Deciding DVT Treatment After ATTRACT: An Expert Panel Discussion

Leading venous interventionalists from around the globe discuss the ATTRACT results and their approach to DVT treatment.

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What were your first thoughts upon hearing the results of the ATTRACT study?

Prof. Sapoval: I was lucky to be at the first presentation of the data in Washington, DC, in early March. I was surprised and disappointed, to some extent, by the results. After listening to the discussions and the more detailed analysis of the data, I think there is still some big hope in the future of the technology to address this problem.

Dr. Silver: The results of the ATTRACT trial were very sobering to me. I think a nearly 50% rate of postthrombotic syndrome (PTS) in both treatment arms in the year 2017 is not acceptable. In particular, in the population of iliofemoral deep vein thrombosis (DVT) patients who have the greatest risk of PTS with medical therapy, we must do better. The approach to endovascular vein intervention has certainly evolved since ATTRACT—in particular the knowledge gained by intravascular ultrasound (IVUS) and newer thrombectomy devices that offer the advantage of a single-session treatment.

Dr. Del Giudice: I think that we can use these results to understand where we have to go, because there are a lot of things that could be better, and we can use that to create a new study in order to examine patients such as iliofemoral patients with the new devices on the market dedicated to intravenous treatment.

Mr. Black: First, Dr. Suresh Vedantham has done wonderfully to get a trial through. It's an enormous effort to get this trial completed and see it through entirely. You need to congratulate somebody on that, regardless of the results.

Dr. de Graaf and I discussed the ATTRACT trial right before the results came out, and we both were expecting, at best, slightly positive, probably equivocal results because of the inclusion of femoropopliteal DVT. My practice does not treat those patients, so I don't expect to see a huge shift in what we do, because we've always focused on iliofemoral.

Dr. Murphy: The ATTRACT trial was a well-intentioned trial that compared best standard interventional practice at the time to traditional anticoagulation for the prevention of PTS after acute proximal DVT. Unfortunately, and only in retrospect, there were major shortcomings in the trial, which significantly limit the ability of this trial to draw conclusions about prevention of PTS using current best interventional strategies for these patients.

What were some of the most meaningful ATTRACT data points for you?

Dr. Silver: The reduction in severity of PTS was a meaningful endpoint in ATTRACT. The primary endpoint itself was approached too binary a fashion. The presence of a Villalta score of > 5 was too strict, realizing that many patients may have had features of abnormal skin pigmentation and venous ectasia before the acute DVT that qualified them to be in ATTRACT. That is why improvement with therapy is an important endpoint, more so than Villalta score > 5, yes or no. In addition, the population of iliofemoral DVT patients who have the greatest risk of PTS and stand the most to gain by intervention were underpowered in ATTRACT.

The ATTRACT data identified a suggested increased benefit for the interventional treatment of DVT in the iliofemoral venous segments compared to the femoropopliteal segments. Are these results representative of what you see in your own practice in regard to success of treating DVT patients?

Prof. Kucher: Iliofemoral DVT is a completely different disease than femoropopliteal DVT. Not only is the location different, but they are two different diseases. Femoropopliteal DVT is always an ascending DVT. It comes from the calf, and it slowly goes up; you have the old clot in the calf, and the fresh clot in the popliteal vein and maybe the femoral vein. Imagine you now put a lysis catheter into these patients. If you're lucky, you lyse some of the fresh clot. The problem is that your inflow is not going to improve after catheter-directed thrombolysis. You will not improve functional inflow in these patients. We stopped treating these patients 10 years ago.

Iliofemoral DVT is the opposite disease. If you have an iliofemoral DVT, where the popliteal vein is open, you have proven that there is a compression. You don't have to look cross-sectional. There's always a compression syndrome there, no exception. The clot in the pelvis is old. It may sometimes be a little bit fresh, but usually it's old. You have the compression, followed by postthrombotic changes of the iliac vein. The fresh clot sits in the leg, so it's vice versa compared to the femoropopliteal disease. When you put a lysis catheter in these patients, you almost always will successfully lyse the clot of your inflow vessel. You get great inflow, you preserve vital function of your femoral vein valves, and you have to finish the treatment. You have to standardize, and you have to find a very good reason not to put a stent in. I think every single step of treatment can be standardized for treating acute iliofemoral DVT.

Dr. Garcia: Approximately 70% to 75% of the acute DVT population I see have some involvement of iliofemoral disease, whether it's iliofemoral alone or iliofemoral extending into the femoropopliteal region. At most, 25% to 30% have femoropopliteal disease alone. Of those

acute patients I treat, they have failed conservative therapy (therapeutic anticoagulation and compression), with serial ultrasound and clinical evaluation demonstrating that they are on their way to developing PTS with significant residual thrombus. As long as I can treat them within 4 weeks from the onset of the symptoms, we are highly successful in resolving the thrombus as well as the signs and symptoms of DVT and PTS. Our results when using the rapid lysis technique 4 weeks from symptom onset have led to our single-center registry demonstrating a > 90% to 95% ability to completely recanalize the deep venous system. The only caveat to waiting out therapeutic anticoagulation is that rare population of true phlegmasia, which would be treated sooner.

Mr. Black: You can standardize a lot of the procedure. I scan patients the next day, and if the stent or vessel is not patent, we take them back and lyse them again. It's aggressive, but with aggressive treatment, appropriate intervention, and appropriate follow-up, we've demonstrated results that are similar to Prof. Kucher's, which is a very low rate of PTS and a Villalta score of 0 in almost 100 patients after 1-year follow-up.

I think with a well-developed, robust program with protocolized treatment and very clear processes, you do get good results. This is not with a massive reintervention rate in the acute cases. We're still reintervening on only about one-fifth of the patients, as compared to the chronic cases, where it's almost half. But that acute group gets exceptionally good results. The patients walk into the clinic 6 weeks later with no symptoms. Their life is back to normal.

What are your acute DVT treatment best practices?

Dr. Silver: DVT management cannot be approached in a one-size-fits-all fashion. The population of iliofemoral DVT patients who have an acceptable risk of intervention, balanced by age, medical comorbidities, and functional capacity, should be considered for interventional therapy. Pharmacomechanical thrombectomy with appropriate, IVUS-driven venous stenting is our practice pattern. In those patients who have intervention, strict follow-up duplex ultrasound surveillance is essential to maximize the chances of maintaining an open vein.

Dr. Murphy: My best practices for the treatment of acute DVT include: (1) proper patient selection (eg, symptomatic patients with iliofemoral DVT and low bleeding risk), (2) intervention within 2 weeks of initial DVT symptoms, (3) intervention to include both complete or near-complete thrombus removal as well as immediate treatment of remaining proximal obstruction after clot removal, and (4) mandatory use of intraoperative IVUS to assess the degree of thrombus removal and guide any stenting procedures. After treatment, best practices include early ambulation, noninterruption of anticoagulation, and adequate follow-up with ultrasound to detect stent problems or need for reinterventions before recurrent thrombosis.

Dr. de Graaf, in the study you are currently conducting, have you experienced a similar screen rate as to what they had for ATTRACT?

Dr. de Graaf: It has been evenly slow. It's very difficult to get a study that will only include iliofemoral DVT. Dr. Vedantham actually said that was one of the reasons why they didn't do that in ATTRACT. We decided to do that for around 7 years. We're almost to the end now, but it's very difficult.

What is your perspective on the bleeding rate demonstrated by ATTRACT?

Dr. Garcia: The trial showed that catheter-directed lytic therapy as well as pharmacomechanical thrombectomy can be safely performed with a very low risk of significant bleeding. When you look at the fact that there were no fatal or catastrophic bleeds in the ATTRACT trial, that is a huge improvement over previous studies, trials, and registries. It's important to recognize that 59% of the population in ATTRACT still had infusion-first therapy, which means they are exposed to lytic therapy for a longer period of time then those receiving one-and-done pharmacomechanical thrombectomy. In our experience, these are the cases that are at a higher risk of a bleeding complication.

What are the key points that referring physician specialties should understand/take away from the ATTRACT trial?

Dr. Murphy: Despite its shortcomings, there are several important take-home points from this trial. First, this trial demonstrates that the risk for PTS after acute proximal DVT is around 50%, which is highly significant given the prevalence of acute DVT. We must do better to prevent this debilitating condition, which can parallel quality-of-life parameters comparable to other severe chronic medical conditions including diabetes, congestive heart failure, and chronic obstructive pulmonary disease.

Second, because patients with iliofemoral DVT are at higher risk for PTS than those with isolated femoropopliteal disease, the number needed to treat before seeing a benefit for femoropopliteal disease is higher. Thus, the inclusion of both patients with iliofemoral and femoropopliteal disease in the same analysis diluted the results. Separate analysis of the iliofemoral segment would have shown a significant reduction of PTS in this cohort.

Further, with data supported by all trials to date, these procedures can be done relatively safely with a low risk of major bleeding events.

Dr. Garcia: The iliofemoral population was trending toward a possible benefit in the reduction of PTS. I think it's important for referring physicians to realize that there may be a subset of patients with DVT who will go on to develop PTS. So, let's work together at trying to identify that population the best we can. If you look across the board over decades of research and studies, anywhere from 25% to 50% of the population that develops DVT goes on to develop PTS. We need to develop an algorithm that works. I truly believe that the algorithm includes early evaluation, early diagnosis, and early standard-of-care intervention with anticoagulation, compression, and ambulation. When the appropriate circumstance arises (when serial evaluation and Doppler studies fail to show improvement within the 4-week window from onset of symptoms), we should then consider whether it's appropriate to intervene.

Show your referring physicians that what you're doing is in the patient's best interest and, in my opinion, is providing the patient with the best medicine.

Dr. Silver: The interpretation of the ATTRACT trial results will be confusing to the referring physicians who, to date, have been transferring patients with iliofemoral DVTs to our tertiary care center for possible intervention. The primary endpoint conclusion, based on a binary interpretation of a Villalta score that there is no efficacy for PTS and more bleeding with intervention, will potentially make them take pause before referring a patient for intervention. The vascular community must give credit to the ATTRACT investigators for executing this very important trial and adding to the body of science, but make clear to the referral doctors that ATTRACT is not the final answer.

Would you change your practice because of the ATTRACT results?

Mr. Black: No. We never treated iliofemoral DVT alone. I think the division of proximal and distal DVT is fundamentally flawed and it came from a hematologic classification years ago that needs to be challenged to some extent. It's below the knee, knee to groin, groin and above; and these are three different things.

It won't change because we don't treat femoral DVT, because you don't see great results. We've had really good results in my iliofemoral program so far.

Dr. Garcia: I actually don't see the results impacting my practice much at all. I say this because many years ago, when we really started building our DVT practice, we realized early on that we needed to develop a way to identify the patient who was really in need of having something done. It's all about risk/benefit ratio. It's identifying that population that it's worth taking a risk on, because the benefit far outweighs the risk involved.

In agreement with our hematologists, we came up with an algorithm. If someone is in the acute phase, we put them on therapeutic anticoagulation and get them to ambulate and use compression. Depending on when they present in relation to their onset of symptoms, we perform serial ultrasound and evaluation, as previously mentioned. If, for a reasonable period of time, there is no improvement using conservative therapy and they are moving toward the risk of developing PTS, then we consider intervention.

What future data are needed?

Dr. Silver: A trial that focuses on iliofemoral DVT patients that incorporates modern-day venous intervention with improved thrombectomy catheters, mandated IVUS-driven venous stenting, and uniform postprocedural imaging to answer the open vein hypothesis must be performed. We owe this to our patients; we cannot accept a 50% rate of PTS.

Mr. Black: If another trial were to be run on iliofemoral DVT now, I think the power would be completely different than what we had with ATTRACT with single-center published results, subgroup inclusion from ATTRACT, and the CAVENT study. Looking at the analysis, you would probably find that you don't need 300 people to run a study.

Dr. Murphy: Interventional techniques have evolved beyond the techniques used in this trial. High-volume interventionalists are experiencing more promising results than suggested by the ATTRACT trial in regard to the ability of early intervention to both prevent and reduce the severity of PTS for patients with iliofemoral DVT. Data demonstrating this are clearly needed. Additionally, data demonstrating the essential role for IVUS are paramount, because experienced operators will tell you that outcomes are strongly tied to this technology. Isolated data for femoropopliteal DVT might also be useful. The number needed to treat to prevent a case of PTS in this group is likely much higher than for iliofemoral DVT and many may not require intervention. However, there may be some patient subgroups with isolated femoropopliteal DVT who benefit from treatment, and these data are lacking. ■