and cellulitis. Especially in patients with cancer, secondary lymphedema of the lower extremities is a common complication after lymphadenectomy and/or radiotherapy. In the literature, it is estimated that 20% to 50% of patients with cancer develop secondary lymphedema.<sup>7</sup> Therefore, leg swelling in patients with cancer is often diagnosed as lymphedema; however, venous dysfunction is a common cause that is under-recognized often. Research on the ideal treatment for patients with venous obstruction and concomitant lymphatic dysfunction is rare. In the present retrospective study, we investigated the patency and clinical outcomes of stent placement in patients with chronic iliofemoral venous obstruction and secondary lymphedema.

Vein drainage and normal lymphatic function play important roles in balancing interstitial fluid volume. Because of the mutual interdependence between the two systems, one system will overload if the other system fails to drain the fluid normally. Fluid accumulation in the interstitial space resulting from venous outflow obstruction and venous hypertension also results in



**Fig 2.** The improvement of all patients in the Villalta and Chronic Venous Insufficiency Questionnaire (CIVIQ) scores at 12 months compared with baseline.

secondary lymphatic damage, which is known as phlebolymphe-  
dema.<sup>8-10</sup> In patients with chronic venous disease, 20% will also have secondary lymphatic damage from fluid overload.<sup>11</sup> Phlebolymphe-  
dema, rather than cancer, was the predominant cause in a large cohort study, accounting for 41.8% of cases of lymphedema in the lower extremity.<sup>12</sup> Thus, phlebolymphe-  
dema will negatively affect the appearance and condition of previ-  
ously abnormal lymphatics after cancer surgery, radiation, recurrent infection, and traumas. It has been proposed that venous stenting can contribute to the clinical relief of patients with phlebolymphe-  
dema.<sup>13,14</sup> In clinical practice, the early stage of lymphedema may be difficult to distinguish from venous disorders on physical examination alone. In addition to the abnormal DUS findings, a history of deep vein thrombosis, the appearance of varicose veins, and skin pigmentation are distinguishable characteristics in differential diagnoses.<sup>4</sup> There are usually a few patients with bilateral lymphedema after surgery of pelvic malignancy. And The occurrence of unilateral lymphedema was probably related to the specific boundaries of lymph node dissection.

We primarily focused on venous obstructive lesions in conditions such as PTS and NIVLs, and tumor compression in the iliofemoral segment, which are recommended for interventional treatment in the literature.<sup>15</sup> Venous stenting for the iliofemoral vein can achieve a high, long-term patency rate of 100% in nonthrombotic disease and 86% in thrombotic disease at a 5-year follow-up.<sup>16</sup> In our series, the primary patency of 16 patients with NIVLs was 100% at 12 months. Most patients with symptomatic NIVLs and concomitant secondary lymphedema from malignancy, improved their stage of lymphedema after stenting. In a registered, prospective study, the primary patency rate of endovenous stent placement for patients with symptomatic iliofemoral venous was 84.0% at the 1-year follow-up.<sup>17</sup> Similarly, the cumulative primary and secondary patency rates in our study were 70.8% and 90.1%, respectively, at the 12-month follow-up. Our analysis shows that lymphedema probably does not have a negative effect on stent patency.

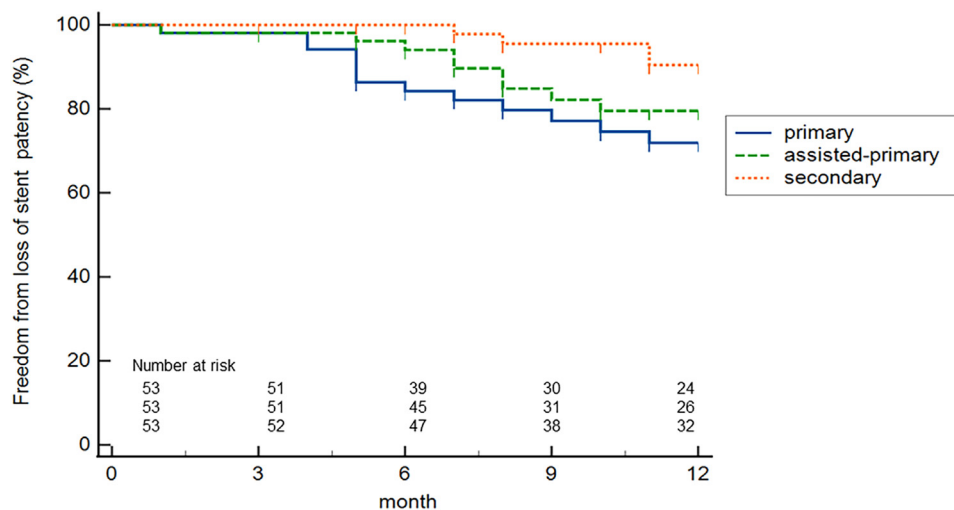
A retrievable inferior vena cava filter was prophylactically inserted in six patients owing to personal experience of the unfortunate encounter of pulmonary embolism during dilation after recanalization. However, prophylactic inferior vena cava filter placement was not recommended. Routine anticoagulation is prescribed perioperatively because endothelial injury develops in the process of balloon dilation and stenting. In the literature, most studies postoperatively administered anticoagulation for 2 to 6 months, followed by aspirin indefinitely.<sup>18</sup> Prolonged anticoagulation is usually given to patients with complicated iliofemoral vein occlusion and PTS, and patients with a known thrombophilia require lifelong anticoagulation.<sup>19</sup>

The department of lymphatic surgery in our hospital is a tertiary referral center that provides comprehensive treatment for lymphatic disorders. At present, the

**Table III.** The Villalta and CIVIQ score at baseline and the 12-month follow-up

	Stage I	Stage II	Stage III
Baseline Villalta	10 (8.5-11.5)	12 (10-16)	17.5 (11-20)
Baseline CIVIQ	50 (45-59)	63.5 (55-67)	67 (57-78)
12-Month Villalta	3 (3-4)	5.5 (5-6)	10 (9-11)
12-Month CIVIQ	22 (19-23)	34.5 (32-45)	54 (50-61)
P Villalta	<.001	<.001	.002
P CIVIQ	<.001	<.001	.017

CIVIQ, Chronic Venous Insufficiency Questionnaire. Values are median (interquartile range).



**Fig 3.** Cumulative primary, assisted primary, and secondary patency rates in all stented limbs. The patient number at the various follow-up intervals is shown at the bottom of the graph. The standard error of the mean was less than 10%.

treatment of secondary lymphedema is divided into conservative treatment, such as compression with elastic stockings, bandages, and pneumatic compression devices, and surgical treatment, such as lymphatic anastomosis, liposuction, and lymph node transfer.<sup>20</sup> Lymphaticovenular anastomosis is a preferred therapy used to avoid the long-term effects of secondary lymphedema, but normal venous function is an important prerequisite. If iliofemoral venous obstruction coexisted in patients with secondary lymphedema, endovascular treatment with stenting was the first step. When venous hypertension is effectively treated after venous stenting, the lymphatic disorder can be cured from the decrease in interstitial fluid volume.<sup>13</sup> According to lymphedema classification, 80% of patients in our study downstaged from stage I to stage 0, and 60% of patients with stage II downstaged to stage I. The Villalta and CIVIQ-20 scores at 12 months indicated significant clinical relief. Ultimately, 86% of patients with secondary lymphedema are spared from surgical treatment. Therefore, most patients could benefit from the treatment of venous obstruction. However, in the subgroup analysis, we found that all cases of grade III lymphedema did not improve according to the lymphedema classification, even after venous hypertension was resolved, and six patients (75%) still underwent liposuction and lymphaticovenular anastomosis. Chronic inflammation and severe fibrosis contribute to the thickness of the limb, rather than simple tissue interstitial fluid accumulation in stage III lymphedema.

Lymphedema-related symptoms, such as heaviness, swelling, pain, and discomfort of the limb, are similar to those of venous hypertension. Despite the revascularization of the iliofemoral vein, lymphedema-related symptoms still have an obvious influence on daily activity.

Although only five patients underwent postoperative lymphoscintigram when seeking lymphatic surgery, we did not find the improvement of lymphoscintigram as Raju et al discovered, in four patients.<sup>13</sup> The primary cause of this difference was that lymphatic dysfunction was induced by venous hypertension in Raju's series, whereas cancer surgery and venous hypertension both contributed to lymphatic damage in our series. In the current study, leg edema results from venous obstruction, phlebolymphe-  
dema, and post-cancer treatment. Patients will benefit from the correction of venous obstruction and phlebolymphe-  
dema with venous stenting. Lymphatic damage induced by the post-cancer treatment may not recover with stenting. It is difficult to determine the actual proportion of phlebolymphe-  
dema and post-cancer treatment. However, the outcome of our study shows that patients with early stages of lymphedema secondary to malignancy can benefit from the treatment of venous outflow obstruction alone.

There are some limitations to our study. First, classifying lymphatic disorders is challenging in that edema can be complicated with venous obstruction and cancer treatment-related lymphedema. Meanwhile, we did not get enough lymphoscintigram staging detail and post-operative lymphoscintigram did not undergo during follow-up. Second, a long-term follow-up could not be achieved because most patients developed malignant tumors. Third, the Villalta score is not suitable for evaluating the severity of illness owing to the high incidence of NIVLs.

## CONCLUSIONS

Good outcomes can be expected in terms of stent patency at 1 year after venous stenting for patients with

iliofemoral venous obstruction and secondary lymphedema. Patients with secondary lymphedema can benefit from clinical improvements when treated in the early stage.

### AUTHOR CONTRIBUTIONS

Conception and design: XLU

Analysis and interpretation: XLI

Data collection: XLI, ZW, ZJ, LN, HZ, YF, CZ, FZ

Writing the article: XLI, ZW, ZJ

Critical revision of the article: LN, HZ, YF, CZ, FZ, XLU

Final approval of the article: XLI, ZW, ZJ, LN, HZ, YF, CZ, FZ, XLU

Statistical analysis: Not applicable

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Overall responsibility: XLU

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