Predicting pelvic congestion syndrome: Concomitant pelvic pain diagnoses do not affect venography or embolization outcomes

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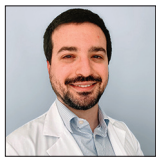
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ABSTRACT

Objectives: Pelvic congestion syndrome (PCS) is a challenging diagnosis to make secondary to nonspecific presenting symptoms and imaging findings. This retrospective review aims to discern predictive factors which can guide the decision to perform catheter-based venography and prognosticate outcomes.

Material and Methods: A retrospective analysis of patients who underwent catheter venography for PCS between January 2014 and December 2019 was performed. Multiple factors, including patient demographics, clinical history, pre-procedural imaging, venographic findings, and treatment outcomes 180 days post-procedure, were included in the analysis. Venographic findings were used to separate patients into two groups (positive or negative), with these factors compared across groups. Regression analysis controlled for the confounding effects of age and body mass index (BMI). Treated subjects were separated based on outcome (partial, no response, complete response, or technical failure), and comparisons were performed.

Results: Eighty patients were included in the initial analysis. Two patients were excluded due to prior embolization or portal hypertension. Seventy-eight patients were included in the final analysis. Sixty-two patients had positive findings, and 16 had no venographic findings to suggest PCS. A history of prior pregnancy was a significant predictor of positive venographic results (odds ratio = 5.99, $P = 0.007$). BMI was significantly lower in those with positive venographic results ($P = 0.047$). Presence of concomitant diagnoses did not affect venographic findings or treatment outcomes. No factors predicted treatment outcomes. Five of the treated patients had subsequent successful pregnancies.

Conclusion: A lower BMI supports the decision to perform venography for suspected PCS. In addition, patients who carried concomitant potentially confounding diagnoses for chronic pelvic pain were found to have similar rates of venographic findings suggesting PCS, as well as similar treatment outcomes.

Keywords: Pelvic congestion syndrome, Venogram, Ovarian vein embolization, Pelvic varicose vein, Embolization

INTRODUCTION

Pelvic venous disorders encompass a range of conditions such as pelvic congestion syndrome (PCS), May-Thurner syndrome, and nutcracker syndrome. Symptomatically, these conditions may include chronic pelvic pain, back pain, pelvic origin lower extremity and vulvar varicosities, obstructive lower extremity varicosity related symptoms, and renal symptoms including

hematuria and flank pain. The vast majority of patients treated for pelvic venous disorders are considered to have PCS, which is a clinical syndrome of chronic pelvic pain in the setting of pelvic venous dilation or incompetence. Symptoms are thought to arise in PCS is due to dysfunctional venous valves leading to venous insufficiency and reflux. This uncompensated reflux leads to venous dilation and venous hypertension which is hypothesized to activate nociceptors and increase pain sensitivity.[1] The venous incompetence may be congenital, induced during pregnancy, or result from a combination of predisposing factors.

PCS is regarded as a challenging diagnosis due to nonspecific findings, absence of definitive criteria and a large differential diagnosis for etiologies of chronic pelvic pain. When evaluating patients with a suspected pelvic venous disorder, other common causes of chronic pelvic pain should be considered. The differential diagnosis includes gynecologic pathologies such as endometriosis and uterine leiomyomas or pathologies stemming from other pelvic or abdominal organs, such as interstitial cystitis, irritable bowel syndrome (IBS), and pelvic floor myalgias. While pelvic venous dilation supports the diagnosis, this finding can also be found incidentally in asymptomatic individuals or may not be the etiology of the patient's pain.[2] Risk factors for PCS include prior pregnancy, prolonged standing, and underlying venous anomalies. Once diagnosed, PCS is treated with embolization of the ovarian veins. Various studies have shown rates of success ranging from 64 to 100%.[3-7]

While some factors can predispose patients to PCS, the decision to perform catheter venography can be challenging. The patients often have undergone extensive workup and multiple office visits before venography is considered. In addition, patients who are treated with embolization for PCS may have persistent symptoms. This retrospective study aims are to identify factors that may predict positive venographic findings and influence successful treatment outcomes to aid in better patient selection for venography.

MATERIAL AND METHODS

The Research Subjects Review Board at the University of Rochester approved this retrospective cohort study. Catheter-based pelvic venograms performed from January 2014 through December 2019 for PCS were included in the analysis. A total of 80 unique patients were identified. Patients were excluded if they had prior embolization or if they had portal hypertension. Out of the 80 included patients, one patient was excluded as she had prior embolization at an outside facility with concern for technical failure or recurrence. In addition, one patient was excluded as their PCS was suspected secondary to extensive portal hypertension with multiple complex intrabdominal portosystemic shunts. The venographic procedure was reviewed to confirm findings of PCS as evidenced by dilated veins, venous reflux with filling of the pelvic veins with stasis and/or drainage into other escape pathways, along with laterality, and treatment. Venography was routinely performed only of the renal veins. The iliac veins were not evaluated. Patient charts were reviewed for multiple factors, including pelvic pain. Chronic pelvic pain was defined as non-cyclic pain lasting for at least 6 months and localized to the anatomic pelvis requiring medical therapy or resulting in functional disability.[8] Symptoms and concomitant diagnosis included dysmenorrhea, dyspareunia, back pain, myofascial pain syndrome, suspected endometriosis, fibromyalgia, and IBS. Obstetric history was defined as a binary variable nulliparous and one or more pregnancies. Prior imaging studies including ultrasound, computed tomography, and magnetic resonance imaging were reviewed. Both the report and images were reviewed for mention of or imaging evidence of PCS by a PGY-5/R4 Radiology Resident. Charts were evaluated for mention of a subsequent pregnancy.

Subjects were separated into two groups based on whether they had a positive or negative venographic findings. Multiple variables were evaluated using Fisher's exact test for binary variables and unpaired *t*-tests for continuous variables. To control for age and body mass index (BMI), independent logistic regression analyses were performed with each variable as the predictor, positive versus negative finding as to the outcome, and age and BMI as confounders. Treated subjects were separated based on outcome (no response, partial response, complete response, or technical failure). This was defined by chart review at various follow-up appointment notes. Patients that experienced no change were defined as no response. Those with some improvement were partial. Only those patients that reported a total resolution of symptoms were recorded as complete. Factors were evaluated using the Chi-squared test for binary variables and ordinary one-way ANOVA for continuous variables. Pairwise comparisons for binary variables were performed using individual Fisher's exact tests, with p values corrected for false discovery rate (FDR). Pairwise comparisons for continuous variables were performed using Tukey's test.

RESULTS

A total of 80 unique patients were identified who underwent catheter venography for PCS; two patients were excluded due to prior treatment and etiology of PCS. Seventy-eight patients were included in the final analysis. Sixty-two patients had positive findings, and 16 had no findings to suggest PCS. Of the variables analyzed, a history of prior pregnancy was the only significant predictor of positive venographic findings (odds ratio = 5.99 (1.63–22.0 95% confidence interval), $P = 0.007$) when controlling for age and BMI. BMI itself was significantly lower in those with positive venographic findings ($P = 0.047$). Full results are found in [Table 1].

There were 26 patients who had a pelvic ultrasound performed before venography for a variety of indications. Among patients who had positive venographic findings, 23 had a prior ultrasound, and 9 of these (40.9%) demonstrated positive findings suggestive of PCS. In contrast, only three patients had an ultrasound in the negative group, none of which showed findings of PCS. Among patients with computed tomography (CT) before venography (*n* = 23) a larger portion had findings of PCS in the positive venographic group compared with the negative venographic findings group (58.8% vs. 33.3%, *P* = 0.57). However, the overall number of CTs performed before venography was low at 29.5%.

Sixty-two patients with positive findings underwent treatment. The vast majority were treated with coil embolization alone, *n* = 49, while the remaining 13 had a combination of coils and an adjuvant embolic, which included glue, sclerosant, and/or gel foam. Charts were evaluated up to 180 days post-treatment. Ten patients did not have any follow-up in our health system and were excluded from further analysis. Of the remaining 52, 57.7% had some symptomatic relief, 13.5% had a complete response, and 44.2% had at least a partial durable response. Approximately, 30% had no change in symptoms at six months. Three patients had treatment failures in which pain initially resolved and returned; all three were found to have recanalization on repeat venography and resolution of

symptoms following re-embolization. No evaluated factors were found to predict treatment outcomes. Full results are found in [Table 2].

The number of patients with treatment failure in our review requiring re-embolization was 4.8%. All three patients were treated with coils. One patient was treated with coil embolization of both the right and left ovarian vein, and found to have a new collateral of the left. Of note this patient had multiple collaterals noted on initial angiogram, which may have predisposed this patient to failure. Of the two remaining patients, one patient was initially treated on the left but had subsequent development of right sided reflux. Finally, one patient was treated on the left and was found to have left sided recanalization.

No major complications (SIR Class C-F) including symptomatic pulmonary embolism occurred. Five of the treated patients had subsequent successful pregnancies.

DISCUSSION

Overall treatment outcomes were similar to prior studies as the majority of patients experienced some reduction of symptomatic relief. A lower percentage of patients had complete relief (13.5%), and a larger percentage of patients experienced no benefit (36.5%), compared

Table 1: Venographic findings.

Variable	Positive venographic finding (*n*=62)	Negative venographic finding (*n*=16)	*P*-value	*P*-value (controlling for age+BMI)
Demographics/risk factors				
Age	36.7±11.2	32.3±8.1	0.15	–
BMI	27.1±6.0	30.9±8.9	0.047	–
Symptoms (%)				
Chronic Pelvic Pain	100 (94.2–100)	100 (79.4–100	>0.99	>0.99
Dysmenorrhea	51.6 (38.6–64.5)	62.5 (35.4–84.8)	0.58	0.54
Dyspareunia	53.2 (40.1–66.0)	43.8 (19.8–70.1)	0.58	0.45
Back Pain	27.4 (16.9–40.2)	25.0 (7.3–52.4)	>0.99	0.89
Concomitant Diagnosis and Risk factors (%)				
Myofascial pain syndrome	39.3 (27.1–52.7)	43.8 (19.8–70.1)	0.78	0.99
Endometriosis	24.2 (14.2–36.7)	25.0 (7.3–52.4)	>0.99	0.86
Fibromyalgia	6.5 (1.8–15.7)	12.5 (1.6–38.3)	0.60	0.46
IBS	14.8 (7.0–26.2)	31.3 (11.0–58.7)	0.15	0.38
Prior Pregnancy	83.9 (72.3–92.0)	43.8 (19.8–70.1)	0.008	0.007
Prolonged Standing	45.2 (32.5–58.3)	50.0 (24.7–75.3)	0.78	0.99
Imaging (%)				
Prior Pelvic US	37.1 (25.2–50.3)	18.8 (4.0–45.6)		
Positive PCS findings on US	40.9 (20.7–63.6)	0.0 (0.0–84.2)	0.51	0.28
Prior Pelvic CT	30.6 (19.6–43.7)	25.0 (7.3–52.4)		
Positive PCS on CT review	58.8 (32.9–81.6)	33.3 (0.8–90.6)	0.57	0.99

Subjects were separated based on whether they had a positive venographic findings of PCS. Binary variables are summarized by percentage (95% confidence interval), while continuous variables are summarized as mean±standard deviation. Reported p values are the results of Fisher's exact test for binary variables and unpaired t-tests for continuous variables. *P*-values controlling for age and BMI are results of logistic regression for each variable, with age and BMI as additional predictors. BMI: Body mass index, CT: Computed tomography, PCS: Pelvic congestion syndrome, IBS: Irritable bowel syndrome

Table 2: Treatment outcome.

Variable	Complete Response (*n*=7)	Partial Response (*n*=23)	No Response (*n*=19)	Technical Failure (*n*=3)	*P*-value (excluding technical failure)
Demographics/Risk Factors					
Age	33.1±9.2	37.9±10.8	36.2±11.8	37.8±1.03	0.60
BMI	25.4±5.7	26.9±6.5	28.4±5.5	27.0±4.9	0.49
Symptoms (%)					
Chronic Pelvic Pain	100 (59.0–100)	100 (85.2–100)	100 (82.4–100)	100	>0.99
Dysmenorrhea	71.4 (29.0–96.3)	60.9 (38.5–80.3)	47.4 (24.4–71.1)	33.3	0.48
Dyspareunia	28.6 (3.7–71.0)	69.6 (47.1–86.8)	57.9 (33.5–79.7)	33.3	0.15
Back Pain	28.6 (3.7–71.0)	26.1 (10.2–48.4)	31.6 (12.6–56.6)	33.3	0.93
Concomitant Diagnosis and Risk factors (%)					
Myofascial pain syndrome	57.1 (18.4–90.1)	54.5 (32.2–75.6)	26.3 (9.1–51.2)	33.3	0.14
Endometriosis	0.0 (0.0–41.0)	26.1 (10.2–48.4)	31.6 (12.6–56.6)	0.0	0.24
Fibromyalgia	0.0 (0.0–41.0)	8.7 (1.1–28.0)	10.5 (1.3–33.1)	0.0	0.68
IBS	14.3 (0.4–57.9)	17.4 (5.0–38.8)	16.7 (3.6–41.4)	0.0	0.98
Prior Pregnancy	85.7 (42.1–99.6)	87.0 (66.4–97.2)	89.5 (66.9–98.7)	100	0.96
Prolonged Standing	42.9 (9.9–81.6)	43.5 (23.2–65.5)	47.4 (24.4–71.1)	33.3	0.96
Imaging (%)					
Prior pelvic US	57.1 (18.4–90.1)	26.1 (10.2–48.4)	36.8 (16.3–61.6)	66.7	
PCS on US review	75.0 (19.4–99.4)	33.3 (4.3–77.7)	33.3 (4.3–77.7)	50.0	0.35
Prior pelvic CT	28.6 (3.7–71.0)	30.4 (13.2–52.9)	26.3 (9.1–51.2)	33.3	
PCS on CT review	0.0 (0.0–84.2)	57.1 (18.4–90.1)	80.0 (28.4–99.5)	57.1	0.16
Catheter Venographic Findings (%)					
Left Reflux/Dilation on venography	85.7 (42.1–99.6)	87.0 (66.4–97.2)	89.5 (66.9–98.7)	100	0.96
Right Reflux/Dilation on venography	57.1 (18.4–90.1)	52.2 (30.6–73.2)	42.1 (20.3–66.5)	33.3	0.73
Unilateral findings	57.1 (18.4–90.1)	56.5 (34.5–76.8)	68.4 (43.4–87.4)	66.7	0.71
Bilateral findings	42.9 (9.9–81.6)	39.1 (19.7–61.5)	31.6 (12.6–56.6)	33.3	0.82

Treated subjects were separated based on outcome (partial, no response, complete response, or technical failure). Binary variables are summarized by percentage (95% confidence interval), while continuous variables are summarized as mean±standard deviation. Reported *P*-values are the results of the Chi-squared test for binary variables and ordinary one-way ANOVA for continuous variables. Pairwise comparisons for binary variables were performed using individual Fisher's exact tests, with *P*-values corrected for FDR. Pairwise comparisons for continuous variables were performed using Tukey's test. *No significant pairwise differences were found for any variables. BMI: Body mass index, CT: Computed tomography, PCS: Pelvic congestion syndrome, IBS: Irritable bowel syndrome

with prior trials ranging from 33.5–60.6% to 4–15%, respectively.[2,4,7,9-11] Among patients with positive findings, 20 patients had bilateral reflux, 36 had unilateral left reflux, and 6 had unilateral right-sided reflux. The sidedness of reflux did not affect outcomes. These findings were similar to prior studies, which have demonstrated that PCS more commonly occurs on the left.[12]

Our results corroborate prior studies, which demonstrated higher rates of chronic pelvic pain secondary to PCS in parous patients.[4] This is hypothesized to occur secondary to the increased pelvic venous capacity that occurs during pregnancy and the distortion of venous structures by the gravid uterus. Both of these factors can alter venous flow resulting in venous varicosities and incompetence.[13] Our review found no difference in treatment outcomes across nulliparous and parous patients. This is likely due to alternative and concomitant conditions resulting in chronic pelvic pain as well as the underlying incidence of PCS in nulliparous women.

BMI was found to be generally lower in patients with positive findings of PCS on venography compared with negative patients. This corroborates a prior study evaluating BMI and venous varicose veins, which found that obese patients are more likely to have lower extremity varices, while patients with lower or normal BMI tended to have ovarian vein dilation.[14] There are several anatomic and biochemical hypotheses that have been proposed to explain this phenomenon. One hypothesis is that abdominal fat may cushion the intrabdominal veins preventing collapse and compression. This is conceptually analogous to prior studies that have found an increased incidence of nutcracker syndrome in patients with lower BMI.[15] This is in contrast to lower extremity varicosities, which are more common in obese patients, likely secondary to larger femoral vein diameters and greater net pressure of lower extremity veins.[14] Another hypothesis revolves around the role of estrogen as a venodilator.[16] Estradiol has been shown to be lower in obese premenopausal women compared with premenopausal

women with a normal BMI. As a result, a higher BMI may indicate lower estrogen levels and decreased venous dilation. The impact of estrogen on venous dilation likely explains the decreased prevalence of PCS in postmenopausal women, as estrogen levels significantly decline following menopause.[17] Finally, recent research has begun to elucidate the role of perivascular adipose tissue in paracrine mediation of arterial vasodilation, which may have implications for venous dilation and the pathophysiology of PCS.[18,19] BMI did not differ across treatment outcomes.

Multiple potentially confounding diagnoses were included in the analysis. It was hypothesized that other concomitant diagnoses resulting in chronic pain would negatively affect rates of PCS findings on venography and positive outcomes. However, concomitant diagnoses did not predict venographic outcomes or treatment response. The majority of patients with prior diagnoses of myofascial pain syndrome and IBS who underwent treatment experienced a complete or partial response. A considerable portion of patients with endometriosis and fibromyalgia experienced a partial response, although they were more likely overall to have no response and none had a complete treatment response. An important limitation was the clinical reporting of endometriosis; several patients had a clinical history or were presumptively diagnosed with endometriosis, as such this diagnosis was not particularly reliable. This finding is multifactorial. It is in part likely due to the patient workup before PCS for chronic pelvic pain, as patients are often presumptively treated for more common etiologies prior to referral for PCS. Secondly, these conditions can occur alongside and overlap symptoms of PCS. However, given our results, patients who experience continued chronic pelvic pain with a known or presumptive diagnosis should also be evaluated for PCS for the aforementioned reasons.

Preprocedural imaging was underutilized in the workup for PCS. The majority of the imaging studies evaluated were for indications unrelated to PCS. Although a larger percentage of patients with positive venographic findings had suggestive findings on prior CT and ultrasound compared with negative venograms, this difference was not significant. Magnetic resonance imaging (MRI) evaluation was only performed on three patients and was excluded from statistical analysis due to a limited sample size. Importantly dedicated studies with Valsalva or dedicated CT venography or MR venography were not routinely performed. Overall, the discrepancies between prior imaging and the gold standard of contrast venography highlight the fact that signs of PCS on diagnostic imaging are variable depending on multiple factors including patient positioning and technique. In addition, a dilated ovarian vein or other imaging findings of PCS are not pathognomonic for the condition.[20-23] However, pre-procedural MRI with venography can help identify dilated veins in patients

suspected of having PCS. These studies can also help identify other confounding conditions including alternative venous pathologies such as May-Thurner and nutcracker syndrome, with sensitivity ranging from 88% to 100% and high specificity if performed with time-resolved venography for reflux. In addition these studies can identify other etiologies of pelvic pain and should be considered at the time of consultation.[24]

Limitations

The retrospective nature of this review limits assessment of certain patient characteristics and introduces bias. Clinical notes which are subject to variability were reviewed to determine outcomes. No standarized outcome instruments, such as a quality of life questionnaire or a visual analog pain scale, were routinely employed.[23,25] In addition, given the variability of patient referrals, there was significant heterogeneity in the workup and imaging of the patients reviewed. However, given the differences that were encountered, this data could be used when developing clinical workflow paradigms or future study protocols. In addition, routing pre-procedural imaging was not obtained in all patients. This is due to the preference of the performing attending interventional radiologists as well as variable sensitivity and specificity of cross-sectional diagnostic imaging compared with the gold standard of contrast venography. Although the lack of prior diagnostic imaging in some patients does preclude potential identification of alternative causes of pelvic pain, the majority of the these patients were clinically evaluated by multiple providers before diagnostic venography.

Finally, in all of the cases reviewed only the renal veins were evaluated. The iliac veins were not routinely evaluated for additional collaterals due to provider preference. This was an important limitation as collaterals can drain to the common and internal iliac veins. In addition, underlying May-Thurner can contribute to venous collaterals. Performing providers annecdotely noted limited benefit in evaluating these other vessels as well as an increased risk of pulmonary embolism for not evaluating and treating collaterals draining to the iliac veins.

CONCLUSION

PCS is a challenging diagnosis for both patients and providers due to significant symptom overlap with other conditions and lack of highly sensitive or specific diagnostic tests. These results suggest that specific predisposing risk factors including a history of prior pregnancy and a lower BMI, along with preprocedural imaging, can support the decision to perform venography for PCS. A larger portion of patients than previously reported may fail to respond to

treatment or fail to achieve a complete treatment response. As presence of a concomitant pelvic pain diagnosis did not affect venographic findings or treatment outcomes, clinicians should be mindful to consider PCS even in patients with concomitant diagnoses.

Declaration of patient consent

Institutional Review Board (IRB) permission obtained for the study.

Financial support and sponsorship

Nil.

Conflicts of interest

Dr. Vikram Dogra is the editor-in-chief of this journal. This manuscript was double-blind peer reviewed by independent reviewers who are not connected with the journal in any personal capacity.

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