Research Article

Incidence and distribution of lower extremity reflux

Nicholaas Scot[1], Karl Gunnar[1], Sanjiv Lakhan [1,2], Candace Pappas [3], Peter Scotti [1,2*]

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Introduction: Women with pelvic venous insufficiency (PVI) often present with lower extremity symptoms and manifestations of chronic venous disorders (CVD). The purpose of this investigation was to determine the incidence of lower extremity CVD and the types and distribution of lower extremity veins involved in patients with a known diagnosis of PVI.

Methods: Between January 2012 and December 2015 we retrospectively reviewed the charts of 227 women with PVI as well as their lower extremity (LE) venous duplex investigations. Presenting symptoms, CEAP class, initial rVCSS and the types of LE veins with reflux and their locations were noted. Patients were also subcategorized according to their primary pelvic disorder as follows: Entire cohort (PVI), Ovarian vein reflux (OVR), iliac vein stenosis (IVS) or both (OVR+IVS).

Results: The study group consisted of 227 women (454 limbs) with documented PVI. The average age was 44.71 ± 10.2. In decreasing order, patients presented with the following lower extremity symptoms: pain (66%), swelling (32%), heaviness (26%), limb fatigue (13%), itching (13%), leg cramps (10%), skin changes or SVT (2%) and ulceration or bleeding (0.004%). Table 1 outlines the CEAP class for 215 of the 227 patients. For the entire cohort 48% of right and 50% of left limbs demonstrated C0 or C1 disease. The incidence and type of symptomatic lower extremity veins were as follows: Any axial vein: 32%, Great Saphenous (GSV): 21%, Small Saphenous (SSV): 11%, GSV and SSV: 5%, Non-saphenous tributaries: 15%, Saphenous tributaries: 12%, Posterior or postero-lateral thigh distribution: 5%, vulvar distribution: 4%, perforators: 4%, deep veins: 2%, and Anterior Accessory Saphenous Veins: 1%. For the GSV and SSV, the following patterns of reflux were observed: Entire GSV: 4%, entire above knee GSV: 2%, entire below knee GSV: 2%, above knee segmental GSV: 20%, below knee segmental GSV: 21%, above and below knee GSV segmental disease 1%, Entire SSV: 4%, SSV segmental disease: 12%. The incidence of reflux in any axial vein, the GSV and AAGSV was greater in the OVR group compared to IVS or OVR+IVS ($p \leq 0.03$). Sixty-four of 227 (28%) patients had a history of prior lower extremity venous ablations: OVR (10/39, 26%), IVS (15/50, 30%) and OVR+IVS (39/127, 9%). The number of ablations per patient was the following: OVR 1.48 ± 0.5, IVS 1.7 ± 0.7 and OVR+IVS was 1.65 ± 0.7.

Conclusion: At least 50% of patients with PVI present with lower extremity venous disease. The incidence of reflux in any axial vein is greatest in the OVR group suggesting a correlation with hormonal fluctuations and pregnancy. The majority of symptomatic patients present with segmental axial GSV or SSV disease. Although vulvar and gluteal escape veins are highly associated with PVI, they are infrequently observed. In patients who experience residual or persistent symptoms after treatment for CVD, a pelvic venous ultrasound should be performed to assess for the presence of PVI.

Key Words: Pelvic venous, swelling and varicosities, iliac vein stenosis

INTRODUCTION

It has been reported that chronic pelvic pain is caused by pelvic venous insufficiency (PVI) in up to 40% of patients [1,2]. The primary etiology of PVI is thought to be ovarian vein reflux [1,2]. A recent publication by our group has indicated that the 80% of patients with PVI have an iliac vein obstruction with or without ovarian vein reflux [3]. Furthermore, the majority of these women presented with lower extremity pain, swelling and varicosities, before a diagnosis of PVI was entertained. It is well known that patients with PVI can present with lower extremity varicosities that emanate from pelvic escape veins through the ovarian veins, internal iliacs, obturator, vulvar, internal pudendal and inferior gluteal veins. Although these veins are often diagnostic for PVI, their incidence is low [4-6]. The purpose of this investigation is to determine the incidence of lower extremity varicosities, their locations, the extent of disease and their relationship to the primary etiologic factor in a group of women with a confirmed diagnosis of PVI.

METHODS

We retrospectively reviewed prospectively collected data from Jan 2012 to September 2015, from our ONC (Office of the National Coordinator for Health Information Technology) certified electronic medical record (Nextgen Healthcare Information Systems™, Irvine California) of 227 women with PVI, treated at the Center for Vascular Medicine. The chart review included all medical records and all non-invasive lower extremity duplex scan reports. Institutional review board (IRB) approval was obtained from RCRC Independent Review Board, LLC., Austin, Texas. Informed consent was not obtained as per the IRB's recommendations. Patients were subcategorized according to their primary pelvic disorder as follows: Entire cohort (PVI), Ovarian vein reflux (OVR) alone, iliac vein stenosis (IVS) alone or both (OVR+IVS). Patient demographics, presenting symptoms, CEAP class, initial rVCSS scores, the types of LE veins with reflux and their locations were noted.

Lower extremity veins and locations were categorized as follows: Any superficial axial vein included the Great (GSV) and Small (SSV) saphenous veins. Vulvar distribution veins included veins in the vulva and high medial thigh branches thought to be escape veins from the internal pudendal (Figures 1a and 1b). Gluteal vein distribution included posterior and postero-lateral thigh veins (Figures 2a and 2b). Deep veins included the common femoral, femoral and popliteal veins. Perforators included any perforator above or below the knee that demonstrated reflux. Saphenous tributaries were any tributary veins that emanated from the GSV or SSV. Non-saphenous tributaries were varicosities that did not emanate from the GSV or SSV above or below the knee.

Differences between treatment groups were analyzed utilizing contingency tables, Chi Square analyses and post hoc assessments utilizing SAS version 9.4 statistical software package (Terry, NC).

[1]*Center for Vein Restoration, Greenbelt, USA*

[2]*Center for Vascular Medicine, Greenbelt, Maryland, USA*

[3]*Gunnarsson Consulting, Jupiter, Florida, USA*

***Correspondence:** Peter Scotti, Center for Vein Restoration, Greenbelt, USA, Tel: 908-766-6801; E-mail: peter.pappas@centerforvein.com*

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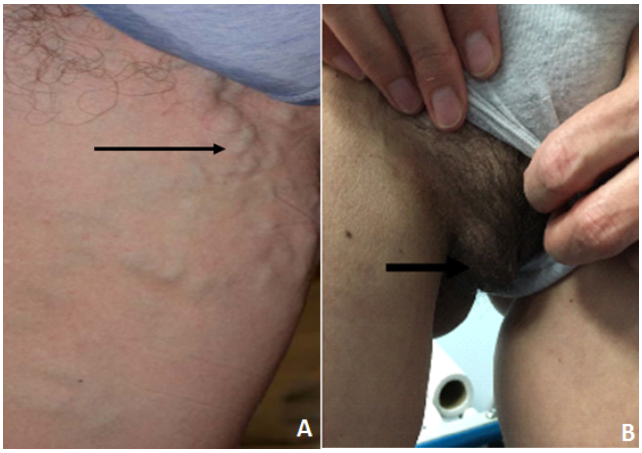
RESULTS

Table 1 demonstrates the demographic distribution for the entire cohort. There were 227 women who had interventions for pelvic venous insufficiency and 454 limbs that were investigated for lower extremity venous reflux with duplex ultrasonography. Of the 227 women in the study, 215 had lower extremity duplex scans available for review. For the 12 patients without scans, they were treated as though no lower extremity disease was present. Of the entire cohort, 64 of 227 (28%) patients had a history of prior lower extremity venous ablations: Ten of 39 patients (26%) in the OVR group, 15 of 50 (30%) patients in the IVS group and 39 of 127 (9%) patients in OVR+IVS group. The number of ablations per patient was the following: OVR 1.48 ± 0.5, IVS 1.7 ± 0.7 and OVR+IVS was 1.65 ± 0.7.

Tables 1: Medical and surgical histories of study groups indicating no significant differences in patient demographics.

	OVR		IVO		OVR+IVO		P-Value*
Medical Demographics	N	%	N	%	N	%	
Total Patients	40	100	50	100	125	100	
Hypertension	6	15	6	12	14	11.2	0.8138
Coronary Artery Disease	2	5	0	0	1	0.8	0.0904
Diabetes	1	2.5	2	4	5	4	0.9028
Hypercholesterolemia	4	10	3	6	5	4	0.3514
Anemia	0	0	1	2	6	4.8	0.2804
Arthritis	4	10	4	8	15	12	0.7323
Thyroid Disease	1	2.5	3	6	14	11.2	0.1766
Deep Vein Thrombosis	1	2.5	2	4	4	3.2	0.9223
Endometriosis	1	2.5	0	0	4	3.2	0.4456
Ovarian Cysts	0	0	0	0	4	3.2	0.2305
Uterine Fibroids	1	2.5	1	2	4	3.2	0.9026
Lumbo-sacral Degenerative Disc Disease	1	2.5	0	0	5	4	0.3462
Gastro-esophageal reflux disease	5	12.5	4	8	10	8	0.6642
Asthma	3	7.5	5	10	8	6.4	0.7145
Depression	2	5	1	2	11	8.8	0.2349
Anxiety	4	10	2	4	15	12	0.273
Surgical Demographics							
Total Patients	40	100	50	100	125	100	
Previous Ablations	10	25	15	30	39	31.2	0.7562
Cesarean sections	12	30	8	16	25	20	0.2481
Cholecystectomy	4	10	6	12	10	8	0.7027
Appendectomy	1	2.5	1	2	1	0.8	0.6671
Inguinal Hernia	2	5	1	2	2	1.6	0.4555
Diagnostic Lap	0	0	0	0	3	2.4	0.3344
Total abdominal hysterectomy	1	2.5	7	14	2	1.6	0.0016
Total abdominal hysterectomy/Bilateral salpingoophorectomy	0	0	0	0	1	0.8	0.6965
Uterine/Fibroid Ablation	0	0	0	0	4	3.2	0.2305
Tubal Ligation	4	10	5	10	15	12	0.8998
Abdominoplasty	2	5	0	0	5	4	0.3184
Unilateral salpingoophorectomy	0	0	0	0	0	0	-
Bilateral salpingoophorectomy	0	0	1	2	0	0	0.1906
Ovarian Cystectomy	0	0	0	0	2	1.6	0.4835

Total hip replacement	0	0	0	0	0	0	-
Total knee replacement	0	0	1	2	2	1.6	0.6918
Arthroscopic knee	1	2.5	1	2	3	2.4	0.9843



Figures 1: High medial thigh varices from the internal pudendal vein (1a). Right sided vulvar varix (1b).

Figures 2: Posterior thigh varix emanating from the gluteal fold (1a). Postero-lateral varix extending from gluteal fold varix (2b).

Table 2 demonstrates the presenting symptoms of the study group. There were no differences in presenting symptoms accept for pain. Pain was more common in the IVS and OVR+IVS groups compared to OVR (Table 2, $p \leq 0.0034$). Tables 3a-3d identify the CEAP classes for the entire cohort and of each of the treatment groups. Of the entire cohort, 95%, were CEAP class three or less. Forty-nine percent were less than or equal to C1 (Tables 3c and 3d) accept for the OVR group where 55% of patients were C1 or less (Table 3b). For the entire cohort 48% of right limbs and 50% of left limbs demonstrated C0 or C1 disease (Table 3a).

Table 4 demonstrates the locations in the lower extremities where symptomatic venous reflux was identified. The incidence and type of symptomatic lower extremity veins were as follows: Any axial vein: 32%, Great Saphenous (GSV): 21%, Small Saphenous (SSV): 11%, GSV and SSV: 5%, Non-saphenous tributaries: 15%, Saphenous tributaries: 12%, Posterior or postero-lateral thigh distribution: 5%, vulvar distribution: 4%, perforators: 4%, deep veins: 2%, and Anterior Accessory Saphenous Veins: 1%. Table 5 documents the patterns of reflux identified. For the GSV and SSV, the following reflux patterns were observed: Entire GSV: 4%, entire above knee GSV: 2%, entire below knee GSV: 2%, above knee segmental GSV: 20%, below knee segmental GSV: 21%, above and below knee GSV segmental disease 1%, Entire SSV: 4%, SSV segmental disease: 12%. The incidence of reflux in any axial vein, the GSV and AAGSV was greater in the OVR group compared to IVS or OVR+IVS ($p \leq 0.03$).

Table 2: Presenting lower extremity symptoms in PVI patients demonstrating an increased incidence of pain in the IVS and IVS+OVR groups compared to OVR alone ($p \leq 0.0034$).

Presenting Limb Symptoms					
Symptoms	OVR	IVS	OVR + IVS	Entire Cohort	P Value
Pain	47	62*	176*	285 (62%)	≤ 0.0034
Swelling	27	35	77	139 (30%)	0.8772
Heaviness	18	24	73	115 (25%)	0.5158
Limb Fatigue	11	12	56	79 (17%)	0.7615
Itching	10	5	39	54 (12%)	0.2063
Cramps	5	10	32	47 (10%)	0.5355
Skin Changes	2	5	3	10 (2%)	0.2775
Superficial Phlebitis	2	0	8	10 (2%)	0.2835
Varix bleeding	1	0	1	2 (0.4%)	0.4579
Ulcer	0	2	0	2 (0.4%)	0.1906

*Compared to OVR

Table 3: CEAP class distribution of a) Entire PVI cohort, b) OVR group, c) IVS group and d) OVR+IVS group. For the entire cohort, 95% of patients were class C3 or less, 49% were C1 or less accept for the OVR group in which 55% of patients were C1 or less.

CEAP Class by limbs (Entire Cohort)			
Right Leg	Number of limbs (n=215)	Left Leg	Number of limbs (n=215)
Class 0	48	Class 0	45
Class 1	56	Class 1	62
Class 2	46	Class 2	43
Class 3	56	Class 3	55
Class 4	7	Class 4	7
Class 5	1	Class 5	1
Class 6	1	Class 6	2
CEAP Class by limbs (OVR Group)			
Right Leg	Number of limbs (n=36)	Left Leg	Number of limbs (n=36)
Class 0	6	Class 0	6

Class 1	14	Class 1	12
Class 2	6	Class 2	9
Class 3	9	Class 3	8
Class 4	1	Class 4	1
Class 5	0	Class 5	0
Class 6	0	Class 6	0
CEAP Class by limbs (IVO Group)			
Right Leg	Number of limbs (n=49)	Left Leg	Number of limbs (n=48)
Class 0	10	Class 0	15
Class 1	14	Class 1	13
Class 2	14	Class 2	10
Class 3	8	Class 3	7
Class 4	2	Class 4	2
Class 5	0	Class 5	0
Class 6	1	Class 6	1
CEAP Class by limbs (OVR + IVO Group)			
Right Leg	Number of limbs (n=119)	Left Leg	Number of limbs N=(120)
Class 0	27	Class 0	26
Class 1	31	Class 1	29
Class 2	21	Class 2	24
Class 3	35	Class 3	36
Class 4	4	Class 4	4
Class 5	1	Class 5	1
Class 6	0	Class 6	0

DISCUSSION

Numerous epidemiologic investigations have reported an increased incidence in the development of varicose veins in women [7-11]. In addition, a history of pregnancy is an independent risk factor that increases the likelihood of lower extremity varicose vein formation [12]. This gender predisposition may be related to changes in estrogen and progesterone receptor levels during pregnancy and the effects of the gravid uterus on venous outflow [13]. Although venodilatation is a normal physiologic response to pregnancy, it is unknown why some women develop varicosities with subsequent pregnancies and others do not [14]. The authors hypothesized that iliac vein outflow obstructive disease (IVS group) would predispose to the formation of lower extremity varicose vein formation more so than isolated ovarian vein reflux. We thought that the increased ambulatory venous hypertension associated with an iliac vein outflow lesion would be associated with a greater likelihood of developing lower extremity varicosities. In addition, we expected that OVR+IVS group would present with a higher incidence of lower extremity varicosities given the combined etiology of this group's PVI. Contrary to our hypothesis, women whose PVI was secondary to OVR and not IVS, had a significantly higher incidence of axial vein reflux. This observation clearly suggests that hormonal variations observed with pregnancy is a greater risk factor in the development of lower extremity varicose veins than isolated iliac vein stenoses.

Table 4: The most common location in the lower extremities for varicose vein formation was in the GSV with a significantly higher incidence in the OVR group compared to IVS and OVR +IVS (p0.0468).

Distribution of lower limb varices				
Vein Type and Location	OVR	IVO	OVR + IVO	P-Value
	(n=80)	(n=100)	(n=254)	
Any Axial	46 (58%)	38 (38%)*	119 (47%)	≤ 0.0335
GSV Alone	36 (45%)	28 (28%)*	78 (31%)*	≤ 0.0468
SSV Alone	4 (5%)	3 (3%)	12 (5%)	0.7407
GSV+SSV	6 (8%)	7 (7%)	29 (11%)	0.3441
AAGSV	8 (10%)	1 (1%)*	7 (3%)*	≤ 0.0402
Saphenous tributary	22 (28%)	16 (16%)	42 (17%)	0.0680
Non-saphenous tributary	15 (19%)	13 (13%)	59 (23%)	0.0913
Vulvar distribution	6 (8%)	5 (5%)	8 (3%)	0.2380
Gluteal distribution	7 (9%)	5 (5%)	10 (4%)	0.2311
Deep veins	1 (1%)	3 (3%)	5 (2%)	0.7034
Perforator	13 (16%)	8 (8%)	15 (6%)	0.5374

*Significantly different compared to OVR

Table 5: A higher incidence of segmental above knee GSV reflux was identified in patients with IVS compared to OVR and OVR+IVS (p ≤ 0.001).

Extent of Reflux					
Vein Location	OVR (n=80)	IVS (N=100)	OVR+IVS (n=254)	Entire Cohort (n=434)	P Value
GSV (Entire)	2 (3%)	3 (3%)	12 (5%)	17 (4%)	0.5798
GSV (Entire AK)	2 (3%)	1 (1%)	8 (3%)	11 (2%)	0.5110
GSV (Entire BK)	1 (1%)	3 (3%)	4 (1.5%)	8 (2%)	0.6077
GSV (Segmental AK)	21 (26%)	43 (43%)*	24 (9.4%)	88 (19%)	≤ .0001
GSV (Segmental BK)	22 (28%)	17 (17%)	54 (21%)	93 (20%)	0.2322

SSV (Segmental)	10 (12.5%)	7 (7%)	31 (12%)	48 (11%)	0.3358

*Compared to OVR and OVR+IVS

It is clear that gender and pregnancy predispose to lower extremity varicose vein formation and that multiple pregnancies are associated with the development of pelvic venous insufficiency [1,2, 15,16]. We previously reported that in the current cohort, the average number of pregnancies in women with PVI was 3.36 ± 1.99 [3]. This observation is similar to other previous reports [1,4,17]. The underlying mechanism of lower extremity vein formation in women with documented PVI is unclear. Perrin et al reported a recurrence rate of 17% in patients with PVI [5]. Asciutto et al. reported that in 71 women with PVI, 53 (75%) had recurrent varicose veins following previous surgery and stripping of the GSV [6]. Of these 53, 47 (66% of the entire cohort) underwent either GSV stripping, redo saphenofemoral junction surgery or phlebectomy. In 58% of these patients, a pelvic venous communication to lower extremity veins was identified suggesting that recurrence of disease was not solely related to neovascularization or poor surgery [6]. In another investigation of 109 male and female patients with PVI, 25.6% presented with recurrent lower extremity varicosities [18]. The incidence increased to 27.9% in women, 30.5% in women with children and 33.3% of women with children and an intact uterus [18]. Few investigations report the incidence of lower extremity varicose vein formation in women with concomitant, documented PVI. To our knowledge, this is the first study to report the simultaneous incidence of the two disease entities at the time of diagnosis and prior to any venous interventions. Our data indicate that the two disease entities can occur together in up to 50% of PVI patients.

The formation of pelvic escape veins secondary to iliac vein reflux, ovarian vein reflux and/or iliac venous obstruction, are known etiologic factors in the development of lower extremity varicosities [1,2,4,6,15,18-23]. These veins typically appear in the vulva, high medial thigh, gluteal fold and postero-lateral thighs [4,18-23]. Despite the known relationship between PVI and the development of lower extremity varicosities via pelvic escape veins, the incidence of these non-saphenous veins is very low. Labropoulos et al reported a 10% incidence of non-saphenous vein reflux in a cohort of 885 limbs [4]. A pelvic venous source was identified by duplex scanning in 34% [4]. In our investigation, non-saphenous venous insufficiency was observed in 35% of the OVR group, 23% of the IVS group and 30% of OVR+IVS group. Of the entire cohort varices in the vulvar and gluteal vein distributions were only observed in 9% of patients similar to that observed by Labropoulos et al. [4]. In the current investigation, 49% of PVI patients were CEAP class 2 or higher. Of those patients 44% were CEAP class 2 or 3. This incidence is an under estimate of disease as 28% of the entire cohort had a history of previous axial vein endovenous ablations (OVR 1.48 ± 0.5, IVS 1.7 ± 0.7 and OVR +IVS was 1.65 ± 0.7). When classic pelvic escape veins are identified on physical exam, symptoms associated with PVI are often sought by clinicians and imaging studies of the pelvis are warranted. In the current study, reflux in the axial GSV and SSV was observed in 47% of women with documented PVI. Therefore, it is clear from this observation that women with PVI will frequently present with lower extremity varicosities and CVI type symptoms and not necessarily associate their pelvic symptoms with their current lower extremity varicosities.

When pelvic and lower extremity symptoms present concomitantly, the clinician must decide which disease process to treat and what order to treat them in. Hartung et al. identified a group of women with PVI from iliocaval obstruction or isolated pelvic vein reflux sources and lower extremity varicose veins. In the women with isolated ovarian vein and internal iliac vein reflux with direct connections to lower extremity varices, embolization did not significantly improve lower extremity varicosity symptoms [24]. Eight-two percent required additional lower extremity interventions to treat their chronic venous insufficiency [24]. Our clinical practice is to treat lower extremity venous disease with minimally invasive techniques first. We look to avoid placing coils and iliac stents given the uncertainty of long term venous stent patency and the recanalization rates of embolized ovarian veins. We only address lower extremity symptoms caused by pelvic lesions if lower extremity symptoms persist after endovenous therapies and phlebectomies are employed or if patients present with classic PVI type symptoms like chronic pelvic pain, dyspareunia, post-coital pain, dysmenorrhea, menorrhagia, pelvic bloating, mid-epigastric pain or urinary frequency. It is currently unknown whether or not lower extremity varicosities will regress if a pelvic source for the varicosities is treated first. In our experience, lower extremity varicosities do not disappear or regress after treatment of ovarian vein reflux or iliac vein stenoses. These observations are important discussion points with patients and help manage patient expectations.

CONCLUSION

Symptomatic lower extremity varicose veins occur simultaneously in women with PVI in at least 50% of women. Axial GSV and SSV reflux are the most common veins observed with segmental disease presenting in the above or below knee saphenous system most often. Women with PVI secondary to OVR have a higher incidence of concomitant disease. In these circumstances it is our clinical practice to address lower extremity disease prior to any pelvic disease. Physicians examining women in their 40s with a history of pregnancy and symptomatic varicose veins should obtain a pelvic venous insufficiency history as part of their clinical evaluation. If the history is suggestive of PVI, a pelvic venous ultrasound should be performed and the patient informed that if endovenous therapies are employed, they may have residual symptoms that are secondary to pelvic venous insufficiency.

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