Lumen Shape: A New Measurement to Consider in Treatment of Iliofemoral Venous Outflow Obstruction

Exploring the role of pre-and post-procedure lumen shape in predicting patient outcomes.

By Michael K.W. Lichtenberg, M.D., FESC

Introduction

With the advent of the first dedicated venous stent in 2011, physicians no longer must rely on repurposed arterial or general utility stents for use in the treatment of venous outflow obstruction (VOO). This is significant for the differences in the anatomy of veins versus arteries, but also for the etiology of the disease addressed in the treatment of VOO. To a far greater degree than ever before, the external compression of the non-thrombotic iliac vein lesion (NIVL) is understood in cases of deep vein thrombosis and chronic venous disease, Clinical, Etiology, Anatomy, and Pathophysiology (CEAP) classification clinical scores C4-C6.[1] As well, the restriction of the elastic collagen bands found in the postthrombotic iliofemoral vein segments present unique challenges for balloon angioplasty and stenting.[2]

The “ideal” dedicated venous stent will comprise a balance of design features which address the needs of the physician in treating VOO. These design features will include open- versus closed-cell architecture, radial strength, coverage, flexibility, ease and accuracy of placement, etc. There are currently six dedicated venous stents with CE Mark approval and four with FDA investigational device exemptions for clinical studies being conducted at centers in the U.S., Europe, and Australia.

The question which must be answered is how to measure the performance of these stents in the treatment of venous disorders? Certainly, the clinical trials will present data on safety and efficacy, but efficacy will, generally, be limited to stent patency. With the current debates about the degree of stenosis and severity of venous disease at which patients should be treated for VOO calls into question patency as a singular measure of stent performance. It is important to know what performance characteristics of dedicated venous stents contribute to improved clinical success.

Fluid Dynamics and Lumen Shape

Raju has provided significant insight into area as a proxy for determining success in venous stenting in the iliofemoral veins. Stents implanted in the iliofemoral veins are subjected to both external compressions at “anatomical choke points” and/or recurrent postthrombotic stenosis. Increases in area should result in greater flow volume and reduced peripheral venous pressure.[3]

The ability to predict patient outcomes through assessment of stenosis using different imaging modalities has also been recently published. Gagne, et al. found that a threshold stenosis of 54% was optimal to indicate stenting in VOO correlative with future clinical improvement. The threshold was higher, 61%, in the subset of non-thrombotic patients.[4]

If one examines the theoretical science of fluid dynamics on flow rate, volume, and pressure, can this be applied to stenting of VOO in the treatment of venous disease? It follows, that there may be other technical performance characteristics of venous stents that bear investigation, as one seeks to better understand the relationship between stent performance and patient outcomes.

Lumen shape is defined by Aspect Ratio. For a vein, this is expressed as a ratio of maximum diameter to minimum diameter. A perfect circle has an Aspect Ratio of 1. As the ovality of the vein increases, so does the Aspect Ratio.

When a perimeter is held constant, the area is dramatically different for various shapes, from a perfect circle to that which is dramatically oval. Figure 1 demonstrates the theoretical changes in flow as a shape, with the same perimeter, increases in Aspect Ratio and ovality.[5] Flow volume is dramatically reduced with an increase in ovality. The science also demonstrates that, in order to maintain the same flow rate, measured as L/min, an increase in pressure would be required to overcome the resistance in flow due to the flatter shape.

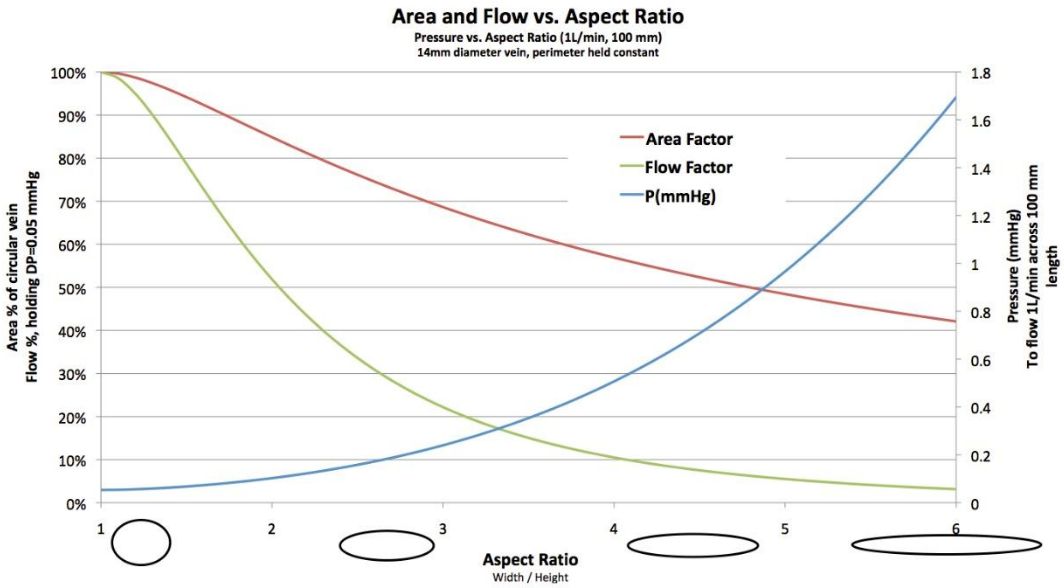

Figure 1. Holding perimeter constant, as Aspect Ratio (ovality) increases, Area decreases.
To maintain the same flow rate, pressure must increase.

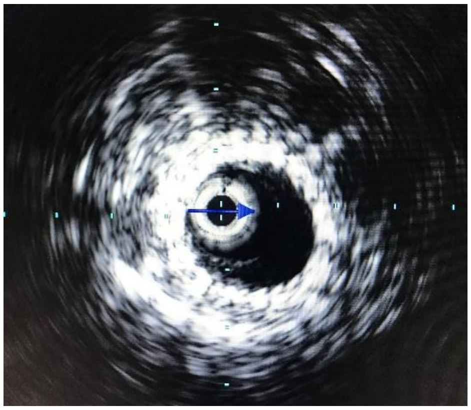

Figure 2. Post-procedure IVUS image of 41-year-old female patient with postthrombotic obstruction. “Round” lumen shape suggests lower and improved Aspect Ratio.

Fluid dynamics suggests that shape matters as it directly impacts area for a given perimeter. Furthermore, the theory of hydraulic diameter implies that shape will have an effect on the cross-sectional flow area (Hydraulic diameter is the effective flow diameter for a non-round shape and for a circle is the diameter). This will then have an impact on flow and pressure. Applying these concepts in clinical practice, and analyzing the outcomes, may provide clinicians with valuable information that could impact long-term clinical success. This research is intended to explore the relationship of changes in venous cross-sectional area (CSA) and lumen shape post-index procedure to patient outcomes at 12-month follow-up.

Methods

The VIRTUS IDE trial of the VICI VENOUS STENT® (VENITI, Inc., Fremont, CA) included a 30-subject Feasibility Cohort that was conducted at 9 centers in the U.S. and Europe. Adult patients ≥18 years with clinically-significant venous obstruction (luminal diameter reduction ≥50%) were eligible. Included patients presented with CEAP-classification clinical score ≥3 or Venous Clinical Severity Score (VCSS) pain score ≥2. Major exclusion criteria were pulmonary emboli within 6 months of enrollment, contralateral venous disease, obstruction extending into the inferior vena cava, active coagulopathy, and intended concurrent venous procedure within 30 days of index procedure.

Notably, the VIRTUS trial included the use of DUS, multiplanar venography, and IVUS, and all were core lab-reviewed. For the purpose of this analysis, the focus was on 8 IVUS measurements of the common iliac vein (proximal, central, distal), external iliac vein (proximal, central, distal), and common femoral vein (proximal and distal) made at both baseline and post procedure. From these measurements, median changes in CSA and lumen shape, as defined by Aspect Ratio, resulting from stent implantation were calculated.

VCSS scores were used as the clinical assessment metric in the lumen shape analysis. VCSS scores were captured in the VIRTUS trial at baseline, 6 months, and 12 months. Specifically, the change in VCSS from baseline assessment to 12 months was used in the analysis of the relationship of changes in CSA and lumen shape to clinical outcomes.

Pearson correlation coefficients (r) measured the strength of the relationship between the following pairs of variables: Post-stent change in CSA and 12-month VCSS score and Post-stent change in Aspect Ratio and 12-month VCSS score.

Results

The 30-patient Feasibility Cohort was composed of 24 women and 6 men with median age of 43 years. The mix of lesion etiology was 19 postthrombotic and 11 non-thrombotic and left-leg lesions were 25 (83%). Fifteen patients had lesions involving more than one vein, including 9 with involvement of the common iliac, external iliac, and common femoral veins. Median baseline stenosis was 91% (range, 50%-100%).

The anatomic changes in CSA and Aspect Ratio, pre- and post-stenting, are presented below:

Median (range)	**Pre Stent**	**Post Stent**	**Pre- to Post-Stent Change**
Area, cm^2	43 (20-76)	130 (73-286)	74% (-18% – 448%)
Aspect Ratio	2.8 (1.2-5.3)	1.3 (1.1–2.2)	-45% (-77% – -0.2%)

Table 1. Anatomic Changes in CSA and Aspect Ratio

Twenty-seven patients with available 12-month VCSS scores were utilized for this analysis. Three patients were outside the 12-month follow-up window 365 +/- 60 days. Median VCSS score declined by 5 points from baseline to 12 months and 23 (85%) patients experienced symptomatic improvement (≥2-point score improvement).

The change in area from pre to post procedure was calculated for each patient, using the formula: post-procedure area – baseline area)/baseline area. Looking at patients' change in vessel area from baseline to post procedure, one would expect to see a positive correlation between area change and clinical improvement; that is, the greater the relative increase in luminal area, the greater the clinical improvement. However, as Figure 3 shows, this was not observed. The correlation coefficient between these variables (r = -.25) indicates a negative relationship between the variables. This finding is surprising but should not be attributed any significance. Consider the strength of the relationship. At -.25, this correlation coefficient does not even meet the threshold of a weak relationship. This is a negligible “relationship”, and one can see that in the graph – there is no clear pattern here. This is also confirmed by the p value of .211.

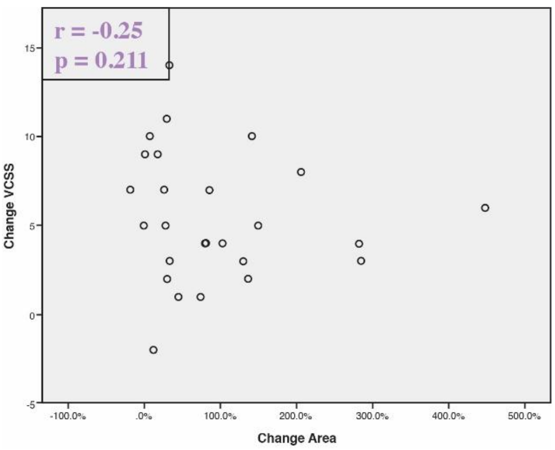

Figure 3. Post-procedure CSA increases from left to right on the x axis. There was no relationship between increase in post-procedure CSA and clinical improvement.

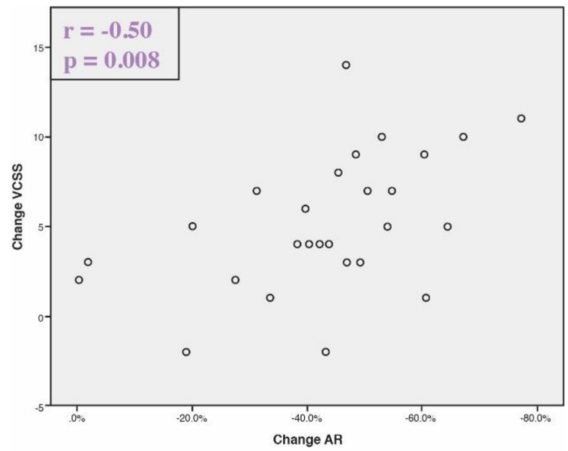

Figure 4. Post-procedure Aspect Ratio improves (lower value) from left to right on x axis. A moderately positive relationship between lower Aspect Ratio and clinical improvement is seen and is significant

Conversely, in Figure 4, there is a clearer relationship in the correlation between post-procedural change in lumen shape and clinical improvement. One sees here a moderately positive relationship (r = .50) between the decreased ellipticity of the stented vessel and clinical improvement. Those patients undergoing the greatest luminal change in the direction of oval to round are most likely to exhibit clinical improvement. This is a significant finding (p = .008).

Conclusion

This research suggests that increased post-stenting CSA is desirable, and change in lumen shape, as defined by Aspect Ratio, may contribute further to positive patient outcomes. Additionally, with further research, Aspect Ratio may be important as predictive factor of clinical improvement in patients treated for VOO. Further research is necessary and forthcoming. Validation of this analysis with the VIRTUS trial 170-patient pivotal cohort is required.

Michael K.W. Lichtenberg, M.D., FESC
Angiology Department / Venous Centre
Klinikum Arnsberg
Stolte Ley
59759 Arnsberg
Germany

+49 2932 952343900
klichte@gmx.net

Disclosures: Michael Lichtenberg receives speaker honoraria from VENITI, Inc., C.R. Bard GmbH, Optimed GmbH, and ab medica GmbH.

---

[1] Raju S. High prevalence of non-thrombotic iliac vein lesions in chronic venous disease: A permissive role in pathogenicity. *J Vasc Surg*. 2006;44:136-144.
[2] Jalaie H, Schleimer K, Barbati ME, et al. Interventional treatment of postthrombotic syndrome. *Gefasschirurgie*. 2016;21(suppl 2):37-44.
[3] Raju S. Ten Lessons Learned in Iliac Venous Stenting. *Endovascular Today*. 2016;15:40-44.
[4] Gagne PJ, Gasparis A, Black S, et al. Analysis of threshold stenosis by multiplanar venogram and intravascular ultrasound examination for predicting clinical improvement after iliofemoral vein stenting in the VIDIO trial. *J Vasc Surg: Venous and Lym Dis*. 2018;6:48-56.
[5] Schifflette JM. *Analytical overview of fluid dynamics science related to venous iliofemoral blood flow and vessel shape.* 2017. Internal VENITI, Inc. report; unpublished.