Evaluation of pelvic varicose veins using color Doppler ultrasound: comparison of results obtained with ultrasound of the lower limbs, transvaginal ultrasound, and phlebography

Avaliação de varizes pélvicas por Doppler colorido: comparação dos resultados obtidos com ultrassom dos membros inferiores, ultrassom transvaginal e flebografia

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Abstract

Introduction: Pelvic varicose veins, one of the main causes of chronic pelvic pain and dyspareunia, are an important source of reflux for lower limb varicose veins, especially in recurrent cases. Color Doppler ultrasound of the lower limbs and transvaginal ultrasound are the noninvasive diagnostic methods most commonly used to assess pelvic venous insufficiency, whereas phlebography is still considered as the gold standard.

Objectives: To determine the prevalence of lower limb varicose veins originating from the pelvis in a group of female patients and to determine the agreement between results obtained via color Doppler ultrasound of the lower limbs, transvaginal ultrasound, and phlebography.

Methods: The sample comprised female patients referred to a vascular laboratory for lower limb screening. Patients diagnosed with deep venous thrombosis were excluded. Data analysis included kappa coefficient of agreement, McNemar’s test, sensitivity and specificity values.

Results: Of a total of 1,020 patients, 124 (12.2%) had findings compatible with reflux of pelvic origin. Among these patients, 51 (41.2%) were recurrent cases. A total of 249 were submitted to transvaginal ultrasound. There was significant agreement between lower limb ultrasonographic findings and transvaginal findings. Phlebography was performed in 54 patients. The comparison between transvaginal ultrasound and phlebography was associated with a 96.2% sensitivity and 100% specificity.

Conclusions: The authors draw attention to the relatively high prevalence of lower limb varicose veins originating from the pelvis, suggesting an important but underdiagnosed cause of recurrent varicose veins.

Keywords: Color Doppler ultrasound, pelvic varicose veins, transvaginal Doppler ultrasound, phlebography.

Resumo

Introdução: As varizes pélvicas, uma das principais causas de dor pélvica crônica e dispareunia, são uma importante fonte de refluxo para as varizes dos membros inferiores, especialmente em casos recorrentes. O Doppler colorido dos membros inferiores e o ultrassom transvaginal são os métodos diagnósticos não-invasivos mais comumente usados para avaliar a insuficiência venosa pélvica, enquanto a flebografia ainda é considerada como o padrão-ouro.

Objetivos: Determinar a prevalência de varizes dos membros inferiores originadas na pélvis em um grupo de pacientes do sexo feminino e determinar a concordância entre os resultados obtidos por Doppler colorido dos membros inferiores, ultrassom transvaginal e flebografia.

Métodos: A amostra incluiu pacientes do sexo feminino encaminhadas para o laboratório vascular para triagem de membros inferiores. As pacientes diagnosticadas com trombose venosa profunda foram excluídas. A análise dos dados incluiu o coeficiente de concordância kappa, o teste de McNemar e os valores de sensibilidade e especificidade.

This study was approved by the Research Ethics Committee of Universidade Federal do Espírito Santo (UFES), register no. CEP 151/08.

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Varicose veins of pelvic origin are a major cause of reflux that is not directly related with the saphenous vein system. They can be restricted to the pelvic region itself or extend to the perineum, vulvar region or lower limbs.

Pelvic varicose veins can be identified during physical examination, indirectly via color Doppler ultrasound (CDU) of the lower limbs or directly via transvaginal Doppler ultrasound or phlebography. The condition can evolve asymptomatically or develop into pelvic congestion syndrome, with symptoms such as abdominal bloating and dyspareunia or presence of varicose veins of the lower limbs with reflux originating from subdiaphragmatic tributaries.

Knowledge of different forms of drainage in the pelvic region is essential for a clear understanding of the pathophysiology and treatment of pelvic varicose veins. The venous plexus located on the broad ligament of the uterus communicates with the uterine plexus, thus forming the gonadal or ovarian veins that usually converge directly into the inferior vena cava on the right side and into the renal vein on the left side. These veins contain valves and are therefore extremely important for drainage; on the other hand, an insufficient number of these veins will result in pelvic varicose veins.

CDU is the method of choice for the assessment of superficial venous insufficiency of the lower limbs. It successfully identifies patterns of saphenous and nonsaphenous reflux, including reflux of pelvic origin. Transvaginal CDU is used to assess organs and circulation in the pelvic region. Finally, selective phlebography is still considered the gold standard for the diagnosis of subdiaphragmatic varicose veins.

The objective of the present study was to identify the prevalence of pelvic varicose veins in female patients referred to a vascular laboratory for superficial venous system screening using three diagnostic methods: CDU of the lower limbs, transvaginal CDU, and phlebography. The results obtained with the three methods were compared so as to determine inter-method agreement.

Material and methods

The sample included all female patients referred to the vascular laboratory at Angiolab-Vitoria, located in the municipality of Vitória, southeast Brazil, for lower limb screening using CDU from January 2006 to April 2008.

Sample size was calculated taking into consideration a total of 10,000 examinations per year, an expected prevalence of pelvic varicose veins of 15%, a significance level of 5%, and a precision level of 2.5%. The minimum sample size was defined as 727 patients submitted to CDU of the lower limbs. In order to measure sensitivity between transvaginal CDU and phlebography, the same sample size was considered, with an expected prevalence of 15%, an expected sensitivity of 95%, a significance level of 5%, and a precision level of 16%. The minimum number of patients necessary for submission to the two diagnostic tests (transvaginal CDU and phlebography) was found to be 54. Indication of transvaginal CDU and phlebography was based on clinical and symptomatic assessment of the patients.

The clinical classification (CEAP) of the sample ranged between 0 and 5. Patients with prior or recent deep venous thrombosis in the iliac, femoropopliteal, and infrapopliteal segments were excluded from the study.

Patients were assessed by a physician specialized in angiography and experienced in vascular ultrasound, using an ATL-Philips HDI 5000 ultrasound device with a 7.5 MHz linear transducer for the assessment of lower limbs and a 4-8MHz endocavity probe for transvaginal ultrasound. The protocol used for lower limb venous mapping followed two stages: 1) patient in the supine position for assessment of the deep venous system; and 2) patient standing for assessment of the main sources of reflux. Significant reflux was defined as the presence of retrograde flow lasting for more than 0.5 s, monitored by placing the pulsed Doppler sample volume longitudinally in the center of the vessel (CDU longitudinal image) with adjustments in gain, filter and pulse repetition settings.

The protocol used for assessment of the pelvic region (transvaginal ultrasound) was as follows: examination performed preferentially in the morning; 6 to 8-hour fasting; an empty bladder during examination.
Transparietal abdominal investigation was carried out to evaluate the patency of the inferior vena cava and iliac vein system, as well as to identify the presence of extrinsic venous compression suggestive of pelvic varicose veins (May-Thurner syndrome and nutcracker syndrome). This exam was performed with patients in the supine position using a low-frequency convex transducer (2-5 MHz).

Transvaginal assessment was carried out with patients in the recumbent position using a 4-8 MHz endocavity probe with a sterile cover (condom). The transducer was introduced into the vaginal canal, allowing the identification of vessels in the bilateral adnexal region.

Pelvic varicose veins were defined as the presence of dilated (diameter ≥ 7 mm), tortuous vessels, with reflux (presence of bidirectional flow during Valsalva’s maneuver) in the adnexal region\textsuperscript{11,13} (Figure 1).

Selective pelvic phlebography was performed using a Philips\textsuperscript{*} device and the Seldinger technique. All operators were specialists in vascular and endovascular surgery. A right upper limb vein was used as access route, followed by selective catheterization with nonionic contrast of renal veins, iliac/gonadal veins and gonadal plexus. Vein diameter and the presence of venous reflux in the pelvic region were evaluated, also trying to identify the direction of blood flow and possible escapes to the lower limbs.

Statistical analysis

Prevalence rates of pelvic varicose veins were calculated for the three examination methods. Sensitivity, specificity, positive predictive values (PPV) and negative predictive values (NPV) obtained for ultrasonographic findings were compared with those obtained with the gold standard method (phlebography).

Kappa coefficients and McNemar’s nonparametric test were used to measure agreement and disagreement between tests, respectively. The SPSS software version 15.0 was used, and the significance level was set at 5%.

The study was approved by the Research Ethics Committee at Universidade Federal do Espírito Santo (UFES), under the protocol no. 101/08.

Results

Prevalence

A total of 1,020 patients were analyzed; mean age was 48.1±14.2 years, and mean number of gestations was 3.3±2.3. CEAP classification ranged from 1 to 2.

CDU of the lower limbs was performed in all 1,020 patients; of these, 249 patients were submitted to transvaginal CDU, and 59 patients to selective phlebography.

The prevalence of pelvic varicose veins according to CDU of the lower limbs was 12.2% (124 positive cases out of 1,020), distributed as follows: 3% (31 cases) bilateral, 4.4% (45 cases) affecting the right limb only, and 4.7% (48 cases) affecting the left limb only. Among the positive cases, 51 patients (41.2%) were recurrent, i.e., had been previously submitted to surgery (great saphenous vein stripping or high ligation of the saphenofemoral junction with preservation of the saphenous vein). These patients included 14 bilateral cases (45.2%), 17 cases (37.8%) affecting the right side only, and 20 cases (41.7%) affecting the left side only.

Reflux of pelvic origin in the lower limbs was as follows: 48 cases (38.7%) of reflux in the posterior aspect of the thigh, 35 (28.2%) converging into the great saphenous vein, 28 (22.6%) in the medial aspect of the thigh (parallel to the saphenous axis), 13 (10.5%) in perijunctional region, three (2.4%) converging into the small saphenous vein, and five (4.0%) in other regions. More than one type of reflux were detected in some patients.

Figure 1 - A) Dilated vessels, with reflux, in the adnexal region identified by transvaginal color Doppler ultrasound; B) measurement of adnexal vein caliber, identified by transvaginal color Doppler ultrasound
According to transvaginal CDU, the prevalence of pelvic varicose veins was 60.2% (150 positive cases out of 249 examinations). The mean diameter of veins with reflux was 8.5 mm (±1.7). With phlebography, the prevalence rate obtained was 98.1% (53 positive cases out of 54 examinations).

There was a statistically significant association between tributaries of pelvic origin in the lower limbs and recurrent varicose veins (chi-square = 26.839; p = 0.001), as shown in Table 1.

**Agreement between CDU of the lower limbs and transvaginal CDU**

Table 2 shows the results obtained with the two tests. Comparison between CDU of the lower limbs and transvaginal CDU (considered as the gold standard in this case) revealed a sensitivity of 41.3%, a specificity of 93.9%, a positive predictive value of 48.5%, and a negative predictive value of 92.0% (predictive values were calculated based on the prevalence obtained with lower limb CDU, 12.2%).

Kappa coefficient for the comparison between the results obtained with CDU of the lower limbs and transvaginal CDU (in this case, no test was considered as gold standard) was 0.309 (p = 0.001), suggesting a statistically significant agreement between both methods. McNemar's test indicated that transvaginal CDU yielded more positive results, i.e., had a higher sensitivity (p = 0.001).

**Agreement between transvaginal CDU and phlebography**

Table 3 shows the results obtained with the two tests. Comparison between transvaginal CDU and phlebography (gold standard) revealed a sensitivity of 96.2%, a specificity of 100%, a positive predictive value of 100%, and a negative predictive value of 94.6% (predictive values were calculated based on the prevalence obtained with transvaginal CDU, 60.2%).

Kappa coefficient for the comparison between the results obtained with transvaginal CDU and phlebography (in this case, no test was considered as gold standard) was 0.486 (p = 0.001), suggesting a statistically significant agreement between both methods. McNemar's test indicated that both tests were equivalent (p = 0.500).

Table 4 summarizes the main results of the present study.

**Discussion**

The pelvic plexus is characterized by venovenous anastomoses connected to the lower limbs, involving or not the saphenous vein system. Although gonadal vein dilatation/insufficiency is not rare among asymptomatic patients, a correlation between pelvic varicose veins on the one hand...
and chronic pelvic pain and recurrent varicose veins of the lower limbs on the other is already known.\textsuperscript{2,6,13,15,16}

According to Labropoulos et al.,\textsuperscript{1} reflux of nonsaphenous origin accounts for 10\% of the varicose veins of the lower limbs; of these, 34\% originate from the pelvic region. Recurrent varicose veins of the lower limbs affect up to 52\% of cases within 5 years; abdominal or pelvic origin account for 17\%.\textsuperscript{17,18}

According to Leal Monedero et al., the etiology of recurrent varicose veins includes recanalizations through pelvic "escape points" to the lower limbs via veins of the broad ligament, i.e., posterior branches that escape through the internal pudendal, obturator and ischiatic veins.\textsuperscript{13}

Geier et al.\textsuperscript{19} showed that 68\% of female patients with pelvic varicose veins confirmed by phlebography presented recurrent varicose veins of the lower limbs after great saphenous vein stripping.

In our sample, the prevalence of reflux of pelvic origin among patients submitted to CDU of the lower limbs was 12.2\%, a similar rate to that reported by Ashour et al.\textsuperscript{4} (15.8\%), but lower when compared to the study by Labropoulos et al. (34\%).\textsuperscript{1} This discrepancy in prevalence rates can be explained, at least in part, by the different degrees of disease severity found in the populations assessed. Labropoulos et al.\textsuperscript{1} inform that 90\% of the sample had a CEAP classification ranging from 1 to 3, compared to classifications 1 to 2 in 87\% of our sample.

The prevalence of patients submitted to great saphenous vein stripping or to high ligation of the saphenofemoral junction with preservation of the great saphenous vein (recurrent cases) in this study was 41.2\%. The association between recurrent varicose veins and tributaries of pelvic origin in the lower limbs was statistically significant (chi-square; p = 0.001), suggesting an important and so far underdiagnosed cause of recurrent varicose veins.

Predominant involvement of multiparous women (having had more than two children) and a higher number of cases affecting the left adnexal region and the left lower limb were similar to reports found in the literature.\textsuperscript{20,21}

It is important to emphasize the presence of collateralization of tributaries into the posterior aspect of the thigh through recanalization of the ischiatic primitive system, as well as transference of the reflux to the saphenous vein system in the presence of ostial competence of the saphenofemoral junction. These findings are extremely relevant because they allow to focus treatment planning on the real source of reflux.

There is no consensus in the literature with regard to the ideal cutoff point for the correlation between adnexal vein diameter measured by transvaginal Doppler ultrasound and presence of reflux, and it is possible to find values ranging from 5 to 8 mm across different studies.\textsuperscript{13,22,23} We considered a cutoff of 7 mm, and the mean diameter of veins with reflux found in our sample was 8.5 mm (±1.7).

Agreement between CDU of the lower limbs and transvaginal CDU with regard to the identification of pelvic reflux was statistically significant. However, sensitivity was low (41.3\%), which suggests that CDU of the lower limbs alone cannot be used as a criterion for the diagnosis of pelvic varicose veins; rather, the performance of transvaginal CDU to confirm the diagnostic hypothesis is required. On the other hand, the specificity 93.9\%, and negative predictive value 92.0\% associated with CDU of the lower limbs suggests that whenever this examination results negative for pelvic varicose veins, further investigation is not necessary.

Phlebography is currently the method of choice for the diagnosis of pelvic varicose veins; however, transvaginal CDU findings were equivalent to those obtained with the gold standard, with the advantage of being a noninvasive and risk-free diagnostic method.

The complex anatomical variations found in the pelvis, associated with the rich network of anastomoses that is characteristic of the region, suggests that endovascular treatment with embolization should be considered as a therapeutic option in cases of pelvic varicose veins.\textsuperscript{6,13,23}

Based on the present findings, the authors propose an algorithm for the investigation of pelvic varicose veins (Figure 2). Patients with gynecological symptoms (pelvic congestion syndrome) or with clinical and ultrasonographic findings suggestive of varicose veins of pelvic origin should be referred for transvaginal assessment. If the presence of varicose veins of pelvic origin is confirmed (diameter ≥ 7 mm and presence of reflux during Valsalva’s maneuver in adnexal vessels), then phlebography is recommended.

Figure 2 - Algorithm proposed for the diagnosis and treatment planning for pelvic varicose veins
Conclusions

The authors draw attention to the relevant prevalence of varicose veins of pelvic origin found in a sample of patients referred to a vascular laboratory for venous screening of the lower limbs. This finding suggests an important and so far underdiagnosed cause of recurrent varicose veins, reinforcing the need to include venous screening of the lower limbs in the therapeutic planning of the treatment of varicose veins. Moreover, the high agreement found between transvaginal CDU and phlebography findings for the diagnosis of pelvic varicose veins suggests that transvaginal CDU is very useful and should be considered as a less invasive diagnostic method prior to phlebography.

References


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NOTA EDITORIAL AO ARTIGO

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O roteiro de avaliação da qualidade de um artigo sobre teste diagnóstico1,2 é formado por três grandes questões, que depois são subdivididas:

1. Os resultados são válidos?
   1.1. Foi realizada uma comparação independente e mascarada do teste diagnóstico com o padrão-ouro?
   1.2. A amostra de pacientes utilizada no teste diagnóstico inclui o espectro encontrado na prática clínica?
   1.3. O resultado dos testes que está sendo avaliado influenciou a decisão de realizar o padrão-ouro?
   1.4. Foi realizada uma descrição do teste diagnóstico com detalhes suficientes para permitir sua reprodução?

2. Quais são os resultados?
   2.1. Os testes diagnósticos são apresentados com sensibilidade e especificidade, valor preditivo positivo, valor preditivo negativo ou os dados estão disponíveis para calculá-los?
   2.2. Os resultados serão aplicáveis aos meus pacientes?
   2.3. Os resultados poderão mudar minha conduta?
   2.4. Os pacientes ficaram melhores com os resultados do teste?

Ao utilizar o roteiro no artigo analisado3, são encontradas, segundo nossa avaliação, as seguintes respostas:

1.1. Foi realizada uma comparação independente e mascarada do teste diagnóstico com o padrão-ouro?
Possivelmente não. A descrição no texto é incompleta para determinar se o novo ultrassom (US) transvaginal e, depois, a flebografia foram realizados de forma que o examinador não soubesse do resultado prévio, pois a indicação dos exames (US transvaginal e flebografia) foi feita de acordo com os sinais e sintomas das pacientes. O melhor seria que todas fossem submetidas aos dois testes e ao padrão-ouro, independentemente dos resultados encontrados. Como o padrão-ouro é a flebografia, torna-se desnecessário o cálculo de sensibilidade ou especificidade da comparação do US de membros inferiores com o US transvaginal. A ausência de um padrão-ouro adequado pode gerar resultados sem aplicabilidade clínica. A comparação entre o US transvaginal e o padrão-ouro em uma amostra com 98% da doença superestima a utilidade do teste diagnóstico.

1.2. A amostra de pacientes utilizada no teste diagnóstico inclui o espectro encontrado na prática clínica?
Não. Foram selecionados os pacientes de um centro de referência que se submeteriam a US de membros inferiores. O mais adequado seria incluir somente pacientes com sinais e sintomas da doença venosa pélvica crônica e submeter todos os indivíduos ao teste diagnóstico e ao padrão-ouro de forma independente e cega.

1.3. O resultado dos testes que está sendo avaliado influenciou a decisão de realizar o padrão-ouro?
Sim. A indicação da realização da US transvaginal e da flebografia foi feita de acordo com sinais e sintomas das pacientes.

1.4. Foi realizada uma descrição do teste diagnóstico com detalhes suficientes para permitir sua reprodução?
Sim. Foi detalhada toda a técnica.

Uma vez respondidas as quatro questões, devemos ter uma avaliação da validade da pesquisa. As respostas negativas para a primeira e a segunda perguntas reduzem a avaliação da qualidade do artigo. Cabe, então, a cada leitor a decisão pessoal de continuar a avaliação. A minha resposta é sim, apesar das limitações apontadas.

Respondendo à pergunta 2.1, sobre a importância: Os testes diagnósticos são apresentados com sensibilidade e especificidade, valor preditivo positivo, valor preditivo negativo ou os dados estão disponíveis para calculá-los?
Sim. Para a avaliação da qualidade em pesquisas sobre testes diagnósticos não interessam os testes estatísticos e os valores de p. Calcular a sensibilidade, a especificidade, a prevalência e as razões de verossimilhança são suficientes. Nesse momento, a ajuda de calculadoras eletrônicas costuma ser útil. Realizados os cálculos, cabe a interpretação.

No entanto, por uma limitação da validade da pesquisa nas primeiras questões, os resultados encontrados são úteis em princípio para gerar boas hipóteses para serem testadas apropriadamente no futuro e, portanto, não seria apropriado continuar com a avaliação de qualidade proposta por Jaeschke et al.1,2.

Assim, a avaliação da qualidade de um artigo é uma habilidade que deve ser desenvolvida e aprimorada por parte de angiologistas e cirurgiões vasculares. O roteiro apresentado é apenas um de uma série de roteiros que existem para avaliação de cada tipo de estudo4,5. Ou seja, para artigos sobre tratamento, as perguntas são outras; para artigos sobre prognóstico, as perguntas também são outras.
Além do uso de roteiros de avaliação, é importante considerar o tipo de estudo. Na pesquisa publicada, existe a possibilidade de o estudo ser retrospectivo, transversal ou prospectivo, o que pode também influenciar na qualidade da pesquisa. Os resultados são mais confiáveis nos estudos prospectivos do que nos retrospectivos por reduzir a possibilidade do viés de aferição.

Referências


RÉPLICA DOS AUTORES

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Em atenção ao comentário editorial sobre nosso artigo, apresentamos uma reflexão sobre medicina baseada em evidência (MBE), o tipo de estudo que realizamos, a forma como conduzimos a pesquisa e sua importância na prática clínica.

Ressaltamos que os comentários realizados foram de alta qualidade teórica. O autor da nota editorial classificou de um teste diagnóstico é obtida em ambientes clínicos, e não em ambientes de pesquisa. Nesses estudos, os médicos utilizam o teste no cuidado com os pacientes e, por questões éticas, não conduzem uma avaliação mais aprofundada quando os testes preliminares são negativos. O problema metodológico advindo de estudos realizados dessa forma é a falta de dados suficientes para a análise.

No nosso estudo, dos três testes de diagnóstico realizados, somente a flebografia (método invasivo e não isento de risco), sofreu parcialmente a falta de dados. Entretanto, o número de pacientes que foram submetidas a esse teste (flebografia) por indicação clínica foi suficiente para a análise estatística de equivalência entre os testes.

3. Nossa pesquisa

A nossa pesquisa estudou pacientes encaminhadas ao laboratório vascular para o mapeamento venoso dos membros inferiores para a avaliação de varizes. O objetivo foi correlacionar o achado de tributárias nos membros inferiores sugestivas de origem pélvica com a real presença de varizes nesse território, visto que em alguns trabalhos essa identificação é feita somente com o estudo ultrassonográfico dos membros inferiores. O ultrassom endovascular é um exame considerado eficaz no estudo da região pélvica, e a flebografia é o exame considerado padrão-ouro para o diagnóstico de varizes pélvicas.

Submeter todas as pacientes ao estudo flebográfico, que não é isento de risco, no nosso entender não seria ético. Assim, coletamos os dados segundo os princípios da amostragem (cálculo de tamanho de amostra com nível de significância de 5%) e analisamos estatisticamente os resultados das pacientes que com a indicação clínica foram submetidas aos três exames. A análise estatística realizada mostra os resultados de sensibilidade, especificidade, valor preditivo negativo e positivo e ainda a equivalência entre os testes.

4. O que aprendemos com nossos resultados

Os resultados da pesquisa foram de grande valia, pois confirmaram com dados estatísticos que o eco-Doppler dos membros inferiores tem uma sensibilidade baixa para identificar o refluxo de origem pélvica, mesmo quando estão presentes tributárias sugestivas dessa origem. A
equivalência entre o eco-Doppler endovaginal e a flebografia foi de crucial importância na prática clínica, visto que a flebografia como diagnóstico de varizes pélvicas poderia ser abolida, sendo reservada apenas para quando o tratamento endovascular fosse indicado.

Referências