Editors' Choice

Inguinal intranodal lymphangiography reveals a high incidence of suprainguinal lymphatic disease in patients with leg edema undergoing stenting for symptomatic chronic iliofemoral venous obstruction

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ABSTRACT

Objective: Recent studies have emphasized the important role lymphatics play in the drainage of interstitial fluid and edema prevention. Although the infrainguinal lymphatics have been studied in some depth, with patterns of pathology identified, such data above the groin are sparse, especially for patients with phlebolymphedema. The present study attempts to evaluate the status of lymphatic flow above the inguinal ligament in patients presenting with edema and undergoing stenting for symptomatic chronic iliofemoral venous obstruction (CIVO).

Methods: A total of 31 lower limbs that underwent pedal lymphoscintigraphy for leg edema and subsequent stenting for symptomatic CIVO formed the study cohort. Each limb underwent intranodal lymphangiography of an ipsilateral inferior inguinal lymph node (10 mL of lipiodol) at the time of stenting. Fluoroscopic visualization of lipiodol transit was performed at 20, 40, and 60 minutes and 3 hours after injection. Enumeration of the lymph nodes and lymphatic collector vessels from above the inguinal ligament to L1, visualization of the thoracic duct, the time delay to visualization of the thoracic duct, and pathologic changes to the thoracic duct when present were all evaluated. These anomalies were independently scored, with the scores combined to generate a total suprainguinal score (range, 0-3). This score was then compared to the limb's lymphoscintigraphically derived infrainguinal score (total infrainguinal score range, 0-3) using the *t* test and Spearman correlation. The clinical outcomes (grade of swelling, venous clinical severity score) after stenting were appraised.

Results: Of the 30 patients (31 limbs), 18 were women, with left laterality noted in 23 limbs. A nonthrombotic iliac vein lesion occurred in 9 limbs and post-thrombotic syndrome in 22 limbs. Of the 31 limbs, 24 (77%) had suprainguinal lymphatic disease (SLD), with 22 of the 24 limbs having severe SLD and 2, mild SLD. When SLD was compared with infrainguinal lymphatic disease, 6 limbs (19%) had the same degree of involvement above and below the groin (1 with normal and 5 with severe disease), 17 limbs (55%) had more severe SLD, and 8 limbs (26%) had more severe infrainguinal lymphatic disease. Three limbs with normal pedal lymphoscintigraphic findings had severe SLD. The Spearman correlation coefficient for the comparison of SLD and infrainguinal disease in the same limb was 0.1 ($P = .69$). At baseline, the limbs with severe SLD had the same degree of leg swelling and venous clinical severity score as the limbs with absent to mild SLD ($P > .1$) with similar improvements after stenting ($P > .4$). Seven limbs underwent complex decongestive therapy (all with severe SLD and concomitant severe infrainguinal disease in one) to treat significant residual leg edema, with improvement.

Conclusions: SLD appears to be common in patients with leg edema undergoing stenting for symptomatic CIVO. Such disease appears to affect the thoracic duct more commonly. Although patients with persistent or residual leg edema after stenting can benefit from complex decongestive therapy, further workup in the form of inguinal intranodal lymphangiography and targeted intervention might need to be considered for those who do not benefit from such therapy. Further study is warranted. (J Vasc Surg Venous Lymphat Disord 2023;11:1192-201.)

Keywords: Phlebolymphedema; Chronic iliofemoral venous obstruction; Lymphangiogram; Lymphoscintigram; Post thrombotic syndrome; May Thurner syndrome

One of the most common causes of lymphedema in western populations is lymphedema secondary to chronic venous insufficiency: phlebolymphedema.[1] Neglen et al[2] and Raju et al[3,4] have demonstrated that of patients with phlebolymphedema associated with chronic iliofemoral venous obstruction (CIVO), 62% can realize partial or complete relief of edema and 73% can experience improvement or

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normalization of lymphoscintigraphic findings. Thus, a definite and sizeable percentage of patients will continue to have quality-of-life impairing symptoms of phlebolymphedema even after stenting for CIVO. In such patients, suprainguinal lymphatic pathology could be a contributing factor. We used inguinal intranodal lymphangiography to evaluate the presence of suprainguinal lymphatic pathology in patients undergoing stenting for CIVO.

ARTICLE HIGHLIGHTS

- **Type of Research:** A single-center, prospective cohort study
- **Key Findings:** In patients with leg edema undergoing stenting for symptomatic chronic iliofemoral venous obstruction, inguinal intranodal lymphangiography revealed that 77% had suprainguinal lymphatic disease (SLD), with most (92%) having severe disease. When SLD was compared to infrainguinal lymphatic disease, 6 limbs (19%) had the same degree of involvement above and below the groin (1 with normal findings and 5 with severe disease), 17 limbs (55%) had more severe SLD, and 8 (26%) had more severe infrainguinal lymphatic disease.
- **Take Home Message:** SLD is a common finding in patients with leg edema undergoing stenting for chronic iliofemoral venous obstruction, and these patients might require further workup in the form of inguinal intranodal lymphangiography and targeted intervention for patients for whom stenting and complex decongestive therapy fail.

METHODS

Study design. We performed a single-center, single-arm, prospective study with patients enrolled from August 2019 to July 2021. The 30 included patients provided written informed consent for all diagnostic tests and procedures. The Franciscan Missionaries of Our Lady University institutional review board approved the study with dissemination of de-identified patient data.

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

Participants. Patients with lower extremity edema (determined by the venous clinical severity score [VCSS]) who underwent stenting for symptomatic CIVO with quality-of-life impairment despite optimal conservative therapy and had undergone lower extremity lymphoscintigraphy before intervention were considered for inclusion. Although the initial diagnosis of CIVO was via duplex ultrasound and cross-sectional imaging via computed tomography venography, intravascular ultrasound (IVUS) was used to confirm the diagnosis. The limbs that underwent stenting after pharmacomechanical thrombectomy and/or catheter-directed thrombolysis for acute deep vein thrombosis or stenting after recanalization of chronic total occlusion were excluded. The patients who underwent technically successful intranodal lymphangiography of the side undergoing stenting concurrent with the stenting procedure formed the study subjects. Conservative therapy included the regular use of compression stockings, leg elevation when feasible, exercise as tolerated, and anticoagulation therapy when appropriate and had been continued for 3 months before the consideration for stenting.

Intervention. With the patient under general anesthesia, access was obtained in the mid-thigh femoral vein under ultrasound guidance and an 11F access sheath placed. IVUS interrogation was performed to confirm the diagnosis of femoral-iliocaval obstruction. Before angioplasty and stenting, a lymph node in the groin on the side that was to undergo stenting was accessed using a 27-guage needle connected to 10 inches of intravenous tubing. The tubing had previously been flushed with saline to remove any air bubbles and connected to a 10-mL syringe with lipiodol. Intranodal lymphangiography was performed by manually injecting the lipiodol (1 mL/3 min) with the tip of the needle positioned at the corticomedullary junction of the lymph node. Such positioning was facilitated by ultrasound guidance. This represents a modification of the technique initially described by Rajebi et al[5] and, subsequently, by Nadolski and Itkin.[6] Antegrade flow of lipiodol was recorded using fluoroscopy. Still images were obtained at 20, 40, and 60 minutes after the start of the lipiodol injection. If the lipiodol had not yet reached the thoracic duct–venous junction by the 60-minute mark, radiographs of the abdomen and chest were obtained 3 hours after the start of the injection. A maximum of 10 mL of lipiodol was used per patient. At the end of the injection, the needle was removed, and manual pressure was applied at the access site for 1 to 2 minutes. Once the injection was complete, the procedure was continued as usual, with predilation, stenting and, postdilation. Completion IVUS interrogation and venography were performed to ensure adequate results had been obtained. Details pertaining to the technique of stenting, stent sizing, perioperative management, use of antithrombotic agents, and follow-up have all been described in previous reports.[2,7,8] All interventions were performed by one surgeon (A.J.).

Anatomy of lymphatic system in lower extremity and trunk. The lymphatic system starts in the interstitial space in the upper dermis with lymphatic capillaries (20-70 um) that drain into precollector vessels (70-150 um) that reside in the lower dermis.[9] The precollector vessels converge into vertically oriented efferent precollector vessels that exit the dermis and drain into collector vessels (150-500 μm) that run in the subcutaneous and subfascial tissue plane and are termed superficial and deep lymphatic collector vessels according to their relationship to the fascia, respectively.[9] Cadaveric dissection has identified a set of superficial collector vessels that begin on the dorsum of the foot and continue around the ankle and up the medial aspect of the leg (along the saphenous vein) to drain into the inguinal lymph nodes.[10] Another superficial set of collector vessels arise from the heel area and lateral foot, continue up the calf, and empty into the popliteal lymph nodes, which then drain into the deep lymphatics. There are also collector vessels that run up the anterior and posterior aspects of the lower leg and travel medially up the thigh. There are usually 2 to 5 lymphatic collector vessels in the lower leg and 5 to 15 in the thigh. There are one to two lymphatic collector vessels that accompany the posterior tibial, anterior tibial, and peroneal arteries.[10] Although these deep lymphatic channels become larger above the popliteal fossa, their numbers continue to remain low. They traverse with the vascular bundle in the adductor canal before emptying into the medial inguinal lymph nodes. The inguinal lymph nodes, which drain the lower extremities, perineum, external genitalia, and lower one half of the anterior abdominal wall and buttock are grouped as superficial and deep according to their relationship to the fascia. There are usually 10 to 20 inguinal lymph nodes on each side.[10] Lymphoscintigraphy and lymphangiography are able to identify only a few of these collector vessels, depending on the site of injection and which lymph vessel was cannulated, respectively. The efferent lymphatic collector vessels drain into the iliac lymph nodes. Above the inguinal ligament, there are three sets of collector vessels (lateral to the external iliac artery [lateral]; medial to the external iliac artery [intermediate]; and medial to the external iliac vein [medial]) and associated lymph nodes. At the level of the common iliac artery bifurcation, the lateral and intermediate chains combine to form a chain lateral to the common iliac artery, the medial chain becomes the intermediate chain, and a set of lymph collector vessels that drain the rectum and pelvic floor become the chain medial to the common iliac vein, thereby maintaining three sets of lymph collector vessels. In the lumbar region, the three chains from each side come together to form the medial and lateral lumbar lymphatic collector vessels on either side of the aorta. These vessels drain the lower extremities and pelvis. Additionally, there are lymphatic collector vessels that drain the alimentary tract that course in front of the aorta. The lymph nodes are grouped as medial aortic, lateral aortic, pre-aortic, and retro-aortic. The right lumbar, left lumbar, intestinal, and retro-aortic lymph collector vessels all join to form the cisterna chyli. The latter lies to the right of the aorta in front of the L1-L2 vertebrae.[10] The thoracic duct arises as the cranial extension of the cisterna chyli that runs up the thorax to the right of the aorta and, at the level of T5, turns left and ascends on the left side of the esophagus before curving to empty into the junction of the left subclavian and internal jugular veins. The right lymphatic duct drains the right head, neck, and arm and has a similar termination as the thoracic duct. Both ducts receive multiple tributaries before their termination. Variations in this anatomy can occur.[10-13]

Lymphoscintigraphy and its interpretation. Bilateral lower extremity lymphoscintigraphy was performed as a part of the initial evaluation of patients presenting to our clinic with suspected lymphedema. The technique has been described previously[3,4] and involves injection of ∼600 mCi of technetium-99m labeled sulfur colloid (filtered) intradermally using a 27-gauge needle and tuberculin syringe between the first and second toes. The patient was then asked to ambulate for 15 minutes. If ambulation was not possible, the feet were massaged for the same duration. Imaging was obtained using a gamma camera with a large field of view and the collimator set on low energy, high resolution, and a parallel hole, with a 20% energy window centered at 140 keV. Scanning was performed in the anterior and posterior configuration with the patient in a supine position from the waist to the toes at 20 minutes after injection using a scan speed of 8 cm/s. In situations in which the pelvis or legs were too large for the imaging field of view, static views were obtained. When a delay in uptake of the radiotracer was noted, repeat images were obtained at 40 and 60 minutes. The images were then saved using a dual-intensity, whole body display with and without masking of the injection sites.

The lymphoscintigram was scored using a combination of visual interpretation and semiquantitative analysis.[14] This method was adapted from the Mayo Clinic transport index, which was originally derived from the scoring system reported by Kleinhans et al[15] and Gloviczki et al.[16] The characteristics used to determine the presence of lymphedema on the lymphoscintigram included a transit time delay in minutes, the presence of dermal backflow, the presence of collateral channels, the intensity of radioisotope uptake in the main channel and lymph nodes, the number of lymph nodes in the groin, and the presence of popliteal lymph nodes. The transit time delay, which is a semiquantitative component of the score, was graded as normal if the time required for the radioisotope to reach the groin lymph nodes was $<$20 minutes. At $>$20 minutes, a delay of 20 to 40 minutes was considered to indicate mild lymphedema; a delay of 40 to 60 minutes, moderate lymphedema; and a delay $>$60 minutes, severe lymphedema. The remaining parameters were scored qualitatively in a binary manner as present or not. For the groin lymph nodes, five or more lymph nodes was used as the cutoff for a normal finding. If fewer than five lymph nodes were

Table I. Lymphoscintigraphic criteria for diagnosis of infrainguinal lymphatic disease

Variable	Normal	Abnormal		
		Mild	Moderate	Severe
Lymph nodes (n)	≥5	≤4	≤4	≤4
Collateral channels	None	Present	Present	Present
Intensity of uptake	Normal	Reduced	Reduced	Reduced
Popliteal lymph nodes	Absent	Present	Present	Present
Transit time delay, minutes	<20	20-40	40-60	>60
Dermal backflow	Absent	Absent	Absent	Present

present, the finding was considered positive for lymphedema. The presence of one or more positive parameters constituted a diagnosis of lymphedema based on the lymphoscintigraphic findings. With one positive parameter, the lymphedema was scored as mild, and with two or more positive parameters, as moderate. Severe lymphedema was considered present if the time delay was >60 minutes and/or dermal backflow was found. Details of the technique and scoring system have been described in a prior report and are presented in Table I.[14]

Interpretation of intranodal lymphangiogram. The technique of intranodal lymphangiography is described in the previous section. Fluoroscopic visualization of lipiodol transit was used to evaluate the different parameters. These included the number of lymph nodes from above the inguinal ligament to L1 (0, severe disease; 1-4, mild to moderate disease; >4 lymph nodes, normal); number of lymphatic collector vessels from above the inguinal ligament to L1 (0, severe disease; 1-4, mild to moderate disease; >4 vessels, normal); opacification of the thoracic duct (0, no opacification [severe disease]; 1, opacification [normal]); time delay to visualization of the thoracic duct (0, <20 minutes [normal]; 1, 21-40 minutes [mild disease]; 2, 40-60 minutes [moderate disease]; 3, >60 minutes [severe disease]); and pathologic changes to the thoracic duct (0, normal; 1, atretic [severe disease]; Table II). These scores were then summed to generate separate scores for disease status up to the cisterna chyli and above the cisterna chyli. The infra-cisterna chyli and supra-cisterna chyli scores were then combined to generate a total suprainguinal score (0, normal; 1, mild; 2, moderate; 3, severe disease). At each stage, the worst score was used to identify the final disease category (ie, normal, mild, moderate, severe). A normal and an abnormal intranodal lymphangiogram are shown in Figs 1, *A-C*, and 2, *A-C*. Because the transit of lipiodol from the cisterna chyli into the thoracic duct is quick, visualization of the cisterna chyli itself was not graded.

Evaluation of clinical parameters and quality of life. The clinical metrics evaluated included the VCSS, grade of swelling (GOS), and visual analog scale (VAS) score for pain (0, no pain; and 10, the worst pain possible). The VCSS was assessed before and after intervention at every follow-up clinic visit. The score was assessed from 0 to 27 (subtracting 3 points for compression). The GOS was objectively assessed and scored as 0, no swelling; 1, pitting, nonobvious swelling; 2, visible ankle swelling; 3, gross swelling involving the leg up to the knee; and 4, gross swelling involving the entire leg, including the thigh. For the quality-of-life assessment, the 20-item Chronic Venous Insufficiency Quality of Life Questionnaire (CIVIQ-20) instrument was used, with a score of 100 indicating the worst possible quality of life and a score of 0 indicating the best possible quality of life.[17,18]

Statistical analysis. Statistical analysis was performed using Prism, version 8 (GraphPad). The suprainguinal score (total suprainguinal score range, 0-3) was compared to the limb's lymphoscintigraphy-derived infrainguinal score (total infrainguinal score range, 0-3) using the *t* test and Spearman correlation coefficient (*r*). The clinical outcomes using the VCSS, GOS, and VAS for pain score after stenting were appraised using *t* tests and χ^2 tests. Kaplan-Meier analysis was used to assess stent patency after the intervention. The limb count used for analysis is noted in the results when appropriate. $P \leq .05$ was considered to indicate statistical significance.

RESULTS

Of 33 limbs, technically successful intranodal lymphangiography could be performed for 31 (30 patients). Intranodal lymphangiography could not be performed for two limbs owing to an inability to adequately access the identified lymph node. Of the 30 patients, 17 were women, with left laterality noted in 23 limbs. A nonthrombotic iliac vein lesion was observed in 9 limbs and post-thrombotic obstruction in 22 limbs. Regarding compliance with conservative therapy before surgery, the patients were compliant for 24 of 31 limbs (77%) with wearing compression stockings. The reasons for noncompliance were intolerance or an inability to put them on. Some of the patients were pursuing daily exercise (25 of 31 limbs [81%]). An inability to pursue daily exercise was due to unrelated medical problems. The baseline characteristics of the group are considered in Table III. The CEAP (clinical, etiologic, anatomic,

Table II. Inguinal intranodal lymphangiographic criteria for diagnosis of suprainguinal lymphatic disease (SLD)

		Abnormal		
Variable	**Normal**	**Mild**	**Moderate**	**Severe**
Lymph nodes, no.	>4	1-4	1-4	0
Lymphatic channels, no.	>4	1-4	1-4	0
TD visualization	Yes	Yes	Yes	No
TD visualization delay, minutes	<20	20-40	40-60	>60
TD pathologic changes	Normal	Normal	Normal	Stenosis

TD, Thoracic duct.

pathophysiologic) clinical class for the nine limbs with a nonthrombotic iliac vein lesion, C4 disease for four and C6 disease for five. Of the remaining 22 limbs with post-thrombotic syndrome, 3 had C3 disease, 14 had C4 disease, 1 had C5 disease, and 4 had C6 disease. The edema in most cases was bilateral (24 of 31 [77%]). At baseline, the limbs with severe suprainguinal lymphatic disease (SLD) had same VCSS, GOS, and VAS for pain score as the limbs with absent to mild SLD ($P > .1$). When the body mass index (BMI) was analyzed, a weak correlation was found between the BMI and lymphoscintigraphically determined infrainguinal lymphatic disease ($r = 0.37$; $P = .04$). However, the correlation between the BMI and intranodal lymphangiographically determined SLD was also weak but not significant ($r = 0.2$; $P = .29$). For the entire cohort, the median stent length and diameter were 160 mm (range, 140-260 mm) and 18 mm (range, 14-24 mm), respectively. The stent size was determined by the inflow channel luminal area and physical properties of the stent, with coverage dictated by the disease extent.[19] The median follow-up time was 20 months. No complications associated with the procedure, including stenting and intranodal lymphangiography, occurred.

Distribution of SLD and infrainguinal lymphatic disease. Of the 31 limbs, 24 (77%) had SLD. Of these 24 limbs, 22 (92%) had severe SLD and 2 (8%) had mild SLD. No limb had moderate SLD. Of the patients with SLD, 10 of 24 limbs (42%) with infra-cisterna chyli disease and all 24 limbs (100%) had thoracic duct disease. Of the 10 limbs with infra-cisterna chyli, 4 (40%) had severe disease and 6 (60%) had mild disease. Of the 24 limbs with thoracic duct disease, 21 (88%) had severe, 1 (4%) had moderate, and 2 (8%) mild disease. Five limbs had the same degree of disease above and below the cisterna chyli.

When SLD was compared to infrainguinal lymphatic disease, 6 limbs (19%) had the same degree of involvement above and below the groin (1 normal and 5 with severe disease), 17 (55%) had more severe SLD, and 8 limbs (26%) had more severe infrainguinal lymphatic disease. Three limbs with normal pedal lymphoscintigraphic findings had severe SLD. The Spearman correlation coefficient was 0.1 ($P = .69$).

Clinical outcomes after stenting and stent patency. After stenting, the VCSS improved for the entire cohort from 7 to 3 at 3 months ($P = .004$). The VCSS was 5 at 6 months ($P < .0001$), 3 at 12 months ($P = .0002$), and 4 at 24 months ($P = .0002$). The GOS for the entire cohort decreased from 3 to 1 at 3 months ($P = .02$) and remained at 1 at 6 months ($P < .0001$), 12 months ($P = .0002$), and 24 months ($P = .002$). The VAS for pain score for the entire cohort improved from 7 to 0 ($P = .002$) at 3 months. It had increased to 1 at 6 months ($P < .0001$), 2 at 12 months ($P = .0002$), and 3 at 24 months ($P < .0001$). The clinical outcomes for the entire cohort and for the limbs with severe and absent to mild SLD are considered in Table IV. At 36 months, the primary patency in the limbs with severe SLD was 95% and the secondary patency was 100% (Supplementary Fig, online only).

Quality-of-life outcomes after stenting. The overall quality of life as evaluated by the CIVIQ-20 score improved for the entire cohort (score decreased from 69 to 29; $P < .0001$). For patients with severe SLD, the CIVIQ-20 score improved from 75 to 44 ($P = .01$) and from 64 to 29 ($P = .0008$) for patients with absent to mild SLD.

Role of complex decongestive therapy. Seven limbs underwent complex decongestive therapy (CDT) after stenting because of significant residual leg edema with continued quality-of-life impairment. All seven limbs had post-thrombotic disease and had had some improvement in the clinical parameters after stenting but not enough to resolve their quality-of-life impairment. CDT involved a period (6-8 weeks with two to three sessions weekly) of manual lymphatic drainage, followed by regular use of a lymphatic pump, complemented with compression stockings. All seven limbs had severe SLD, with one also having concomitant severe infrainguinal disease. After the manual lymphatic drainage, improvement occurred in the size of the lower extremities at the knee, upper calf, mid-calf, malleolus, and mid-foot that was statistically significant. Improvement also occurred in the lymphedema life impact scale and

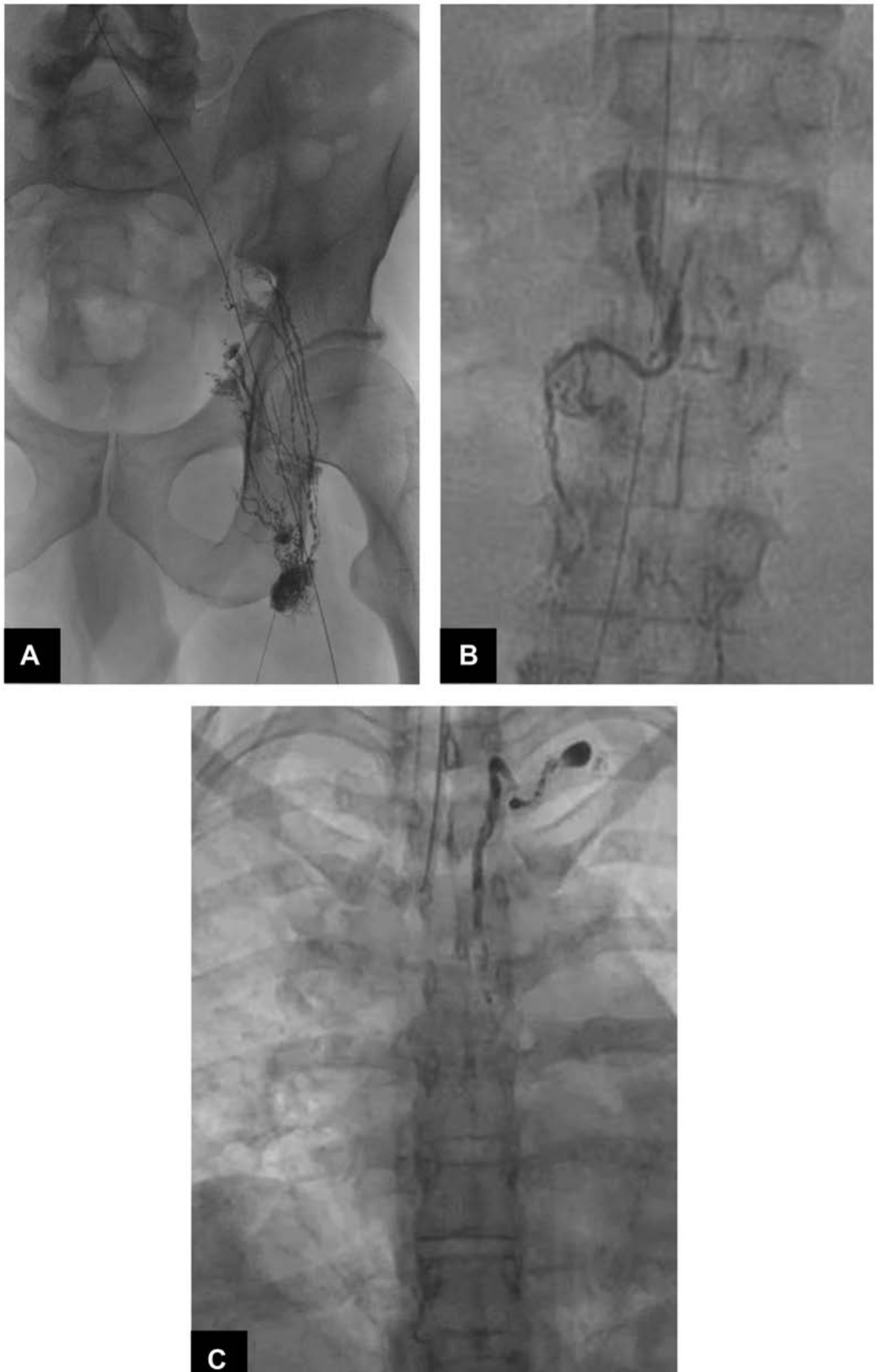

Fig 1. Inguinal intranodal lymphangiogram with normal findings showing inguinal lymph nodes and lymphatic channels (**A**), cisterna chyli (**B**), and thoracic duct (**C**).

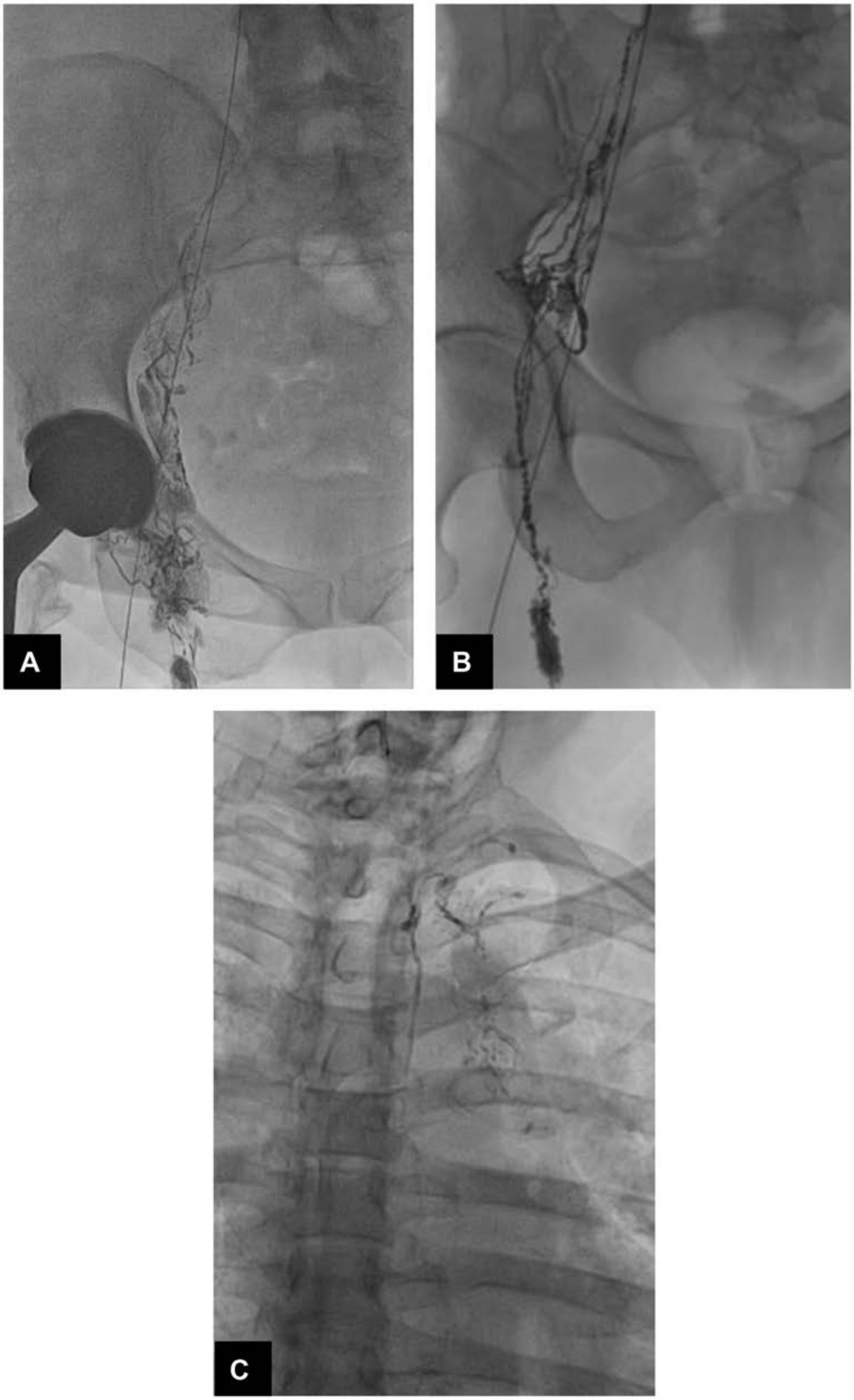

Fig 2. Inguinal intranodal lymphangiogram with abnormal findings showing a paucity of lymphatic collector vessels above the inguinal ligament (**A**), a paucity of lymph nodes above the inguinal ligament (**B**), and stenotic thoracic duct with reflux (**C**).

Table III. Baseline cohort characteristics

Variable	Value
Age, years	59 (41-76)
BMI, kg/m^2	33 (22-53)
NIVL	1
PTS	2
Ulcers	5 (16)
MLD therapy	7 (23)
Reintervention	4 (13)
VCSS for edema	3 (1-3)
CEAP clinical class	
C0-C2	0 (0)
C3	5 (16)
C4	19 (61)
C5	2 (6)
C6	5 (16)

BMI, Body mass index; *CEAP,* clinical, etiologic, anatomic, pathophysiologic; *MLD,* manual lymphatic drainage; *NIVL,* nonthrombotic iliac vein lesion; *PTS,* post-thrombotic syndrome; *VCSS,* venous clinical severity score.
Data presented as median (range) or number (%).

the degree of impairment, although the difference was not statistically significant (Supplementary Table, online only). The CIVIQ-20 score also improved from 61 after stenting in this small group to 29 after CDT ($P = .001$). No statistically significant improvement was found in the VCSS, VAS for pain score, GOS, or quality of life for these seven limbs from before to after stenting or from before to after CDT, possibly because of the small sample size.

DISCUSSION

Large studies of patients undergoing stenting for chronic iliofemoral obstruction have reported a rate of complete or partial relief of swelling of ~60% to 70%.[20] The remainder of patients who undergo CDT experience improvement of their swelling. However, potentially, a small cohort of patients will likely have persistent and/or residual swelling with impairment of their quality of life despite undergoing these previously described measures. Lymphatic impairment in the suprainguinal territory could possibly explain this given that CDT is unlikely to offer much help with such impairment because a functioning lymphatic system is likely required in the suprainguinal territory to complement the CDT. Although the lymphatic collector vessels are multiple with extensive cross-connections up to the cisterna chyli, this is not the case for the thoracic duct. Thoracic duct pathology can lead to retrograde lymphatic hypertension and result in a lack of relief from CDT and significant residual swelling.

Distribution of SLD in patients with CIVO. Although the sample size is small, the present study found that an overwhelming majority of limbs that underwent stenting for quality-of-life impairing CIVO had SLD (77%). Additionally, using the previously described system of diagnosing SLD, 22 of the 31 limbs (71%) had severe SLD and 2 (6%) had mild SLD. When SLD was divided into below and above the cisterna chyli (thoracic duct), it seems that disease involving the thoracic duct is far more common than disease affecting the lymphatic collector vessels that drain into the cisterna chyli. Every limb (100%) that had SLD demonstrated a degree of pathology in the thoracic duct. Slightly >40% of the limbs with SLD had involvement of the lymphatic collector vessels below the cisterna chyli. The status of the precollector system could not be assessed, given the nature of the study. A previous study has demonstrated involvement of both precollector and collector vessels in patients with secondary lymphedema.[21] Whether this would be true for patients with phlebolymphedema remains to be determined.

Another key finding was that the SLD can exist, irrespective of the presence of infrainguinal lymphatic disease. Three limbs (10%) had normal lymphoscintigraphic findings but demonstrated severe SLD. Only 6 of the 31 limbs (19%) had the same degree of involvement both above and below the inguinal ligament. In contrast, 17 limbs (55%) had more severe disease in the suprainguinal territory, and 8 limbs (26%) had worse infrainguinal lymphatic disease. Finally, in this cohort, no limb had neither SLD or infrainguinal lymphatic disease. The correlation between SLD and infrainguinal lymphatic disease was poor ($r = 0.1$).

Clinical and quality-of-life improvement after stenting and CDT in patients with SLD. Improvements in the clinical and quality-of-life scores occurred, not only in the entire cohort, but also in those with severe SLD. These improvements were seen across the VCSSs, VAS for pain scores, and GOS. The differences were all statistically significant ($P < .05$). This improvement across all three metrics was maintained even at 24 months after stenting ($P < .05$). The quality of life, as determined by the CIVIQ-20 questionnaire, improved by 40 points ($P < .0001$) for the entire cohort and 31 points ($P = .01$) for the patients with severe SLD. Thus, although 22 of the 31 limbs (71%) undergoing stenting for CIVO had severe SLD, most of them (15 of 22 [68%]) experienced significant improvement with just stenting alone. Seven limbs (32%) required additional CDT to help with persistent or residual edema. None required further intervention after CDT. However, this represents a small sample, and it possible that there will be a small cohort for whom these measures will fail.

Role of SLD and future directions. Patients with residual or persistent lower limb edema with impairment of their quality of life after stenting and CDT might benefit from an evaluation of their suprainguinal lymphatic

Table IV. Clinical outcomes after stenting for entire cohort and limbs with severe suprainguinal lymphatic disease (SLD)

Follow-up, months	Parameter	Limbs, no.	Score		*P* value
			Before stenting	After stenting	
All limbs (n = 31)					
6					
	VCSS	21	8	5	**<.0001**
	GOS	21	3	1	**<.0001**
	VAS	19	7	1	**<.0001**
12					
	VCSS	19	7	3	**.0002**
	GOS	19	3	1	**.0002**
	VAS	19	7	2	**.0002**
24					
	VCSS	17	8	4	**.0002**
	GOS	17	3	1	**.001**
	VAS	17	7	3	**<.0001**
Limbs with severe SLD (n = 24)					
6					
	VCSS	13	8	5	**.0005**
	GOS	13	3	1	**.008**
	VAS	11	6	0	**.004**
12					
	VCSS	12	7	3	**.012**
	GOS	12	3	1	**.012**
	VAS	12	8	1	**.008**
24					
	VCSS	12	8	5	**.01**
	GOS	12	3	1	**.012**
	VAS	12	7	2	**.002**

GOS, Grade of swelling; *SLD*, suprainguinal lymphatic disease; *VAS*, visual analog scale (for pain); *VCSS*, venous clinical severity score.
Boldface *P* values represent statistical significance.

system via inguinal intranodal lymphangiography. If thoracic duct obstruction is found, potentially relieving the obstruction via stenting of the thoracic duct might help. This could be accomplished in an antegrade manner via transabdominal access of the cisterna chyli or retrograde venous access via the subclavian vein. Cases of stenting of the thoracic duct have been reported; however, these were for chylothorax rather than for obstructive pathology. Further study is certainly warranted.

Study limitations. The limitations of the present study include its small sample size. Additionally, diagnostic criteria of SLD for patients with CIVO is nonexistent. Thus, the present study represents an effort to determine diagnostic criteria for SLD in patients with CIVO presenting with edema. Risks are associated with intranodal lymphangiography, including pulmonary and cerebral embolization.[22] These can be minimized by limiting the amount of lipiodol used to <10 mL and evaluating patients for right to left shunting before intranodal lymphangiography. Technical challenges can be encountered when the lymph nodes are small, in obese patients, and when lymph node venous networks are present. When the latter is noted on duplex ultrasound, it is best to avoid accessing such a lymph node to prevent large volume embolization to the lungs. An alternate lymph node without such networks should be identified for access. Despite these limitations, the present study, to the best of our knowledge, represents the first study to reveal the existence of SLD in patients with symptomatic CIVO and raise the possibility of a role for intranodal lymphangiography for patients with persistent or residual edema after stenting and CDT. However, more research in this area, including the utility of noninvasive imaging techniques such as magnetic resonance imaging to evaluate the suprainguinal lymphatic system before focused lymphatic intervention is clearly required.

CONCLUSIONS

SLD appears to be common in patients with leg edema undergoing stenting for symptomatic CIVO with such disease most commonly affecting the thoracic duct. Although patients with persistent or residual leg edema after stenting can benefit from CDT, additional workup using inguinal intranodal lymphangiography and targeted intervention might need to be considered for those who do not benefit from such therapy. Further study is warranted.

AUTHOR CONTRIBUTIONS

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

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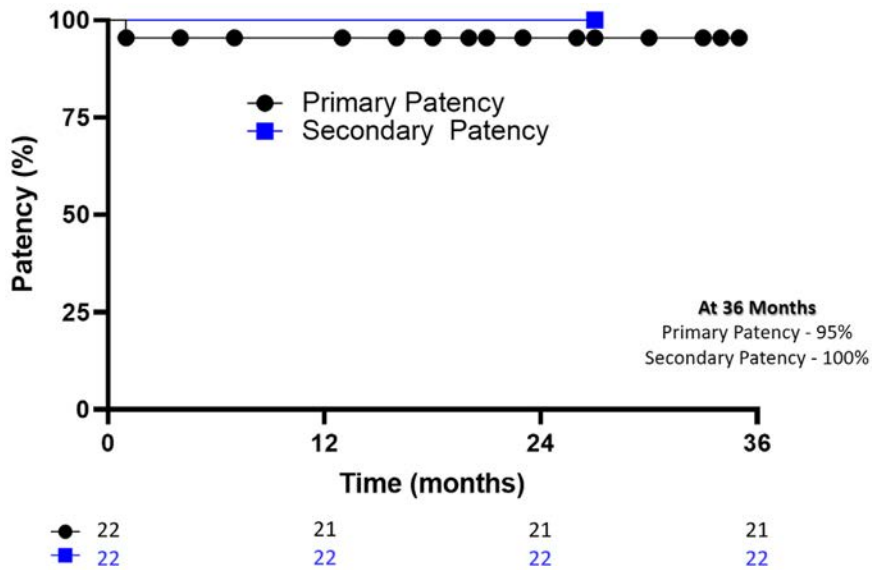

Supplementary Fig (online only). Stent patency for patients with severe suprainguinal lymphatic disease (SLD; standard error of the mean, <10%).

Supplementary Table (online only). Clinical outcomes after manual lymphatic drainage (MLD) for limbs with symptomatic persistent or residual edema after stenting

		Median MLD, cm			
Parameter	Limbs, no.	Before	After	Median change, %	*P* value (before vs after)
Lower extremity measurements (n = 7)					
Knee	7	42	40.6	−1.8	**.03**
Upper calf	7	46	41	−5.8	**.01**
Mid-calf	7	30	27	−5.2	**.01**
Malleolus	7	28	25	−5.5	**.007**
Mid-foot	7	24	22.5	−1.6	**.03**
Lymphedema clinic outcomes (n = 7)				NA	
Pain					
Best	5	0	0		.9
Worst	5	7	0		.13
Present	5	2	0		.50
LLIS	5	38	17		**.07**
Impairment, %	5	57	23		**.06**

LLIS, Lymphedema life impact scale; *NA,* not applicable.
Boldface *P* values represent statistical significance.