The Critical Need for an Iliofemoral Venous Obstruction Classification System

An overview of a potential classification system to better identify and treat iliofemoral venous outflow obstruction.

BY WILLIAM MARSTON, MD

Understanding of the importance of venous obstructive disease and its impact on venous hemodynamics and clinical symptoms has dramatically increased in the past decade. Severe obstruction of the iliac veins and/or vena cava may result in severe lower extremity symptoms, including chronic debilitating pain, edema, and venous claudication, occasionally leading to intractable ulceration. Compression therapy, the typical treatment for these symptoms, is poorly tolerated by patients with iliocaval venous obstruction (ICVO), as symptoms worsen in the compressed limb with ambulation as the limb swells due to the increased blood flow associated with exercise.

Neglen et al demonstrated that the iliac veins and inferior vena cava (IVC) could be successfully reopened using stents that were initially designed for the arterial system or the biliary tract, even in patients with veins that had been occluded for years.[1] That pioneering study combined with the availability of improved devices for recanalization and intervention have led to an exponential increase in the number of procedures performed for the treatment of ICVO.

In their classic report, May and Thurner described the anatomy of the aortic bifurcation and IVC confluence and the resultant compression of the left iliac vein in 22% of the cadavers they studied (Figure 1).[2] Subsequently, it has been recognized that compression of the iliocaval outflow tract can occur at multiple locations, including the hypogastric origin and the inguinal ligament, among others.[3,4] Patients experience symptoms from anatomic compression alone (primary obstruction) and may also develop postthrombotic obstruction after iliac or caval deep vein thrombosis (secondary obstruction).

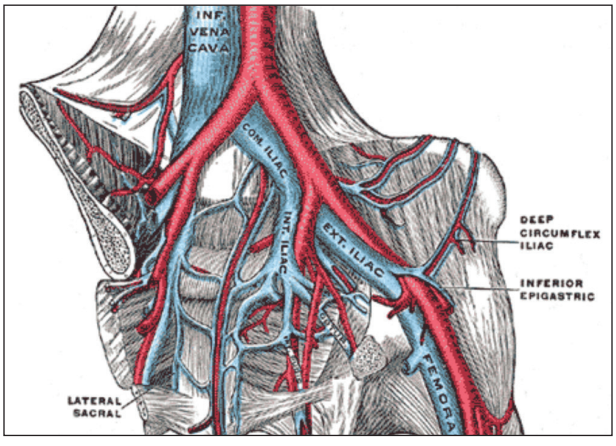

Figure 1. Pelvic venous anatomy indicating potential sites of compression of the iliac vein and vena cava. Reprinted from Wikimedia Commons, the free media repository. Gray's Anatomy plates, plate 586. https://commons.wikimedia.org. Accessed June 28, 2017.

Patients with ICVO develop varying anatomic involvement of the venous system. In some cases, obstruction involves only a short segment of common iliac vein where the contralateral iliac artery crosses over, leading to stenosis of the underlying vein (Figure 2). In other

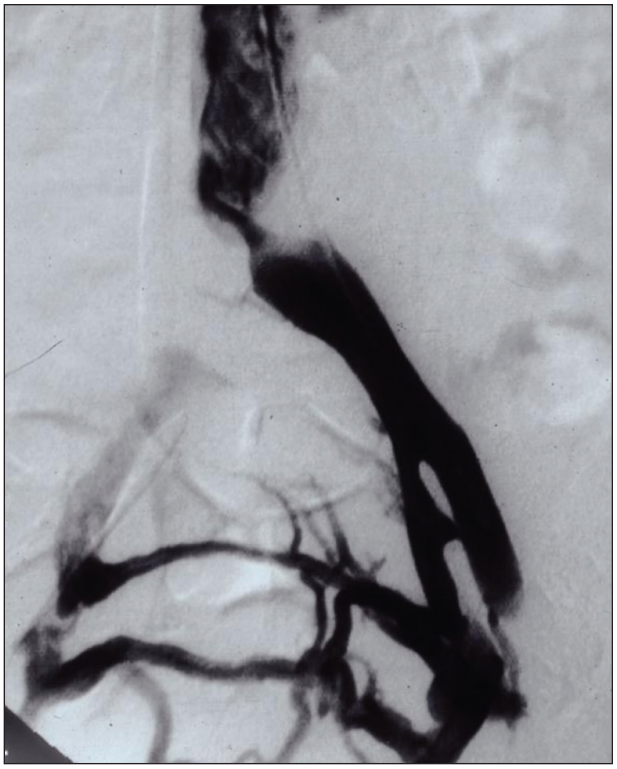

Figure 2. Venogram of localized compression of the left iliac vein at the confluence into the IVC with collateralization to the contralateral iliac vein.

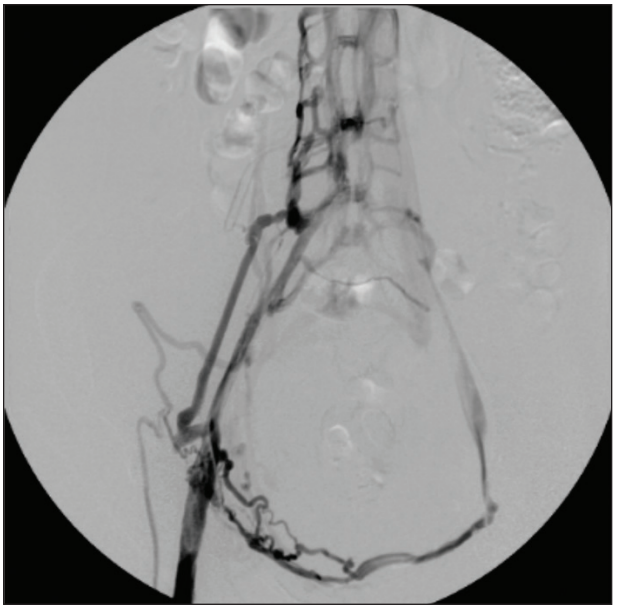

Figure 3. Venogram of complete occlusion of the external and common right iliac veins and IVC with collateralization into the left iliac vein and azygous system.

situations, the entire venous system from the common femoral vein through the vena cava is occluded (Figure 3). When considering methods of intervention to treat these problems, it is obvious that the varying anatomy of venous obstruction may require different tools and strategies to optimize results. If we are to compare results between treatment strategies, we should be sure that we are comparing cases with similar levels of complexity typical to interventional treatment of arterial and aneurysmal disease.

DEVICE OPTIONS

Currently, the stainless steel self-expanding Wallstent (Boston Scientific Corporation) is the most commonly used stent for venous intervention in the United States. The Wallstent, initially designed over 20 years ago for biliary intervention, has some positive characteristics for use in the venous system including flexibility, large-diameter sizes, and fracture resistance. The results reported by numerous investigators with this device have been favorable.[1,5] However, there are shortcomings, including a lack of strength at the ends of the stent that may lead to failure to resist compression when placed at the iliac confluence, migration, and significant foreshortening at deployment. In some cases, nitinol self-expanding stents are used as well.

Recently, multiple medical device manufacturers have developed stents designed specifically for the venous system (Figure 4). Several are CE Mark approved and in use in Europe, while clinical trials are ongoing in the United States (Table 1). There is great interest in the performance of these venous stents to determine which is best to use in the venous system. However, when considering the design of any stent, there are significant engineering trade-offs that must be considered. In general, engineering a stent that is stronger and better able to resist the forces of external compression may result in increased stiffness or density, which may have negative performance characteristics in certain situations. For example, placing a stiff stent in a tortuous venous segment may straighten that segment but lead to significant angulation or kinking at the ends of the stent with resultant obstruction of flow. Given the variability of the anatomic distribution and extent of disease, one venous stent design may not be the best for all situations encountered by the venous interventionalist. A stent that performs well in a nonthrombotic patient with localized compression at the iliac vein confluence may not be ideal for a postthrombotic patient with chronic total occlusion of the iliac vein. It is therefore important that we compare outcomes with devices in specific anatomic situations to determine which venous devices will perform best for individual patients with ICVO.

TABLE 1. CURRENT STATUS OF VENOUS-SPECIFIC STENTS	
Stents in Clinical Trials in the United States	**Stents With CE Mark Approval in Europe**
Venovo venous stent (Bard Peripheral Vascular, Inc.)	Venovo venous stent
Vici venous system (Veniti, Inc.)	Vici venous system
Zilver Vena venous stent (Cook Medical)	Zilver Vena venous stent
	sinus-Obliquus (OptiMed GmbH)
	sinus-Venous (OptiMed GmbH)
	sinus-XL (IVC only; OptiMed GmbH)
	sinus-XL Flex (OptiMed GmbH)

CLASSIFYING DISEASE SEVERITY

As interventional therapies for the arterial system evolved, it became apparent that the extent and severity of disease affecting the artery related closely to outcomes. The TransAtlantic InterSociety Consensus (TASC) criteria and subsequent TASC II criteria were developed to classify arterial disease severity and provide a framework for clinicians to study technical success of interventions and long-term success of a treatment plan over time.[6] Currently, no anatomic classification scheme has been validated for use in the treatment of ICVO. Neglen et al reported that patients with postthrombotic ICVO had significantly higher rates of stent occlusion during follow-up.[1] Another study related the lower patency rates in postthrombotic patients to the effects of diffuse venous thrombosis on the femoral and profunda femoral veins, leading to compromised inflow into the iliac venous segments.[7] However, no further information on the outcomes of ICVO intervention have been available related to the anatomic extent of disease. Other factors, such as the presence of an IVC filter, bilateral disease, and the extent of ipsilateral femoral disease, have not been evaluated to determine their effect on poststenting outcomes.

A group of venous interventionalists created an initial classification system, such as the TASC criteria for iliac arterial disease, that included four types of ICVO based on the extent of venous involvement and the severity of obstruction (Table 2).[8] In this system, a patient with stenosis of a single venous segment in the outflow tract (common femoral vein, external iliac vein, common iliac vein, or IVC) was defined as a type I. Those with multiple segments identified with stenosis (defined as > 50% narrowing) were assigned to type II. A single segment with complete occlusion was defined as type III, and multiple segments of occlusion were categorized as type IV.

This initial classification system was tested in a retrospective study of ICVO patients undergoing intervention at two vascular centers. Classification can be performed

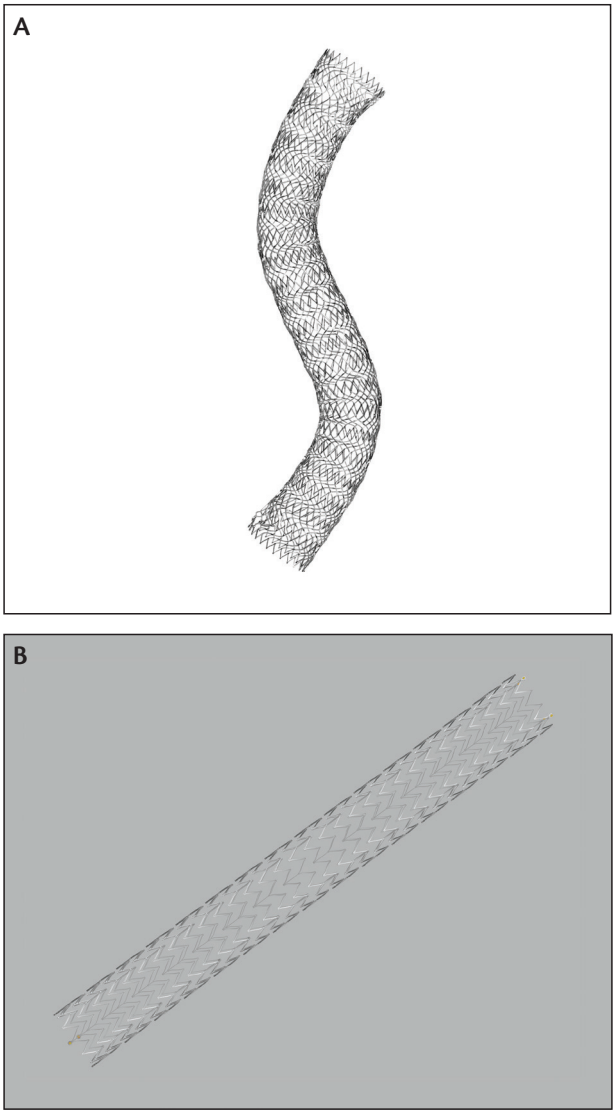

Figure 4. Stents engineered for the venous system nearing completion of clinical trials in the United States include the Vici venous system* (A) and Zilver Vena venous stent† (B).

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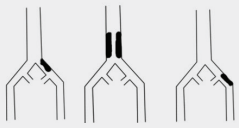
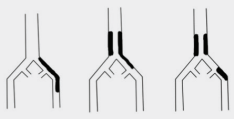
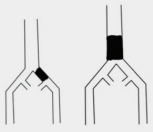
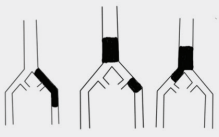
†Permission for use granted by Cook Medical, Bloomington, Indiana. Not approved for sale in the US. Caution: Investigational device. Limited by Federal (or United States) law to investigational use.

TABLE 2. ICVO CLASSIFICATION SYSTEM

Classification Type	Disease Characteristics	Examples
Type I	Single segment of stenosis	
Type II	Multiple segments of stenosis	
Type III	Single segment of occlusion	
Type IV	Multiple segments of occlusion	

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using a variety of diagnostic methods, as long as imaging of the venous system from the femoral vein to the suprarenal IVC is performed. CT venography and magnetic resonance venography are acceptable tests if venous contrast is well timed to image the system and identify areas of significant obstruction.[9] This allows identification of the classification type before intervention to better counsel patients. The classification type was confirmed using intravascular ultrasound whenever it was performed. One-hundred twenty patients were identified as having clinically significant ICVO and intervention was attempted.[8] Forty-two percent of those patients were in the type I group, and the remainder were evenly distributed between types II, III, and IV. Technical success in reestablishing unobstructed venous outflow was achieved more often in types I and II than in types III and IV (P = .003) (Table 3). Iliocaval patency was measured at 6 months after intervention and showed significantly better results in types I and II than in types III and IV (P = .02) (Table 3). The classification system can provide additional predictive information that cannot be determined by classifying the patients as postthrombotic or nonthrombotic. Patients with postthrombotic disease

TABLE 3. INITIAL TECHNICAL SUCCESS AND EARLY FAILURE RATE BY ANATOMIC TYPE*

Type	No. of Patients	Procedural Success	Early Failure Rate (within 6 mo)
I	51	50/51 (98%)	4/51 (7.8%)
II	23	23/23 (100%)	1/23 (4.3%)
III	16	13/16 (81.3%)	2/16 (12.5%)
IV	30	24/30 (80%)	8/30 (26.7%)

*Fisher's exact P value for types I and II versus III and IV: procedure success is P = .003; early failure rate is P = .02.
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who were type I had better outcomes than type IV postthrombotic cases.

This initial report supports the belief that a well-designed, validated classification system for ICVO cases could appropriately identify the expected risk and outcomes for the spectrum of disease encountered in this growing area of intervention. Just as the TASC system has done for arterial intervention, varying treatment strategies can be compared for specific types of disease and the outcomes that follow, ensuring that similar anatomic levels of disease are involved in the comparison. Inevitably, the venous space will evolve as the arterial space did before it and, hopefully, have not one but multiple venous stents of varying design that may be employed where their design characteristics yield the best results. Other devices specific to the venous system, such as a bifurcated venous stent for the management of iliac confluence obstruction would also benefit from the use of an ICVO classification system to facilitate clinical studies.

This novel classification system is likely too simple to adequately capture all the key predictors of outcomes associated with intervention for ICVO. The presence of IVC filters associated with caval occlusion, as well as the presence of bilateral disease and a history of prior interventions on the affected venous outflow tract, may all have a significant bearing on outcomes. It is also widely believed that inflow into the iliac venous segments is critical to maintaining patency of stents implanted in this location. Raju et al previously related the lower patency rates in postthrombotic patients to the effects of diffuse venous thrombosis on the femoral and profunda femoral

veins leading to compromised inflow into the iliac venous segments.[7] It will be important for a well-developed classification system to capture these important factors to provide the best predictive information to guide treatment and device development moving forward.

CONCLUSION

The treatment of venous obstruction is currently experiencing phenomenal growth as physicians discover the capability that intervention offers to improve patient symptoms and heal recalcitrant wounds. However, this growing field has yet to successfully define which patients can benefit most from these procedures. It appears clear that a multinational consensus of venous specialists is needed to create and validate a classification system to facilitate patient counseling, device development, and the selection of the most appropriate treatment strategies for specific types of disease. As information from ongoing clinical trials in venous stenting becomes available, the generated data may be useful in further defining and validating this type of system. Further use in a prospective manner can then reveal its relevance.

A final, and potentially most important, possibility is the ability to relate the extent of disease to symptom improvement after ICVO intervention. One of the most vexing problems surrounding this area concerns the severity of disease that is required to cause significant patient symptoms. It is not well known whether a stenotic but nonoccluded lesion causes symptoms that are as severe as a complete occlusion nor whether a short segment of stenosis is as severe as a more extended area of disease. A classification system that relates the type of anatomic disease to symptom improvement after intervention may provide meaningful information on the quality of life improvement that can be expected after venous intervention. For these reasons, it is critical that a classification system is developed to support further advancement in the treatment of patients suffering from the effects of ICVO. ■

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Disclosures: Principal Investigator and member of the steering committee for Veniti, Inc., related to clinical trials of the Veniti Vici stent, and receives compensation for his time related to these duties.