Efficacy and safety of ovarian vein embolization with N-butyl-2 cyanoacrylate for pelvic venous disorder: Analysis of 100 cases

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ABSTRACT

Objective: The aim of this study was to evaluate the safety and efficacy of ovarian vein embolization using N-butyl-2 cyanoacrylate (NBCA) for treating pelvic venous disorder-associated chronic pelvic pain.

Methods: This retrospective study analyzed 100 patients who underwent ovarian vein embolization with NBCA at a single institution between February 2018 and June 2024. Pelvic venous insufficiency was confirmed by duplex ultrasound and abdominal computed tomography or magnetic resonance imaging, and NBCA was the sole embolic agent. Pain levels were assessed pre- and post-procedure using the Visual Analogue Scale (VAS) in three categories: pain on standing, dyspareunia, and menstrual pain. Follow-up included clinical evaluation and VAS scoring at 1 to 3 months and annually. Statistical analysis determined the significance of pain reduction.

Results: Technical success was achieved in all cases, with complete occlusion of the target veins. Clinical success was observed in most patients, with significant improvement in VAS scores across all categories ($P < .05$). Due to symptom recurrence, four patients (4%) required reintervention during follow-up. No NBCA-related complications were reported.

Conclusions: In our study, ovarian vein embolization with NBCA appears to be a safe and effective treatment for pelvic venous disorder-associated chronic pelvic pain, providing significant pain relief. Additionally, it offers advantages over permanent metal implants such as the potential for gradual polymer degradation over time and avoiding interference in future imaging studies. (J Vasc Surg Venous Lymphat Disord 2025;■:102256.)

Keywords: Chronic pelvic pain; N-butyl-2 cyanoacrylate; Ovarian vein embolization; Pelvic venous disorder

Pelvic venous insufficiency is one of the causes of pelvic venous disorder (PeVD), characterized by chronic symptoms such as chronic pelvic pain (CPP), perineal heaviness, urinary urgency, and dyspareunia.[1] CPP is defined as noncyclic pelvic pain lasting more than 6 months.[2]

Despite growing awareness, the exact cause of CPP secondary to PeVD remains unclear and is likely influenced by multiple factors. Pelvic vein incompetence, with retrograde flow in the varicose utero-ovarian plexus, is considered a major contributor.[3] Symptoms of pelvic congestion syndrome appear to result from increased pelvic venous pressure, leading to venous distension around the uterus. This is likely due to hormonal, genetic, and hemodynamic factors that cause venous dilation, reduced elasticity, and venous valve incompetence.[2]

Endovenous embolization of the gonadal vein, with or without concomitant treatment of the internal iliac vein or its branches, is the standard procedure for treating CPP in these patients due to its effectiveness and low complication rate (recommendation class 2A, level of evidence B).[4] The goal of embolization is to occlude incompetent veins, thereby reducing venous pressure in the pelvic vein plexus.[5] Previous studies have reported success rates of 96% to 100%, with recurrence rates of up to 32%, whereas embolization-related complications are rare and nonfatal.[4]

Various approaches to ovarian vein embolization have been described, with differences in access techniques and embolic agents, including sclerosants, coils, and plugs. New embolic materials, such as absorbable polymer plugs, continue to emerge.[6] However, comparative studies on embolization agents are lacking, and no trials have shown significant differences in clinical outcomes between them.[7]

Liquid embolic agents like N-butyl-2 cyanoacrylate (NBCA) are widely used to achieve hemostasis in acute arterial haemorrhage.[8] A key advantage of NBCA is its rapid polymerization, making it a potential option for treating PeVD. Its mechanism of action provides a dual benefit: it ensures complete occlusion independent of

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the coagulation cascade and induces vessel sclerosis through endothelial necrosis followed by an inflammatory reaction. As a liquid agent, it also diffuses through collateral pathways, potentially increasing procedural efficacy.[9] However, few studies have reported on NBCA use for PeVD-related CPP. This study aimed to evaluate the safety and efficacy of ovarian vein embolization using NBCA for PeVD treatment.

METHODS

This report presents the initial experience with the first 100 patients treated at a single institution using a standardized protocol for ovarian vein embolization with NBCA as the sole embolic agent.

This study was approved by the Institutional Review Board of Clínica Universidad de Navarra (Approval Number: 2024.289) and conducted in accordance with current ethical guidelines, including the Declaration of Helsinki. Patient data were pseudonymized to ensure confidentiality and privacy. Written informed consent was obtained from all patients for the publication of images related to their procedures.

In this retrospective study, we analyzed data from our medical database covering February 2018 to June 2024, including demographic and pathological variables: age, sex, number of births, clinical presentation (chronic pelvic pain, vulvar varices, lower limb varicose veins), diagnostic methods (ultrasound, computed tomography [CT], magnetic resonance imaging [MRI], or phlebography) and anatomical location of the embolized veins (left ovarian vein, right ovarian vein, bilateral or isolated pelvic varices).

This study included patients referred to the Unit of Vascular Surgery and Interventional Radiology for CPP evaluation or lower limb varicose veins. Per our institutional protocol, all patients were assessed for symptoms, particularly chronic lower abdominal pain relieved by lying down and worsened by standing or during the premenstrual period. This pain, often accompanied by dyspareunia and leg fullness, had to persist for over 6 months. Patients were also examined for potential PeVD signs (varicose veins in the perineum, buttocks, or lower extremities) and evaluated by an experienced gynecologist to rule out other CPP causes. All suspected cases underwent venous abdominal Doppler ultrasound and contrast-enhanced abdominal imaging (CT or MRI venogram). Baseline Visual Analogue Scale (VAS) scores were recorded for three CPP symptoms: menstrual pain, pain while standing, and pain during intercourse.

Ultrasound diagnostic criteria included visualization of a dilated ovarian vein axis (>6 mm in the supine position), dilated tortuous arcuate veins in the myometrium communicating with bilateral pelvic varices, slow blood flow (<3 cm/s), and reversed caudal or retrograde flow in the left ovarian vein.

ARTICLE HIGHLIGHTS

- **Type of Research:** Single-center retrospective cohort study
- **Key Findings:** Among 100 patients undergoing ovarian vein embolization with N-butyl-2 cyanoacrylate (NBCA) for pelvic venous disorder-associated chronic pelvic pain, technical success was achieved in all cases. Significant pain reduction was observed across all assessed categories ($P < .05$), with a 4% reintervention rate and no NBCA-related complications.
- **Take Home Message:** Ovarian vein embolization with NBCA appears to be a safe and effective treatment for chronic pelvic pain caused by pelvic venous disorder, offering complete vein occlusion and significant symptom relief without permanent metal implants.

MRI or CT findings compatible with PCS were defined as:[1] ovarian vein dilation >5 mm on T2-TRUFI sequences,[2] varicose dilation and tortuosity of the hypogastric veins,[3] and reversal flow in the ovarian and/or parauterine veins on TWIST sequences (Fig 1).

Patients with compatible symptoms and imaging criteria were offered embolization.

Procedure. The procedures were performed by a vascular surgeon and an interventional radiologist in a hybrid operating theater (Artis Pheno; Siemens Healthcare) under local anesthesia and sedation. Access was obtained via the right basilic vein using a 4 Fr (11 cm) sheath (Radiofocus Introducer II; Terumo Europe). A standard 0.35-inch (260 cm) hydrophilic Glidewire (Terumo Europe) and a multipurpose catheter (Tempo Aqua; Cordis) were advanced into the left renal vein to reach the left ovarian vein origin. A left renal venogram was initially obtained using the diagnostic catheter.

Selective catheterization of the left ovarian vein was performed using the same 4 Fr (100 cm) multipurpose catheter and hydrophilic guidewire. Retrograde venography confirmed reverse flow and valvular incompetence in the left ovarian vein.

In cases with a dilated and incompetent periuterine venous plexus, catheterization was performed using a 165-cm, 2.7 Fr pre-shaped torqueable microcatheter with a preloaded guidewire (Direxion Transend 14 System Preloaded Torqueable Microcatheter; Boston Scientific). A coaxial technique was used from the 4 Fr diagnostic catheter positioned in the left ovarian vein to initiate injection at this level.

All patients received an embolic agent consisting of ethiodized oil (Lipiodol Ultra Fluid; Guerbet) and NBCA (Glubran2; GEM). The mixture was emulsified at a 5:1 ratio (5 parts Lipiodol to 1 part NBCA) using two clean, dry Luer

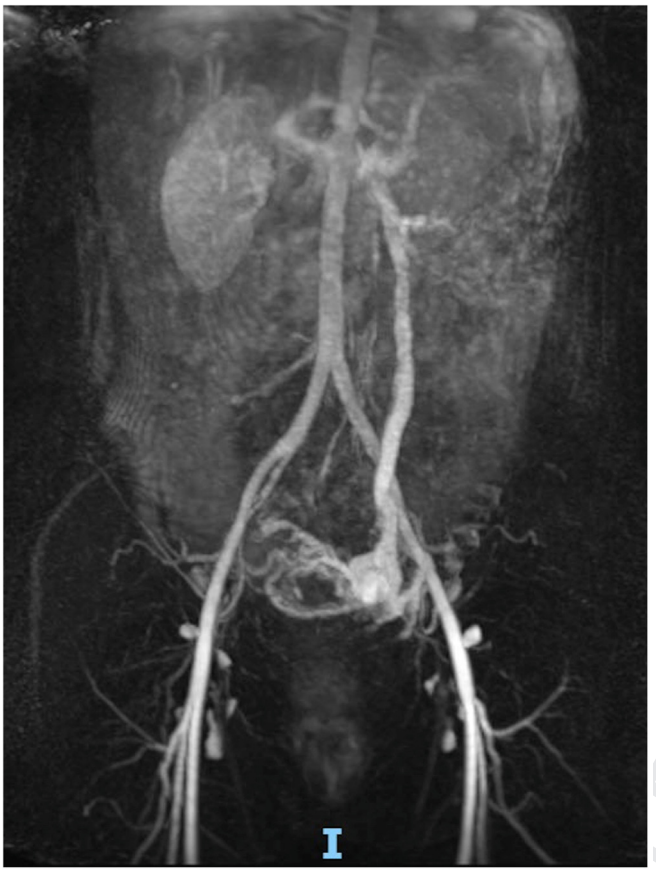

Fig 1. Magnetic resonance imaging (MRI) showing left gonadal vein insufficiency with associated peri-uterine varicose veins.

lock disposable syringes and a three-way tap. To prevent premature polymerization within the microcatheter, its dead space was prefilled with 5% dextrose solution before injection. The Lipiodol-NBCA mixture was injected under fluoroscopic guidance using a pullback technique and continuous manual injection, allowing real-time distribution across the pelvic varices and the left gonadal vein axes (Fig 2, *A*).

In the event that the vein to be embolized was the right gonadal vein, a similar procedure was done, with selective catheterization of the right gonadal vein and embolization using NBCA as with the left gonadal vein (Fig 2, *B*).

If bilateral embolization was performed, to access the right ovarian vein, the uterine venous plexus was visualized and catheterized to facilitate a crossover anterograde approach through the left ovarian vein using a microcatheter to navigate through the uterine plexus. This technique was described and published by our group[10] (Fig 3).

Efficacy, safety, and follow-up. The efficacy of ovarian vein embolization with NBCA was evaluated both technically and clinically. Technical success was defined as complete occlusion of the target incompetent varicose ovarian vein and reflux pelvic veins on final venography.[5]

As part of our institutional protocol, VAS scales were self-administered at each follow-up consultation to assess pain perception using a dedicated questionnaire covering three categories: pain on standing, dyspareunia, and menstrual pain. The VAS score ranged from 0 to 10, with 0 indicating no pain and 10 indicating the worst pain possible.

Clinical success was defined as complete or slight improvement in CPP symptoms without the need for repeat endovascular treatment.

Safety was evaluated based on complications observed during NBCA embolization and postintervention. Clinical efficacy was assessed by comparing preoperative and follow-up VAS scores.

Demographic, intraoperative, and follow-up data were recorded in a dedicated database and analyzed using STATA version 14.2 (StataCorp). The Shapiro-Wilk test was used to assess the normality of quantitative distributions. Numeric pain perception scores were analyzed using the paired Student's *t*-test, with results presented as means and standard deviations. Statistical significance was set at a *P*-value of $< .05$.

RESULTS

Diagnostic confirmation of pelvic venous insufficiency was achieved through abdominal ultrasound and abdominal imaging (CT scan or MRI [Fig 1]) in 89 patients (89%), whereas abdominal duplex ultrasound alone was used in eight patients (8%).

Additionally, three patients were referred from other institutions with a diagnostic phlebography.

NBCA was used as the sole embolic agent in all 100 patients.

The demographics, clinical presentation, and lesion locations of patients with CPP who underwent ovarian vein embolization are summarized in Table I. The treated conditions included CPP in 77 patients (77%), vulvar varices in 12 patients (12%), and lower limb varicose veins in 50 patients (50%).

The anatomical distribution of embolized veins was as follows: 77 cases (77%) involved the left ovarian vein, five cases (5%) involved the right ovarian vein, 11 cases (11%) involved both ovarian veins, and seven cases (7%) involved only periuterine varicose veins (Fig 4).

Final venography revealed complete occlusion of all targeted varicose veins, confirming technical success in all patients.

No NBCA-related complications occurred intraoperatively or postintervention.

The mean fluoroscopy time per procedure was 13.8 ± 9.4 minutes, whereas the mean total intervention time was 41.2 ± 15.2 minutes. These times reflect the feasibility of the technique and its relatively short duration compared with other published studies with coils and

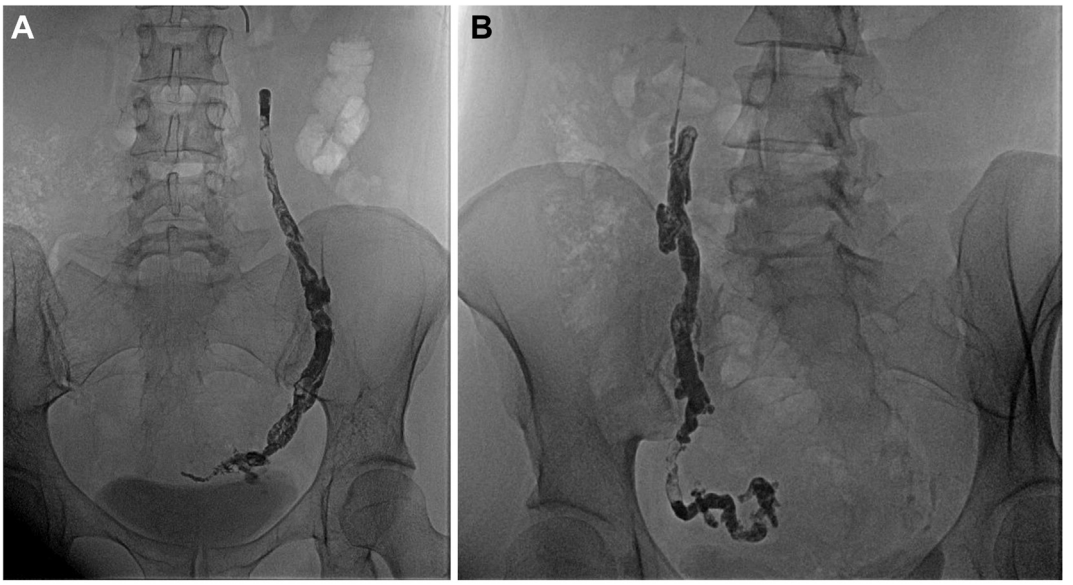

Fig 2. A, N-butyl-2 cyanoacrylate (NBCA) embolization of the left gonadal vein. **B,** NBCA embolization of the right gonadal vein.

glue.[11,12] The use of NBCA allowed for efficient vein occlusion without the need for repositioning or multiple embolic deployments, which may contribute to procedural efficiency.

At the first follow-up visit (mean, 41.3 ± 11.1 days; range, 7-83 days), all dominant symptoms showed considerable improvement, with a significant reduction in all VAS categories.

Mean pre-procedural VAS scores were 7.1 ± 1.3 for pain on standing, 6.5 ± 1.5 for dyspareunia, and 6.8 ± 1.4 for menstrual pain. Post-procedural VAS scores at last follow-up were significantly lower in all categories: 2.3 ± 1.1 for pain on standing, 2.0 ± 1.2 for dyspareunia, and 1.9 ± 1.0 for menstrual pain ($P < .05$ for all categories). This improvement remained consistent over time (Table II), with final VAS scores at the last follow-up visit significantly lower than preintervention values ($P < .05$).

Seventeen patients (17 % of the cohort) gave birth to 22 healthy babies during the follow-up period.

Eleven patients (11%) had recurrent symptoms after treatment, and four (4%) of them required new embolization.

DISCUSSION

CPP of venous origin is one of the most common causes of CPP in women, resulting from pathologic hemodynamics in the ovarian and uterine venous plexus. The estimated prevalence of CPP is 3.8% among women aged 15 to 73 years, which is higher than that of migraine (2.1%) and similar to that of asthma (3.7%) or back pain (4.1%).[13] In primary care settings, 39% of women report pelvic pain, and 16% of all women experience CPP.[14]

In 1993, Edwards et al published the first case of bilateral gonadal embolization with coils.[15] Although other treatment options, such as endoscopic ligation,[16] have demonstrated good short-term outcomes, endovascular embolization remains the preferred approach.[4]

Various embolic agents have been used in ovarian vein embolization, with coils being the most common. Several retrospective case series have documented their effectiveness.[17-19] Kim et al reported a significant reduction in VAS scores from 7.6 pre-procedure to 2.9 at

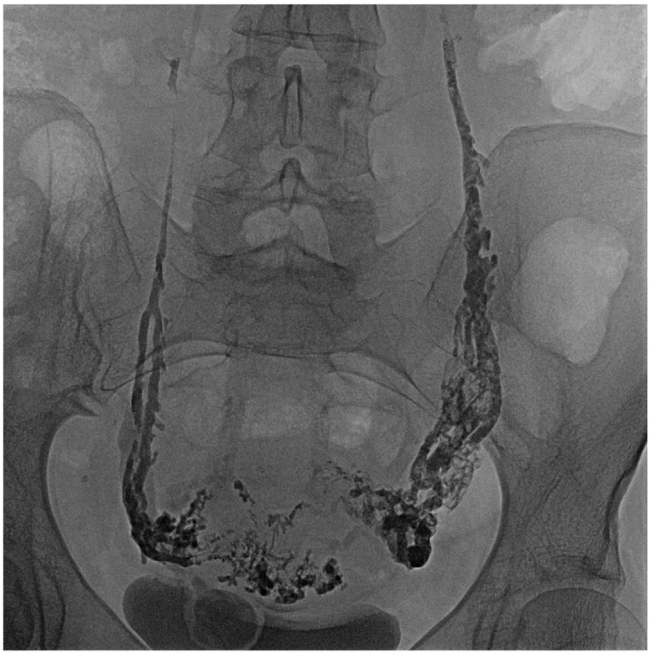

Fig 3. Bilateral gonadal vein embolization through a crossover technique with N-butyl-2 cyanoacrylate (NBCA).

Table I. Demographics, presentation and lesion location of patients with chronic pelvic pain (*CPP*) who underwent ovarian vein embolization with N-butyl-2 cyanoacrylate (NBCA)

Characteristic	Value
Age, years	40.2 ± 9.4 (25–71)
Female sex	100 (100)
Births	3.01 ± 1.91 (0–9)
Diagnostic	
CT + US	26 (26)
RI + US	63 (63)
Duplex US	8 (8)
Phlebography	3 (3)
Location	
LOV	77 (77)
ROV	5 (5)
Bilateral	11 (11)
Isolated pelvic varicose veins	7 (7)
Clinical presentation	
Chronic pelvic pain	77 (77)
Vulvar varices	12 (12)
Lower limbs varicose veins	50 (50)
CPP symptoms (VAS score)	
Pain on standing	7.74 ± 1.03
Dyspareunia	7.22 ± 1.3
Menstrual pain	4.63 ± 3.1

CT, Computed tomography; *LOV*, left ovarian vein; *MRI*, magnetic resonance imaging; *ROV*, right ovarian vein; *US*, ultrasound; *VAS*, visual analogue scale.
Data are presented as number (%) or mean ± standard deviation.

45 months post-embolization using foam sclerosant.[19] Laborda et al observed a similar reduction in VAS scores, from 7.34 to 0.78, at a 5-year follow-up in patients treated with metal coil embolization.[17] However, no studies have definitively proven the superiority of one embolic agent over another.

Our experience with NBCA embolization has progressively evolved over time. During the initial phase, some patients were treated with a combination of NBCA and other embolic agents—such as detachable coils or polidocanol foam—particularly in territories where NBCA control was still being optimized. These cases were excluded from the current analysis, which focuses exclusively on patients treated with NBCA as the sole embolic agent.

Based on accumulated experience, we have developed a structured treatment protocol tailored to the hemodynamic relevance of each venous territory. Gonadal veins and the periuterine venous plexus are the primary targets for embolization, as they are usually the main contributors to pelvic venous hypertension. Obturator and pudendal veins are systematically assessed, but only

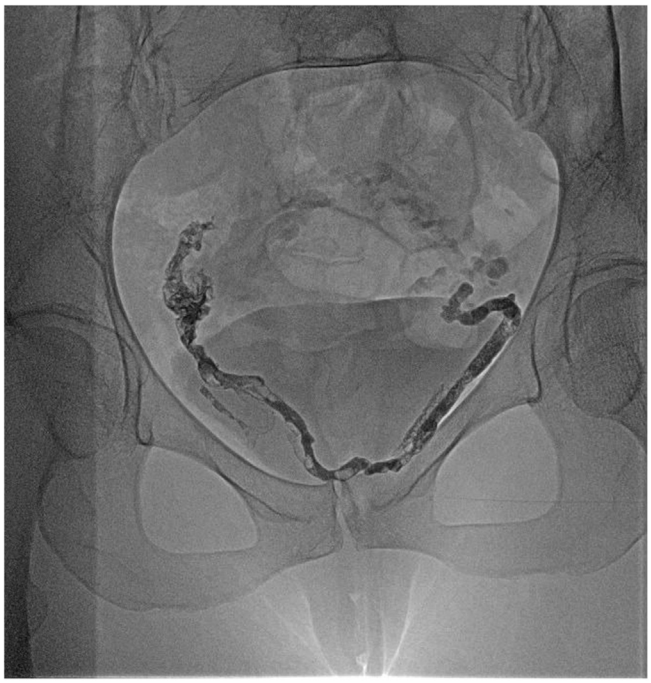

Fig 4. N-butyl-2 cyanoacrylate (NBCA) embolization of periuterine veins.

embolized when clear hemodynamic involvement is confirmed. In these cases, we prefer to use polidocanol foam due to the complex and tortuous anatomy of these veins.

In this study, NBCA was used with excellent and consistent results, significantly reducing VAS scores across the three evaluated categories: pain while standing, dyspareunia, and menstrual pain. The success of NBCA may be attributed to its unique physicochemical properties, allowing polymerization to occur independently of the coagulation cascade. Upon contact with blood, NBCA polymerizes immediately, leading to rapid and complete occlusion of insufficient venous axes.[5]

Our findings suggest that NBCA may provide effective relief for CPP by treating not only the main ovarian veins but also the multiple small varicose tributaries that often contribute to recurrence. Despite this advantage, 11 patients in our study did not experience substantial symptom relief, and four required repeat embolization using NBCA.

Safety is a crucial consideration in ovarian vein embolization. Although complications are rare, the most significant concern is the risk of non-target embolization, particularly pulmonary migration of embolic material.[20,21] This event is typically related to suboptimal glue concentration or inappropriate coil sizing, which may result from an inaccurate assessment of pelvic vein caliber in the presence of vasospasm.[22] This risk of pulmonary embolization is inherently higher in ovarian vein embolization than in treatments for lower limb

Table II. Changes in Visual Analogue Scale (VAS) pain before and after embolization procedure

Clinical condition	Preoperative	1-3 months	1 year
Pain on standing	7.74 ± 1.03	2.16 ± 1.86[a]	1.77 ± 1.31[a]
Dyspareunia	7.22 ± 1.3	2.55 ± 1.66[a]	2.33 ± 1.22
Menstrual pain	4.63 ± 3.10	2.22 ± 1.92[a]	1.77 ± 1.32[a]

Data are presented as mean ± standard deviation.
[a] $P < .05$ compared with previous assessment.

varicose veins due to differences in venous outflow dynamics. To prevent these complications, the NBCA-to-Lipiodol ratio can be adjusted to tailor the density and viscosity of the embolic mixture. Higher NBCA concentrations yield a more viscous solution with reduced migratory potential, allowing greater control during injection and minimizing the likelihood of distal embolization. These characteristics are essential for ensuring both the safety and efficacy of pelvic vein embolization. Fortunately, no such complications were observed in our study, likely due to NBCA's properties and meticulous preoperative planning.

Other complications, such as hypersensitivity reactions, have been reported with the use of NBCA for endovenous ablation in the lower limbs.[23] However, in our study, none of these "phlebitis-like" reactions were observed. This absence may be explained by the anatomical differences between the treated veins. Unlike the saphenous vein, which is located just beneath the skin, the ovarian veins lie deeper, potentially reducing the local inflammatory response. Additionally, variations in NBCA formulations influence tissue reactions. Glubran2 extends the polymerization time, improves the exothermic reaction, and reduces the inflammatory response[24] in comparison to cianoacrilate used for saphenous vein ablation. These factors may account for the lower incidence of inflammatory reactions observed in our cohort.

A key consideration when using NBCA for embolization is its long-term behavior within the treated veins. Some case reports[25,26] have found residual polymer several years post-procedure, even though an animal model found that cyanoacrylate was completely degraded within 3 months,[25] suggesting that polymer persistence may depend on multiple factors, including vessel caliber, hemodynamic conditions, and the specific formulation used. The NBCA formulation employed in our study (Glubran2) differs from those in prior investigations, as it incorporates metacryloxysulfolane, which has been associated with reduced histotoxicity and potentially altered degradation kinetics.[24] These characteristics reinforce one of the key advantages of NBCA over traditional embolization techniques such as coils: the absence of permanent metal implants. Although NBCA polymer may persist for a variable period, evidence suggests it undergoes progressive degradation rather than remaining permanently in the tissue. Additionally, avoiding permanent metal implants may reduce the risk of post-implant syndrome and coil protrusion, complications that sometimes require surgical intervention due to persistent pain.[27] Furthermore, NBCA minimizes imaging artefacts during follow-up assessments.

Studies indicate that NBCA embolization does not affect hormone levels or reproductive function.[5,19] Liu et al suggested that pelvic embolization could be a potential treatment option for infertility in women struggling to conceive.[28] Although current data are insufficient to confirm this hypothesis, our study observed that 17 patients (17% of the cohort) successfully gave birth to 22 healthy babies following NBCA ovarian vein embolization. Among them, three patients had two pregnancies, whereas one had three successful pregnancies. However, four of these 17 patients experienced recurrent symptoms during follow-up, with two requiring repeat embolization.

This study has several limitations. Because pain perception is subjective, using the VAS to assess CPP may have introduced some bias. Additionally, a comprehensive evaluation of quality-of-life scores was not performed. Moreover, as this study focused on assessing the initial outcomes of ovarian vein embolization with NBCA for CPP due to PeVD, it did not include a direct comparison with other embolic agents, which would be valuable for future research. Lastly, due to the retrospective study design, a multicenter prospective study is warranted to obtain more conclusive results.

Despite these limitations, to our knowledge, this study represents the largest case series evaluating NBCA as the sole embolic material for treating CPP associated with PeVD. In conclusion, in our series, ovarian vein embolization with NBCA has been proven to be a feasible and safe treatment option for CPP caused by PeVD, allowing complete embolization of pelvic varicosities. However, prospective studies are necessary to further validate these findings.

DECLARATION OF GENERATIVE AI AND AI-ASSISTED TECHNOLOGIES IN THE WRITING PROCESS

During the preparation of this work, the author used ChatGPT to translate some paragraphs from Spanish to English. After using this tool, the author reviewed and

edited the content as needed and takes full responsibility for the content of the publication.

AUTHOR CONTRIBUTIONS

Conception and design: JH, AA, RC, JL
Analysis and interpretation: JH, JL
Data collection: JH, RC, MP, JL
Writing the article: JH, AA, JL
Critical revision of the article: JH, AA, RC, MP, JL
Final approval of the article: JH, AA, RC, MP, JL
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