From the American Venous Forum

Iliac vein stenosis is an underdiagnosed cause of pelvic venous insufficiency

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ABSTRACT

Background: Reflux in the ovarian veins, with or without an obstructive venous outflow component, is reported to be the primary cause of pelvic venous insufficiency (PVI). The degree to which venous outflow obstruction plays a role in PVI is currently ill-defined.

Methods: We retrospectively reviewed the charts of 227 women with PVI who presented to the Center for Vascular Medicine from January 2012 to September 2015. Assessments and interventions consisted of an evaluation for other causes of chronic pelvic pain by a gynecologist; preintervention and postintervention visual analog scale (VAS) pain score; complete venous duplex ultrasound examination; and Clinical, Etiology, Anatomy, and Pathophysiology classification. All patients underwent diagnostic venography of their pelvic and left ovarian veins as well as intravascular ultrasound of their iliac veins. Patients were treated in one of six ways: ovarian vein embolization (OVE) alone (chemical ± coils), OVE with staged iliac vein stenting, OVE with simultaneous iliac vein stenting, iliac vein stenting alone, OVE with venoplasty, and venoplasty alone.

Results: Of the 227 women treated, the average age and number of pregnancies was 46.4 ± 10.4 years and 3.36 ± 1.99, respectively. Treatment distribution was the following: OVE, n = 39; OVE with staged stenting, n = 94; OVE with simultaneous stenting, n = 33; stenting alone, n = 50; OVE with venoplasty, n = 8; and venoplasty alone, n = 3. Seven patients in the OVE and stenting groups (staged) and one patient in the OVE + venoplasty group required a second embolization of the left ovarian vein. Eighty percent (181/227) of patients demonstrated an iliac stenosis >50% by intravascular ultrasound. Average VAS scores for the entire cohort before and after intervention were 8.45 ± 1.11 and 1.86 ± 1.61 ($P \leq .001$). In the staged group, only 9 of 94 patients reported a decrease in the VAS score with OVE alone. VAS score decreased from 8.6 ± 0.89 before OVE to 7.97 ± 2.10 after OVE. After the planned staged stenting, VAS score decreased to 1.33 ± 2.33 ($P \leq .001$). Similarly, in the simultaneous group, preintervention scores were 8.63 ± 1.07 and decreased to 2.36 ± 2.67 after OVE + stenting ($P \leq .001$).

Conclusions: The majority of patients in our series (80%) demonstrated a significant iliac vein stenosis. These observations indicate that the incidence of iliac vein outflow obstruction in PVI is greater than previously reported. In patients with combined ovarian vein reflux and iliac vein outflow obstruction, our data suggest that pelvic venous outflow lesions should be treated first and that ovarian vein reflux should be treated only if symptoms persist. In women with an outflow lesion, ovarian vein reflux, and a large pelvic reservoir, we recommend simultaneous treatment. (J Vasc Surg: Venous and Lym Dis 2017;■:1-10.)

Chronic pelvic pain (CPP) is a major cause of disability in women.[1,2] The differential diagnosis is extensive (Table I), and it has been estimated that up to 40% of CPP is secondary to pelvic venous insufficiency (PVI), also known as pelvic congestion syndrome (PCS).[3,4] The underlying cause of PVI is reflux in the ovarian or internal iliac veins, with or without an obstructive cause.[3-7] Compression of the left renal vein by the superior mesenteric artery (nutcracker syndrome) is a well-described cause of ovarian vein obstruction.[8,9] Iliac vein obstruction has been reported as a rare and infrequent cause of PVI.[7,10,11] Currently, ovarian vein reflux with or without internal iliac vein reflux has been reported as the primary cause of PVI. The purpose of this investigation was to determine the incidence of iliac vein obstruction in PVI and the role of stenting in the management of PVI.

METHODS

From January 2012 to September 2015, a retrospective chart review of 227 women with PVI treated at the Center for Vascular Medicine (CVM) was performed. Institutional Review Board approval for the study was obtained from RCRC Independent Review Board, LLC,

From the Center for Vein Restoration[a]; and the Center for Vascular Medicine.[b]

Author conflict of interest: none.

Presented at the Twenty-ninth Annual Meeting of the American Venous Forum, New Orleans, La, February 14-17, 2017.

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The editors and reviewers of this article have no relevant financial relationships to disclose per the Journal policy that requires reviewers to decline review of any manuscript for which they may have a conflict of interest.

2213-333X

https://doi.org/10.1016/j.jvsv.2017.09.007

Austin, Texas. Informed consent was not obtained per the Institutional Review Board.

All patients with PVI who were referred to CVM were first evaluated by a vein specialist at the Center for Vein Restoration (CVR). CVR is a physician-run outpatient health care delivery organization that focuses on the diagnosis and management of patients with chronic venous disorders. Established in 2004, CVR is currently composed of 70 centers in 11 states throughout the United States: Alabama (n = 1), Connecticut (n = 8), Indiana (n = 5), Maryland (n = 19), Michigan (n = 5), Ohio (n = 2), Pennsylvania (n = 2), New Jersey (n = 11), New York (n = 4), Virginia (n = 12), and Florida (1). The PVI patients in this investigation originated from the 31 CVR centers in Maryland and Virginia.

The initial evaluation consists of a bilateral, infrainguinal lower extremity venous duplex ultrasound examination for reflux and obstruction of the deep, superficial, and perforator veins, followed by a complete history and physical examination by a vein specialist. The noninvasive ultrasound examination is a standard protocol used by all CVR vascular technologists. CVR has a robust vascular technology quality assurance program that ensures all aspects of the vascular laboratory protocol are followed. As part of the quality assurance program, CVR is seeking Intersocietal Accreditation Commission accreditation for all its noninvasive vascular laboratories and outpatient vein centers. To further ensure standardization of data collection, all patient data are recorded in CVR's Office of the National Coordinator for Health Information Technology-certified electronic medical record (NextGen Healthcare Information Systems, Irvine, Calif). NextGen is a template-driven electronic medical record with discrete data elements. In addition to standard demographic data, a complete Clinical, Etiology, Anatomy, and Pathophysiology (CEAP) classification and revised Venous Clinical Severity Score are recorded for every new patient and on completion of a treatment plan. Patients who reported a history of pelvic pain, dyspareunia, postcoital pain, pelvic fullness, or bloating or had evidence of escape veins were referred to the CVM.

At CVM, a standardized assessment protocol was used. All patients had data prospectively recorded on standardized data collection forms. A complete history and physical examination were conducted and visual analog scale (VAS) pain scores recorded. All patients had a transabdominal, suprainguinal ultrasound examination of the pelvic veins. The inferior vena cava, common iliac veins, external iliac veins, common femoral veins, and left ovarian vein were interrogated with duplex ultrasound for the presence of reflux, any obstructive or stenotic venous outflow lesions, cross pelvic collaterals, or ascending lumbar collaterals. The right ovarian vein was not routinely interrogated. Transvaginal ultrasound was not performed by CVM physicians. Patients with strong history, physical examination, or suprainguinal duplex ultrasound findings were subsequently considered for diagnostic venography, intravascular ultrasound (IVUS), venous stenting, and ovarian vein embolization (OVE). Before proceeding with venography, all PVI patients were evaluated by a gynecologist to ensure that no other possible causes of the patient's pelvic pain existed. Once the patient was cleared by a gynecologist, we proceeded with venography and possible therapeutic endovascular interventions. The gynecologic evaluation was left up to each individual gynecologist. The number of women who had transvaginal ultrasound, axial computed tomography imaging, or diagnostic laparoscopies was not assessed in this retrospective review. After an intervention was performed, all patients returned between 3 and 7 days for a postoperative femoral vein duplex ultrasound scan to rule out an insertion site deep venous thrombosis. Patients were asked to return for a follow-up evaluation at 12 weeks. At this visit, transabdominal ultrasound was performed to assess the patency of any stents placed and the continued occlusion of any embolized ovarian veins.

ARTICLE HIGHLIGHTS

- **Type of Research:** Retrospective, multicenter cohort study
- **Take Home Message:** Of 227 women with pelvic venous insufficiency, 80% had >50% iliac vein stenosis by intravascular ultrasound. Treatment with ovarian vein embolization (OVE) and either staged or simultaneous iliac vein stenting provided better symptom relief at 3 months than OVE alone ($P < .001$).
- **Recommendation:** In patients with pelvic venous insufficiency and combined iliac vein stenosis and ovarian vein reflux, the authors suggest that pelvic venous outflow lesions be treated first and that ovarian vein reflux be treated if symptoms persist. They suggest simultaneous iliac vein stenting and OVE in women with an iliac vein stenosis and ovarian vein reflux with a large pelvic reservoir.

Intervention protocol. The majority of the endovascular procedures were performed by two interventionalists (G.L. and V.S.) at one CVM outpatient ambulatory center in Greenbelt, Maryland. On the day of the procedure, patients were placed supine on a floating table and sedated. The patient's legs were placed in the frog leg position, and an on-table duplex ultrasound examination was performed. The location of the femoral veins in the midthigh was identified and marked with a marking pen. Once the patient was prepared and draped, bilateral ultrasound-guided midthigh femoral vein cannulations were performed. All diagnostic and therapeutic interventions were performed through a femoral vein

Table I. Differential diagnosis of chronic pelvic pain (CPP)

Gynecologic	Psychiatric	Urologic	Neurologic	Musculoskeletal	Gastroenterologic	Hematologic/ oncologic
Endometriosis	Major depression	Interstitial cystitis	Neuralgia of ilioinguinal, genitofemoral or pudendal nerves	Pelvic floor myalgia	Irritable bowel syndrome	Cancer or metastases
Chronic pelvic inflammatory disease	Somatization	Recurrent urinary tract infections	Neuropathic pain	Myofascial pain (trigger points)	Inflammatory bowel disease	Porphyria
Fibroids	Sleep disorder	Urethral diverticulum	Herniated nucleus pulposus	Piriformis syndrome	Diverticular disease	Sacroiliac joint pain
Ovarian cysts	Physical, sexual, or substance abuse		Abdominal epilepsy/migraine	Psoas inflammation	Chronic constipation	Hip joint disease
Adhesions					Hernia	Fractured coccyx
Uterine prolapse						Fibromyalgia

approach. Jugular vein access was not used. Initially, a 10F introducer sheath (Boston Scientific, Marlborough, Mass) was placed in the left femoral vein and an 11-cm, 6F sheath was placed in the right femoral vein for diagnostic venography of the iliofemoral veins. The left renal-ovarian vein was cannulated with either a left internal mammary artery or RIM catheter (Cook Medical, Bloomington, Ind) or a Bern catheter (Cordis, Hialeah, Fla) and a stiff angled Glide Wire (Terumo Medical Corp, Somerset, NJ). The right ovarian vein was not assessed because of technical difficulties in cannulating the orifice from a femoral vein approach. For patients requiring OVE, chemical embolization with 3% sodium tetradecyl sulfate (Mylan Institutional LLC, Rockford, Ill) or Interlock coils (Boston Scientific) were used. The 3% sodium tetradecyl sulfate was made into a foam using the Tessari method. Between 12 and 16 mL of foam per patient was used. Balloon occlusion venography was not a technique used during embolization. On completion of the embolization, the 6F sheath was exchanged for a 10F, 11-cm sheath (Boston Scientific). After venography and embolization, IVUS was performed. IVUS was performed using the Volcano IVUS system, Volcano console model is GEST190XX-POXX-BT, and the Visions PV 0.035 catheter (Philips, Amsterdam, The Netherlands). IVUS was performed bilaterally over a 180-cm stiff angled Glide Wire. The interrogation started in the inferior vena cava and included the common iliac veins, external iliac veins, common femoral veins, and femoral veins. Area-reducing lesions of 50% or greater were considered clinically significant and treated with stenting. Wallstents (Boston Scientific) were used for all stenting procedures. Stent diameter and length were determined by the findings on IVUS. During this study, stents were routinely oversized by 20%. Since 2016, we now oversize by 10%.

Intervention types. Patients with positive findings were treated in one of six ways: OVE alone (n = 39, chemical ± coils), OVE with staged iliac vein stenting (n = 94), OVE with simultaneous iliac vein stenting (n = 33), iliac vein stenting alone (n = 50), OVE with venoplasty (n = 8), and venoplasty alone (n = 3). In patients with venographic evidence of ovarian vein reflux and IVUS-confirmed iliac vein obstruction (area reduction of 50% or greater), it was our policy to perform OVE first, followed by a staged stenting procedure at a second setting. If patients had resolution of their symptoms with OVE alone, stenting was not performed. Simultaneous OVE and stenting were performed in patients with travel restrictions who were unable to return for a staged stenting procedure or in patients who preferred simultaneous treatment. Venoplasty was performed only when patients refused stenting. VAS pain scores were obtained at the patient's initial assessment and 3 months after the last intervention. Finally, CEAP classification was obtained as part of the patient's initial CVR assessment.

RESULTS

Table II outlines the demographic distribution of our population of patients. The average age of the entire cohort was 46.4 ± 10.4 years. The median age distribution of patients treated for PVI was between 41 and 50 years, with 69% of the overall treatment group younger than 50 years (Fig 1). Fifty-two percent had three or fewer pregnancies, with an average of 3.36 ± 1.99 pregnancies for the entire cohort (Fig 2). A significant number of women had concomitant gynecologic diseases: endometriosis (48/227 [21%]), fibroids (28/227 [12%]), and ovarian disease (13/227 [9%]). Nine percent had a history of a previous deep venous thrombosis and three patients had a hypercoagulable disorder (two methylenetetrahydrofolate

Table II. Demographics of patients demonstrating no difference in age, number of pregnancies, and medical or surgical histories

	Entire group (N = 227)	OVE alone (n = 39)	OVE + stenting (n = 127)	Stenting alone (n = 50)	OVE + venoplasty (n = 8)	Venoplasty alone (n = 3)	*P* value
Medical history							
Age, years, average	46.41 ± 10.15	46.41 ± 10.15	44 ± 4.89	45.82 ± 11.70	46.25 ± 8.94	35.67 ± 15.33	.4668
No. of pregnancies, average	3.36 ± 1.99	3.55 ± 2.22	3.52 ± 2.01	2.81 ± 1.53	3.63 ± 1.80	2 ± 2.83	.3761
Diabetes	19	2	9	4	3	1	.4605
Hypertension	48	10	20	14	3	1	.1312
Coronary artery disease	1	0	1	0	0	0	1.000
Hypercholesterolemia	33	5	20	6	2	0	.3837
Degenerative disk disease	37	2	26	8	1	0	.3354
Hypercoagulable disorders (protein C, protein S, antithrombin 3, MTHFR)	3	0	2	1	0	0	1.000
Deep venous thrombosis	8	1	5	2	0	0	.4725
Concomitant gynecologic disorders							
Endometriosis	17	2	13	2	0	0	.4250
Previous hysterectomy	39	3	16	10	0	0	.4040
Previous myomectomy	1	1	0	0	0	0	.5005
Fibroids	14	4	5	5	0	0	.3669
Previous ovarian surgery	8	0	6	2	0	0	.4665
Ovarian cysts	3	0	2	1	0	0	1.000

MTHFR, Methylenetetrahydrofolate reductase; *OVE*, ovarian vein embolization.

reductase and one protein C/S deficiency). Twenty-three percent of women had a previous hysterectomy.

Treatment distribution was the following: OVE, n = 39; OVE with staged stenting, n = 94; OVE with simultaneous stenting, n = 33; stenting alone, n = 50; OVE with venoplasty, n = 8; and venoplasty alone, n = 3. All OVEs were of the left ovarian vein. The right ovarian vein and branches of the internal iliac veins were not selectively interrogated with venography or subjected to embolization. A total of 188 (80%) patients had iliac vein lesions identified by IVUS with an average area reduction of 70.12% ± 10.67%. Of the 177 patients who received stents, all but 2 were placed in the left iliac venous system. Two patients had stents placed in right iliac venous segments. Table III outlines the locations of the stents and the types of OVE. The remaining 11 patients had OVE + venoplasty (n = 8) or venoplasty alone (n = 3). The distribution of stent diameters is outlined in Fig 3. Ovarian vein diameters were recorded in 70 of the 227 patients. The average vein diameter was 5.94 ± 1.99 mm.

The average pain score by VAS on initial assessment for all patients was 8.45 ± 1.1. Table IV indicates the initial and postintervention pain scores by treatment type. Patients available for a 3-month follow-up assessment were as follows: OVE, 23 of 39; OVE + stenting, 113 of 127; stent alone, 44 of 50; OVE + venoplasty, 7 of 8; and venoplasty alone, 2 of 3. Overall follow-up was 83% (189/227). The OVE patients were used as the control group because OVE is currently the accepted standard of care. Results of all interventions were therefore

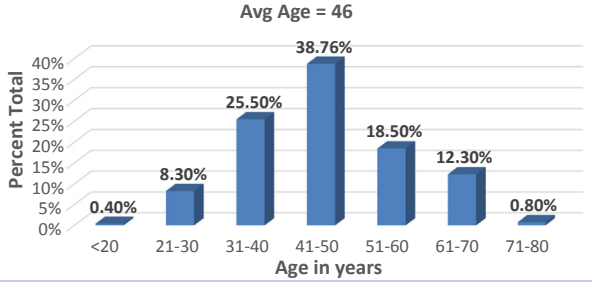

Fig 1. Age distribution of women treated for pelvic venous insufficiency (PVI).

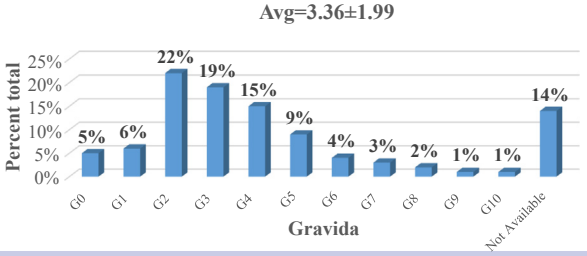

Fig 2. Number of pregnancies at the time of initial intervention for the entire cohort.

Table III. Intervention type indicating types of interventions, location of stent placement, and average area reduction according to treatment regimen

	Location	No. of patients	Area reduction, %, average	Stent size, mm, average
OVE alone	Left ovary (n = 39)	Chemical: 28	N/A	N/A
		Chemical + coil: 10	N/A	N/A
		Coil alone: 1	N/A	N/A
OVE + stenting	Left ovary (n = 127)	Chemical: 111		21.51 ± 2.11
		Chemical + coil: 14		
		Coil alone: 2		
	IVC + LCIV	99	70.12 ± 10.67	
	IVC + LCIV + LEIV	27	76.89 ± 9.89	
	IVC + RCIV + REIV	1	N/A	
Stenting alone				21.37 ± 2.62
	IVC + LCIV	43	70.12 ± 10.67	
	IVC + LCIV + LEIV	4	80.5 ± 8.65	
	IVC + RCIV + REIV	2	90 ± 0	
	RCIV + LCIV	1	60 ± 0	
OVE + venoplasty	Left ovarian vein	Chemical: 7		17.75-mm balloon
		Chemical + coil: 1		
		Coil alone: 0		
	IVC + LCIV	6	49.8 ± 10.42	
	IVC + LCIV + RCIV	1	N/A	
	IVC + LCIV + LEIV	1	77 ± 0	
Venoplasty				12-mm balloon
	IVC + LCIV	2	70.5 ± 9.5	
	IVC + RCFV	1	N/A	

IVC, Inferior vena cava; *LCIV,* left common iliac vein; *LEIV,* left external iliac vein; *N/A,* not applicable; *OVE,* ovarian vein embolization; *RCFV,* right common femoral vein; *REIV,* right external iliac vein.

compared with OVE alone. Initial VAS scores were significantly lower in the OVE group compared with all other groups (Table IV). After intervention, VAS scores were significantly decreased in the OVE + stenting and stenting alone groups. To assess the role of stenting for alleviation of pain in patients with ovarian vein reflux and iliac vein occlusive disease, we analyzed the OVE + stent staged and simultaneous groups separately. In the staged group, only 9 of 94 patients reported a decrease in the VAS score with OVE alone. In this group, VAS score decreased from 8.6 ± 0.89 before embolization to 7.97 ± 2.10 after OVE ($P \leq .01$). The remaining 85 reported no improvement in pain. After the planned staged stenting, VAS score decreased further to 1.33 ± 2.33 ($P \leq .001$). Similarly, in the simultaneous group, preintervention scores were 8.63 ± 1.07 and decreased to 2.36 ± 2.67 after OVE + stenting ($P \leq .001$). The postintervention scores between the staged and simultaneous groups were significantly different, with the staged patients reporting greater pain relief ($P \leq .04$; Fig 4).

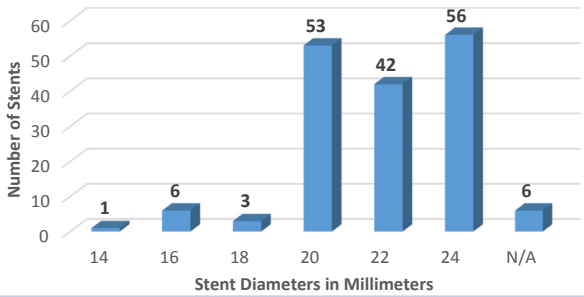

Fig 3. Number of stents placed and their diameters.

In addition to VAS, a global assessment of pain relief was analyzed by determining the degree of complete,

Table IV. Visual analog scale (*VAS*) pain scores by treatment type

	OVE	OVE + stenting	Stenting alone	OVE + venoplasty	Venoplasty alone	*P* value
Initial pain score on presentation	7.41 ± 1.33[a]	8.62 ± 0.96	8.78 ± 0.83	8.75 ± 0.83	8.67 ± 0.47	<.006[a]
Pain score 3 months after intervention	3.15 ± 3.10	1.63 ± 2.36[a]	1.48 ± 2.57[a]	1.89 ± 2.20	1.33 ± 1.25	<.01[a]
Preintervention vs postintervention pain score	$P < .001$	$P < .001$	$P < .001$	$P < .001$	$P = .25$	

OVE, Ovarian vein embolization.
[a]The OVE group was utilized as the control group. Initial assessment VAS scores in the OVE group were significantly less that the other four groups. After intervention, the OVE + stenting and the stenting groups demonstrated a significant improvement in VAS compared to OVE. Compared to initial VAS scores, all postintervention scores demonstrated an improvement except for venoplasty.

partial, and no symptom resolution (Table V). Of the six therapies employed, complete, partial, or no symptom resolution was observed as follows: OVE alone, 35%, 54%, and 5%; OVE + stenting, 58%, 36%, and 5%; stenting alone, 70%, 20%, and 10%; OVE + venoplasty, 50%, 50%, and 0%; and venoplasty alone, 33%, 63%, and 0%. Dyspareunia and fullness responded best to OVE + stenting and worst to OVE alone.

CEAP scoring indicated that a significant number of patients demonstrated lower extremity varicosities. Left and right leg chronic venous insufficiency was observed in 58% and 56% of patients, respectively (Table VI). Forty-seven women (21%) presented with vulvar varicosities (7 in the OVE group, 29 in the OVE + stent group, 10 in the stent only group, and 1 in the venoplasty and embolization group).

DISCUSSION

A great deal of information about the etiology of PVI has been learned since Taylor's original description of pelvic varicosities as a cause of "venous congestion" in 1949.[1,2] The majority of recent publications have focused on ovarian vein reflux with or without internal iliac vein reflux as the primary etiologic factor in the development of PVI.[3-7,13,14] Compression of the left renal vein by the superior mesenteric artery, nutcracker syndrome, is a well-described cause of left ovarian vein outflow obstruction and reflux.[8,9] Although iliac vein obstruction (May-Thurner syndrome) is a common cause of lower extremity edema and pain, it is uncommonly identified as a contributing or causative factor in the development of PVI.[8,10,11] In our retrospective analysis, we have determined that iliac vein obstruction, with or without ovarian vein reflux, is an underdiagnosed cause of PVI in women suffering from CPP. In the current series, all 227 patients complained of pelvic pain. Additional signs and symptoms included pelvic fullness in 189, dyspareunia in 122, and vulvar varices in 47. Of interest is the associated gynecologic disorders that presented concurrently with the patient's PVI. Table II indicates that 17% reported a history of endometriosis, 12% had fibroids, and 8% reported a history of ovarian cysts or ovarian surgery. These findings emphasize the fact that despite the presence of known gynecologic disorders associated with CPP, PVI can occur concurrently.[15] In addition, 23% of women reported a history of a previous hysterectomy before the development of PVI. This observation suggests that previous gynecologic surgery may predispose to the development of a compressive or fibrotic lesion in the left iliofemoral venous distribution.

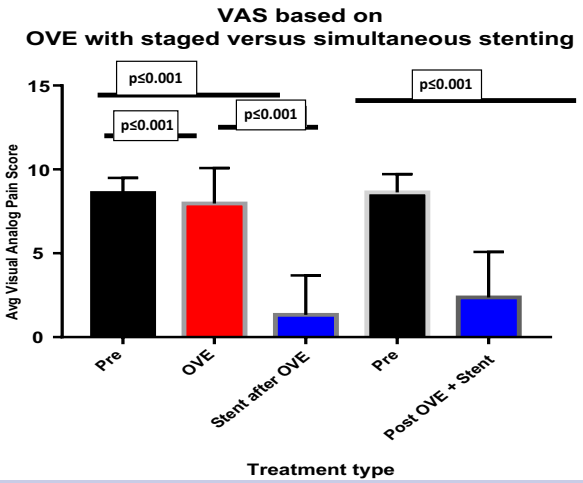

Fig 4. Change in visual analog scale (*VAS*) pain scores in women with ovarian vein embolization (*OVE*) with staged or simultaneous stenting. Only 9 of 94 women in the staged group reported an improvement in VAS score after OVE. After stenting, a significant improvement in VAS score was noted. The overall improvement in VAS score was greater for the staged patients compared with the patients with simultaneous stenting.

A review of pelvic venous anatomy emphasizes the impact that iliac vein occlusive disease can have on the development of pelvic engorgement and pain.[16,17] The ovarian vein forms from three or four branches that arise from veins of the pampiniform plexus in the broad ligament.[4] This broad ligament plexus collateralizes with branches from the uterine veins.[4] The uterine veins arise as branches from the anterior division of the internal iliac vein.[16-18] The internal iliac veins do not have valves in >90% of patients, and the common iliac veins are valveless.[18]

Therefore, obstruction of the common iliac veins can lead to reflux into the internal and external iliac venous systems with the resultant development of

Table V. Specific symptom resolution by type of intervention

Pelvic symptoms	OVE alone (n = 39)	OVE + stenting (n = 127)	Stenting alone (n = 50)	OVE + venoplasty (n = 8)	Venoplasty alone (n = 3)
Pelvic pain					
Complete	14/39 (35)	74/127 (58)	35/50 (50)	4/8 (50)	1/3 (33)
Partial	21/39 (54)	46/127 (36)	10/50 (20)	4/8 (50)	
No improvement	2/39 (5)	7/127 (5)	5/50 (10)		
Dyspareunia					
Complete	4/22 (18)	50/72 (69)	16/19 (84)	3/6 (50)	0/3 (0)
Fullness					
Complete	6/34 (18)	76/107 (71)	34/39 (87)	2/6 (33)	2/3 (66)

OVE, Ovarian vein embolization.
Values are reported as n/N (%).

venous hypertension. Venous hypertension of the lower extremities due to venous outflow obstruction is a well-recognized cause of lower limb swelling, pain, and venous ulceration.[19-21] Similarly, reflux in the ovarian veins can lead to venous congestion of the uterine veins and other branches of the internal iliac vein. As a result, it is a common venographic observation to see cross pelvic collaterals through the uterine veins as egress routes from the pelvis to the contralateral deep veins of the iliac and inferior vena cava.[6,13] In addition, nonaxial venous reflux and varicose vein formation in the medial thigh, vulva, and posterior and lateral thigh, commonly referred to as escape veins, are well-described consequences of internal iliac venous hypertension.[18,22-28] High medial thigh veins often emanate from the internal pudendal vein. Vulvar varicosities can arise from a recanalized round ligament or from the obturator vein. Gluteal fold and lateral thigh veins often arise from the superior gluteal vein. These egress points in the pelvis are referred to as the P (pudendal), I (inguinal), O (obturator), and G (gluteal) points.[17] In our investigation, 56% and 58% of right and left legs, respectively, demonstrated evidence of chronic venous insufficiency based on CEAP

Table VI. Clinical, Etiology, Anatomy, and Pathophysiology (*CEAP*) classification

	Unknown	E	V	E + V	S	E + S + V	Total
Left leg CEAP score by treatment							
0	0	1	0	1	4	9	15
1	0	16	1	2	12	31	62
2	1	6	0	1	15	22	45
3	0	6	1	1	8	30	46
4	0	0	0	0	0	0	0
5	0	0	0	0	0	1	1
6	0	0	0	0	1	0	1
Other	0	2	0	1	3	8	14
Total	1	31	2	6	43	101	184
Right leg CEAP score by treatment							
0	0	2	0	0	7	7	16
1	0	15	0	2	15	30	62
2	1	7	1	1	11	24	45
3	0	5	1	2	5	29	42
4a	0	2	0	0	4	6	12
4b	0	0	0	0	0	1	1
5	0	0	0	0	0	2	2
6	0	0	0	0	1	0	1
Other	0	0	0	1	0	2	3
Total	1	31	2	6	43	101	184

E, Embolization; *S*, stenting; *V*, venoplasty.
Evidence of lower extremity chronic venous insufficiency was demonstrated by 58% of left legs and 56% of right legs.

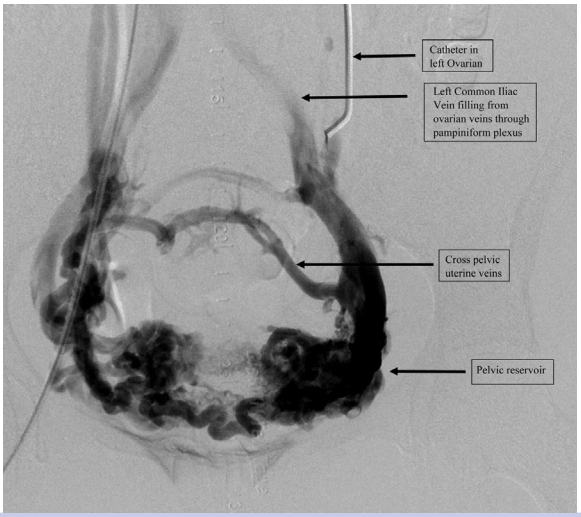

Fig 5. Selective left ovarian vein venogram demonstrating large pelvic venous reservoir, cross pelvic collaterals through the uterine vein, and filling of the common iliac veins bilaterally through collaterals from the pampiniform plexus.

classification. Vulvar varicosities were observed as presenting signs in 47 women.

In the current investigation, we observed iliac vein occlusive disease in 80% (188/227) of patients presenting with signs and symptoms of PVI. This observation is in stark contrast to previously published investigations. Hartung et al[7] reported that in 44 patients treated with stenting for chronic nonmalignant iliocaval venous occlusive disease, 10 presented with signs and symptoms of PCS. Similar to our experience, five were previously treated with OVE and required further treatment for residual symptoms. In a review of five patients presenting with PCS secondary to nutcracker syndrome, Hartung et al[8] described one patient with prior iliac vein stenting. The largest series of PCS with iliac vein stenoses is from Daugherty and Gillespie.[11] These investigators described 19 patients whose PCS was secondary to 18 iliac and one inferior vena cava stenosis. Nine of the patients originally presented with symptoms of PCS and 10 presented with lower extremity edema. All patients were treated with stenting, and although 7 of 19 patients had evidence of ovarian vein reflux, only one patient required OVE. Fifteen of 19 patients had complete symptom resolution, and 14 of 17 reported complete resolution of their dyspareunia. VAS pain scores were not reported. In our series, patients with ovarian vein reflux and evidence of iliac vein stenosis did not respond well to OVE before stenting. Of 94 patients treated with staged OVE followed by stenting, only nine patients demonstrated a decrease in pelvic pain by VAS score. The remaining 85 demonstrated no symptom improvement until iliac vein stenting was performed. This finding suggests that in women with combined ovarian vein reflux and iliac vein stenosis, the iliac vein outflow obstruction is the primary etiologic factor of their pelvic pain. We agree with Daugherty and Gillespie that in patients with uncompensated iliac vein occlusive disease, pelvic stenting should be performed first.[10,11] This raises the question of when OVE should be performed when a hemodynamically significant iliac vein lesion is also present. Our data demonstrated that VAS pain scores were significantly improved in the staged group compared with the simultaneous OVE + stenting group. We suspect this observation is secondary to the presence of compensated venous outflow in patients with ovarian and iliac vein reflux or obstruction. The embolization of patients with large pelvic reservoirs followed by stenting resulted in a superior overall reduction in pain compared with the simultaneous OVE + stenting group. Therefore, in patients with OVE, iliac vein stenoses, and large pelvic reservoirs (Fig 5, compensated disease), we recommend thorough pelvic reservoir embolization and simultaneous stenting. In the absence of compensated disease, we would stent the iliac lesion and stage the

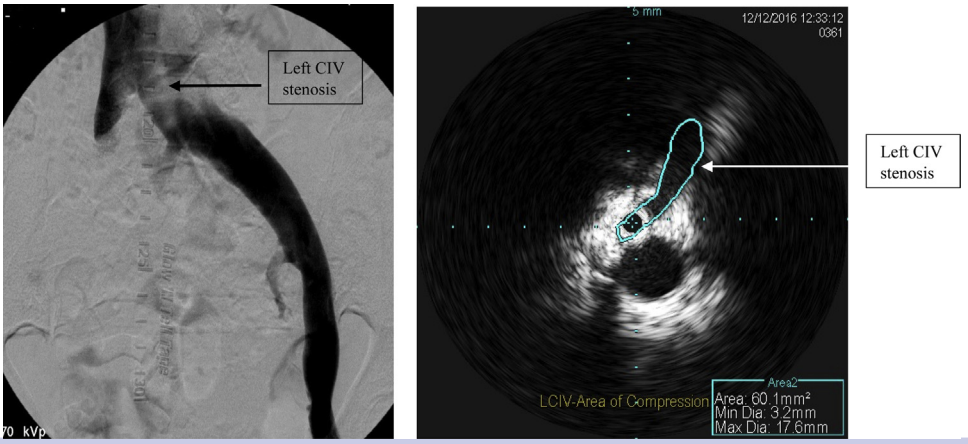

Fig 6. Venogram and intravascular ultrasound (IVUS) demonstrating an uncompensated left common iliac vein (*CIV*) stenosis in a woman with pelvic pain.

embolization of the ovarian vein reflux only if residual symptoms persisted (Fig 6).

The goal of invasive treatment of PVI is complete symptom resolution. Despite significant decreases in pain symptoms as reported by VAS score, a significant number of patients reported only partial symptom resolution. For example, in our OVE alone group, only 35% of patients reported complete symptom resolution, with 54% reporting partial improvement. Despite excellent results in patients receiving iliac vein stents, up to 36% reported some residual pain. The existence of residual pain is a commonality in all investigations of PVI regardless of treatment modality.[3,29-31] We hypothesize that residual pain in women suffering from PVI is secondary to undiagnosed iliac vein obstruction or untreated symptomatic reflux of a large pelvic reservoir. In the current series, IVUS was routinely used to assess the iliac veins for lesions with area reductions of 50% or greater. Venography, compared with IVUS, misses iliac vein lesions in 50% of patients, as recently reported by the Venogram vs IVUS for Diagnosing Iliac vein Obstruction (VIDIO) investigators at the 2016 American Venous Forum meeting. Therefore, patients presenting with PVI should routinely have IVUS performed as part of a complete pelvic venous assessment. In the current investigation, the right ovarian vein and the internal iliac veins were not routinely assessed for pelvic reflux at initial diagnostic venography. It is therefore possible that residual venous disease was left untreated and the reason that some women reported only partial symptom relief. This supposition is further supported by the observation that compared with the other treatment groups, the OVE group demonstrated the poorest degree of symptom improvement, suggesting that residual disease was left untreated. The need to treat internal iliac vein reflux in the presence of untreated common iliac occlusive disease appears unwarranted, given the fact that treatment of occlusive disease with stenting may in and of itself correct internal iliac reflux. Whether to treat residual symptoms should be determined by the impact on quality of life that continued pain imposes. For many patients, a significant pain improvement may be enough. Given the current findings, it is clear that iliac vein occlusive disease in patients with PVI is underdiagnosed. We believe this underassessment is directly related to over-reliance on multiplanar venography. As stated before, the VIDIO investigators clearly demonstrated that multiplanar venography misses hemodynamically significant venous outflow lesions in 50% of patients. Our observations are similar to those of the VIDIO investigators, and we believe our routine use of IVUS is the reason that so many iliac vein lesions were identified.

CONCLUSIONS

In the current investigation, we identified hemodynamically significant iliac vein outflow obstructions in 80% of patients because of the routine use of IVUS. In women who received OVE with iliac vein stenting, significant reductions in pain were identified. Although women who received OVE before their stenting did not report immediate pain reduction before stenting, their overall pain reduction compared with the simultaneous OVE + stenting group was superior. In PVI patients with ovarian vein reflux and iliac vein occlusive lesions, we recommend simultaneous OVE and stenting only in women with significant pelvic reservoirs. In women with ovarian vein reflux, no significant pelvic reservoir, and an iliac occlusive lesion, we recommend stenting followed by a staged OVE only if symptoms persist.

AUTHOR CONTRIBUTIONS

Conception and design: RS, PP, SL, GL
Analysis and interpretation: RS, PP
Data collection: RS, PP, SL, GL, MM, VS
Writing the article: PP
Critical revision of the article: RS, PP, SL, GL, MM, VS
Final approval of the article: RS, PP, SL, GL, MM, VS
Statistical analysis: RS, PP
Obtained funding: Not applicable
Overall responsibility: PP
RS and PP contributed equally to this article and share first authorship.

REFERENCES

1. Daniels JP, Khan KS. Chronic pelvic pain in women. BMJ 2010;341:c4834.
2. Mathias SD, Kuppermann M, Liberman RF, Lipschutz RC, Steege JF. Chronic pelvic pain: prevalence, health-related quality of life, and economic correlates. Obstet Gynecol 1996;87:321-7.
3. Phillips D, Deipolyi AR, Hesketh RL, Midia M, Oklu R. Pelvic congestion syndrome: etiology of pain, diagnosis, and clinical management. J Vasc Interv Radiol 2014;25:725-33.
4. O'Brien MT, Gillespie DL. Diagnosis and treatment of the pelvic congestion syndrome. J Vasc Surg Venous Lymphat Disord 2015;3:96-106.
5. Durham JD, Machan L. Pelvic congestion syndrome. Semin Intervent Radiol 2013;30:372-80.
6. Venbrux AC, Chang AH, Kim HS, Montague BJ, Hebert JB, Arepally A, et al. Pelvic congestion syndrome (pelvic venous incompetence): impact of ovarian and internal iliac vein embolotherapy on menstrual cycle and chronic pelvic pain. J Vasc Interv Radiol 2002;13(Pt 1):171-8.
7. Hartung O, Otero A, Boufi M, De Caridi G, Barthelemy P, Juhan C, et al. Mid-term results of endovascular treatment for symptomatic chronic nonmalignant iliocaval venous occlusive disease. J Vasc Surg 2005;42:1138-44; discussion: 1144.
8. Hartung O, Grisoli D, Boufi M, Marani I, Hakam Z, Barthelemy P, et al. Endovascular stenting in the treatment of pelvic vein congestion caused by nutcracker syndrome: lessons learned from the first five cases. J Vasc Surg 2005;42:275-80.
9. Scultetus AH, Villavicencio JL, Gillespie DL. The nutcracker syndrome: its role in the pelvic venous disorders. J Vasc Surg 2001;34:812-9.

10. Daugherty SF. Nonthrombotic venous obstructions cause pelvic congestion syndrome. J Vasc Surg Venous Lymphat Disord 2015;3:117-8.
11. Daugherty SF, Gillespie DL. Venous angioplasty and stenting improve pelvic congestion syndrome caused by venous outflow obstruction. J Vasc Surg Venous Lymphat Disord 2015;3:283-9.
12. Duncan CH, Taylor HC Jr. A psychosomatic study of pelvic congestion. Am J Obstet Gynecol 1952;64:1-12.
13. Ganeshan A, Upponi S, Hon LQ, Uthappa MC, Warakaulle DR, Uberoi R. Chronic pelvic pain due to pelvic congestion syndrome: the role of diagnostic and interventional radiology. Cardiovasc Intervent Radiol 2007;30:1105-11.
14. Cordts PR, Eclavea A, Buckley PJ, DeMaioribus CA, Cockerill ML, Yeager TD. Pelvic congestion syndrome: early clinical results after transcatheter ovarian vein embolization. J Vasc Surg 1998;28:862-8.
15. Pacheco KG, Fortes de Oliveira MR. The prevalence of ovarian varices in patients with endometriosis. Ann Vasc Surg 2016;34:135-43.
16. LePage PA, Villavicencio JL, Gomez ER, Sheridan MN, Rich NM. The valvular anatomy of the iliac venous system and its clinical implications. J Vasc Surg 1991;14:678-83.
17. Kachlik D, Pechacek V, Baca V, Musil V. The superficial venous system of the lower extremity: new nomenclature. Phlebology 2010;25:113-23.
18. Kachlik D, Pechacek V, Musil V, Baca V. The venous system of the pelvis: new nomenclature. Phlebology 2010;25:162-73.
19. Neglen P. Stenting is the "method-of-choice" to treat iliofemoral venous outflow obstruction. J Endovasc Ther 2009;16:492-3.
20. Neglen P. Chronic deep venous obstruction: definition, prevalence, diagnosis, management. Phlebology 2008;23:149-57.
21. Neglen P. Chronic venous obstruction: diagnostic considerations and therapeutic role of percutaneous iliac stenting. Vascular 2007;15:273-80.
22. Asciutto G, Asciutto KC, Mumme A, Geier B. Pelvic venous incompetence: reflux patterns and treatment results. Eur J Vasc Endovasc Surg 2009;38:381-6.
23. Jin KN, Lee W, Jae HJ, Yin YH, Chung JW, Park JH. Venous reflux from the pelvis and vulvoperineal region as a possible cause of lower extremity varicose veins: diagnosis with computed tomographic and ultrasonographic findings. J Comput Assist Tomogr 2009;33:763-9.
24. Whiteley AM, Taylor DC, Dos Santos SJ, Whiteley MS. Pelvic venous reflux is a major contributory cause of recurrent varicose veins in more than a quarter of women. J Vasc Surg Venous Lymphat Disord 2014;2:411-5.
25. Whiteley MS, Dos Santos SJ, Harrison CC, Holdstock JM, Lopez AJ. Transvaginal duplex ultrasonography appears to be the gold standard investigation for the haemodynamic evaluation of pelvic venous reflux in the ovarian and internal iliac veins in women. Phlebology 2015;30:706-13.
26. Labropoulos N, Tiongson J, Pryor L, Tassiopoulos AK, Kang SS, Mansour MA, et al. Nonsaphenous superficial vein reflux. J Vasc Surg 2001;34:872-7.
27. Creton D, Hennequin L, Kohler F, Allaert FA. Embolisation of symptomatic pelvic veins in women presenting with non-saphenous varicose veins of pelvic origin—three-year follow-up. Eur J Vasc Endovasc Surg 2007;34:112-7.
28. Hobbs JT. Varicose veins arising from the pelvis due to ovarian vein incompetence. Int J Clin Pract 2005;59:1195-203.
29. Rundqvist E, Sandholm LE, Larsson G. Treatment of pelvic varicosities causing lower abdominal pain with extraperitoneal resection of the left ovarian vein. Ann Chir Gynaecol 1984;73:339-41.
30. Beard RW, Kennedy RG, Gangar KF, Stones RW, Rogers V, Reginald PW, et al. Bilateral oophorectomy and hysterectomy in the treatment of intractable pelvic pain associated with pelvic congestion. Br J Obstet Gynaecol 1991;98:988-92.
31. Gargiulo T, Mais V, Brokaj L, Cossu E, Melis GB. Bilateral laparoscopic transperitoneal ligation of ovarian veins for treatment of pelvic congestion syndrome. J Am Assoc Gynecol Laparosc 2003;10:501-4.

Submitted May 16, 2017; accepted Sep 8, 2017.