Intravascular Ultrasound (IVUS) for the Treatment of Venous Disease

Studies, awareness, and training help drive improved outcomes.

The views, opinions, and clinical experiences expressed in this article are those of the physicians being interviewed. Any individual case results, opinions, or experiences are not predictive of future results.

Paul J. Gagne, MD
Section Head, Vascular Surgery
Norwalk Hospital
Southern CT Vascular Center
Darien, Connecticut
Disclosures: Consultant and Global Principal Investigator for Philips Volcano.

Erin Murphy, MD
Vascular Surgeon
Director of Venous and Lymphatic Intervention
Sanger Heart & Vascular Institute
Charlotte, North Carolina
Disclosures: Consultant and National Principal Investigator for Medtronic.

Paul M. Khait, MBA
Senior Director, Global Training & Education
Market Enablement
Image Guided Therapy
Philips Volcano
San Diego, California
Disclosures: Employee of Philips Volcano.

Mahmood K. Razavi, MD, FSIR, FSVM
Medical Director, Comprehensive Aortic Center
Director, Department of Clinical Trials
St. Joseph Heart & Vascular Center
Phoenix, Arizona
Disclosures: Member of the ATTRACT trial steering committee; Principal Investigator of the VIRTUS trial.

Technologies are emerging rapidly and having a significant impact on patient outcomes in peripheral vascular disease. Clinical studies to validate these new technologies, coupled with awareness building among specialists, referring physicians, patients, and industry, will be important steps in moving this field forward with better outcomes.

Philips Volcano is focusing on three pillars to improve patient outcomes in this relatively new and expanding area of venous disease. Through innovative product development, empirical data generation, and best-in-class device training and medical education, Philips is collaborating with physicians to improve diagnosis and treatment. This article examines the use of intravascular ultrasound (IVUS) in the diagnosis and treatment of venous disease, such as occlusions and compressions, deep vein thrombosis (DVT), and postthrombotic syndrome (PTS), among others. These diseases are often misdiagnosed and therefore mistreated with standard of care alone. However, with IVUS, patients receive a more accurate

diagnosis, precise sizing and placement of a balloon/stent (if required), and immediate assessment of posttreatment therapy.

Criticisms of the ATTRACT study included the lack of IVUS and the low stenting rate used in the iliofemoral veins. Do you foresee the data affecting your decision making in cases of iliofemoral DVT?

Dr. Murphy: At the time ATTRACT was designed, the use of IVUS was not yet the standard of care. Although this makes the lack of IVUS use understandable, it also leads to several concerns regarding the initial results of the trial. First, when looking at the clot burden assessment after thrombolysis or pharmacomechanical thrombolysis, we know the venogram is falsely reassuring compared to the same assessment performed with IVUS. Thus, the degree of clot removal in the trial patients was likely overestimated when based solely on venography. Because we now know that a lower degree of clot removal has been associated with both decreased venous patency and an increased risk of PTS, the patients in this trial were likely at increased risk for both compared to patients treated today under IVUS guidance.

Second, even after thrombus removal, IVUS detects more underlying lesions requiring stenting when compared to venography. Experience would suggest that the rate of stenting is near 90% after iliofemoral DVT when using IVUS guidance. In ATTRACT, the rate of stenting for iliofemoral DVT was approximately 50%.[1] Therefore, it is entirely possible that many trial patients were left with a persistent, untreated obstruction with resultant risk for rethrombosis and PTS.

Furthermore, the lack of IVUS was combined with another major gap in data collection—a lack of follow-up ultrasound exams to document procedural success. After the initial DVT treatment, there was no ultrasound or any other imaging mandated to prove the vein was patent at follow-up visits. I believe this point invalidates the ability to draw conclusions from this study. The question asked was, "Does early restoration of venous blood flow prevent PTS?" but the trial studied a population that likely had high rates of remaining obstruction and rethrombosis due to a lack of IVUS combined with the low stenting rates, and then follow-up was not conducted to determine whether restoration of flow was maintained beyond the original procedure. Because of these data gaps, conclusions regarding care should not be altered based on this study.

Dr. Razavi: There are valid shortcomings of the ATTRACT trial, including the choice of primary endpoint (any degree of PTS as opposed to the more clinically relevant moderate to severe PTS) and lack of imaging follow-up, but a low stent rate cannot be one of them. Certainly, IVUS has advantages over catheter venography in diagnosing venous lesions, and it would have been valuable using it in postinterventional patients. However, the criticism ignores the reality of a study funded by the National Institutes of Health and its timing. The funding limitations did not allow the addition of IVUS; at the time of the grant submission, the literature on IVUS and venous disease was insufficient to support increased trial resources.

I believe the "low stent rate" claims are not supported by the literature. Over half of the patients in the experimental arm of ATTRACT underwent stent placement, which is in line with that of the more experienced centers, as well as the National Venous Registry. I disagree that a majority of patients with DVT will require stent placement after clot removal. That assumes that outflow obstruction is the main risk factor for DVT in most patients, which is not necessarily true. Existing data suggest that approximately half of patients with iliofemoral DVT have outflow obstructive lesions; hence, they are suitable candidates for stent placement. Stents should be placed only when there is a physiologically significant obstructive lesion.

Regarding the VIDIO clinical trial, can you share any key takeaways?

Dr. Gagne: The original hypothesis of the VIDIO (Venography versus Intravascular ultrasound for Diagnosing Iliofemoral vein Occlusive disease) trial was to evaluate the relative diagnostic sensitivity of IVUS versus multiplanar venography. Our central conclusion is that IVUS is significantly more sensitive for identifying venous outflow obstructions, in part because IVUS is more accurate in identifying the severity of a lesion compared to venography, even multiplanar. In this 100-patient study, venograms missed 26% of > 50% diameter-reduction lesions. In addition, IVUS determined stenoses were 10.9% more severe than when viewed on venogram.[2]

From a procedural standpoint, as an investigator, the decision to stent changed in 60% of the patients due to IVUS. Further, in 50 patients, the number of stents increased from 0 to 1 or from 1 to 2. In my opinion, IVUS is the best guide for stent intervention and, without it, we are undertreating patients with iliac/common femoral vein obstruction.

An additional benefit of IVUS is that you can potentially minimize the amount of radiation and contrast the patient is exposed to while making that diagnosis. We need to consider the increased radiation costs to the patient and medical team when evaluating diagnostic technologies.

What should the next venous IVUS clinical trial look like?

Dr. Gagne: There are two studies that would be critical for moving the peripheral vascular field forward with IVUS. The first is to evaluate the different proposed venogram measurement criteria for a preintervention iliac/common femoral vein obstruction in nonthrombotic patients and correlate cutoff values with clinical improvement in a larger data set. This should enable us to stratify the predictive capability of various vein stenosis criteria for predicting improvement in clinical outcomes once treated with a stent.

The second is a prospective study comparing time to healing using standard of care (eg, compression, wound debridement) for chronic venous ulcer (ie, clinical C6) patients versus early intervention for iliofemoral venous outflow obstruction and standard-of-care treatment. The endpoint would determine whether we can accelerate wound healing and decrease recurrence rates. We know the current standard of care often results in long healing times, with some patients healing, and some not. The objective would be to change the paradigms at the wound centers to prove that you can significantly accelerate venous ulcer healing if you evaluate and treat any underlying venous disease early and appropriately.

Dr. Murphy: I would suggest two studies. One would use IVUS to detect the degree of remaining clot burden after acute interventions and correlate with clinical outcomes. The second would use IVUS to determine the degree of iliac vein stenosis that should prompt intervention to achieve improved clinical outcomes of both PTS iliac lesions and nonthrombotic iliac lesions. The intervention thresholds are likely different for both patient groups.

Dr. Razavi: The utility of IVUS in deep venous interventions is clear to all IVUS practitioners, but high-quality data remain scant in the literature. During interventions in the deep venous system, we make assumptions that have not been validated by robust prospective trials. One of the major questions is, what is a physiologically significant obstruction? For example, the presence of collaterals, > 50% area stenosis, and translesion pressure gradient of 2 to 3 mm Hg have all been proposed, but none has been rigorously examined.

Similarly, the correlation between obstructive lesions and pathologic conditions, such as DVT or venous reflux disease, needs to be investigated. An important prerequisite for conducting such studies is the utilization of diagnostic tools with a high degree of accuracy and reproducibility. Currently, IVUS is the only method to achieve this and should be included in all future trials.

Several venous stents are currently available in Europe but not yet in the United States. What role do you see IVUS playing as we try to evaluate how these stents will perform?

Dr. Gagne: A fundamental consideration as we move into using these stents in the United States is that the material that they are made of and the stent structure is fundamentally different than what many physicians in the United States have used for iliac vein procedures. Because of the change in the stent structure and deployment, the forces on points of compression—specifically between the spine and the iliac arteries—may be different than what patients have been subjected to in the past with the self-conforming Wallstent (Boston Scientific Corporation) that is commercially available and used regularly for this purpose.

We need to be extra careful and thoughtful in the sizing and placement of these large-caliber nitinol venous stents. To complicate things, because of the vagaries of measuring veins and the evidence that we have from the VIDIO study, measurements can be off by as much as 10% compared to IVUS. If you oversize the stent, it may create forces that have a long-term adverse effect on the adjacent artery. Alternatively, if you place a small stent into a big vein, then we might see embolization and injury to the patient.

Dr. Razavi: IVUS is an important diagnostic tool and particularly useful in venous stent placements. The ovoid nature of the veins, especially in segments prone to external compression, makes it difficult to accurately determine the dimensions of the vein, hence the appropriate stent size. IVUS is a helpful modality for such assessments.

As far as I am aware, only the VIRTUS trial required IVUS. This substantially added to the confidence of the investigators and the sponsor regarding correct sizing of the stents. Experience has so far indicated that stent undersizing may have a deleterious effect on long-term patency of the stent and vessel. Alternatively, gross oversizing of the new generation of venous stents marked by higher radial force may promote vascular injury over time and patency loss. Although not yet confirmed in veins, the latter has been proven in the arterial system. Hence, correct sizing of stents plays an important role in long-term stent patency. For this reason, use of IVUS in deep venous interventions is highly advisable.

Philips Volcano is one of the first companies to invest in medical education for the diagnosis and treatment of deep venous disease. What

programs are offered for professionals who want to learn more?

Dr. Gagne: Philips Volcano has taken a broad approach to raising awareness regarding venous hypertension and chronic venous insufficiency, the bane of a large segment of people within our population. The result we hope for is that through increased awareness and education, physicians will be able to provide better care for these patients who in the past have had few options for leading a better life.

There are multiple educational opportunities available for physicians who want to learn more and hone their procedural approach. The first is a quarterly course called the Deep Venous Summit, which focuses on all aspects of venous disease. From superficial venous insufficiency to acute DVT, including diagnosis, treatment, and management, this comprehensive course enables physicians with limited experience in this arena to begin understanding the breadth and depth of deep vein issues.

Philips Volcano also provides an opportunity to expand beyond didactic learning with lectures and reading to actually viewing how venous cases are done in real time within the office or cath lab. Physicians see how workflow proceeds and decision making evolves to obtain the best outcome for patients with iliac and other outflow obstructions.

Last, Philips Volcano offers an ELIITE Fellows 3-day course designed to raise the awareness of peripheral vascular disease by exposing fellows in training and young attending physicians to aspects of venous disease diagnosis and treatment. The course includes the workup of patients, including proper evaluation through history, physical, and imaging modalities, so that patients can be vetted for either further evaluation or treatment.

Upcoming Training Opportunities

Philips Volcano is committed to supporting customers new to our technology by providing a comprehensive medical education curriculum. From basic to advanced educational opportunities, we guide customers to clinical independence through a variety of learning forums that best meet their unique training needs.

- Deep Venous Summit:
  September 29–30, 2017 in Boston, Massachusetts
- ELIITE Fellows symposium:
  October 12–14, 2017 in Chicago, Illinois

Contact your local Philips Volcano representative for more information.

Mr. Khait: Much of venous disease is an underdiagnosed and unmet patient need. As an industry leader in the diagnosis and treatment of peripheral vascular disease, Philips Volcano has a responsibility to create broader awareness and understanding of the disease state for the betterment of medical practice and patient care. There's the awareness that deep venous disease exists, and then there's the innovation around intervention, what you can actually do to help these patients get back to normal, healthier lives. But industry can't succeed alone; we need partnering physicians.

For the awareness part, we are preparing to launch a formalized venture into disease state recognition and discernment. To build the program, we collaborated with physician advisors to understand the landscape dynamics of the market and how we can create a partnership for education. We realize that a crucial component for physicians is on the referring side, so we are also partnering with a third-party medical education company to create a continuing education program that provides disease state awareness. Our goal is to educate between 3,000 and 5,000 referring physicians in the United States on venous disease and then connect them with appropriate points of care.

Philips Volcano representatives are valuable resources and a great entry point. We do a substantial amount of education for our internal sales team, as they tend to be the first contact for our technology. We also closely evaluate what programs we should be running to help train our customers that directly participate in venous programs. We leverage and tailor a variety of training methods for our medical advisors and customers. For example, recognizing we live in a digital world, there are virtual technologies and simulation technologies that we can employ for some customers. There's also a Venous IVUS App that is pretty remarkable. Between our apps, our tailored programs, our website, and our physician partnerships, we are creating both the awareness and interventional education necessary for improved outcomes in the venous disease arena. ■

Download the most popular Philips Volcano app by searching for Venous IVUS in the iPad App store.

1. Vedantham S. The acute venous thrombosis: thrombus removal with adjunctive catheter-directed thrombolysis (ATTRACT). Presented at: Society of Interventional Radiology; March 4–9, 2017; Washington, DC.
2. Gagne PJ, Tahara R, Fastabend C, et al. Venogram versus intravascular ultrasound for diagnosing and treating iliofemoral vein obstruction (VIDIO): abstract from a multicenter, prospective study of iliofemoral vein interventions. J Vasc Surg. 2016;4:136.