A Comprehensive Ultrasound Approach to Lower Limb Varicose Veins and Abdominal-Pelvic Connections

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#### Title:

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#### **Short running title:**

Ultrasound Approach to Lower Limb Varicose Veins and Abdominal-Pelvic Connections

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#### **ARTICLE HIGHLIGHTS**

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2 **Type of Research:** Case-control

3 Key Findings: 44 patients in group 1 (patients with LL varicose veins and pelvic escape points - PEP) and 35 4 patients in group 2 (patients with LL varicose veins without PEP - control group) were studied, matched by age. 5 The median age was 43 years in both groups. The calculated BMI was lower in group 1 (23.4 kg/m2) compared 6 to the control group (25.4 kg/m<sup>2</sup>) and this difference reached statistical significance (p<0.001). The presence of 7 pelvic varicose veins (PV) by transvaginal ultrasound was 86% in group 1 and 31% in group 2. Perineal PEP were 8 the most prevalent, being found in 35 patients (79.5%), more frequent on the right (57.14%) than on the left 9 (42.85%) and associated with bilateral PVs in 65.7% of the times. In group 1, 23 (52%) patients reported recurrent varicose veins versus 8 (23%) in the control group (p = 0.008). Regarding the complaint of dyspareunia, a 10 11 significant difference was identified between the groups (p = 0.019), being reported in 10 (23%) patients in group 12 1 against 1 (2.9%) patient in the control group. The median diameters in the transabdominal approach of the left gonadal veins were 6.70 mm for group 1 and 4.60 mm for group 2 (p<0.001). In patients with PV in group 1, the 13 14 median diameter of PEPs at the trans-perineal window was 4.05 mm. In the transvaginal examination, the mean diameter of the veins in the peri uterine region was 8.71 mm on the left and 7.04 mm on the right. Take home 15 16 Message: Understanding the venous connection between abdomen, pelvis and the lower limbs holds promise for 17 tailoring more precise treatment strategies, potentially diminishing recurrence rates and enhancing patient 18 outcomes. The proposed methodology presents distinct advantages in diagnosing and managing lower limb 19 varicose veins by directly addressing pelvic venous reflux, offering a more comprehensive investigative approach 20 than current methods.

#### TABLE OF CONTENTS SUMMARY

- In this case-control study, a significant association was found between pelvic varicose veins, pelvic escape points,
- 23 and the recurrence of varicose veins in the lower limbs. The study suggests a comprehensive 4-step ultrasound

- 1 investigation protocol, incorporating transabdominal, transperineal, and transvaginal approaches for venous
- 2 mapping in suspected pelvic venous origin of reflux.

#### 3 **ABSTRACT**

4 **Introduction:** Pelvic venous reflux may be responsible for pelvic venous disorders and/or lower limb (LL) 5 varicose veins. Ultrasound investigation with Doppler allows a complete study of the entire infra-diaphragmatic 6 venous reservoir. **Objectives:** To guide and standardize the investigation of the pelvic origin of venous reflux in 7 female patients with LL varicose veins. **Method:** In this case-control study, we applied a comprehensive 8 ultrasound investigation protocol, which involved four steps: 1. Venous mapping of the lower limbs, 2. 9 Transperineal and vulvar approach, 3. Transabdominal approach, and 4. Transvaginal approach. Results: 44 patients in group 1 (patients with LL varicose veins and pelvic escape points - PEP) and 35 patients in group 2 10 11 (patients with LL varicose veins without PEP - control group) were studied, matched by age. The median age was 12 43 years in both groups. The calculated BMI was lower in group 1 (23.4 kg/m2) compared to the control group 13 (25.4 kg/m2) and this difference reached statistical significance (p<0.001). The presence of pelvic varicose veins 14 (PV) by transvaginal ultrasound was 86% in group 1 and 31% in group 2. Perineal PEP were the most prevalent, 15 being found in 35 patients (79.5%), more frequent on the right (57.14%) than on the left (42.85%) and associated 16 with bilateral PVs in 65.7% of the times. In group 1, 23 (52%) patients reported recurrent varicose veins versus 8 17 (23%) in the control group (p = 0.008). Regarding the complaint of dyspareunia, a significant difference was 18 identified between the groups (p = 0.019), being reported in 10 (23%) patients in group 1 against 1 (2.9%) patient 19 in the control group. The median diameters in the transabdominal approach of the left gonadal veins were 6.70 20 mm for group 1 and 4.60 mm for group 2 (p<0.001). In patients with PV in group 1, the median diameter of PEPs 21 at the trans-perineal window was 4.05 mm. In the transvaginal examination, the mean diameter of the veins in the 22 peri uterine region was 8.71 mm on the left and 7.04 mm on the right. **Conclusion:** The identification of PEP by 23

venous mapping demonstrates the pelvic origin of the reflux and its connections with the LL varicose veins. For

- a more adequate treatment plan, we suggest a complete investigation protocol based on the transabdominal and
- 2 transvaginal study to rule out venous obstructions, thrombotic or not, and confirm the presence of varicose veins
- 3 in the pelvic adnexal region.
- 4 **Keywords:** pelvic vanishing point, pelvic varicose veins, chronic pelvic pain, color Doppler ultrasound, venous
- 5 compression.

#### 6 INTRODUCTION

- 7 Pelvic venous insufficiency may be responsible for varicose veins located in the pelvic reservoir or for varicose
- 8 veins in the perineal region and/or lower limbs<sup>1,2</sup>, being frequently one of the causes of chronic pelvic pain, known
- 9 as Pelvic Congestion Syndrome (PCS) which was recently defined in the document of Transatlantic
- 10 Interdisciplinary Consensus (VEIN-TERM) as chronic symptoms that may include pelvic pain, perineal
- heaviness, urination urgency and post-coital pain, caused by reflux and/or obstruction of pelvic veins, which may
- be associated with vulvar, perineal and/or lower limb varicose veins. PCS most commonly affects women of
  - reproductive age (20-45 years) and the incidence is related to the number of pregnancies.<sup>3</sup> Doppler
  - ultrasonography is considered the first-line investigation method for pelvic venous disorders (PVD), as it is non-
- invasive, easily accessible, and inexpensive, in addition to allowing the exclusion of other pelvic pathologies.<sup>4</sup>
- Pelvic escape points (PEP) connect pelvic reflux with lower limb varicose veins and are easily identified by
- studying the transperineal region during venous mapping. Unsatisfactory results of traditional treatments for PCS
- may be related to an incomplete investigation. Based on this, an accurate diagnosis protocol of the entire infra-
- diaphragmatic venous reservoir becomes indispensable for hemodynamic compression of all these connections.

#### **METHOD**

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- 21 This is a case-control study in which a group of patients with varicose veins in the lower limbs and PEP with
- 22 reflux and another group with varicose veins in the lower limbs without PEP (control group) were evaluated using
- 23 an ultrasound investigation protocol for confirmation or not of pelvic varicose veins. Epidemiological,

- anthropometric, and clinical data and variables resulting from the ultrasound evaluation were collected. This study
- 2 was approved by local Research Ethics Committee under approval number 5.931.954.

#### 3 Study population

- 4 A convenience sample was used consisting of 79 patients referred to the researcher's vascular laboratory from
- 5 March 2022 to March 2023. Of these, 44 patients had varicose veins in lower limbs and PEP with reflux (group
- 6 1) and 35 patients had varicose veins in the lower limbs without PEP (group 2), all of them female and matched
- 7 by age. After orienting the patient and signing the Free and Informed Consent Form, the consultation was carried
- 8 out, consisting of the following steps: anamnesis, physical examination, Symptoms-Varices-Pathophysiology
- 9 (SVP) classification<sup>7</sup> and CEAP (Clinical-Etiology-Anatomy-Pathophysiology) classification<sup>8</sup> (**figure 1**), all
- patients underwent ultrasound examination of the veins of the lower limbs, abdomen, and pelvis following a
- standard protocol performed by the same examiner. On average, the complete examination took 60 minutes per
- patient. The exams were performed with the Epiq 5G Philips device and the transducers used were: Linear 3-12
- 13 MHz, convex pure wave 1-5 MHz, and endocavity 3-10 MHz.
- 14 The sample size was calculated to test the difference in the values of a quantitative variable between two groups,
- for paired samples. The Wilcoxon test for paired samples was considered. At a significance level of 5%, minimum
- power of 80%, for an average effect size, at least 35 cases and 35 controls would be needed to conduct the study.
- 17 The sample size was calculated using the G\*Power 3.1.9.4 program.
- Patients with lower limbs varicose veins and PEP identified during venous mapping, aged between 25 and 60
- 19 years, were included in group 1. Patients with isolated lower limb varicose veins and with corresponding age were
- 20 included in the control group (group 2). All patients had previous gynecological ultrasounds without alterations,
- such as endometriosis, uterine myomatosis and adenomyosis. Male patients, patients with deep venous thrombosis
- or post-thrombotic sequelae, pregnant women, female subjects who had not attained menarche or undergone
- 23 penetrative intercourse were not included in the study.

- 1 Pelvic varicose veins investigation protocol step by step (figure 2)
- 2 **STAGE 1:** Conventional venous mapping
- 3 The first step of the investigation protocol for pelvic varicose veins follows the same recommendations proposed
- 4 for the venous mapping of lower limb varicose veins, 9 paying attention to varicose veins connected to the pelvic
- 5 territory.
- 6 **STAGE 2:** Investigation of pelvic leak points
- With the patient in a standing position, reflux in the PEP was induced with the Valsalva maneuver. A linear
- 8 transducer was used for the conventional venous mapping. The PEP and their anatomical relationships are shown
- 9 in Figure 3 and described below.<sup>10</sup>
- Perineal point (P point): The transducer was positioned at the junction of the posterior \(^1\)4 and anterior \(^3\)4 laterally
- to the labia majora, close to Alcock's canal, where the perineal veins continue after receiving the labial tributaries,
- thus connecting the internal and external pudendal systems. Slight movements are made in a medial direction
- towards the pubis with the thigh slightly flexed (**figure 4**).
- 14 **Inguinal point (I point):** The transducer was placed on the inguinal ligament, above the saphenofemoral junction
- 15 (SFJ), and moved in the superior and medial direction to about 1 cm above and lateral to the pubic bone to assess
- 16 for the presence of varicose veins exteriorizing in the superficial inguinal ring. This escape point has three
- 17 peculiarities: an ultrasound image with a concave aspect, it is associated with varicose veins in the pubic region,
- and, in most cases, it is related to varicose veins in the peri uterine or parametrical region (**figure 5**).
- 19 **Gluteal point (G point):** In the greater sciatic notch, the superior gluteal vein passes above the piriformis muscle
- 20 whereas the inferior gluteal vein passes below the piriformis muscle and the gluteal point is located along the
- 21 intrapelvic passage of the gluteal veins. The venous plexus of the sciatic nerve can be seen in the posterior
- proximal aspect of the thigh and is drained by the inferior gluteal vein (**figure 6**).

- 1 **Obturator point (O point):** It is located at the level of the saphenofemoral junction, in the obturator canal, and
- 2 connects the deep veins of the anterior thigh muscles with the internal iliac vein. The transducer is placed between
- 3 the great saphenous vein and the femoral vein in the inguinal region to visualize this point. (**figure 7**).
- 4 **STAGE 3:** Transabdominal approach
- 5 The patient was examined in the supine and left lateral positions to assess the iliac axis and renal veins for
- 6 compression. We used anatomical and velocimetry criteria for diagnosing iliac and renal venous compression. <sup>12,13</sup>
- 7 The gonadal vein was identified using the psoas major muscle and the iliac vessels as a reference. Caliber and
- 8 flow direction were evaluated bilaterally (**figure 8**).
- 9 **STAGE 4:** Transvaginal approach
- The patients with empty bladders were placed in the lithotomy/reverse Trendelenberg position, and the following
- criteria were used to assess the pelvic varicose veins: 1) The diameter of the parametrical veins greater than 7 mm
- and 2) Alteration in the amplitude of the retrograde flow during the Valsalva maneuver. 14,15 The gonadal veins,
- periuterine and perivaginal venous plexuses, internal iliac veins, and perineal escape points were evaluated (**figure**
- 14 9). All patients received a cartography of the pelvis and abdomen with all the data found during the examination
- attached to the medical report<sup>26</sup> (**figure 10**).
- 16 Statistical analysis
- 17 Qualitative variables were presented as frequencies, and quantitative variables as mean  $\pm$  standard deviation
- [median]. Quantitative variables were submitted to the Shapiro-Wilk normality test. To compare quantitative
- 19 variables between cases and controls, Student's t-test or Wilcoxon test for paired samples were used, and
- 20 McNemar's chi-square test was used to verify the association between qualitative variables. Analyzes were
- 21 performed using the R program version 4.2.0 and p<0.05 was considered significant.
- 22 **RESULTS**

- 44 patients in group 1 (patients with lower limbs varicose veins and PEP with reflux) and 35 patients in group 2
  (patients with lower limbs varicose veins without PEP control group) were studied, matched by sex and age. The
- 3 median age was 41 years in group 1 and 44 in group 2. The calculated body mass index (BMI) was lower in group
- 4 1 23.4 kg/m<sup>2</sup> (21.3, 25.1) compared to the control group 25.4 kg/m<sup>2</sup> (23.9, 29.2) and this difference reached
- 5 statistical significance (p<0.001). The number of previous pregnancies ranged from 0 to 5 in both groups, with a
- 6 predominance of 2 pregnancies, corresponding to 42% in group 1 and 37% in group 2. No patient had iliac venous
- 7 compression, and only one patient in group 1 had compression left renal vein (table 1).
- 8 The presence of pelvic varicose veins by transvaginal ultrasound according to the pre-established criteria for its
- 9 diagnosis was 86% in group 1 and 31% in group 2 (**graphic 1**). In group 1, pelvic varicose veins on transvaginal
- ultrasound were bilateral in 59.1% of cases, left in 22.7% of cases, right in 4.5% of cases, and absent in 13.6%
- 11 **(graphic 2)**.
- Perineal PEP was the most prevalent, being found in 35 patients (79.5%) in group 1, more frequent on the right
- 13 (57.14%) than on the left (42.85%) and is associated with varicose veins bilateral pelvic vessels in 65.7% of the
- times (graphic 3).
- 15 Inguinal PEP was observed in 11 patients (25%) in group 1, being more frequent on the left (63.6%) and associated
- with bilateral pelvic varicose veins in 44.5% of cases, and without pelvic varicose veins in 27.3 % of cases.
- Gluteal PEP was identified in 6 patients (13.6%) in group 1, being more prevalent on the right (83.3%) and being
- associated with bilateral pelvic varicose veins in 66.7% of cases. Obturator PEP was the least prevalent, being
- observed in only 3 patients (6.8%), found more to the right (66.7%), and is associated with bilateral pelvic varicose
- veins in 2/3 of the cases.
- Of the 38 patients with pelvic varicose veins confirmed by transvaginal ultrasound in group 1, 5 patients (13.2%)
- had 1 previous pregnancy, 16 (42.1%) had 2 previous pregnancies, 14 (36.8%) had 3 previous pregnancies, 1
- 23 (2.5%) had 4 previous pregnancies, and 2 (5.3%) had 5 previous pregnancies.

1 The rate of recurrence of lower limbs varicose veins was determined for all patients who underwent surgical 2 intervention/removal of superficial varicose veins (crossectomy, stripping, phlebectomy, sclerotherapy with 3 polidocanol foam). In group 1, 23 (52%) patients had recurrent varicose veins against 8 (23%) in the control 4 group, with a p-value of 0.008 (table 2). Of these 23 patients with recurrent varicose veins in the lower limbs in 5 group 1, 19 (82.6%) had pelvic varicose veins on transvaginal examination, with the number of previous 6 interventions ranging from 1 to 3. In group 1, 17 (39%) patients underwent 1 previous intervention, 5 (11%) 7 patients underwent 2 previous interventions, and 1 (2.3%) patient underwent 3 previous interventions. In the 8 control group, 6 (17%) patients underwent 1 previous intervention, 1 (2.9%) patient underwent 2 previous 9 interventions, and 1 (2.9%) patient underwent 3 previous interventions. It is indicated that the groups are not independent, that is, there is a statistically significant association. In the control group, in which 8 patients (23%) 10 11 had recurrent and/or recurrent varicose veins, 3 (37.5%) had pelvic varicose veins on transvaginal ultrasound. 22 12 patients in total with recurrent lower limb varicose veins in both groups, 15 (68%) had bilateral pelvic varicose 13 veins on transvaginal ultrasound. 14 Regarding pelvic symptoms, pelvic pain was reported in 11 (25%) patients in group 1 and in 5 (14%) in group 2, 15 without reaching statistical significance between groups. With regard to the complaint of dyspareunia, Fisher's 16 exact test showed that there is a significant difference between the groups (p = 0.019), with dyspareunia being 17 reported in 10 (23%) patients in group 1 and in 1 (2.9%) patient in group 1. group control (table 3). The median 18 diameter of the left periuterine plexus was significantly greater (p = 0.037) in patients with 9.00 mm dyspareunia 19 (8.45, 9.28) than in patients without 7.45 mm dyspareunia (6.00, 9.30) in group 1 (table 4). 20 The difference in diameters in the transabdominal approach of the gonadal veins between the groups reached 21 statistical significance (p<0.001), being 6.70 mm (6.10, 7.30) for group 1 and 4.60 mm (4.00, 5.50) for group 2 22 on the left. On the right, it was 5.10 mm (4.45, 5.60) for group 1 and 4.00 mm (3.20, 4.50) for group 2 (table 5).

In patients with pelvic varicose veins (n=38) in group 1, the diameter of the right gonadal vein was 5.20 mm (4.60,

- 5.68) and that of the left gonadal vein was 6.70 mm (6.30, 7.40) in transvaginal ultrasound, with no significant
- 2 difference with the measurements taken in the transabdominal stage. Of these 38 patients, the median diameter of
- 3 PEP in the transperineal window was 4.05 mm (3.58, 4.65) (table 6), in the transvaginal examination, the average
- 4 diameter of the periuterine plexus was 8.71 mm on the left and 7.04 mm on the right.

#### DISCUSSION

- 6 In our study, the median age of patients in the PEP group was 41 years, indicating that investigation in the age
- 7 group over 40 years should be considered. The prevalence of pelvic symptoms tends to decrease with age, with a
- 8 reciprocal effect on the increase in symptoms in the legs<sup>16</sup> which could be explained by the flaccidity of the pelvic
- 9 floor and drainage in the pelvic reflux towards the lower limbs through the leakage points that become insufficient.
- We found a significant difference in BMI between groups 1 e 2 [23.4 (21.3, 25.1) kg/m2 vs 25.4 (23.9, 29.2)
- kg/m2], respectively (p<0.001). This data suggests that pelvic venous disorders are more prevalent in patients
- with normal or lower BMI, consistent with the findings of Nanavati et al. <sup>17</sup> About 41% of the women in both
- groups had at least 2 pregnancies with no statistically significant difference between the groups, suggesting that
- the number of previous pregnancies may not be a risk factor for the presence of PEP with reflux and pelvic
- 15 varicose veins.
- 16 The transabdominal approach can assess for iliac and renal venous compression, pelvic varicosities, and gonadal
- vein insufficiency. Whereas a 6 mm gonadal vein on transabdominal ultrasound has a 96% positive predictive
- value for pelvic varicose veins, 18 we identified that the median diameter of the left gonadal vein in group 1 was
- 19 6.70 mm (6.10, 7.30) and reached statistical significance (p<0,001) compared to group 2, which was 4.60 mm
- 20 (4.00, 5.50). Although diameter measurements by itself do not correlate well with gonadal vein reflux, <sup>19</sup> our study
- suggests a positive association between the diameter of the left gonadal vein with the presence of pelvic varicose
- veins and PEP with reflux. There was no significant correlation between venous compressions and the finding of

pelvic varicose veins, as no patient had iliac venous compression, and only one patient in group 1 had compression 1 2 of the left renal vein. 3 The agreement between the lower limbs venous mapping and the transvaginal ultrasound regarding the 4 identification of pelvic reflux was statistically significant in a previous publication of our group, however, the 5 sensitivity was low (41.3%), which suggests that the venous mapping of the lower limbs alone cannot be used as 6 a criterion for the diagnosis of pelvic varicose veins; instead, transvaginal ultrasound is required to confirm the 7 diagnostic hypothesis. On the other hand, the specificity of 93.9% and the negative predictive value of 92.0% 8 associated with the venous mapping of the lower limbs suggest that whenever this test is negative for pelvic varicose veins, no further investigation is necessary.<sup>2</sup> 9 10 The transvaginal investigation approach offers better visualization of the pelvic venous plexus compared to the 11 transabdominal one. Despite its accuracy has not been validated by phlebography in all cases and it is not able to assess renal and iliac veins.<sup>3</sup> The presence of pelvic varicose veins on transvaginal ultrasound according to the 12 13 pre-established criteria for its diagnosis (presence of circular or linear venous structures with a diameter greater 14 than 6 mm) was 86% in group 1 and 31% in group 2. This finding suggests PEP with reflux is strongly correlated 15 with pelvic varicose veins, corroborating the need for a broader study of the abdominopelvic territory in these 16 patients, as well as the frequent finding (31%) of pelvic varicose veins in patients without clinical suspicion. 17 Due to the presence of valved venous plexuses vertically and horizontally connecting all the pelvic viscera and the pelvic wall, the venous flow follows the pressure gradient.<sup>20</sup> This explains the finding that even perineal PEP 18 19 is unilateral most of the time (86,3%) and are associated with bilateral pelvic varicose veins in 59.1% of cases. 20 This complex anatomy, combined with the fact that reflux often affects more than one pelvic region, makes it 21 difficult to identify and treat all points of reflux and, on the other hand, facilitates the development of collateral

pathways given the fact that one vein with reflux has been successfully treated.<sup>21</sup>

1 The perineal pelvic leak was the most prevalent in our study, being found in 35 patients (79.5%) in group 1, results comparable to 60% of all PEP treated in women<sup>22</sup> and 70.8%<sup>23</sup> according to the literature. One data to be 2 3 considered is that it was more frequent on the right (57,14%) than left (42,85%) and was associated with bilateral 4 pelvic varicose veins 65,7% of the time. The other points of pelvic leaks found (25% inguinal, 13,6% gluteus, and 5 6,8% obturator) also corresponded to the order of prevalence described in the literature.<sup>20</sup> 6 In recent years, many studies have evaluated patients with chronic venous disease of the lower limbs for evidence 7 of pelvic venous reflux origin using pelvic phlebography, transvaginal and/or transperineal ultrasound. It was 8 identified that approximately 15-20% of patients have reflux of pelvic origin.<sup>24</sup> The percentage rises to 30% in 9 patients with recurrent varicose veins initially treated by conventional surgery or minimally invasive intravenous 10 techniques. 15 Likewise, in Perrin's study of 170 patients, pelvic reflux was present in approximately 17% of patients with recurrent varices after surgery. 25 In our study, 23 patients 5 (52%) in group 1 had recurrent varicose 11 12 veins, and of these 23, 19 (82%) had pelvic varicose veins on transvaginal ultrasound versus 8 (23%) recurrent 13 veins in the control group, with a p-value of 0.008. These results corroborate the fact that pelvic reflux is an 14 important risk factor to be considered for recurrence of lower limb varicose veins. 15 We did not find any studies in the literature evaluating the relationship between pelvic symptoms and periuterine 16 plexus diameters. In our study, there was a significant difference between the groups (p = 0.019) from the 17 complaint of dyspareunia in 10 (23%) of the patients in group 1 and in 1 (2.9%) patient in the control group, and 18 the median diameter of the periuterine plexus on the left was significantly greater (p = 0.037) in patients with 19 dyspareunia (9.00 mm) than in patients without dyspareunia (7.45 mm) in the group 1. This data leads us to believe 20 that there is a significant correlation between the diameter of the pelvic venous plexuses and the complaint of 21 dyspareunia. It is noteworthy that 20% of all patients evaluated (n = 79) reported chronic pelvic pain, being a 22 prevalent complaint in 25% of patients in group 1 and 14% of patients in group 2, with no statistically significant 23 difference between groups, and therefore takes us to raise intriguing questions regarding the potential influence

1 of PEP with reflux on pelvic pain symptoms, emphasizing the need for in-depth investigations to better understand 2 the relationship between pelvic venous disorders and chronic pelvic pain. Among all patients with pelvic varicose 3 veins in group 1 (n = 38), the median PEP diameter at the transperineal window was 4.05 mm (3.58, 4.65). There 4 is still no cut-off diameter for PEP in the literature that is associated with the presence of pelvic reflux and dilation 5 of the periuterine plexuses, but according to our results, we recommend values > 3.5 mm. In the transvaginal stage, the median diameter of the periuterine plexus was 8.71 mm on the left and 7.04 mm on the right for patients 6 7 in group 1 with pelvic varicose veins. However, taking into account only the diameter for treatment indication 8 may be questionable. The lack of knowledge and technical skills in assessing the flow of the gonadal and internal iliac veins for a better 9 hemodynamic understanding of the origin of pelvic reflux can be a crucial factor for tactical errors in the treatment. 10 11 Based on our experience, one of the main causes for the maintenance or recurrence of signs and symptoms of 12 lower limb varicose veins is pelvic escape points. This protocol, recommended by us, involves the comprehensive 13 investigation of the infra-diaphragmatic venous reservoir, making it the most comprehensive approach to studying 14 this issue. 15 Our findings reveal a significant correlation between pelvic varicose veins, recurrent lower limb varicose veins, 16 and dyspareunia in PEP patients. This association strongly suggests a connection between pelvic venous reflux 17 and lower limb varicosities, providing a solid basis for investigating the pelvic origin of venous reflux. This 18 includes exploring its role in post-procedural recurrent varicose veins, as well as in patients with groin, perineal, 19 and vulvar varicosities, and dyspareunia. This approach allows for a more targeted investigation into the pelvic 20 origin of venous reflux in individuals exhibiting these particular manifestations. 21 Understanding this connection holds promise for tailoring more precise treatment strategies, potentially 22 diminishing recurrence rates and enhancing patient outcomes. The proposed methodology presents distinct

- advantages in diagnosing and managing lower limb varicose veins by directly addressing pelvic venous reflux,
- 2 offering a more comprehensive investigative approach than current methods.
- 3 Considering the practicality of implementing these methods, specialized training can render this protocol cost-
- 4 effective and readily integrated into routine clinical practice. In our study, a singularly experienced vascular
- 5 ultrasound specialist conducted the protocol, emphasizing the importance of expertise in its application. We
- 6 recommend that these investigations be carried out by physicians or technologists specialized in this field within
- 7 their respective countries.
- 8 One limitation of this study was the lack of a quality-of-life questionnaire to assess the extent of symptoms, as
- 9 well as the absence of data regarding the specific timeframes of prior surgical interventions on the lower limbs,
- which could enhance the understanding of varicose vein recurrence management.

#### 11 **CONCLUSION**

- 12 The connection between lower limb varicose veins and the pelvic and abdominal venous territory is well
- 13 established. This consideration underscores the creation of a comprehensive protocol that guides its investigation,
- consequently leading to a more precise treatment plan with a reduced risk of recurrence.

#### 15 **REFERENCES**

- 16 1- Labropoulos N, Tiongson J, Pryor L, Tassiopoulos AK, Kang SS, Mansour MA, Baker WH.
- Nonsaphenous superficial vein reflux. J Vasc Surg. 2001 Nov;34(5):872-7.
- 18 2- Barros FS, Perez JMG, Zandonade E, Salles-Cunha SX, Monedero JL, Hilel ABS, et al. Evaluation of
- 19 pelvic varicose veins using color Doppler ultrasound: comparison of results obtained with ultrasound of the lower
- 20 limbs, transvaginal ultrasound, and phlebography. J Vasc Bras. 2010 Jun;9(2):15–23.
- 21 3- Antignani PL, Lazarashvili Z, Monedero JL, Ezpeleta SZ, Whiteley MS, Khilnani NM, et al. Diagnosis
- and treatment of pelvic congestion syndrome: UIP consensus document. Int Angiol. 2019 Aug;38(4):265-283.

- 1 4- De Maeseneer MG, Kakkos SK, Aherne T, Baekgaard N, Black S, Blomgren L, et al. Editor's Choice -
- 2 European Society for Vascular Surgery (ESVS) 2022 Clinical Practice Guidelines on the Management of Chronic
- 3 Venous Disease of the Lower Limbs. Eur J Vasc Endovasc Surg. 2022 Feb;63(2):184-267. doi:
- 4 10.1016/j.ejvs.2021.12.024. Epub 2022 Jan 11. Erratum in: Eur J Vasc Endovasc Surg. 2022 Aug-Sep;64(2-
- 5 3):284-285.
- 6 5- Francheschi C, Bahnini A. Treatment of lower extremity venous insufficiency due to pelvic leak points in
- 7 women. Ann Vasc Surg. 2005 Mar;19(2):284-8.
- 8 6- Smith PC. The outcome of treatment for pelvic congestion syndrome. Phlebology. 2012; 27:74-77.
- 9 7- Meissner MH, Khilnani NM, Labropoulos N, Gasparis AP, Gibson K, Greiner M, et al. The Symptoms-
- Varices-Pathophysiology classification of pelvic venous disorders: A report of the American Vein & Lymphatic
- Society International Working Group on Pelvic Venous Disorders. J Vasc Surg Venous Lymphat Disord. 2021
- 12 May;9(3):568-584.
- 13 8- Lurie F, Passman M, Meisner M, Dalsing M, Masuda E, Welch H, et al. The 2020 update of the CEAP
- classification system and reporting standards. J Vasc Surg Venous Lymphat Disord. 2020 May;8(3):342-352. doi:
- 15 10.1016/j.jvsv.2019.12.075. Epub 2020 Feb 27. Erratum in: J Vasc Surg Venous Lymphat Disord. 2021
- 16 Jan;9(1):288.
- 17 9- Bottini O, Rodriguez Santos F, Boroda A, Arias F, Calcina D, Agüero Wagner C, et al. The First Latin
- American Consensus on Superficial and Perforating Venous Mapping. Int Angiol. 2023 Feb;42(1):45-58.
- 19 10- Lemasle, P; Greiner, M. Duplex ultrasound investigation in pelvic congestion syndrome: technique and
- 20 results. Phlebolymphology. 2017;24(2):79-87.
- 21 11- Krzanowski M, Partyka L, Drelicharz L, Mielnik M, Frolow M, Malinowski KP, et al. Posture commonly
- 22 and considerably modifies stenosis of left common iliac and left renal veins in women diagnosed with pelvic
- venous disorder. J Vasc Surg Venous Lymphat Disord. 2019 Nov;7(6):845-852.e2.

- 1 12- Esposito A, Charisis N, Kantarovsky A, Uhl JF, Labropoulos N. A Comprehensive Review of the
- 2 Pathophysiology and Clinical Importance of Iliac Vein Obstruction. Eur J Vasc Endovasc Surg. 2020
- 3 Jul;60(1):118-125.
- 4 13- Ananthan K, Onida S, Davies AH. Nutcracker Syndrome: An Update on Current Diagnostic Criteria and
- 5 Management Guidelines. Eur J Vasc Endovasc Surg. 2017 Jun;53(6):886-894.
- 6 14- Monedero JL, Zubicoa Ezpeleta S, Perrin M. Pelvic congestion syndrome: an update. Phlebolymphology
- 7 2013; 20:145-9.
- 8 15- Whiteley MS, Dos Santos SJ, Harrison CC, Holdstock JM, Lopez AJ. Transvaginal duplex
- 9 ultrasonography appears to be the gold standard investigation for the haemodynamic evaluation of pelvic venous
- reflux in the ovarian and internal iliac veins in women. Phlebology. 2015 Dec;30(10):706-13.
- 11 16- Sulakvelidze L, Tran M, Kennedy R, Lakhanpal S, Pappas PJ. Presentation patterns in women with pelvic
- venous disorders differ based on age of presentation. Phlebology. 2021 Mar;36(2):135-144.
- 13 17- Nanavati R, Jasinski P, Adrahtas D, Gasparis A, Labropoulos N. Correlation between pelvic congestion
- 14 syndrome and body mass index. J Vasc Surg. 2018 Feb;67(2):536-541. doi: 10.1016/j.jvs.2017.06.115.
- 15 18- Park SJ, Lim JW, Ko YT, Lee DH, Yoon Y, Oh JH, Lee HK, Huh CY. Diagnosis of pelvic congestion
- syndrome using transabdominal and transvaginal sonography. AJR Am J Roentgenol. 2004 Mar;182(3):683-8.
- 17 19- Dos Santos SJ, Holdstock JM, Harrison CC, Lopez AJ, Whiteley MS. Ovarian Vein Diameter Cannot Be
- Used as an Indicator of Ovarian Venous Reflux. Eur J Vasc Endovasc Surg. 2015 Jan;49(1):90-4.
- 19 20- Delfrate, R. Anatomy of Pelvic leak points in the context of varicose veins. Phlebologie 2021; 50: 42-50.
- 20 21- Asciutto G, Asciutto KC, Mumme A, Geier B. Pelvic venous incompetence: reflux patterns and treatment
- results. Eur J Vasc Endovasc Surg. 2009 Sep;38(3):381-6.
- 22 22- Delfrate, R., Bricchi, M., & Franceschi, C. Minimally invasive procedure for pelvic leak points in
- women. Veins and Lymphatics. 2019; 8.

- 1 23- Gianesini, S. & Antignani, P. & Tessari, L. Pelvic congestion syndrome: Does one name fit all.
- 2 Phlebolymphology. 2016; 23 (3):142-145.
- 3 24- Marsh P, Holdstock J, Harrison C, Smith C, Price BA, Whiteley MS. Pelvic vein reflux in female patients
- 4 with varicose veins: comparison of incidence between a specialist private vein clinic and the vascular department
- of a National Health Service District General Hospital. Phlebology. 2009 Jun;24(3):108-13.
- 6 25- Perrin MR, Labropoulos N, Leon LR., Jr Presentation of the patient with recurrent varices after surgery
- 7 (REVAS) J Vasc Surg. 2006;43:327–334.
- 8 26- Gail PS, Lozanski L, Kelly D. Antonucci L. Inside Ultrasound Venous Reference Guide. 2nd ed, Vail:
- 9 Inside Ultrasound: 2022.

#### **FIGURES**

Figure 1. Collected variables

Figure 2. Pelvic varicose veins investigation protocol

**Figure 3**. Watercolor painting with emphasis on pelvic veins and pelvic escape points (arrows). Authors archive.

**Figure 4.** (a) Location of the perineal escape point on transperineal ultrasound examination. (b) Varicose veins in the perineal region and root of the thigh. (c) Perineal

escape point with reflux on color-Doopler. Authors archive.

**Figure 5.** (a) Location of the inguinal escape point on transperineal ultrasound examination. (b) Varicose veins in the inguinal region. (c) Inguinal escape point with

reflux on color-Doopler. Authors archive.

**Figure 6.** (a) Location of the gluteal escape point on transperineal ultrasound examination. (b) Gluteal and posterior thigh varicose veins (c) Gluteal escape point with

reflux on Color-Doopler. Authors archive.

**Figure 7.** (a) Location of the obturator escape point on transperineal ultrasound examination. (b) Adapted schematic from Gail PS, 2023 demonstrating probe placement.<sup>26</sup> (c) Illustration depicting anatomical landmarks of the obturator escape point. SFJ: saphenofemoral junction; CFV: common femoral vein; GSV: great saphenous vein; SEPA: superficial external pudendal artery; PMF: pectineus muscle

fascia; ACFV: anterior circumflex femoral vein; OP: obturator point. Authors archive.

**Figure 8.** (a, b) Location of the left gonadal vein and periuterine veins on transabdominal ultrasound examination (c, d) Left gonadal vein and periuterine veins

on color-Doppler. Authors archive.

**Figure 9.** (a) External iliac, internal iliac, and left gonadal veins (b) dilated and insufficient peri-uterine and peri-vaginal plexuses, and (c) perineal escape point on transvaginal ultrasound examination. Authors archive.

**Figure 10.** Pelvic Venous Disorders Duplex Worksheet. Adapted from Inside Ultrasound Venous Vascular Reference Guide, 2023. <sup>26</sup>

#### **GRAPHICS**

Graphic 1. Prevalence of pelvic varicose veins on endovaginal ultrasound by group

**Graphic 2.** Relationship between pelvic escape points and pelvic varicose veins on endovaginal ultrasound

Graphic 3. Laterality of pelvic escape points

#### **TABLES**

**Table 1.** General characterization of the sample

**Table 2.** Recurrent varicose veins and number of previous surgeries per group

**Table 3.** Symptoms by Group

**Table 4.** Relation of the symptom 'dyspareunia' with the diameters of the periuterine plexuses in the transvaginal ultrasound

**Table 5.** Diameter of gonadal veins in the transabdominal approach by group

**Table 6.** PEP diameter in the transperineal approach in patients with pelvic varicose veins

Characteristics	Per Group					
	<b>Total</b> , N = 79 <sup>1</sup>	<b>Group I</b> , $N = 44^{1}$	Group II, $N = 35^1$	Value p <sup>2</sup>		
Age	43 (37, 50)	41 (37, 50)	44 (38, 51)	0.2		
IMC	24.3 (22.2, 26.8)	23.4 (21.3, 25.1)	25.4 (23.9, 29.2)	<0.001		
Weight (kg)	65 (60, 70)	64 (58, 67)	68 (62, 77)	0.007		
Gestation				>0.9		
0	3 (3.8%)	1 (2.3%)	2 (5.7%)			
1	13 (16%)	6 (14%)	7 (20%)			
2	32 (41%)	19 (43%)	13 (37%)			
3	24 (30%)	14 (32%)	10 (29%)			
4	4 (5.1%)	2 (4.5%)	2 (5.7%)			
5	3 (3.8%)	2 (4.5%)	1 (2.9%)			

<sup>&</sup>lt;sup>1</sup>Median (AIQ); n (%)

<sup>&</sup>lt;sup>2</sup> Wilcoxon rank sum test; Fisher's exact test.

			ns and Previous Surgeries Group	
Characteristics	<b>Total</b> , N = 79 <sup>1</sup>	Group I, $N = 44^1$	Group II, $N = 35^1$	Value p <sup>2</sup>
Recurrent Varicose Veins				0.008
No	48 (61%)	21 (48%)	27 (77%)	
Yes	31 (39%)	23 (52%)	8 (23%)	
Surgery / Varicose Veins				0.030
0	48 (61%)	21 (48%)	27 (77%)	
1	23 (29%)	17 (39%)	6 (17%)	
2	6 (7.6%)	5 (11%)	1 (2.9%)	
3	2 (2.5%)	1 (2.3%)	1 (2.9%)	

<sup>&</sup>lt;sup>1</sup>n (%)

<sup>&</sup>lt;sup>2</sup> Chi-square independence test; Fisher's exact test

	Symptoms by Group						
Characteristics	<b>Total</b> , $N = 79^1$	<b>Group I</b> , $N = 44^{1}$	<b>Group II</b> , $N = 35^1$	Value p <sup>2</sup>			
Leg Pain				0.3			
No	35 (44%)	17 (39%)	18 (51%)				
Yes	44 (56%)	27 (61%)	17 (49%)				
Dyspareunia				0.019			
No	68 (86%)	34 (77%)	34 (97%)				
Yes	11 (14%)	10 (23%)	1 (2.9%)				
Pelvic Pain				0.2			
No	63 (80%)	33 (75%)	30 (86%)				
Yes	16 (20%)	11 (25%)	5 (14%)				

<sup>&</sup>lt;sup>1</sup>n (%)

<sup>&</sup>lt;sup>2</sup> Chi-square independence test; Fisher's exact test

Characteristics	Dyspareunia					
	<b>Total</b> , $N = 44^{1}$	$n, N = 34^1$	$s, N = 10^1$	Value p <sup>2</sup>		
Periuterine plexus diameter on the right	7.10 (5.08, 7.80)	7.05 (4.78, 7.80)	7.40 (6.13, 7.55)	0.5		
Periuterine plexus diameter left	7.95 (6.80, 9.33)	7.45 (6.00, 9.30)	9.00 (8.45, 9.28)	0.037		

<sup>&</sup>lt;sup>1</sup>Median (AIQ)

Journal Pre-Proof <sup>2</sup> Wilcoxon rank sum test

	Diameter of gonadal veins by groups				
Characteristics	<b>Total</b> , N = 79 <sup>1</sup>	<b>Group I</b> , N = 44 <sup>1</sup>	<b>Group II</b> , N = 35 <sup>1</sup>	Value p <sup>2</sup>	
RIGHT gonadal vein diameter	4.60 (4.00, 5.20)	5.10 (4.45, 5.60)	4.00 (3.20, 4.50)	<0.001	
LEFT gonadal vein diameter	6.25 (4.53, 6.80)	6.70 (6.10, 7.30)	4.60 (4.00, 5.50)	<0.001	

<sup>&</sup>lt;sup>1</sup>Median (AIQ)

<sup>&</sup>lt;sup>2</sup> Wilcoxon rank sum test

			icose veins ginal US		
Characteristics	<b>Total</b> , N = 38 <sup>1</sup>	<b>bilat</b> , N = 26 <sup>1</sup>	Right, $N = 2^1$	<b>Left,</b> $N = 10^1$	Value p <sup>2</sup>
PEP diameter / transperineal window	4.05 (3.58, 4.65)	4.15 (3.60, 4.80)	5.60 (5.60, 5.60)	3.70 (3.50, 4.40)	0.2

<sup>&</sup>lt;sup>1</sup>Median (AIQ). PEP: pelvic escape point; US: ultrasound

<sup>&</sup>lt;sup>2</sup>Test of Kruskal-Wallis

### **Epidemiological and clinical variables**

- Age, gender, weight, height, body mass index
- Number of pregnancies
- Pelvic and/or lower limb symptoms
- Prior surgery and recurrence of varicose veins
- Family history of varicose veins

#### Vascular examination

- SVP and CEAP classifications
- Venous mapping of the lower limbs and transperineal
- Transabdominal ultrasound
- Transvaginal ultrasound

#### PELVIC VARICOSE VEINS INVESTIGATION PROTOCOL

#### Stage 1. Vascular ultrasound of the lower limbs and transperineal

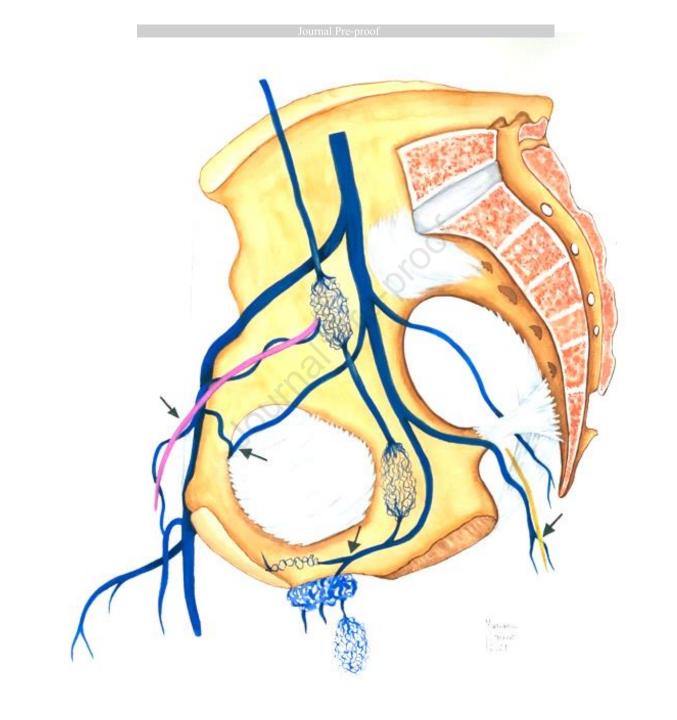
- 1.1 To select patients with lower limb varicose veins that connect to the pelvic territory through pelvic vanishing points using the transperineal ultrasound window.
- 1.2 To identify the pelvic vanishing points (Inguinal, Perineal, Gluteal, and Obturator).

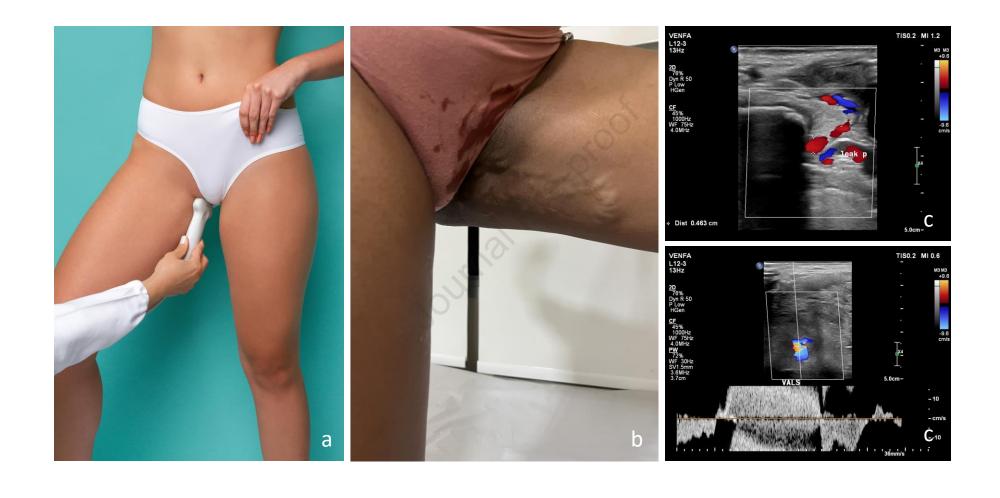
#### Stage 2. Transabdominal vascular ultrasound

- 2.1 To evaluate the presence of iliac and renal venous compressive syndrome.
- 2.2 To evaluate the gonadal and internal iliac veins.
- 2.3 To assess the patency of the inferior vena cava and iliac axis.

### Stage 3. Transvaginal vascular ultrasound

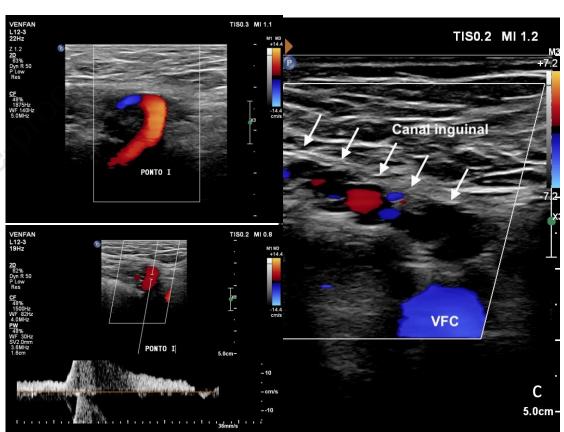
- 3.1 To identify the presence of periuterine varicose veins.
- 3.2 To assess the flow in the gonadal and hypogastric veins.
- 3.3 To assess the patency of these vessels.



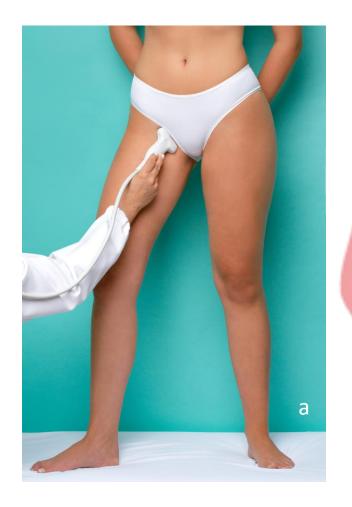


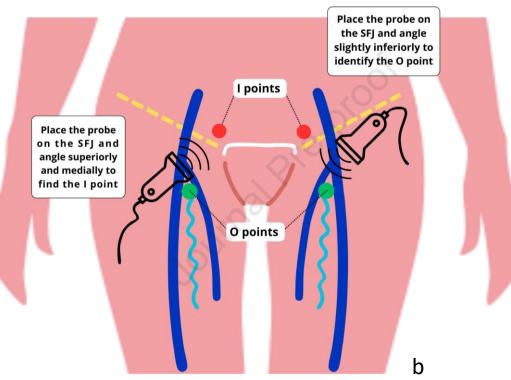


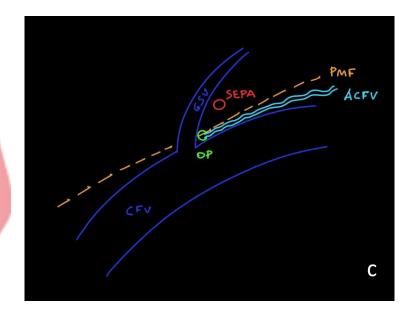


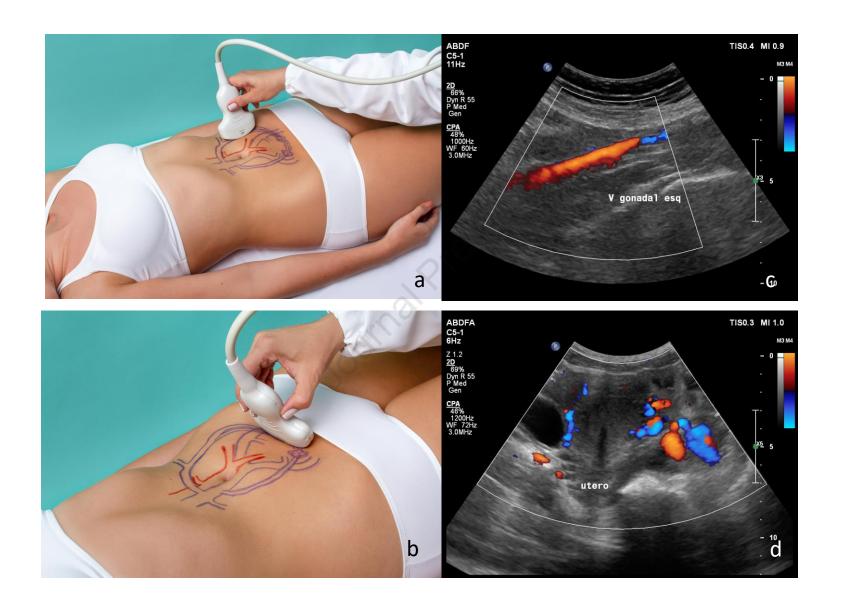


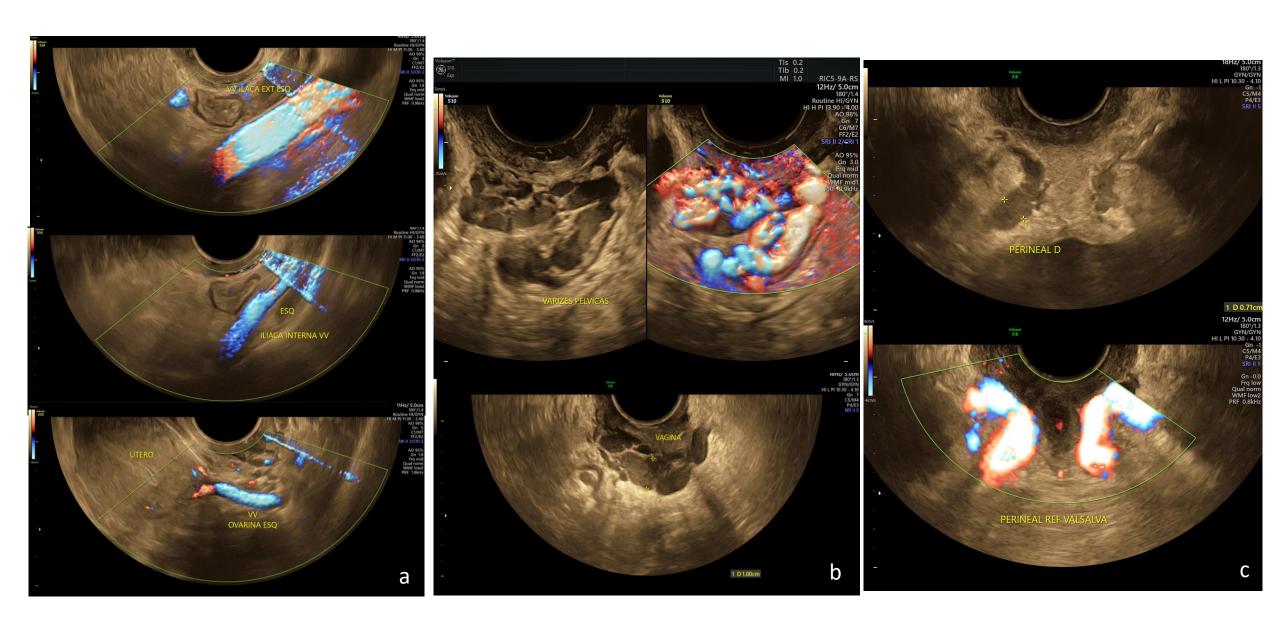












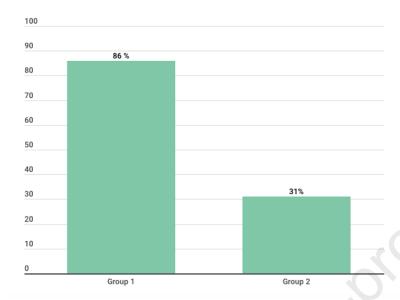
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lame:	Date:/	
OOB:/		
xam indication:		
	Left Renal Vein	
	PVV (cm/sec) Peripheral At obstruction	
Diameter	Diameter (mm) Peripheral At obstruction	
	Velocity Ratio Diameter Ratio	
	Gonadal / IIV Reflux  Gonadal: Right yes no / Left yes no  IIV: Right yes no / Left yes no	$\bigcirc$
	Left Common Iliac Vein  PVV (cm/sec) Peripheral At obstruction	
$\mathbb{V} \subset \mathbb{V} $	Diameter (mm) Peripheral At obstruction	
	Velocity Ratio Diameter Ratio	
0 1,000 pg 0	Pelvic Varicose Veins	
Diameter Diame	ter Right Adnexa yes no	
	Left Adnexa yes no	
	Transuterine yes no	
	*Diameter:	

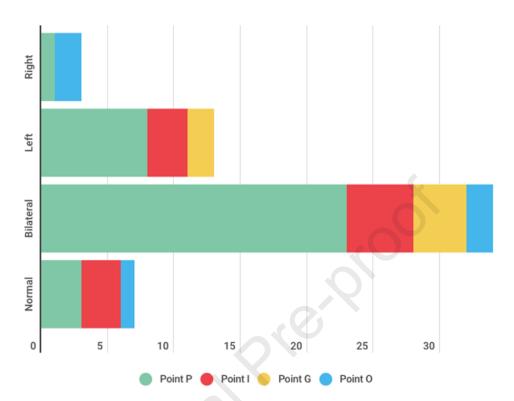


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## **Pelvic Varicose Veins**



# **Pelvic Varicose Veins**



# **Pelvic Leak Points**

