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VENOUS THERAPY

CONSIDERATIONS AND DECISIONS

REFLUX DECISIONS | DVO UNKNOWNS | C-TRACT & PE-TRACT | FEMALE PeVD | ACUTE DVT TREATMENT | THERMAL & NONTHERMAL OPTIONS | ULCER APPROACHES

Venous Therapy Considerations and Decisions


As the ability of the vascular community to deliver therapies for a variety of venous diseases continues its rapid expansion, it is a good time to reflect and share our experiences, both positive and negative, to ensure safe and appropriate delivery of care. At a time when practice is outpacing data collection, it is important to be candid in our communications. With this in mind, this edition of *Endovascular Today* invites candid commentary prompted by challenging questions probing what we know, and just as importantly, what we do not. To provide a more balanced discussion, we have sought expertise from both sides of the Atlantic.

Interspersed throughout this issue are expert panel discussions on charged topics and key developments in the venous world. In the first of these panels, Suman M. Wasan, MD, asks Misaki Kiguchi, MD; Michael Lichtenberg, MD; Mahmood Razavi, MD; and Suresh Vedantham, MD, about the landscape of acute deep vein thrombosis intervention in 2021, examining the clinical ramifications of recent trial data and recent changes in the technology.

Then, moderator Gerard O'Sullivan, MD, asks Mohammad E. Barbati, MD; Dr. Desai; Dr. Jalaie; Erin H. Murphy, MD; and Emma Wilton, MD, how we each tackle various chronic deep venous occlusion challenges. Continuing on the topic of deep venous obstruction is an article by Nicos Labropoulos; Suat Doganci, MD; and Stephen A. Black, MD, who outline the primary needs for progress in chronic venous obstruction management.

Next, Suresh Vedantham, MD, and Akhilesh K. Sista, MD, share insights and updates on the C-TRACT and PE-TRACT trials, respectively, framing their potentially significant impact on venous care.

Continuing our panel format, moderator William Marston, MD, leads a discussion on venous ulcers with deep obstruction and superficial reflux through the lens of complex patient presentations. Joining him in the discussion as panelists are Irwin Toonder, RVT, and Marie Josee van Rijn, MD. Patient-centered decision-making also comes into play in Dr. med. Tobias Hirsch's panel on thermal and nonthermal solutions for varicose vein treatment, where panelists Antonios Gasparis, MD; Ramona Gupta, MD; and Kathleen Ozsvath, MD, provide insights on the basis for their decision-making regarding the variety of therapeutic modalities, the pros and cons of each, and potential complications to be aware of.

In our last panel, Raghu Kolluri, MD, posits questions to Steve Elias, MD, and Eri Fukaya, MD, regarding their treatment of venous reflux. The conversation includes advanced disease therapy decisions, differences in perforators versus axial disease, and considerations on deep system involvement.

Closing out our venous coverage is an update from representatives for the International Pelvic Venous Disorders in Women Work Group. Kathleen Gibson, MD; Neil Khilnani, MD; and Mark H. Meissner, MD, explain how the new SVP (symptoms, varices, pathophysiology) instrument for classifying variations of pelvic venous disorders works in practice and introduce some of the group's other projects to improve pelvic disease care.

This issue also features an interview with Tiago Bilhim, MD, on his journey in prostatic artery embolization work, tips for quality medical writing, raising awareness for interventional radiology, and more.

We hope the experiences shared by this esteemed group of global venous experts assist with the challenges you face in your practice, and we welcome your feedback and insights as well. ■

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PANEL DISCUSSION

Perspectives on Acute Deep Vein Thrombosis in 2021

Moderator: Suman M. Wasan, MD
Panelists: Misaki Kiguchi, MD; Michael Lichtenberg, MD, FESC; Mahmood Razavi, MD; and Suresh Vedantham, MD

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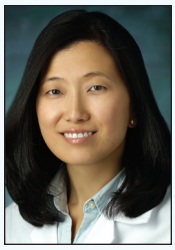

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Key developments in deep vein thrombosis (DVT) in recent years include the publications of the landmark ATTRACT trial and the CAVENT trial. In addition, several dedicated venous stents have been approved, two of which were recently recalled by their manufacturers. This expert panel seeks to explore the practical ramifications of recent trial data and changes in the technology landscape.

Patients with acute DVT may not be offered endovascular intervention initially, but often present 7 to 14 days after their initial event with continued pain and swelling seeking relief. In addition, patients who are candidates for intervention rarely present with an isolated iliac-common femoral vein and more often have involvement of the femoral and popliteal veins. Given the results of these recent trials with a primary outcome of prevention of postthrombotic syndrome (PTS), which patients are ideally suited for endovascular intervention?

Dr. Vedantham: The routine use of endovascular thrombolysis for proximal DVT does not exert a large effect in preventing PTS. It does increase major bleeding (1.4% absolute increase in ATTRACT) and it is not cost-effective (in ATTRACT, $220,041 per quality-adjusted life-year gained). Therefore, it should not be routinely used for "all comers" with proximal DVT.

However, patients presenting with acute iliofemoral DVT appear likely to benefit. The definition of "iliofemoral DVT" used in ATTRACT was the one endorsed by the Society of Interventional Radiology and the American Heart Association—DVT involvement of the iliac and/or common femoral vein with or without additional (eg, femoral, popliteal) veins. Using that definition, ATTRACT found that the use of pharmacomechanical catheter-directed thrombolysis (PCDT) in iliofemoral DVT resulted in greater resolution of leg pain and swelling within 30 days, a reduction in the point prevalence of PTS at 6 months (but not later), and a reduction in PTS severity during 2 years, compared with no PCDT. PCDT led to a sizable quality of life (QOL) benefit for the first 6 months; beyond that, the QOL benefit was smaller.

In the overall trial, patients aged > 65 years experienced reduced efficacy (ie, more PTS) with PCDT and worse safety in nearly all of the observed major bleeds.

Therefore, select younger, highly symptomatic patients with acute iliofemoral DVT and low expected bleeding risk can be reasonably considered for endovascular thrombolysis in addition to anticoagulation. This consensus is now supported by medical (2020 American Society of Hematology) and surgical (2021 European Society for Vascular Surgery) society guidelines.[1,2]

Dr. Razavi: Patient selection for catheter-based therapies in the setting of acute DVT (thrombectomy, thrombolysis, recanalization/stent placement, etc) should be based on patient symptoms. Although proximal clot location (such as iliofemoral) is a strong determinant of the risk of PTS, we do offer intervention in patients with isolated femoropopliteal DVT who are severely symptomatic. In general, ambulatory patients with symptomatic acute iliofemoral DVT who have a reasonable life expectancy are the best candidates for catheter-based therapies. The decision to intervene in symptomatic patients with significant frailty or with limited life expectancy is a complex one. The risks of intervention, degree of symptoms, and symptom improvement on anticoagulation alone are the main decision-making drivers in such patients in our practice.

Dr. Kiguchi: PTS is often underrecognized, and intervention at the time of diagnosis can reduce the risk of PTS or decrease its severity in select patients, as shown in the CAVENT and ATTRACT trials, respectively. Our department strives to offer same-day office and vascular lab appointments to ensure timely initiation of treatment, whether medical or surgical, to our patients to ensure an optimal outcome. In our patient population, any patient with adequate life expectancy with acute iliofemoral DVT is offered intervention to decrease clot burden, and thus, the severity of PTS.

What is the ideal timing of these interventions to assess the effectiveness of anticoagulation therapy alone and subacute presentation of many of these patients?

Dr. Kiguchi: Early intervention is important, as true thrombus age is often difficult to determine from clinical history alone. If a patient is newly diagnosed with an iliofemoral DVT and is an appropriate patient for intervention to decrease clot burden (appropriate life expectancy, low bleeding risk, benefit from decreased severity of PTS, etc), intervention is offered in addition to anticoagulation. Lytic-based therapeutic interventions are often most effective within the first 2 to 3 weeks of DVT occurrence. Mechanical thrombectomy can be more effective for older, newly diagnosed DVT.

Dr. Razavi: Ideally, the sooner the intervention, the better the results. Although not examined for statistical significance, patients within 7 days of symptom onset appeared to do better in the ATTRACT trial as compared to those with 7 to 14 days of symptoms. In our practice, we tend not to wait for symptom improvement in patients with iliofemoral involvement but do so in those with isolated femoropopliteal DVT. Although 14 days is a reasonable cutoff for the definition of acute clot, in practice the efficacy of clot removal versus time of symptom onset likely follows a logarithmic curve. Hence, we do offer catheter-based therapy to symptomatic patients with iliofemoral DVT beyond 2 weeks.

It is important to note that there are no data to show that thrombectomy alone is effective in "subacute" or

chronic thrombosis. Although in the ACCESS-PTS registry there was a signal for symptom reduction, their observations should be considered preliminary since it was a single-arm study with a small number of patients. ACCESS-PTS was a multicenter, single-arm, prospective study of venoplasty and ultrasound-accelerated thrombolysis in patients with chronic DVT and PTS (Villalta score ≥ 8).

Dr. Lichtenberg: Many patients are referred for treatment at a late stage, on average 7 to 10 days after the first symptoms of DVT. Typical reasons for this are misdiagnosis and ignorance of the fact that iliofemoral DVTs can be treated safely. Patients are usually quite compromised in this "subacute" phase. In these scenarios, the interventionalist is confronted with a large quantity of thrombotic material adherent to the wall. This has an impact on technical and procedural success rates; not every existing technique is able to remove organized thrombotic material. Therefore, I always recommend treatment at a very early stage. Enhancing awareness is crucial for this purpose.

Please comment on the necessity and placement of an inferior vena cava (IVC) filter prior to CDT.

Dr. Kiguchi: IVC filter use as an adjunct to CDT remains controversial and selective. Filters should not be used routinely, as CDT and pharmacomechanical and mechanical thrombectomy haven not been shown to increase the rate of pulmonary embolism (PE). Filters may be used in patients with established large symptomatic PE and/or evidence of right heart strain if there is significant concern for a "second hit" intolerance. Filters are important in cases of high-risk thrombus such as visualized mobile or tethered proximal thrombus. If an IVC filter is used, there should be clear clinical pathway for removal.

Dr. Lichtenberg: The placement of an IVC filter is no longer advisable. As we now have efficient and safe mechanical thrombectomy systems, CDT is not performed at my institution. Mechanical thrombectomy devices usually do not need a filter protection because they permit very efficient thrombus extraction. If a protective device is needed in specific circumstances (IVC, floating thrombus), we use a retrievable IVC filter.

Many interventionalists still prefer to perform thrombolysis/thrombectomy and venoplasty without placement of a venous stent during initial treatment and reassess for stent placement later. What do recent studies and experience indicate about the timing of venous stent placement?

Dr. Vedantham: There are no comparative studies with which to inform decisions on venous stent placement. Observational studies, shared anecdotes, and personal

experience have convinced me that residual stenosis on venography after CDT is associated with a high risk of early rethrombosis. When I have reintervened on patients with acute rethrombosis, often I have discovered residual obstructive lesions (ie, lesions not stented, or incomplete coverage of lesions with stents), so I use a relatively low threshold to place iliac vein stents in that situation.

Dr. Lichtenberg: An iliofemoral DVT usually has an underlying cause outside the vein (such as tumor compression or May-Thurner syndrome) or within the iliofemoral venous system itself. Thrombectomy or thrombolysis relieves the immediate symptoms. Patients feel better directly after effective thrombus removal. However, the treatment is incomplete without final venous stenting because the underlying cause is not remedied. During the procedure, the interventionalist needs to decide whether inflow is stable and sufficient after thrombectomy, as this is a prerequisite for final stenting. Stenting should be performed from one healthy vein to another. In the absence of sufficient inflow, stenting should be postponed to a later time during follow-up. I refer to this staged procedure as "stenting when possible."

Do intravascular ultrasound (IVUS) findings affect this decision?

Dr. Lichtenberg: To define sufficient inflow, I usually employ IVUS and Doppler to assess morphology and flow. Based on our recent analysis, our threshold for stenting is at least a 30 cm/second Doppler flow from the deep femoral or femoral vein into the common femoral vein.

Dr. Kiguchi: IVUS is imperative in every venography procedure.[3] Venograms alone may be falsely misleading in predicting residual clot burden, and thus, any residual clot seen on IVUS should be retreated with pharmacomechanical thrombectomy or additional days of lysis. Residual stenosis > 50% should be retreated with stent at the time of initial treatment to ensure no rethrombosis.[4]

Dr. Razavi: IVUS facilitates many aspects of venous stenting and interventions, but its role in the decision to stage the procedures has not been rigorously investigated. Anecdotal experience from our center and others suggest that beyond the delineation of stenoses, IVUS may identify diseased venous segments better than single view venography.

Are there any nuances in women of childbearing age?

Dr. Kiguchi: Limited evidence suggests pregnancy affects the outcomes of iliocaval stents placed after lysis or DVT or May-Thurner syndrome, according to a few published studies, and thus, stenting is not contraindicated in women of reproductive age, but I suggest close clinical and ultrasound follow-up during and after pregnancy.[5,6]

Dr. Vedantham: The literature suggests that pregnancy-associated stent fractures are infrequent and often asymptomatic, with consequences usually limited to stent stenosis or rethrombosis. Hence, childbearing capacity does not generally deter me from placing stents to manage venous obstruction when it is present. For patients undergoing CDT, the potential for stent placement and the potential risks (known and unknown) should be discussed with the patient beforehand.

Dr. Razavi: The evidence is weak so far but suggests a protective role for the use of stents to relieve venous obstructions. We do advise all our patients as such and do not hesitate to use stents in pelvic veins when necessary.

With the recent recall of two venous stents for migration and placement issues (Vici [Boston Scientific Corporation] and Venovo [BD Interventional], respectively), please comment on potential changes to the approval and postmarketing device surveillance process?

Dr. Vedantham: The FDA continues to review the information available on these devices. In general, I believe that long-term data collection should be mandated during the early years after approval of permanent (and many nonpermanent) device implants. However, FDA mandates are only one part of the solution here. Far more importantly, it is crucial for the culture among endovascular physicians to evolve to where we report every device malfunction into the MAUDE database quickly, so that we become aware of such issues as soon as possible and act to mitigate risk to our patients. We should be objective in assessing possible device causality, and we should not "pull punches" in transparently sharing device-related problems we encounter with each other.

Dr. Razavi: It should be clarified that both venous stent recalls were completely voluntary by the manufacturers and not FDA mandated. Such recalls and needs for improvements are not rare and are an important reason why postapproval studies are necessary. To my knowledge, neither platform had any issues during their pivotal studies. Problems were identified when a larger number of stents were deployed by a wider group of practitioners. This confirms the need for continued postmarket surveillance.

Dr. Lichtenberg: At this stage, our knowledge about the recent recall is incomplete. We have no official statements that would permit definitive conclusions that may have an impact on the approval process and the device surveillance process. Venous recanalization has been a safe and effective treatment for millions of patients with acute DVT and PTS. Any hasty conclusion may compromise trust in this therapy, which would be undesirable. The industry, as well as regulatory authorities and physicians, are called upon to achieve complete clarification. With the new medical device regulation in Europe, I believe we now have a very efficient and strong approval system.

Postprocedure care including prescription of anticoagulation and antiplatelet agents as well as venous stent patency surveillance often falls to the vascular medicine specialist. It is my clinical observation that immediately postprocedure, patients often have significant recurrent thrombosis in treated veins prior to or just after the sheath being pulled. Can you comment on the timing on the first dose of anticoagulation postprocedure?

Dr. Razavi: Recurrent thrombosis in the immediate postprocedural period is becoming more common. There are several reasons for this trend as outlined below.

1. With the more widespread use of PMT devices that need large-bore access (≥ 10 F) in the popliteal vein, postprocedural rethrombosis should be expected, especially in the popliteal and femoropopliteal veins. Venous punctures usually heal by a process of layered thrombosis, and when the ratio of venous puncture size to its diameter exceeds a certain limit, total access site thrombosis occurs at a higher frequency. Furthermore, it is unknown whether an aggressive scraping of vessel walls in the already inflamed veins has an additive effect in promoting rethrombosis.
2. To reduce the risk of bleeding after placement of a large-bore access, many practitioners delay the onset of anticoagulation. This increases the risk of rethrombosis in freshly thrombectomized and inflamed venous segments.
3. Finally, pharmacomechanical thrombectomy devices do not effectively reestablish inflow if the access site (popliteal vein) is thrombosed. Poor popliteal inflow in turn increases the risk of femoropopliteal rethrombosis.

Given the above, I use the following guidelines in my practice: (1) minimize venous access sheath size to the extent possible; (2) use adjunctive CDT or thrombolytics (if not contraindicated) in patients with access site thrombosis; (3) resume full therapeutic anticoagulation after the procedure, usually within 30 minutes—my preference is to use heparin or heparinoids in the immediate postprocedure period; and (4) apply sequential compression devices to the ipsilateral calf immediately after the sheath is pulled. It may be discontinued as soon as the patient is ambulatory.

Dr. Vedantham: For patients on low-molecular-weight heparin (LMWH), we simply continue it before, during, and after the CDT/PCDT procedure, without interruption. For patients on unfractionated heparin, we will sometimes briefly stop the infusion to enable the sheath to be pulled, but we restart anticoagulation within 1 hour after hemostasis. We do not allow a prolonged "off" period because postintervened patients are prone to reclot.

What is the current recommendation for anticoagulation and antiplatelet treatment after intervention ± venous stenting, dose and duration?

Dr. Razavi: After interventions for acute DVT, we prefer therapeutic LMWH for 3 to 4 weeks before switching to oral anticoagulants. Duration of anticoagulation is per American Society of Hematology guidelines for the management of patients with DVT.[1]

After venous stent placement, we use the same protocol as was used in the VIRTUS trial. In patients with nonthrombotic obstruction, we prescribe antiplatelets only unless there are risk factors for DVT such as history of malignancy. For patients with chronic postthrombotic obstruction or history of DVT, we use therapeutic anticoagulation for a minimum of 3 to 6 months. It is then discontinued if the stented segment is patent and there is no history of thrombophilia. Anticoagulation may be extended if there is coexistent femoropopliteal disease with suboptimal inflow.

We have observed asymptomatic partial stent thrombosis shortly after discontinuation of anticoagulation in a few patients. Resumption of anticoagulation for an additional 3 months has been sufficient so far in such patients.

Dr. Vedantham: In general, patients who undergo CDT or who receive stents during the management of acute DVT (ie, after lysis) or chronic DVT (treatment of established PTS) should receive anticoagulant therapy for at least 3 to 6 months. Stent recipients may also receive an antiplatelet drug. Patients stented for symptomatic nonthrombotic iliac vein lesions (ie, no DVT history) seem to have very high stent patencies and can usually receive antiplatelet therapy without anticoagulation.

However, current recommendations are not based on rigorous studies in endovascular therapy recipients but are extrapolated from medical DVT treatment guidelines in nonintervened patients. This is problematic, because patients selected/referred for endovascular therapy may represent a highly prothrombotic subgroup of patients, and catheter manipulations can contribute to venous injury that increases the predilection to rethrombose.

Taking stock of ATTRACT, although PCDT was statistically significantly associated with more bleeding, the absolute increase in major bleeds (1.4%) was smaller than expected, and there were no PCDT-related fatal or intracranial bleeds. However, the efficacy of PCDT was worse than expected—no effect on PTS prevention—and has been linked to the reformation of thrombus. Specifically, despite venograms showing good thrombus removal, a substantial share of PCDT-treated vein segments were noncompressible at 1 month, and noncompressibility of the common femoral vein correlated with more PTS, more moderate-or-severe PTS, and worse venous QOL. Hence, I believe more aggressive antithrombotic regimens are needed and that close attention must be paid to ensuring adequate anticoagulation during the initial postintervention weeks. We also need comparative studies to assess which regimens work best. In our practice, we have evolved towards routinely using LMWH for at least 1 to 3 weeks postintervention prior to transition to oral therapy, but the feasibility of doing so depends on patient-specific factors.

Dr. Lichtenberg: Anticoagulation therapy started prior to the intervention is continued after the intervention, usually for 3 months in nonthrombotic cases, and 6 to 12 months in acute DVT and PTS cases. Over the last few years, I recommend even more prolonged anticoagulation because this seems to have a positive impact on the prevention of restenosis and rethrombosis. When using vitamin K antagonists for anticoagulation, the clinician should aim to achieve a target international normalized ratio of 2.5 to 3.5. When the value drops below minimum, it would be advisable to additionally administer LMWH in a therapeutic dose. New oral anticoagulants are being used to an increasing extent, but we still lack sufficient experience with these agents.

What is the recommended timing of postprocedure vascular ultrasound surveillance to identify restenosis and what degree of stenosis warrants reintervention?

Dr. Vedantham: In our clinical practice, we do not perform routine surveillance ultrasound because we would not be likely to reintervene unless the patient was symptomatic. If this is to be done, then I suggest it should be done 7 to 10 days after the intervention, to enable lysis of recurrent/residual thrombi. Unlike the arterial system, even small degrees of stenosis (eg, 30%-40% narrowing) can limit flow and increase peripheral venous pressure. However, the problem with reintervening for stenosis is that to be beneficial, the improvement in luminal caliber that one gains (which is hard to predict with venous angioplasty) must be large enough to outweigh the prothrombotic effects of angioplasty-mediated endothelial injury. However, if a patient has residual or recurrent symptoms, repeat ultrasound is very helpful in distinguishing the etiology—either by identifying residual/recurrent obstruction, superficial venous reflux, or other causes.

Dr. Lichtenberg: We believe intensive postprocedure surveillance is a significant factor in preventing restenosis and rethrombosis. At our institution, we perform duplex ultrasound investigations at 2 to 4 weeks, 3 to 6 months, and 12 months after the procedure, followed by an annual examination. I believe that a 50% restenosis is associated with a high risk of rethrombosis. If the patient is completely free of symptoms, I usually schedule another analysis after 4 to 6 weeks. If the restenosis has progressed at this time, I recommend urgent reintervention. The same applies to patients with 50% restenosis plus symptoms such as new venous claudication and/or swelling.

Dr. Kiguchi: We perform duplex ultrasound surveillance should be continued at regular intervals (4 weeks, 3 months, 6 months, and then annually). I encourage all patients to present urgently if clinical conditions suddenly worsen. Any patient with > 50% stenosis and/or residual unresolved symptoms should be considered for reintervention. ■

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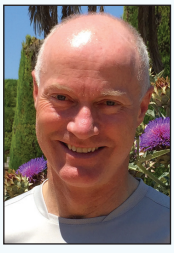
PANEL DISCUSSION

The Most Challenging Chronic Deep Venous Occlusions

Moderator: Gerard O'Sullivan, MD
Panelists: Mohammad E. Barbati, MD, FEBVS; Kush R. Desai, MD, FSIR; Houman Jalaie, MD; Erin H. Murphy, MD, FACS; and Emma Wilton, MD, FRCS



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In which deep venous occlusion cases will you definitively not stent?

Dr. Desai: In cases where inflow is irreparably compromised, any iliofemoral stent is often consigned to fail. With postthrombotic occlusions, this is most frequently when the femoropopliteal segment and, more importantly, the profunda femoris are occluded such that there simply is no flow to support stent patency. In these cases, I feel that placing a stent has a much greater likelihood of failure than success. As we all know, restoring patency can be enormously difficult when stents fail, and an occluded stent may exclude patients from any future therapies that would more definitively restore inflow and support a future stent reconstruction.

Dr. Murphy: Although stenting for deep vein occlusions can be extremely rewarding, these cases can also prove challenging. I find that the outcomes of these cases are highly dependent on sound judgment and attention to the technical details of the operation. I avoid stenting patients when a good outcome is unlikely, even if the best operative techniques are employed to achieve the best-case scenario technical result. The most frequent reason for operative exclusion in my practice is severely diseased, two-vessel, occlusive inflow disease (profunda and femoral veins [FVs]). If these vessels are wholly occluded, the likelihood of a successful outcome is very low. My inflow requirements include at least one suitable inflow vessel (femoral or profunda), or if both inflow vessels are involved, I look for < 50% occlusive disease in both. In borderline patients, I may stent in conjunction with inflow venoplasty, although this achieves inconsistent results. On occasion, I may offer endophlebectomy to patients initially excluded from stenting based on inflow, if the inflow vessels 1 to 2 cm caudal to the confluence are healthy.

In addition to anatomic exclusions, I do not offer stenting to patients with medical conditions I feel would unreasonably limit the benefits of stenting. Examples include patients with severe morbid obesity (body mass index > 40-45 kg/m^2) or other advanced prohibitive medical conditions (chronic obstructive pulmonary disease on oxygen, decompensated heart failure). These conditions cause increased operative risk as well as significantly elevated venous pressures, which limits the benefits of intervention. Lastly, I do not offer high-risk interventions (ie, those with severe inflow disease) to patients who are routinely noncompliant until a track record of follow-up compliance proves otherwise.

Miss Wilton: Our main reason for not stenting is inadequate inflow, as this is required to maintain stent patency. This would have been assessed prior to undertaking the reconstruction. You need to stent from normal vein to normal vein to try to ensure stent patency over time. However, it is very rare that if we were able to cross the occlusion satisfactorily, we wouldn't stent in the iliac vein/common femoral vein (CFV) region. Consideration also needs to be given to the patient's age and the proposed extent of stenting, particularly iliocaval reconstructions. However, as with all venous cases, severity of symptoms, quality of inflow, and patient factors all need to be balanced.

Drs. Jalaie and Barbati: Case selection is a key factor when patients are considered for endovascular treatment. If the inflow is severely impaired (eg, involvement of both the FV and deep FV [DFV]) and the probability of a long-term patency rate is really low, then recanalization and stenting should be avoided. In our opinion, in such a case, neither a hybrid procedure nor stenting into one of the inflow veins is advisable. Moreover, in most patients with asymptomatic chronic venous obstruction, when anticoagulation is contraindicated and in immobile patients, conservative treatment should be considered as the treatment of choice.

When do you consider an arteriovenous fistula (AVF)?

Dr. Murphy: Patients with extensive CFV disease are generally treatable with endovascular methods alone (ie, stenting to the profunda femoral confluence), as long as there is adequate inflow. Therefore, I reserve AVF creation for patients with poor femoral and profunda inflow. Endophlebectomy and AVF creation may be helpful in these cases. Occasionally, AVF without endophlebectomy is performed in cases of single-vessel diseased inflow proven insubstantial for stent maintenance.

Drs. Jalaie and Barbati: Please bear in mind that AVF creation is not a routine procedure in daily practice. It should be considered a temporary solution in carefully selected patients to improve the inflow and keep the affected vein segments patent. The more important aspects after venous intervention are long-term patency rates and clinical improvement of the patients thereafter. Artificially improved inflow into the iliocaval segment in a patient with obstructed FV and DFV will increase venous hypertension and likely even increase complaints and discomfort of the affected leg. Moreover, after closing the AVF, the preexisting insufficient inflow is not enough to keep the treated segments open. Unfortunately, a standardized technique to measure the venous flow in chronic obstructed venous segments and the threshold

of minimum necessary inflow could not be quantified until now.

Creation of AVF should be considered in the following patients/situations: (1) those who have vigorous synechiae at the level of femoral confluence covering the ostium of a patent DFV and need an endophlebectomy to ensure sufficient inflow; (2) to keep the reconstruction patent in patients with early reocclusion after successful initial thrombus removal and in whom the reason of the rethrombosis is unclear; and (3) patients with an acute iliofemoral thrombosis who have undergone a surgical thrombectomy.

Miss Wilton: In our opinion, an AVF temporarily maintains stent patency but does not address the underlying inflow issues and may in fact potentiate them. We prefer endovascular strategies to improve inflow rather than AVF, which we rarely perform.

Dr. Desai: Creation of an AVF may have a role when the inflow is of such poor quality that the stent is doomed to fail. However, as our surgical colleagues will probably attest, the outcomes of these interventions are incompletely described. Do AVFs address a short-term problem (ie, maintaining immediate stent patency) without a clear signal of long-term symptom reduction in any significant number of patients? Do the AVFs remain open relatively unassisted? I do believe that they have a role, but we need to define it a bit better.

With a compromised CFV, is it technically better to go from above or below?

Miss Wilton: We generally try from below first and are usually successful. However, there are certain disease patterns that commonly require dual access from the right internal jugular vein (IJV) as well as the FV, for example in patients with a history of intravenous drug misuse. This is because the disease is isolated to the lower external iliac vein (EIV) and CFV, and the occlusion does not have the usual trabeculations and microchannels but has a more obliterative, hard, fibrotic appearance.

Drs. Jalaie and Barbati: Even with a compromised CFV, an antegrade (popliteal or midfemoral) approach should be the first choice. The advantages of this access are the ability to evaluate the quality of inflow veins, no need for longer wires and catheters (compared to transjugular access), more stability of wires on recanalizing the iliofemoral obstruction without needing to change to a longer sheath, and more accessibility to the contralateral side in cases of bilateral iliocaval obstruction.

The advantage of a jugular approach is easy access for DFV vein dilation and stenting. Consequently, the jugular approach should be the first choice only in patients with planned DFV stenting. However, it remains a very important option because jugular assistance will be necessary in some cases to traverse the occlusion. In our daily work, we always position, prep, and drape the patient in a way that bilateral femoral access and jugular approach are feasible.

Dr. Desai: I think this is a matter of operator preference. I know several in both camps who have had tremendous success. My personal approach is to work from below the occlusion. For me, this means from an access in the popliteal fossa. I achieve access in the small saphenous vein immediately caudal to the saphenopopliteal junction (if the patient has one), the high calf posterior tibial vein immediately caudal to the popliteal vein, or my least preferred, the popliteal vein itself. These accesses require that the patient is prone. Others use the mid-FV, which is again a matter of preference. Coming at the occlusion from below has the benefit of working with flow, meaning you can directly observe what the inflow to a stent will be. Working from below has the disadvantage of potentially needing a reverse-curve catheter to select the profunda femoris should it be necessary, although this is not terribly cumbersome in my experience.

Approaching an occlusion from above allows you to easily select critical branch vessels such as the profunda with a standard angle-tip catheter. However, you will be working against flow. The operator needs to advance the catheter past the area of interest for adequate venography. Working from the neck also requires some ergonomic adjustments. We are all used to working with our tools on a table, and adjustments need to be made to work from above so that you are not working in the air. One potential benefit of working from above, particularly in an occluded CFV, is that it allows you to "stick the landing" of a stent at the profunda origin so that it is not inadvertently covered. Again, numerous skilled operators have done remarkable work from a neck access. It is a matter of what works for you.

Dr. Murphy: Ultrasound-guided ipsilateral FV access in the upper to midthigh is my preferred access for iliofemoral occlusive disease. This location gives excellent pushability for crossing diseased venous segments. The access must be low enough in the thigh so that the sheath tip lies below the lesser trochanter (the expected location for the profunda femoral confluence), allowing visualization and treatment of the entire CFV.

This approach has a high success rate even in FV occlusions, which often accompany extensive CFV disease. Venous occlusions are not solid but rather trabeculated, and the wire usually passes with ease.

Alternatively, access from above via the right IJV can be a solid choice. This access is particularly well suited for a patient with a patent ipsilateral cranial common iliac vein (CIV). However, patients with a compromised CFV often have accompanying ipsilateral EIV and CIV disease. In these cases, the presence of a tight stenosis or occlusion of the cranial CIV may prohibitively increase the difficulty of selecting the vessel from above. Occasionally, if crossing the occlusion is challenging, an approach from above and below to cross the lesion with an eventual body floss technique is also helpful.

In inferior vena cava (IVC) occlusions, do we need to be more careful with renal vein inflow?

Drs. Jalaie and Barbati: Stent placement across the ostium of renal veins is very common during iliocaval stent reconstruction and is necessary in patients with postthrombotic trabeculation extending into the juxtarenal and suprarenal IVC.

Until now, there was no or minimal evidence of renal function impairment after IVC stenting with jailing of renal veins. A literature search showed that there was only one report of renal function impairment and one report of renal vein thrombosis without renal dysfunction after overstenting the renal veins.[1-3] In our own patient population, we haven't seen any detectable renal function impairment or renal vein thrombosis after stenting across the renal vein inflow. We are confident that implanting a stent in an already obstructed IVC and jailing renal veins with porous dedicated venous stents will not further decrease the renal venous flow.

Dr. Murphy: IVC occlusions most often involve the distal portion of the IVC up to the level of the renal veins. Less commonly, occlusions will involve the suprarenal IVC or even the intrathoracic IVC. I generally use Wallstents (Boston Scientific Corporation) in the nonbranched portion of the IVC because they are available in sizes large enough to accommodate the IVC (22-24 mm). The Wallstent is used in combination with Z-stents (Cook Medical) across the renal and hepatic veins as needed. Z-stent interstices are significantly larger than the small interstices of the Wallstent. These larger openings may prevent the jailing of confluences over time. An additional technical detail to avoid jailing the renal veins is to avoid overlapping stents across the vessel conflux with the IVC.

When stents do cross the renal vein confluence with the IVC, anticoagulation can likely help preserve renal blood through stent sidewalls in the same way that anticoagulation helps prevent contralateral deep vein thrombosis after confluence jailing by iliac vein stents. Indefinite anticoagulation is already required in most patients undergoing caval reconstructions secondary to complex stent configurations, associated compromised inflow, and concomitant thrombophilias. Protection against renal vein compromise secondary to jailing is another reasonable consideration for use in these patients.

Notably, although I follow these practices to preserve renal flow, it does not greatly concern me when closed-cell stents cross the renal veins. This is because the renal veins are very high flow, which is often enough to maintain flow through the stent sidewalls. In addition, as stated, most patients are on anticoagulation, which is likely protective. Lastly, the renal outflow is typically very well collateralized. Thus, renal vein compromise is often without significant deleterious effects.

In summary, we should mind the renal venous inflow with attention to technique and consideration in anticoagulation decisions. However, in cases where they are compromised, minimal clinical impact is expected.

Dr. Desai: This is a frequent area of debate. We have heard anecdotal discussions of caval side branch occlusion, such as the renal veins, when stents extend across the ostia. The issue arises when the occlusion approximates these major side branches such that appropriate stent placement mandates at least a portion of the stent will cover the branch ostia. My personal preference in these cases is to place large-diameter, large-interstice tracheobronchial stents in an off-label application at the level of the caval side branches. Then, I place double-barrel-configuration nitinol stents the level of major caval side branches. On the other hand, we have all seen cases where no normal renal vein inflow into the cava is present, and the kidneys drain via collaterals to the azygos or phrenicoadrenals. Is this concern justified? It is unclear. One area where narrow-interstice stents may be an issue is adjacent to the hepatic veins. Here, hepatic vein occlusions may theoretically cause Budd-Chiari syndrome, which could cause portal hypertension and liver failure. Like so much of what we are discussing, the bottom line is that we have a lot to learn.

Miss Wilton: Stenting across the renal vein inflow when treating IVC occlusions is something we do consider, but as with all venous disease, the key is to ensure that the entire disease segment is treated. The limited

evidence and our experience show that it is safe to stent across the renal vein inflow if required. We have not had any compromise in renal function or other complications from stenting across the renal vein inflow, such as renal vein thrombosis.

Is it acceptable or justifiable to perform complex deep venous reconstruction without (1) good-quality preoperative MR venography (MRV) or CT venography (CTV) or (2) intraoperative intravascular ultrasound (IVUS)?

Dr. Murphy: In my opinion, the short answer is no. These cases are complex, and appropriate preoperative planning with high-quality duplex imaging and CTV (or MRV) helps plan the access, predict likely stent landing zones, prevent surprises, and guide outcome expectations, which can guide patient and physician decision-making.

In complex venous cases, IVUS is often a key determinant of eventual stent outcomes, and it is essential to select appropriate stent landing zones, protect confluences, and ensure maximal technical success. It is significantly harder to fix stent errors or occlusions resulting from shortcuts than to do these procedures correctly the first time.

Miss Wilton: We always perform cross-sectional imaging with either an MRV or CTV prior to undertaking any complex deep venous reconstruction. This allows discussion and planning of our operative approach in detail before undertaking the procedure. It also allows us to decide on extra strategies that we may need to employ to try to cross the lesion—for instance, whether to access from the FV and/or the right IJV. We also think of adjuncts that may be needed during the procedure to help cross the occlusion, such as a Rösch-Uchida access set (Cook Medical). We are also aware of the anatomy to help guide us across the occlusion. Cross-sectional imaging is useful to ensure that there is no other cause for the occlusion, such as malignancy or external compression. Additionally, to ensure adequate inflow, we perform direct venography on a separate occasion before undertaking complex deep venous reconstruction.

We use IVUS in all cases to confirm we are in the correct place, plan stent placement from normal vein to normal vein, and accurately land the stent. With IVUS, we can also assess the stent once it has been deployed to ensure there is no compromise, such as residual compression, loss of luminal diameter, and flattening of the stent. We also find it useful to reduce the radiation dose to both patient and operator.

Dr. Desai: So much of the procedure is in planning. You need high-quality imaging to determine the cause of occlusion (ie, in a caval occlusion, is it a filter?) because this will significantly impact your procedure, from your access sites to what tools you'll need (eg, filter removal tools, sharp recanalization techniques) to your anesthetic plan and how long it will take to get it done! So, preprocedural imaging is mandatory in my opinion. In the most complex venous occlusions, I think CTV of the abdomen/pelvis is mandatory. I prefer CTV based on its availability and how quickly it can be obtained, but use of MRV is perfectly valid. The exception for MRV is for filter-related occlusions as the filter will cause a terrible artifact with MRV.

I used to perform these cases without IVUS, but I would not now. IVUS provides so many tangible benefits, including addressing inflow, outflow, and postplacement stent expansion. It has given me more confidence in the intervention and has likely prevented many occlusions from occurring by demonstrating areas that I have not sufficiently addressed.

Drs. Jalaie and Barbati: Complex venous reconstruction requires profound preoperative preparation consisting of anamnesis, clinical examination, and imaging. A good MRV or CTV, in addition to a thoroughly performed duplex ultrasound, is mandatory and a premise for good results. It is important to carefully assess the inflow veins and the CFV to plan the procedure and predict the outcome. We also must remember the importance of having a detailed, reliable preoperative conversation with the patient about the procedure, patency rate, and probable clinical outcome. During the procedure, it is highly recommended to use IVUS to determine the proximal and distal landing zones.

What is your stent type of choice for crossing the inguinal ligament: open-cell nitinol, closed-cell nitinol, or a braided design? If you believe that one particular type of stent is preferred to cross it and go to the ligament, where should the overlap zone be, and why? How would you achieve this stent placement?

Dr. Desai: Stent placement across the hip is a hot topic at the moment. There is increasing recognition that not placing a stent into the CFV when it is obstructed is a frequent cause of occlusion. However, this is counterbalanced by concerns of stent fracture. One of the stent trials demonstrated a single-digit rate of fracture for closed-cell stents, but it is not clear whether fracture routinely impacted patency. I have seen some instances of fracture with open-cell nitinol stents and

with braided stents as well less frequently. Work done by several venous leaders, including Stephen Black, MD, and colleagues, has shown that the ligament is likely not the cause of fracture. Rather, it is caused by the superior pubic ramus and stress placed on the stent in leg extension.[4]

Technique is key. Stent overlap at the level of the ligament or the femoral head/pubic ramus can lead to failure because the "stent joint" is then at a dynamic position. I aim to have my stent overlap occur above the ligament (in the pelvis) and have a single stent exit the pelvis, cross the joint, and terminate at the profunda inflow. Thankfully, this is easier to do now that we have long dedicated venous stents.

Miss Wilton: When treating chronic iliac venous occlusions, we regularly place a stent across the inguinal ligament (84% of our cases) because the disease often extends from the caval confluence to the CFV confluence. In the vast majority of cases, we've used a closed-cell nitinol stent. The overlap zone is in the EIV proximal to the pelvic brim. This is to ensure that the overlap zone is not on a bend where the flexion/extension movement would increase the risk of stent fracture. We achieve this using IVUS. We land the distal stent accurately just at/proximal to the CFV confluence.

Drs. Jalaie and Barbati: There is no best stent for crossing the ligament. This area has the highest range of motion and high external compression, so ensuring flexibility and radial force is crucial. Overlapping segments of two stents will have less flexibility and should be avoided at the level of the ligament. We have very rarely seen fracture of dedicated venous stents in our patients, and none of the fractures we did see resulted in obstruction of the reconstruction or relapse of patient symptoms. Amid measuring the length of the pathologic segment that needs to be stented, it should be noted that the overlapping zone remains at the level of the EIV.

Dr. Murphy: Dedicated venous stents are relatively new to the venous space. Although there is a long-standing track record of braided stents crossing into the CFV without fracture, a lack of deployment predictability and precision motivated the development of newer nitinol stents. As the clinical experience has increased, we've found that some more contemporary stent designs are associated with infrequent fractures when extending past the ligament. Trials have yet to demonstrate whether these fractures are clinically deleterious or insignificant over time. Nonetheless, when faced with stenting into the CFV, we have stents that are associated with stent fracture and stents that are not. To this point, when crossing the ligament, I tend to rely on either braided elgiloy stents or open-cell nitinol stents that have no known incidence of stent fracture in this scenario. However, in the absence of clinically impactful data, I cannot voice a strong recommendation.

Regardless of stent selection, avoiding stent overlap under the ligament is important because this likely increases the risk of stent fracture. With the increased availability of longer stents, overlap zone location should be easily controlled and is part of appropriate stent selection. ■

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Probing the Unknowns of Deep Venous Obstruction in 2021

The three main areas for progress in chronic venous obstruction management.

By Nicos Labropoulos; Suat Doganci, MD; and Stephen A. Black, MD, FRCS(Ed), FEBVS

Significant progress has been made in the diagnosis and treatment of patients with chronic venous obstruction (CVO). The diagnosis of obstructive disease is easier and faster, and treatment can be performed by a variety of specialists and in a timelier fashion. More patients are now treated due to this progress, but there are still several areas to be addressed to optimize the management of patients with CVO.[1] This article discusses three of the main areas where progress can be made.

EVALUATION OF INFLOW

One of the most common modes of treatment failure after stent placement is inadequate inflow. With stents being placed from the inferior vena cava (IVC) to the distal part of the common femoral vein, the femoral vein (FV) and deep femoral vein (DFV) define the inflow.[1,2] The great saphenous vein can be included in select patients because it does not usually carry a significant amount of blood.[3] In patients with CVO with or without acute vein thrombosis, the DFV is typically patent and seems to have adequate inflow to support a more proximal intervention on its own. Typically, the FV or DFV must be patent. A good number of patients have a previous deep vein thrombosis that affects both the FV and DFV. If both veins are occluded, then inflow needs to be established first. If recanalization of these veins cannot be achieved, a small arteriovenous fistula at the groin can be created to provide enough flow.

In patients with partial recanalization, various types of flow are seen. An anatomic classification of the obstruction has been proposed that is based on the most commonly encountered patterns of inflow.[4] This classification describes the patterns of obstruction in the iliofemoral veins but does not include the IVC. Given the lack of data on evaluating outcomes based on this classification and the type of inflow, more work is needed to evaluate its use in clinical practice.

Flow patterns and blood flow estimation with ultrasound have been suggested, as well as the use of contrast flow rate during venography alone or in combination with ultrasound findings. Venography is empirical and not standardized and, as such, is very subjective. Currently, there are no robust techniques to quantify the inflow, and therefore, no cutoff values are available to dictate when a procedure can be safely or predictably performed.

Further issues arise with the fact that almost all measurements are done in the supine position, but the obtained values may not be indicative of what will happen when the patient stands up. Research in this area is needed to understand how to accurately evaluate the inflow and determine the values that would permit stent deployment with a low failure rate and a reduction in reintervention to preserve stent patency.

DIAGNOSIS OF SIGNIFICANT OBSTRUCTION

In routine clinical practice, CVO is diagnosed with direct morphologic evaluation by determining the location, extent, and diameter reduction. Indirect hemodynamic assessment is based on identifying the presence of collateral veins and denoting their number, size, and flow patterns.[1,3,5,6] Such hemodynamic assessment is empirical and not easy to apply in decision-making for managing CVO. Methods for diagnosing CVO include duplex ultrasound, intravascular ultrasound (IVUS), venography, CT venography (CTV), MR venography (MRV), and pressure measurements. Some centers also use plethysmography.[5,6] Most patients have symptoms during standing or physical activity. Unfortunately, nearly all of the daily testing for CVO is morphologic evaluation performed in the supine position. Although this position is convenient for both the patient and examiner, it cannot reproduce the hemodynamic conditions during standing or walking and can

be misleading.[1,5-7] There is less controversy regarding intervening in patients with postthrombotic disease and clear signs and symptoms, such as venous claudication, extensive swelling, or skin damage. However, even these patients may have other factors that contribute to the development of signs and symptoms, such as reflux in the lower limb veins, obesity, lack of physical activity, foot static disorders, joint issues, or right heart failure. These factors can be equally bad and sometimes may contribute more in the disease severity than the CVO. In patients with nonthrombotic CVO, determining the significance of the stenosis is controversial, particularly as we gather more evidence toward positional stenosis.[1,7,8] As previously mentioned, in most patients, the symptoms are more evident during standing or walking; however, nonthrombotic stenosis is found in the supine position and reduces or disappears in the standing position or when the patient is placed on the left side.[8] Clearly, we need to improve our diagnosis by performing more dynamic testing to define which patients are likely to benefit from interventions.

POSTINTERVENTION FOLLOW-UP AND EVALUATION

Some experience has been gained recently in following-up patients with interventions for CVO. Early detection of obstruction, issues with stent fracture, migration, malapposition, or not covering all the affecting area are important.[2,9] Duplex ultrasound has been shown to be a good postintervention method, but there are only a few studies, and none are robust regarding determining the diagnostic accuracy.[10-12] CTV or MRV should be used selectively because they are not appropriate to routinely use at follow-up. Venography and IVUS are more likely to be used when there is intention to treat. Currently, an imaging test is done within the first month from intervention; at 3, 6, and 12 months; and then yearly thereafter. Patients with changes in signs and symptoms are examined promptly. This surveillance program parallels the experience from the arterial interventions because there are no robust data on the venous side.

Another issue is how to manage different findings. On many occasions, experience and common sense guide the management because more definitive work needs to be done in this area. The findings also must be placed in context with the patient risk factors, type and number of interventions, material used, location and extent of the disease, and remaining disease that was not addressed by choice or was missed. Disease progression can occur without failure of the intervention due to existing problems such as reflux and obstruction in the limb, development of varicose veins, weight gain, or development of organ failure. Understanding the pathophysiology behind the development of in-stent stenosis is also needed to help guide both preventive and interventional strategies. Current options to manage in-stent stenosis are crude and prone to failure, leading to repeated reintervention. ■

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Playing Offense in Postthrombotic Syndrome: The C-TRACT Trial Opportunity

Why a randomized controlled trial is important to evaluate iliac vein stenting in PTS and how the C-TRACT trial can help resolve unanswered questions.

By Suresh Vedantham, MD

The C-TRACT trial is a multicenter, randomized controlled clinical trial evaluating the ability of endovascular iliac vein stent placement to reduce the severity of the postthrombotic syndrome (PTS) and improve quality of life in patients with previous deep vein thrombosis (DVT).[1] This study and its development have been funded by the National Heart Lung and Blood Institute (NHLBI), part of the National Institutes of Health (NIH), in a United States taxpayer commitment of > $12 million. The C-TRACT trial is being conducted at 30 clinical centers nationwide and is coordinated by researchers at Washington University in St. Louis, Missouri (clinical coordinating center); McMaster University in Hamilton, Ontario, Canada (data coordinating center); Massachusetts General Hospital in Boston, Massachusetts (vascular ultrasound core laboratory); and the Mid America Heart Institute in Kansas City, Missouri (health economic core laboratory). As of May 21, 2021, the study has enrolled 105 patients (targeted accrual is 374 patients).

BETTER LATE THAN NEVER

The history of endovascular intervention in chronic venous disease management dates back > 25 years, during which clinical practice development was largely driven by shared anecdotes, case series, and retrospective analyses that suggested that clinical improvement may often be observed in PTS patients who have their iliac veins reopened. In recent years, the use of iliac vein stents has seen a steep increase due to the advent and subsequent FDA approval of stents bioengineered for venous use, improved diagnosis of venous lesions by intravascular ultrasound (IVUS), and greater awareness of this form of treatment.[2]

Then, why conduct a randomized trial in 2021, so many years down the line? Don't we already understand this treatment modality? Certainly, we have made many worthwhile observations, but there remain a number of important unanswered questions.

First, does iliac vein stent placement produce benefits that are sufficiently large and durable to be worth the risks, costs, inconveniences, and uncertainties of permanent device implantation? There are good reasons to ask this loaded question. To date, there is no prospective evidence of efficacy for stent placement in PTS or any convincing characterization of the degree of benefit that is sustained beyond a single, small (n = 50) pilot randomized trial with a mixed group of patients followed for 6 months.[3] Previous studies indicate that perhaps one-third of stented PTS patients will require additional procedures to manage stent stenosis or occlusion during the first few years after placement.[4] Even when stents remain patent, some patients do not sustain the initial benefit achieved due to changes in other factors such as weight, cardiovascular status, superficial venous disease, and unknown variables. To responsibly recom-

mend stent therapy to patients, physicians need high-quality data to understand the nature of the associated benefits.

Second, the long-term safety of stents has not been systematically evaluated. Stent restenosis and occlusion are known complications, but the stability and mechanical integrity of new venous stents remain to be determined over a longer time horizon. Even in the first few years after FDA approval, two stents have already developed possible safety issues that have prompted global device recalls.[5,6]

Third, there is robust payer attention to the medical necessity of stent placement. A 2016 MEDCAC panel convened by the Centers for Medicare & Medicaid Services concluded that there was limited randomized trial data on which to base assertions of efficacy for chronic venous disease interventions. Private payers have also started to look more carefully at this practice, with updated policies introducing new barriers over the past few years. Absent high-quality data, insurers are likely to make decisions that have negative effects upon patients' access to quality care.

PLAYING OFFENSE

The above study rationale is valid but may seem inherently "defensive," especially to providers who are already sold on stent placement. Speaking as an experienced provider of medical, compressive, and endovascular PTS care, I respectfully disagree and would contend that the C-TRACT trial is actually the only ongoing initiative that can produce a large-scale quantum increase in well-justified stent placements.

As endovascular physicians, it is important to realize that our clinical referrals represent only the tip of the iceberg. From our experience with the ATTRACT trial, we know that a 500-bed hospital will see an average of 450 acute DVT cases per year, and that 10% to 20% of these patients will develop moderate-or-severe PTS over 2 years. But the majority of these patients have their DVT managed by their primary care physicians and hematologists; only a tiny fraction are ever referred to an endovascular provider. In addition, most localities only have a limited number of endovascular-capable specialists who manage the challenging PTS population, which further limits awareness among medical physicians. Although the cocktail of clinical experience, shared anecdote, exciting new devices, and single-arm studies may suffice to justify stent placement in the eyes of endovascular physicians, it has little chance of meaningfully expanding quality stent-based care because it is poorly suited to (1) define which patients benefit and (2) convince medical physicians (who are not inclined to subject their patients to risky interventions without evidence) to consider this option for their PTS patients. In fact, there is only one thing that can convince them: a rigorous multicenter, randomized controlled trial conducted with strong precautions against bias, showing compelling evidence of efficacy and safety. Until a trial of that nature is completed, stenting proponents will not be able to speak effectively to their medical colleagues and the majority of patients with moderate-to-severe PTS and reversible iliac vein lesions will live with disability, oblivious to the potential to be helped.

For many reasons, the C-TRACT trial is ideally suited to solve this problem. It was developed in close collaboration with and is led by highly credible leaders from the medical and endovascular DVT provider communities. In developing the protocol, study organizers queried and integrated the real-world clinical practice preferences of clinicians who manage PTS patients. It studies a highly relevant patient population—patients with moderate-to-severe PTS who have iliac vein occlusion or ≥ 50% stenosis and excludes patients who may be less likely to benefit (mild PTS or poor venous inflow). All patients in both arms receive close monitoring and optimal PTS care that includes medications, compression therapy, and (if needed) quality venous ulcer care. For patients randomized to stent placement, dilatation of stents to an adequate diameter is required, as are pre- and poststenting IVUS and postprocedure antithrombotic therapy. Although follow-up is for 2 years, the primary outcome of the study is the Venous Clinical Severity Score at 6 months, adjusted for baseline. Hence, C-TRACT stands a strong likelihood of being positive if completed as planned. If that proves to be the case, endovascular therapy proponents will have a highly attentive audience of medical physicians, creating a potential to greatly expand the number of patients who benefit.

The C-TRACT study protocol has been adapted to accommodate the real-world conditions posed by the coronavirus pandemic and currently requires just two to three in-person visits. Study patients benefit from close monitoring, free compression garments (donated by MediUSA), and independent safety oversight. Please type "C-TRACT" into your cellphone's app store, download the study's HIPAA-compliant Referral App, and efficiently refer your patients to the study (which takes about 15 seconds). Please visit https://bloodclotstudy.wustl.edu/c-tract/health-provider-referral/ for more information.

We are grateful to our study participants and to our partners who have publicly endorsed the study:

(Continued on page 68)

(Continued from page 65)
the American Venous Forum, the American Vein and Lymphatic Society, the National Blood Clot Alliance, the North American Thrombosis Forum, the Society of Interventional Radiology Foundation, and the Society for Vascular Medicine. Please join this incredible community that is driving forward best care for PTS! ■

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The Importance of the PE-TRACT Trial

A discussion of why PE-TRACT is so badly needed at the present time.

By Akhilesh K. Sista, MD, FSIR, FAHA

Intermediate-risk (submassive) pulmonary embolism (PE) has seen a flurry of interventional clinical trial activity in the last 7 years. In 2014, the first and only randomized controlled trial of catheter-directed thrombolysis (CDT) was published (ULTIMA).[1] In 2015, the Ekos catheter (Boston Scientific Corporation) was cleared by the FDA after publication of the SEATTLE II study.[2] In 2018, results of the OPTALYSE study were published, which investigated whether shorter durations and lower doses of thrombolytics were effective.[3] In 2019 and 2021, two studies that described the safety and efficacy of two novel aspiration thrombectomy devices (FLARE[4] with the FlowTriever device [Inari Medical] and EXTRACT-PE[5] with the Indigo aspiration system [Penumbra, Inc.]) facilitated FDA clearance for each.

WHY PE-TRACT IS IMPORTANT

Despite the previously mentioned studies, we remain woefully short of answering the fundamental question of whether catheter therapy should be routinely used to treat intermediate-risk PE. There are two reasons.

1. Lack of randomization: More than 1,500 patients have been randomized to systemic thrombolysis versus anticoagulation (AC) alone, whereas only 59 have been randomized to CDT versus AC alone. Therefore, it is unknown whether early CDT is better than prompt initiation of AC, close monitoring, and advanced supportive care.
2. Insufficient outcomes data: Since SEATTLE II, the standard outcome measure has been the right ventricular/left ventricular ratio 48 hours postprocedure. Although this outcome served as a useful surrogate in preliminary and pilot studies, it has outlived its use and has taken on outsized importance because the FDA has accepted it as the primary efficacy measure. Data are needed on short-term clinical deterioration and longer-term exercise tolerance, functional capacity, and quality of life in the year after a PE—outcomes that matter to patients and physicians—to truly assess catheter therapy.

The PE-TRACT study is designed to overcome these shortcomings. It is in submission to the National Heart, Lung, and Blood Institute within the National Institutes of Health (the same institute that funded the ATTRACT trial and funds the C-TRACT trial). If funded, PE-TRACT would be the largest study to date (approximately 500 patients) of CDT for PE, and its rigorous, randomized comparison of CDT to AC alone is exactly what is needed in the interventional PE space.

However, PE-TRACT would accomplish so much more than addressing this single question. Just as the ATTRACT trial provided major insights into the biology of deep vein thrombosis (DVT) and which patients with proximal DVT should be considered for catheter therapy, PE-TRACT would (1) clarify the long-term natural history of PE, as we are just now starting to understand the scope of the long-term toll PE takes on patients, with nearly 50% having a below-normal peak oxygen consumption during exercise 1 year after PE per the ELOPE study[6]; (2) identify novel risk factors (eg, blood biomarkers, baseline comorbidities, hemodynamic parameters) for the development of long-term disability and short-term deterioration; and (3) offer biological insights that would drive research toward novel device and pharmacologic therapies. Consequently, PE risk stratification will become more refined and precise, delineating which patients with submassive PE are at highest risk for short-term deterioration and death, those at highest risk for long-term disability, and those who will truly benefit in the short and long term from targeted reperfusion therapy. PE-TRACT will also begin to offer insight into some of the technical aspects of catheter therapy, including correlating the amount of thrombus removed with clinical out-

comes. In addition, PE-TRACT will increase precision around major bleeding estimates.

SUMMARY

Ultimately, the PE community must demand more rigorous studies of catheter-based devices used to treat intermediate-risk PE. The rapid increase in CDT procedures may be putting patients at risk without evidence-based benefit. The true opportunity lies in gaining a deeper knowledge about the disease and (if PE-TRACT is positive) improving the short- and long-term cardiopulmonary health of thousands of patients. ■

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PANEL DISCUSSION

Venous Ulcers With Deep Obstruction and Superficial Reflux: How I Do It

Moderator: William Marston, MD
Panelists: Irwin Toonder, RVT, and Marie Josee van Rijn, MD, PhD

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A patient is referred from a wound clinic with a 15-month history of left leg ulceration. The ulcer is large (50 cm^2), located on the medial aspect of the ankle, and has not been responding well to the wound clinic's treatment using topical wound therapies and compression therapy. They suspect that venous disease is the primary etiology of the wound. What testing protocol do you use to evaluate the venous system for abnormal reflux or obstruction? Do you use duplex ultrasound imaging alone or also obtain axial imaging using CT, MRI, or other?

Dr. van Rijn: I always start with duplex ultrasound, which I perform myself. At our outpatient clinic, all deep venous experts have been trained to perform duplex ultrasound, and we train our residents as well. Performing the duplex investigation myself allows me to really study the venous anatomy in detail and look for possible abnormalities, with specific focus on wounds and other clinical signs and symptoms. I will investigate the leg as well as the abdomen, and after the first visit, I will know this patient's superficial and deep venous status of leg and abdomen with respect to both reflux and obstruction. I will perform additional imaging only when I am considering a deep venous intervention such as an iliac vein stent.

Dr. Toonder: I first exclude possible peripheral artery disease and measure ankle-brachial indices. Then, with the patient in the supine position, I perform extensive duplex ultrasound of the inferior vena cava (IVC) and iliac tract, excluding possible compression and obstruction and identifying venous scarification and intra-abdominal collaterals. In an upright position, I confirm

suspected iliac vein compression and assess venous valvular function of the complete venous system of the legs. If and when there is an intention to treat, in the case of obstructive venous disease, complementary diagnostic imaging is advisable.

Venous ultrasound studies have identified that the patient with left leg ulceration described in the previous question has abnormal reflux in the great saphenous vein (GSV) throughout its length with diameters of 6 to 8 mm in the calf and 8 to 10 mm in the thigh. The deep system in the leg is patent with no evidence of obstruction or reflux. On ultrasound or CT/MRI, there is evidence of compression of the left common iliac vein (CIV) by the right common iliac artery that appears to be between 50% and 70%. What treatment would you recommend for this patient: ablation of the GSV alone, venography/intravascular ultrasound (IVUS) and possible stenting of the CIV, or both? If both, would you stage the procedures or perform them simultaneously?

Dr. Toonder: Compression of 50% to 70% on CT/MRI is a common finding in healthy patients and in and of itself should not be considered as a pathologic finding. I assess suspected CIV compression with ultrasound with the patient in an upright position. The compression will become less significant in the majority of cases. Always assess the flow direction of the ipsilateral internal iliac vein, and pay attention to the presence or absence of pelvic collateral veins. Ablation of the GSV is the primary treatment of choice.

Dr. van Rijn: Considering the diameter of the GSV, the extent of the reflux, and the fact that the patient only has a potentially significant compression of the CIV and not a postthrombotic obstruction, I would start with ablation of the GSV alone and evaluate the effect on the wound closely. I choose this strategy because I believe that the refluxing GSV has a large negative impact on healing of the wound, and I am less sure at this stage about the negative impact from the CIV compression. Also, an iliac vein stent is a more invasive treatment, with a higher complication rate and the need for temporary anticoagulation with additional risks. Even if I consider both treatment options, I would stage the two procedures, starting with the less invasive one.

For a patient with a venous leg ulcer and evidence of ipsilateral nonthrombotic iliac vein compression, how do you determine whether compression of the iliac vein is severe enough to inhibit healing, warranting placement of a stent? Do you go by IVUS-derived diameter reduction, area reduction, presence of collaterals, or other?

Dr. Toonder: First, I assess suspected CIV compression with ultrasound with the patient in an upright position. As previously mentioned, the compression will become less significant in the majority of cases. Assess the flow direction of the ipsilateral internal iliac vein and whether pelvic collateral veins are present or absent. The fact that you can examine the patient in an upright position is the strongest attribute of duplex ultrasound. No other diagnostic tool can provide this vital information to date. IVUS should only be used to identify true venous scarification such as fibrotic wall lesions and intraluminal synechia. Diameter or lumen reduction without evidence of fibrotic venous lesions is an insufficient ground for treatment. Extrinsic compression should be confirmed with a complementary diagnostic tool.

Dr. van Rijn: This can be tricky and difficult to determine. With a patient in supine position, the amount of compression of the CIV can be overestimated, so I always also examine the patient in a half-sitting position, although this makes the duplex investigation more challenging. I look at a combination of things to determine whether the compression is inhibiting ulcer healing. Of course, the amount of compression is one of them, and if this is not > 50%, I don't think a venous stent is indicated. Besides duplex ultrasound, I prefer phlebography with pressure measurements together with IVUS to measure area reduction. On phlebography, you can also see the presence of collaterals, which make a strong case for the significance of the obstruction. I combine this information with other items like: "Are there other possible factors that inhibit ulcer healing (impaired walking, inadequate edema reduction, diabetes mellitus)?" and "Does the patient complain of venous claudication or other symptoms that correspond with venous outflow obstruction?" Based on all of the above, I decide if stent placement is warranted.

A patient is referred with a recalcitrant left leg ulcer that has been present for over a year and is not responding to compression therapy and wound care. The patient has a history of several episodes of deep vein thrombosis (DVT) in the left leg over the last 10 years. Venous studies indicate that there is reflux in the GSV, which measures 3 to 5 mm below the knee and 5 to 7 mm in the thigh. There is evidence of postthrombotic changes in the popliteal and femoral veins, but they are patent with reflux. The left iliac vein appears occluded on pelvic

venous imaging. What treatment would you recommend for this patient: ablation of the GSV alone, stenting of the iliac vein, or both? If you would recommend both, would you stage the procedures or perform them simultaneously?

Dr. van Rijn: In this case, my strategy is less "standard" compared to the previous nonthrombotic iliac vein lesion (NIVL) case, and it is suspected that the negative contribution of the occluded left iliac vein on ulcer healing is much larger than the NIVL. Whether it is larger than the GSV reflux depends on the diameter of the GSV and the extent of the reflux; 5 to 7 mm at the thigh and smaller toward the lower leg is not very large, so in this case, the obstruction might be the most important factor. I like the strategy Raju et al proposed in which they treated patients with a venous leg ulcer according to the following algorithm: (1) incompetent GSV ablation only if the vein diameter was ≥ 5 mm and specific clinical features associated with iliac vein obstruction (significant limb swelling, severe diffuse venous limb pain) were absent; (2) iliac vein stenting plus GSV ablation if the vein diameter was < 5 mm or features of iliac vein obstruction were considered dominant; and (3) iliac vein stenting only if there was no GSV reflux with demonstrated iliac vein obstruction.[1] Raju et al found that long-term ulcer healing at 5 years was 75% overall, with no differences between the three groups. I would probably treat the GSV first, also because it can be easily and quickly done. If the common femoral vein (CFV) is not too affected with postthrombotic changes and there is good inflow from either the deep femoral vein (DFV) or femoral vein, I probably won't wait too long with stenting in case there are no signs of wound healing within 2 to 3 weeks.

Dr. Toonder: Deep venous obstruction causes a higher degree of venous hypertension than that caused by hydrostatic pressure due to valvular incompetence. Therefore, resolution of the iliac vein obstruction should be the preferred therapy. Of course, stent patency is dependent on the flow received from the affected femoral and popliteal veins. Even short-term patency may offer ample opportunity for ulcer healing. If the femoral and popliteal veins are diminished due to postthrombotic changes, even an incompetent dilated GSV can function as an important collateral. Theoretically, ablation of the GSV will not resolve the hydrostatic pressure because the deep system also has reflux.

For the patient described in the previous question, describe the technical details of intervention for chronic occlusion of the iliac vein. How do you position the patient, and what are the access location(s), preferred method of crossing the chronic occlusion, and preferred stent type and configuration?

Dr. van Rijn: I position the patient in supine position, and with duplex ultrasound, find a spot where the femoral vein is next to the artery instead of completely underneath. I position the neck in a way that I can also achieve access from the right internal jugular vein. In the leg, I make sure that the tip of the sheath (10 F) is caudal to the confluence of the DFV and femoral vein so the stent can land in the CFV if necessary. I use a hydrophilic wire and a multipurpose catheter to cross and always check once with a lateral image that my wire coursed ventral from the lumbar spine into the IVC because it can pass into spinal collateral veins. If I can't get through from below, I will also access from the neck, sometimes using a snare to catch the wire, creating a through-and-through wire. I predilate the whole segment with a 14- to 16-mm percutaneous transluminal angioplasty (PTA) balloon, but these balloons may be too big to pass initially, so a smaller diameter may be required initially. I prefer to exchange for a stiff wire (Glidewire Advantage, Terumo Interventional Systems) as soon as I have crossed the obstruction, and I do an IVUS run to mark May-Thurner, occluded and open parts of the veins, and the femoral confluence and perform multiplanar venography as well to check for collaterals (after stenting, I want to see they have disappeared). I perform PTA of the CIV with a 16-mm-diameter balloon and use a 14-mm-diameter noncompliant balloon in the external iliac vein (EIV)/CFV. If there is some stenosis in the femoral vein, I will perform PTA with a 10-mm-diameter balloon in that segment as well (in cases of severe stenosis, be certain that you have enough inflow from the DFV, otherwise the stent will block). With another IVUS run, I check to ensure my previously marked start and endpoints for stent placement are accurate. I prefer the Abre stent (Medtronic), using a 16-mm stent in the CIV and 14-mm stent in the EIV/CFV. After deployment, I postdilate the stents with the same size PTA balloon. I perform another IVUS run to check for residual stenosis in the stents and ensure the proximal and distal landing points of the stents are correct. In severe postthrombotic syndrome with extensive iliofemoral obstruction, stent extension into a single inflow vein may be a valuable option. This is usually the DFV, which has to be stented into from a jugular approach. On final venography, I check for rapid washout of contrast, with disappearance of collateral veins. During the procedure, patients are heparinized and receive low-molecular-weight heparin postprocedure in a therapeutic dose as soon as possible, as well as intermittent pneumatic compression.

Dr. Toonder: The European Venous Center Aachen-Maastricht is led by Dr. Houman Jalaie. The patient is positioned supine. Then, the ipsilateral femoral vein is accessed under ultrasound guidance at least 10 cm caudal to the femoral confluence, a 7-F introducer set is placed, 5,000 units of heparin are administered, and a stiff

Glidewire (Terumo Interventional Systems; 0.035-inch, 180-cm angled wire for routine use or a reversed 0.018-inch wire for sharp recanalization) is introduced and then replaced with a superstiff Amplatz guidewire. Then, the 7-F sheath is exchanged for a 11-F, predilation Atlas balloon (BD Interventional) at a maximum of 18 atm, and the iliac confluence is identified with fluoroscopy with contrast and/or IVUS to assess cranial landing zone and sizing. Depending on patient anatomy, stent size should be 16/18-mm diameter with 120- to 150-mm length for the CIV and 14/16-mm diameter with 100- to 120-mm length for the EIV. The 16-mm-diameter CIV and 14-mm-diameter EIV are the most commonly used configurations. Currently, Abre and the Beyond venous stents (Bentley) are used in our center. The Optimed sinus-venous stent (Optimed) is not FDA approved. Despite this, Maastricht has the largest cohort of patients treated adequately with Optimed in The Netherlands, using the 16-mm diameter and 100- to 120-mm length for the CIV and the 14-mm diameter and 100- to 120-mm length for the EIV.

Our center also has extensive experience with the Venovo stent (BD Interventional), which has been recalled due to faulty deployment issues; the Vici stent (Boston Scientific Corporation) has been recalled due to reported stent migration without clear cause. Wallstent (Boston Scientific Corporation) and Blueflow (plus medica GmbH & Co) stents tend to extend, making landing difficult at overlapping segments. I collaborate extensively with Professor Suat Doganci in Turkey, who achieves effective results using the Wallstent. He most commonly uses the 16-mm diameter for the CIV and 14-mm diameter for the EIV, with lengths of 90, 60, or 40 mm, and often lands below the ingiunal ligament without seeing stent fractures. One should always avoid overlapping stents at the inguinal ligament to avoid pain. It can be said that all stents have advantages and disadvantages that should be recognized by those deploying them. In conclusion, the preferred stent and configuration is not yet on the market and still needs to be developed.

A patient is referred with a chronic nonhealing ulcer of the right lower leg. Venous imaging demonstrated abnormal reflux in a large GSV measuring 6 to 8 mm in the calf and 8 to 10 mm in the thigh. The patient has a history of prior right leg DVT and evidence of complete occlusion of the femoral vein throughout the thigh. The CFV is open, and there is no evidence of significant obstruction of the right iliac veins. What would you recommend for this patient? Would you proceed with GSV ablation despite the occluded femoral vein, recanalize and dilate the femoral vein, or both? Or, would you have other recommendations?

Dr. van Rijn: If I really suspect that the GSV is not refluxing but serving as a collateral, I will not ablate it. Physicians are often afraid to ablate a refluxing GSV in the presence of postthrombotic changes in the femoral vein; however, if the GSV is incompetent, it will only do harm. The duplex ultrasound image of a collateral GSV is different from an insufficient GSV. However, it is sometimes difficult to be sure if the GSV is serving as a collateral or not. I have not performed PTA in patients with a solely occluded femoral vein because there is not enough evidence to support this, but results from the ACCESS PTS study are promising with respect to patency.[2]

Dr. Toonder: Deep venous obstruction causes a higher degree of venous hypertension than that caused by hydrostatic pressure due to valvular incompetence. An incompetent dilated GSV can function as an important collateral. If we consider Stevin's law, the diameter of the GSV is irrelevant. The height or length of the incompetent vein in an upright position is important. Simply formulated, when vertical, a 1-m-long tube with a diameter of 2 mm will have the same pressure value at the base when compared to a 1-m-long tube with a 12-mm diameter. Currently, there is insufficient evidence for effective femoral vein recanalization.

Do you feel that intervention is useful for occluded femoral veins in patients with chronic ulceration? If so, what technique do you prefer? Is there ever a reason to stent the femoral vein?

Dr. Toonder: As mentioned, there is currently insufficient evidence for effective femoral vein recanalization. Standard balloon dilation after crossing the femoral vein has shown to have short-term patency. Even a short-term patency may offer ample opportunity for ulcer healing. Ultrasound-assisted balloon dilation of the femoral vein momentarily has no added value compared to standard balloon dilation. Stent failure with dire patency rates in the femoral vein is the only reason not to stent.

Dr. van Rijn: I have not treated solely occluded femoral veins because of the lack of evidence to support it. I expect a bigger role for PTA than stenting in this area. I have a couple of patients in my practice with iliac vein stents also extending way down into their femoral vein (these procedures were performed years ago), but in all of them, the stents below the femoral confluence are occluded, and the proximal stents are still patent. ■

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PANEL DISCUSSION

Thermal or Nonthermal? Decision-Making, Pros and Cons, and Complications to Watch For

Moderator: Dr. med. Tobias Hirsch
Panelists: Antonios Gasparis, MD, FACS; Ramona Gupta, MD; and Kathleen Ozsvath, MD

Over the last 2 decades, endovenous procedures have become a standard form of varicose treatment. International guidelines recommend radiofrequency ablation (RFA) and laser treatment as first-line therapies, as they provide excellent results and are backed by a lot of evidence. Nonthermal, nontumescent (NTNT) procedures that avoid thermal trauma and tumescent anesthesia, such as foam sclerotherapy, mechanochemical ablation (MOCA), and acrylate sealing, round off the treatment portfolio. As a result, we now have a wide variety of devices at our disposal. Having more than one instrument in our toolbox means that an optimal solution can be found for every patient. To illuminate further on this topic, I've posed varying questions to Drs. Tony Gasparis, Ramona Gupta, and Kathleen Ozsvath about the basis for their decision-making.

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Disclosures: Consultant for Medtronic; receives honoraria from Kreussler, Medtronic, Merit Medical; event sponsoring from Kreussler, Biolitec, Medtronic, and Intros.

Dr. Gasparis, do we have data on the percentage of patients undergoing saphenous ablation for varicose vein treatment in the United States that utilizes NTNT methods? If not, what do you believe is the percentage?

Dr. Gasparis: NTNT refers to treatments such as polidocanol injectable foam (Varithena, Boston Scientific Corporation), cyanoacrylate (VenaSeal, Medtronic), and MOCA (ClariVein, Merit Medical Systems, Inc.). Accurate data on the percentage of patients undergoing saphenous ablation for varicose vein treatment in the United States that utilizes NTNT methods are not readily available. Thermal technology (TT) remains the predominant treatment modality partially because it has been around for > 20 years, but mostly because some insurance carriers still consider NTNT technologies experimental.

When reviewing the Centers for Medicare & Medicaid database (2018 data only available), NTNT accounted for approximately 20% of all ablation procedures performed in the Medicare population.[1] In the general population, I would think this number is lower because of reimbursement issues with private insurance carriers. In 2021, with some increase in coverage since 2018, my estimate is that NTNT treatment accounts for 10% to 20% of all ablation procedures in the United States.

Which of your patients would you primarily advise to have a nonthermal procedure such as polidocanol injectable foam, MOCA, or cyanoacrylate?

Dr. Gasparis: I discuss the options with patients. Most patients have questions before we even begin the dialogue. I start the discussion with their anatomy and review the reflux studies. The results of these studies together with patients' expectations will help determine which procedure is best. No matter which technique we decide upon, the risks and benefits, closure rates, recanalization rates, and possible complications are discussed.

From an anatomic perspective, patients with axial reflux in a below-knee great saphenous vein that needs to be treated and those with small saphenous vein pathology are patients in whom nerve injury with thermal ablation may be higher. Therefore, I advise NTNT treatment for these patients, as it has an extremely low incidence of nerve injury. From a patient perspective, for anxious patients with low pain tolerance, I offer NTNT because it does not require tumescent anesthesia.

Do anatomic conditions play a role (anatomy of the junctions, diameter, length of the reflux?)

Dr. Gasparis: Each technology has instructions for use (IFU) that the manufacturer has published and recommended. I strongly believe in following the IFU, but equally important is training and experience. With respect to anatomic conditions and treatment options:

- Vein diameter: For veins ≥ 12 mm, I preferentially use TT over NTNT
- Vein length: For vein < 10 cm in length, I favor TT over NTNT
- Location: For below-the-knee veins, I choose NTNT over TT

Which cases definitely warrant a "robust" thermal procedure?

Dr. Gasparis: The case in which a "robust" thermal procedure I feel is needed would be the patient with a large (> 12 mm) saphenous vein.

Do you see a special benefit of NTNT for the treatment of recurrent veins?

Dr. Gasparis: With respect to recurrent veins, NTNT has the following special benefits:

- If recurrence is due to failure of thermal closure of the saphenous vein, using a NTNT technology such as VenaSeal would be my next step to close the saphenous vein.
- If recurrence is due to neovascularization or there are extensive postthrombotic changes in the saphenous vein, using a NTNT technology such as a Varithena may be more appropriate.
- If recurrence of disease is due to below-knee saphenous disease, NTNT technology would be preferential.

1. Centers for Medicare & Medicaid Services. Medicare provide utilization and payment data: physician and other supplier. Accessed June 15, 2021. https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/Medicare-Provider-Charge-Data/Physician-and-Other-Supplier

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Dr. Gupta, acrylate embolization has been used in vascular medicine for > 30 years. Why do you think that the topic of hypersensitivity did not enter scientific discourse until it started being used to treat varicose veins?

Dr. Gupta: Cyanoacrylates are widely used "super glues" with many applications across vascular medicine and also with uses in dentistry and the cosmetic industry. Cutaneous allergic reactions to cyanoacrylates are type IV hypersensitivity reactions (HSRs) that are a T lymphocyte–mediated response to a recognized foreign antigen, not an antibody-mediated reaction as in other HSRs. Similar type IV HSRs with other medical uses of cyanoacrylates are well described in the literature including reactions to Dermabond (Ethicon) for skin closure and adhesives used for glucose sensors, eyelash extensions, and artificial nails.

The superficial venous space has seen significant growth in the past 10 years with the emergence of newer NTNT technologies, one of these being VenaSeal cyanoacrylate adhesive closure (CAC). Given this competitive market, clinicians must engage in discourse regarding the efficacy of the newer therapies as compared with other new and existing treatment options. For example, the risk of an HSR with VenaSeal may be preferable to the risk of a skin burn using a thermal, tumescent technology in a patient with a suprafascial great saphenous vein. Recent studies indicate that the rate of HSRs after CAC of incompetent saphenous veins is approximately 6%.[1] Awareness and recognition of an HSR enables clinicians to initiate appropriate treatment, avoid misdiagnosis, and/or delay treatment.

What form of assessment do you use to identify patients who might react to the material?

Dr. Gupta: Our protocol is to screen patients for allergies in general and known hypersensitivities to adhesives and glues. We also question patients regarding their history of skin conditions such as psoriasis and atopic dermatitis. In those patients with an uncertain allergy history, we partner with our colleagues in allergy/immunology to offer skin testing. In those patients who have a positive skin test, CAC is not offered as a treatment option.

Various data show that insufficient perforator veins have a particularly high recurrence rate. Do you see any advantages of thermal treatment using laser or RFA over ultrasound-guided foam sclerotherapy (UGFS)?

Dr. Gupta: Insufficient perforator veins play a well-known role in the development of chronic venous insufficiency and ulceration, and successful closure of incompetent perforators is predictive of wound healing. UGFS is my first-line therapy in the treatment of perforators. As compared to RFA and laser, UGFS is fast, technically straightforward, minimally painful, and less expensive. Closure rates with UGFS are lower than RFA/laser, and all three modalities show a higher failure rate in those patients with morbid obesity (body mass index > 50 kg/m^2). When UGFS fails, laser and RFA are excellent second-line therapies with reliably high closure rates.

1. Gibson K, Minjarez R, Rinehardt E, Ferris B. Frequency and severity of hypersensitivity reactions in patients after VenaSeal™ cyanoacrylate treatment of superficial venous insufficiency. Phlebology. 2020;35:337-344. doi: 10.1177/0268355519878618

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Dr. Ozsvath, a frequently discussed side effect of acrylate bonding is the development of a phlebitis-like reaction within the first few days after treatment. Have you also observed this reaction in your patients?

Dr. Ozsvath: When cyanoacrylate was first released, practitioners were inexperienced in recognizing and treating this particular side effect. Once discussion ensued among vein specialists, we gained insight. As data were collected, papers were published regarding identifying and treating this HSR. We also began to understand the pathophysiology behind it. When I first encountered it, I reached out to colleagues who were able to describe their management of the reaction. I also worked with a local allergist at my institution to come up with a reasonable treatment plan that we have since made into our standard protocol for this issue.

Understanding and recognizing the HSR is the most important first step. I screen patients to find out if they get HSRs to adhesives. Because most patients who do have hypersensitivity to adhesives are aware of it, asking about it will bring it to light. This has essentially made it much easier to rule out the use of cyanoacrylate in that patient population. For others, it is a very good option to consider. Fortunately, the reaction can be treated and controlled effectively in most cases. I have never had any patient with a HSR have any long-term sequelae. I have never had to remove such a vein, although it has been described in the literature.

Do you see any way to prevent or minimize this reaction?

Dr. Ozsvath: The easiest and best way is to ask the patient if they have sensitivity to adhesives. Most people don't think of a dermal reaction to a bandage as an allergy, per se. If you ask about drug allergies, this may be omitted. I have patients take nonsteroidal anti-inflammatory medications periprocedurally, and I explain the reaction as a possible risk. The patients are educated before the procedure and then are told to call with any questions. If they develop an issue, they are seen in the office. Then, depending on severity, an oral steroid taper is prescribed together with an antihistamine. I have also spent time teaching the office staff, nurses, and mid-level practitioners to recognize the reaction.

Another important technical detail is the importance of resheathing the catheter prior to removing it from the vein so that cyanoacrylate is not exposed to the skin and subcutaneous tissue. Additionally, I am careful to make the final administration of cyanoacrylate at the distal end of the treated vein in a way that the adhesive is not too close to the venipuncture site. This minimizes the risk of extravasation into the surrounding tissue. As with all techniques, patient selection is paramount.

In your opinion, are nerve lesions a relevant issue in thermal procedures?

Dr. Ozsvath: Neuropathy is certainly well described and can definitely complicate thermal ablation. I discuss this with patients as a possible complication. There are several things I do to help minimize this risk. From an anatomic point, it is important to think about where to access the vein and how far distally the vein actually needs to be treated. Sometimes other techniques can be used to treat distally diseased veins if needed, concurrently or separately. I also use plenty of tumescent solution to "push" the nerve away from the vein especially in areas that are at risk. In my experience, I have found that RFA has a lower rate of post-procedural neuropathy compared to laser. Additionally, there is a learning curve with all procedures. Early in my experience, although neuropathy occurred rarely, it was fortunately self-limiting. Proper patient selection, access location, and plenty of tumescent solution have greatly diminished the frequency of neuropathy in patients I treat with thermal ablation. ■

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PANEL DISCUSSION

Venous Reflux Treatment Decisions

A discussion on selecting optimal therapies, ensuring long-term outcomes and comfort, and complication avoidance.

Moderator: Raghu Kolluri, MD, MS, FSVM
Panelists: Steve Elias, MD, FACS, FACPh, and Eri Fukaya, MD, PhD

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Dr. Kolluri: What are some keys to achieving optimal outcomes and lower complications when using foam sclerotherapy in more severe disease settings? To begin, Dr. Elias, how should we time or stage our course?

Dr. Elias: In more advanced disease states (C4 and above, patients who have superficial axial reflux), I tend to treat the branch varicosities at the same time in hopes of preventing further progression or improving ulcer healing. However, in less severe disease (eg, C2), I usually do not treat the varicosities with foam or anything else at the same time. Essentially, the more advanced the disease, the more you should do.

Dr. Kolluri: Excellent. What is your advice on how best to prevent foam-induced thrombosis?

Dr. Fukaya: I think it is a common concern among those new to using foam. If I'm particularly concerned, I use ultrasound to identify calf perforators, and I mark the leg thoroughly so I know where they are connecting. As I inject, I scan in real time to see where the foam is spreading, and if it is close to the perforator, I'll apply pressure at the perforator to prevent flow into the deep system. Because that perforator may be refluxing, even if some foam were to go in, it could be argued that the foam will dilute by the time it gets into the deep vein. There are times when we see a little thrombus when they come back a week or so later, but I have never had the thrombus persist. Again, this step may not be necessary, but it gives me assurance when I'm concerned about preventing foam going into the deep system.

Dr. Elias: Foam is inactivated fairly quickly by the time it gets into the system, and there's a significant amount

of flow in the deeper system compared to the varicosities, so if I'm doing an ablation plus foaming, I will ablate, then foam, and then have the patients move and basically wash it out of the system. Like Dr. Fukaya said, if there are a few small areas, I'm not too concerned, and I don't perform ultrasound routinely when we first see them again unless they have significant complaints. I think it is a mostly theoretical concern, and if you move patients right after you inject, the risk is relatively low.

Dr. Kolluri: The most common question I get from my fellows-in-training is when do you use sotradecol and when do you use polidocanol?

Dr. Elias: In general for varicosities, I use sotradecol. I don't think there is necessarily much difference, but it's perhaps a bit stronger, so to speak. I tend to use polidocanol foam for smaller varicosities, or I'll use it as a liquid for spider veins or reticular veins. In general, if I'm making my own foam for advanced venous disease patients, I use sotradecol.

Dr. Fukaya: Especially with advanced disease, even if patients don't have ulcers, they may have thin-walled varices that can be prone to ulcerating, so I tend to use polidocanol in veins that are more superficial, with the thinking that it's less irritating.

Dr. Kolluri: What is your practice with regard to trapped coagulum? Do you bring these patients routinely or only when they are symptomatic?

Dr. Fukaya: Due to the nature of how sclerosants work, many patients will have trapped blood, and some may experience pain. They will get better with time, but it does help if you have them come back in 2 weeks (when I like to see them postoperatively anyway) to assess for this. If they are having pain, I may remove the trapped blood within areas they complain are painful. If it is a larger area, giving a bit of lidocaine helps. I also recommend use of nonsteroidals after the procedure.

Dr. Kolluri: Dr. Elias, when do you give nonsteroidals or cold or warm compresses versus puncturing or lancing the area?

Dr. Elias: It depends on how the patient is feeling in terms of pain and also what the overlying skin looks like. If there's a significant inflammatory reaction 2 to 3 weeks after the initial treatment, even without pain, I may evacuate the coagulum. I tend not to use an 11 blade,

instead preferring to try a 21-gauge needle first. The needle is pretty sharp, and I'm still amazed how much coagulum you can get out with just a 21-gauge needle stick, so that's my go-to. Then, yes, I use nonsteroidal anti-inflammatory medication if there is any erythema or pain. I don't use warm compresses on an inflamed area. I suggest icing it, which makes more sense to me if it's painful, but there is not much data on which to recommend cold versus hot.

Dr. Kolluri: What about concentration strength? What do you use and when?

Dr. Fukaya: If the veins are very superficial and thin-walled, I use 0.5% polidocanol for the reasons I mentioned earlier. If they are deeper, I want to make sure the veins close, so I'm less concerned with using something stronger.

Dr. Elias: I think size is one determinant, as well as where it is located with regard to the skin level. In general, for advanced disease with skin changes or even an advanced ulcer, we're clearly not going to do a phlebectomy, so I would tend to foam the varicosities in that area. If there are others higher up, such as in the mid-calf region, and they are large, I remove the larger ones in the areas of good skin and foam those in the areas of bad skin that may be 4 to 5 mm. In terms of concentration, I use 1.5% sotradecol in these varicosities, and I'll only go lower if there are areas much closer to the skin, where I'll use 1%. I stick to the rules in terms of volume, 10 mL per session; it's important to that keep in mind, as well as that you can always bring patients back and treat more if necessary.

Dr. Kolluri: Moving on to perforators, why do you feel the results we see here are not as good as with axial disease, regardless of modality?

Dr. Fukaya: I think it is a combination of the technical difficulty related to anatomic variance—the tortuosity and length of the perforator—and also the pressures coming from the deep system.

Dr. Elias: I believe it's mostly technical in the beginning, and I agree with Dr. Fukaya that with the perforators being very close to the deep system, the level of reflux and hypertension is different than a superficial axial vein running parallel to the system. I'm not sure we'll ever get to 90% technical success, unless the glue trials show us we can do better than we have so far. In terms of preferred modalities, foam is not the best option for perforator veins, with my preference being thermal or off-label use of glue.

Dr. Kolluri: Assuming you've algorithmically decided the perforator needs to be treated, and it is timed properly with respect to any other treatment that might be necessary, do you administer adjunctive foam in cases involving perforators? If so, is your postprocedural compression any different with and without foam?

Dr. Elias: Most of the time, I'm ablating the perforator thermally and then using foam for the varicosities, so patients will be in compression anyway. In patients with advanced disease, I have them go back to utilizing the compression they previously had been, but if I've used foam, I keep them in continuous compression day and night, except for showering, for 3 to 5 days before returning to normal compression. I would also note that it can be dangerous to directly access the perforator if you're using foam because you might also access the accompanying artery. If you inject the accompanying artery, you'll get very significant skin necrosis in that area.

Dr. Fukaya: If there is a large reservoir of veins around the perforator that can build up pressure, you want to obliterate as much as you can with foam. You do not need to be worried about going into to the deep system if you have ablated the perforator. Compression is very important after this, and I will often apply a multilayer wrap or unna boot, especially if they have wounds.

Dr. Kolluri: Conducting clinical trials in patients with advanced disease is challenging, in large part due to the need to collect and assess long-term results, increased interest in patient-reported outcomes, and the difficulties inherent in accounting for the wide variety of factors when randomizing patients, which may require impossibly large numbers of patients to be enrolled. In looking at the big picture, what do we need to see next? What would be most beneficial to address or demonstrate in a trial?

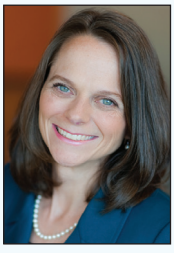
Dr. Elias: I would like to see a trial further exploring the role of maintenance treatment once the initial ulcer or significant dermatitis episode is addressed—what happens if you treat the underlying venous pathology in an ongoing fashion, before the patient progresses to have another ulcer? Can we decrease the ulcer recurrence rate and demonstrate whether the benefits of treating venous disease in a prophylactic manner after the initial ulcer is healed? Many of us are doing this already, but it would be beneficial to show the overall health care cost savings to society and individuals. ■

ROUNDTABLE DISCUSSION

Making Sense of Chaos: Formalizing an Approach to Female Pelvic Venous Disorder and Setting a Research Agenda

An update from the International Pelvic Venous Disorders in Women Work Group.

With Kathleen Gibson, MD; Neil Khilnani, MD, FSIR, FAVLS; and Mark H. Meissner, MD



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In October 2017, a Society of Interventional Radiology Foundation (SIRF) research consensus panel identified several tools that are necessary to develop in order to execute high-quality clinical studies to strengthen the evidence base related to treatment of pelvic venous disorders (PeVDs).[1] Since that time, many of the panelists have been working to accomplish these recommendations. We are joined by three members of the International PeVD in Women Work Group, Drs. Kathleen Gibson, Neil Khilnani, and Mark Meissner, to discuss the group's progress.

Dr. Khilnani, can you tell us about the PeVD work group?

Dr. Khilnani: The work group is composed of physicians and researchers from multiple disciplines interested in advancing the evidence base related to PevD. It developed as an extension of the SIRF consensus panel and includes physicians from gynecology, interventional radiology, and vascular surgery, representing many of their larger specialty societies. Also contributing to our work are scientists in patient-centered outcomes research and study methodology.

The most recent accomplishment of our work group has been the development of an instrument called SVP (symptoms, varices, pathophysiology), which can precisely classify all clinical, anatomic, and pathophysiologic variations of PeVD.[2,3]

Dr. Gibson, how would you explain the SVP tool? Can you share some examples of how it works?

Dr. Gibson: Much like the CEAP classification (clinical, etiology, anatomy, pathophysiology), the SVP instrument was designed as a discriminative tool to place patients in homogeneous groups based on their symptoms, the location of their varices, and their pathophysiology. It is not meant to be a tool that measures disease severity or be responsive to change with treatment. It will allow us to speak a "common language" in clinical practice and research when discussing or writing about patients with PeVD. There are three domains. "S" describes the location of symptoms in different anatomic zones: the left renal venous reservoir (S1, flank pain/hematuria), pelvis (S2, chronic pelvic pain [CPP]), genital pain (S3a, vulvar or scrotal), pain in the extrapelvic pelvic-origin escape point–derived varicose veins of the perineum and upper thighs (S3b), and venous claudication (S3c). "V" refers to location of varices: V1 (left renal hilum), V2 (pelvic venous plexus), V3a (vulva, scrotum), and V3b (extrapelvic pelvic-origin lower extremity veins varicose veins). The "P" refers to pathophysiology and has three subdomains: anatomy (A), hemodynamics (H), and etiology (E). Anatomy refers to the vein(s) involved using easy-to-remember abbreviations. Hemodynamics are designated as either reflux (R) or obstruction (O), and etiology is defined as nonthrombotic (NT), thrombotic (T), or congenital (C).

To give examples of how the instrument works, let's classify three different patients with CPP. The first patient is a woman in her early 40s. She is a P3G3 with symptoms of pelvic aching, heaviness, and dyspareunia; nonpainful vulvar varices on exam; and imaging that shows left ovarian vein reflux, left internal iliac vein reflux, and pelvic and left vulvar varicose veins. Her SVP classification would be S_2 (symptoms in the pelvis), $V_{2,3a}$ (varices in the pelvis and vulva), and $P_{LOV,R,NT;LIIV,R,NT;LPELV,R,NT}$ (left ovarian vein reflux, nonthrombotic; left internal iliac vein reflux, nonthrombotic; and pelvic escape point vein, reflux, nonthrombotic). The second patient is a woman in her mid-30s with CPP and left leg bursting pain with exercise. On duplex ultrasound, she has nonthrombotic extrinsic compression of her left common iliac vein, reflux in her left internal iliac vein, and large parauterine veins. Her SVP classification would be $S_{2,3c}$ (symptoms in the pelvis and venous claudication), V_2 (varices in the pelvis), and $P_{LCIV,O,NT;LIIV,R,NT}$ (left common iliac vein, obstruction, nonthrombotic; left internal iliac vein, reflux, nonthrombotic). The final patient is a woman in her late 20s, who is nulliparous with CPP and has no visible lower extremity varicose veins, with left renal vein compression, left ovarian vein reflux, and dilated pelvic veins. Her SVP classification would be S_2 (symptoms in the pelvis), V_2 (varices in the pelvis), and $P_{LRV,O,NT;LOV,R,NT}$ (left renal vein, obstruction, nonthrombotic; left ovarian vein, reflux, nonthrombotic). Although this seems complex, this classification scheme becomes straightforward with practice.

Dr. Meissner, as leader of the SVP project, why is SVP so important to advancing research on PeVD in women? Where can our readers learn more about this instrument and how to use it?

Dr. Meissner: Much of the previous research regarding PeVDs used historical nomenclature such as "pelvic congestion," ''nutcracker syndrome," and "May-Thurner syndrome" to classify patients. Unfortunately, both the pathophysiology and symptoms associated with these syndromes overlap to a substantial degree, making classification of patients in clinical communication and research studies very imprecise. For example, ovarian vein reflux and left common iliac vein compression can both cause CPP in women. The SVP instrument allows these two different clinical scenarios to be precisely characterized. Identifying homogeneous patient populations is important to developing the outcomes instruments and clinical trials necessary to advance the field. For example, women with pelvic pain secondary to left common iliac vein compression should not be included in trials evaluating the efficacy of ovarian vein embolization.

It is recognized that like pelvic venous disease, the SVP classification is complex. However, when the structure of the classification is understood, it becomes

much more intuitive and should become the standard for clinical communication, research, and publication. Concurrent publication in the *Journal of Vascular Surgery: Venous and Lymphatic Disorders and Phlebology* will ensure the manuscript is widely available,[2,3] and translation into several languages is also planned. The American Vein & Lymphatic Society has developed several aids to assist in adoption of the classification, including smartphone apps (available at www.myavls.org/svp-classification.html) and a soon-to-be-released educational workbook.[4]

Dr. Khilnani, can you comment on other projects the work group is addressing?

Dr. Khilnani: Nearly all the published evidence related to PeVD in women have been single-arm retrospective case series. In addition, most of the studies related to CPP from a venous source have relied on pain scores as the primary outcome measure. However, we know that the impacts of CPP affect other domains of health, such as social, professional, relationship, and behavioral function. We are currently applying for grant funding to perform qualitative, patient interview research to develop a quality-of-life instrument that can be used as a primary outcome measure in comparative drug and device trials in women with CPP of venous origin. Scientists from Evidera, an outcomes research organization that supports patient-centered research by academia and industry, are collaborating with us to develop the tool. One of the members of our work group from Evidera was involved in developing and validating the Uterine Fibroid Symptom and Quality of Life instrument, the most-used tool for drug and device trials related to uterine fibroids.[5] We plan to recruit women with CPP and a likely venous cause from CPP gynecologic practices at several academic- and nonacademic-affiliated sites in North America to develop our tool. Then, we'll assess the differences in how women with CPP of a nonvenous cause are impacted by asking them to comment on the items in the tool we developed in separate qualitative interviews. Finally, we plan to perform preliminary validation of the tool's responsiveness to change in patients before and after endovascular therapy.

Another member of the work group, Dr. Ronald Winokur from Sidney Kimmel Medical College at Thomas Jefferson University Hospital, is in the final stages of preparing a grant application to support a randomized controlled trial to explore the value of ovarian vein embolization. The study will recruit women with ovarian vein reflux and CPP felt to be of a venous origin ($S_2V_2P_{BGV,R,NT}$, $S_2V_2P_{RGV,R,NT}$, or $S_2V_2P_{LGV,R,NT}$). Patients found with clinically significant left renal vein and left common iliac vein compression will not be included. Women will be randomized after venogram/intravascular ultrasound confirmation of their classification to either bilateral ovarian vein and periuterine/ovarian venous plexus embolization or conservative care. The patients will be blinded as to what group they are assigned to. A variety of outcome measures will be used at fixed intervals before and after the procedures, including the novel quality-of-life tool we are currently developing, as well as other generic and women's health-related tools. The study will extend for 6 months before unblinding patients, allowing them to pursue additional therapy as needed. ■

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Real-world use of the Indigo® System Lightning® 7 and Lightning 12 Intelligent Aspiration in arterial, pulmonary embolism, and venous cases.

Thrombotic disease puts patients at high risk of mortality, poor quality of life, and poor treatment outcomes. Treatment options for thrombus have been limited in function and efficiency. Lytic infusions are associated with higher risks of bleeding, while other devices are linked to incomplete thrombus removal, distal emboli, or further bleeding complications. The Lightning® Intelligent Aspiration System (Penumbra, Inc.) shows potential to be a successful treatment option for thrombotic disease.

Lightning, first introduced in July 2020, includes 7-, 8-, and 12-F catheter sizes and uses an "intelligent" device that has the ability to detect thrombus during the procedure and potentially reduce blood loss. The microchip design utilizes a thrombus detection algorithm meant to detect when the catheter is in patent flow or when it is in thrombus, initiating intermittent aspiration to mitigate blood loss. The system also provides audible feedback that alerts the operator when the catheter is transitioning between areas of thrombus in the form of clicking. The operator can focus on removing thrombus completely rather than being limited by the estimated blood loss (EBL).

The second component of the system is the catheter. Lightning 7 and Lightning 12 have laser-cut hypotube technology designed to enhance the deliverability of power aspiration in hard-to-reach vasculature. The trackability and torqueability is bolstered by the hypotube that aims to support the removal of thrombus from large vessels with wall-adherent thrombus. The Lightning unit and catheter create a mechanical thrombectomy system that is simple to use compared to other products.

From personal experience, we have seen quicker procedure times and higher rates of single-session therapy with reduced lytic use. The Lightning Intelligent Aspiration System has the capacity to change the way physicians manage and treat thrombotic disease in high-risk patients.

–Amit Srivastava, MD, FACC, FABVM

LIGHTNING 7 THROMBUS REMOVAL IN THE SFA VIA PEDAL ACCESS

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Disclosures: Speaker for and consultant to Abbott Vascular, Cardiovascular Systems Inc., Penumbra, Terumo, and W.L. Gore.

PATIENT PRESENTATION

A woman in her early 80s with Rutherford class 4 claudication of the right lower leg with a known contralateral common femoral artery (CFA) occlusion presented with leg pain and a thrombosed right superficial femoral artery (SFA) stent 3 months after the first intervention. The patient had been noncompliant with antiplatelet therapy and also had a history of tobacco use, hypertension, and hyperlipidemia.

INTERVENTION

Under ultrasound guidance, the right posterior tibial artery was accessed using a 6-F GlideSheath Slender

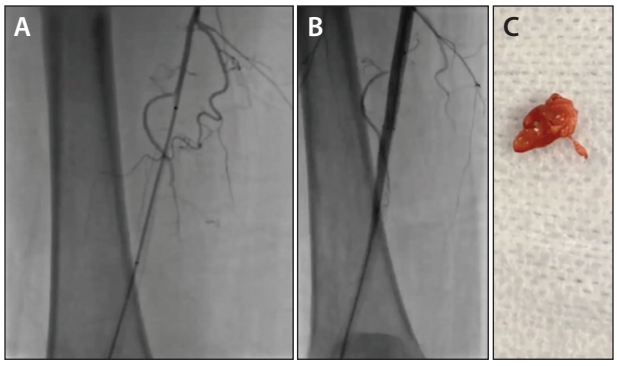

Figure 1. Lightning 7 thrombus removal case images.

introducer sheath (Terumo Interventional Systems) that allowed Lightning 7 to be used with a 6-F access site. After gaining tibial/pedal access, fluoroscopy revealed thrombosed stents in the right lower extremity with presence of collaterals (Figure 1A). The catheter was advanced over a wire into the sheath using an introducer packaged with Lightning 7.

Using the circumferential sweep and the Separator 7 (SEP7; Penumbra, Inc.), wall-adherent thrombus was removed from the stent, allowing the catheter to work in a 360° fashion throughout the posterior tibial artery (Figure 1C). Due to severe residual stenosis in the SFA, a prolonged percutaneous transluminal angioplasty (PTA) was performed in a retrograde fashion. Good flow was restored through the SFA to the distal popliteal segment (Figure 1B).

DISCUSSION

An advantage of mechanical thrombectomy is that you can choose to go antegrade or retrograde while potentially minimizing the risk of distal embolization. In this case, where contralateral femoral access was not an option, we were able to get pedal access with the Lightning 7. **Paired with the 1:1 torqueability of the catheter, in this case, the Lightning technology also helped mitigate blood loss while removing stubborn wall-adherent thrombus in stenosed arteries**.

LOWER EXTREMITY ARTERIAL THROMBUS REMOVAL USING LIGHTNING 7

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Disclosures: Owns public stock in Penumbra.

PATIENT PRESENTATION

A patient in his late 60s presented with history of coronary artery disease, congestive heart failure, and peripheral vascular disease. He presented with 2 to 3 weeks of right lower extremity claudication at 100 feet after stopping dual antiplatelet therapy for 3 days for an unrelated procedure. His right thigh and medial foot and ankle were cool to the touch on examination. Arterial Doppler ultrasound demonstrated proximal long-segment right SFA occlusion.

INTERVENTION

Left groin access was achieved using a 5-F sheath. An aortogram and pelvic angiogram demonstrated patent aortoiliac inflow without significant stenosis to the bilateral lower extremities. Right lower extremity runoff angiography demonstrated patency of the right CFA and profunda femoris artery with proximal long-segment occlusion of the right SFA, including in-stent occlusion with distal reconstitution (Figure 1).

The 5-F sheath was upsized to a 7-F Destination sheath (Terumo Interventional Systems) and an 0.018-inch

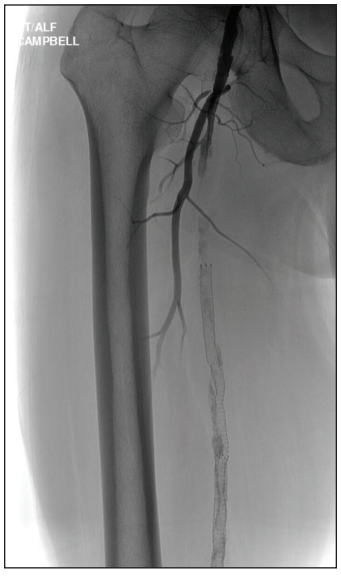

Figure 1. Right lower extremity runoff angiogram demonstrating proximal long-segment occlusion of the SFA with distal reconstitution.

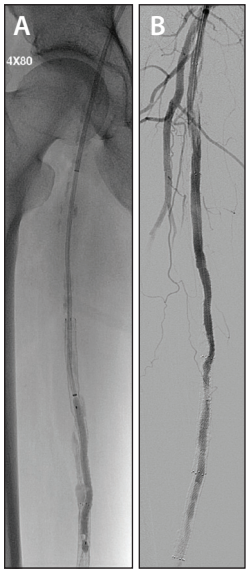

Figure 2. Balloon-assisted CAT7 crossing of the stent (A). Post CAT7 thrombectomy angiogram (B).

crossing catheter and wire were used to cross the occluded segment into the popliteal artery. The Indigo® Lightning® Intelligent Aspiration System CAT™ 7 (Penumbra, Inc.) was then used to perform over-the-wire mechanical aspiration thrombectomy of the long-segment SFA occlusion. The CAT7 was preloaded with an 0.018-inch 4- X 8-mm Ultraverse balloon (BD) to assist in crossing the stent struts (Figure 2A).

After a few passes, postthrombectomy angiography demonstrated restoration of in-line flow through the right SFA stent (Figure 2B).

No tissue plasminogen activator (tPA) was given for the case. The patient was discharged the same day without an overnight stay.

DISCUSSION

Acute lower extremity ischemia, defined as a rapidly developing or sudden decrease in perfusion to the lower extremity, often results in threatened limb viability. Frequently, this is due to arterial occlusion, as was the case with this patient. Rapid revascularization is indicated when the limb is viable and salvageable.

Catheter-directed therapy can be performed using catheter-directed thrombolysis or endovascular thrombus aspiration. Thrombolysis generally requires multiple interventions, longer lengths of stay, added costs, and places patients at risk of intracranial bleeding.

The Indigo System CAT7 with Lightning Intelligent Aspiration technology provides a new and excellent alternative for endovascular revascularization. The catheter has a convenient low 7-F profile but maintains a robust inner diameter at 0.082 inches. Coupled with the high-power Penumbra ENGINE™, it is a potent tool in endovascular peripheral arterial thrombectomy. The Lightning 7 Intelligent Aspiration technology provides intraprocedural audiovisual cues to help detect thrombus, as well as dual-pressure sensors for real-time flow monitoring. **The new XTORQ tip design provides the directional ability needed to tackle eccentric wall-adherent thrombus.** These design features allow our team to perform revascularization while minimizing tPA use. In many cases, such as in this patient, full revascularization can be achieved with no tPA administration, and hospital length of stay can be kept to a minimum.

PERCUTANEOUS EMBOLECTOMY TO TREAT ACUTE LIMB ISCHEMIA

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Disclosures: Consultant to Penumbra, Inc.

PATIENT PRESENTATION

The patient was admitted to the emergency room with report of leg pain. CT revealed bilateral popliteal emboli (Figure 1A), so the patient was taken directly to the catheterization lab.

INTERVENTION

Left and right popliteal embolectomy was performed using Lightning 7. Access was gained in the opposite CFA using an 8-F, 65-cm Pinnacle sheath (Terumo Interventional Systems). The catheter was used up and over with the SEP7 to maintain luminal patency as thrombus was aspirated. Once the left side was cleared, access was gained in the left CFA with the same sheath to clear the right popliteal. Throughout the procedure,

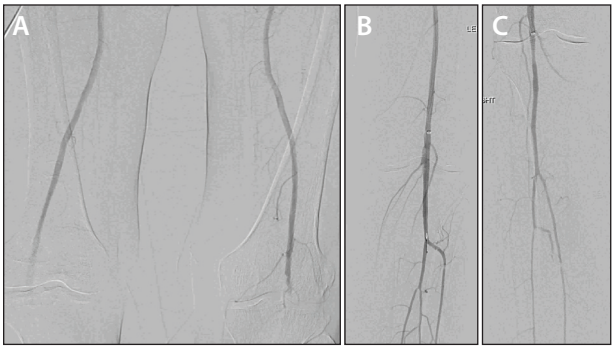

Figure 1. Angiogram of occluded left and right popliteal arteries (A). Angiogram showing restored flow to left popliteal artery (B). Flow restored to right popliteal artery (C).

the Lightning device flashed yellow without any clicking, indicating thrombus was most likely occluding the catheter. The hemostasis valve adapter was removed from the sheath and the catheter pulled back to reveal heavy thrombus corked at the tip of CAT7. Flow was restored to both popliteal arteries with good distal runoff (Figure 1B and 1C). No tPA was used, EBL was only 110 mL, and the patient was released the next day.

DISCUSSION

Lightning 7 is a great alternative to surgical embolectomy for acute limb ischemia (ALI) patients. In years

past, this patient would have been taken straight to the operating room for an open procedure. **With percutaneous embolectomy, our practice has seen no issues of surgical site incisions, infections, or complicated fasciotomies**. With the inherent risks of using tPA, a mechanical thrombectomy option that can minimize the need to use tPA and may reduce intensive care unit (ICU) stay is ideal.

TREATING TOTAL OCCLUSION OF TIBIOPERONEAL TRUNK AND ANTERIOR TIBIAL ARTERY WITH LIGHTNING 7

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Disclosures: Consultant to, speaker for, and research support from Penumbra, Inc.

PATIENT PRESENTATION

The patient presented in the emergency room as an ALI case with irregularity of the distal left superficial femoral artery (SFA) and a total occlusion of the tibioperoneal (TP) trunk, with further thrombus in the anterior tibial (AT) artery (Figures 1A and 1B). Intravascular ultrasound (IVUS) revealed irregularity within the vessel in the form of ectatic aneurysm with free-floating thrombus.

INTERVENTION

Via contralateral access, Lightning 7 was used to aspirate thrombus in the TP trunk in conjunction with the SEP7 to break up the dense clot in stepwise fashion. The catheter was advanced into the peroneal, and clot was quickly removed (Figure 2A). The catheter was then further advanced into the posterior tibial (PT) artery and completely cleared the vessel (not shown). After this, we advanced the Lightning 7 into the AT, which had mid-vessel occlusion. This was quickly cleared with restoration of three-vessel runoff to the foot (Figure 2B). An 11- X 5-cm Viabahn covered stent (Gore & Associates) was deployed across the lesion with complete exclusion (Figure 2C).

DISCUSSION

In ALI cases, the Lightning 7 device serves as a great option to access clot not only above the knee but also below. The laser cut, hypotube design allows nearly the aspiration capacity of the 8-F CAT 8 catheter in a 7-F form factor (0.006-inch inner diameter difference). The lower profile facilitates access in small vessels while the larger surface area increases contact with thrombus. In my experience, combined with the Lightning Intelligent Aspiration system, blood loss and procedural time is significantly reduced; moreover, these features have been shown to facilitate single-session therapy.

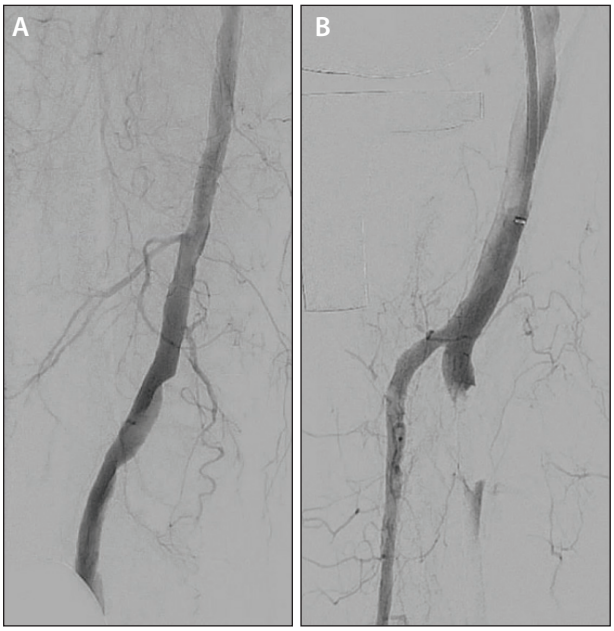

Figure 1. Occlusion in the AT artery (A) and TP trunk (B).

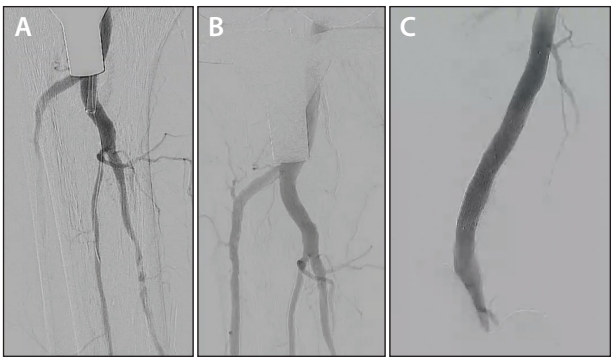

Figure 2. Flow restored to the peroneal artery (A) and to the AT artery (B). Stent placed to reduce irregularity from the ectasia (C).

LIGHTNING 12 THROMBECTOMY FOR BILATERAL PULMONARY EMBOLISM

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Disclosures: None.

PATIENT PRESENTATION

A female patient in her mid-60s with a history of recent lung transplant presented with hypoxemic respiratory failure. CT demonstrated extensive pulmonary emboli (PE) bilaterally and suggestion of right heart strain (Figure 1). Echocardiogram confirmed systolic and diastolic septal flattening suggestive of right ventricle pressure and volume overload; normal right ventricular size was noted, as were moderately reduced systolic function and a hypokinetic right ventricular free wall. The patient was also found to have elevated cardiac enzymes.

Given the patient's limited reserve secondary to idiopathic pulmonary fibrosis within the native right lung and developing infarcts within the transplant left lung, the PERT decided to proceed with thrombectomy and possible lysis.

INTERVENTION

A 12-F sheath was placed within the right internal jugular vein (Figure 2). The pulmonary arterial system was catheterized using a Swan-Ganz catheter that was subsequently exchanged for a 5-F pigtail catheter for angiography and pressure measurement. Initial pulmonary angiography demonstrated extensive clot burden throughout the bilateral pulmonary vasculature, greatest in the right-upper and left-lower segmental arteries. Using a 1-cm Floppy 0.035-inch Amplatz wire, Lightning 12 was advanced into the right PA and aspiration thrombectomy was performed. The catheter was then carefully advanced into the left lobar and segmental transplant PA for thrombectomy. Postintervention digital subtraction angiography demonstrated improvement of vascular flow in the bilateral PAs (Figure 3).

The patient's clinical status improved on the table and served as an endpoint for intervention along with the improved appearance of the pulmonary angiogram. Postintervention echocardiography demonstrated normal right ventricular size, mildly reduced systolic function, and normal PA systolic pressure.

DISCUSSION

The Lightning 12 is made of a laser-cut stainless steel hypotube with large lumen to maximize thrombus engagement. The catheter has a multipitch hypotube for 1:1 torque transfer and advanced deliverability. In our experience, the Lightning 12 system offers an easy-to-use large-bore thrombectomy device within the Penumbra thrombectomy device portfolio that is easily navigated from the right PA into the left.

A Separator device (Penumbra, Inc.) intended to clear the catheter lumen can be used in conjunction to allow continuous aspiration and macerate clot at the tip of the catheter. The Separator is designed with a solid piece of wire, distally containing a radiopaque polymer bulb for increased visualization under fluoroscopy. The bulb is used to break up the clot as it is pulled into the reperfusion catheter to decrease catheter lumen obstruction with clot. This process is repeated throughout aspiration as the aspiration catheter is advanced to engage the thrombus.

Patients with lung transplants present unique challenges in the treatment of PE given the lack of bronchial artery

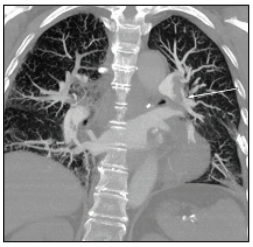

Figure 1. Submassive PE within the right main and left lobar pulmonary arteries (PAs).

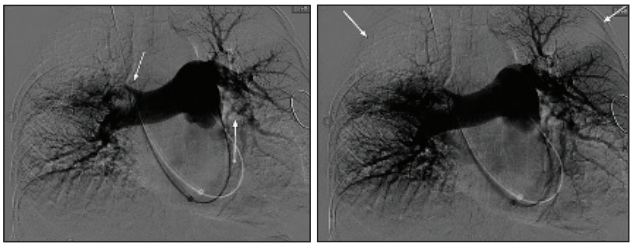

Figure 2. Balloon catheter advanced into the PA from the right internal jugular vein approach.

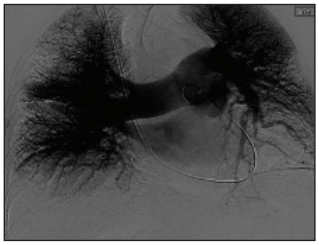

Figure 3. Postintervention angiography demonstrated a significant decrease in thrombus burden with improved parenchymal flow throughout the right and left upper lobes.

circulation as seen in native lungs. There is an increasing concern for lung reserve with pulmonary infarcts as well as caution related to pulmonary hemorrhage within the infarcted tissue with the initiation of lysis.

As mechanical thrombectomy becomes a more standard technique for PE treatment, patient selection and optimizing technique become critical as many PE patients are critically ill and will not tolerate prolonged time in the interventional radiology suite. In our experience, the Lightning 12 Intelligent Aspiration system has effectively removed clot with minimal complications. Penumbra's partnership with RapidAI, an app for PE meant to streamline communication and standardize workflow for PE patients, shows the potential to connect hospital systems and improve patient outcomes and experiences.

THROMBUS REMOVAL IN LEFT AND RIGHT SIDE PULMONARY ARTERY

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Disclosures: Consultant to Abbott Vascular, Boston Scientific Corporation, Medtronic, and Penumbra, Inc.

PATIENT PRESENTATION

A woman in her early 40s with no significant prior medical history was evaluated in the emergency room after experiencing syncope and identified as having a large saddle PE (Figure 1A). Echocardiography showed questionable thrombus in transit, significant right heart strain, and right ventricular enlargement and hypokinesis.

INTERVENTION

Right femoral vein access was obtained using a micropuncture kit. A 14-F DrySeal sheath (Gore & Associates) was inserted into the main PA over a Supra Core guidewire (Abbott). Then, Lightning 12 was taken first into the left PA where there was a smaller amount of thrombus that was cleared quickly. At that point, attention was turned to the right PA where there was a large amount of thrombus. With the assistance of the Separator (Figure 1B), several passes were made into the upper, middle, and lower lobes after first clearing the right PA itself (Figure 1C). A large amount of thrombus was removed successfully (Figure 1D). The PA pressure was lowered from 42 to 26 mm Hg during the procedure. More importantly, the patient noticed that her breathing had improved on the table. Her initial oxygen requirement of 10 L upon arrival to the cardiac catheterization laboratory was lowered to room air when she was taken back to her room.

DISCUSSION

In many instances, PE requires emergent interventions. There are data to support thrombolytic therapy as well as some evidence that mechanical intervention can be clinically useful. The emergence of newer technologies such as Lightning 12 may be an example of where technology has outpaced clinical data. It will be important to see in the future if case representations such as this are the norm and the paradigm shifts to more emergent intervention of intermediate to high-risk PE.

In terms of ease of use, Lightning 12 is easy to manipulate not only in the main PA but also distally into the lobar PA. Additionally, the audiovisual cues from Lightning and the thrombus detection algorithm are very helpful when removing thrombus from the PA. The audio cues in the form of clicking help with clot detec-

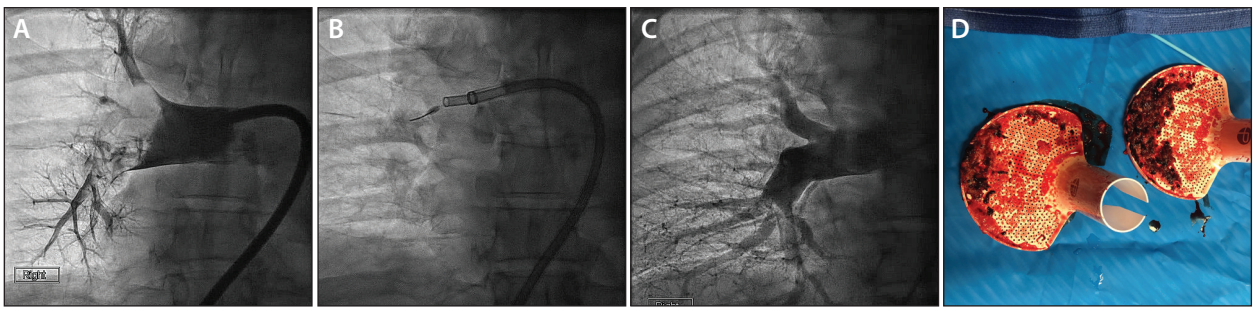

Figure 1. Angiogram showing thrombus in the right PA (A). Lightning 12 and SEP12 being used in the right PA (B). Flow restored to the right PA (C). Thrombus removed during the procedure (D).

tion to optimize thrombus removal and enables the operator to focus on the screen rather than monitoring how much blood is flowing through the tubing and canister. The Separator is also of great utility when trying to remove large volumes of thrombus. The blood loss remains well within acceptable limits thanks to the intelligent aspiration system that optimizes thrombus removal primarily by helping distinguish thrombus from blood.

LIGHTNING 12 THROMBECTOMY FOR ILIAC VEINS AND IVC

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Disclosures: None.

PATIENT PRESENTATION

A teenaged patient was transferred from an outside hospital for swelling, redness, heaviness, and discomfort in the right lower extremity over the previous 2 weeks. Imaging revealed extensive deep venous thrombosis of the right iliac veins (Figure 1) and a partially thrombosed, ectatic left-sided inferior vena cava (IVC; Figure 1A).

INTERVENTION

A 12-F sheath access was obtained in the right popliteal vein with the patient supine. The Lightning 12 aspiration catheter was used to perform mechanical thrombectomy in the clotted veins, including the anomalous IVC, after lacing the thrombus with alteplase. Post-thrombectomy images showed complete resolution of the thrombus (Figure 2). Significant clot was aspirated with minimal blood loss (Figure 3).

DISCUSSION

In this case, the Lightning system was used in anomalous vascular anatomy and demonstrated excellent torqueability and suction capacity. Most notably, the volume of blood loss, which is critical in younger patients, was well-controlled and insignificant. The sound alert system when the catheter tip is not in the clot is an excellent audible cue for the operator to reposition the catheter in the clot. The catheter tip is soft to mitigate the risk of intimal damage or vascular perforation, a factor to consider in younger patients. The system was easy to assemble and use. All of the clot was aspirated in one session without the need for extended-infusion thrombolysis or additional procedures to regain vascular patency. This helped reduce extended in-hospital monitoring and stay.

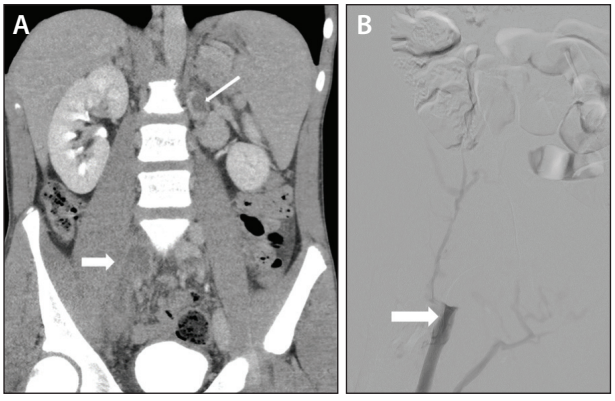

Figure 1. Contrast CT of the abdomen showing large clot burden filling and expanding the right iliac veins (wide arrow) (A). Also noted is the thrombus in the anomalous left-sided IVC (thin arrow). Venogram confirming complete thrombotic occlusion of the right iliac veins above the femoral vein (arrow) (B).

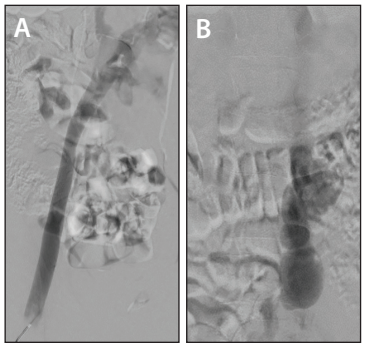

Figure 2. Post-thrombectomy venogram showing complete recanalization of the right iliac veins (A) and patency of the left-sided IVC (B).

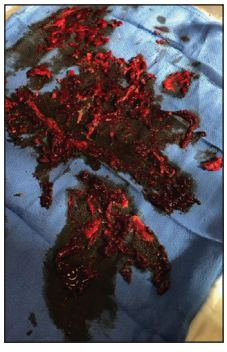

Figure 3. Picture of thrombus aspirated using the Lightning 12 aspiration catheter.

IVC THROMBUS REMOVAL USING LIGHTNING 12

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NYU Langone Health
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Disclosures: Speaker for Cook Medical, Inari, and Penumbra, Inc.

PATIENT PRESENTATION

A man in his early 60s with a remote history of bilateral iliocaval stenting at an outside hospital presented with a 2-week history of right leg swelling. A venous duplex ultrasound identified extensive venous thrombosis extending from the popliteal vein to the external iliac vein on the right. CT venography of the abdomen and pelvis was performed, which revealed an extension of the thrombus to the IVC. The stents placed on the left had migrated to encroach across the caval confluence (Figure 1). Finally, the patient had splenomegaly from a history of idiopathic thrombocytopenic purpura (ITP) and newly identified small bowel carcinoid. The biology of the carcinoid was favorable and given the severity of the symptoms, an intervention was planned.

INTERVENTION

The patient was placed in the prone position and right popliteal access was obtained. The Lightning 12 system was used to perform mechanical thrombectomy from the native popliteal to the common femoral vein. It was next advanced through the right venous stent up to the confluence of the IVC (Figure 2). Extensive thrombus was removed (Figure 3).

IVUS was performed that demonstrated encroachment of the right common iliac vein outflow by the left venous stents. Left popliteal venous access was obtained to correct the migrated stent (Figure 4).

DISCUSSION

The Lightning 12 aspiration catheter has excellent torqueability and a curved tip that allows for a 360° sweep. The catheter is soft, has an atraumatic design, and can be used with or without the wire. Using this catheter without a wire increases the aspiration lumen and allows the catheter to form a curve, increasing the circumferential sweep. Coupled with Lightning's intelligent aspiration, the system is effective in thrombus retrieval and designed for blood loss reduction. In this case, the thrombus was > 2 weeks in age with some organized elements that were likely present along the stent wall. The fresh thrombus was easily removed. Using the catheter without a wire worked particularly well along the stent in aspirating some of the more adherent thrombus as well.

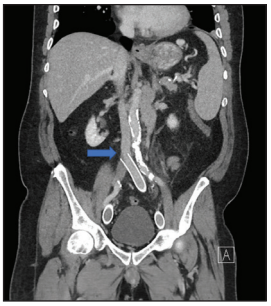

Figure 1. CT demonstrating left iliac stent migration. The blue arrow points to the encroachment of the left iliac vein stent.

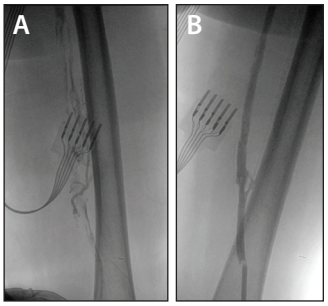

Figure 2. Femoral vein before (A) and after (B) thrombectomy.

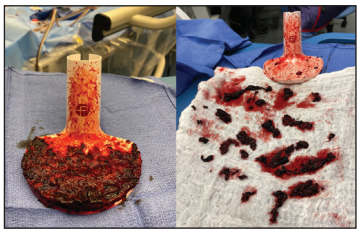

Figure 3. Thrombus removed.

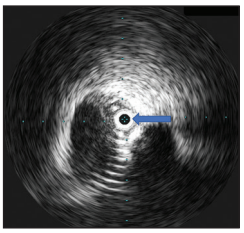

Figure 4. IVUS demonstrating outflow obstruction on the right. The blue arrow points to the right common iliac vein at the confluence of the IVC.

THROMBUS REMOVAL IN LEFT LOWER EXTREMITY USING LIGHTNING IN PATIENT CONTRAINDICATED TO SYSTEMIC LYTICS

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Disclosures: Speaker for Bard and Acera Surgical Wound Care.

PATIENT PRESENTATION

A man in his early 50s presented in the emergency department with left lower extremity swelling and increased pain and numbness. The patient had a history of venous thrombus from 1 year ago while being on anticoagulants, and a spinal tumor that contraindicated him for systemic tPA. Extensive left lower extremity venous thrombus was detected (Figure 1A). CTA revealed acute bilateral PE, for which high-dose heparin was prescribed as the patient exhibited no shortness of breath.

INTERVENTION

The patient was laid in a supine position with access gained in the popliteal vein using a 12-F, 13-cm Check-Flo introducer (Cook Medical). Lightning 12 was used to successfully remove thrombus from the iliac to the popliteal vein. After a majority of thrombus was removed and flow established, a small amount of tPA was administered locally. The patient had an area of stenosis in the common femoral vein that was angioplastied, resulting in good flow (Figure 1B-1D). A significant amount of thrombus was removed throughout the left lower extremity (Figure 1E). The patient tolerated the procedure well, with an immediate decrease in swelling and leg pain.

DISCUSSION

The Lightning 12 device was a good option for the removal of thrombus from the iliac to the popliteal vein. Compared to other devices currently on the market, it allows more thrombus to be removed in a short amount of time, therefore, leading to less use of thrombolytics. As the patient was contraindicated to systemic lytics and presented with leg pain and bilateral PE, immediate relief was needed and the Lightning 12 technology proved to be an important tool in our armamentarium to enable treating this patient. ■

Disclaimer: The opinions and clinical experiences presented herein are for informational purposes only. The results may not be predictive of all patients. Individual results may vary depending on a variety of patient-specific attributes.

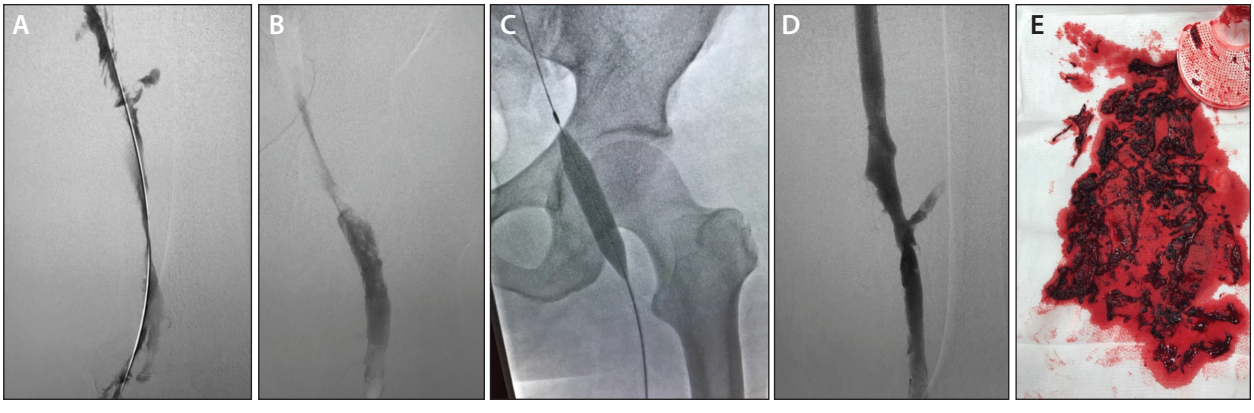

Figure 1. Angiogram of left femoral vein (A). Angiogram showing stenosis of common femoral vein (B). Angioplasty of stenosed vessel (C). Good flow was restored to the femoral vein postintervention (D). Thrombus removed during procedure (E).

Building a VTE Center of Excellence

How one institution introduced dedicated care coordinators to identify, triage, and follow patients with venous thromboembolic disease.

With Michael Knox, MD, FACR; Trevor Cummings, MD, FACEP; and Erin VanDyke, MPAS, PA-C

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When an ST-segment elevation myocardial infarction (STEMI) or stroke patient presents to the emergency department (ED) at any hospital in the United States, their care pathway is largely predetermined. For these patients, care has become standardized over time, with programs that have evolved to ensure they will be appropriately identified, triaged, and treated in short order and with minimal variance. The same is not true for patients who present with high-acuity venous thromboembolism (VTE) disease, where systematic and coordinated care is lacking and variability common.

Based on years of research on risk stratification and recent developments in mechanical thrombectomy, an enthusiastic team of providers at Spectrum Health in Grand Rapids, Michigan, set out to change that, developing an advanced VTE program similar to what has become familiar in STEMI and stroke care. They created a paradigm shift in care at their institution with a groundbreaking program that introduced a vital new role: a dedicated VTE care coordinator. Their program has changed practice and allowed them to more aggressively treat more VTE patients, leading to improved outcomes. We interviewed Dr. Michael Knox, Dr. Trevor Cummings, and advanced practice provider (APP) Erin VanDyke to learn how their program came to be, how patient pathways emerged, and how they plan to take their successes to the next level to become a VTE Center of Excellence, sharing data, best practices, and providing leadership to other institutions.

There's no better example of a successful VTE program than what you have developed at Spectrum Health. When did your interest begin, and what was it like before you launched this program?

Dr. Cummings: About 10 years ago, there was a big paradigm shift for those of us trying to move the needle on VTE treatment. Direct oral anticoagulants (DOACs) came out, giving us an oral medication that was instantly therapeutic for a patient. DOACs allowed us to treat some VTE patients as outpatients rather than placing them on a heparin drip, admitting them, and having them spend days in the hospital. Around that time, there was also a lot of work on risk stratification for VTE and trying to find optimal treatment options for different patient populations.

Dr. Knox: We became interested in treating submassive pulmonary embolism (PE) about 12 years ago when catheter-directed thrombolytic therapy was becoming more accepted at some of the more progressive institutions. We started with ultrasound-facilitated thrombolysis, and through that experience, our clinicians saw the clinical benefits and became very supportive of treating submassive (intermediate-risk) patients more aggressively than with anticoagulation alone. We tried some mechanical devices but never latched on to one that was effective and safe until the FlowTriever System (Inari Medical) came along.

Erin VanDyke: PE intervention was driven by a single question during risk assessment: "Can this patient have thrombolytics, and if so, does the benefit outweigh the risk?" When you've seen life-altering complications from the use of lytics, it's very difficult to assess a clinically stable patient and recommend exposing them to thrombolysis. As we started to see a paradigm shift and introduced FlowTriever as a reliable and safe intervention, the risk profile during clinical assessment for PE intervention dropped to nearly zero at our institution. This shift promoted changes to the clinical assessment of PE patients, as well as recommendations for intervention. Patients who previously would not have been considered candidates due to contraindications for thrombolysis could now be considered for intervention.

Many VTE patients come in through the ED. Who diagnosed and followed these patients back then, and how did communication happen?

Dr. Cummings: Without the current standards in place, there was a lot of variation—in evaluation, diagnostic testing, and treatment. I would still risk stratify but mostly to identify low-risk patients. I would also look to identify massive and submassive PE but only to determine where to put them. A massive PE would clearly go to the intensive care unit (ICU), but a submassive PE was more challenging. I would call the hospitalist for these "in betweener" patients, and they were at risk for being moved through the system with wide variations in management and varying follow-up that could put them at risk. They could be lost in the system easily with past approaches.

Before we set up our VTE program, we wouldn't call interventional radiology (IR) or other proceduralists on our patients. We would admit them and leave that to the inpatient side of things. Some IR operators were interested; however, because what they could do was not universally accepted and thought to involve some risk, they left it to the inpatient service to decide which patients got a consult.

Erin VanDyke: Prior to current standards, we didn't have algorithms in place for VTE. The ED had variable direction for who and when to contact and no criteria to follow for VTE diagnosis from an interventional service. If IR was not consulted from the ED, the patient would be admitted and depend on the inpatient teams to guide additional consults. Often, these consults were based on clinical stability alone. There was a silo effect where our communication wasn't congruent. As we worked to decide on the best intervention, communication could be separated by hours or days, depending on the patient's status and what services were involved.

Dr. Knox: Similarly, posttreatment follow-up for these patients was very inconsistent. Nurses would perform clinical follow-up from our IR outpatient office on those patients who had catheter-based intervention. Most PE patients would be called on the phone; occasionally they would be seen in the office, but not often. They were frequently seen in follow-up by their primary care doctor and infrequently by a pulmonologist. PE patients who were treated with anticoagulation alone received limited and inconsistent follow-up for VTE sequelae.

What was your motivation for setting up a dedicated VTE program, and how long did it take to develop it?

Dr. Cummings: We recognized that there wasn't standardized care around this patient population, best practice wasn't defined, and there were barriers for admitted patients. Our hospital services commonly operate in silos. When a service comes by to see a patient, they write notes and move on. That service doesn't call anybody or talk to other services. We wanted to do better for these patients.

Dr. Knox: Our VTE program took time to develop, including finding the right people to bring to the table, so we were a small group at first: physician champions from IR,

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—Erin VanDyke, MPAS, PA-C

pulmonary/critical care, cardiothoracic surgery, hospitalist medicine, and the ED. We put our heads together and realized we needed to do a better job at risk stratifying these patients and deciding how best to treat them. At about that time, Massachusetts General Hospital developed the concept of a pulmonary embolism response team (PERT). We jumped on board to develop a program where we could take care of these patients more consistently.

It took over a year to birth the PERT team, but we brought together people from all walks of our institution, from nursing leaders to pharmacy and informatics, information technology, research, and all the clinician groups. We had many meetings to put all the pieces together and went live with our PERT process in November 2019. Since then, we have seen steady growth in terms of referrals, and today we have had more than 300 PERT activations (ie, approximately four or five per week). This all came as a result of engagement by a core of interested physicians who demonstrated the value to others in our institution and generated widespread support.

What was the rationale for creating the VTE coordinator role?

Erin VanDyke: The birth of the VTE program originated with physician champions who had an interest in VTE work. They first modeled the program on pathways such as acute coronary syndrome or stroke, which were already highly used and functional in the system. VTE algorithms, including PERT, were designed to offer a similar service that would identify candidates for intervention based on specific criteria and clinical presentation and then trigger a multidisciplinary conversation to determine next steps. The VTE coordinator role evolved to bring the entire picture together—building workflows, creating algorithms and order sets, training and supporting other APPs on the IR team to assist with specialized evaluation of VTE patients, and coordinating care. It allows IR to collaborate with other services such as the hospitalist, ED, pulmonary, critical care, oncology, and primary services.

Dr. Cummings: We recognized that smooth transitions and handoffs are really important. The VTE coordinator role creates eyes and ears on the floor for the operators. They are the boots on the ground, relaying information back to the proceduralist and creating a seamless, efficient, and safe system.

What challenges did you need to overcome when developing your VTE program?

Dr. Knox: There were certainly challenges in setting it up. For example, depending on where and when they trained, some clinicians were more resistant than others to treating submassive PE aggressively. We also encountered concerns from nursing education because these interventions were new, and managing these patients postprocedure was not something nurses were used to (eg, care of a larger sheath site).

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The other significant hurdle was the perceived cost of intervention. Our hospital's value analysis team had reservations initially given that some of the mechanical thrombectomy devices we use are expensive. However, they hadn't factored in the cost-avoidance benefits. Irrespective of the clinical and patient risk-benefit ratio of mechanical intervention over lytic therapy, there are cost-avoidance benefits related to decreased length of hospital stay, no ICU stay, and no cost of tissue plasminogen activator.

Further, what are the cost savings of having preserved cardiopulmonary function and avoiding chronic congestive heart failure, chronic thromboembolic disease, or pulmonary hypertension? We have to consider not only the clinical benefit to each patient but also the costs to the system for taking care of those who develop sequelae of PE, as well as the impact on population health. There's a much bigger picture to consider than simply device cost. Well-designed studies of long-term clinical benefit from early intervention are critically important, and some are currently in progress.

How did you develop the IR care pathways, and what are their key features?

Dr. Cummings: The ED physician must operate on several levels, focusing on patients, volume and capacity, and throughput. This program makes it easier for me because I can take a systematic approach to an individual patient. I know where I'm going and what I'm doing with them pretty early into their stay. Having standardized what we do when we find these patients takes a lot of the pressure off. As with STEMI, it's easier because everything is now hardwired. You don't have as much variance or the mental gymnastics of figuring out what to do with them because we've standardized our process.

Erin VanDyke: We decided to tackle the PE care pathways first. Due to the clinical presentation for PE, our care

pathways originate in the ED. Dr. Cummings was a valuable asset in streamlining processes between the ED and IR. Together, we created comprehensive and directive workflows for each of our teams, identifying clinically pertinent data points in the ED, such as elevated biomarkers, large-volume PE on CTA with associated right ventricular strain, ultrasound, echo, and clinical history. Each of these points was found to be very effective for supporting PERT activation and multidisciplinary guidance and in providing a seamless transition to the IR team.

We also collaborated with diagnostic physicians to ensure that dictation on CTA would include the presence of right heart strain to assist in initiating the correct algorithm in the ED.

The IR algorithm we developed directs ED providers to initiate a screening call to decide whether the case warrants a multidisciplinary PERT conversation. Based on the screening call, the IR APP is included in the care pathway to further assess clinical status and indications for intervention. The APP assessment will often occur before or at the same time as PERT activation. The primary service caring for the patient will present the case to the IR attending, the IR APP, or both, as well as pulmonary and critical care. The multidisciplinary discussion includes recommendations for catheter intervention, inferior vena cava (IVC) filter placement, and any support the patient may require based on clinical status. If intervention is recommended by the PERT, the interventional team is activated, and the IR algorithm is initiated.

Each pathway has separate, customized order sets, notes, and data points that help navigate the patient to and from the IR department. The type of intervention the patient received and their postprocedure clinical status determine the floor they go to for recovery, how they are monitored, and their nursing assessment needs. Each pathway has a designated order set that the physicians can choose.

When Dr. Knox performs a preprocedure assessment or documents a postprocedure note, he uses customized notes and lists that are easily navigated and specific to each type of intervention. These order sets default to IR current practice standards for specific interventions and can be modified for unique clinical circumstances per the provider's discretion. The order sets are also based on system standard policies and protocols for nursing assessments and monitoring.

We are very fortunate in that we can keep most of our mechanical thrombectomy patients out of the ICU. We currently use a cardiac step-down unit where the staff have received dedicated training on closure device removal and postvenous intervention assessment.

Dr. Knox: Front-end triage by the ED staff gets the patient to evaluation by the PERT, and then it's up to the interventionalist to determine what intervention would be most effective. A lot of that may be based on the clot burden, clot anatomy, location, and degree of right ventricular dilatation. Our experience has been that mechanical embolectomy works well, safely, and with very low risk in terms of clinical deterioration or bleeding. We've had very few complications, and these patients almost universally improve significantly on the table. They can be quickly transitioned to oral anticoagulants, and we are finding their length of stay is decreased significantly.

You mentioned prepopulated forms. How were these developed, and how do you keep them updated?

Erin VanDyke: When our health care system went on board with Epic electronic medical record (EMR; Epic Systems), the IR team decided to standardize IR workflows into customized notes and order sets for use by the providers in our department. Any updates to workflows, best practices, notes, and order sets are entered into the system by me and shared with the IR APPs and physicians. These changes are universal, meaning clinicians are always working from the same customized forms, and updates are automatic once placed into the EMR. My fellow APPs provide significant support as well, creating new notes and documentation and sharing with the IR provider team. This helps maintain group standardization as opposed to having multiple varying order sets and different note structures coming through from the same department.

Dr. Knox: The benefit to these prepopulated forms is consistency. For everyone receiving patients, there is a uniform set of orders and expectations. It makes my world much easier because we've already decided how to monitor these patients and all the details. Erin builds the order sets, and most orders are prechecked, but I can easily make modifications as appropriate to each case. It certainly makes me more efficient.

How would an IR APP follow one of the predetermined pathways?

Erin VanDyke: The IR APP team is the glue that holds these processes together. Dr. Knox and the physician team are in the IR department performing life-saving procedures. They rely on the APP team to assess VTE patients, relay any concerns or challenges, and make sure they get to IR safely and ready for intervention. IR APPs see patients after a PERT call or sometimes even initiate the PERT based on a screening call and clinical assessment. The IR APP team has been trained in VTE assessment and algorithms, can

expedite clinically declining patients to intervention, and provides ongoing communication and reassessment.

If the patient meets the criteria for a PERT, even if intervention is not pursued, the IR APPs are automatically sent to assess and follow-up to make sure all points along the established workflows and algorithms are followed for each patient. This ensures the patient will have appropriate follow-up from our pulmonary clinic, as well as recommendations for follow-up imaging.

Dr. Knox: Our IR APP service owns some of the inpatient clinical follow-up as well, even with patients who don't undergo intervention. If we do a PERT call and the patient is seen by the IR APP, but we decide to anticoagulate without advanced intervention, we follow the patient to see if they trend better over time on anticoagulation. If they're not improving and show signs of deterioration, we need to reassess and consider intervention. That's a decision we don't necessarily want to leave in the hands of a busy hospitalist who may not have time to re-evaluate frequently or be as familiar with subtle clinical changes. We have a low threshold to have another PERT call to discuss change of treatment strategy.

How does change happen in the VTE program, with day-to-day processes and in the bigger picture?

Erin VanDyke: When we develop care flows, we anticipate pinch points and alternate tracks that may need to be addressed. When we discover a need for additional coverage, standardization, or optimization to an existing algorithm, as the VTE coordinator, I'm there to close the gap. I start by collaborating with Dr. Cummings in the ED, the support staff or providers on the floors, or in the IR department and attempt to standardize and create additional algorithms that may streamline the workflows for all involved. This can be as simple as offering additional education or as challenging as recommending a new system policy or designing a new order set.

We also have to consider how our teams are communicating nonverbally through notes, order sets, and transitions of care. This includes our physicians, APPs, residents, and other more transient practitioners we interact with to ensure everyone has the resources and information they need to take the best care of the patients we serve. Typically, orders flow through Epic, and there is a standard expectation of care in our system. However, in medicine, nothing is black and white. When an atypical case arises, we have to be flexible and communicative with the teams that help support the transition of patients through the IR department. This allows for smooth and seamless care, even in unique situations. We also can be advocates for VTE patients on the inpatient floors and with services who may be new to this paradigm shift.

Dr. Cummings: Dr. Knox, Erin, and I are continuously invested in this program, and we meet much more often than the larger group to plan and collaborate. When we went live, the larger group would meet every few weeks, and because the issues weren't as great and we reached a steady state, we were able to back off. At this point, we touch base quarterly, but the frequency will soon pick up as we pursue becoming a VTE Center of Excellence.

Do you see a difference between where you were before you put this program in place and where you are now?

Dr. Knox: We performed our first FlowTriever case in July 2019, and the PERT process went live in November 2019. The timing was great. Our experience has been driven by the synergism between a very effective device that is low risk and dramatically improves patients immediately and a robust process for identifying patients who can benefit from intervention. Multidisciplinary communication and consideration of best practices, as well as our own experience, are key in deciding optimal treatment for each patient.

One indicator of programmatic success is the volume of patients who are evaluated by our PERT and considered for intervention, which has increased dramatically over the last few years. This is a result of a more comprehensive process to identify these patients and get them to evaluation, leading to intervention when appropriate.

We have done a lot of education with our ED physicians and hospitalists, but we still have some room to grow because we are a system with 11 or 12 hospitals, and we do not have the capability to do advanced intervention at the smaller regional facilities. Patients are transferred to the central hospital for treatment when appropriate, and we need to make sure that the education is available to the physicians and APPs at those hospitals so they know when to reach out to our PERT.

Erin VanDyke: Prior to the availability of an effective mechanical device for PE intervention, the decision to expose an otherwise clinically stable patient to thrombolytic medications weighed heavily on providers. The FlowTriever System supported the growth of this program by giving us a completely different, more inclusive clinical approach to offer patients. Patients who might have been excluded from intervention in the past are now candidates for mechanical treatment and often have clinical improvement of their PE symptoms on the IR table.

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How do you market the program, and what sort of outreach are you doing at the more remote hospitals?

Dr. Knox: Dr. Cummings' group of emergency medicine physicians covers most hospitals within the system, so by communicating the algorithms through champions at Spectrum Health Butterworth Hospital, we have been able to deliver education throughout the network. Even so, many physician groups whose patients could benefit (eg, obstetrics/gynecology, oncology, pediatrics) still have relatively little knowledge about what we can offer their patients. It will take time and effort, but we recognize that it needs to be done to deliver the best care to as many patients as we can.

What advice do you have for those interested in setting up a program like this?

Dr. Knox: To roll out a robust program and help drive it forward, assemble a group of collaborative physicians from different specialties who are passionate about treating VTE. Erin's role as VTE coordinator has helped with the logistics of moving these patients through the system and dealing with order sets and workflows: the things that make my job easier. These types of upfront efforts make a tremendous difference in terms of acceptance and success of the VTE program.

Dr. Cummings: If an institution is just getting started, the process may be shorter than it was for us because there are now models that work well. So, find a model that works for your institution. Invite key players and leaders to group meetings to decide logistics and work out the process, then integrate that knowledge with the leaders of the facility. Once you go live, track your outcomes. Follow-up to see what you can improve, and keep moving forward because a program like this is a garden you need to tend.

Erin VanDyke: My advice is simply to invite those who doubt the effectiveness of this intervention to watch a case. We've found the most compelling thing you can do to spread word quickly is to experience the pre- and post-clinical presentations of PE patients and see the physical evidence produced during the case. Post the clot pictures in the patient's chart. It's a great way to get your hospital—and any other practitioner—to understand. They pull up the patient chart and see these huge clots and the reaction is, "Wow! No wonder that patient feels better." It offers a point of conversation and an introduction to the paradigm shift that is occurring for VTE treatment.

What's next for the program? How do you plan to develop into a VTE Center of Excellence?

Dr. Knox: We're excited about smartphone applications that may allow the PERT call to be facilitated with fingertip access to images and clinical data needed to make informed decisions about how to treat patients. We're also planning to establish a multidisciplinary follow-up clinic with dedicated space and time to see patients postdischarge. We have assembled a group of physicians, APPs, nurses, research personnel, and administration to drive this forward because follow-up care is a significant problem for many patients. We can have a major impact on their quality of life by developing a robust and consistent follow-up process. This will also allow the gathering of important long-term clinical outcomes data, supporting our research initiatives.

Dr. Cummings: Regarding the VTE Center of Excellence, we already have a process in place, but next is the research arm and tracking to truly define best practice. Once we have that, we'll begin to report out, and the world can benefit from what we learn. That's really exciting because it's the work that will get VTE care to where we are with STEMI and stroke.

Erin VanDyke: We've worked hard to develop algorithms and a robust pathway for PE patients, and we are now working on developing a similar deep vein thrombosis (DVT) pathway. One other area we need to target now that we have things more streamlined is the population of patients who are diagnosed with PE while they are inpatient. We need to introduce those patients into the algorithm by meeting with our colleagues who provide primary inpatient services.

Any closing thoughts on the advantages of a dedicated VTE program?

Dr. Cummings: We are changing the outcomes for these patients and saving their lives. That's why it's exciting—we're doing something that helps people

instantly and with on-the-table changes. It's as gratifying as STEMI care. I had a thrombectomy patient return to the ED postintervention during the pandemic when our hospitals were full and there were no ICU beds. She was a different person pre- versus postprocedure. I received all the "thank you"s I need for 3 years! It was moving to see we are truly making a difference in people's lives.

Because we haven't had great therapies for most higher-risk VTE patients, standards similar to STEMI and stroke have not come into play yet. Well, here it is. It's coming, and I think it is the Inari devices and mechanical thrombectomy. It will take time because of the nature of what VTE care has been, but in my mind, VTE will be just like STEMI care in the future.

Postpartum Patient Rescued From the PE Death Spiral With FlowTriever Mechanical Thrombectomy

By Michael Knox, MD, FACR, and Erin VanDyke, MPAS, PA-C

An otherwise healthy 40-year-old multiparous woman had three syncopal episodes the day after an uncomplicated vaginal delivery. At 4 days postpartum, she presented to the ED at a small community hospital with shortness of breath, chest discomfort, and presyncope. Her symptoms had worsened over the previous 24 hours. The patient was diagnosed with a large PE with evidence of right heart strain based on a CT scan. She reported no history of DVT or PE.

The patient's clinical presentation and available clinical information were presented by the community hospital ED provider to the interventional radiologist at Spectrum Health during a screening call—the first step to engage the interventional team and determine candidacy for PERT initiation. Based on the screening call, a decision was made to transfer the patient to Spectrum Health Butterworth. The IR department's PE algorithm and workflow were set in motion, and the IR team's APP was notified of the patient's arrival at Spectrum's ED.

A PERT call was initiated, and a multidisciplinary conversation occurred between the ED physician, pulmonologist/critical care physician, IR attending physician, and IR APP. A decision was made to perform mechanical embolectomy with the FlowTriever System.

Acting as a clinical extension of the IR attending physician and specifically trained in PE assessment, the IR APP identified a decline in the patient's clinical status since the time of the screening call. The patient was noted to have very elevated brain natriuretic peptide (4736 ng/L) and high-sensitivity cardiac troponin T levels (63 ng/L) with increasing tachypnea, tachycardia, and increased oxygen demand requiring a nonrebreather. Her clinical decline prompted the IR APP to initiate the IR care flow for PE, which included placing orders and communicating with the IR charge nurse to expedite transition to the IR department for immediate intervention. An echocardiogram was not completed prior to intervention due to the patient's declining clinical status, but a limited lower extremity ultrasound demonstrated acute left iliofemoral vein thrombosis.

Within 30 minutes of the IR APP assessment, the patient had been moved from the ED to the IR prep and recovery area to be seen and consented by the IR attending. While the IR team was diligent to prepare for the procedure and provide expedited care, the patient's condition continued to deteriorate. She was becoming more hemodynamically unstable and declining, appearing pale and ashen, with conversational dyspnea. It was very apparent to the IR attending and IR APP that her appearance indicated a progressive failing right ventricle.

PROCEDURAL OVERVIEW

Due to the patient's instability, minimal sedation was used. Access to the right common femoral vein was achieved using ultrasound guidance. After access, a quick contrast injection in the iliac vein and IVC detected no thrombus but very stagnant venous flow (Figure 1A). Right pulmonary angiography revealed a large volume of thrombus, with near-complete occlusion of the truncus anterior and limited flow to the interlobar artery, with minimal right lung perfusion (Figure 1B). A saddle embolus was seen extending from the right main pulmonary artery (PA) into the main PA and left PA.

The access site was dilated, and a 24-F sheath was placed. The 24-F Triever24 aspiration catheter (Inari Medical) was introduced and advanced over a guidewire to the target thrombus in the right PA (Figure 1C). FlowTriever mechanical thrombectomy was initiated, and a large volume of thrombus was removed after the first aspiration. The patient's skin color immediately improved, the tachycardia lessened, and her oxygen saturation levels increased.

An additional aspiration in the right PA cleared further thrombus in the right lung, and follow-up angiography showed clearance of the saddle embolus and central left PA thrombus. The Triever24 catheter was advanced to the left PA, and additional aspirations were performed to extract residual, smaller-volume thrombus. Completion arteriography in the main PA demonstrated marked improvement in perfusion bilaterally (Figure 1D).

After removal of the majority of thrombus (Figure 1E) and the patient's dramatic clinical improvement, it was decided to place a retrievable IVC filter in the infrarenal vena cava to address the residual large-volume left leg DVT.

The access site was closed with a cerclage technique, and manual pressure was held for 10 minutes to achieve hemostasis.

From in-suite, preprocedure presentation to postprocedure, the patient's blood pressure improved from 79/39 to 111/69 mm Hg, her respiratory rate dropped from 40 to 28 breaths/minute, and her pulse dropped from 137 to 101 bpm. Her main PA pressure was 45/22 mm Hg with a mean of 31 mm Hg prior to intervention. Postbilateral thrombectomy, her main PA pressure was 24/9 mm Hg with a mean PA pressure of 16 mm Hg. The total length of time from patient sedation to departure from the IR suite was 55 minutes.

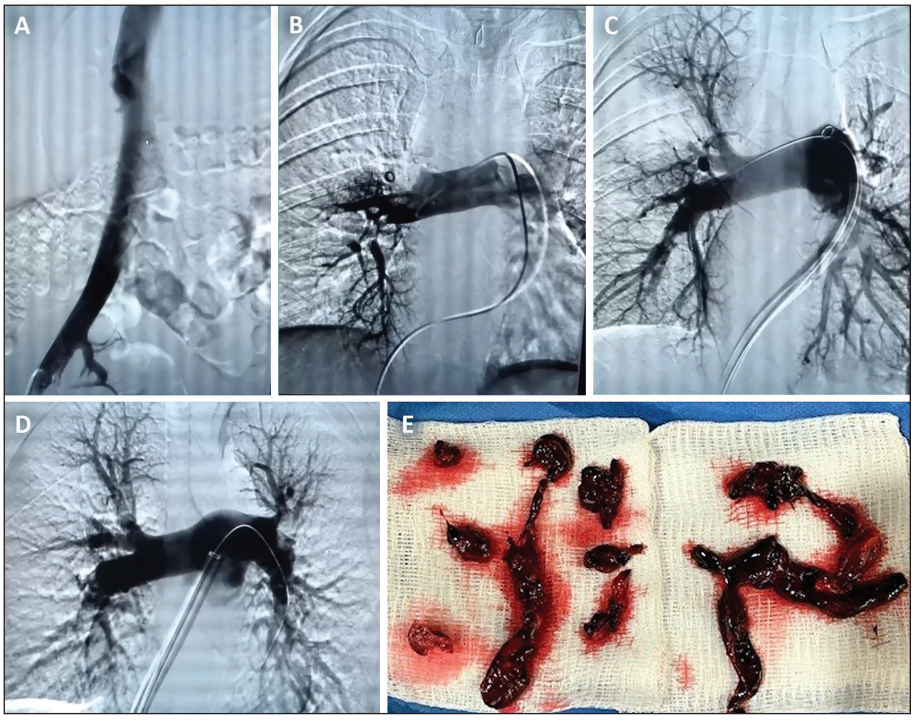

Figure 1. Intraprocedural angiography before thrombectomy showed very sluggish venous flow in the iliac vein and IVC but no thrombus (A). Right pulmonary angiography revealed a large volume of thrombus, with complete occlusion of the truncus anterior and limited flow to the interlobar artery and minimal right lung perfusion (B). The FlowTriever aspiration catheter was advanced to the right PA, and after a single aspiration, marked improvement in right lung perfusion was demonstrated, as well as clearance of the saddle embolus (C). The FlowTriever aspiration catheter was advanced to the left lower lobe, and aspiration was performed, with final main PA injection demonstrating markedly improved perfusion in right and left PAs (D). Extracted thrombus (E).

POSTPROCEDURE COURSE

Using the postprocedure IR algorithms, the patient was assigned a non-ICU bed and transferred to the cardiac step-down unit. There, the care team followed the standardized postprocedure orders developed by the IR team. A few hours later, the IR APP went to evaluate the patient at her bedside and found her sitting up, eating lunch, and talking with her husband while he held their newborn baby. She was off oxygen, had no conversational dyspnea, and her vitals had returned to normal. She had no left lower extremity pain or groin pain and informed the IR APP that although she had noticed significant leg swelling in the waning days of her pregnancy, she no longer had pain or other DVT symptoms.

The patient was seen by the IR APP again the next day to ensure that the cerclage suture had been removed appropriately by the trained nursing staff. There were no complications with the puncture site, and the patient continued to tolerate intravenous anticoagulation.

The patient was followed by the hospitalists, and after discussion and assessment, an appropriate oral anticoagulant was chosen. The patient was discharged after one overnight stay and no time in the ICU.

At her 3-month follow-up with the pulmonologist, the patient was doing well and had complete resolution of PE-associated symptoms. She was followed by the IR team for her IVC filter, and an ultrasound verified that there was no residual DVT. The patient underwent uncomplicated, successful IVC filter removal 11 weeks after her intervention. She was taken off anticoagulation by the pulmonologist at 6 months postprocedure. ■

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Iliac Vein Stenting: Best Practices for Patient Safety and Successful Outcomes

By Kathleen Gibson, MD, FACS, FAVLS

Venous stenting first emerged as a treatment for iliofemoral venous outflow obstruction in the 1990s. Recently, several factors have led to a significant increase in the volume of these procedures being performed around the world. There has been an increased awareness of the contribution of venous outflow obstruction to the causation of disabling symptoms such as venous claudication, chronic edema and/or venous ulceration, and other manifestations of postthrombotic syndrome (PTS). Venous outflow obstruction may be secondary to iliofemoral deep vein thrombosis (DVT) or nonthrombotic iliac vein lesions (NIVLs, previously termed May-Thurner syndrome). The development of improved endovascular skill sets among various specialties, improving awareness of the treatment of venous disorders, and an expansion of endovascular treatment into nonhospital-based facilities have all likely contributed to an increase in venous stenting. Additionally, the development of stents specifically designed for venous indications, providing more straightforward deployment, has increased enthusiasm for the treatment of venous outflow obstruction.

Although an increase in the accessibility of venous stenting procedures will undoubtedly help improve patient quality of life, overuse or misapplication of the technology can be harmful. Two of the venous-dedicated stents have recently been withdrawn from the marketplace, allegedly due to issues with stent deployments and migrations (whether these are permanent or temporary recalls is not known at this time). As with any burgeoning technology, proper patient selection, physician training, and patient aftercare and follow-up are key to safe, successful treatment of venous outflow obstruction.

VENOUS STENTS: AN OVERVIEW

The use of self-expanding stents for the treatment of venous outflow obstruction was reported by Drs. Neglén and Raju more than 20 years ago.[1] Their described technique included the use of the venous Wallstent™* endoprosthesis stent (Boston Scientific Corporation), a braided, self-expanding stent composed of Elgiloy (a Co-Cr-Ni alloy). Although the venous Wallstent was not initially designed as a venous stent, its large diameters, compression (crush) resistance, radial force, and fracture resistance lent itself well to venous stenting. Over the ensuing decades, venous stenting techniques using Wallstents were refined. Despite its strengths, there are several drawbacks to the venous Wallstent. Their deployment accuracy can be imprecise because they can foreshorten considerably depending on the diameter of the vessel in which they are deployed. Additionally, the ends of the stent lack the radial force present throughout the rest of the stent body and are prone to collapse. As the point of maximal compression in the case of NIVLs is typically at the confluence of the left common iliac vein (CIV) and the inferior vena cava (IVC), the venous Wallstent typically needs to be extended cranially into the IVC to avoid collapse and potential subsequent occlusion if the weakest portion of the stent is placed too caudally. If the stent is placed too far into the IVC, there is risk of the stent covering the confluence of the contralateral iliac vein, which can lead to contralateral limb thrombosis.[2] Due to this lack of radial force at the end of the stents, care also must be taken with the venous Wallstent to ensure appropriate overlap when more than one stent is placed.

The need for accurate deployment to avoid complications with placement of the venous Wallstent coupled with their tendency to foreshorten somewhat unpredictably makes for

a steep learning curve for successful deployment. Even in the most expert hands, a perfect venous Wallstent placement can be an elusive endeavor. Although the venous Wallstent has a long and successful track record in the treatment of venous outflow obstruction, its shortcomings spurred the development of various venous dedicated stents. The ideal venous stent would be adaptable to a variety of venous anatomic features, available in a wide range of diameters and lengths, strong and able to resist both recoil and compressive forces, flexible and able to negotiate the curves of the venous anatomy in the pelvis without kinking or distorting the vein, durable and able to withstand repetitive movement without loss of integrity, and able to offer accurate and precise deployment at both stent ends.

Four dedicated venous stents have received FDA approval after investigational device exemption (IDE) trials: Vici venous stent™* system (Boston Scientific Corporation; VIRTUS IDE trial), Venovo™* venous stent system (BD Interventional; VERNACULAR IDE trial), Zilver™* Vena™* venous self-expanding stent (Cook Medical; VIVO IDE trial), and Abre™ venous self-expanding stent system (Medtronic; ABRE IDE trial). With the exception of the VIRTUS trial, all of these IDE trials included patients with acute and chronic obstructions and showed acceptable efficacy and safety.[3-9] The Vici stent is a closed-cell stent, and the other approved dedicated venous nitinol stents are open cell. Characteristics of the approved stents are listed in Table 1. At the time of this publication, both the Vici venous stent and the Venovo venous stent system have been pulled from the market.

PATIENT SELECTION

Proper patient selection, both in terms of clinical presentation and anatomic findings, is essential to successful treatment of symptomatic venous outflow obstruction. In all clinical scenarios where a venous stent is being considered, the patient's symptoms and the impact of these symptoms on their quality of life is of primary consideration. Venous stents are permanent implants, and as such, diligent consideration should be given as to whether the patient's symptoms have a significant enough impact on quality of life to warrant their consideration. Placement for minor symptoms such as mild ankle edema is discouraged by most venous experts.

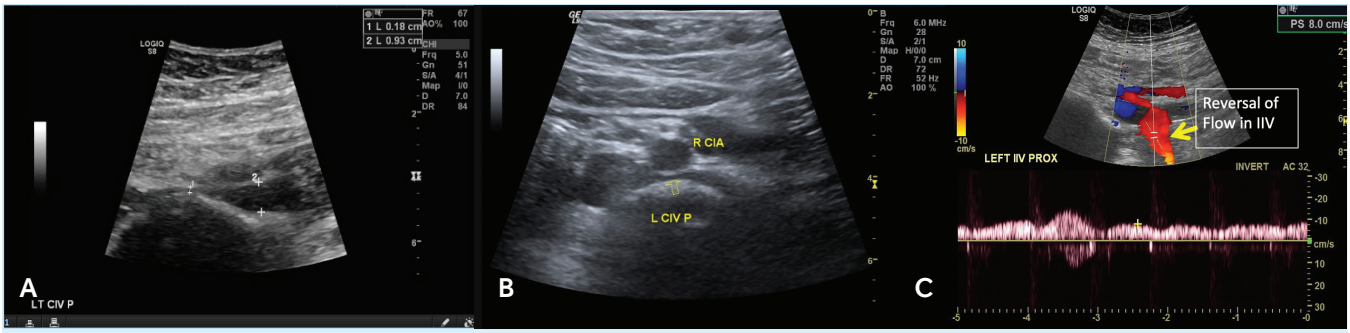
In patients with chronic PTS and venous ulceration, current Society for Vascular Surgery/American Venous Forum clinical practice guidelines recommend venous outflow obstruction be considered to speed ulcer healing if anatomically appropriate.[10] Other symptoms impacting patient quality of life such as pain, significant edema, and venous claudication can be alleviated or improved with venous stenting.[11] It is generally accepted that as long as adequate thrombus resolution has occurred in patients with acute DVT who have undergone thrombolysis, iliac stenting improves vessel patency and lowers PTS rates.[12] In patients with chronic postthrombotic outflow obstruction, anatomic considerations are important in addition to symptom assessment. An axiom for proper venous stenting is to stent from "healthy to healthy." With the exception of a chronically occluded IVC, which can be recanalized with advanced maneuvers, inadequate venous outflow is not usually a limiting anatomic factor for successful stenting. Significant inflow disease, typically involving the common femoral vein (CFV), is likely the primary anatomic cause of stent failure.[13] As such, it is incumbent on the treating physician to be certain that adequate inflow is feasible prior to placement of a venous stent.

Proper patient selection is most critical and controversial in patients with NIVLs because the risk/benefit ratio in this group is less clear. Symptom complexes in these patients can vary and can include chronic pelvic pain,[14] venous claudication,

TABLE 1. CHARACTERISTICS OF FDA-APPROVED VENOUS STENTS IN THE UNITED STATES

Stent	Deployment	Availability	Structure	Size (mm)
Wallstent endoprosthesis stent	Coaxial, 10 F	Approved, available	Braided, Elgiloy	D: 12-24 L: 20-90 (depending on diameter)
Vici venous stent system	Coaxial, 9 F	Approved, unavailable due to voluntary recall	Closed cell, nitinol	D: 12-16 L: 60-120
Venovo venous stent system	Triaxial dual thumbwheel, 8-10 F	Approved, unavailable due to voluntary recall	Open cell, nitinol	D: 10-20 L: 40-160
Abre venous self-expanding stent	Triaxial thumbwheel, 9 F	Approved, available	Open cell, nitinol	D: 10-20 L: 60-150 (40 mm also available in 10-mm diameter)
Zilver Vena venous self-expanding stent	Coaxial, 7 F	Approved, available	Open cell, nitinol	D: 10-16 L: 40-140

Abbreviations: D, diameter; L, length.



Courtesy of Kathleen Gibson, MD, FACS, FAVLS.

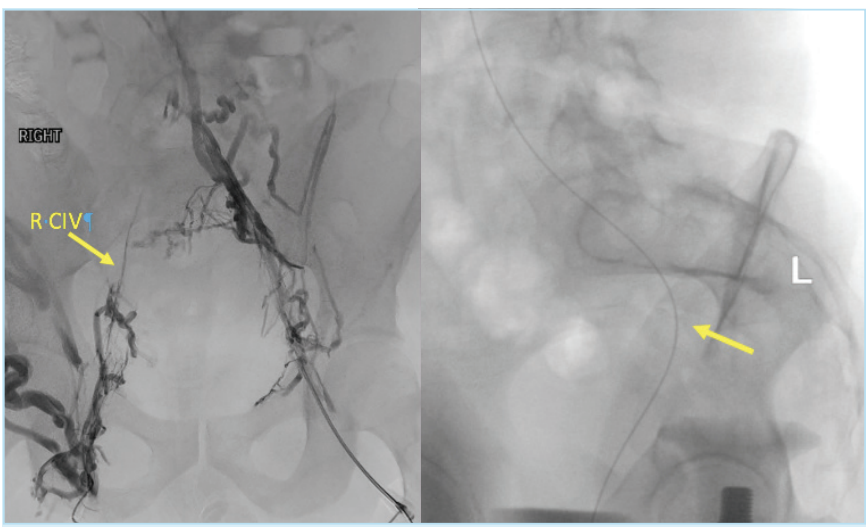
Figure 1. Longitudinal images of left iliac vein compression. CIA, common iliac artery.

and edema. Many patients with anatomic venous compression found on imaging are asymptomatic,[15] and venous stenting should never be contemplated prophylactically in such patients. Consideration of an interventional procedure with rare but potentially serious or even fatal outcomes (such as migration of a stent to the right atrium, which is more common in NIVL patients than patients with PTS) must be carefully balanced against any potential long-term benefit for the patient. In particular, intervention for the edema relief alone is fraught with potential disappointment for the patient and the physician because limb edema may have many causes and improvement after stenting is not assured.[16] Management of patient expectations to expect improvement but not necessarily resolution of symptoms attributable to NIVLs is crucial.

PROPER IMAGING: PRIOR TO AND DURING INTERVENTION

Preprocedural imaging should be performed for diagnostic purposes and case planning. The technology used is institutionally dependent but could include CT venography (CTV), MR venography, or diagnostic transabdominal duplex scans. At our institution, we rely primarily on transabdominal duplex imaging, reserving CTV for cases of acute thrombosis, chronic occlusive disease involving the IVC, or in patients where an etiology such as malignancy or compression from a nonvascular etiology is being considered (eg, previous back surgery, radiation). With proper training, excellent images can be obtained with duplex ultrasound. For NIVL patients, we follow imaging protocols as described by Labropoulos and colleagues.[17] A visible difference in venous diameter at the point of compression, a peak vein velocity ratio > 2.5 in the area of compression, and a reversal of flow in the internal iliac vein (IIV) are all indications of a clinically significant stenosis (Figure 1).

Appropriate confirmatory diagnostic imaging on an "intent-to-treat" basis prior to stenting is critical. A combination of multiplanar venography and intravascular ultrasound (IVUS) are gold standards for proper stent placement to identify the degree of stenosis and length of disease. In the case of postthrombotic obstruction, venography demonstrates collateral flow, and the "pathway" to traverse to reach the IVC is often visible (eg, the patient with a chronic bilateral iliac and IVC occlusive disease after DVT in Figure 2). When crossing a chronic occlusion, it is vital to obtain an oblique or lateral view to ensure the wire is in the proper location anterior to the spine because inadvertent stenting into the obturator vein or spinal canal has been reported (Figure 3).[18] Venography for NIVL cases will typically demonstrate a "pancaking" of the left CIV, with prestenotic dilatation and a lag in contrast emptying, retrograde flow in the IIV, and cross-pelvic and paraspinous collaterals (Figure 4). For NIVL lesions, IVUS is used to confirm the degree of area reduction in the area of compression (Figure 5). The comparative reference vessel could be the patient's own ipsilateral normal CIV, their



Courtesy of Kathleen Gibson, MD, FACS, FAVLS.

Figure 2. Venography in a patient with occlusion of the right CIV and IVC.

Figure 3. Proper course of a wire crossing the pelvis in a patient with chronic occlusion of the left CIV.

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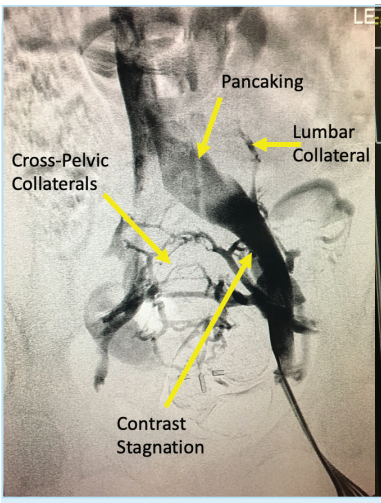

Figure 4. Venography of a NIVL demonstrating "pancaking of vein," contrast stagnation, and cross-pelvic and lumbar collaterals.

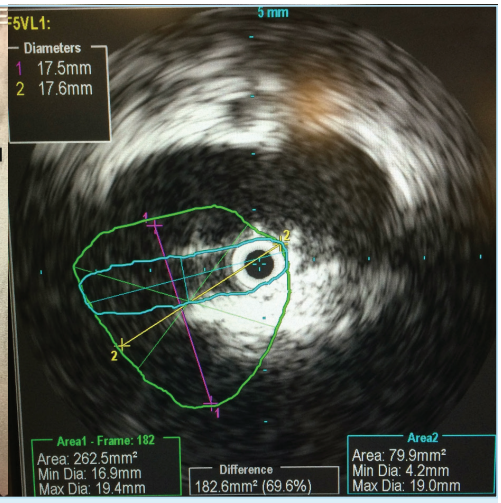

Figure 5. IVUS determination of cross-sectional area reduction in a NIVL.

contralateral CIV, or a reference from anatomic literature.[19] The VIDIO trial demonstrated that compared to multiplanar venography, IVUS was more sensitive in detecting lesions with > 50% cross-sectional area reduction, an anatomic threshold that, although controversial, is often used to determine which lesions may benefit from stenting.[20]

PROPER ACCESS AND STENT PLACEMENT

The choice of access vessel for stent placement depends on the extent and location of the venous disease. In patients with acute venous thrombosis, stenting is often performed in conjunction with thrombolysis or mechanical thrombectomy. The most common venous access site for acute interventions is the popliteal vein, although the posterior tibial vein is increasingly being used. In patients with chronic occlusive disease, it is important to determine the caudal-most extent of disease, as there must be enough room between the end of the venous sheath and the end of the stent to facilitate placement. Although many physicians prefer the popliteal vein for chronic occlusive disease access, I prefer the midfemoral vein if it is patent because it allows the patient to remain in a supine position and permits easy access to the jugular vein. If the femoral vein is diseased, my preferred approach is via the right jugular vein. Occasionally, I will use great saphenous vein access to cross the occlusion from below, snaring the wire in the IVC placed via internal jugular vein (IJV) access and redirecting the IJV wire into the profunda vein or diseased femoral vein. This allows precise stent landing at the lesser trochanter, which is the usual location of the confluence of the profunda and femoral veins (Figure 6).

Once proper access is achieved, confirmatory imaging is completed, and systemic heparinization is administered, the length of the venous segment that requires stenting and diameter of the stent to be used is then determined. For a chronically occluded vein, stent sizing can be based on known normal diameters of iliac veins: 14 to 16 mm for the CIV, 12 to 14 mm for the external iliac vein (EIV), and 10 to 12 mm for the CFV.[19] The length of stent(s) needed is determined most efficiently by the IVUS catheter, which has radiopaque markers. With long segments of disease in PTS patients, more than one stent is usually required, and the physician must account for allowance of sufficient overlap between stents (common practice is a minimum 2-cm overlap). If the length of disease extends from the iliac confluence to the lesser trochanter, three stents are usually needed when using the venous Wallstent in an average-sized patient, whereas the longer lengths of the newer nitinol stents will often allow this to be achieved with two stents. IVUS is used to determine the landing zones cranially and caudally, with a goal of stenting from "healthy to healthy" vessel.

The choice of stent sizing is more controversial in NIVL cases and is critically important because the majority of stent migration cases occur in these clinical scenarios. The cross-sectional area of the CIV at the point of compression may be quite reduced, but the length of this area reduction may be quite short and the vein caudal to the compression point quite dilated, creating a significant size mismatch. Placing a short but anatomically appropriately sized stent (14 or 16 mm) in the wall apposition existing only at the point of compression creates a dependence on that very short stretch of constricted vein to hold the stent in place as the caudal end of the stent is "floating" in the dilated segment. If the cross-sectional view of the vein in the area of compression is not accurately measured and the stent is undersized, migration of the stent may occur.

Two opposing strategies exist to overcome the issue of stent migration, and there are no published data supporting one strategy over the other. The first is to place a stent with a diameter matching the size of the CIV caudal to the area of compression. In some cases, this could necessitate the placement of an 18- or 20-mm stent. The advantage to this strategy is the much longer length of vein wall apposed to the stent. The main disadvantage is an increase in the incidence of postprocedure back pain with larger stents. The severity and duration of back pain after venous stenting procedures has not been well characterized, but it is a common

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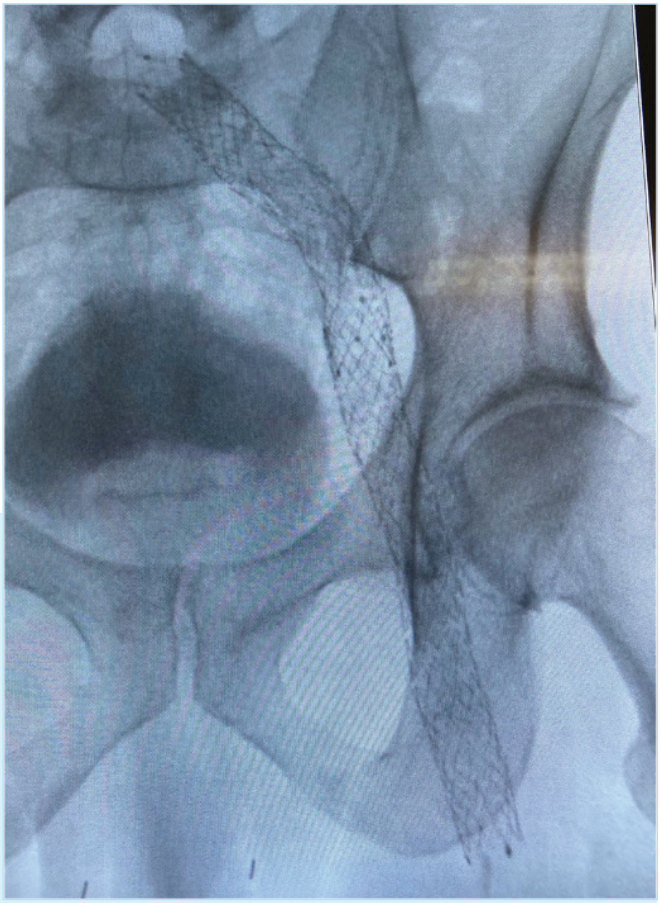

Figure 6. Placement of a venous stent from IVC confluence to confluence of the profunda and femoral veins at the lesser trochanter.

patient complaint; it is not typically long-lasting, but it can be distressing. Although rare, chronic back pain after venous stenting can occur, and stent explantation has been required in some cases.[21] The second approach used to prevent stent migration is to place a longer stent by extending the stent into the EIV past the curve in the pelvis. The stent has venous wall apposition at the confluence and along the length in the EIV, so the stent diameter can be smaller (usually 14-16 mm). Proponents of this approach point to a theoretical decrease in migration and a decrease in postprocedure pain. Opponents argue this approach has a disadvantage of placing more stent material in healthy vein and covering the IIV, which could theoretically complicate future access of this vessel.

With either approach to venous stent placement in NIVL cases, accurate IVUS assessment is important. Veins are not "round" throughout their entire course and can vary in size depending on patient position, hydration status, and respiration. Patients are commonly instructed to be NPO (nothing by mouth) for a period of time prior to a procedure, so intravenous prehydration is a good practice. Asking the patient to perform a Valsalva maneuver during IVUS measurement can also be helpful. Most practitioners determine vein diameter on IVUS either by adding the major diameter to the minor diameter and dividing that number by two or by taking the square root of the area, dividing by π, and multiplying by two (area = πr^2). The chosen stent should be 1 to 2 mm larger than the calculated vein diameter. The caudal end of a venous stent should not land at the "dip" in the pelvis (yellow arrow, Figure 3) or the inguinal ligament. Placement at the curve in the pelvis can lead to straightening or kinking of the vein, and placement at the inguinal ligament subjects the stent to a significant amount of repetitive motion and stretch; both could theoretically lead to stent thrombosis.

Pre- and postdilatation of venous segments to the chosen stent diameter is recommended (the Abre venous stent instructions for use requires predilatation and recommends postdilatation), typically with a high-pressure balloon. For chronic venous occlusion, serial dilatation with balloons of increasing diameter may be necessary. Predilatation to the intended stent diameter allows the stent to expand more easily. For NIVL cases, predilatation also allows an important safety check on sizing. Some physicians will inflate a balloon to nominal size and then perform venography. If contrast passes readily around the balloon, the vein diameter may have been undermeasured, or there might be no clinically relevant compression. Another technique is to inflate a balloon at the point of compression and gently pull the balloon caudally. If it pulls back easily, as with the previous technique, vein measurement or the need for stent placement should be reassessed. Postdilatation of venous stents is also important, particularly for nitinol stents as the maximal resistive force of the alloy is not achieved without dilatation to its nominal diameter. Postdilatation venography and IVUS are also performed; ideally, venography will demonstrate prompt antegrade emptying of contrast and an absence of collaterals, and IVUS will show good wall apposition and expansion of the stent(s) to its nominal diameter.

POSTPROCEDURAL FOLLOW-UP AND ANTICOAGULATION

The success or failure of a venous outflow intervention does not end with stent placement. In my clinical practice, full heparinization is administered after placement of a large venous sheath (usually 9 or 10 F), and the heparin is redosed throughout the procedure as needed. In practices where an activated clotting time (ACT) is measured, it is typical to aim for an ACT > 250 sec during treatment. A variety of anticoagulation regimens have been suggested for thrombotic and nonthrombotic patients poststenting, with no evidence for superiority of any particular approach. For thrombotic patients (acute or chronic), most practitioners will prescribe twice-daily enoxaparin for 3 to 4 weeks and then transition to either a vitamin K antagonist or a direct oral anticoagulant (DOAC) for a variable period of time. For patients with unprovoked DVT or hypercoagulable states, indefinite prophylactic-dose DOACs

should be considered after treatment with standard anticoagulation. For a NIVL patient, the need for anticoagulation after a stenting procedure is less clear, with regimens of antiplatelet agents, DOACs, heparins, or vitamin K antagonists being used by various practices. Some would argue that no anticoagulation is necessary in these cases. Postprocedural imaging within weeks of the procedure to assess for flow disturbance in the stents and the presence of any mural thrombus is recommended. Early intervention should be considered to prevent stent failure if any significant narrowing or flow disturbance is found on follow-up imaging. In our practice, follow-up imaging via duplex ultrasound after the initial postprocedural scan occurs every 6 months for 2 years, then annually.

SUMMARY

Venous stenting for venous outflow disease has the potential to improve the quality of life for millions of patients, but to prevent poor outcomes, proper patient selection and careful technique are of paramount importance. The introduction of dedicated venous stents is welcome, but the recent withdrawal of some of these stents from the market is a caution that education and training in the use of these stents, focusing on their safe placement, is imperative. ■

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AN INTERVIEW WITH...

Tiago Bilhim, MD, PhD, EBIR, FCIRSE, FSIR

Dr. Bilhim shares about his journey in prostatic artery embolization work, tips for quality medical writing, raising awareness for interventional radiology, and more.

Please tell us about your own journey in researching prostatic artery embolization (PAE). What interested you most about this procedure?

My PAE journey started in 2008 when my mentor Professor João Pisco challenged me to pursue my PhD thesis on a new interventional radiology (IR) procedure for patients with benign prostatic hyperplasia (BPH). I designed the study protocol and had to decide which outcome measures to assess and when to assess them postintervention. I never thought the PAE technique itself would be so challenging. The first 10 procedures each lasted > 3 hours, and Prof. Pisco kept asking: "Is this the prostatic artery? Can we embolize this safely?" At the time, I was already teaching anatomy at NOVA Medical School, so anatomy was "part of my business." I was surprised to find out that after so many centuries of great anatomy studies and books, the knowledge on anatomy of the prostatic arteries was so scarce. Wow! For me it was mind-blowing to have the feeling that we were looking at things never seen before.

At that time, Saint Louis Hospital had a very old angiography machine unit that could not perform cone-beam CT. We only had two-dimensional digital subtraction angiography (DSA) to rely on! So, it was quite obvious that we needed something else to guide us during PAE and make sure we were embolizing the right arteries. I still remember when I showed Prof. Pisco my first CTA from a patient before PAE. He said to me, "You have your PhD thesis here." He was right! We published several studies on the anatomy of the prostatic arteries based on CTA and DSA.

This feeling of exploring new boundaries and excitement with the adventure was rather unique for me. One of my major concerns when we were still in the early years of PAE was that no one would be able to replicate our methods and results and that PAE would be considered "bogus," but one of our major accomplishments was seeing other groups replicate our findings and having amazing interventional radiologists from all over the globe acknowledging our work.

Last August, you and colleagues published a study on repeat PAE for BPH, concluding a limited impact in patients who didn't show a response to the initial PAE.[1] How do you address these nonresponders?

I was really enthusiastic about this study, which followed our publication in *Radiology* in 2016 focusing on understanding clinical outcomes after PAE.[2] Trying to identify baseline predictors of clinical outcomes is important because it can help optimize results through better patient selection. This *Journal of Vascular and Interventional Radiology* (*JVIR*) study from August 2020 expanded on the concept that not all BPH patients respond to PAE the same way. Even if you perform a successful bilateral embolization, you may have a minority of patients that do not improve after PAE (roughly 10%-20%). These patients, whom we labeled in 2016 as "nonresponders" because they didn't improve post-PAE, are quite different from patients who improve the first 6 months after PAE but have relapsing symptoms after. We called those patients "relapsers." With the August 2020 *JVIR* study, we were able to show that clinical outcomes differ when you repeat PAE for these two types of patients. With relapsers, you may still have good clinical outcomes after PAE. However, PAE does not work for most nonresponders, and other options are better suited.

These two studies suggest that patient selection rather than technique is essential to enhancing clinical outcomes after PAE. Choosing the right patients is key because PAE is not a perfect fit for all BPH patients. Nowadays, and after learning from these studies, we don't offer repeat PAE to nonresponders, just for relapsers. With nonresponders, we usually try medical therapy for a few months. If residual symptoms are very bothersome, we counsel patients for other minimally invasive treatments, transurethral resection of the prostate, or laser prostatectomy.

(Continued on page 96)

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What do you see as the remaining hurdles to PAE's acceptance?

From my point of view, the process is quite different when comparing the United States with Europe and the rest of the world, and these differences are reflected in the urology and national guidelines. For example, in the urology guidelines of United Kingdom, Brazil, and Europe, PAE is already an accepted treatment option for patients with BPH. However, it is still considered experimental in the United States and is only recommended under clinical trials. The reasons for this are political and economic rather than scientific. The data are already there and are robust enough to allow for PAE to be compared with all existing minimally invasive treatment options for BPH patients, and PAE has the most robust supportive data of all those options.

What tips do you have for working with those who remain skeptical?

You must understand the pros and cons of minimally invasive treatment options for patients with BPH and team up with open-minded urologists who will accept PAE. As with uterine artery embolization for fibroids/adenomyosis, the challenge is more about who treats the patient than the treatment itself. To convince urologists to explore a PAE practice, you can propose a clinical research study or simply provide an additional treatment option for a dedicated BPH clinic. If you are a urologist with a strong BPH clinical practice, you will want the practice to be able to offer PAE as an option, irrespective of who is performing it. At the end of the day, this team strategy will give you more options for your patients.

How would you summarize your recent publication[3] of results from the BestFLR trial for patients with liver cancer?

In one sentence: Glue is better and faster than particles plus coils for liver hypertrophy after portal vein embolization. I was really happy with this study. It is the main study from Dr. José Hugo Luz, a PhD student who worked with us for 5 years. This study reflected a huge effort from him but also from everyone on the team involved and is a good example of how we should strive to collect and report data from IR. Prospective randomized controlled trials are always better than retrospective case series without controls. We should make all efforts to improve the quality of data from IR studies. We already knew from retrospective studies that glue was better. However, we had no randomized trials proving this. Like Norah Jones says in the song "One Flight Down," "Now you know."

What were some of the important insights gleaned on a well-run, effective morbidity and mortality meeting from the "CIRSE Standards of Practice on Conducting Meetings on Morbidity and Mortality" document[4] you and colleagues published in May 2021?

This team effort was led by Dr. Joo-Young Chun from St George's Hospital in the United Kingdom. It was a commendable initiative from the Cardiovascular and Interventional Radiological Society of Europe focusing on a rarely reported but immensely important aspect of IR: assessing and learning from errors in order to improve patient safety. The publication provides all the key aspects relevant for interventional radiologists on how to implement and organize morbidity and mortality meetings at IR units. IR procedures are less invasive than conventional surgical procedures, but you will always run into complications along the way. The only way to monitor and correct any possible mistakes is through morbidity and mortality meetings, which are already mandatory for most surgical departments. However, many IR departments still need to understand the true value of the meetings and implement them recurrently. Where I work, I was fortunate enough to help implement these recurrent meetings for the past 3 years. This allowed us to correct practices that were not optimized and improve patient safety. We were able to minimize errors in a departmental culture that values shared learning in a blame-free environment.

As Section Editor for embolization at *CardioVascular and Interventional Radiology* (*CVIR*), Associate Editor for *Acta Radiológica Portuguesa*, previous Associate Editor for *JVIR*, and the recipient of several *JVIR* Top Reviewer awards, what advice can you share about medical writing and producing a quality manuscript?

My first piece of advice is that you should like doing it. I am passionate about medical writing, though I should also say that it might be a bit easier for me as my wife deals with science and scientific writing on a daily basis. When I see a poorly written paper that might otherwise be of interest, I appreciate the opportunity to help the authors improve their manuscript quality, and it is rewarding to see the publication of a paper you helped improve. My second piece of advice is to learn how to write scientifically, including rigorous reporting of data and adhering to established standards. There are numerous guidelines and checklists online for authors to use in reporting data, and *CVIR* has valuable tips on its website. There are also scientific publications available on how to

review papers.[5] When reviewing papers, you also learn a lot from authors and from other reviewers' and editors' comments.

One final tip: Make sure your research topic is novel and relevant. You do not want to waste time and energy reinventing the wheel or finding something that has no implications for patient care.

On your website (tiagobilhim.pt), you've provided informative patient resources on embolization treatments, including Q&As, blogs, and videos. What advice do you have for colleagues who might want to start their own site?

We need to raise community awareness about IR. Some interventional radiologists still believe that we should only work for other physicians and should not have direct patient referrals, but I learned from my first few years with Prof. Pisco that angio room work is only a small fraction of all IR work. Our practices should be centered on patient care before, during, and after the procedures. However, direct patient referral to IR is almost impossible because the general community and even most medical doctors do not know about IR, and awareness initiatives teach patients and doctors about IR and the minimally invasive treatment options we can provide.

For patients, I like to compare this to a holiday stay at a fancy hotel. Most people take virtual tours of the hotel website, watch videos, and view photos and comments from other clients. Patients appreciate knowing exactly what to expect before their intervention.

If you are starting your own site, you should be very specific about your goals. In my experience, the primary focus should be on the patients and diseases rather than the treatments. Seeking professional expertise is also paramount—do not try to do everything yourself. ■

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