

# Factors influencing peripheral venous pressure in an experimental model

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## ABSTRACT

**Background:** Peripheral venous hypertension and microvascular injury have merged as central features of chronic venous disease. Peripheral venous pressure in the lower limb is controlled by central and peripheral mechanisms. In the current manuscript, we examine the role of peripheral factors, particularly conduit capacitance compliance, focal stenosis, and arterial inflow into the calf.

**Methods:** An experimental venous model using Penrose tubing as a venous analogue was used where the aforementioned parameters could be manipulated. Volume-pressure curves were derived in the static mode. The dynamic model attempted to simulate key pressure parameters of lower limb venous flow.

**Results:** Decreasing compliance resulted in progressive reduction of conduit capacitance affecting both bending and stretching regimens and the relative distribution between the two, rotating the volume-pressure curve toward the x-axis. Increased postcapillary (arterial) inflow increased conduit pressure. For a given inflow, pressures varied inversely to conduit caliber. Decreased compliance led to a smaller functional caliber at working pressures. Sideline capacitance with stagnant flow connected to the flow channel (simulating calf vein network) did not influence conduit pressure. Focal stenosis increased “venous pressure” if it was narrower than “optimum outflow caliber,” defined as the minimum outflow conduit caliber required to balance inflow. Percentage stenosis as traditionally calculated using adjacent lumen as denominator was uncorrelated to pressure increase.

**Conclusions:** Conduit pressure is increased with smaller native or functional (poor compliance) caliber, focal stenosis, and increased postcapillary inflow. Many of these features appear to be present in limbs clinically suspected of chronic venous disease. The importance of the geometric factor of Poiseuille equation in pressure effects of caliber reduction and collateralization is discussed. (J Vasc Surg: Venous and Lym Dis 2017;5:864-74.)

Peripheral venous hypertension has emerged as a main instigator of microvascular injury and chronic venous disease.<sup>1</sup> In a previous publication, we showed that a set of central mechanisms extrinsic to the peripheral venous bed influences venous pressure in the lower limb.<sup>2,3</sup>

In this manuscript, we aim to examine the role of intrinsic properties of the peripheral venous bed in the control of peripheral venous pressure, specifically the pressure effects of capacitance and compliance changes and their interaction with focal stenosis. An experimental model whereby these parameters can be manipulated is used. Based on the experimental findings, the concept of “optimal” outflow caliber is advanced. Conduit caliber appears to be a major factor in pressure control. Clinical implications of the geometric factor in the Poiseuille equation related to caliber are discussed.

## METHODS

**Experimental model.** Penrose tubing was used as the experimental analogue for veins. Compliance characteristics of this material at physiologic pressure ranges have been shown to be nearly identical to biologic veins except near the lower end of the volume-pressure curve (V-P curve). The Penrose tube tends to collapse into dumbbell-shaped geometry in cross section, whereas the vein maintains a cylindrical shape to total collapse.<sup>4</sup>

**Terminology.** When the Penrose tube is full without stretching the wall, its caliber is referred to as unstretched or native caliber; when the wall is stretched, the resulting caliber is referred to as stretched caliber. The caliber at a specified internal pressure is referred to as functional caliber with the pressure specified. Physiologic terms are often interchangeably used with model features for ease of description.

A static model and a dynamic model with flow were used (Fig 1). A 2:3 mixture of glycerin and water was used with viscosity similar to blood. Rheologic effects apparent in non-newtonian microvascular flows are negligible in large (>0.5 mm) conduit flows as used in the model (ie, viscosity is independent of velocity).<sup>5,6</sup>

In the dynamic model, flow occurred from a header tank through polyethylene tubing (inner diameter [ID],  $\frac{1}{8}$  to 1 inch to vary inflow rate) into the Penrose tubing setup (“venous bed”). Penrose tubing 45 cm in length was horizontally mounted between large nonrestrictive

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Author conflict of interest: S.R. holds a U.S. patent regarding intravascular ultrasound diagnostics in chronic venous disease and has stock in Veniti.

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connectors at either end. Capacitance of the venous bed was varied by using different caliber Penrose tubing (ID,  $\frac{3}{8}$  to 1 inch). Compliance of the Penrose tubing was varied by additional layers (single layer to five ply). Input pressure from the header tank was held constant by continuous replenishment at 24 mm Hg, resembling mean capillary pressure. Discharge was to the atmosphere (0 mm Hg, similar to right atrial pressure) through the end of the Penrose tube. Pressure within the Penrose tubing setup was monitored by an electronic transducer (Sper Scientific, Scottsdale, Ariz) positioned 8 cm into the Penrose tube at the inflow end. The basic dynamic model was slightly modified in some experiments, which are described in context.

There is no provision in the model to simulate reflux or calf pump function. Experiments are solely focused on the hemodynamics of obstruction. Patient consent and Institutional Review Board permission were not obtained as no human data are included.

**Statistics.** A Student two-tailed unpaired *t*-test ( $\alpha = .05$ ) was used to analyze categorical variables. All analyses were performed with commercial software (Prism Corporation, Irvine, Calif).

## RESULTS

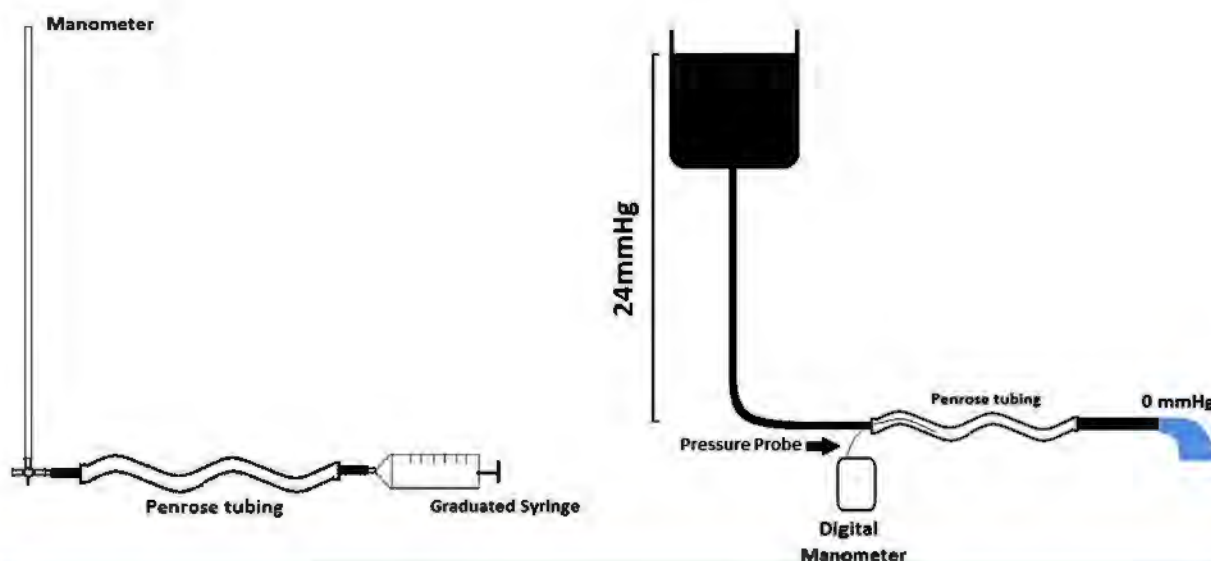
### Experimental model

**Conduit compliance.** Static V-P curves of different caliber Penrose tubes ( $\frac{1}{8}$  to  $\frac{3}{4}$  inch) were qualitatively similar; curves obtained with single-ply, two-ply, three-ply, four-ply, and five-ply  $\frac{3}{8}$ -inch Penrose conduits

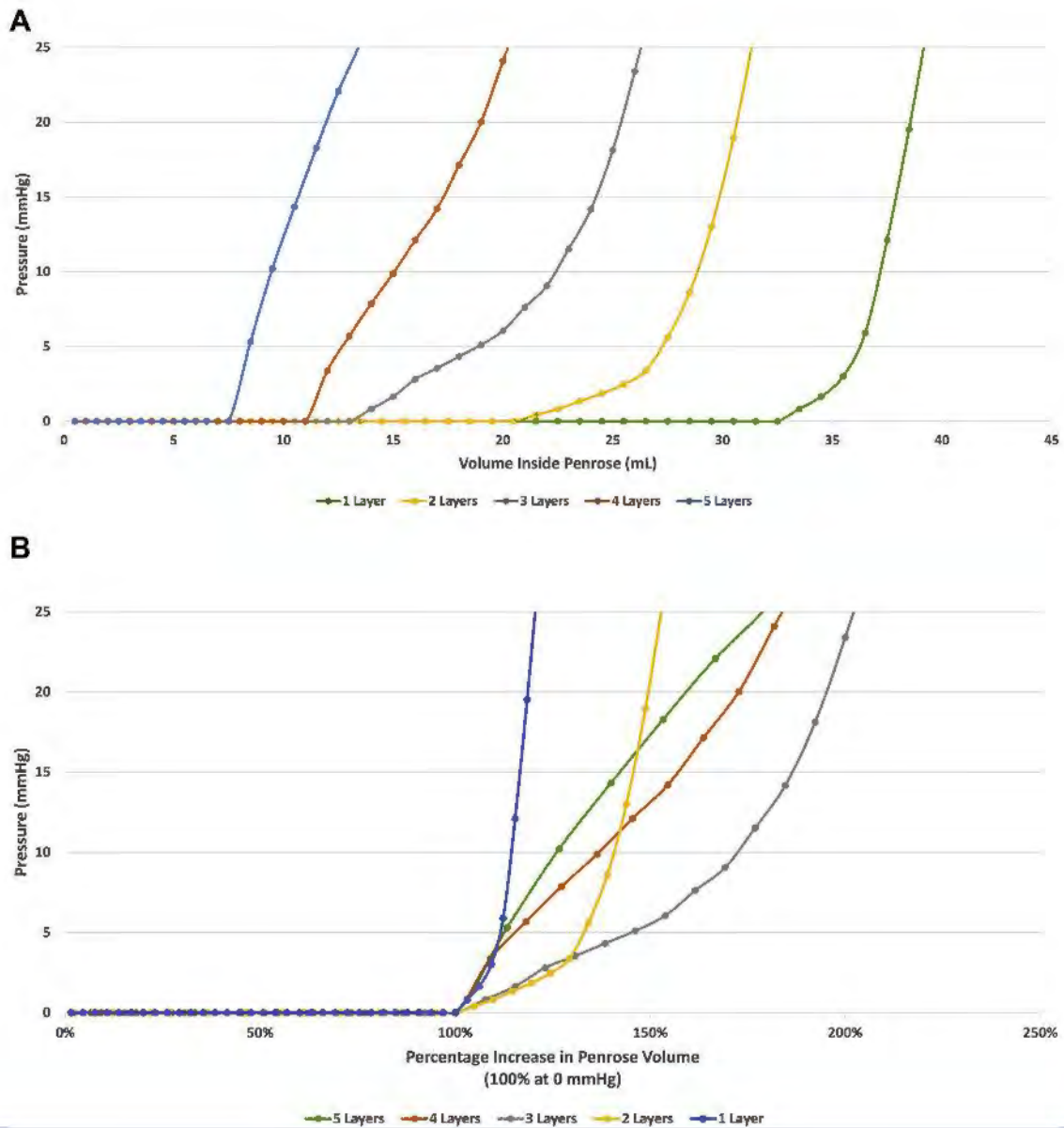
### ARTICLE HIGHLIGHTS

- **Type of Research:** Ex vivo experimental model using Penrose tubing as a venous analogue
- **Take Home Message:** In this model, conduit pressure increased with smaller native or functional (poor compliance) caliber, focal stenosis, and increased postcapillary inflow.
- **Recommendation:** The authors suggest that traditional calculation of vessel stenosis alone is not satisfactory to determine the functional effects of a venous stenosis in patients with chronic venous insufficiency.

are shown in Fig 2. The curves have a horizontal and a slanted vertical component. The initial horizontal component represents filling of the Penrose tube without an increase in the perimeter (bending regimen). The vertical component represents additional filling by wall stretch (stretching regimen). Substantial reduction in total conduit volume occurs with increasing wall (one ply to five ply) thickness (Fig 2, A). For example, the single-ply Penrose tube exhibits a conduit volume of  $\approx 32$  mL in the bending regimen and an additional  $\approx 8$  mL in the stretching regimen for an 80%/20% split. The corresponding figures for the four-ply Penrose tube are  $\approx 12$  mL and 10 mL for nearly a 50%/50% split distribution. With increasing wall thickness, the volume ratio between the bending regimen and the stretching regimen changes as shown in Table I. Fig 2, B shows



**Fig 1.** Static and dynamic experimental models. In the static model (*left*), pressure inside the Penrose tube was monitored when it was inflated with saline from a graduated syringe through a three-way stopcock and attached water manometer. In the dynamic model (*right*), flow from a header tank at constant pressure flowed through the Penrose tube to an open end. The input and output pressures were 24 mm Hg and 0 mm Hg, resembling mean capillary and right atrial pressures, respectively. Volumetric flow through the Penrose tube could be varied by varying the caliber of the tube connecting the header tank to the Penrose tube. See text.



**Fig 2. A and B,** Volume-pressure (V-P) curves obtained with the static model. Absolute volumes in milliliters are plotted on the x-axis in **(A)**. The horizontal portion of the nonlinear curve represents the bending regimen and the vertical portion the stretching regimen. Note the decline in total volume of the curve as wall thickness (ply) increases and the compliance decreases. **B,** Relative volume distribution between the bending and stretching regimens. Full unstretched volume is 100%. The capacitance of the stretching regimen declines in relative percentage as compliance decreases with increasing wall thickness. Note the curve in the stretching regimen as three-ply, four-ply, and five-ply Penrose tubes become flatter, rotating toward the x-axis. See text.

V-P curves plotted in terms of relative volume change (unstretched volume = 100%). The upper part of the V-P curve (stretched component) progressively rotates (particularly evident in three-ply, four-ply, and five-ply conduits) toward the x-axis, becoming flatter. Each ply adds only 5 mL of physical wall thickness volume per 25-cm length of Penrose tube (0.2 mL/cm) as determined by water displacement in a graduated jar. Thus, the reduction in conduit caliber is less from physical

mass but mostly due to reduced functional caliber at a given pressure. The caliber of a 1-cm circular conduit calculated from static V-P data (Fig 2, A) for various wall thicknesses is shown in Fig 3. A change in caliber has an exponential effect on conductance (hence pressure); conductance is  $\propto r^4$  (the geometric factor) per the Poiseuille equation. The respective values of the geometric factor are also shown in Fig 3 for various functional calibers in physiologic pressure ranges.

**Table I.** The effect of compliance on conduit volume (mL)

Penrose tube wall thickness	Bending regimen volume <sup>a</sup>	Stretching regimen volume at 20 mm Hg <sup>b</sup>	Total conduit volume	Ratio bending/stretching
Single ply	32	7	39	5:1
Two ply	21	9	30	2:1
Three ply	13	12	25	1:1
Four ply	11	8	19	1:1

<sup>a</sup>Unstretched volume.  
<sup>b</sup>Stretched volume.

**Dynamic pressures**

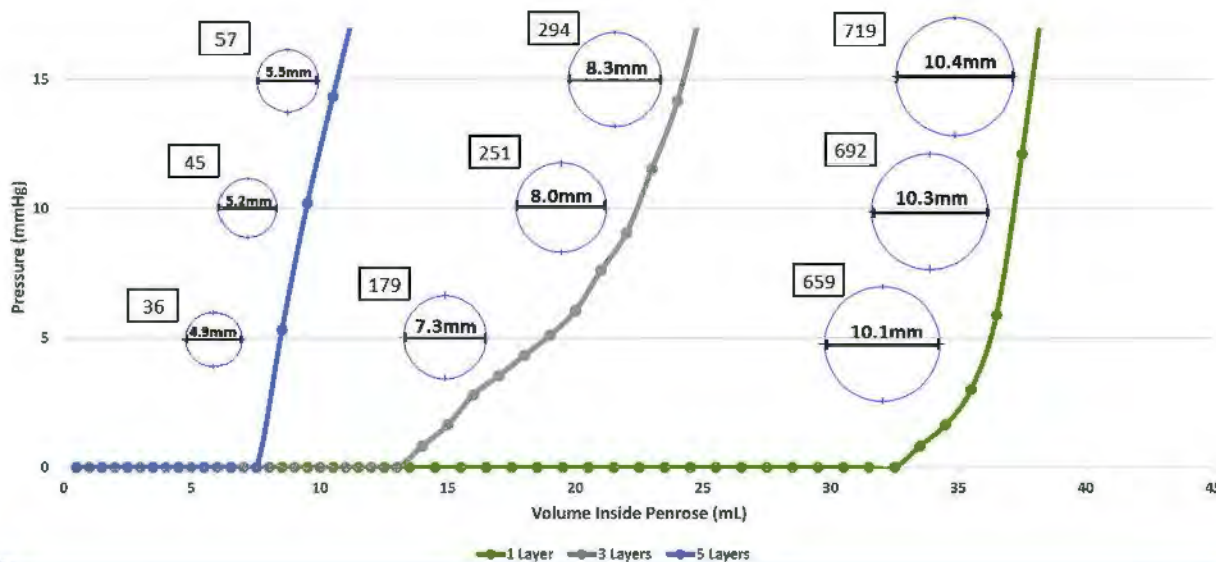
**Effect of postcapillary inflow and native caliber.** The inflow line connecting the header tank (at 24 mm Hg) to the Penrose tube was varied from 1/8- to 1-inch ID, which varied inflow into the Penrose tube. The pressure varies directly with inflow and inversely with Penrose tube native caliber (Fig 4).

**Effect of sideline capacitance.** Two Penrose tubes, each with one end tied off, were connected to the main Penrose tube, with flow through a T connector adding sideline capacitance but without active flow (Fig 5). The arrangement mimics axial flow in the tibial veins connected to the relatively stagnant large network of nonaxial calf veins. The additional stagnant capacitance does not significantly modify the pressure (Table II) per Pascal law.

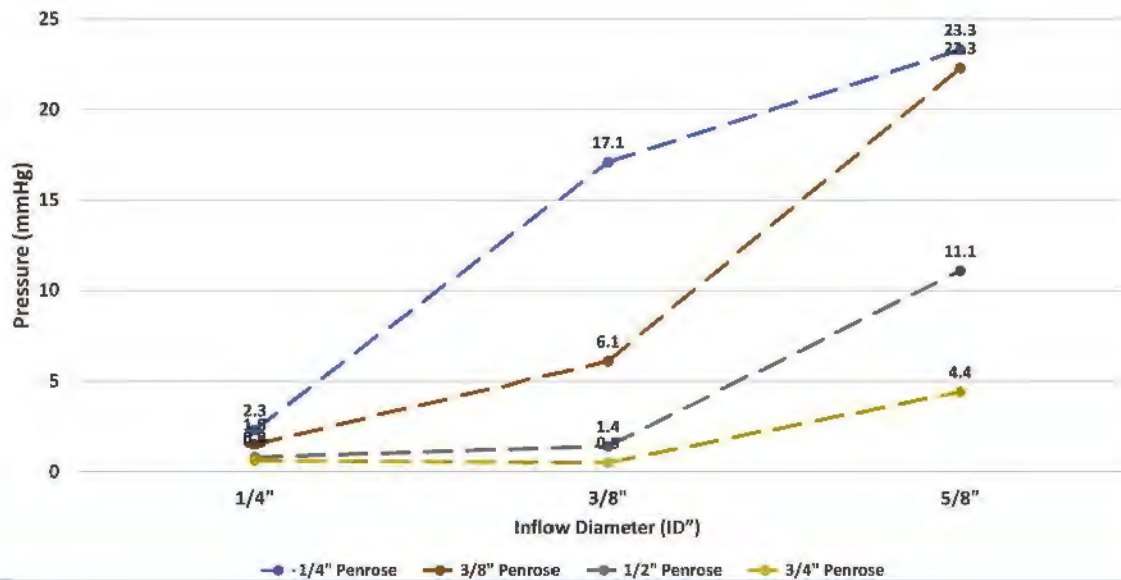
**Influence of native conduit caliber and focal stenosis.** Single-ply Penrose tubes of 1/4 to 3/4 inch were used in this modified dynamic model (Fig 6). Short rigid

plastic end pieces (1/8- to 5/8-inch ID) were connected to the outflow end of the Penrose tube to create focal stenosis at the end.

The 3/8-inch Penrose tube can be considered the optimum outflow caliber as it exactly balances inflow from the 3/8-inch inflow tube. The pressure inside the 3/8-inch Penrose tube is used as the reference pressure. Pressures were higher or lower in Penrose tubes of smaller or larger calibers, respectively. The 3/8-inch optimum caliber acts as a threshold for focal stenosis created by end pieces of known ID. Pressures rose if the focal stenosis narrowed the lumen further beyond the threshold (red arrow). The one exception is the 1/4-inch Penrose tube with already high pressures as its caliber was narrower than the optimum threshold of 3/8 inch. Pressure in it rose further when focal stenosis of 1/8 inch narrowed the lumen even more (blue arrow). Thus, the optimum caliber is the threshold for calculating conduit or focal stenosis. Pressure increase was not as well correlated to



**Fig 3.** Compliance and functional conduit caliber. Functional caliber in 3/8-inch Penrose tube with increasing wall thickness (one, three, and five ply) at various physiologic pressure ranges (y-axis). The caliber (diameter in millimeters) is derived from static volume-pressure (V-P) curves converting absolute volume (45-cm length) at corresponding pressure into volume of a 1-cm-long cylinder. Corresponding geometric factor (r<sup>4</sup>) in arbitrary units derived from diameter is shown in a box above the caliber circles. With decreasing compliance, functional caliber becomes smaller. Note that relative change in caliber has a much larger effect on conductance. Functional caliber for five ply is roughly half that for single ply, yet the geometric factor is 10 to 20 times smaller. See text.



**Fig 4.** Postcapillary inflow and venous pressure. Conduit pressure in Penrose tubes of varying caliber (color-coded dashed lines) shown with inflow tubing of different calibers (shown below x-axis) connected to the header tank. Pressure varies directly with inflow and inversely with Penrose tube caliber. ID, Inner diameter.

percentage stenosis calculated using adjacent native caliber of the Penrose tube as denominator.

**Effect of poor compliance and focal stenosis.** Pressure rises stepwise in the dynamic model (Fig 7) when Penrose tube wall thickness is increased (one to five ply). The mechanism is reduced functional caliber; decreased compliance results in a smaller functional caliber and increased pressure as shown in Fig 3. The pressures in multiple-ply Penrose tubes are higher than in corresponding single-ply Penrose tubes shown in Fig 6. Interaction with additional focal stenosis is similar as well with a  $\frac{3}{8}$ -inch threshold.

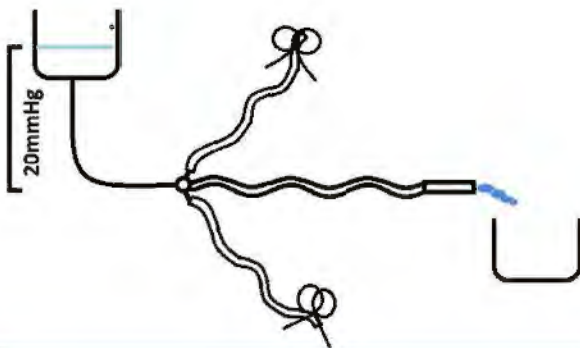
## DISCUSSION

The experimental model findings explain the relationship between conduit caliber and pressure in chronic venous disease limbs. In the erect position, a large gravity component is added to the foot venous pressure, and

the arterial inflow is variably reduced by about 50% (venoarterial reflux).<sup>7</sup> Complex modeling is required for simulation of the calf pump and reflux, which is not attempted here.

**Homeostasis of peripheral venous pressure.** Supine peripheral venous pressure is  $\leq 11$  mm Hg and has two components: (1) a static component related to venous fill, often referred to as "dead man" pressure, which is  $\approx 7$  mm Hg; and (2) an additional dynamic component generated by flow from heart action.<sup>8-10</sup> Venous pressure is further modulated by a set of central and peripheral mechanisms summarized in Table III.

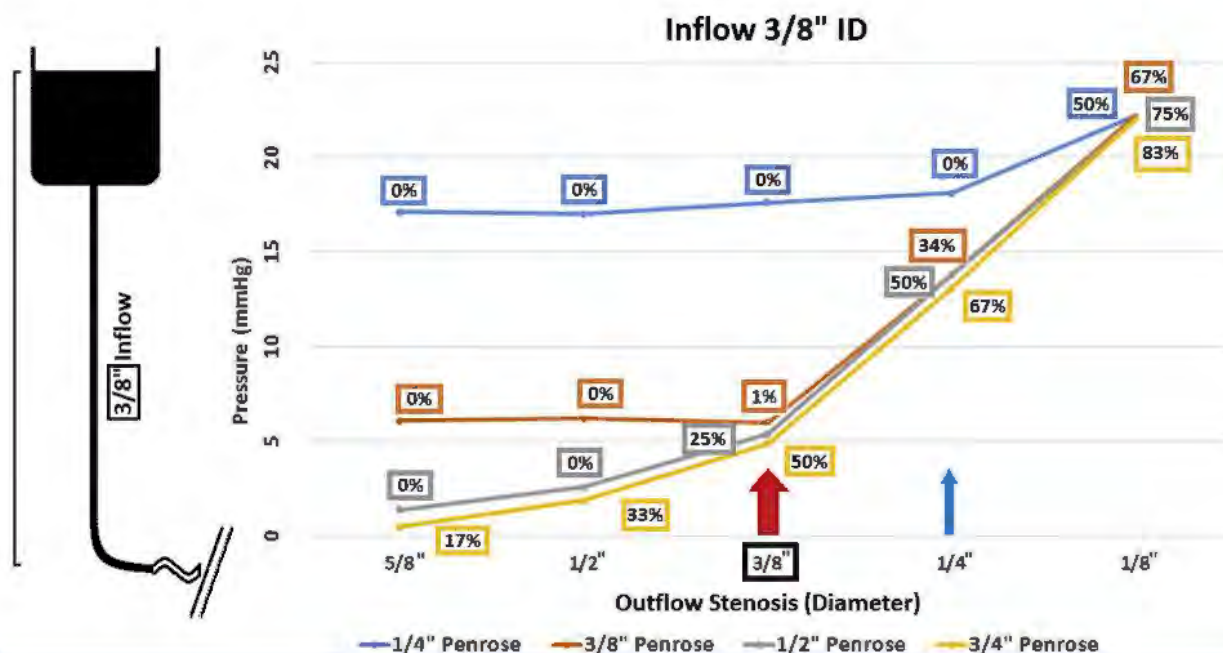
Normal venous pressure is 4 to 6 mm Hg higher than right atrial pressure, which is normally  $\approx 0$  mm Hg.<sup>9</sup> The actual supine or ambulatory pressure threshold that causes or potentiates microcirculatory damage is not known. If the normally profuse venous outflow is substantially reduced or occluded as in common iliac vein thrombosis or phlegmasia cerulea dolens, respectively, there is stagnation of venous flow, and the venous pressure will passively begin to reflect arterial upstream pressure like a closed tube connected to it.<sup>11,12</sup> This is similar to the principle underlying "wedge pressure."



**Fig 5.** Model of sideline capacitance. Capacitance is tripled by adding two additional Penrose tube side arms to the flow channel. The side arms are connected but have stagnant flow.

**Table II.** Effect of sideline capacitance on pressure

Penrose tube wall thickness	Pressure with sideline capacitance, mm Hg	Pressure without sideline capacitance, mm Hg
Single ply	3	2.6
Two ply	4.8	3.9
Three ply	5.2	5.9
Four ply	10	10.8



**Fig 6.** Effect of conduit caliber and focal stenosis on venous pressure. Pressures in single-ply Penrose tubes of various unstretched calibers (color key) are shown. Inflow was provided by a connector tube of 3/8-inch inner diameter (ID) for all of the Penrose tubes. Outflow stenosis created by end pieces of known calibers are shown below the x-axis. Discrete pressure measurements recorded in the various Penrose tubes are plotted above corresponding end stenoses. The 3/8-inch Penrose tube (red) represents optimum outflow caliber as it exactly balances inflow through the connector from the header tank, which is also 3/8-inch ID. Pressure in the 3/8-inch Penrose tube (red) is used as the reference pressure for comparisons. Pressures in Penrose tubes larger than 3/8-inch caliber (yellow and gray) are lower. Pressures rise when end stenosis exceeds optimum caliber of 3/8 inch. The 1/4-inch Penrose tube (blue) is narrower than the optimum outflow caliber, and the pressure remains higher than the reference pressure throughout until an end stenosis of 1/8 inch further narrows the flow channel; additional pressure rise is seen at this point (blue arrow). Percentage stenosis relative to the adjacent Penrose tube caliber (colored squares) has poor correlation to the pressure. This is particularly evident in the 3/4-inch (yellow) and 1/4-inch (blue) Penrose tubes. A better correlation is seen when optimum caliber (3/8 inch) is used as a threshold (red arrow). See also Fig 8.

In the experimental model, conduit pressure can never rise above input reservoir pressure of 24 mm Hg as only postcapillary circulation is simulated—the arterial side is not part of the system.

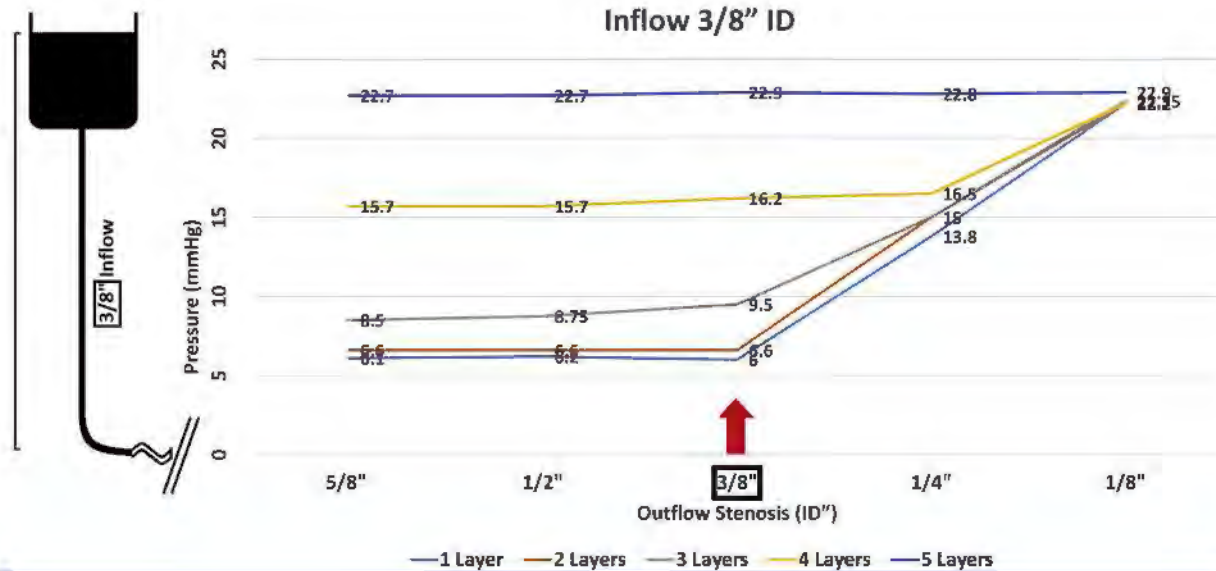
**Peripheral mechanism of venous pressure control.** The primary peripheral mechanism of pressure control is the caliber (and stenoses) of the venous flow channel. The experiments described show that a reduction in capacitance or compliance of the axial flow channel results in a smaller caliber, and a smaller caliber raises venous pressure. All of these elements are commonly present in post-thrombotic limbs; organized thrombus occupying the lumen may further decrease physical luminal caliber.

Regardless, caliber reduction can be viewed as a long stenosis. When diffuse stenosis and focal stenosis occur in combination, the higher of the two in terms of resistance will set the pressure as shown in Figs 6 and 7. When such clinical combination occurs in post-thrombotic disease, correction of the focal stenosis may not yield complete relief.<sup>13</sup>

**Venous caliber and the geometric component of Poiseuille equation.** The Poiseuille law in expanded form is written  $F = \pi/8 \times 1/\eta \times r^4/l$ , composed of numeric, viscosity, and geometric factors, respectively.<sup>5</sup> In this presentation, we simply use  $r^4$  for the geometric factor, omitting  $l$  as its value is unity for caliber comparisons. Because the geometric factor enters the equation in the fourth power, the magnitude of effects related to caliber (and therefore pressure) can be surprising. This is illustrated in three relevant situations (Fig 8) in venous flow: (1) caliber upsizing at venous confluences, (2) collateralization, and (3) focal stenosis.

There has been very little work on dimensions of the venous tree using modern morphometric techniques. Many questions, such as variations with sex or body mass differences, are unknown.

**Optimal venous caliber.** There is an optimal caliber for the axial outflow at each anatomic level to match arterial inflow to keep venous pressure stable. This is best illustrated by using the example of a storage reservoir fed



**Fig 7.** Compliance and focal stenosis. Venous pressure (y-axis) in 3/8-inch Penrose tube (one to five ply, color key) is shown with plastic end stenosis of varying calibers. Inflow was provided by a connector tube of 3/8-inch inner diameter (ID) for all. The curves reflect smaller functional caliber with decreasing compliance and are qualitatively similar to those in Fig 6 showing pressure effects in Penrose tubes of different native calibers. A pressure increase is noted in one-, two-, and three-ply Penrose tubes when end stenosis exceeds the 3/8-inch optimum threshold (red arrow). Pressure in the four-ply (yellow) is already high, but a further pressure increase is seen with an end stenosis of 1/4-inch ID end piece. With a five-ply 1/8-inch Penrose tube, the basal pressure is nearly the highest possible in the system (24 mm Hg) that an additional focal end stenosis up to 1/8-inch ID has no apparent additional effect on pressure. Penrose tubes of small native or functional caliber are analogous to long diffuse stenosis. The effect of additional focal stenosis in tandem will depend on which is narrower. See text.

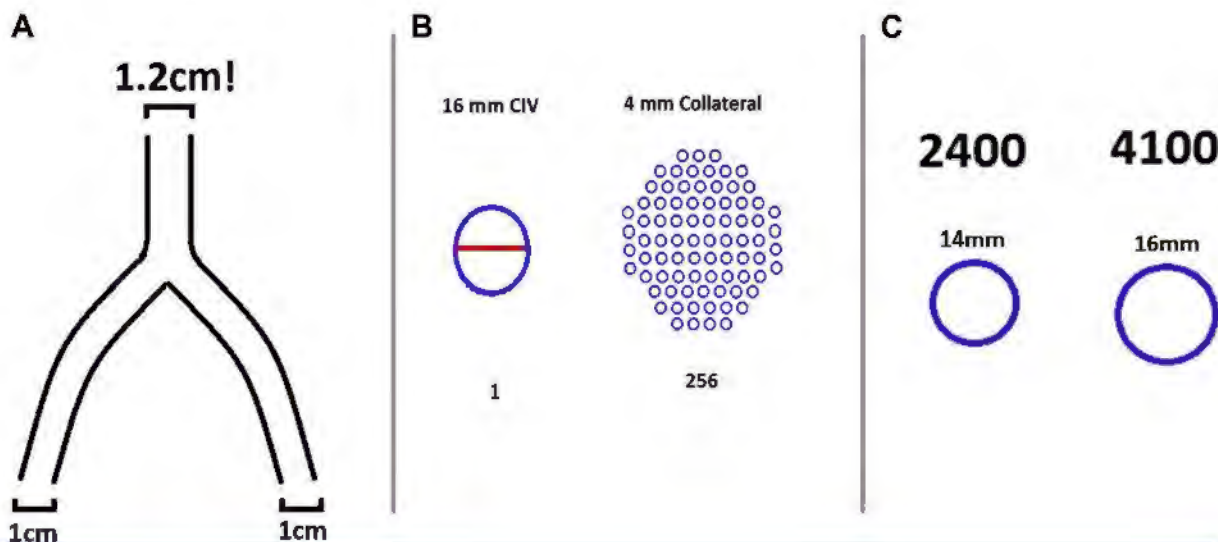
by a river (Fig 9). Water depth in the reservoir is the open channel analogue of pressure in conduit flows.<sup>14</sup> The water level will be stable if the outflow caliber equals inflow, but it will rise or fall if outflow is larger or smaller, respectively. Elements of this concept can be seen in experimental results shown in Figs 6 and 7. We suggest that percentage venous stenosis should be calculated on the basis of optimal caliber rather than adjacent "normal" caliber as is the current practice. The latter method will

underestimate lesions associated with long diffuse lesions that are not uncommon in the iliac veins.<sup>15</sup> Optimal caliber of iliac veins can be calculated from generic common iliac flow data, which is a fixed fraction of cardiac index.<sup>16</sup> More precise individualized data await more precise measurement of common iliac flow than is currently available. The potential for adequate collateralization to normalize conductance varies according to functional anatomy.

**Table III.** Control of peripheral venous pressure<sup>a</sup>

Central mechanisms		Clinical analogue or comment
Increased arterial inflow into the limb		Arteriovenous fistula
Elevated right atrial pressure		Congestive heart failure
Increased intra-abdominal pressure		Morbid obesity
Iliac vein stenosis		May-Thurner syndrome
Peripheral mechanisms		
Decreased native unstretched caliber	Maldevelopment; insufficient upscaling at venous confluence	
Decreased compliance	Decreased compliance reduces functional caliber. Organized thrombus can reduce luminal caliber.	
Focal stenosis	Nearly two-thirds of the general population will have silent iliac vein stenosis.	
Venous tone	Quantitative caliber effect of venous tone is unknown.	
Postcapillary inflow	Rate of arterial inflow into the calf is increased in chronic venous disease limbs.	

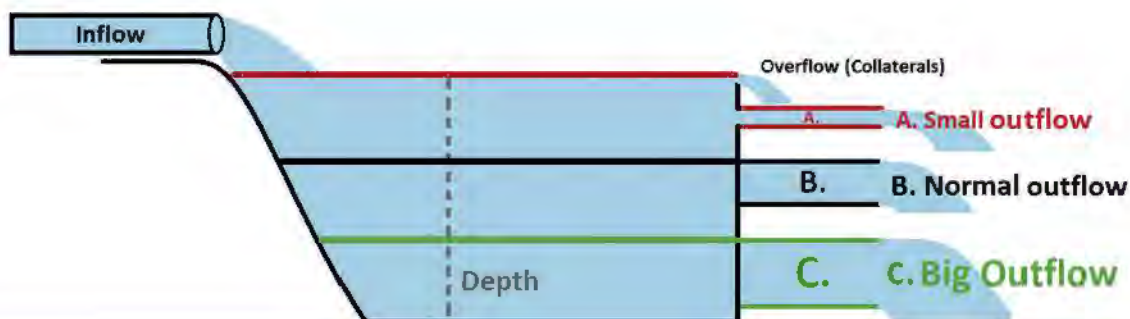
<sup>a</sup>See text.



**Fig 8. A,** Upsizing at venous confluences. Consider a venous confluence where two tributaries, each 1 cm in diameter and of equal volumetric flow, coalesce into a larger trunk. Surprisingly, the trunk needs to be only 20% larger (1.2 cm) than a *single* tributary to accommodate both tributary flows without raising pressure. By calculation, the geometric factor ( $r^4$ ) of the trunk equals twice the  $r^4$  value of each tributary. This is because a small increase in base  $r$  results in a very large product for the fourth power of  $r$ . It is easy to see how small defects in needed caliber upscaling at confluences due to maldevelopment or disease can result in elevation of venous pressure. **B,** Geometric factor in collateralization. The power of the geometric factor works in reverse in collateralization. An occluded common iliac vein (CIV) 16 mm in diameter will require 256 pelvic collaterals one-fourth the size (4 mm) each to equal the conductance of the occluded trunk. Caliber of individual collaterals is more powerful than their number to preserve conductance. **C,** Stenosis and conductance. Consider a common iliac vein stenosis that is seemingly “minor”: the stenosis measures 14 mm in diameter, a mere 2-mm diameter reduction from the norm of 16 mm (13% diameter stenosis). Yet the geometric factor ( $r^4$ ) is nearly half (2400) compared with normal caliber (5100). Without collateral compensation, backpressure will nearly double with this minor stenosis. Flow will also roughly halve if the pressure gradient remains the same. There is potential to increase the venous gradient up to a limit, perhaps doubling, which can maintain flow. Any further increase in stenosis will require collateral compensation to maintain flow.

**Functional anatomy.** In the calf, the superficial veins (great and small saphenous veins), deep axial veins (three pairs of tibial veins accompanying named tibial arteries), muscular veins, and sinusoidal and perforator veins form

a dense interconnected network open to easy pressure-neutral collateralization (Fig 10).<sup>17,18</sup> Isolated acute or chronic tibial vein occlusions rarely exhibit symptoms of elevated venous pressure. There is abrupt coalescence of



**Fig 9.** Optimal outflow caliber. Outflow channel will have to have adequate caliber to maintain pressure equilibrium in the limb. A storage reservoir fed by a river is shown. Reservoir depth is the analogue of venous pressure in conduit flows. The pressure will rise or fall if the outflow conduit is narrower or larger than optimum. When the outflow is narrow, the increased pressure will open up dormant collateral channels, shown here as overflow over the dam. In anatomic territories where volumetric outflow is known (eg, common iliac vein), the optimal caliber can be calculated from flow equations. Percentage stenosis calculated relative to the projected optimal outflow will be more reflective of pressure increase than relative stenosis based on adjacent vein caliber. See text.





**Fig 10.** Coalescence of calf vessels. The named and unnamed veins in the calf form a functionally single network with free to and fro flow. Conductance-neutral collateralization is possible in this setting because of alternative flow pathways of similar caliber. Pressure-neutral collateralization becomes more difficult higher up when the calf network abruptly coalesces into the much larger popliteal trunk (*arrow*). See text.

the calf network of 2- to 3-mm-caliber vessels into the larger femoropopliteal trunk at the popliteal fossa. This means conductance-neutral collateral compensation becomes increasingly difficult from here on up.

**Axial caliber and collateralization.** Recruitment and enlargement of collaterals are generally more rapid after acute venous occlusions compared with arterial occlusions.<sup>10</sup> Venous pressures are higher when larger caliber veins occlude. Venous pressures of up to 18, 51, and 83 mm Hg have been recorded in acute thrombosis of popliteal, femoral, and iliac vein thromboses, respectively.<sup>11</sup>

The increased pressure opens up higher resistance preformed venous channels where there was little or stagnant flow previously. The recruitment of additional flow channels and their subsequent rapid enlargement brings the peripheral pressure to nearly normal levels.<sup>10</sup> When there is occlusion of a femoropopliteal segment, collateral replacement by smaller caliber collaterals

alone is likely to be inadequate as shown in Fig 8, B. A special collateral mechanism in the thigh is axial transformation of the profunda femoris vein, which has an embryologic basis (Fig 11).<sup>19</sup> Acute symptoms of femoral vein occlusion usually regress in most individuals by 1 year unless the profunda femoris is also involved in the thrombotic process.

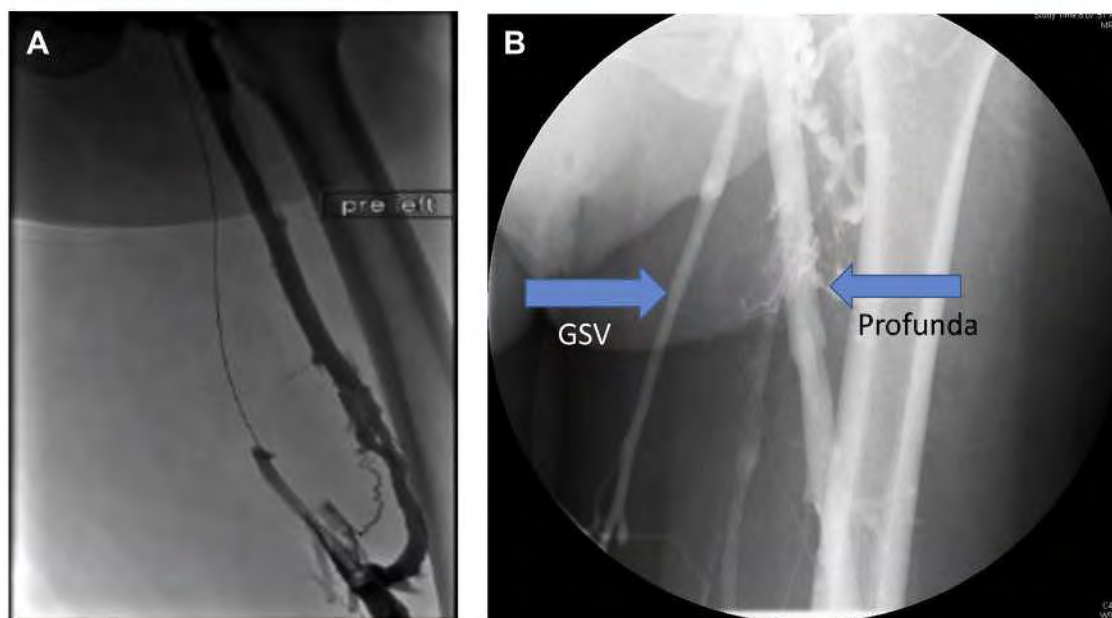
The great saphenous vein is a potential collateral in femoropopliteal venous occlusions but is often inadequate (Fig 11, B).<sup>20</sup> About half the size of the femoral vein, roughly 16 saphenous size collaterals will be required to equal the occluded femoral vein in conductance. Furthermore, the inflow perforators are even smaller, with valves against the flow providing a severe bottleneck.<sup>21</sup> The saphenous vein can be safely ablated without sequelae in the presence of chronic deep venous obstruction.<sup>22</sup> This will be a consideration only when there is substantial saphenous reflux requiring ablation, offsetting its collateral potential.

The iliac veins are the most disadvantaged in terms of collateral compensation. Because of their large caliber ( $\approx 16$  mm), an impossible number of small-caliber veins are required to carry the flow and to maintain pressure equilibrium. Many patients with extensive collaterals on venography continue to be symptomatic.<sup>23</sup> Collaterals often “disappear” when a lower resistance pathway is opened by venous stenting.

It is believed that aggregate volumetric outflow is rapidly restored after most acute venous occlusions, including of major trunks, except in rare instances.

Inefficient collaterals raise peripheral pressure but do not compromise volumetric flow. A reverse finding is that venous pressure falls after stent correction of iliac vein stenosis, but quantity of venous flow remains the same.<sup>2,24</sup>

**Venous tone.** The infrainguinal veins have a substantial muscle component ( $\approx 60\%$ - $70\%$  in the leg, declining to  $\approx 30\%$  at the groin) and are subject to contraction (venous tone) under autonomic control.<sup>10</sup> Very little is known about this in quantitative terms in control of peripheral venous pressure. Pressure increase in venous tone is mediated through caliber reduction. The muscle content of iliac veins is sparse ( $\approx 10\%$ ) and loosely organized. Venous tone is unlikely here for this anatomic reason. The iliac veins appear “full” (not collapsed) at normal supine pressures on intravascular ultrasound examination.<sup>15</sup> Because the iliac veins are essentially collagenous thin-walled tubes, they become full with as little as 2 mm Hg pressure.<sup>25</sup> Unless there is severe dehydration, functional caliber is unlikely to be affected, which comports with intravascular ultrasound observation in our experience. In contrast, the vena cava is partially collapsed in normal individuals because of its organized muscle component, and volume status is a factor.<sup>26</sup>



**Fig 11. A,** The profunda femoris is a “natural” dormant collateral for the femoral vein. It opens up when venous pressure rises after femoral vein occlusions to overcome the slightly higher resistance in this pathway. Venographic flow can be seen as early as a few hours after femoral vein thrombosis (*arrow*). A guidewire can be seen in the thrombosed femoral vein. **B,** An axially transformed deep femoral vein is often mistaken for the native femoral vein because of similarity of caliber (different patient from limb shown in **A**). Note more medial course overlying bone compared with femoral vein. The great saphenous vein (*GSV*, *arrow*) is much smaller in caliber and an inferior collateral in comparison. See text.

**Implications for iliac vein stenting.** Many authors consider a stenosis of >50% significant in this location. This threshold concept is transmigrated from arterial experience, where there is no drop-off of flow until a 70% stenosis threshold is reached in most territories. This is due to the presence of arteriolar resistance downstream acting as a stenosis in tandem and compensatory vasodilation, which are not factors in venous stenosis. Venous pressure (not flow) is the critical factor in venous stenosis and rises with as little as 13% diameter stenosis in experimental models and in theoretical projections of Poiseuille law.<sup>2</sup>

The concept of optimal outflow caliber as described is a useful threshold to assess stenosis in the terminal outflow of common iliac vein. It follows that stent correction of iliac vein stenosis should aim to achieve post-stent caliber that equals this optimum caliber. At present, there are no clinical data correlating percentage stenosis by either method with venous pressure.

**Study limitations.** The elements of the experimental model are not scaled for high-fidelity simulation. Results offer only qualitative insights.

## CONCLUSIONS

Peripheral venous pressure is controlled by central and peripheral mechanisms. An important peripheral mechanism is reduced venous caliber due to disease, poor compliance, or focal stenosis as shown in the

experimental model used. Poor compliance causes smaller functional caliber at working pressures. Small caliber elevates venous pressure.

## AUTHOR CONTRIBUTIONS

Conception and design: SR  
Analysis and interpretation: SR, WC, WB  
Data collection: SR, WC, WB  
Writing the article: SR  
Critical revision of the article: SR, WC, WB  
Final approval of the article: SR, WC, WB  
Statistical analysis: SR, WB  
Obtained funding: SR  
Overall responsibility: SR

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