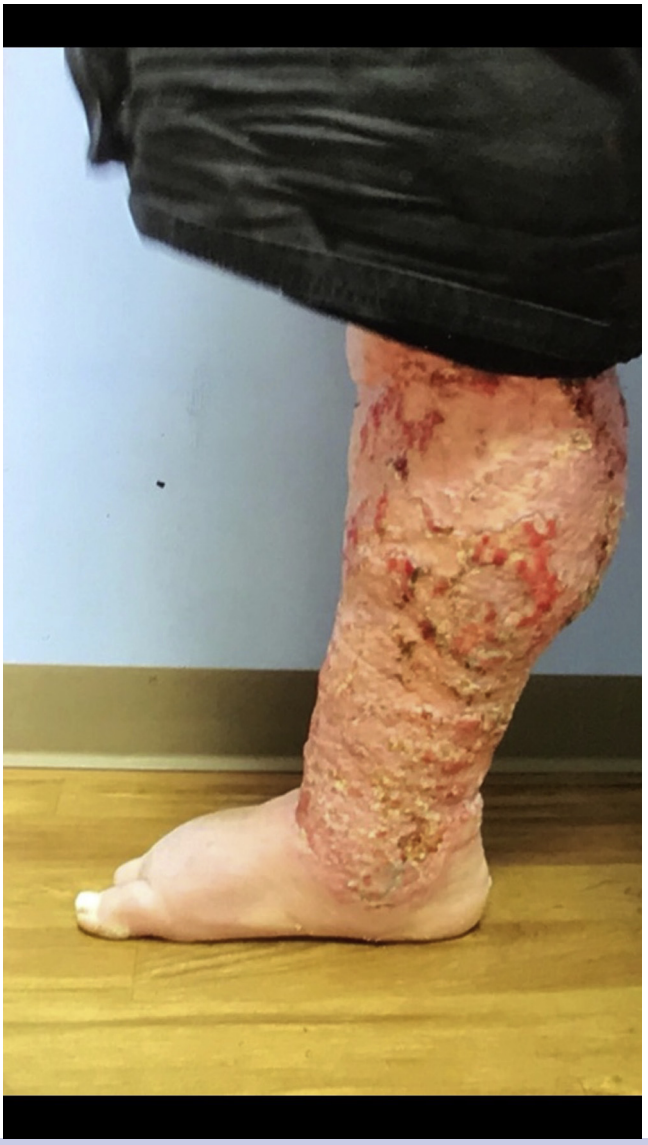

Fig 2. Image 6 weeks after Charles procedure.

Methods: Two patients (mean age, 42.5 years) were selected to undergo surgical reduction of severe lower extremity lymphedema. A skin incision was made exposing subcutaneous tissues. A Harmonic scalpel (Ethicon, Somerville, NJ), was used to cut and to coagulate tissues down to the level of the fascia while maintaining hemostasis. The dissection was then carried circumferentially around the extremity to resect all skin and lymphedematous tissue. The specimen was removed and weighed. Split-thickness skin grafts were constructed using the resected specimen and applied to the operative defect. Finally, a negative pressure vacuum system was applied to facilitate wound healing. The patients were observed in the hospital until medically appropriate for discharge and subsequently followed up in the outpatient clinic.

Results: Mean operative time was 8 hours 55 minutes, and blood loss was 2450 mL. Patients were observed for wound healing and quality of life improvement. At 2 months postoperatively, patient 1 had significant wound epithelialization. He found employment and was able to walk >1 mile daily. At 4 months postoperatively, the main complaint was focal wound tenderness. Fig 1 is a preoperative image and Fig 2 is a 4-month postoperative image. He continues to express satisfaction and improved functionality leading to overall improved quality of life. Patient 2 required readmission 1 week postoperatively for inadequate home wound care assistance. The patient has experienced improved mobility thus far. No significant wound complications have been encountered for either patient.

Conclusions: Direct surgical excision with reconstruction is an invasive treatment option with potentially severe complications. Initial results in our patients suggest that the modified Charles procedure is an effective management option for severe lymphedema refractory to conservative therapy. En bloc removal of lymphedematous tissue increases functionality and improves quality of life. Further longitudinal follow-up is needed to assess progression of wound healing and percentage skin graft take. A multidisciplinary approach to minimize operative time and blood loss and to optimize skin grafting results appears to benefit this population of difficult patients.

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Primary Chronic Venous Insufficiency Is Distinguished by Attenuated Circulating Inflammatory Mediators and Healing Networks

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Objective: Inflammation promotes venous leg ulcers (VLUs) in post-thrombotic syndrome. However, it is not clear how inflammation affects VLU in primary venous reflux. Computational modeling has demonstrated differences in cytokine and chemokine networks in other wound healing paradigms. We hypothesize that serum inflammatory mediators are differentially expressed and disorganized in primary chronic venous insufficiency (CVI), which may be a mechanism for future VLU.

Methods: Participants were recruited prospectively with Institutional Review Board approval. Blood was obtained during sclerotherapy or endovenous thermal ablation for primary CVI without ulcer (Clinical, Etiology, Anatomy, and Pathophysiology [CEAP] class C2-C4). Control patients without CVI underwent phlebotomy from great saphenous and antecubital veins. Demographics, Venous Clinical Severity Score, and body mass index (BMI) were collected. Twenty-five mediators previously shown to be important in wound healing were measured in serum with Luminex. Values were compared using Mann-Whitney *U* test. Pearson correlations among mediators (nodes; Fig, ●) that were above a specific threshold prompted connection between nodes (edges; Fig, —). Correlations were mapped as networks (MATLAB; MathWorks, Natick, Mass). "Complexity" was determined from number of connections for each mediator and total number of mediators. A

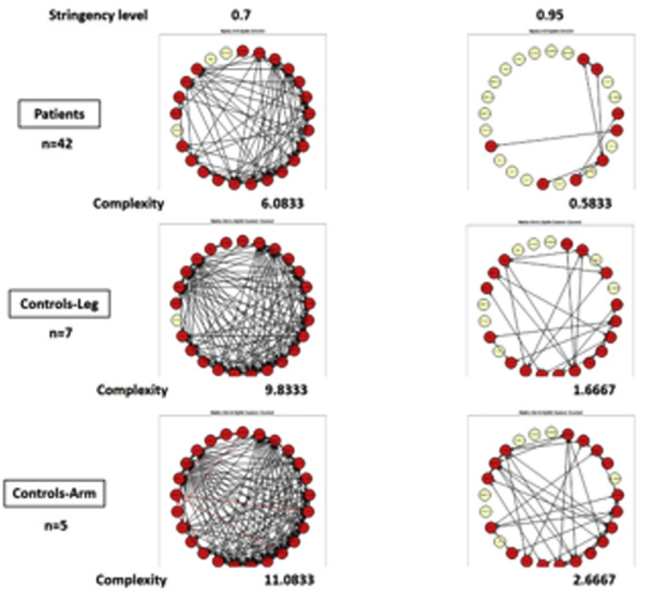

Fig. Inflammatory mediator networks in chronic venous insufficiency (CVI) patients and controls.

Table. Demographics for inflammatory mediators drawn from leg veins of patients and controls

	Patients (N = 42)		Controls (N = 7)		
	Mean	SEM	Mean	SEM	*P*
GM-CSF	19.1	3.6	61.6	0.0	<.001
IFN-γ	23	5.4	58.9	0.0	<.001
IL-12p70	12.9	2.6	41	0.0	<.001
IL-17A	10.1	2.2	27.5	0.0	<.001
IL-7	10.3	1.5	30.5	0.0	<.001
MIG	1227.2	195.4	313.4	0.0	<.001
sIL-2RA	696.9	62.3	252.1	0.0	<.001
IL-10	18	3.1	51.5	0.0	.001
IL-1b	7.5	1.5	20.9	0.0	.001
IL-4	37.7	9	107.4	0.0	.001
IFN-α2	51.8	12.4	110.5	0.0	.002
IL-1RA	117.8	21.9	306.9	0.0	.002
MIP-1β	33.3	2.6	55.6	0.0	.003
IL-12p40	116.6	28.7	252.1	0.0	.005
IP-10	685.3	65.3	311.1	0.0	.005
IL-15	12.9	2.4	24	0.0	.009
TNF-α	27.6	4.8	48.2	0.0	.011
IL-5	5	1.5	7.8	0.2	.012
IL-2	4.9	1.1	7.6	0.1	.015
IL-13	32.8	12.7	37.2	0.3	.045
IL-6	8.7	1.5	20.8	0.0	.059
IL-8	14.2	3.2	14.8	0.4	.157
Eotaxin	100.6	8.1	113	0.4	.265
MCP-1	343.7	29.9	334.7	0.3	.658
MIP-1α	5.9	1.8	2.6	0.2	1
		Range		Range	
Age, years	55.7	31-88	34.7	21-47	.008
BMI, kg/m^2	32	19-48	23	20-26	.004
VCSS	6.5	2-14	1.1	0-2	<.001
Female	71%		43%		

BMI, Body mass index; *GM-CSF,* granulocyte-macrophage colony-stimulating factor; *IFN,* interferon; *IL,* interleukin; *MCP,* monocyte chemotactic protein; *MIG,* monokine induced by γ interferon; *MIP,* macrophage inflammatory protein; *SEM,* standard error of the mean; *sIL,* soluble interleukin; *TNF,* tumor necrosis factor; *VCSS,* Venous Clinical Severity Score.
Values are reported as picogram/milliliter unless otherwise indicated.

robustness index measuring network strength was calculated by dividing number of connections at a Pearson correlation threshold of 0.95/0.7

Results: Demographics, BMI, Venous Clinical Severity Score, and mean and standard error of the mean mediator values for patients (N = 42) and controls (leg; N = 7) are shown in the Table. Significant differences ($P < .05$) were demonstrated in 20 of 25 mediators; most reflected lower concentrations in patients. In controls, arm and leg values were nearly identical to one another and across patients. The Fig demonstrates networks of inflammatory mediators for each group, showing lower network complexity and robustness in CVI vs controls. The robustness index for patients, control leg, and control arm was 0.096, 0.169, and 0.241, respectively.

Conclusions: CVI associates not only with age and BMI but also with diminished expression of many inflammatory compounds instrumental for wound healing. The relationship among these mediators is similarly weak. In contrast, mediators within competent veins show little variability and a high degree of correlation that is lacking in CVI. Dysregulated inflammatory networks in response to injury from venous hypertension may be a predisposing factor to further venous damage and VLU. Normalizing venous competency may improve baseline cytokine and chemokine interactions and the response to microstresses that can lead to wounds.

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Reduced Left Jugular Venous Remodeling and Graft Patency in a Preclinical Model

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Objective: Venous remodeling, the adaptive structural and functional reorganization of the venous wall after intervention, is still not well understood. Up to 60% of arteriovenous fistulas fail to mature adequately to sustain hemodialysis as the vein fails to adequately thicken and dilate in response to arterial flow. To examine venous remodeling, we used a pig arteriovenous graft (AVG) model to expose veins to arterial flow without changing their geometry. Because humans have smaller diameter and cross-sectional area of the left internal jugular vein (IJV) compared with the right IJV, we hypothesized that left-sided AVGs may have different remodeling and patency compared with right-sided AVGs in a preclinical model.

Methods: Ten Yorkshire male pigs (mean weight, 48 kg; age, 3.4 months) underwent ipsilateral or bilateral placement of AVGs from the