Venous Stenting: Expectations and Reservations

A panel of experts discusses patient selection, follow-up, and ideal technologies for the future.

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When and why do you place a venous stent?

Dr. Razavi: Stents may become necessary when venous patency is not adequately achieved with angioplasty alone, possibly from symptomatic venous obstructions due to chronic thrombosis and/or some venous compression disorders. A typical scenario would be in a patient with deep vein thrombosis (DVT) who is discovered to have an underlying obstruction of the central veins after the clot is removed. Other common indications for venous stenting in our practice include recanalization of chronically occluded central veins or outflow venous obstructions in patients with symptomatic reflux. I like to emphasize "central veins" because venous stenting of the peripheral veins using today's available devices has not been particularly effective. In particular, these are locations peripheral to the thoracic outlet (subclavian or axillary veins) in the upper extremities and caudal to the saphenofemoral junction in the lower limbs.

Dr. Williams: I place a venous stent in the setting of chronic DVT and recanalization, whenever the post-angioplasty lumen is ≤ 50% of the expected diameter of the vessel in question. In the setting of residual narrowing after thrombolysis for acute and subacute venous thrombosis, I place a venous stent whenever there is a compressive lesion, such as related to the left common iliac vein and right common iliac artery; left innominate vein and innominate artery; or whenever there is ≥ 50% residual thrombus resistant to thrombolytic treatment. In these settings, I place a stent because I believe long-term patency requires good inflow and good outflow through the treated venous segment. I determine significance of residual narrowing using a combination of intravascular ultrasound and contrast injections.

Dr. Spencer: Venous stents are placed in the inferior vena cava (IVC), common iliac, external iliac, and com-

mon femoral veins for chronic venous obstructions and/or May-Thurner syndrome. May-Thurner syndrome is not only a compressive phenomenon, in which the right common iliac artery crosses on top of the left common iliac vein, but there is also hyaline scar formation within the vein lumen itself. This relationship explains why angioplasty alone is not effective, especially in the common iliac vein.

Dr. Raju: Most venous stenting in my practice has been confined to central veins in the abdomen that drain the lower limbs. A crucial difference between arterial and chronic venous disease is that the latter seldom poses a threat to limb or life. For that reason, intervention is not indicated, even in severe lesions, unless there are disabling symptoms that do not respond to conservative treatment.

What are your current device options? What are their capabilities and limitations?

Dr. Razavi: Our options are currently somewhat limited when dealing with patients who have deep venous pathologies. Stent configurations and sizes are suboptimal, recanalization tools are not designed for chronic venous occlusions, effective thrombectomy catheters do not exist, and of course, antireflux devices have all failed so far.

This does not mean that we cannot presently deal with most venous pathologies. Patients with acute DVT are treated with thrombolysis or lytic-assisted devices, and venous obstructions are stented with what we presume to be suboptimal stents. The development of a new generation of venous stents is an important step in the right direction.

Dr. Raju: Venous stenting is performed to reduce peripheral venous hypertension, which is the basis of symptoms. The stent has to decompress the obstructed vein reducing congestion in the tissues. Merely establishing flow across the lesion is not enough. For this reason, venous stents have to approximate the size in normal anatomy. This generally means a 16-mm-diameter stent for the common iliac vein and even larger for the IVC. Only one make of stent, the Wallstent (Boston Scientific Corporation, Natick, MA), has been available in such large sizes and has seen predominant use in venous applications. Other choices are in the offing.

Dr. Spencer: Options for venous stenting include stainless steel and nitinol stents, as well as covered stent grafts. The stainless steel choice is the Wallstent, which offers strength and flexibility. The downside to the Wallstent is that it is the weakest at the end, which is where you need the most strength with May-Thurner syndrome, and foreshortening makes precise placement difficult. The benefit is that it is retrievable up to a certain point before complete deployment. The concern for the free-floating portion of a stent in the IVC to be even weaker is often not discussed. Anchoring is critical for the stent to maintain strength; therefore, I only use the Wallstent for larger sizes in the IVC and not in patients with May-Thurner syndrome.

Nitinol stent options include the SMART (Cordis Corporation, Bridgewater, NJ), Zilver (Cook Medical, Bloomington, IN), Protégé (Covidien, Mansfield, MA), Supera Veritas (Idev Technologies, Inc., Webster, TX), and Epic stents (Boston Scientific Corporation). The benefits of these are that they allow precise placement. The Protégé stent is the best for accurate placement in my opinion, because the stent is 95% deployed before the base with round ball feet is released. This is a slightly weaker stent, but I believe precise placement is more important. I retreat many patients whose stents have not been placed far enough proximally into the edge of the IVC, so this is my preferred stent. The Supera is flexible and very strong but elongates significantly at times, so precise placement is difficult. There is no weakness at the end—great for crossing the groin—but it is only available up to an 8-mm inner diameter, which works great in larger stents that are compressed/won't open (eg, in a radiated pelvis with scar).

For covered stent grafts, the Viabahn device (Gore & Associates, Flagstaff, AZ) is good for ruptured vessels—a very rare phenomenon. For a contained leak, I still treat with uncovered stents because a low-pressure system (venous) tends to thrombose as soon as anticoagulation has been stopped. In a patient with invasive cancer and very tight narrowing where there is concern for tumor erosion, the iCast balloon-expandable stent graft (Atrium Medical Corporation, Hudson, NH) works well.

Dr. Williams: There are numerous nitinol stents that are 14-mm diameter or smaller and the stainless steel Wallstent, which extends up to diameters exceeding 20 mm. In the IVC, I prefer a stent that is ≥ 18 mm in diameter. In the common iliac vein, I prefer a stent that is 14 or 16 mm in diameter, and in the external iliac and common femoral vein, I prefer a stent that is 14 mm in diameter. If I have to extend into the deep femoral or femoral vein, I would use a 12-mm stent. The nitinol stents are technically easier to insert, because there is no significant foreshortening during deployment. Most stents are rated by hoop strength, whereas in the setting of extrinsic compression, it may be more appropriate to use resistance to vise-like compression. I have occasionally seen nitinol stents flattened by the right common iliac artery in May-Thurner anatomy.

What are the ideal characteristics of a venous stent? If you had a wish list for stent development, what would it include?

Dr. Williams: The ideal venous stent would deploy without foreshortening, be capable of transitioning from full diameter to two-thirds diameter over a distance of 2 or 3 mm without pursing of either end, have high resistance against compression as well as high hoop strength, be MR-compatible, resistant to thrombus formation and platelet adherence. Ideally, it would come in diameters ranging from 10 to 22 mm and lengths ranging from 4 to 10 cm. It should tolerate a radius curvature of 2 cm without protrusion of metallic components of the cell structure, reach and retain its target diameter by balloon angioplasty, and (as long as we are dreaming here) be inexpensive. If a biodegradable stent could disintegrate without return of venous compression, that would be a bonus.

Dr. Raju: The iliac veins pursue a complex curve in the pelvis. While diffuse stenosis is present in postthrombotic disease, focal stenosis also occurs at anatomical "choke" points caused by arterial or other compressive elements at the iliocaval junction, iliac bifurcation, and (less often) behind the inguinal ligament. For some reason, thrombus resolution is poor at these locations. These are also the sites of nonthrombotic stenoses, not only due to compression, but from mural fibrosis and luminal webs from trauma of repetitive arterial pulsations. The ideal stent has to be reasonably long and flexible, yet provide adequate radial strength to withstand opposing forces at the choke points. The iliocaval junction is particularly critical. Persistence or recurrence of symptoms is likely if this lesion is not adequately traversed. Crossing the inguinal ligament is also a concern, but the Wallstent appears to be free of fractures and erosions that are more common in the arterial system.

Dr. Spencer: The ideal stent would be flexible with moderate radial force, no foreshortening, and allow for very precise and accurate placement.

Dr. Razavi: Some desirable features are common to all stents, not just venous devices, and include precise deployment, good visibility, and flexibility of both a low-profile delivery catheter and the deployed stent. However, certain attributes are more suited for venous applications, such as larger diameters (≥14 mm) and appropriate levels of radial force and crush resistance.

Although, in terms of "appropriate radial force," we really do not know what the optimal radial force in veins should be. We know that most 10- to 14-mm nitinol stents currently available in the United States do not have high enough radial force and crush resistance to deal with venous compression syndromes, nor to maintain patency in the fibrotic chronically occluded veins. On the other hand, veins have thin walls devoid of the muscular layer present in arteries. This means that there is the theoretical possibility of erosion of stent struts through the vessel wall, especially if the end of a rigid stent with high radial force is placed at a bend.

I would also like to see fenestrated or beveled stents for points of venous confluence where only one side needs a stent.

In what ways might some desirable stent characteristics affect others, such as flexibility versus radial force?

Dr. Spencer: To gain radial force and maintain flexibility, you give up the ability to precisely place a stent, which, in my opinion, is the key reason some stented patients rethrombose. I think the focus on greater and greater force is not the key issue. Technique is the key issue.

Dr. Razavi: With advances in technology and design, flexibility versus radial force is a false tradeoff. For example, the Supera Veritas stent is arguably one of the most flexible stents on the market today and also has the highest radial force. The tradeoff there is accuracy of placement.

I think physicians, as end-users of medical devices, and our patients, as the recipients of devices, should challenge our engineer partners to not think of tradeoffs but rather strive to achieve all of the desired characteristics in one device. As a respected engineer and entrepreneur once told me, "All engineering problems, by definition, are solvable. You just have to find the right engineer to do it."

Dr. Raju: Placing an undersized stent in the iliacs is pretty much an irretrievable situation most of the time. Symptoms persist or, worse, the stent occludes. Hopefully, a dedicated iliac vein stent with optimal size will help reduce this all-too-common problem.

Dr. Williams: In clinical practice, I have not found the tradeoff between flexibility and radial force to be a significant issue.

How might clinical study parameters differ from arterial stents? What would be the most critical endpoints?

Dr. Spencer: Study parameters should look at quality of life, swelling, venous stasis changes, and ulceration (eg, VEINS score, CEAP, Villalta scale, etc.). Primary and secondary patency and relief or improvement in deep venous reflux is important as well. One great misperception is that deep venous reflux plays a major role in

symptoms from venous disease. Venous obstruction and superficial venous reflux are actually the key culprits in symptomatology.

Dr. Williams: A stent that could be brought to its target diameter by simple balloon angioplasty would save 1 or 2 hours of procedure time. A stent resistant to platelet adherence and thrombus formation would improve short- and long-term patency rates.

A nitinol stent is MR-compatible and less radiopaque, which is important for MR and CT evaluations of the pelvis later in life, considering that patients with iliac vein compression tend to be young or middle-aged.

Dr. Razavi: It is important for all those involved in the upstream processes, such as the design, development, testing, and regulatory cycles, to understand that veins and arteries have significant differences. Veins are more than just conduits. They are physiologic organs that have humoral, capacitance, antireflux, and conduction functions.

In terms of study endpoints, we have to examine the reasons that we perform each step during venous interventions. The problem we encounter in the case of venous stenting is that stents are only one step in the complex therapeutic plan that often consists of management of clot, prevention or treatment of venous reflux, establishment of good inflow and outflow, and prevention of disease recurrence. Hence, the clinical objectives of therapy are dependent on multiple factors, not just stents. The role of stents in this complicated algorithm is to maintain venous patency.

I am pleased by the recent efforts on the part of industry to understand the venous space better (especially the deep system), but I am somewhat concerned that the regulatory agencies may not completely appreciate that achieving clinical success in this arena is often dependent on the function of a series of steps, not just one.

What kind of patient or case characteristics can significantly influence long-term stent performance? How do failures manifest?

Dr. Williams: In patients with prothrombotic syndromes, personal commitment to compliance with anticoagulation is important for long-term stent performance. I personally think that anticoagulation in the perioperative and immediate postoperative period is also crucial to stent patency. I tell our interventional radiology fellows that, in venous stent biology, flow is trump. Warfarin will not salvage a stent with poor inflow, emphasizing the need to ensure good inflow and good outflow during the recanalization procedure. Stent failure usually manifests as recurrence of the dominant symptoms with which the patient presented in the first place. I emphasize to the patient that keeping a stent open is easier than reopening an occluded stent.

Dr. Raju: Iliac vein stents have excellent long-term patency. In nonthrombotic disease, only three stents among over 1,000 that were followed up to 10 years (cumulative) have occluded—an astonishing statistic. On a cumulative basis, about 10% of stents placed in postthrombotic limbs become occluded over time; the majority of these are in chronic total occlusion recanalizations. Acute stent occlusion is only rarely silent—most of the time, the patient knows that something has happened from the sudden deterioration of the clinical status of the limb.

Dr. Razavi: The function of stents is to keep the vessel patent, so I think this discussion should revolve around optimization of stent patency. The majority of stent failures occur early in the venous system. This suggests a thrombotic etiology. There are both patient and operator factors that can affect stent thrombosis. Important among these are the proper use of stents (location and size), establishment of good inflow and outflow, and optimal transition from postprocedural, heparin-based therapies to oral anticoagulants. Stent failures may be acutely asymptomatic but predispose the patient to recurrent venothromboembolic disease, pain, edema, or other manifestations of both acute and chronic venous disease.

Dr. Spencer: From a patient standpoint, factors that lead to failure (we've already discussed that technique is the greatest issue) include hypercoagulable states with poorly managed anticoagulation. Lupus anticoagulant tends to be one of the worst. Patients with DVT who were not able to be anticoagulated (bleeding concerns, intracranial surgery, trauma, etc.) tend to have more problems in the infrainguinal veins. Therefore, inflow problems and poor landing zones for stents make these cases challenging to get lasting results. Also, patients with significant superficial venous disease need to have it addressed to keep flow in the deep system antegrade.

What is your follow-up protocol for stented patients? Does it differ from those who do not receive stents?

Dr. Razavi: Our protocol for patient follow-up is independent of whether or not stents were used. Routine follow-up for nontrial patients are performed at 1, 3, 9, and 18 months after intervention. After that, patients are seen if their symptoms recur. We use duplex ultrasound as the imaging method of choice in our venous patients, including those who require imaging of their iliac veins.

Dr. Spencer: My follow-up is the same for all DVT patients, stents or not. Acute DVT patients receive warfarin or rivaroxiban immediately. Chronic DVT patients are treated with enoxaparin for 1 month. All patients undergo ultrasound imaging and are seen at the clinic visit at 3 weeks. If all is well, chronic patients are converted to oral anticoagulants, and if not, they receive 3 months of enoxaparin before 6-month follow-up with ultrasound. If patients are asymptomatic and this is their first episode, they come off anticoagulants, go on aspirin, and undergo one more ultrasound and follow-up 6 months later. If the veins are still abnormal and if there are any symptoms, they stay on anticoagulants indefinitely, with 6-month follow-ups. Everyone undergoes yearly clinical follow-up with ultrasound as needed.

Dr. Williams: Our patients are discharged on Lovenox 1 mg/kg twice a day for 2 weeks, 81 mg of aspirin per day, and on 75 mg Plavix per day after appropriate loading. They return to the clinic in 2 weeks, at which time we transition to warfarin. In patients already familiar with warfarin, we may start the transition earlier, even in the hospital. The patients return for follow-up venography at 6 months, 12 months, and 24 months. If we see in-stent stenosis at venography, we biopsy the adherent material, trying to distinguish between ongoing thrombosis and mature, organized thrombus. The Plavix is discontinued at 2 months. If the patient has an indication for lifelong warfarin, then of course that continues unabated. If the patient has no indication for long-term anticoagulation, then at 5 months (while the patient is on aspirin and warfarin), we will obtain a D-dimer. If the D-dimer is negative, we will maintain aspirin but discontinue warfarin, obtaining a second follow-up D-dimer in 2 weeks. If that remains negative, the patient stays off of warfarin. The patient returns for the 6-month venogram 2 weeks following the second D-dimer (4 weeks after discontinuing warfarin). If venography shows no in-stent stenosis and if the D-dimers have been negative, then we think it is safe to continue off warfarin. If the D-dimer is positive or if biopsy of in-stent stenosis shows ongoing thrombosis, we would encourage further continuation of warfarin. We communicate frequently with colleagues in vascular surgery, vascular medicine, and hematology for patients with complex thrombotic issues or recurrent thrombosis.

Dr. Raju: I think stent surveillance is important in postthrombotic patients, particularly those who undergo chronic total occlusion recanalizations. In the latter subset, we perform duplex stent checks weekly for 3 to 4 weeks initially, then monthly for a few months, and less often as time goes on. Surveillance can be less rigid and at greater intervals in stenting of stenotic lesions. In nonthrombotic limbs, a 6-month or yearly routine stent check is sufficient. Of course, regardless of the etiology, duplex imaging or venography is called for if there is persistence or recurrence of symptoms. ■

Note: This article has been updated to reflect a correction in the materials of the Idev Supera stent.