

# C-TRACT: What We've Learned About DVT Trial Design

Dr. Suresh Vedantham discusses his experience with C-TRACT and other DVT trials and their potential implications on future trial design and treatment standards.



## What can you tell us about the goals, design, and timeline of the C-TRACT study?

**Dr. Vedantham:** The Chronic Venous Thrombosis: Relief With Adjunctive Catheter-Directed Therapy (C-TRACT) study is a multicenter randomized controlled trial that will evaluate the

use of endovascular therapy in patients with advanced postthrombotic syndrome (PTS). Patients will be randomized to receive either optimal standard therapy (including medical, compressive, and ulcer care therapies) or optimal standard therapy plus endovascular therapy (stent placement for occluded iliac veins followed by endovenous ablation for major saphenous vein reflux). The primary objective of the study is to determine whether endovascular therapy provides greater improvement in health-related quality of life and PTS severity than standard therapy alone. The study's development was supported by a clinical trial planning grant from the National Heart, Lung, and Blood Institute (NHLBI). A grant application for the full trial has been submitted to the NHLBI and is under review. If funded on the first attempt, the trial could begin as early as spring 2017.

## How has your work as principal investigator of the ATTRACT trial helped in designing C-TRACT? In other words, what lessons from ATTRACT can be applied to future study designs?

**Dr. Vedantham:** The C-TRACT study is proposed by the same group (with a few changes) of deep vein thrombosis (DVT) research leaders who successfully conducted the NHLBI-sponsored ATTRACT trial. For that study, we used NHLBI funds to support a clinical coordinating center

(Washington University in St. Louis), data coordinating center (Ontario Clinical Oncology Group at McMaster University), ultrasound core laboratory (VasCore at Massachusetts General Hospital), and economic core laboratory (Mid America Heart Institute), as well as to build a consortium of United States-based clinical centers with multispecialty investigator teams that bring strong expertise in the medical and endovascular aspects of DVT care. Collectively, we are eager to realize the full impact of this unique infrastructure by taking on the challenge of determining whether endovascular therapy can alleviate suffering in patients with advanced PTS. The ATTRACT trial was very challenging to complete, but we believe that through that experience, the DVT community has gained tremendous capabilities in terms of being able to answer new questions through pivotal clinical trials.

## Although it is still early, have there been any lessons learned in designing C-TRACT?

**Dr. Vedantham:** No two trials are the same. The main lesson we have applied to our C-TRACT planning is the importance of optimizing scientific rigor and real-world feasibility by obtaining the input of a wide range of physicians who manage PTS in diverse practice settings on a daily basis. Among other steps, our planning process included hosting an expert panel meeting that was attended by 35 PTS experts of diverse backgrounds. This has provided us tremendous insight into how PTS is managed around the country, enabling us to estimate the pros and cons of different choices we could make in designing the study. Once the trial starts, I'm sure we will encounter new challenges that need to be managed.

### In what ways is C-TRACT more challenging?

**Dr. Vedantham:** Two obvious challenges of C-TRACT are (1) the fact that most PTS patients are outpatients who are not rapidly referred to a vascular specialist (ie, the challenge will be how to make them “visible” to hospital-based research teams), and (2) the fact that advanced PTS is a life-limiting condition, which can make patient randomization and adherence to the assigned treatment arm challenging. We feel confident that we can overcome this barrier with robust education and protocol flexibility.

### Can trials in this population overcome the heterogeneity of patients and how they are managed?

**Dr. Vedantham:** Heterogeneity is indeed a challenge, and there certainly are limits to our ability to address different patient subgroups in a study of a few hundred participants. We will be restricting enrollment to patients with advanced PTS, as defined by higher scores on validated PTS measures—that will provide one level of uniformity. We will provide guidelines for the use of endovascular and noninvasive PTS therapies in the trial, but physicians will still have flexibility to individualize care, which will discourage outlier practices. We expect to be collecting blood samples from enrolled participants for genomic and other analyses in the hope that any markers identified can be used to better understand subgroups of responders and nonresponders.

### When do you anticipate the publication of the ATTRACT data?

**Dr. Vedantham:** We expect the primary ATTRACT data to be published in early 2017, with additional publications appearing in print during the remainder of 2017 and 2018.

### What do you predict the impact of favorable outcomes would be?

**Dr. Vedantham:** If ATTRACT finds that pharmacomechanical catheter-directed thrombolysis (PCDT) indeed prevents PTS, we hope physicians will move toward routine consideration of PCDT for patients with proximal DVT who are deemed to be at low risk for bleeding. This would hopefully involve ensuring that local work flows support rapid referral of DVT patients to vascular specialists near the time of initial diagnosis and strong monitoring schemes during treatment. A positive study would send a clear message to payors and to research sponsors that having an “open vein” is crucially important to a patient’s long-term outcome. As health care reform continues, it is important for the venous community to highlight the value of including PTS prevention

as an essential measure of quality care in DVT patients—at present, the metrics are centered only around prevention of pulmonary embolism and recurrent DVT. Finally, the real long-term value of ATTRACT may be to spur investment in better and safer ways to remove thrombus, enabling many more patients to be treated.

### What about the potential impact of negative outcomes?

**Dr. Vedantham:** There are different kinds of negative outcomes. If ATTRACT does not show a PTS prevention benefit for PCDT, we would explore the data to determine if (1) the operators did not successfully open the veins, (2) the operators did open the veins but patients developed recurrent DVT and PTS during follow-up, or (3) the operators did open the veins but patients developed PTS anyway, and recurrent DVT does not seem to be the mechanism. Each of these possibilities would have different effects, and research might need to be redirected to explore what other factors beyond clot removal and venous patency explain the onset of PTS in this population. But any way you cut it, given the risks of PCDT, we would expect the clinical threshold for use of thrombolytic therapy to rise significantly if the study does not show a significant clinical benefit.

### What other trials in the “TRACT” family are in the works?

**Dr. Vedantham:** The “PE-TRACT” Trial is a multicenter randomized controlled trial evaluating the use of CDT for patients with submassive pulmonary embolism. Akhilesh Sista, MD, with New York University is the national principal investigator for this study, and a grant application will be submitted to the National Institutes of Health later this year. I am very excited about this study, and I hope the venous thromboembolism research community will provide Dr. Sista the same determined support that they so graciously have provided to me. ■

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