LITERATURE HIGHLIGHTS

# C-TRACT Trial Insights

A closer look at the landmark trial that evaluated iliac vein stenting for postthrombotic syndrome and how to apply its findings in practice.

**With Suresh Vedantham, MD**

In a randomized controlled trial (RCT) evaluating endovascular therapy for postthrombotic syndrome (PTS), Vedantham et al found that iliac vein stenting plus standard care significantly reduced PTS severity and improved quality of life (QOL) compared with standard care alone, although bleeding rates were higher with intervention. Results of the C-TRACT trial were published online in *The New England Journal of Medicine* (*NEJM*).[1]

Investigators conducted the phase 3, multicenter, open-label, assessor-blinded, National Institutes of Health (NIH)–sponsored C-TRACT trial across 29 United States centers from July 2018 through June 2025, enrolling 225 patients with moderate or severe PTS and imaging-confirmed iliac vein obstruction after prior deep vein thrombosis (DVT). Patients were randomized 1:1 via a Web-based central randomization system to receive either endovascular therapy consisting of iliac vein stent placement plus enhanced antithrombotic therapy and standard PTS care or standard PTS care alone. Standard therapy included compression therapy, anticoagulation, guidance on lifestyle modifications (eg, exercise, smoking cessation), and ulcer management when appropriate.

Eligible patients had substantial venous symptoms affecting daily function, including chronic pain, swelling, skin changes, or venous ulcers. PTS was defined as chronic venous disease in the ipsilateral leg of a patient who had DVT at least 3 months before enrollment. Moderate or severe PTS was defined as a Venous Clinical Severity Score (VCSS) ≥ 8, a Villalta score ≥ 10, or the presence of an open venous ulcer. Baseline demographics and disease severity were well balanced between groups, with mean VCSS scores of approximately 12 points in both arms.

The primary endpoint was PTS severity at 6 months, measured using the validated VCSS tool by evaluators blinded to treatment assignment. Secondary outcomes included venous disease–specific and overall QOL at 6 months (assessed using the VEINES-QOL questionnaire and SF-36, respectively), Villalta scores, calf volume, venous ulcer status, recurrent venous thromboembolism (VTE), bleeding, and mortality. Investigators used linear mixed models adjusted for baseline severity, stratification factors, and clinical center effects.

## KEY FINDINGS

- The addition of endovascular iliac vein stenting to standard care significantly reduced PTS severity compared with standard care alone.
- Patients undergoing endovascular therapy experienced substantial improvements in venous disease–specific and overall QOL at 6 months.
- Iliac vein stenting successfully restored venous patency in most treated patients, with procedural success achieved in > 96% of cases.
- Bleeding events were more common in the endovascular therapy group, primarily driven by nonmajor bleeding associated with intensified antithrombotic therapy.
- Rates of recurrent VTE, venous ulcers, and death were low and similar between treatment groups.

At 6 months, patients treated with endovascular therapy had significantly lower PTS severity scores than patients receiving standard care alone (mean [± SD] VCSS, 8.1 ± 5.1 vs 10.0 ± 4.9; adjusted difference, −2.0; 95% CI, −3.2 to −0.8; $P = .001$). A substantially larger proportion of patients in the endovascular arm shifted into lower severity VCSS and Villalta categories over follow-up.

Venous disease–specific and overall QOL also favored intervention. Mean VEINES-QOL scores were signifi-

cantly higher in the endovascular group (62.8 ± 24.6 vs 48.6 ± 26.7; adjusted difference, 14.5 points; 95% CI, 9.5-19.4; $P < .001$). Overall physical SF-36 scores similarly improved with intervention (56.0 ± 16.4 vs 49.9 ± 17.1; adjusted difference, 6.1 points; 95% CI, 2.8-9.3; $P < .001$). The prevalence of open venous ulcers and calf volume changes were similar between groups.

Endovascular procedures were successfully completed in 96.1% of attempted cases (median time to intervention, 16 days; IQR, 9-28 days), with a median of 2.1 stents implanted per patient. Complete occlusion decreased from 51.5% (52/101 patients) preprocedure to 5.0% (5/101 patients) postprocedure, as shown on venography and intravascular ultrasound (IVUS).

Bleeding events occurred more frequently in the endovascular therapy group than in the standard care group (11.6% vs 3.6%; risk ratio, 3.22; 95% CI, 1.07-9.69; $P = .03$), driven primarily by nonmajor bleeding associated with intensified antithrombotic therapy. Major bleeding was uncommon and no fatal bleeding events occurred. Rates of recurrent VTE and death were low and similar between groups.

Investigators noted several limitations, including the open-label design, relatively short 6-month follow-up, variability in physician-directed standard care, reduced final sample size compared with the original target enrollment, and limited applicability to lower-volume centers with less venous intervention experience. Long-term follow-up is ongoing to better define durability, stent patency, ulcer outcomes, and extended safety profiles.

This RCT demonstrated that the combination of endovascular iliac vein stenting and standard care improved symptom burden and health-related QOL in patients with moderate or severe PTS and iliac vein obstruction. The findings provide some of the strongest prospective evidence to date supporting venous stenting in carefully selected patients with advanced postthrombotic disease, while underscoring the need to balance symptomatic benefit against bleeding risk.

## *ENDOVASCULAR TODAY ASKS…*

**Suresh Vedantham, MD, lead investigator of C-TRACT, commented on the study's findings and what they mean for current practice.**

### How can the C-TRACT findings affect the role of iliac vein stenting in the routine management of patients with moderate or severe PTS?

For many years, endovascular proceduralists have observed clinical improvement in many patients with PTS after Iliac vein stenting. However, the degree of change varied and the incremental benefit over standard care had not been quantified in a multicenter RCT. This was an important limitation given that stents are permanent implants, and there are inherent risks related to the endovascular intervention and the intensified antithrombotic therapy afterward. Practitioners can now move forward with confidence that stenting does offer incremental benefits to patients that are clinically meaningful. Patients with PTS should be referred to knowledgeable specialists. Patients with clinical features that suggest iliofemoral segment involvement (eg, history of iliofemoral DVT, thigh symptoms, entire-limb swelling, venous claudication, sonographically abnormal common femoral vein anatomy or Doppler waveform) should have the iliac vein evaluated if they have symptoms that limit activities of daily living. On the other hand, patients with mild symptoms, poor inflow to the common femoral vein, or high bleeding risk are not optimal stenting candidates.

### C-TRACT demonstrated meaningful improvements in both VCSS and QOL measures. What is the magnitude of this finding for patients in day-to-day practice?

The VCSS was chosen as C-TRACT's primary outcome measure for a few reasons: (1) It can be objectively assessed by a blinded examiner, avoiding bias; (2) it has good discrimination at the more severe end of the venous disease spectrum; (3) being derived directly from the CEAP (clinical, etiologic, anatomic, pathophysiologic) classification system, it clearly measures elements of chronic venous disease. Drawbacks are that it mostly assesses clinical signs (not symptoms), and, even with successful treatment, many clinical signs of chronic venous disease change slowly over time. In considering the between-arm VCSS change in C-TRACT over 6 months and the rigorous methodology with which these data were obtained and analyzed, physicians can have very high confidence that endovascular therapy meaningfully affected PTS (the disease). The improvement in QOL, which is likely to stem from symptom changes, was more than double the minimal clinically important differences on the scales, so stenting is very likely a high-impact procedure for most patients through 6 months.

### Bleeding rates were higher in the endovascular arm, largely due to intensified antithrombotic

**therapy. How should clinicians balance symptom improvement against bleeding risk when selecting patients for intervention?**

During the initial clinic assessment, once it is determined that iliac vein stenting may be indicated, each patient should undergo an individualized assessment of their risk of bleeding. In the PTS population, anticoagulation will almost always be essential after stent placement. If a patient has a very high risk of bleeding with anticoagulation, stenting may not be advisable, but other active methods to address PTS symptoms can be used. For patients with substantial disability and a moderate risk of bleeding, the duration of therapy and the approach to concomitant antiplatelet therapy use can be adjusted to help optimize risk and benefit. The ARIVA study[2] and hopefully other studies will be helpful in tailoring care in the future, and the potential for new classes of antithrombotic medical to strike a better balance in optimizing patency versus bleeding is exciting. Collaboration with a stenting-aware hematologist or vascular internist is strongly encouraged.

**The study included experienced operators at specialized centers. What are the best steps that can be taken to ensure these results are generalizable? What are the implications for training, credentialing, and procedural standardization?**

Recanalizing chronically occluded iliac veins is challenging, with a steep learning curve. Updated procedural tools are helping new providers execute the technical aspects of stent placement with greater ease, but patency loss can also stem from poor patient selection (eg, patients with poor inflow) and deficiencies in postprocedure care. Guidelines from the Society of Interventional Radiology and the European Society for Vascular Surgery are among the excellent resources that providers are encouraged to review as they start caring for the PTS patient population.[3,4] Where possible, local proctorship mechanisms should be established to help less-experienced providers avoid the common causes of failure. The recent proposal of an anatomic categorization system (Jalaie classification system)[5] is a positive step in developing a common language that can lead to shared understanding of which PTS subpopulations should or should not be treated. I expect the C-TRACT trial's secondary analyses to provide a stronger understanding of predictors of success or failure that can ultimately be broadly shared with practitioners. The development of regional centers of excellence around advanced thrombosis care is also an idea worthy of consideration.

**What can you share about the importance of long-term surveillance to ensure durable patency? What should operators and their practices have in place in terms of follow-up?**

Prospective studies and large case series have shown that a substantial minority of patients with PTS will develop stent restenosis or occlusion during the first few years after stent placement. With timely reintervention, secondary patency rates can be acceptable when weighed against the serious PTS-related disability that many patients face. Therefore, long-term clinic follow-up is crucial to identify symptom recurrence, and patients should be regularly reminded to (1) attend routine follow-up visits; (2) comply with recommended antithrombotic therapy; and (3) notify the provider immediately if the pattern of daily symptoms changes for the worse or if there is suspicion for bleeding. The commitment to provide excellent follow-up should be considered a prerequisite for delivering stent-based therapy. Providers should be able to see patients in clinic and obtain duplex ultrasound on relatively short notice and schedule patients for venography and IVUS when applicable. To optimize decision-making with respect to antithrombotic therapy and ensure that patients can quickly obtain a re-supply of their medications, local collaborations among endovascular providers and medical thrombosis experts can be very helpful.

**What questions remain regarding durability, stent patency, ulcer healing, and the long-term risk/benefit profile of intervention?**

Many questions remain to be answered, and the C-TRACT data will help with some of it. Clinically, it will be important to understand the durability of the observed QOL benefits and the incremental cost-effectiveness of intervention (both of these analyses are underway). We did not observe a difference in the overall prevalence of venous ulcer at 6 months, but we will describe in more detail the impact of iliac vein stenting on the healing of preexisting venous ulcers. The study evaluated iliac vein patency and superficial and deep venous valvular reflux by ultrasound—it will be interesting to see what (if anything) changed after intervention and to correlate any anatomic and physiologic changes with the clinical outcome findings. The size of the VCSS change was modest and we did not see a difference in measured calf volume, so it will be interesting to dive deeper to learn what PTS elements (symptoms and clinical signs) and QOL domains were improved after endovascular therapy. We also plan to explore predictors of bleeding after stenting, both in terms of baseline patient characteristics and posttreatment use of antithrombotic agents.

**Let's talk more about what this means for patients with this condition, whom you've said**

**often suffer in silence. How can these results and their publication in *NEJM* improve awareness and referral pathways? What steps need to be taken to ensure improvement on both fronts now that the benefits are established?**

The demonstrated benefit in a rigorous NIH-sponsored trial with strong precautions against bias will hopefully help encourage medical providers to refer their PTS patients for consultation. At present, PTS is often ignored, so our broad ambition should be to ensure that every patient affected by PTS receives individualized assessment and targeted care, whether or not it includes stenting. Formation of local multidisciplinary teams to guide the care of all patients who present with high-risk DVT and identify appropriate stenting candidates would be a terrific outcome. I hope that C-TRACT can help to catalyze this kind of transformational change in our approach to extensive DVT. We have shown that even severe PTS is treatable and that an open iliac vein is important! ■

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