

INTERVIEW

Best Practices for Anticoagulation Management After Venous Interventions

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01/21/2020

Vascular Disease Management spoke with Raghu Kolluri, MD, MS, RVT, FSVM, President for the Society for Vascular Medicine and System Medical Director, Vascular Medicine at OhioHealth Riverside Methodist Hospital. Dr. Kolluri discussed challenges surrounding anticoagulation therapy and venous interventions. He will be presenting on these topics at the 2020 International Symposium on Endovascular Therapy (ISET) in Hollywood, Florida.

Tell us about some current challenges regarding anticoagulation and venous interventions, particularly in relation to clinical trials.

Anticoagulation guidelines are not very helpful as they do not stipulate the anticoagulation treatment prescription after a venous stent placement. Current clinical trial protocols also do not typically dictate standard anticoagulation after venous intervention, and this lack of standardization results in heterogeneity in patient treatment. For example, we normally start anticoagulation in a certain manner when treating deep vein thrombosis (DVT) or pulmonary embolism (PE). We might recommend beginning treatment with enoxaparin (Lovenox) and then transition to warfarin (Coumadin) over 5 to 7 days. However, some physicians are proponents of using enoxaparin for 6 weeks, before switching the patient to warfarin. Alternatively, other physicians prefer to start with direct oral anticoagulants (DOACs) such as rivaroxaban (Xarelto) and apixaban (Eliquis) immediately after the intervention, without having any bridge with enoxaparin or heparin. There is back and forth discussion between the two approaches. Some physicians will cite anecdotal failures with DOACs, and others will say they have not had such failures with DOACs and do not understand the reasoning behind 6 weeks of enoxaparin treatment.

How does treatment of venous disease differ from treatment of coronary artery disease or peripheral artery disease (PAD)?

Disease manifestation is not clear cut in venous disease, unlike in coronary artery disease or PAD. We often treat for a certain percentage of stenosis or occlusion in coronary artery disease or PAD, whereas the treatment is more complex in venous disease. We could be treating for just a stenosis, or we could be treating stenosis with extensive fibrosis, or stenosis with fresh clot. What are the different approaches that we should take to treat each one of patients? We do not have an answer to that question.

What would you like to see happen to address the problem of better, individualized treatment for patients?

Venous stent related clinical trials have been typically IDE studies that are focused on obtaining FDA approval. Now that we have venous stents on label, we should begin collecting data to create treatment algorithms for the optimal therapy for patients with venous stents. We need to develop evidence-based approaches rather than the current approaches that are based on personal and anecdotal experience.

What are some of the challenges surrounding antiplatelet therapy in patients with venous stents?

There are no data for optimal antiplatelet therapy. The typical approach is to use clopidogrel (Plavix) for 6 weeks and then stop clopidogrel and switch to aspirin. However, no one knows the true answer to the question of optimal antiplatelet therapy. We may be surprised with the real-world adverse events related to antiplatelet and anticoagulation therapy as more venous stents go on label.

In the absence of guidelines, what are some changes you would like to see in the way that anticoagulation is handled with venous patients?

One could consider dividing these patients into 3 broad groups – 1) patients that need to be treated more aggressively with medications such as enoxaparin for several weeks 2) patients that need standard approach of enoxaparin/heparin to warfarin bridge and 3) patients who can be treated with DOAC immediately. We don't have much data to answer these simple anticoagulation management related questions. A recent coronary study called the TWILIGHT study randomized 7,000 patients in each arm to assess the efficacy of ticagrelor monotherapy vs ticagrelor and aspirin therapy.¹ On the other hand, a recent meta-analysis of both anticoagulation and antiplatelet therapy after venous stents had fewer than 100 patients available at 12 months. These low numbers

of patients in studies are a profound deficiency that we need to overcome. Now that venous stents have been approved, we need to take the steps necessary to better understand anticoagulation. Steady state anticoagulation is important. Suboptimal anticoagulation will lead to stent thrombosis. Similarly, too much anticoagulation and bleeding complications can lead to interruption of anticoagulation, which in turn can lead to stent thrombosis.

Do you have any tips for colleagues on optimally managing anticoagulation duration?

Anticoagulation duration should depend on the reason for the deep vein thrombosis (DVT) itself, not the stent. Did the person have an idiopathic DVT? Did the person have a circumstantial or provoked DVT? Additionally, in the case of a provoked DVT, does that patient have continued risks for having that provocation? For example, a morbidly obese, bed-bound patient who has a DVT will need different treatment than a healthy 52-year-old who has a DVT after a major operation.

The Einstein Choice trial compared 10 mg of rivaroxaban to aspirin **81mg.**² There was no significant difference in bleeding in both groups. As a result of this trial, I am lot more comfortable recommending long-term anticoagulation to patients who require it. Ultimately, duration of anticoagulation is based on shared decision making and should be individualized, and a typical consultation time for anticoagulation recommendation may take up to 40 minutes.

There will be a live physical examination at ISET, and you are participating on the panel. Can you tell us more about the examination?

Physical examination is a lost art in many cases due to decreasing reimbursement and lack of incentive to spend time spent with our patients. The physical examination is a key part of ISET, and I am glad it will be performed by Michael Jaff, MD, and highlighted at ISET.

Are there any upcoming studies that you are closely watching?

There are several venous stent IDE trials in progress. We are also the core lab for the Treatment of Acute Iliofemoral Deep Vein Thrombosis (CLEAR-DVT) trial, an investigator-initiated trial that follows on the heels of the Acute Venous Thrombosis: Thrombus Removal with Adjunctive Catheter-Directed Thrombolysis (ATTRACT) trial. CLEAR-DVT is focusing on contemporary treatment of DVT that probably has less of a bleeding risk than what ATTRACT used. I am looking forward to the results of CLEAR-DVT because it has some functional, patient-reported components such as 6-minute walking distance.

What are the main takeaways from your talk at ISET?

Don't ignore anticoagulation. Don't ignore antiplatelet therapy. Clinical trialists and high-volume centers need to generate post-market data and outcomes so that all of us can learn. In the meantime, clinicians should tailor therapy to individual patients' needs in a systematic way in the three groups that we discussed: heparin to warfarin, DOACs, and extended enoxaparin therapy.

References

1. Mehran R, Baber U, Sharma SK, et al. Ticagrelor with or without aspirin in high-risk patients after PCI. *N Engl J Med.* 2019;381(21):2032-2042.
2. Weitz JI, Lensing AWA, Prins MH, et al. Rivaroxaban or aspirin for extended treatment of venous thromboembolism. *N Engl J Med.* 2017;376(13):1211-1222.