Many members of the vascular community were sobered by the findings reported from the ATTRACT randomized controlled trial of a near 50% rate of postthrombotic syndrome (PTS) in both treatment arms. The ATTRACT trial randomly assigned 692 patients with acute proximal deep vein thrombosis (DVT) to receive either anticoagulation alone (control group) or anticoagulation plus pharmaco-mechanical catheter-directed thrombolysis (PCDT; catheter- or device-mediated intrathrombus delivery of recombinant tissue plasminogen activator and thrombus aspiration or maceration, with or without stenting). The primary outcome was the occurrence of PTS between 6 and 24 months of follow-up.

ARE WE UNDERTREATING?
From our perspective, absolutely yes, especially for patients with iliofemoral DVT who have the highest risk of PTS with standard anticoagulation. In addition to the ATTRACT trial, recent prospective studies suggest that proximal DVT is associated with a twofold increased risk of PTS as compared with distal disease. In fact, the presence of residual thrombus in the iliofemoral distribution is a strong predictor of recurrent thrombosis and development of PTS as compared with distal thrombus. Finally, despite the use of anticoagulation and other adjunctive noninvasive therapies for proximal DVT, more than 50% of patients with this condition develop signs and symptoms consistent with PTS.

ARE WE OVERTREATING?
Based on the ATTRACT trial, the answer may seem to be yes. Not only was there no benefit in the rate of PTS at 24 months with PCDT, but the conclusion also stated that PCDT “did result in a higher risk of major bleeding.” However, from our perspective, there are some limitations of the ATTRACT trial worth highlighting for the vascular community to show that we have not yet fully answered the question of overtreatment.

The ATTRACT investigators deserve congratulations on executing this very important body of work. Furthermore, we must recognize that the field of venous intervention has gained considerable experience and improvements in technology since the start of the ATTRACT trial in 2009. However, we must also acknowledge the following shortfalls from the ATTRACT trial conclusions listed here:
1. The ATTRACT results do not apply to patients we see every day. Only 1 in 50 patients screened were randomized, which means that the results are not generalizable.
2. There was no true clinical equipoise demonstrated in enrollment among the investigators. Complete trial enrollment took 5 years (2009–2014) across 56 sites.
3. The primary endpoint was flawed, with the Villalta score applied in a binary fashion (ie, PTS: yes or no). The simple presence of a Villalta score of > 5 should not define a lack of clinical benefit.
4. ATTRACT was underpowered to evaluate the group with the highest risk of PTS, as only 57% of patients had iliofemoral DVT.
5. Only 68% of patients in the control arm completed the full 24-month follow-up, which likely underestimated the benefit of PCDT.
6. Venography was used as the endpoint to define the use of stenting; however, intravascular ultrasound
(IVUS) has been shown to be superior to venography for clinical decision-making.\(^5\)

7. Only 28% of patients with iliofemoral DVT underwent venous stenting. Research has shown that the majority of patients with an iliofemoral DVT have an underlying anatomic etiology (ie, extrinsic iliac vein compression).\(^6\)

8. The median thrombolysis duration was 21 hours. With modern-day thrombectomy, this long thrombolysis time is rarely needed, and the thrombolysis time drives the bleeding risk.

As physicians and scientists, we must continue to advance the field of venous intervention and not accept a 50% rate of PTS for our patients with acute proximal DVT.

**PARAMETERS FOR FUTURE AREAS OF STUDY**

It is humbling to consider that the incidence of venous thromboembolism in the general population may reach approximately 1.92 per 1,000 person-years.\(^7\) The incidence is increased in women of childbearing years and can reach as high as 130 per 100,000 patient-years in men.\(^8\) In fact, it is estimated that there are more than 900,000 new venous thromboembolic events per year in the United States alone.\(^9\) Therefore, an important next step involves the unequivocal development of better means for preventing DVT. The goal of future research should be the prevention, diagnosis, and treatment of acute proximal DVT. It will be critical that hospitals, practitioners, and ultimately payers adopt behaviors, algorithms, and an approach that properly acknowledges the DVT problem and provide patients with the safe prophylaxis that they deserve.

**Enhanced Diagnostics**

Before discussing considerations on the future of DVT treatment, we must first uncover a more rational and accurate way to promptly diagnose DVT within hours to days of symptom onset. As accurate as compression ultrasound is,\(^10\) it remains very operator dependent and has severe limitations in the pelvis, abdomen, upper chest, and small veins. To overcome these shortcomings, new imaging techniques have been developed and tested, such as single-photon emission CT, CT venography (CTV), positron emission tomography (PET), and various MRI techniques. From a practical standpoint, if a compression ultrasound study identifies thrombus in either the common femoral or external iliac vein, axial imaging (CTV or MRV) should be considered to better define the entire iliac venous system and inferior vena cava. The majority of patients with iliofemoral DVT documented on compression ultrasound will have some anatomic abnormality (ie, May-Thurner syndrome, extrinsic compression, venous stricture) in addition to thrombus on CTV.\(^6\) Newer techniques such as magnetic resonance direct thrombus imaging and fluorodeoxyglucose PET scanning will both be valuable in the diagnosis of recurrent ipsilateral DVT, because both can make the distinction between residual thrombi and an acute recurrent DVT.\(^11\)

Moving forward, it will be important that contemporary venous intervention for iliofemoral DVT always incorporates IVUS guidance. Studies have found that in comparison to IVUS, standard venography had poor sensitivity (45%) and negative predictive value (49%) in the detection of a venous area stenosis of > 70%.\(^12\) Importantly, when IVUS was used compared with venography during treatment for iliofemoral DVT, the treatment plan changed in 60 of 100 patients and the decision to stent changed in 50 of 100 patients, as described in the recently published VIDIO trial.\(^5\) These findings from the VIDIO trial led to the conclusion that without IVUS, iliofemoral vein occlusive disease would have been undertreated in the majority of patients studied.\(^5\)

**Improved Devices**

Great advances have been made in acute proximal DVT thrombectomy devices that have allowed for faster and more efficient treatment times since the ATTRACT trial publication.\(^7\) A new 8-F AngioJet catheter, the ZelanteDVT (Boston Scientific Corporation), has a venous-only indication and offers four times the thrombectomy power over the 6-F AngioJet thrombectomy system (Figure 1). Using Power Pulse lytic delivery technology, the ZelanteDVT catheter delivers the thrombolytic agent directly into the thrombus; then, after a 30-minute dwell time, additional thrombectomy is performed. In our experience, the ZelanteDVT catheter provides an “on the table” result two-thirds of the time, alleviating the need for a prolonged thrombolytic infusion with the associated costs and bleeding risks.

Another catheter-based thrombectomy system, the ClotTriever (Inari Medical Corporation) offers an additional option to patients with acute iliofemoral DVT. The advantages of the ClotTriever system include the ability to capture and remove large thrombus volumes, mechanically core clot from the vein wall, treat in a single session, and potentially reduce or eliminate the need for thrombolytics. The system is composed of the 13-F ClotTriever sheath (Figure 2A) and the ClotTriever catheter (Figure 2B), which includes the coring element with the collection bag that can contour to effectively treat vessels as small as 6 mm and as large as 16 mm.
Importantly, both of these newer, more efficient thrombectomy devices diminish or, at times, completely negate the need for a prolonged thrombolytic infusion, which should theoretically lower the bleeding risk.

Lastly, a catheter-based thrombectomy system, the Indigo mechanical thrombectomy catheter (Penumbra, Inc.) can be used to remove emboli and thrombi from the venous system (Figure 3A). It is indicated for use on its own when thrombolytic therapy and surgery may be contraindicated, as well as in conjunction with thrombolysis to shorten lengthy infusions and costly intensive care unit stays. These features are driven by the Indigo system’s Pump Max (Figure 3B) and proprietary Separator technologies, which maximize aspiration power and efficiency. These two technologies ensure continuous aspiration throughout the system without clogging the catheter’s tip. This percutaneous system is available in five diameter options (CAT3, CAT5, CAT6, CAT8, and CATD) ranging from 3.4 to 8 F and lengths ranging from 85 to 150 cm.

There have also been considerable advances in the design and manufacturing of dedicated venous stents. Many dedicated venous stents have been available outside the United States for years and are currently under clinical trial in the United States. These newer design features will hopefully have a positive effect on long-term vein patency (see the Characteristics of an Ideal Venous Stent sidebar).

Considering Biological Factors
It is important to also increase attention to the accumulating evidence that the factors influencing venous thrombosis are not restricted to the coagulation system alone, but also include the immune system, which is closely involved with formation and resolution of thrombosis. A recent study documented that patients with a history of unprovoked DVT have long-term increased levels of inflammatory markers and markers of endothelial damage. As more clinical observations and mounting laboratory evidence support a complex interplay between inflammation, innate immunity, and the coagulation system, novel preventive and treatment modalities will most certainly be integral to future investigation.

CHARACTERISTICS OF AN IDEAL VENOUS STENT

- High resistance to compression
- Deploys without foreshortening or lengthening
- Designed to adapt to flexion points
- Good visibility
- Reaches and retains target diameter with postdilation
- Resistant to thrombus formation
- MRI compatible
- Low-profile delivery catheter
**CONCLUSION**

It is imperative that a modern-era venous intervention trial be executed post-ATTRACT and incorporate many of the advances discussed. This new trial should include only acute iliofemoral DVT patients, incorporate mandated use of IVUS, and have uniform postprocedure imaging in all patients to truly investigate the open vein hypothesis. Improved mechanical thrombectomy devices not available during the ATTRACT trial would be utilized, which should substantially lower exposure times to thrombolysis and significantly lower bleeding risks. Postprocedure pharmacology would be per protocol and hopefully provide the data to advance this aspect of venous intervention where there is currently no uniformity or guidelines. Finally, to address the issue of clinical equipoise, patients who are randomized to the control arm would have the ability to be crossed over to intervention if they fail medical therapy up to 21 days.

For now, venous intervention must still be part of the treatment algorithm for patients with acute iliofemoral DVT, taking into account the patients' functional status, life expectancy, bleeding risk, and available local expertise.

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**Figure 3.** The Indigo mechanical thrombectomy catheter (A) with Pump Max technology (B).