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Optimal sizing of iliac vein stents

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Abstract

Background: Iliac vein stenting has emerged as a therapeutic option in chronic venous disease. The optimal stent size is unknown but should match normal caliber at a minimum.

Methods: *Teleology*: The iliac-femoral outflow caliber was measured by Duplex in healthy volunteers to determine normal caliber. *Patient IVUS data:* The distribution curve of IVUS planimetry data in 345 chronic venous disease limbs was analyzed: values at the right tail end of the curve should approach normal values according to distribution theory. The optimal stent size was also projected using *Poiseuille equation* and *Young's scaling rule*.

Results: The optimal stent sizes in the common iliac, external iliac, and common femoral vein segments are: 16, 14, and 12 mm diameters, respectively.

Conclusion: Stent correction of iliac vein stenosis should aim to restore the lumen to the minimum recommended caliber during the initial procedure and later re-interventions.

Keywords

Iliac vein stent, May–Thurner syndrome, post-thrombotic syndrome, iliac vein compression, endovenous stent, chronic venous disease

Introduction

Iliac vein obstruction is a major component of chronic venous disease (CVD). Iliac vein stenting is increasingly used after conservative therapy has failed. It has an attractive therapeutic profile with good long-term patency, safety, and efficacy. The therapeutic effect is due to relief of venous hypertension.[1] There is decompression of the peripheral venous tree following iliac vein stenting with significant reduction of foot venous pressure.

Iliac vein stents should be of a size that provides outflow with low resistance to normalize elevated venous pressure in the limb. What is the "optimum" outflow/stent size? The answer to this question is more difficult than it would seem. We describe below several approaches to a solution, difficulties encountered and our recommendation of optimal stent size to be used.

Patients and methods

Methods to determine optimal size

Teleology. We attempted to determine optimal iliac vein stent size by measuring the caliber of iliac-femoral vein segments in a set of normal healthy volunteers. This approach failed, as many of the "normal" volunteers were found to have silent iliac vein stenosis as is known to occur.

Intravascular ultrasound (IVUS) planimetry in patients. The distribution curve of IVUS planimetry in a large subset of CVD patients was analyzed. The extreme right end of the curve should represent nonstenotic normal values according to the distribution theory. Median area in limbs that populate the right tail of the curve beyond a Z-score 1.65 was determined for this calculation.

Poiseuille equation. The Poiseuille equation was used to calculate outflow resistance offered by various caliber stents. The Poiseuille equation is: $F = \Delta P/R$. Therefore, $\Delta P = FR$, which expands to $\Delta P = Fx\frac{8\eta l}{\Pi r^4}$.

The arterial inflow into both lower limbs and pelvis and (by inference, outflow through common iliac vein (CIV)) is $\approx$1500 mL in normal individuals at rest. This represents a constant fraction ($\approx$21%,) of cardiac

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index.[2–4] Each common iliac outflow (*F* in the formula) is 750 mL/min occurring mostly in expiration. Using the normal inspiratory/expiratory ratio of 1:2 the value of F in the equation is 19 mL/s. The value for l is 4 cm (length of the CIV) and η is 0.04 Poise. With these inputs, the pressure gradient offered by a given caliber stent can be calculated from the Poiseuille equation. As an example, resistance in dynes/cm^2 for a 10 mm diameter (0.5 cm radius) stent will be based on the formula, $19Fx\frac{8{*}.04\mathrm{P}{*}4l}{(3.14)0.5\,\mathrm{cm}^4}$, yielding a resistance value = 124 dynes/cm^2. Normally, there is little measurable gradient in the abdominal veins during phasic periods of flow.[2,5] An optimum size for the stent should yield a negligible gradient with margin to spare to account for 3× flow increase with exercise and in-stent restenosis (ISR) that occurs commonly after stent placement.

Young's scaling rule. It has been known that parent to daughter branches in the vascular system had a diameter ratio of 1.26:1 (or a daughter to parent ratio of 0.79:1) that held constant across several generations of vascular branching. This scaling rule is generally attributed to Thomas Young, but probably predated him.[6] This is a fundamental law of efficient branching to maximize flow with the least expenditure of energy.[7] The scaling proportion tends to optimize several key flow parameters such as flow volume, velocity, resistance/conductance, and Reynolds number.[8–10] The relative caliber of iliac vein segments can be projected using the scaling rule from femoral vein caliber, which is known. The projections yield the upper limit of upscaling required of the parent vein as confluence of equal caliber daughter veins is assumed; the external iliac vein (EIV) and CIV are both born of the confluence of large and smaller tributaries (CFV and saphenous; EIV and hypogastric).

Subjects

Normal volunteers

Supine foot venous pressure and diameters of the iliac-femoral vein segments by Duplex ultrasound (DUS) were obtained in 10 normal healthy volunteers without history or clinical signs of CVD. This was an effort to establish "normal" caliber of these veins.

Patients

IVUS subset: The lumen area derived from IVUS planimetry of CIV, EIV, and common femoral vein (CFV) in a large subset of patients ($n = 345$) who underwent IVUS examination for indications since 2011 were analyzed. The demographics of IVUS subset is shown in Table 1.

Table 1 Demographics of IVUS subset (345 limbs).

Age	
Median (Range)	60 (17–92)
Sex	
Male	115 (33%)
Female	230 (67%)
Pathology	
MTS	63 (20%)
PTS	208 (65%)
MTS+PTS	35 (11%)
Other	14 (4%)
Diseased side	
Right	146 (43%)
Left	197(57%)

Table 2. Duplex diameters and foot venous pressures in the left lower limb of healthy volunteers.[c]

	Iliac femoral vein duplex diameters (mm)			Supine dorsal foot venous pressure (mmHg)
	CFV	EIV	CIV	
Volunteer 1	11.3	13.8	10.2	12[b]
Volunteer 2	10.4	13	8.7	N/A
Volunteer 3	13.3	13.1	13.9	5
Volunteer 4	14.8	13.9	12.5	12[b]
Volunteer 5	13.9	15.8	12.6	13[b]
Volunteer 6	13.8	13.2	11.5	17[b]
Volunteer 7	15.3	15.8	11.5	7
Volunteer 8	14	13.3	11	12[b]
Volunteer 9	12.6	11	13.9	6
Volunteer 10	10.9	11	10.3	N/A
Median (Range)	13.6 (10.4–15.3)	13.3 (11–15.8)	11.5 (8.7–13.9)[a]	12 (5–12)

[a] Smaller than CFV, p-value = 0.0185.
[b] Higher than "normal" foot venous pressure of 11 mmHg; see text.
[c] Data were obtained in the left lower limb.
N/A: not available; CIV: common iliac vein; EIV: external iliac vein; CFV: common femoral vein.

Techniques

Duplex technique: A color Duplex instrument (Logiq 9, GE Medical Systems, Waukesha, WI) was used. A 6 Hz curved probe and 9 Hz linear probe with 60° angle of insonation were used for the native and stented iliac-caval and femoral segments, respectively. B mode/B flow/Color flow images were used in combination to define vein lumen/flow channel and measure its

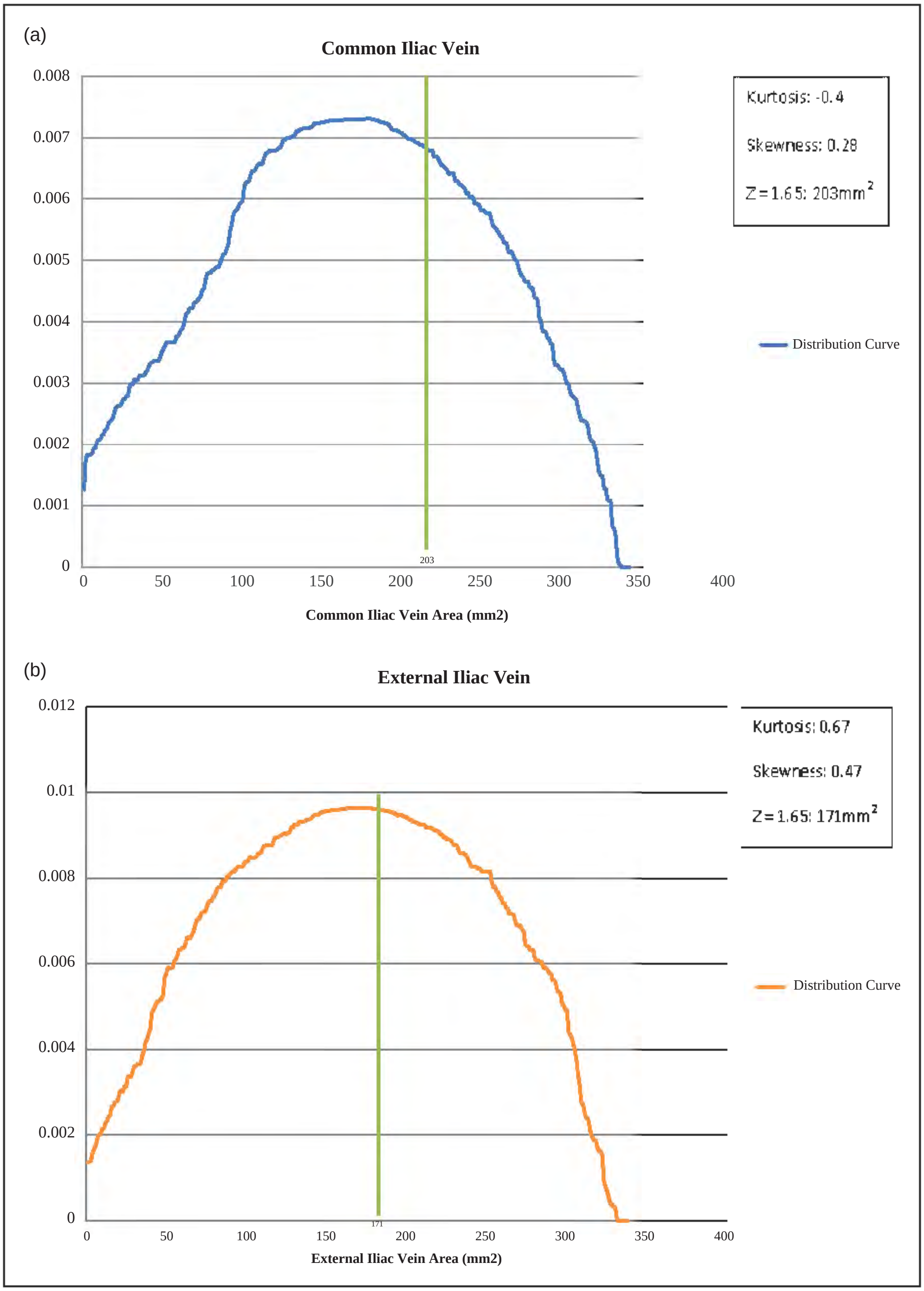

Figure 1. Distribution curve of common iliac (a), and external iliac (b), vein segments. The skewness (s) and kurtosis (k) are shown in the top right of the graph and the values are considered within an acceptable range. "Normal" values are (s) = −0.5 to 0.5; (k) −3 to 3, according to the National Institute of Standards and Technology (www.nist.gov).

diameter at its widest point. This was confirmed in transverse views when good quality images of adequate segment length were available.

IVUS examination: A 6 Fr coaxial system (Volcano, San Diego. CA) was used. The stenotic area was traced by electronic pen and the area was provided by system software.

Informed consent: All procedures in patients as well as healthy volunteers were performed with informed consent. Institutional review board (IRB) permission was obtained for volunteer participation, data collection from volunteers and patients, and their analysis for publication.

Statistics

Distribution curve of IVUS areas for the various segments were analyzed for skewness and kurtosis. A commercially available statistics program (Prism5.0, Mountainview, CA) was used.

Results

Iliac vein lumen area in normal volunteers

Duplex diameter measurements of supine peripheral venous pressure in normal volunteers in our laboratory are shown in Table 2. Many had stenosed common iliac vessels that were smaller than their respective EIV or CFV. The resting venous pressure was also elevated in many of these individuals. Normal supine foot venous pressure is ≤ 11 mmHg.[4,11–13] Silent iliac vein stenoses are known to occur in as many as 66% of the general population.[14] The data are therefore useless in gauging the "normal" caliber of the iliac vein to guide optimal stent size.

IVUS planimetry in patients

The CIV is about 2 cm in size on gross inspection during open vascular procedures. The EIV and CFV are a few mm smaller. The three vein segments (CIV, EIV, and CFV) frequently measure ≈16, 14, and 12 mm respectively on IVUS examination of segments free of disease.

IVUS area distribution curves of iliac femoral vein segments display a wide range (Figure 1(a) and (b)). The data points at the extreme (5%) right tail of the curve a (Z-score of > 1.65) are or should approach normal (nonstenotic) values per distribution theory. Respective Z line intersection (> 1.65) values for the vein segments are shown in Table 3. Normal lumen of the various segments is expected to be circular or nearly so with normal hydration.[15] Lumen diameters shown in Table 3 are derived values from the area, based on this assumption.

Table 3. Normal area (Z-score > 1.65) from IVUS distribution curves of various vein segments. The respective calculated diameters are also shown as Wallstents assume a circular shape at deployment.

Sample from each distribution curve with a Z-score > 1.65	*n*	Median (range) area (mm^2)	Median (range) diameter (mm)
CIV	16	220 (203–290)	17 (16–19)
EIV	21	183 (172–277)	15 (15–19)

CIV: common iliac vein; EIV: external iliac vein.

Poiseuille equation

The pressure gradient in stents of different caliber is shown in Table 4. Values are shown for flow at rest, during exercise (3× resting flow) and when the stent is involved in 50% diameter stenosis due to ISR/compression. The optimal size of the stent for the CIV appears to be ≈18 mmHg

Young's scaling rule

Diameters of EIV and CFV (two generations) can be projected from the CIV diameter estimated by the

Table 4. Pressure gradient in stents of different calibers at resting flow and exercise with and without 50% diameter stenosis due to ISR/compression.

	Pressure (dyne/cm^2)[a]			
Stent diameter (mm)	Resting flow	Exercise flow (3×), no stenosis	50% diameter stenosis, resting flow	50% diameter stenosis, exercise flow (3×)
8	302	907	4838	14,515
10	124	372	1982	5945
12	60	179	956	2867
14	32	97	516	1548
16	19	57	302	907
18	12	35	189	566
20	8	23	124	372
22	5	16	85	254

[a] 1 mmHg = 1333 dyne/cm^2.

Table 5. Diameter estimates of for the iliac-femoral vein segments derived from various methods.

Vein segment	From distribution curve of IVUS area in patients ($n = 346$)[a]	Poiseuille's law	Young's scaling law[b]
CIV	17	18	19
EIV	15	N/A	15
CFV	N/A	N/A	12[c]

[a] With a Z-score of greater than 1.65; see text.

[b] Scaling projections from IVUS data, Poiseueille calculations and Fronek's data. See text.

[c] Duplex CFV diameter in a large population study by Fronek; see text.

CIV = common iliac vein; EIV = external iliac vein; CFV = common femoral vein; N/A: not calculated because of lack of reliable flow estimates.

above two methods (IVUS distribution curve and Poiseuille law). The projected CFV diameter by the scaling law closely corresponds to actual femoral vein diameter (mean 11.8 mm) recorded by Fronek in a large ($n = 3539$ limbs) population study;[16] the estimated "normal" caliber of the three iliac-femoral vein segments derived from the various methodologies described above are closely similar as shown in Table 5. Table 6 shows our recommendation of the optimal size of stent to be used for the various segments. This is also the target size in reinterventions to correct ISR/stent compression.

Discussion

Optimal caliber of iliac-femoral outflow tract

Peripheral venous pressure is controlled by a set of central and peripheral factors. Central factors have been previously described.[1] The most important peripheral variable is vein caliber as conductance/resistance (hence pressure) is related to the *fourth power* of radius. Caliber of the iliac-femoral outflow is a key variable in the control of peripheral venous pressure because it is correctible while other variables such as compliance or inflow are not. The purpose of stent correction is to restore the lumen area to an optimal value that would provide maximal decongestion of the peripheral venous bed and lower peripheral venous pressure. The optimal outflow caliber should match rate of inflow to maintain stable peripheral venous pressure. This is best understood using as an example the open channel flow of a river dam as shown in Figure 2. Water level height/depth (h) in open channel flow is the analogue of pressure (P) in conduit flows.[17] Reservoir depth (i.e. venous pressure) will be stable at the desired normal level when outflow through sluice gates equals inflow. When outflow is less, depth/pressure rises and overflow over the dam spillway (collaterals) occurs. The reservoir analogy also helps explain another nonintuitive feature of venous flow. Arterial inflow, like river flow, is unaffected by chronic venous obstruction (i.e. the dam). Arterial inflow remains the same after stent correction of the chronic obstruction as would be the case with river flow if the dam were to be removed.[1]

Table 6. Recommended stent diameter and post-stent IVUS area for different vein segments.

Vessel segment	Diameter	Area
CIV	16–18 mm	200–254 mm[a]
EIV	14 mm	150 mm^2
CFV	12 mm	110 mm^2

[a] The ideal diameter/area of 18 mm/254 mm^2 may not be achievable in post-thrombotic cases due to tough fibrotic band underneath the artery. Post stent area of 200 mm^2 is achievable in most.

CIV = common iliac vein; EIV = external iliac vein; CFV = common femoral vein.

The estimations from Poiseuille law provided herein are derived from generic inflow data. More precise individualized estimations may be possible if common iliac arterial flow can be determined with accuracy. Noninvasive technology to do this is not available yet.

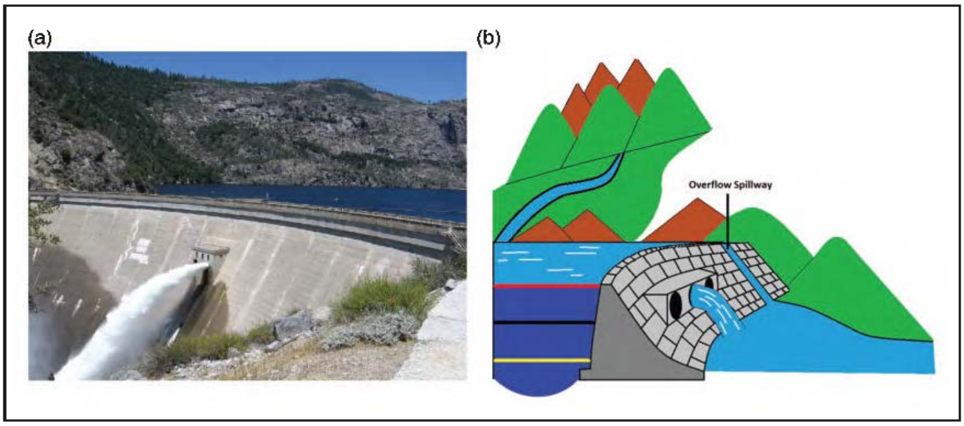

Figure 2. (a) O'Shaughnessy Dam in Yosemite National Park, California, reproduced under the following creative commons license: https://creativecommons.org/licenses/by-sa/3.0/.[19] It impounds Tuolumne River, forming the Hetch Hetchy Reservoir. The reservoir is the source of water and power to the San Francisco Bay area. The Reservoir level can be varied according to water or power demand by adjusting the number of sluice gates that are opened. (b) If the outflow exactly equals inflow from the Tuolumne River, the reservoir level will be stable (Black line). Overflow spillway (collateral flow) to the right is used during flood season when water level is the highest (red line) because outflow is less than inflow even with all sluice gates open. During summer season when demand is at its peak, water level may be lowered (yellow line) by temporarily increasing outflow over supply from the river. Changes in the level in the reservoir will not significantly affect existing river flow into the reservoir as the headwaters are in the Sierra Nevada Mountains several thousand feet above the reservoir level. Venous flow and collateralization work in similar ways in case of obstruction. See text.

Undersizing a stent is more harmful than slight oversizing. Undersizing the iliac vein stent is a cause of permanent iatrogenic stenosis that is not easily corrected. This frequently occurs from the mistaken belief that restoration of perfusion and patency is the primary goal as in arterial stent practice. Adequate stented caliber is essential for relief of venous hypertension.

Practical considerations

Since iliac venous outflow has an ''optimal'' caliber, grading the severity of stenosis should be based on this optimal caliber rather than adjacent or contralateral lumen as comparators. The latter method may result in underestimation of the stenosis particularly when long diffuse lesions (Rokitanski stenosis) is present.[15] Elevated peripheral venous pressure from causes other than outflow stenosis (e.g. congestive failure, A-V fistula) will have a normal outflow caliber on IVUS examination.

We oversize the stent by 2 mm beyond recommended caliber but post dilatation is restricted to the optimum outflow caliber for the segment. This allows for later aggressive dilatation during re-interventional correction when necessary.

Stent function is open to decay by development of instent restenosis (ISR). Up to 25% reduction in flow channel diameter is common.[18] Stent compression from outside by development of recurrent stenosis in the native vein also occurs.[15]

Conclusion

The ''normal'' caliber of the iliac outflow tract is not easily determinable by direct measurement. A variety of indirect methods have been used to arrive at estimation. The optimal recommended caliber is the target to restore diseased lumen during initial stent placement and also at reinterventions.

Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: Stock and Royalty, Veniti Inc. US Patent, IVUS diagnostics. US Patent, Iliac vein stent design.

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Ethical approval

Informed Consent: All procedures in patients as well as healthy volunteers were performed with informed consent. Institutional review board (IRB) permission was obtained for volunteer participation, data collection from volunteers and patients, and their analysis for publication.

Guarantor

Seshadri Raju

Contributorship

SR: Conception, data collection and analysis, statistics, manuscript writing, and overall responsibility; WB and WC: Data collection and analysis, statistics, and manuscript writing; AJ: Data collection, writing manuscript.

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