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The beneficial role of complex decongestive therapy in patients with symptomatic chronic iliofemoral venous obstruction with phlebolymphedema

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ABSTRACT

Objective: Phlebolymphedema has been noted to be one of the most common causes of lymphedema in the lower extremity in western societies. Although complex decongestive therapy (CDT) represents the mainstay of lymphedema treatment, its role for phlebolymphedema arising from chronic iliofemoral venous obstruction (CIVO) merits further exploration. We evaluated this through the use of a protocol of CDT first for limbs with CEAP (clinical, etiologic, anatomic, pathophysiologic) clinical C3 disease and stent correction of obstruction before CDT for those with more advanced disease (CEAP C4-C6). In the present study, we analyzed the outcomes after the use of such a protocol.

Methods: We analyzed prospectively collected data for 192 limbs (166 patients) that underwent treatment of quality-of-life (QoL) impairing symptoms from CIVO due to lymphoscintigraphically determined phlebolymphedema between 2017 and 2022. The characteristics evaluated included CEAP clinical class, venous clinical severity score (VCSS), grade of swelling (GOS), visual analog scale (VAS) pain score, QoL (CIVIQ-20 [20-item chronic venous disease quality of life questionnaire]), stenting for CIVO, and outcomes related to CDT and stenting. For the limbs undergoing CDT or stenting followed by CDT, the outcomes were evaluated at 6 weeks and 3, 6, and 12 months after completion of CDT. Paired and unpaired *t* tests, χ^2 tests, and analysis of variance were used for comparisons of clinical variables. Kaplan-Meier analysis was used to evaluate stent patency, with the log-rank test used to discriminate between different curves.

Results: Of the 192 limbs (166 patients) in the entire cohort, 74 were in the C3 group and 118 were in the C4-C6 group. The median patient age was 63 years; 57 were men and 109 were women. In the C3 group, after CDT, improvement had occurred in the VCSS and VAS pain score at 6 weeks ($P < .0001$) and at 3 ($P < .0001$), 6 ($P < .0001$), and 12 ($P < .0001$) months. Improvement in the GOS was noted at 6 ($P < .0001$) and 12 ($P = .0005$) months. The CIVIQ-20 score improved from 63 to 38 ($P = .009$). Nine limbs (12%) in the C3 group required stenting after CDT. In the C4-C6 group, of the 118 limbs, 75 (64%) underwent stenting only and 43 (36%) underwent stenting followed by CDT for persistent QoL impairing symptoms. For this latter group, after CDT, improvement occurred in the VCSS, GOS, and VAS pain score at 6 weeks ($P < .0001$) and 3 ($P < .0001$), 6 ($P < .0001$), and 12 ($P < .0001$) months. The CIVIQ-20 score improved from 61 to 34 ($P < .0001$). The primary, primary assisted, and secondary patency in the C4-C6 group at 36 months was 92%, 100%, and 100%, respectively.

Conclusions: For CEAP C3 patients with phlebolymphedema due to CIVO, CDT should be a part of the first line of treatment. Stenting should be reserved for those with QoL impairing symptoms despite the use of CDT. Additionally, CDT helps provide symptom relief for patients with more advanced CEAP C4-C6 disease with persistent or residual edema after stenting. Further study is warranted. (J Vasc Surg Venous Lymphat Disord 2024;12:101686.)

Keywords: Phlebolymphedema; Chronic iliofemoral venous obstruction; Iliac vein stenting; Post thrombotic syndrome; May Thurner syndrome; Lymphedema

Lymphedema due to chronic venous insufficiency has been demonstrated to be the most common cause of lymphedema in the lower extremity in western societies, accounting for 41.8% of limbs with lymphedema.[1] Such lymphedema, termed "phlebolymphedema," has been noted to be present in ~20% to 30% of patients with chronic iliofemoral venous obstruction (CIVO).[2] CIVO can lead to the development of venous hypertension with consequent overloading of the lymphatic transport capacity leading to the development of phlebolymphedema. The treatment of patients with CIVO impairing their quality of life (QoL) despite conservative therapy (ie, use of compression stockings, leg elevation when feasible, exercise as tolerated) traditionally has been

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through intravascular ultrasound (IVUS) interrogation to confirm the diagnosis, followed by stenting to relieve the confirmed obstruction. However, after stent placement for correction of such obstructions, up to 30% of patients will experience no relief from their edema.[3,4] This brings forth the potential role of alternative therapies for such patients either before or after stenting. Thus, we decided to pursue a protocol of complex decongestive therapy (CDT) first for limbs with CEAP (clinical, etiologic, anatomic, pathophysiologic) clinical C3 disease and stent correction of CIVO first for those with more advanced CEAP C4-C6 disease. Such an approach was hypothesized to provide symptomatic relief and reduce the need for femoroiliocaval stenting in patients with CEAP C3 disease. However, for patients with advanced chronic venous insufficiency (CEAP C4-C6), given the presence of skin and/or soft tissue damage (ie, severe venous hypertension), stent correction of the obstruction was prioritized. Further treatment after these initial therapies was determined by the presence of residual symptoms. For the CEAP C3 cohort, if QoL impairing symptoms remained after CDT, IVUS interrogation and stenting were pursued. However, for the CEAP C4-C6 patients with residual QoL impairing edema after stenting, CDT was pursued. In the present study, we evaluated the results of this approach.

METHODS

Study design. We performed a single-center retrospective analysis of prospectively collected data from 2017 to 2022. The Franciscan Missionaries of Our Lady University institutional review board approved the present study and dissemination of de-identified patient data. All the patients provided written informed consent for all tests and procedures.

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

Participants. Symptomatic patients with CIVO diagnosed using duplex ultrasound and computed tomography venography and phlebolymphedema (confirmed by lower extremity lymphoscintigraphy) that impaired their QoL in whom conservative therapy had failed formed the study cohort. Those with CEAP C3 disease underwent CDT as the first treatment and those with CEAP C4-C6 disease underwent IVUS interrogation followed by iliofemoral venous stenting once the diagnosis of CIVO was confirmed. Stenting was pursued for C3 limbs with QoL impairing symptoms after CDT, and CDT was pursued for C4-C6 limbs with QoL impairing edema after stent correction of their obstruction. Patients with phlebolymphedema in the setting of acute deep vein thrombosis or chronic total occlusive lesions of the femoroiliocaval segments and pregnant women were excluded. Also excluded were patients who were noncompliant with any component of CDT.

ARTICLE HIGHLIGHTS

- **Type of Research:** A single-center analysis of prospectively collected data
- **Key Findings:** Complex decongestive therapy (CDT) provides clinical and quality-of-life improvement for patients with phlebolymphedema due to chronic iliofemoral venous obstruction. This improvement is seen even for patients with advanced CEAP (clinical, etiologic, anatomic, pathophysiologic) clinical (C4-C6) disease.
- **Take Home Message:** For patients with phlebolymphedema due to chronic iliofemoral venous obstruction (CEAP C3), CDT should be a part of the first line of treatment options, with stenting reserved for those with quality-of-life impairing symptoms despite CDT. In patients with more advanced (C4-C6) disease, CDT helps with symptomatic persistent or residual edema after stenting.

Lymphoscintigraphy. Patients presenting to our clinic with symptomatic lower extremity edema underwent bilateral lower extremity lymphoscintigraphy as a part of the diagnostic evaluation protocol. Lymphoscintigraphy was performed by injection of ~600 mCi of technetium-99m–labeled sulfur colloid (filtered) into the intradermal space between the first and second toes using a 27-guage needle and tuberculin syringe. The patient was then asked to ambulate for 15 minutes. If ambulation was not possible, the feet were massaged for 15 minutes. Lymphoscintigraphy was then performed using a gamma camera with a large field of view, high resolution, and the collimator set on low energy. When a delay occurred in radiotracer uptake, repeat images were obtained at 40 and 60 minutes. These images were then saved on dual intensity whole body display with masking and unmasking of the injection sites. The lymphoscintigraphy findings were scored using a combination of semiquantitative analysis and visual interpretation. This scoring represents an adaption of the Mayo Clinic transport index originally derived from the scoring system described by Kleinhans et al.[5,6] Each limb was scored as normal or having mild, moderate, or severe lymphedema. The lymphoscintigraphy technique and scoring system have both been described in a prior report.[7]

Complex decongestive therapy. CDT involved the use of manual lymphatic drainage (MLD) for 2 to 3 sessions each week for 6 to 8 weeks as determined by a certified lymphedema therapist. This was followed by the use of a lymphedema pump (sequential pneumatic compression device) that extends from toes to the groins twice daily in conjunction with the use of compression stockings or compression wraps (pressure, 20-30 mm Hg). Leg elevation at night was recommended.

Stenting and follow-up. Patients presenting with QoL impairing symptoms due to CIVO (CEAP C4-C6 disease or CEAP C3 disease with failed conservative therapy and CDT) underwent IVUS interrogation for confirmation of the diagnosis and subsequent stenting. These clinical manifestations included pain, swelling, heaviness, tiredness, venous claudication, hyperpigmentation, lipodermatosclerosis, and/or venous leg ulcers. Access was obtained in the femoral or popliteal vein (as dictated by the best possible inflow). Venography was then performed to evaluate the flow characteristics, followed by IVUS interrogation. Normal minimal luminal areas of 125 mm^2, 150 mm^2, and 200 mm^2 in the common femoral, external iliac, and common iliac veins, respectively, were used as cutoffs to diagnose obstruction via IVUS. Any luminal area less than these values in a patient with a QoL impairing clinical presentation in whom conservative therapy had failed merited predilation, stenting, and postdilation. The stent sizes were determined by the inflow channel luminal area, and the stent length extended from an area of good inflow to an area of good outflow.[8] Completion IVUS interrogation was performed to ensure adequacy of stenting, and venography was performed to ascertain the final flow dynamics. The technique of stenting, peri- and postoperative care, and follow-up have been described previously.[4,9,10]

Reintervention. Patients who developed recurrence of QoL impairing clinical manifestations underwent repeat IVUS interrogation and consequent correction of the etiology of their stent malfunction. This malfunction varied from in-stent restenosis (ISR) to stent compression to a combination of ISR and stent compression to stent occlusion. The technique of diagnosis and treatment of stent malfunction has also been previously described.[11-13]

Measurements. The clinical metrics evaluated included the venous clinical severity score (VCSS; range, 0-27 [range, 3-30 for compression stockings]), grade of swelling (GOS; score range, 0-4), and the visual analog scale (VAS) pain score (score range, 0-10). The GOS was categorized 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. All scores were appraised at every clinic follow-up visit. QoL was assessed using the CIVIQ-20. For the CIVIQ-20, the maximum score of 100 indicates the worst possible QoL, and a score of 0 indicates the best possible QoL.[14,15] The last follow-up response available was used in the postoperative outcome analysis. For the lymphedema outcomes, the best, worst, and present pain for each patient was recorded at the first and last visit of MLD therapy. The lymphedema life impact score (LLIS) and the percentage of impairment data were also recorded before and after treatment completion. LLIS was developed as a comprehensive, lymphedema-specific instrument to assess the effects of lymphedema on any extremity.[16] Finally, circumferential measurements of the knee, upper calf, mid-calf, malleolus, and midfoot (in cm) were taken at each visit to record any decrease in swelling with MLD. The measurements before and after the last MLD visit were used for analysis. For those patients who underwent CDT and those who underwent stenting followed by CDT, the follow-up times were 6 weeks and 3, 6, and 12 months after completion of MLD.

Statistical analysis. Statistical analysis was performed using Prism, version 8 (GraphPad). Comparisons were performed at baseline and after CDT or stenting using unpaired and paired *t* tests. The limb count used for analysis is noted in the results when appropriate. Kaplan-Meier analysis was used to assess stent patency after intervention, with the log-rank test used to discriminate between the curves. $P \leq .05$ was considered statistically significant.

RESULTS

A total of 192 limbs (166 patients) were included in the present study, with 74 limbs (35%) in the CEAP C3 group and 118 limbs (65%) in the CEAP C4-C6 group. The median age for the entire cohort was 63 years, with a preponderance of women (n = 109) and left laterality (n = 104 limbs). Twenty-six patients had bilateral involvement. The median body mass index was 38 kg/m^2. The median duration of conservative therapy before being deemed a failure was 3 months (range, 1-61 months). Of the limbs that underwent IVUS interrogation, 88 were noted to have post-thrombotic obstruction and 39 had a non-thrombotic iliac vein lesion (NIVL). Of the 192 limbs, 41 (21%) had deep venous reflux. Of these 41 limbs, 16 (39%) had segmental reflux and 25 (61%) had axial deep venous reflux. In the CEAP C3 group and CEAP C4-C6 group, 8 of 74 limbs (11%) and 33 of 118 limbs (28%) had deep venous reflux. Lower extremity lymphoscintigraphy demonstrated mild lymphedema in 99 limbs (52%), moderate lymphedema in 37 limbs (19%), and severe lymphedema in 56 limbs (29%; Table I). The demographic characteristics are presented in Table I. The clinical outcomes for the VCSS, GOS, VAS pain score, and QoL for all limbs are listed in Tables II and III. Regarding the supine foot venous pressure, the CEAP C3 group had a median pressure of 10 mm Hg and the CEAP C4-C6 group had a median pressure of 14 mm Hg ($P = .0054$). Of the 127 limbs that underwent IVUS interrogation and subsequent stenting, 12 (9%) underwent concomitant endovenous laser ablation for superficial venous reflux. The median follow-up for the overall cohort was 17 months (11 months for the C3 group and 19 months for the C4-C6 group).

Table I. Baseline characteristics for entire cohort (192 limbs; 166 patients)

Variable	CEAP C3 CDT (n = 74 limbs)	CEAP C4-C6 (n = 118 limbs)	
		Stenting only (n = 75 limbs)	CDT after stenting (n = 43 limbs)
Age, years	60 (23-82)	64 (17-86)	65 (40-83)
Gender			
Male	10	31	16
Female	40	42	27
Laterality			
Left	13	41	24
Right	13	30	19
Bilateral	24	2	0
NIVL	NA	26	12
PTS	NA	49	31
BMI, kg/m^2	38 (23-70)	37 (21-62)	38 (23-57)
Lymphoscintigram severity			
Mild	29 (39)	44 (59)	26 (61)
Moderate	18 (24)	15 (20)	4 (9)
Severe	27 (37)	16 (21)	13 (30)

BMI, Body mass index; *CEAP,* clinical, etiologic, anatomic, pathophysiologic; *CDT,* complex decongestive therapy; *NA,* not applicable; *NIVL,* non-thrombotic iliac vein lesion; *PTS,* post-thrombotic syndrome.
Data presented as median (range), numbers, or number (%).

Outcomes in limbs with CEAP C3 disease

Clinical outcomes.

Venous clinical severity score. The VCSS improved from 6 to 5 ($P < .0001$) at 6 weeks and 3 months, with improvement to 4 at 6 months ($P < .0001$) and an increase to 5 at 12 months ($P = .0003$).

Grade of swelling. The GOS demonstrated an initial improvement at 6 months, decreasing from 3 to 2 ($P < .0001$), and remained at 2 at 12 months ($P < .0001$).

VAS pain score. The VAS pain score improved from 7 to 4 ($P < .0001$) at 6 weeks, remained at 4 ($P < .0001$) at 3 months, with an improvement to 3 ($P < .0001$) at

Table II. Clinical and quality of life (QoL) outcomes for C3 group

Follow-up	Patients, No.	Before CDT	After CDT	*P* value
6 Weeks				
VCSS	40	6	5	<.0001
GOS	40	3	3	.0035
VAS score	34	7	4	<.0001
3 Months				
VCSS	42	6	5	<.0001
GOS	42	3	3	.0001
VAS score	27	6	4	<.0001
6 Months				
VCSS	46	4	6	<.0001
GOS	46	3	2	<.0001
VAS score	40	7	3	<.0001
12 Months				
VCSS	37	6	5	.0003
GOS	37	3	2	.0005
VAS score	25	8	4	<.0001
QoL	13	63	38	.0089

CDT, Complex decongestive therapy; *GOS,* grade of swelling; *VAS,* visual analog scale for pain; *VCSS,* venous clinical severity score.
Data presented as median scores.

Table III. Lymphedema outcome measures for C3 and C4-C6 groups

Parameter	Patients, No.	Score before MLD	Score after MLD	Change, %	*P* value
C3, CDT only (n = 74)				NA	
Pain best	53	1	0		<.0001
Pain worst	53	6	3		<.0001
Pain present	53	3	0		<.0001
LLIS	54	37	19		<.0001
Impairment	54	54	28		<.0001
Location			Circumference, cm		
Knee	62	45	45	−4.0	<.0001
Upper calf	62	45	42	−5.3	<.0001
Mid-calf	62	32	30	−6.9	<.0001
Malleolus	62	29	27	−7.4	<.0001
Mid-foot	61	24	23	−3.1	<.0001
C4-C6, CDT after stenting (n = 43)				NA	
Pain best	39	0	0		.0021
Pain worst	39	6	2		<.0001
Pain present	40	2	0		<.0001
LLIS	38	30	13		<.0001
Impairment, %	38	49	19		<.0001
Location			Circumference, cm		
Knee	43	45	43	−4.0	<.0001
Upper calf	43	43	41	−4.5	<.0001
Mid-calf	43	30	28	−5.8	<.0001
Malleolus	43	28	27	−6.9	<.0001
Mid-foot	43	24	24	−2.6	<.0001

CDT, Complex decongestive therapy; *LLIS,* lymphedema life impact score; *MLD,* manual lymphatic drainage.

6 months and a slight increase to 4 ($P < .0001$) at 12 months after CDT.

Quality of life. The CIVIQ-20 score improved from 63 to 38 ($P = .009$) after CDT. The clinical and QoL outcomes are presented in Table II.

Lymphedema outcomes. The pain scores, LLIS, percentage of impairment data, and circumferential measurements of the knee, upper calf, mid-calf, malleolus, and mid-foot demonstrated improvement after MLD (Table III).

Stent outcomes for C3 limbs. Of the 74 limbs that underwent CDT, 9 (12%) had persistent symptoms impairing the patients' QoL and required stenting. The median time to stenting was 14 months. The primary, primary assisted, and secondary patency in the C3 group at 5 months was 100%, 100%, and 100%, respectively.

Outcomes in limbs with CEAP C4-C6

The CEAP C4-C6 group was divided into those limbs that required stenting alone (n = 75; 64%) and those that required CDT after stenting (n = 43; 36%) for persistent QoL impairing symptoms. Their clinical outcomes are presented in Table IV. The median IVUS-determined luminal area stenosis across the iliofemoral segment for the C4-C6 group that required stenting alone was 37% and was 35% for those who received CDT after stenting, a reflection of the inability of the degree of stenosis to predict the clinical presentation or outcome.

Clinical outcomes after CDT and stenting.

Venous clinical severity score. Following CDT after stenting, the VCSS improved from 7 to 4 ($P < .0001$) at 6 weeks, increased to 6 ($P < .0001$) at 3 months, and remained at 6 ($P < .0001$) at 12 months before decreasing to 5 ($P < .0001$) at 12 months.

Grade of swelling. The GOS improved from 3 to 1 ($P < .0001$) at 6 weeks, increased to 2 ($P < .0001$) at 3 months, remained at 2 at 6 months, and decreased to 1 ($P < .0001$) at 12 months.

VAS pain score. The VAS pain score after CDT improved from 7 to 4 ($P < .0001$) at 6 weeks, remained at 4 ($P < .0001$) at 3 months, improved to 3 ($P < .0001$) at 6 months, and increased to 4 ($P < .0001$) at 12 months.

Ulcer healing. The healing rate of leg ulcers for the entire cohort was 80% (8 of 10), with a recurrence rate of 20% (2 of 10). For the limbs that received stenting

Table IV. Clinical and quality of life (QoL) outcomes for C4-C6 group stratified by treatment

Follow-up	Patients, No.	Score before stenting	Score after stenting	Score After CDT	*P* value
Stenting only (n = 75)				NA	
6 Weeks					
VCSS	66	8	4		<.0001
GOS	66	3	1		<.0001
VAS score	62	7	1		<.0001
3 Months					
VCSS	35	7	3		<.0001
GOS	35	3	1		<.0001
VAS score	34	7	2		<.0001
6 Months					
VCSS	74	8	5		<.0001
GOS	74	3	1		<.0001
VAS score	69	7	1		<.0001
12 Months					
VCSS	74	8	4		<.0001
GOS	74	3	1		<.0001
VAS score	72	7	1		<.0001
QoL	52	58	24		<.0001
CDT after stenting (n = 43)					
6 Weeks					
VCSS	31	8	6	4	<.0001
GOS	33	3	3	1	<.0001
VAS score	26	7	5	3	<.0001
3 Months					
VCSS	27	9	6	6	<.0001
GOS	27	3	3	2	.0006
VAS score	25	7	5	3	.0001
6 Months					
VCSS	32	10	6	6	<.0001
GOS	32	3	3	1	<.0001
VAS score	31	7	5	3	<.0001
12 Months					
VCSS	31	9	6	5	<.0001
GOS	31	3	3	1	<.0001
VAS score	30	7	5	2	<.0001
QoL	26	62	57	33	<.0001

CDT, Complex decongestive therapy; *GOS*, grade of swelling; *NA*, not applicable; *VAS*, visual analog scale for pain; *VCSS*, venous clinical severity score.

only, 75% (6 of 8) healed and 25% (2 of 8) recurred. For the limbs that underwent CDT after stenting, 100% of the ulcers healed (2 of 2) with no recurrence.

QoL after CDT and stenting. The CIVIQ-20 score improved from 61 to 34 ($P < .0001$) after CDT in the limbs that had previously undergone stenting.

Lymphedema outcomes after CDT and stenting. Of the limbs with C4-C6 disease that underwent stenting, 43 (36%) required CDT after stenting for persistence of QoL impairing symptoms. The median time to CDT after stenting was 2 months. The pain scores, LLIS, percentage of impairment data, and circumferential measurements of the knee, upper calf, mid-calf, malleolus, and mid-foot demonstrated improvement after MLD in the patients who had previously undergone stenting (Table III).

Stent outcomes for C4-C6 limbs. The primary, primary assisted, and secondary patency in the C4-C6 group at

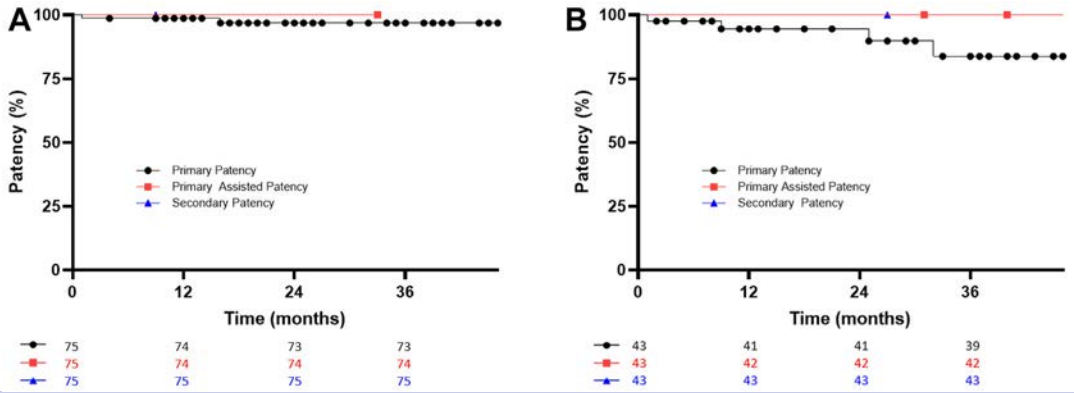

Fig 1. Plots demonstrating primary, primary assisted, and secondary stent patency for CEAP C4-C6 cohort. **A,** Limbs that underwent stenting only. **B,** Limbs that underwent stenting, followed by complex decongestive therapy (CDT). Standard error of the mean: <10%.

36 months was 92%, 100%, and 100%, respectively. The C4-C6 patients who underwent stenting only had primary patency of 97%. However, the patients who underwent CDT after stenting had primary patency of 84% ($P = .03$). The primary assisted and secondary patency for both groups was 100% (Fig 1). Reintervention was required for 2 of 75 patients (3%) who underwent stenting only and 5 of 43 patients (12%) who received CDT after stenting ($P = .05$). The reasons for reintervention in the C4-C6 group with stenting only included ISR in one of two limbs (50%), stent occlusion in one of two limbs (50%), ISR in two of five limbs (40%), stent occlusion in one of five limbs (20%), and ISR plus stent compression in two of five limbs (40%).

DISCUSSION

Stenting has become the first-line treatment for patients with QoL impairing symptoms of CIVO in whom conservative therapy fails. Patients presenting with CIVO can have concomitant lymphedema (phlebolymphedema) that contributes to their symptoms.[2,17] Although conservative therapy can help with the edema, the key question to pose if such therapy fails, is whether the next step should be IVUS interrogation and stenting or focused treatment of the phlebolymphedema, such as CDT, with stenting reserved for those in whom CDT fails. This study explores this aspect by dividing patients with QoL impairing symptoms of CIVO in whom standard conservative therapy has failed into those with less advanced disease (CEAP C3) and more advanced disease (CEAP C4-C6) and evaluating the role of CDT for each group. Given presence of tissue damage from venous hypertension in patients with C4-C6 disease, IVUS interrogation with an intent-to-treat first approach was pursued. In this regard, the supine foot venous pressure, which is a surrogate for CIVO and an indicator for venous hypertension,[18] had a median value of 10 mm Hg in the CEAP C3 group and was 4 mm Hg higher (14 mm Hg) in the CEAP C4-C6 group ($P = .0054$), indicative of more severe venous hypertension in the limbs with tissue damage.

Role of CDT for patients with CIVO and phlebolymphedema. Of the 74 limbs with CIVO and phlebolymphedema manifesting as C3 disease, only 9 (12%) required stenting after CDT secondary to inadequate symptom relief. Of these nine limbs, two (22%) had mild, two (22%) had moderate, and five (56%) had severe lymphedema found on lymphoscintigraphy. Overall, after CDT, the VCSS and GOS improvements were mild, with the GOS requiring 6 months to register a statistically significant improvement. However, a statistically significant change in the VAS pain score was noted at 6 weeks after CDT, with the improvement persisting over time. This likely reflects fact that even in limbs with edema, pain and discomfort represent the major symptom components. The VCSS instrument appears to be unable to capture this, given the narrow scaling the instrument uses for the pain and/or discomfort component. Another useful set of metrics in this context is the lymphedema-specific metrics (eg, LLIS, leg circumference measurements, and percentage of impairment). These are also able to capture early the benefit that the MLD component of CDT provides. We found statistically significant improvement in the QoL of C3 patients undergoing CDT, as evidenced by the 25-point improvement in their CIVIQ-20 score after CDT. Another aspect is that even in limbs with C4-C6 disease, CDT has a role to play. Of the limbs with C4-C6 disease, 43 (36%) underwent stenting and then CDT because of persistent QoL impairing symptoms. Of these limbs, 26 (60%) had mild, 4 (9%) had moderate, and 13 (30%) had severe lymphedema on lymphoscintigraphy. After CDT, statistically significant improvement was found in the VCSS, VAS pain score, and GOS at 6 weeks, which was maintained at 3, 6, and 12 months. Again, patients experienced QoL improvement as shown by the 27-point improvement of their CIVIQ-20 score after CDT. Significant improvements in

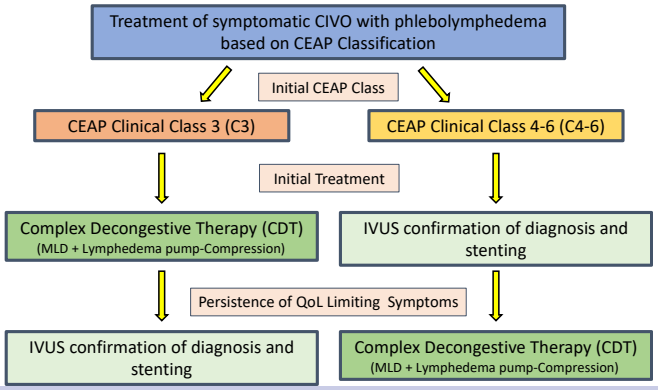

Fig 2. Algorithm for treatment of chronic iliofemoral venous obstruction (CIVO) with phlebolymphedema in patients with quality-of-life (QoL) impairing symptoms for whom conservative therapy failed (details provided in the text). *CEAP,* Clinical, etiologic, anatomic, pathophysiologic; *IVUS,* intravascular ultrasound; *MLD,* manual lymphatic drainage.

lymphedema-specific metrics (eg, LLIS, leg circumference measurements, and percentage of impairment) were also noted. One difference in the C4-C6 cohort is that, after CDT, the improvement in the VCSS and GOS appears to be greater than in that in the C3 cohort, with the improvement in GOS also occurring earlier.

Role of stenting in patients with CIVO and phlebolymphedema. Stenting, although an invasive intervention, has a role to play for patients with CIVO and phlebolymphedema and should be the first-line treatment for limbs with evidence of tissue damage (CEAP C4-C6 disease) because such damage is indicative of disease progression from temporary symptoms to permanent tissue damage. However, these patients do not uniformly benefit from stenting, as evidenced by the sizeable percentage of patients who experience an absence or minimal relief of their edema after stenting.[3,4] Such patients should be offered CDT. The benefit from the latter is significant in such limbs and can have positive effects on their QoL. On analysis, at baseline, patients who underwent CDT after stenting had similar incidence of severe lymphedema on lymphoscintigraphy as patients who did not undergo CDT after stenting. However, patients who underwent CDT after stenting had significantly higher VCSSs (6 vs 4; $P = .0007$), GOSs (3 vs 1; $P < .0001$]), and VAS pain scores (5 vs 1; $P < .0001$) at 6 weeks after stenting compared with those who did not, indicating that the severity of lymphedema on lymphoscintigraphy might not be able to prognosticate symptom improvement or the necessity for CDT after stenting. In patients with less severe disease (CEAP C3 disease), stenting should only be pursued for those patients with persistent or residual symptoms that impair their QoL despite CDT. This is because disease progression from C3 to C4-C6 is not certain. The use of such a protocol will reduce the requirement for iliofemoral venous stenting in patients with QoL impairing CIVO and optimize outcomes. However, this requires a comprehensive evaluation of the venous and lymphatic system at the initial evaluation before the formulation of a treatment regimen. An algorithm that outlines this approach is suggested in Fig 2.

Study limitations. The relatively small size of the study sample and the loss of patients to follow-up after treatment represent shortcomings. These deficiencies are difficult to counter and likely have a bearing on the results of the study. Additionally, the absence of a comparator group is a limitation. However, IVUS interrogation and stenting is an invasive intervention with periprocedural morbidity, in addition to a 20% long-term reintervention rate. These factors must be considered when using a comparator such as an invasive intervention in limbs without tissue damage (C3 limbs). The use of historical controls has multiple inherent inadequacies. In addition, in limbs with tissue damage (C4-C6), the venous hypertension has become severe enough to cause tissue damage. Thus, in this setting, the etiology (ie, iliofemoral venous obstruction) must be corrected, instead of focusing on symptom alleviation. Access to qualified therapists is a limiting factor in pursuing CDT. Also, lymphedema pump availability is subject to insurance approval. It should also be emphasized that long-term follow-up is essential to determine compliance with lymphedema pump and compression therapy and consequent maintenance of improvement over time.

CONCLUSIONS

For CEAP C3 patients with phlebolymphedema due to CIVO, CDT should be a part of the first line of treatment. Stenting should be reserved for those with QoL impairing symptoms despite CDT. CDT also helps provide symptom relief for patients with more advanced CEAP C4-C6 disease with persistent or residual edema after stenting. Further study is warranted.

AUTHOR CONTRIBUTIONS

Conception and design: AJ
Analysis and interpretation: AJ, DT
Data collection: DT
Writing the article: AJ, DT
Critical revision of the article: AJ
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DISCLOSURES

None.

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