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

proximal common carotid artery to the distal IJV using polytetrafluoroethylene (6 mm in diameter, 6-7 cm in length). Pigs were observed for 1 week, 2 weeks, or 3 weeks. Select pigs underwent ultrasound measurements of flow and ultrasound and caliper measurements of vessel diameters before graft placement. Vessels were harvested from two additional pigs that had undergone procedures unrelated to the IJV for control measurements. Grafts and vessels were excised and analyzed with histologic evaluation.

Results: At baseline, there was no significant difference in peak systolic or end-diastolic velocities between the left and right IJVs. The left and right IJVs also did not demonstrate any difference in caliper-measured diameters or ultrasound-measured luminal diameters. Histologic analysis of preoperative bilateral IJVs showed no difference in wall thickness or intima-media surface area. There were 10 left-sided and 8 right-sided polytetrafluoroethylene grafts placed; 4 of 10 (40%) were patent on the left and 7 of 8 (88%) were patent on the right ($P = .03996$, χ^2 test). Postoperatively, the right IJV showed an increase in wall thickness (0.15 to 0.35 mm; $P < .0001$) and intima-media surface area (0.17 to 0.35 mm^2; $P = .0024$) compared with baseline, but significant thickening was not seen on the left side. Left-sided grafts had increased luminal macrophages at the arterial anastomosis compared with right-sided grafts, but there was no significant difference in macrophage number at the venous anastomosis.

Conclusions: Left-sided jugular veins do not thicken to the degree that right-sided veins thicken on exposure to the AVG environment. Lack of left jugular venous remodeling was associated with reduced graft patency in this preclinical model. These data suggest anatomic differences in different venous beds, emphasizing the need to understand the biology of venous remodeling to optimize graft patency.

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AMERICAN VENOUS FORUM ANNUAL MEETING ABSTRACTS

Venous Thromboembolism Prophylaxis and Its Association With Postoperative Venous Thromboembolism, Morbidity, and Mortality in a Modern Postsurgical Cohort

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Objective: Evidence-based recommendations for venous thromboembolism (VTE) prevention include assessment of risk and application of mechanical or pharmacologic prophylaxis. Trials and patient cohort series have suggested benefit compared with no prophylaxis. However, whether this translates into real-world benefit is less clear. We hypothesized that prescription of VTE prophylaxis is high and that it confers a decreased VTE incidence and mortality benefit using a multihospital quality consortium.

Methods: This statewide, retrospective cohort study analyzed the primary outcomes of VTE incidence, morbidity, and mortality among postsurgical patients with and without VTE prophylaxis between April 2013 and September 2017 from 73 hospitals. All inpatient surgical procedures (>24-hour admission) with complete variables regarding VTE prophylaxis were included. Logistic regressions with cluster robust standard errors were then used to evaluate independent risk factors for postoperative VTE despite appropriate VTE prophylaxis adjusting for patients' demographics, premorbid conditions, family and personal history of deep venous thrombosis (DVT), intraoperative risk factors, and case complexity.

Results: Among 39,430 operations, the mean age was 60 ±15 years, and 63% (n = 24,765) were female. There were 572 (1.45%) postoperative VTEs, including 214 (0.54%) pulmonary embolisms and 404 (1.02%) DVTs. The overall mortality rate was 1.84% (n = 727). VTE events were associated with a significantly increased mortality (odds ratio [OR], 1.83; 95% confidence interval [CI], 1.18-2.83; $P = .007$) and postoperative complications (OR, 3.24; 95% CI, 2.67-3.95; $P < .001$) after adjusting for confounders. At the hospital level, there was a significant positive correlation between hospital postoperative VTE and mortality ($r = 0.27$; $P < .05$). In examining various VTE prophylaxis regimens, those receiving heparin three times a day and low-molecular-weight heparin were significantly more likely to develop a postoperative VTE event (1.71% vs 0.99%; OR, 1.39; 95% CI, 1.03-1.86; $P = .029$) compared with those who received no therapy. There was no difference in mortality between the two groups. Further analysis of patients receiving appropriate VTE chemoprophylaxis identified presence of other complications (OR, 3.21; 95% CI, 2.54-4.04; $P < .001$), having a personal history of DVT (OR, 2.34; 95% CI, 1.84-2.96; $P < .001$), receiving packed red blood cells during surgery (OR, 1.80; 95% CI, 1.32-2.44; $P < .001$), not smoking (OR, 1.37; 95% CI, 1.06-1.78; $P = .015$), not having prior history of peripheral vascular disease (OR, 1.97; 95% CI, 1.37-2.83; $P < .001$), and having high-risk procedures as independent risk factors for development of breakthrough postoperative VTE.

Conclusions: In modern day postsurgical care, VTE represents a continued source of morbidity and mortality. Contrary to our hypotheses, we found that postoperative VTE prophylaxis was broadly applied yet was associated with increased rather than decreased postoperative VTE and no effect on mortality.

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Use of the Caprini Score Integrated With a Thrombodynamics Test Reduces the Incidence of Unpredicted, Postoperative Deep Venous Thrombosis

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Objective: Thrombodynamics (TD) is a global assay for hemostasis that makes it possible to follow changes in parameters such as hypercoagulation and to control an individual's response to blood thinners. The aim of this study was to compare how well the classic Caprini 2005 score and its modified version, taking into account the results of TD, predict postoperative deep venous thrombosis (DVT) in surgical patients with colorectal cancer.

Methods: This prospective observational clinical study involved 80 patients (33 men and 47 women; mean age, 73.9 ± 7.2 years) with colorectal cancer who underwent surgery. The patients were at a high risk for postoperative VTE (mean Caprini score, 9.9 ± 2.0) and received combined prophylaxis (antiembolism stockings and enoxaparin 40 mg once daily) until discharge. Enoxaparin was administered at a fixed hour according to the time of blood sampling for TD. Duplex ultrasound was performed to detect postoperative DVT before and 5 to 7 days after surgery.

Results: DVT was noted in 21 of the patients. Caprini scores significantly predicted DVT ($P < .0001$; area under the curve [AUC] = 0.839 ± 0.045). Analysis of receiver operating characteristic (ROC) curve coordinates revealed a cutoff score of 11 points, with a sensitivity of 76.2% and a specificity of 74.6%.

The results of the TD test revealed significant hypercoagulation despite administration of enoxaparin to patients with DVT. Regression analysis and ROC curves demonstrated that initial velocity of clot growth and clot size, measured 12 and 24 hours after enoxaparin administration (AUC = 0.697 ± 0.063 and AUC = 0.790 ± 0.059; AUC = 0.847 ± 0.059 and AUC = 0.803 ± 0.069, respectively), best predicted postoperative DVT. The cutoff points for DVT prediction appear to be initial velocity of clot growth >62.5 to 64.5 μm/min (normal range, 35-56 μm/min) and clot size >1351.5 to 1333.5 μm (normal range, 800-1200 μm).

The identified thresholds for the TD parameters have been integrated into the Caprini score. The total Caprini scores were recalculated for patients with at least one TD parameter that exceeded the cutoff; we also reanalyzed the ROC curves. The best predictability was found for Caprini score considering the elevation of all four TD parameters together (AUC = 0.924 ± 0.029) and increased cutoff up to 12 points with sensitivity of 85.7% and specificity of 81.4%. Using cutoffs for the original and modified scores, we calculated the number of patients whose values were under the cutoff level but who developed DVT nonetheless: 10.2% and 5.9%, respectively.

Conclusions: Integrating TD parameters into the Caprini score increases one's ability to predict postoperative DVT and to reduce the number of unpredicted complications.