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Experimental analysis of aspect ratio in iliac vein stenosis

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ABSTRACT

Background: Veins are thin-walled tubes. Their lumen is roughly circular with an aspect ratio close to 1:1 under physiologic pressures. When they collapse owing to decreased internal pressure or external compression, the aspect ratio changes. The vertical diameter is usually diminished more than the transverse, with a considerable decrease in the lumen area. The recent emergence of stent correction of many venous compression syndromes, particularly iliac vein stenosis, has brought attention to the importance of the aspect ratio, quite apart from an overall decrease in caliber. The iliac vein pressure is influenced not only by stenosis, but also intra-abdominal pressure, right atrial pressure, and collaterals. We investigated the impact of aspect ratio in an experimental model incorporating these factors.

Methods: Inflow was provided from a header tank at 25 mm Hg pressure into a Penrose tubing enclosed in a polyethylene cylinder pressurized (Starling pressure) to simulate intra-abdominal pressures of 5 and 10 mm Hg. The Penrose drained into an outflow tank with a pressure of 7 mm Hg, simulating right atrial pressure. Stenosis was simulated with a series of three-dimensional, printed plastic nozzles with caliber areas of 50, 100, and 200 mm^2 and varying in aspect ratios of 1:1 to 1:4. The flow and pressure in this system was monitored with the use of overflow collaterals in some experiments.

Results: Free flow from the header tank through the Penrose (zero Starling pressure) with a 200 mm^2 circle nozzle into the outflow tank with zero pressure resulted in flow pressure of approximately 1.5 mm Hg. Using nozzles of a smaller caliber or an increased aspect ratio resulted in an increase of flow pressures of up to approximately 3.7 mm Hg. Flow into an outflow tank of 7 mm Hg simulating right atrial pressure further increased flow pressures by approximately 7 mm Hg. The addition of Starling pressures of 5 and 10 mm Hg simulating abdominal pressure increased flow pressure even further to the 10 to 17 mm Hg range. When the Starling pressure was dominant, the additional contribution of nozzle caliber stenosis or aspect ratio reduction to the overall flow pressure ranged from 2 to 6 mm Hg. Collateral overflow varied inversely with collateral resistance. Some experiments yielded an anomalous flow/pressure phenomena known to occur in collapsible tube flows.

Conclusions: A decrease in the caliber or the aspect ratio of iliac vein stenosis was among several other factors that generate peripheral venous hypertension in an experimental model. Increased intra-abdominal pressure is a major influence that amplifies the pressure effects of aspect ratio or caliber reduction. (J Vasc Surg Venous Lymphat Disord 2021;9:1041-50.)

Clinical Relevance: The influence of aspect ratio has been suggested as a significant source of venous hypertension in iliac vein stenosis. We investigated the importance of the aspect ratio in combination with other known elements that influence peripheral venous pressure using an experimental flow model. Flow nozzles of various aspect ratios, and lumen calibers used in the model were fabricated in a three-dimensional printer. The aspect ratio, caliber of the stenosis, intra-abdominal pressure, and right atrial pressure were shown to influence venous pressure related to iliac vein stenosis. Both aspect ratio and lumen caliber should be restored to normal in its treatment.

Keywords: Iliac vein stenosis; Aspect ratio; Venous hypertension; Peripheral venous pressure; Intra-abdominal pressure; Iliac vein caliber

The flow dynamics in veins as they deflate from a round shape to an oval or even further into a flatter lumen ("fish mouth") has long been a matter of interest.[1] The subject has attracted renewed attention recently, with increasing awareness of May-Thurner syndrome.[2] The stenosis related to iliac vein compression often presents as an oval or fish mouth on intravascular ultrasound examination. A progressive deformation of a circular iliac vein into an oval to fish mouth will decrease the aspect ratio as well as its area. The flow may deteriorate from laminar to turbulent. All of these events result in greater flow resistance and peripheral venous hypertension—the

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pathophysiologic basis of chronic venous disease. Caliber reduction without aspect ratio deformation as may occur in post-thrombotic stenosis will also increase the peripheral venous pressure. The intra-abdominal pressure and right atrial pressure also influence the lower limb venous pressure.[3] Collateral flow will tend to decrease the peripheral venous hypertension resulting from iliac vein stenosis.

The aim of the current analysis was to assess the relative influence of these various factors on iliac venous flow and pressure in an experimental model of iliac vein stenosis. It is possible to separate the effects of aspect ratio change from caliber area reduction in an experimental model unlike in vivo.

ARTICLE HIGHLIGHTS

- **Type of Research:** A study of aspect ratio and stenosis caliber in an experimental model of iliac vein stenosis
- **Key Findings:** A number of factors that include aspect ratio, stenosis caliber, intra-abdominal pressure, right atrial pressure, and collaterals influence venous hypertension of iliac vein stenosis.
- **Take Home Message:** Both the aspect ratio and the lumen caliber are correctible causes of venous hypertension and should be restored to normal in endovascular treatment of iliac vein stenosis.

METHODS

Experimental model

The basic iliac vein flow model (Fig 1, *A*) consisted of a header tank and a Penrose drain as described previously.[3] The system was filled with a 2:3 mixture of glycerol and water with a viscosity of .04 poise. The fluid levels in the header and discharge tanks were maintained at 25 and 7 mm Hg, simulating the mean capillary and right atrial pressures, respectively. The flow from the header tank was controlled by an adjustable ball valve. It was set at a flow rate of 600 mL/min, simulating the normal common iliac vein flow. The inflow and outflow volumes were measured by noting the volume change in the respective tanks at the end of each run.

Individual modules were added to the basic flow model to simulate abdominal pressure (Starling resistor), iliac vein stenosis (nozzles), and collateral flow (collateral arcade). In some experiments, the outflow tank pressure was kept at 0 mm Hg.

Starling resistor. The Penrose drain was mounted between short plastic connectors within a Plexiglas cylinder sealed by rubber stoppers at either end (Fig 1, *B*). The cylinder was filled with water through a side hole which could be pressurized ("Starling pressure") to the desired level by gravity flow from a pressurizing tank. Pressure within the Penrose was monitored by a digital manometer (Sper Scientific; Scottsdale, Ariz) through a 5F catheter passed through drill holes in the plastic connector.

Flow nozzles. A series of nozzles (Fig 2, *A*) varying in shape (a circle, an oval, and a fish mouth) with three different caliber areas each (200, 100, and 50 mm^2) were inserted in the flow stream between the Starling resistor and the outflow tank to simulate normal and stenotic common iliac vein calibers. The 200 mm^2 nozzles represented normal caliber with circular, oval, and fish mouth shapes. The smaller caliber nozzles represented stenosis of these three shapes. The aspect ratios of the nozzles are shown in the table accompanying Fig 2, *A*. The large caliber despite the decreased aspect ratio was possible by a large increase in transverse diameter, which does not occur in vivo.

The nozzles were designed using engineering software (Autodesk, Inc.; San Rafael, Calif) and fabricated in a commercial three-dimensional printer (Flashforge USA, City of Industry, Calif).

Collaterals. In some experiments, collaterals were simulated by inserting a flow bypass module between the header tank and the Starling resistor (Fig 2, *B*). The module had a series of vertical tubes—a 4-mm internal diameter increasing in height from 5 to 10 to 15 cm such that the "collateral" overflow would occur through the selected vertical tube (others were plugged) when the flow pressure exceeded the fluid gravity pressure in the selected vertical tube. When the collateral module was used, the overflow was allowed to drain into a base pan and separately measured.

Experiments

Each component of the flow module affected flow and pressure. Successive runs were made with different combinations of individual components to record the changes. Each run was replicated at least five times and the results averaged. The intra-run coefficient of variation (n = 81 runs) was 13.3% for flow rate and 4.5% for pressure. Changes in flow or pressure in the various experiments were tested for significance only when they exceeded these limits. Variations within these limits were marked as nonsignificant (ns).

Statistics

Two-way paired *t*-tests and analyses of variance were used in the analyses. All analyses were performed with commercial software (Prism Corporation, Irvine, Calif).

Permissions

No ethical permission was required for this experimental study or its publication.

RESULTS

Table I shows a representative selection of experiments where the Penrose pressure and nozzle flow are shown

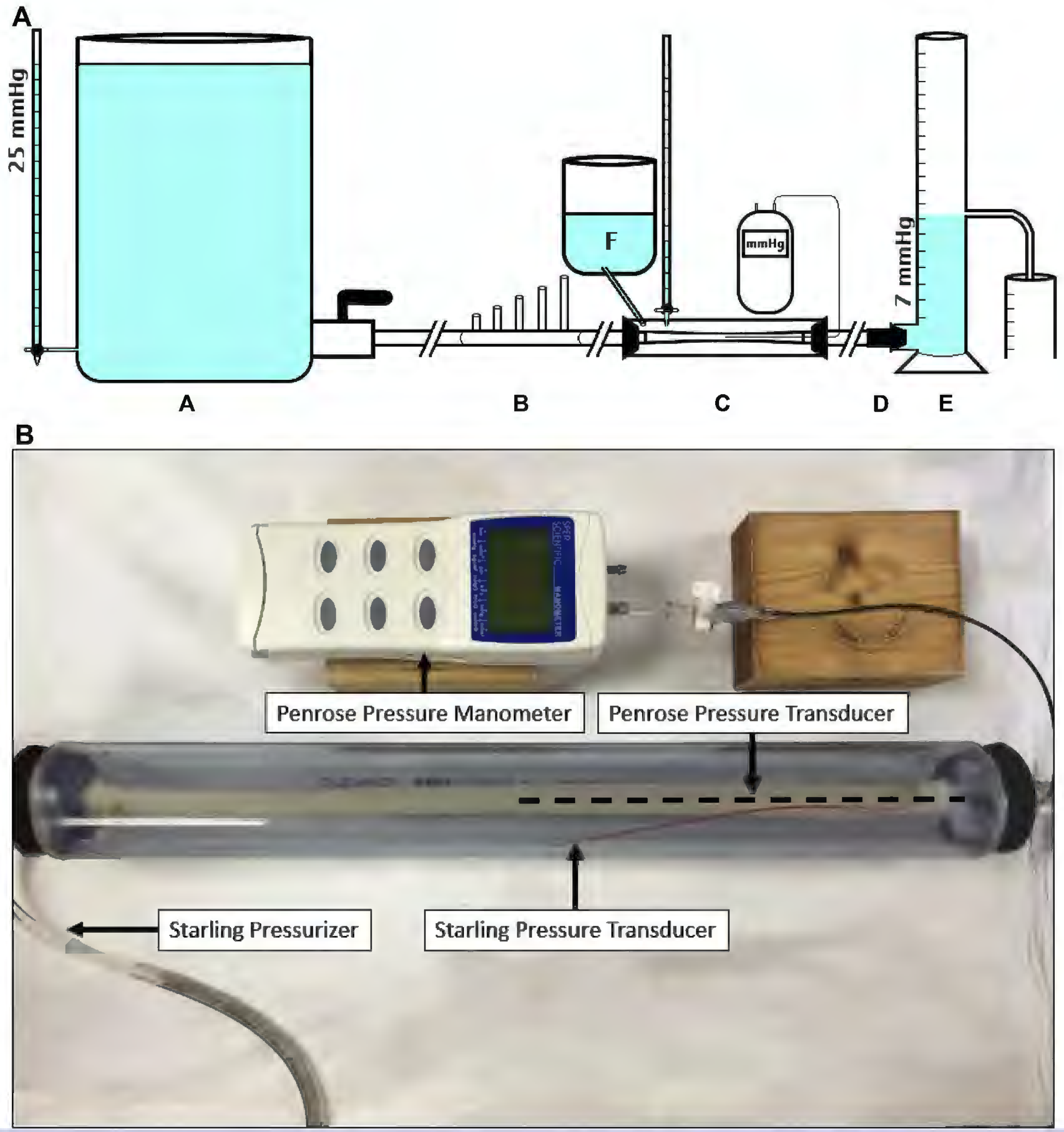

Fig 1. A, Individual modules were added to the basic flow model to simulate mean capillary pressure (A, header tank), collateral flow (B, collateral arcade), abdominal pressure (C, Starling resistor), iliac vein stenosis (D, nozzles), right atrial pressure (E, discharge tank). (F, Starling resistor pressurizing tank). **B,** Starling resistor.

when different components of the system were deployed alone or in combination. The flow valve was set to yield 600 mL/min with the 200 mm^2 round nozzle in these experiments. The noted changes in flow and pressure in the various experiments in Table I was due to variable resistance to flow provided by the different components. Pertinent statistical significance of results is shown in Table II.

Experiment 1. Nozzle flows and Penrose pressures with different nozzles are shown in this experiment. The Starling resistor pressure was set at zero, and the nozzle flow emptied into an empty outflow tank without any outflow back pressure. The Penrose pressure with the 200 mm^2 nozzle was 1.5 mm Hg. A stepwise reduction in nozzle area by one half from 200 to 100 to 50 mm^2 resulted in about 1 mm Hg stepwise increment in the Penrose pressure. The intranozzle differences where lumen shape decreased in aspect ratio while the caliber area remained the same resulted in a pressure increment of about 0.5 mm Hg. The 50 mm^2 fish mouth nozzle representing the maximum combination of area

A

Nozzle Shape	Aspect Ratio (n:n)	Area (mm^2)	Minor Diameter (mm)	Major Diameter (mm)
Circle	1 : 1	200	15.96	15.96
		100	**11.28**	**11.28**
		50	7.98	7.98
Oval	**1 : 1.5**	**200**	**13.03**	**19.54**
		100	9.21	13.82
		50	**6.51**	**9.77**
Fish Mouth	1 : 4	200	7.98	31.92
		100	**5.64**	**22.57**
		50	3.99	15.96

B

Fig 2. A, A series of nozzles varying in shape (a circle, an oval, and a fish mouth) with three different caliber areas each (200, 100, and 50 mm^2) were inserted in the flow stream to simulate normal and stenotic common iliac vein calibers. The aspect ratios of the nozzles are shown in the accompanying table. **B,** Collateral arcade. The pipes indicated by stars (internal diameter of 4 mm; height 5, 10, and 15 cm representing 3.7, 7.4, and 11.0 mm Hg gravity pressure, respectively) were open individually for this experiment; others were plugged shut. The collaterals would offload if the flow pressure exceeded these limits.

and pressure decrease resulted in a Penrose pressure of only 3.7 mm Hg ($P = .001$ vs the 200 mm^2 circular nozzle) in this experiment. These pressures are quite low compared with peripheral venous pressure in vivo (≤11 mm Hg).[4]

Experiment 2 (atrial pressure). An outflow tank with a back pressure of 7 mm Hg was added to the setup in the previous experiment; Starling pressure was kept at zero. Penrose pressure increased by approximately 7 mm Hg over previous experiment to approximately 10 mm Hg ($P < .001$),approximating the normal peripheral venous pressure. The flow is modestly decreased from approximately 600 to approximately 300 mL/min ($P < .0001$) when an outflow pressure of 7 mm Hg was added to the model, decreasing the pressure gradient (ΔP) from 25 mm Hg to 18 mm Hg.

Experiment 3 (5 mm Hg Starling pressure). A Starling resistor with a 5-mm Hg Starling pressure was added to the flow setup in experiment 2; the outflow back pressure at 7 mm Hg was retained. System flow is decreased further ($P < .0001$) and the flow pressure was increased ($P < .0001$). The Starling resistor was the dominant influence on pressure and flow in many of the experiments. For example, all three 200 mm^2 nozzles (round, oval, and fish mouth) with different aspect ratios yielded quantitatively similar flows (195, 192, and 189 mL/min, respectively; $P = .80$) and pressures (11.9, 12.5, and 12.2 mm Hg, respectively; $P = .78$). However, a further decrease in the nozzle caliber to less than 200 mm^2 resulted in a further significant increase of the Penrose pressure ($P < .001$) (Tables I and II). Aspect ratio reduction significantly increased the pressure among smaller caliber nozzles (<200 mm^2) (Table II). The pressure associated with the 50 mm^2 nozzle (17.9 mm Hg) was among the highest recorded in this series of experiments.

Experiments 3 and 4 (anomalous flow increase). The setup in experiment 4 was similar to experiment 3, except that the outflow drained into an empty tank and the outflow pressure was zero. Starling pressure was maintained at 5 mm Hg. An anomalous increase in nozzle flows occurred in experiments 3 and 4 when the nozzle caliber or the aspect ratio was decreased (Table I). The flow increase was anomalous because a decrease in the nozzle caliber or aspect ratio increases resistance and should result in a decrease in the flow per Poiseuille's law. The 200 mm^2 nozzles yielded a flow of 141 mL/min with the round shape, increasing to 184 mL/min with the oval, and further increasing to 239 mL/min with the fish mouth. These flows were significantly different ($P < .001$).

Experiment 5 (10 mm Hg Starling pressure). This experiment used a 25 mm Hg inflow pressure, a 10 mm Hg Starling pressure, and a 7 mm Hg outflow pressure. The ΔP was 18 mm Hg. The setup was the same as in experiment 3, except that the Starling pressure was increased from 5

Table I. Penrose pressure and nozzle flow rate when different components of the system are deployed alone and in combination

Aspect ratio	Area, mm^2	Penrose pressure, mm Hg	Flow rate, mL/min	Anomalous flow increase, %	
Experiment 1: Starling pressure = 0 mm Hg, outflow vessel pressure = 0 mm Hg					
Circle	200	1.5	606		
	100	2.74	597		
	50	2.76	590		
Oval	200	2.5	573		
	100	2.4	570		
	50	2.5	567		
Fish mouth	200	2.7	550		
	100	3.7	559		
	50	3.7	535		
Experiment 2: Starling pressure = 0 mm Hg, outflow vessel pressure = 7 mm Hg					
Circle	200	9.8	358		
	100	9.8	322		
	50	10.2	281		
Oval	200	9.2	319		
	100	9.7	289		
	50	10.1	263		
Fish mouth	200	10.1	334		
	100	10.0	276		
	50	10.5	242		
Experiment 3: Starling pressure = 5 mm Hg, outflow vessel pressure = 7 mm Hg					
Circle	200	11.9	195		
	100	10.7	221		
	50	16.3	123		
Oval	200	12.5	192	Base[a]	
	100	13.8	230	+20%[a,b]	
	50	16.8	121		
Fish Mouth	200	12.2	189		
	100	13.1	136		
	50	17.9	100		
Experiment 4: Starling pressure = 5 mm Hg, outflow vessel pressure = 0 mm Hg, anomalous flow increase despite increased gradient compared with experiment 3					
Circle	200	14.0	141	Base[a]	Base[c]
	100	14.8	175	+24%[a,d]	
	50	15.1	131		
Oval	200	14.3	184		+30%[b,c]
	100	14.2	153		
	50	14.6	140		
Fish mouth	200	13.4	239		+70%[c,d]
	100	13.9	144		
	50	14.5	135		
Experiment 5: Starling pressure = 10 mm Hg, outflow vessel pressure = 7 mm Hg					
Circle	200	15.8	82		
	100	17.1	77		
	50	16.7	81		
Oval	200	16.3	77		
	100	17.3	79		

(Continued on next page)

Table I. Continued.

Aspect ratio	Area, mm^2	Penrose pressure, mm Hg	Flow rate, mL/min	Anomalous flow increase, %
	50	17.0	80	
Fish mouth	200	16.9	74	
	100	16.9	85	
	50	17.2	82	
Experiment 6: Starling pressure = 10 mm Hg, outflow vessel pressure = 0 mm Hg				
Circle	200	15.4	85	
	100	14.9	85	
	50	15.5	78	
Oval	200	15.1	94	
	100	15.3	78	
	50	15.1	80	
Fish mouth	200	15.3	92	
	100	15.0	76	
	50	15.2	75	

Significant anomalous flow increases with a decrease in the aspect ratio compared with the base flow (see text).
Significant anomalous flow increases with a decrease in the nozzle area compared with the base flow (see text).
[a]Anomalous flow increase associated with changes in aspect ratio.
[b]$P < .05$.
[c]Anomalous flow increase associated with changes in caliber.
[d]$P < .001$.

to 10 mm Hg. The Penrose pressures in this experiment were higher than in experiment 3. All pressures were significantly increased to more than 11 mm Hg, which is considered the normal threshold for peripheral venous pressure. Even the 200 mm^2 circle nozzle yielded a pressure of 15.8 mm Hg, the lowest in the group. Pressure increase with caliber reduction or aspect ratio was significant among some nozzles (Table II).

Experiment 6. The setup was similar to experiment 5, with a 10 mm Hg Starling pressure; however, outflow pressure was 0 mm Hg. This setup resulted in slightly lower pressures than in experiment 5. The Starling pressure was the dominant factor in experiments 5 and 6, because the Penrose pressure and nozzle flows varied within a very narrow range among the various nozzles.

Experiments 3-6 (flow limitation). The outflow pressure was 7 mm Hg in experiments 3 and 5 whereas it was 0 mm Hg in experiments 4 and 6. The inflow pressure was 25 mm Hg in all four experiments. A 39% increase in the ΔP was, therefore, present in experiments 4 and 6 compared with experiments 3 and 5. However, the expected proportionate increase in flow (Poiseuille's law) did not occur in any of the nozzle flows in experiments 4 and 6 (Table III). The flow decreased in most nozzles.

Experiment 7 (collaterals). The setup was the same as in experiment 5, except the collateral arcade was added between the input reservoir and the Starling resistor. Collateral flow increases with decreasing resistance (height) of the overflow collateral tube (Fig 3, *A* and *B*). A decrease in the caliber or aspect ratio of the nozzles seems to have only a minor effect on collateral flow (Supplementary Table, online only). The Penrose pressure trends lower with increasing collateral flow ($P = .05$). The Penrose pressure is greater than the collateral tube height with all three collateral tubes tested, that is, the collateral flow did not lower the flow pressure to nominal levels set by the collateral tube height.

DISCUSSION

Model findings. This experimental model simulates a number of factors that contribute to iliac vein pressure, which in turn influences peripheral venous pressure. Intra-abdominal pressure (normally approximately 2-7 mm Hg) and right atrial pressure (normally approximately 7 mm Hg) are major contributors to peripheral venous pressure.[5,6] A decrease in the caliber or aspect ratio by themselves, result in quantitatively trivial elevation (up to approximately 3 mm Hg) of Penrose flow pressures. However they become important raising flow pressures to the 15 to 20 mm Hg range when abdominal and atrial pressures are added to the mix.

The normal common iliac flow is approximately 600 mL/min.[7] Resting iliac-femoral pressures are in the range of 10 to 15 mm Hg.[4] Any increase in flow resistance presented by iliac vein stenosis increases pressure and decreases flow, resulting in venous claudication in the clinical setting. Collateral flow will tend to compensate for this.

Table II. Statistical significance of Penrose pressure parameters[a]

	Circle nozzles, mm Hg	Oval nozzles, mm Hg	Fish mouth nozzles, mm Hg	
Experiment 1				b
200 mm^2	1.5	2.5[c,d]	2.7	c,e
100 mm^2	2.7[e,f]	2.4	3.7[c,d,f]	c,e
50 mm^2	2.8	2.5	3.7[c,d]	c,d
g	e,f		d,f	
Experiment 2				b
200 mm^2	9.8	9.2[c,e]	10.1[c,e]	
100 mm^2	9.8	9.7	10.0	
50 mm^2	10.2	10.1	10.5	
g				
Experiment 3				b
200 mm^2	11.9	12.5	12.2	
100 mm^2	10.7[d,f]	13.8[c,d,f,h]	13.1[d,f]	c,e
50 mm^2	16.3[f,h]	16.8[f,h]	17.9[c,d,f,h]	c,e
g	f,h	f,h	f,h	
Experiment 4				b
200 mm^2	14.0	14.3	13.4[c,e]	c,e
100 mm^2	14.8[e,f]	14.2	13.9	c,e
50 mm^2	15.1	14.6	14.5	
g	e,f			
Experiment 5				b
200 mm^2	15.8	16.3	16.9	c,e
100 mm^2	17.1[e,f]	17.3[e,f]	16.9	
50 mm^2	16.7	17.0	17.2	
g	d,f			

[a]A matrix tabulation is used where different calibers are compared across columns and aspect ratio across rows. The last column and row compares columns I and III and rows I and III, respectively.
[b]Fish mouth nozzle versus circle nozzle *P* value.
[c]Significant Penrose pressure change with a decrease in the nozzle aspect ratio as compared with the previous column.
[d]$P < .05$.
[e]$P < .01$.
[f]Significant Penrose pressure change with a decrease in the nozzle area as compared with the previous row.
[g]The 50 mm^2 nozzle versus the 200 mm^2 nozzle *P* value.
[h]$P < .001$.

Aspect ratio versus caliber. The aspect ratio was examined using circular, oval, and fish mouth configurations with different calibers. These came in normal common iliac vein caliber (200 mm^2) and stenotic sizes of 100 and 50 mm^2 caliber areas representing 50% and 75% stenosis, respectively.[8]

Most iliac vein stenoses involve both aspect ratio and area reductions. The findings herein suggest that stent correction should aim to correct caliber reduction and restore aspect ratio as close to 1 (circle) as feasible. Restoration of the aspect ratio alone may not yield sufficient and durable relief of symptoms. Successful correction of both caliber and aspect ratio is largely dependent on structural properties of the stent.

Intra-abdominal pressure. Earlier work has showed that a caliber stenosis of greater than 80% yielded a peripheral venous hypertension equal to that produced by a Starling pressure of 20 mm Hg.[3] In experiment 5, 100 and 50 mm^2 nozzles representing 50% and 75% area stenoses, respectively, yielded Penrose pressures higher than those seen with normal caliber (200 mm^2) nozzles when combined with 10 mm Hg Starling pressure.

The increased intra-abdominal pressure in obese patients is often associated with organic iliac vein stenosis with cardiovascular disease manifestations.[9] In about 10% of obese patients, intra-abdominal pressure may contribute to peripheral venous hypertension by compression of the iliac-caval veins, as in the Starling resistor in these experiments.[10] Stenting may shield the central veins from compression by external pressure. Stenting results are inferior in obese patients.[10] The stent option should be considered only when the patient adamantly refuses to consider bariatric treatments (many do from fear or other psychosocial reasons).

Table III. Flow limitation[a]

Aspect ratio	Area, mm^2	Experiment 3[b] Flow rate, mL/min	Experiment 4[c] Flow rate, mL/min	Flow change, %	Experiment 5[d] Flow rate, mL/min	Experiment 6[e] Flow rate, mL/min	Flow change, %
Circle	200	195	141	−28%	82	85	+4%
	100	221	175	−21%	77	85	+10%
	50	123	131	+7%	81	78	−4%
Oval	200	192	184	−4%	77	94	+22%
	100	230	153	−33%	79	78	−1%
	50	121	140	+16%	80	80	0%
Fish mouth	200	189	239	+26%	74	92	+24%
	100	136	144	+6%	85	76	−11%
	50	100	135	+35%	82	75	−9%

[a]The pressure gradient (ΔP) was increased 39% in experiment 4 versus 3 and also in experiment 6 versus 5. A corresponding 39% flow increase did not occur in any of the nozzles. Flow decreased in many nozzles. (See text.)
[b]Starling P = 5 mm Hg; inflow P = 25 mm Hg; outflow P = 7 mm Hg; ΔP = 18 mm Hg.
[c]Starling P = 5 mm Hg; inflow P = 25 mm Hg; outflow P = 0 mm Hg; ΔP = 25 mm Hg (+39%).
[d]Starling P = 10 mm Hg; inflow P = 25 mm Hg; outflow P = 7 mm Hg; ΔP = 18 mm Hg.
[e]Starling P = 10 mm Hg; inflow P = 25 mm Hg; outflow P = 0 mm Hg; ΔP = 25 mm Hg (+39%).

Collaterals. The role of collaterals in iliac vein stenosis is not completely understood. Collaterals are visible in only approximately 30% of symptomatic patients. Curiously, patients with profuse collaterals are more symptomatic with higher venous pressures.[11] Because conductance decreases exponentially (r^4) with conduit size, an improbable number of collaterals will be required to completely neutralize the hypertension of iliac vein stenosis.[12] Lower resistance collaterals were shown to provide greater flow in these experiments, but did not normalize the Penrose pressures. This is partly because the collateral arcade was mounted before the Starling resistor; even the shortest collateral tube tested here had to work against a gravity column and a smaller caliber than the Penrose offering significant resistance to collateral flow. The influence of abdominal pressure on collateral flow has not been studied and was not explored in this experiment.

Anomalous flow. The experimental model displays several curious flow features known to occur in collapsible conduits. The flow pattern is bimodal, that is, friction dominated (Poiseuille's law) when the conduit is full, transitioning to inertia dominated flow (turbulent) when collapsed.[13] Griffiths showed that flow velocity may exceed the phase velocity (that transmits pressure information upstream) in partially collapsed tubes.[14] This supercritical flow is associated with many anomalous features that run counter to our understanding of Poiseuille's flow principles. Flow limitation as occurs in a waterfall (the flow is insensitive to downstream water level) is a curious feature. Flow in a downward sloping Penrose tubing ranges from subcritical to supercritical with a shock-like transition between the two.[13] Pressure-flow relationships are inverted in the two types of flows. The Starling resistor can display both types of flow, with the Penrose remaining full in the midsection and collapsing near the exit if the outflow pressure is less than the Starling pressure. Shapiro[13] showed that a number of factors such as stenosis, wall stiffness, erect posture, Starling pressure, and outflow pressure can precipitate non-Poiseuille flows in the Starling resistor. In certain combinations of Penrose pressure and outflow pressure where the difference is small, the flow becomes unstable, changing from supercritical to subcritical (and vice versa). Unlikely as it may seem, these flow anomalies have been shown to be present in many biologic flows.[5]

The counterintuitive increase in flow with the diminishing caliber of nozzles in some experiments (eg, experiment 4) is likely an example of this anomalous flow behavior.[13,15]

Experiments 4 and 6 (Table III) display flow limitation, where flows do not show a proportionate flow increase compared with experiments 3 and 5, despite a 39% increase in the ΔP. Flow limitation is associated with tube collapse near the outflow end of the Starling resistor when the outflow pressure is lower than the Starling pressure. Although the increased ΔP tends to increase flow velocity, the caliber of the outflow end tends to become smaller from tube collapse, limiting the overall flow and functioning as a negative feedback control mechanism.

Study limitations. This experimental model, although adequate to demonstrate general principles, is not a high-fidelity simulation. For example, the flow mechanics in May-Thurner syndrome with luminal webs and strands likely behave differently from the simple Penrose collapse used in this model. Penrose, although collapsible like veins, has differences in compliance

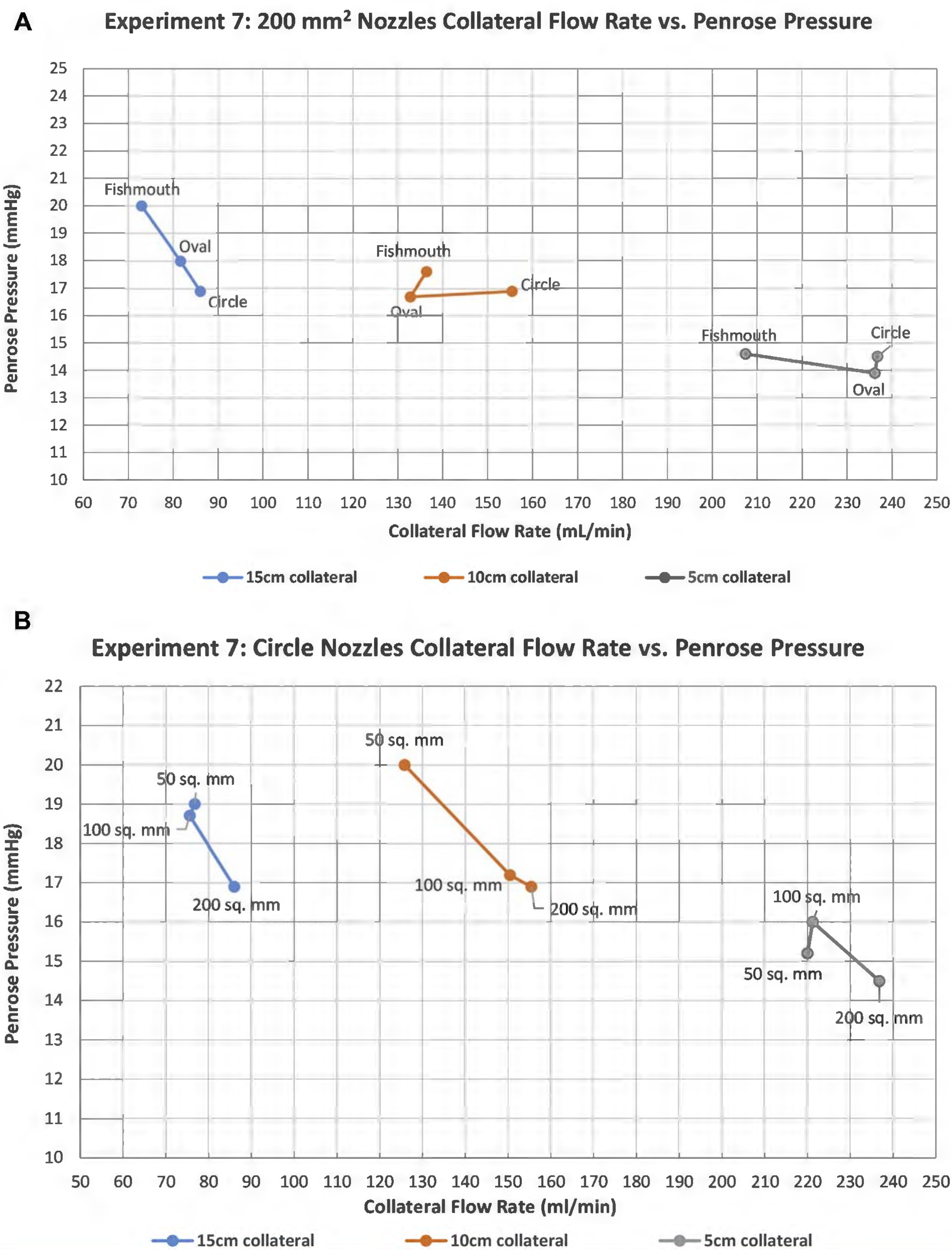

Fig 3. A, Experiment 7: 200 mm^2 nozzles collateral flow (15-, 10-, or 5-cm tubes) versus the Penrose pressure. The aspect ratio has a minimal effect on the collateral flow. (See text.) **B,** Experiment 7: circle nozzles collateral flow (15-, 10-, or 5-cm tubes) versus the Penrose pressure. Caliber reduction appears to have a minor effect on collateral flow. (See text.).

charecteristics.[16] Venous flow is generally regarded as quasisteady despite its phasicity. Phasic variations are not simulated in this experimental model.

CONCLUSIONS

A decrease in the aspect ratio or caliber of iliac vein stenosis were but two of several factors that result in peripheral venous hypertension in an experimental model of iliac vein stenosis. Intra-abdominal pressure is a dominant influence on iliac vein pressure. High-grade iliac vein stenosis may add to the pressure effects of intra-abdominal pressure. Stent correction of iliac vein stenosis should attempt to normalize both caliber area and aspect ratio because they are tightly interconnected in vivo.

AUTHOR CONTRIBUTIONS

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

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Supplementary Table (online only). Statistical significance of collateral flow in experiments 7A, 7B, and 7C[a]

	Circle nozzles	Oval nozzles	Fish mouth nozzles
Experiment 7A collateral flow (15 cm collateral)			
200 mm^2	86	82	78
100 mm^2	76	83	82
50 mm^2	77	79	85
Experiment 7B collateral flow (10 cm collateral)			
200 mm^2	155	133[b,c]	136
100 mm^2	150	142	119
50 mm^2	126[c,d]	137	148[d,e]
Experiment 7C collateral flow (5 cm collateral)			
200 mm^2	237	236	207
100 mm^2	221	200[c,d]	231
50 mm^2	220	215	249[b,c]

Values are milliliters per minute.
[a]A matrix tabulation is used where different calibers are compared across columns and aspect ratio across rows.
[b]Significant collateral flow change with reduction in nozzle aspect ratio as compared with the previous column
[c]$P < .05$.
[d]Significant collateral flow change with reduction in nozzle area as compared with the previous row.
[e]$P < .001$.