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INTERVENTIONAL RADIOLOGY

ORIGINAL ARTICLE

Transcatheter cyanoacrylate embolization vs. pharmacologic therapy for gonadal vein reflux in symptomatic pelvic venous disorders: a randomized controlled trial

Mohamed I. Eleissawy[1]
Hossam M. Mokhtar[1]
Mai N. Ageez[2]
Mohamed A. Eleiwa[1]
AbdelRahman A. Nagy[1]

[1]Tanta University Faculty of Medicine, Department of Vascular and Endovascular Surgery, Tanta, Egypt

[2]Tanta University Faculty of Medicine, Department of Obstetrics and Gynecology, Tanta, Egypt

PURPOSE

Pelvic venous disorders (PeVDs) with gonadal vein reflux are a frequently overlooked cause of chronic pelvic pain in women. Although embolization is increasingly used in practice, high-quality comparative evidence—particularly for cyanoacrylate glue—remains limited. This randomized controlled trial compares cyanoacrylate embolization with conservative pharmacologic management in women with symptomatic PeVDs.

METHODS

Forty women with imaging-confirmed gonadal vein reflux were randomized (1:1) to receive either micronized purified flavonoid fraction (Daflon®, 500 mg twice daily) or transcatheter cyanoacrylate embolization. The primary endpoint was the change in pelvic pain measured by the visual analog scale (VAS). Secondary outcomes included dyspareunia and dysmenorrhea VAS scores, clinical success, symptom recurrence, and adverse events over 12 months.

RESULTS

Embolization yielded earlier and more durable symptom improvement. At 12 months, mean pelvic pain VAS scores were significantly lower in the embolization group (3.20 ± 0.77 vs. 5.10 ± 0.97; $P < 0.001$). Additionally, dyspareunia improved significantly with embolization (1.75 ± 0.91 vs. 3.95 ± 1.91; $P < 0.001$), whereas dysmenorrhea outcomes were comparable between groups. Clinical success was achieved in 95% of patients who received embolization, compared with 70% of those who received Daflon®, although this difference did not reach statistical significance ($P = 0.091$). Lower recurrence was observed in the embolization arm (10% vs. 45%, $P = 0.031$). Kaplan–Meier analysis demonstrated superior recurrence-free survival with embolization (log-rank $P = 0.013$), and Cox regression identified embolization as an independent protective factor against recurrence (hazard ratio: 0.12; 95% confidence interval, 0.02–0.74; $P = 0.021$). No major complications were reported.

CONCLUSION

In women with symptomatic gonadal vein reflux, cyanoacrylate embolization, compared with conservative pharmacologic therapy, appears to provide significantly greater and more durable symptom relief, with low recurrence and an excellent safety profile, although the difference in clinical success rates did not reach statistical significance.

CLINICAL SIGNIFICANCE

In this randomized trial, cyanoacrylate embolization was particularly beneficial for women with documented gonadal vein reflux and symptoms dominated by non-cyclic pelvic pain and dyspareunia. In appropriately selected patients, early intervention may reduce recurrence and avoid prolonged medical therapy with limited durability. Although these preliminary findings support embolization as a potential definitive therapeutic option, larger confirmatory studies are needed before it can be recommended over second-line status.

KEYWORDS

Cyanoacrylate glue, embolization, pelvic congestion syndrome, pelvic varicose veins, PeVDs, venous insufficiency

Corresponding author: AbdelRahman A. Nagy

E-mail: abdelrahman.nagy@med.tanta.edu.eg

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Pelvic venous disorders (PeVDs) are an unrecognized but significant cause of chronic pelvic pain in women, with a reported prevalence ranging from 27% to 50%, most commonly affecting those between 30 and 45 years of age.[1,2] PeVDs are characterized by venous reflux, dilatation, and varicosities within the ovarian and pelvic venous plexuses. Clinically, patients typically present with non-cyclic pelvic pain, dyspareunia, urinary urgency, painful defecation, and occasionally, perineal or lower limb varicosities. Symptoms are often exacerbated by prolonged standing, menstruation, or increased intra-abdominal pressure.[3]

Diagnosis remains challenging due to non-specific clinical features and overlap with gynecologic conditions. Imaging findings typically demonstrate dilated, tortuous gonadal and pelvic veins, retrograde flow, venous stasis, and the formation of convoluted collateral pelvic venous networks.[4] The Symptoms–Varices–Pathophysiology (SVP) classification has improved diagnostic standardization; however, therapeutic decision-making continues to rely primarily on symptom severity rather than imaging findings alone.[5]

Management strategies aim to reduce venous hypertension, improve venous tone, and alleviate inflammation.[6,7] Venoactive agents such as micronized purified flavonoid fraction (MPFF; Daflon®) are frequently used as a first-line treatment, although the available evidence suggests that symptom improvement may be modest and often not durable.[6,8] Other pharmacological options—including progestins, hormonal therapies, and analgesics—have shown variable efficacy and may be limited by systemic side effects.[9]

Main points

- In women with imaging-confirmed gonadal vein reflux, cyanoacrylate embolization provided greater symptom relief than conservative pharmacologic therapy.
- Transcatheter cyanoacrylate embolization resulted in more durable improvement and lower recurrence rates over 12 months.
- Non-cyclic pelvic pain and dyspareunia responded more consistently to reflux elimination than dysmenorrhea.
- By directly occluding incompetent gonadal veins, cyanoacrylate embolization offers a definitive interventional treatment option for pelvic venous disorders.

Endovascular embolization has emerged as an effective alternative that aims to occlude incompetent gonadal and pelvic veins to prevent venous stasis in the pelvic reservoir, thereby reducing excessive pelvic blood flow.[9,10] Multiple embolic agents such as coils, sclerosing foam, and plugs have shown effectiveness, but concerns remain regarding coil migration, allergic reactions, foreign-body burden, and procedural complexity.[11] Cyanoacrylate offers several theoretical advantages, including rapid polymerization, durable vein wall adhesion, reduced migration risk, and potentially a shorter procedural time and lower cost, making it an attractive alternative.

Although multiple studies have evaluated coil or sclerosant embolization for ovarian vein reflux, evidence supporting cyanoacrylate glue remains limited to small case series and retrospective non-comparative or non-randomized cohorts.[12-15] Accordingly, this randomized controlled trial was designed to evaluate the safety and efficacy of transcatheter cyanoacrylate embolization and to test the hypothesis that cyanoacrylate embolization provides superior symptom relief compared with pharmacologic therapy in patients with symptomatic PeVDs related to gonadal vein reflux.

Methods

Study design and selection criteria

This single-center randomized, controlled, open-label trial enrolled 40 women aged 30–50 years presenting with non-cyclic pelvic pain for at least 6 months. The study was approved by the Ethical Committee of Tanta University (approval code: 36264PR752/7/24, date: 15.07.2024) and registered at ClinicalTrials.gov (ID: NCT06560294). Written informed consent was obtained from all participants. No important changes to the study protocol were made after trial commencement. No interim analysis or stopping rules were planned.

This study was conducted from August 2024 over 18 months to allow for completion of patient recruitment and to ensure a minimum 12-month follow-up for all participants.

The diagnosis of PeVD was established using transvaginal ultrasound (TVUS) and computed tomographic venography after excluding alternative gynecological or compressive causes. Reflux was defined as retrograde venous flow lasting longer than 1 second on Doppler interrogation during the Valsalva maneuver. Additional diagnostic criteria included gonadal vein dilatation ≥ 6 mm, the presence of dilated parauterine veins ≥ 5 mm in diameter, and the presence of a tortuous pelvic venous plexus with slow or reversed flow. Transabdominal Doppler ultrasound was considered an alternative imaging approach when TVUS was not feasible or contraindicated. However, in the present study, TVUS was successfully performed in all enrolled patients.

Patients were classified according to the SVP system described by Meissner et al.[5] as $S_2 V_2 P_{GV, R, NT}$ (S_2: chronic pelvic pain of venous origin; V_2: pelvic varices; P_{GV}: gonadal vein involvement; P_R: reflux; P_{NT}: non-thrombotic pathology).

Exclusion criteria included pregnancy at any gestational age, childbirth within the previous 12 months, current breastfeeding, known contrast allergy, renal impairment, gynecologic causes of chronic pelvic pain (e.g., endometriosis, fibroids, adenomyosis, or ovarian cysts), and any previous intervention for PeVDs.

Randomization and blinding

Patients were randomly assigned in a 1:1 ratio to the embolization group or the conservative treatment group using a computer-generated randomization sequence. Randomization was performed using simple random allocation without blocking or stratification. The 1:1 allocation ratio was chosen to ensure balanced group sizes and maximize statistical efficiency, given the anticipated sample size. Allocation concealment was achieved using sequentially numbered, opaque, sealed envelopes, prepared by a researcher not involved in the patient recruitment or outcome assessment. Envelopes were opened only after participant enrollment to ensure that treatment assignment remained concealed during the recruitment process.

Participants were assigned to the following groups:

• Group A (conservative therapy): MPFF (Daflon®), 500 mg twice daily.

• Group B: Transcatheter gonadal vein cyanoacrylate embolization (Figure 1).

No additional interventional or hormonal therapies were administered during the study period.

Due to the differing nature of the interventions, the study was open-label, and the

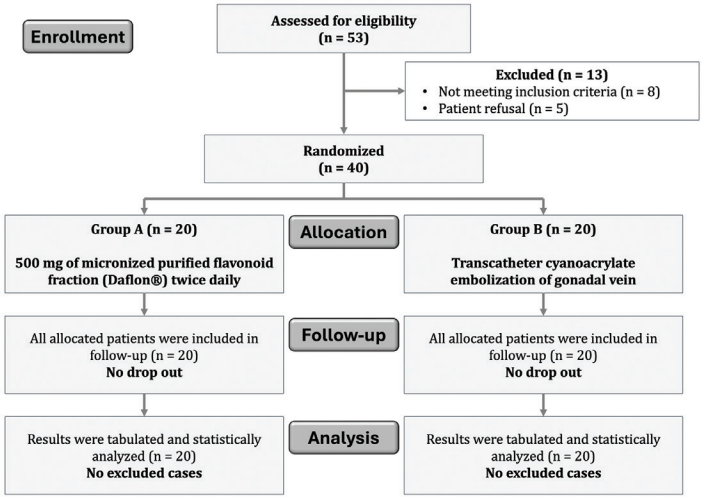

Figure 1. Flow diagram of patient enrollment, allocation, follow-up, and data analysis.

blinding of participants and operators was not feasible. However, outcome assessment was standardized at each follow-up visit and performed using standardized questionnaires administered by an investigator who was blinded to treatment allocation.

Embolization technique

All embolization procedures were performed according to a standardized institutional protocol by experienced interventional vascular surgeons with more than 10 years of experience in venous embolization. Procedures were performed under fluoroscopic guidance using a standardized technique.

The procedure was performed under local anesthesia in an operating room equipped with a Portable high-quality C-arm fluoroscopy; Ziehm Vision® FD (Ziehm Imaging, Nuremberg, Germany). Vascular access was achieved via a 6-French sheath inserted into the femoral vein in 15 patients and the right internal jugular vein in 5 patients.

Diagnostic venography was conducted using a 5-F Cobra or Simmons catheter (femoral approach) or a 5-F multipurpose catheter (jugular approach). Approximately 20 mL of iodixanol contrast (Visipaque™ 320) was manually injected to visualize the iliac veins, inferior vena cava, and left renal vein, with and without the Valsalva maneuver. Because intravascular ultrasound (IVUS) was unavailable, venographic assessment was used to rule out compressive syndromes such as May–Thurner or nutcracker phenomena. Patients were placed in the supine Trendelenburg position. Retrograde venography confirmed ovarian vein incompetence based on reflux and uterine plexus opacification.

In addition to gonadal vein reflux, the pelvic venous system was evaluated for additional reflux pathways, including internal iliac vein tributaries and pelvic venous collaterals. The primary treatment target was the refluxing gonadal vein. Adjunctive embolization of other pelvic venous tributaries was not routinely performed to maintain procedural standardization within the study protocol.

Depending on the venous anatomy and reflux pattern, embolization was performed on the left, right, or both gonadal veins. The number of treated veins per patient and the distribution of unilateral vs. bilateral embolization were recorded.

A 2.8-F, 130-cm coaxial microcatheter (Merit Maestro®) was advanced through the guiding catheter to the target embolization site. The microcatheter dead space was primed with 5% dextrose solution to prevent premature polymerization of the cyanoacrylate.

The embolic mixture was prepared in a 2:1 ratio of Lipiodol® Ultra Fluid (lipiodized oil) to n-butyl-2-cyanoacrylate (Histoacryl®, B. Braun). Under fluoroscopic guidance, the mixture was injected using gentle thumb pressure in a slow pullback technique, beginning distally from the sacroiliac level and continuing proximally. The patient was positioned semi-upright with intermittent Valsalva maneuvers performed to optimize delivery, adjust injection speed based on cyanoacrylate propagation and venous flow, and minimize non-target embolization.

Following the injection, the microcatheter was rapidly withdrawn into the guiding catheter, and both were removed together (to avoid glue spill and non-target embolization). Final venography was performed with a new catheter to confirm complete occlusion (Figures 2, 3).

All patients were observed for 24 hours post-procedure. Pain was managed with non-steroidal anti-inflammatory drugs, and early complications (e.g., hypersensitivity reactions or exothermic-induced perivascular inflammation) were clinically monitored.

Follow-up and definitions

After discharge, patients were advised to rest for 5 days and were followed up virtually after 1 week, then monthly for 3 months, then again at 6 and 12 months. These visits aimed to assess clinical outcomes and monitor for delayed adverse events, such as chronic pelvic inflammation or late-onset pulmonary hypertension following embolization. Additional unscheduled visits were allowed if new or recurring symptoms developed. Outcome assessment in our study was performed by a blinded assessor who was unaware of the treatment allocation.

The primary endpoint was the change in pelvic pain, assessed using the visual analog scale (VAS), a 10-point subjective scale ranging from 0 (no pain) to 10 (worst imaginable pain).[16]

Secondary endpoints included dyspareunia VAS, dysmenorrhea VAS, clinical success, symptom recurrence, and adverse events, including hypersensitivity reactions and non-target embolization.

Clinical success was defined as a reduction of ≥ 2 points in VAS scores sustained at 3 and 6 months, with no major treatment-related complications.

Symptom recurrence was defined as an absolute increase of ≥ 2 points from the lowest VAS scores achieved.

Adverse events were prospectively recorded during follow-up visits and classified according to the Society of Interventional Radiology adverse event reporting standards.

Sample size calculation

Sample size was estimated using G*Power 3.1.9.2 (Universität Kiel, Germany). Based on previously reported mean VAS scores of 4.8 ± 3.2 with MPFF[6] and 1.6 ± 0.67 with embolization,[11] the effect size was 1.384. To achieve 95% power, a value of α: 0.05 and a 1:1 allocation ratio with 20 patients per group were required, with 5 additional cases included to account for potential dropout.

The initial sample size estimation was based on detecting a clinically meaningful difference in VAS pain scores between the treatment groups at follow-up. However, because pain scores were collected at multiple time points, the final analysis used a more robust linear mixed-effects model (LMM) to account for repeated measurements among individuals.

Statistical analysis

Analysis was performed according to the intention-to-treat principle, including all randomized patients. No imputation for missing data was performed; analyses were conducted using available case data.

Data were analyzed using SPSS v.27 (IBM Corp., Armonk, NY, USA). Normality was assessed via the Shapiro–Wilk test and histogram inspection. Continuous variables were compared using independent t-tests or Mann–Whitney U tests, and categorical variables using a chi-square or Fisher's exact test. Data were presented as mean ± standard deviation, median and interquartile range, or frequency (%).

Longitudinal VAS scores were analyzed using an LMM to account for within-subject repeated measures. Post-hoc pairwise comparisons were performed to assess between-group differences at each time point for pelvic pain, dyspareunia, and dysmenorrhea VAS scores. Given the exploratory nature of these comparisons, and to avoid potentially masking clinically meaningful signals, no adjustment for multiple comparisons was applied. All reported *P* values are nominal, and findings should be interpreted accordingly. Kaplan–Meier analysis with a log-rank test assessed recurrence-free survival, and univariate Cox regression identified predictors of recurrence. Statistical significance was set at a P value < 0.05.

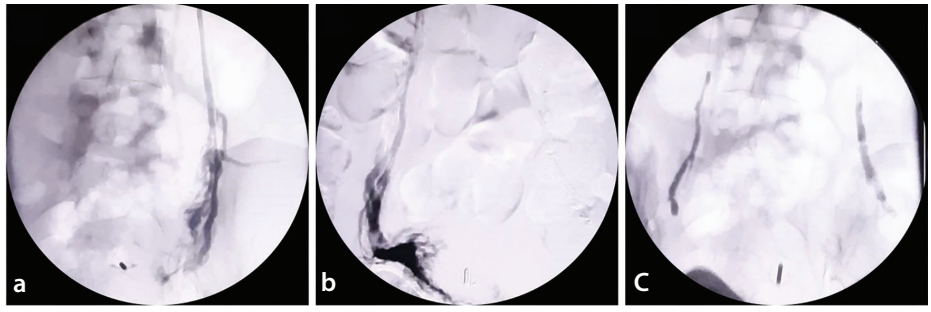

Figure 2. Transcatheter cyanoacrylate embolization (via jugular approach) of both ovarian veins of a 34-year-old patient presenting with chronic pelvic pain and dyspareunia. **(a)** Refluxing left ovarian vein; **(b)** refluxing right ovarian vein; **(c)**, final venography after embolization.

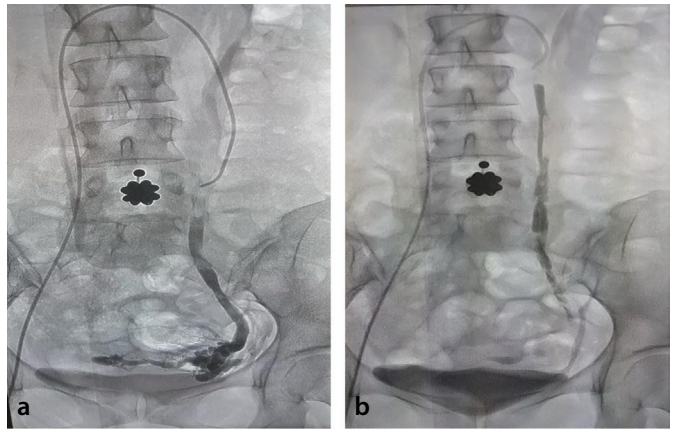

Figure 3. Transcatheter cyanoacrylate embolization (via right femoral approach) of the left ovarian vein of a 28- year-old patient presenting with dyspareunia and dysmenorrhea. **(a)** Dilated left ovarian vein and uterine plexus; **(b)**, final venography after embolization.

Table 1. Baseline demographic and clinical characteristics of the study participants

Variable	Group A, n = 20	Group B, n = 20	*P* value
Age (years)	41.8 ± 6.4	39.2 ± 5.2	0.162
Weight (kg)	76.4 ± 13.0	79.8 ± 9.5	0.344
Height (cm)	168.6 ± 5.9	166.0 ± 6.9	0.207
BMI (kg/m^2)	27.0 ± 5.1	29.2 ± 4.5	0.161
Parity	3 (2–3.25)	2.5 (2–3.25)	0.502
Age at first presentation (years)	35.4 ± 8.2	32.7 ± 5.9	0.237
Symptoms-to-diagnosis interval (months)	61.8 ± 31.0	64.8 ± 19.6	0.716

Data are presented as mean ± SD, median (IQR), or frequency (%). BMI, body mass index; SD, standard deviation; IQR, interquartile range.

Results

Of 53 patients assessed for eligibility, 8 did not meet the inclusion criteria, and 5 declined participation. The remaining 40 patients were randomized equally into 2 groups (Figure 1). No patients were lost to follow-up at 12 months.

Baseline demographic and clinical characteristics were comparable between the groups. The mean age was 41.8 ± 6.4 years in Group A and 39.2 ± 5.2 years in Group B (P = 0.162). No significant differences were found in weight, height, body mass index (BMI), parity, age at first presentation, or duration of symptoms before diagnosis (all $P > 0.05$) (Table 1).

The Pelvic Venous Clinical Severity Score (PVCSS)[17] is a 10-domain tool that scores each symptom from 0 (absent) to 3 (severe); the maximum total is 30, and it was applied only at baseline to provide a comprehensive profile of clinical presentation. However, it was not employed during follow-up due to challenges in standardizing the assessment of certain domains (e.g., urinary and bowel symptoms), and because pain was the primary endpoint. The VAS was selected for longitudinal tracking due to its simplicity, reproducibility, and sensitivity to clinical change.

At baseline, the distribution of pelvic symptoms and the PVCSS scores did not differ significantly between the 2 groups ($P > 0.05$ for all individual items and the summary score) (Table 2). The median PVCSS was 13 in both groups, indicating moderate-to-severe baseline symptom burden.

Component analysis of the PVCSS provided further insight into the nature of symptom presentation among participants. The most frequently reported symptoms were non-cyclic abdominal pain and abdominal heaviness, with both groups showing similar prevalence. Dyspareunia, discomfort in the sacrum/coccyx, and dysuria were also com-

monly reported. In contrast, perineal tenderness and edema were observed in only a minority of cases, while atypical varicosities and menstrual irregularities were infrequent.

Embolization was performed on the left gonadal vein in 15 patients, the right gonadal vein in 1 patient, and bilaterally in 4 patients (20% of the embolization group). Overall, a total of 24 veins were treated in 20 patients. The mean injected volume of the Lipiodol–Histoacryl solution was 2.81 ± 0.15 mL per treated vein. The presence of additional reflux pathways (internal iliac tributaries) was identified in 2 patients, all within the embolization group (10%). However, these were not treated as per protocol.

Pelvic pain, dyspareunia, and dysmenorrhea visual analog scale outcomes

Both groups showed progressive improvement in pelvic pain VAS scores over time, with significantly earlier and greater pain relief in the embolization group. Baseline scores were comparable between Group A (8.35 ± 0.58) and Group B (8.15 ± 0.67; $P = 0.322$). At 1 month, Group B had a substantially lower pain score (5.30 ± 0.57) than Group A (7.75 ± 0.97; $P < 0.001$), a difference that persisted at 3 months (3.20 ± 0.77 vs. 6.35 ± 1.14; $P < 0.001$), 6 months (3.15 ± 0.75 vs. 4.30 ± 1.08; $P < 0.001$), and 12 months (3.20 ± 0.77 vs. 5.10 ± 0.97; $P < 0.001$) (Table 3).

Dyspareunia VAS outcomes followed a similar pattern, with significantly lower scores in the embolization group at all follow-up points ($P < 0.001$ at 1 and 3 months, $P = 0.020$ at 6 months, and $P < 0.001$ at 12 months). Dysmenorrhea VAS outcomes showed modest improvement in both groups, with a statistically significant difference only at the 6-month time point ($P = 0.012$) (Table 3).

These trends are depicted in Figure 4, illustrating the trajectory of pelvic pain (a), dyspareunia (b), and dysmenorrhea (c) VAS scores across the 12-month follow-up period.

Follow-up and treatment outcomes

Clinical success was achieved in 14 patients (70%) in Group A and 19 patients (95%) in Group B ($P = 0.091$), favoring embolization (Table 3). Symptom recurrence occurred significantly more frequently in the conservative group (9 patients, 45%) compared with the embolization group (2 patients, 10%, 1 of whom initially achieved clinical success but experienced symptom recurrence at the 9-month follow-up visit, which was captured in the recurrence analysis and reflected in the Kaplan–Meier curve) ($P = 0.031$) (Table 3).

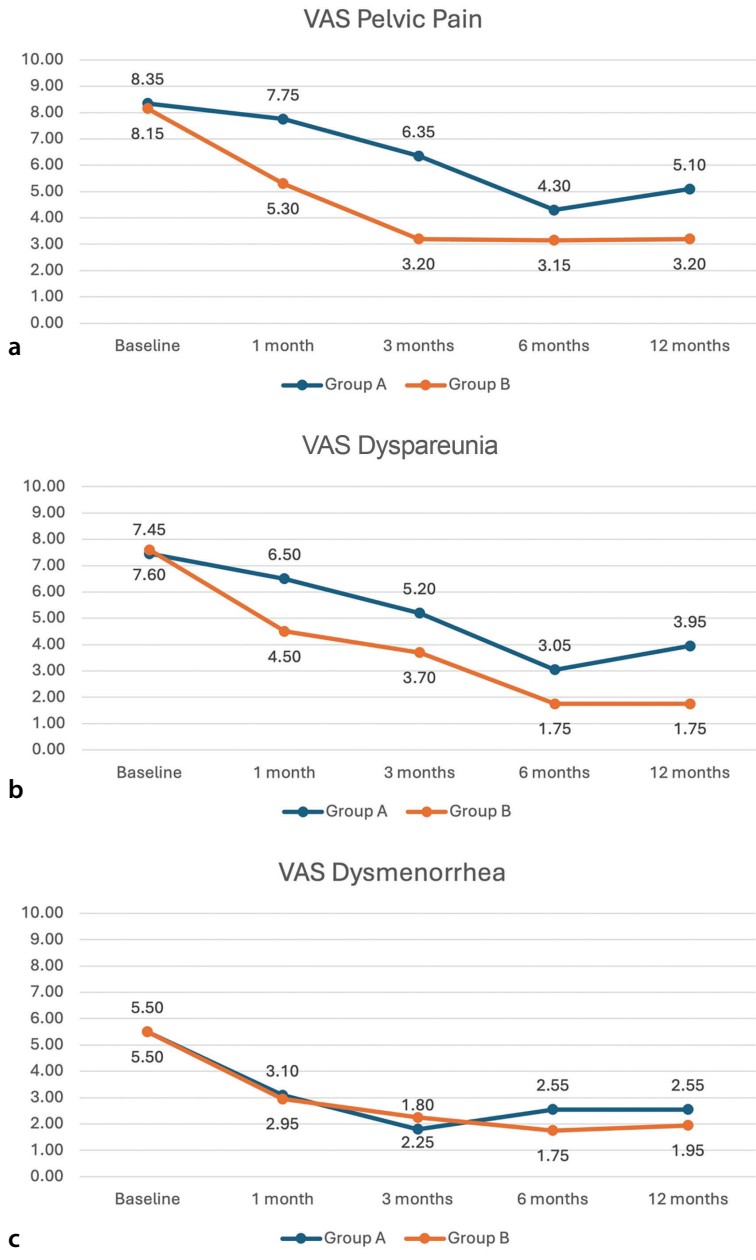

Figure 4. Trends in visual analog scores over 12 months in both treatment groups. VAS, visual analog scale.

Table 2. Pelvic Venous Clinical Severity Score domains at baseline in both groups

Variable	Group A, n = 20	Group B, n = 20	*P* value
Abdominal pain (not during menstruation)	3 (3–3)	3 (3–3)	0.604
Abdominal heaviness	2 (1–2)	2 (1–2.25)	0.703
Abdominal discomfort	1 (1–1.25)	1 (0–1)	0.297
Pain in the sacrum and coccyx	1 (0.75–2)	1 (1–2)	0.781
Dysuria	1 (0–1.25)	1 (0–1)	0.947
Atypical varicosities	0 (0–0)	0 (0–0)	0.801
Dyspareunia (during and/or after intercourse)	2 (2–3)	2.5 (2–3)	0.598
Menstrual disorders	1 (1–1)	1 (1–1)	0.842
Tenderness in the external genitalia area and perineum	1 (1–2)	1 (0–1)	0.173
Edema in the external genitalia area and perineum	0 (0–1)	0 (0–1)	0.723
Summary score	**13 (11–15)**	**13 (12–14)**	**0.531**

Kaplan–Meier survival analysis demonstrated a significantly higher recurrence-free survival in the embolization group (Log-rank test: X^2: 6.12, $P = 0.013$) (Figure 5), suggesting that, beyond the number of relapses, embolization provided more durable symptom relief over time.

Univariate Cox regression analysis identified embolization as the only significant protective factor against symptom recurrence (hazard ratio: 0.12, 95% confidence interval: 0.02–0.74, $P = 0.021$). Other variables, including age, BMI, parity, baseline VAS scores, and duration of symptoms, were not significantly associated with recurrence (Table 4).

Adverse events

In the embolization group, 3 patients (15%) experienced mild post-embolization syndrome, presenting with low-grade fever, pelvic discomfort, and fatigue. One patient (5%) developed a small femoral access site hematoma, which was managed conservatively. No allergic reactions, non-target embolization, or major complications were observed. All adverse events were self-limited and resolved spontaneously within 1 week. Apart from occasional mild gastrointestinal disturbances, such as epigastric discomfort, nausea, and abdominal bloating, no major adverse events were reported in the conservative treatment group.

Table 3. Visual analog scale scores for pelvic pain, dyspareunia, and dysmenorrhea over time and outcome data

Variable	Group A, n = 20	Group B, n = 20	*P* value
Pelvic pain VAS			
Baseline	8.35 ± 0.58	8.15 ± 0.67	0.322
1 month	7.75 ± 0.97	5.30 ± 0.57	< 0.001*
3 months	6.35 ± 1.14	3.20 ± 0.77	< 0.001*
6 months	4.30 ± 1.08	3.15 ± 0.75	< 0.001*
12 months	5.10 ± 0.97	3.20 ± 0.77	< 0.001*
Dyspareunia VAS			
Baseline	7.45 ± 0.89	7.60 ± 0.82	0.582
1 month	6.50 ± 1.05	4.50 ± 0.89	< 0.001*
3 months	5.20 ± 0.83	3.70 ± 0.98	< 0.001*
6 months	3.05 ± 1.32	1.75 ± 1.21	0.020*
12 months	3.95 ± 1.91	1.75 ± 0.91	< 0.001*
Dysmenorrhea VAS			
Baseline	5.50 ± 0.89	5.50 ± 0.89	1.000
1 month	3.10 ± 1.17	2.95 ± 1.10	0.678
3 months	1.80 ± 1.28	2.25 ± 0.97	0.218
6 months	2.55 ± 1.10	1.75 ± 0.79	0.012*
12 months	2.55 ± 1.43	1.95 ± 1.05	0.603
Clinical success	14 (70%)	19 (95%)	0.091
Recurrence events	9 (45%)	2 (10%)	0.031*

VAS values are presented as mean ± SD. *P* values are derived from a linear mixed-effect model for repeated within-subjects measures. Clinical success was assessed at the 3- and 6-month follow-up time points, while recurrence refers to symptom relapse after an initial successful response. *P* value ≤ 0.05 is considered significant (*).
VAS, visual analog scale; SD, standard deviation.

Table 4. Univariate Cox regression analysis of predictors for symptom recurrence

Variable	HR	95% CI		*P* value
		Lower	Upper	
Age (years)	1.07	0.81	1.43	0.619
Weight (kg)	0.96	0.34	2.68	0.927
Height (cm)	0.89	0.34	2.34	0.810
BMI	1.01	0.07	15.43	0.990
Parity	1.54	0.67	3.55	0.307
Age at first presentation (years)	0.78	0.60	1.02	0.708
Symptoms-to-diagnosis interval (months)	1.02	0.98	1.05	0.342
Intervention (embolization)	0.12	0.02	0.74	0.021*
Pelvic pain baseline VAS	1.99	0.49	8.13	0.342
Dyspareunia baseline VAS	1.31	0.55	3.17	0.544
Dysmenorrhea baseline VAS	1.25	0.36	4.41	0.727

P value ≤ 0.05 is considered significant (*). BMI, body mass index; CI, confidence interval; HR, hazard ratio; VAS, visual analog scale.

Discussion

PeVDs are increasingly recognized as an important but underdiagnosed cause of chronic pelvic pain in women. However, optimal management remains the subject of ongoing debate, where clinical guidelines and practice patterns vary widely, largely due to a lack of high-quality comparative data between medical and endovascular therapies[4,5] Although embolization has gained broader acceptance, most studies have evaluated traditional agents such as coils or foam, while prospective evidence supporting cyanoacrylate glue remains limited.[12-15] Additionally, direct comparisons between interventional treatments and pharmacologic therapy are scarce, with most available studies limited to case series or observational designs.[18] Accordingly, this randomized controlled trial provides higher-level evidence addressing both of these gaps.

The present study demonstrates that transcatheter cyanoacrylate ovarian vein embolization provides superior and more durable symptom relief compared with conservative therapy in patients with pelvic venous disease. Patients undergoing embolization experienced earlier pain reduction, superior 12-month pelvic pain scores, higher—yet non-significant—clinical success rates (95% vs. 70%, $P = 0.091$), and significantly lower recurrence (10% vs. 45%; $P = 0.031$). Conversely, patients who were managed conservatively showed only partial and less durable benefit over time. This difference likely reflects embolization's ability to directly eliminate pathological venous reflux, offering a more definitive therapeutic strategy than medical modulation of venous tone alone.

These findings support the concept that the correction of underlying venous reflux offers a more definitive therapeutic strate-

gy than medical modulation of venous tone alone.

MPFF (Daflon®) is widely used for PeVDs due to its venoactive, anti-inflammatory properties and microcirculatory effects. However, evidence regarding its long-term efficacy in PeVDs remains inconsistent. In our study, patients treated with Daflon® experienced only modest symptom improvement, with mean pelvic pain VAS scores decreasing from 8.35 ± 0.58 at baseline to 5.10 ± 0.97 at 12 months. Clinical success was achieved in only 14 of 20 patients (70%), and nearly half experienced symptom recurrence (45%) during follow-up. These findings are consistent with those of Akhmetzianov and Bredikhin,[6] who reported a 12.7-point reduction in pain scores (on a 100-mm scale) after 2 months of Daflon® therapy ($P < 0.05$), along with improvement in global quality of life in 90.5% of patients. However, Simsek et al.[19] found no significant difference between Daflon® and a placebo in pain relief, while Tsukanov et al.[20] and Gavrilov et al.[7] reported only partial symptom relief in small cohorts.

Although MPFF is generally considered safe, gastrointestinal disturbances—including epigastric discomfort, nausea, and abdominal bloating—are reported as adverse effects.[7] Although typically mild, such symptoms may negatively affect compliance in patients requiring prolonged therapy. On the other hand, embolization is a one-time intervention that eliminates the need for continuous medication. Therefore, differences in treatment burden and adherence may partially explain the higher recurrence observed in the conservative group.

At 1 month, pelvic pain VAS scores decreased markedly in the embolization group compared with a modest reduction noted in the conservative group. This trend continued across all follow-up points. Notably, in the conservative group, pelvic pain scores worsened between 6 and 12 months, suggesting that the symptom relief provided by MPFF may be transient and wane over time. This supports the concept that pharmacological therapy does not address the underlying hemodynamic abnormality of gonadal vein venous reflux.

Our results align closely with prior studies demonstrating significant and sustained symptom reduction following embolization. Kim et al.[10] reported long-term improvement after coil embolization (a VAS reduction from 7.6 to 2.9 over nearly 4 years), whereas Laborda et al.[21] observed a sustained decrease from 7.34 to 0.78 after 5 years with metal coils. More directly relevant, Gong et al.[13] demonstrated that Glubran-2 glue reduced VAS scores from 7.57 ± 1.81 to 0.86 ± 0.69 at 6 months. The present study extends these findings by providing randomized controlled evidence that directly compares cyanoacrylate embolization with pharmacological therapy. The rapid polymerization, effective vein wall sealing, and minimal risk of migration may enhance durable venous occlusion. Additionally, cyanoacrylate embolization may offer economic advantages over coil embolization because it generally requires fewer materials and shorter procedure times. However, a formal cost-effectiveness analysis was not performed in this study, and future studies incorporating economic evaluation are warranted.

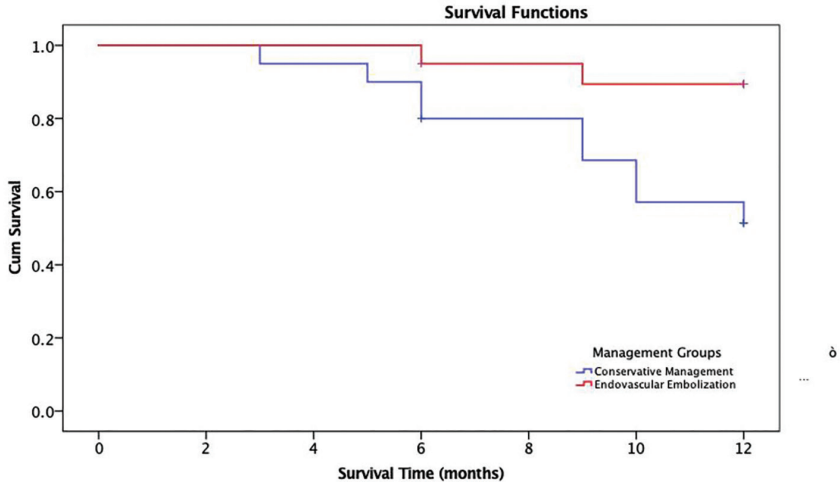

Figure 5. Kaplan–Meier curve for symptom recurrence-free survival. Log rank (Mantel–Cox): X^2: 6.12, $P = 0.013$*.

Dyspareunia, a hallmark and often distressing symptom of PeVDs, responded more favorably to cyanoacrylate embolization than to conservative therapy in our study. Baseline dyspareunia VAS scores were similar between groups (7.45 ± 0.89 in the conservative group vs. 7.60 ± 0.82 in the embolization group; $P = 0.582$). However, by 12 months, the embolization group showed a significantly greater reduction (1.75 ± 0.91) compared with the conservative group (3.95 ± 1.91; $P < 0.001$). This supports the role of embolization in alleviating venous congestion-related pain during intercourse, an issue often insufficiently addressed by conservative management. Our findings align with those of Gong et al.,[13] who demonstrated substantial dyspareunia improvement with Glubran-2 embolization, and Maleux et al.,[12] who found that 72% of women with pre-procedure dyspareunia experienced relief after embolization. In contrast, Akhmetzianov and Bredikhin[6] reported persistent dyspareunia in 61.9% of patients treated with Daflon®, underscoring the limited effectiveness of pharmacologic therapy for this symptom. Collectively, these results suggest that dyspareunia—often refractory to conservative measures—may be more effectively addressed with endovascular intervention.

Nevertheless, dysmenorrhea demonstrated only modest and less consistent between-group differences. Menstrual pain is multifactorial and primarily mediated by prostaglandin-induced uterine hypercontractility, hormonal fluctuations, and inflammatory mechanisms independent of venous reflux.[22,23] Although pelvic venous congestion may exacerbate menstrual discomfort, it is unlikely to represent the principal driver of dysmenorrhea in most patients. Systematic reviews of embolization for PeVDs have similarly demonstrated more consistent improvement in non-cyclic pelvic pain than in menstrual pain.[18] Consequently, embolization may exert a secondary rather than primary effect on dysmenorrhea.

Cyanoacrylate embolization was well tolerated in our cohort, with no major complications observed. Mild post-embolization syndrome—manifesting as low-grade fever and transient pelvic discomfort—occurred in 3 patients (15%), and 1 patient (5%) developed a small femoral access site hematoma that resolved with conservative management. All adverse events were self-limited and resolved within 1 week. These findings are consistent with those of Maleux et al.,[12] who reported no major complications in their series of glue embolization.

This study has some limitations. First, the modest sample size limited subgroup analyses and reduced the statistical power to detect certain between-group differences or late events. A post-hoc power calculation for the clinical success outcome (95% vs. 70%, $P = 0.091$) yielded an observed power of 55.1%, indicating limited power to detect differences of this magnitude and suggesting a potential risk of type II error.

Second, although an outcome assessment was performed by a blinded assessor to mitigate investigator-related bias during data collection, patient-reported outcomes remain susceptible to expectation bias inherent to the open-label design. Assessor blinding cannot fully mitigate this effect. Although a sham-controlled design could theoretically reduce such bias, its feasibility in this clinical context is limited due to ethical and procedural considerations.

Third, the single-center design and the high level of operator experience may limit generalizability, particularly in centers with less experience in venous embolization.

Fourth, IVUS was not available to systematically exclude potential compressive syndromes. In addition, the study protocol focused on embolization of the refluxing gonadal vein, and adjunctive embolization of other pelvic venous tributaries was not routinely performed. This may have undertreated some patients with multilevel reflux and represents a methodological limitation that could affect the generalizability of our findings.

Fifth, the conservative treatment arm consisted of MPFF monotherapy. Although MPFF is widely used for chronic venous disorders and may improve venous symptoms, conservative management of PeVDs may also include hormonal therapy or combination regimens. Therefore, MPFF alone may not fully represent the spectrum of conservative strategies used in clinical practice, although it was selected to provide a standardized pharmacologic comparator. Additionally, compliance with twice-daily MPFF therapy was not objectively measured and was assumed based on patient reporting. Variations in adherence may have influenced outcomes and represent a potential unmeasured confounder.

Finally, follow-up was limited to 12 months, precluding assessment of long-term durability.

Future multicenter studies with larger populations, longer follow-up, and direct comparisons of different embolic materials are warranted to further validate these findings.

In women with symptomatic gonadal venous reflux, transcatheter cyanoacrylate embolization provided greater and more durable symptom relief than conservative treatment with MPFF. Embolization was associated with superior improvement in pelvic pain and dyspareunia, lower recurrence rates, and an excellent safety profile.

By directly addressing the underlying venous reflux, cyanoacrylate embolization offers a definitive therapeutic approach, particularly in patients with documented reflux who have failed or declined medical therapy. These findings support its role as a safe and effective interventional option in the management algorithm of PeVDs.

Footnotes

Conflict of interest disclosure

The authors declared no conflicts of interest.

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