Evaluation of common femoral vein thickness as a diagnostic tool for Behçet's disease in a non-endemic area

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Abstract

Objective

To evaluate common femoral vein thickness (CFVT) as a diagnostic tool in Brazilian patients with Behçet's disease (BD) and to analyse associations between increased CFVT and disease features.

Methods

A cross-sectional study was performed including 100 BD patients and 100 controls. The CFVT and the diameters of great saphenous vein (GSV), and small saphenous vein (SSV) were measured by Doppler ultrasound.

Results

BD patients had higher right CFVT [0.600mm (0.500-0.700) vs. 0.525mm (0.450-0.637); p=0.012] and left CFVT [0.550mm (0.450-0.650) vs. 0.500mm (0.450-0.550); p=0.004] compared to controls. Vascular involvement of BD and previous deep venous thrombosis were associated with increased CFVT (p<0.05). The number of vascular events correlated with right and left CFVT (Rho=0.475 p=0.030 and Rho=0.429 p=0.052, respectively). The 0.575mm cut-off point of right and left CFVT had area under the curve (AUC) of 0.602; 95% confidence interval (95% CI): 0.524-0.680 and AUC: 0.615; 95% CI: 0.537-0.693, respectively. The right and left CFVT had a sensitivity for BD diagnosis of 52% and 43%, and a specificity of 64% and 77%, respectively. No significant differences were found between BD patients and controls regarding the GSV and SSV diameters in both legs (p>0.05).

Conclusion

In this study, CFVT measurement was not shown to be a reliable diagnostic test for BD. CFVT was increased in BD patients presenting vascular involvement and correlated with the number of previous events.

Key words

Behçet's disease, ultrasound, common femoral vein thickness

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Introduction

Behçet's disease (BD) is a systemic inflammatory disease classified as a variable vessel vasculitis (1). It is more prevalent in countries along the Silk Road, such as Turkey, Iran, and China, as well as in Mediterranean nations (2). The spectrum of BD manifestations is wide, ranging from isolated mucocutaneous symptoms to severe presentations including posterior uveitis, central nervous system involvement, and vascular disease (3). The vascular involvement of BD is one of the major causes of morbidity and mortality in BD. In particular, pulmonary artery aneurysm carries mortality as high as approximately 25 percent. Therefore, early recognition of BD is important (4).

The diagnosis of BD relies on a compilation of clinical symptoms and signs, and it poses a challenge for rheumatologists and clinicians in daily practice, especially in non-endemic areas for BD, including Brazil. To date, there are no validated tests or serum biomarkers to aid the diagnosis of BD (3, 5). The pathergy test is a complimentary test to the investigation of BD diagnosis (6, 7). However, this test has lost its sensitivity over the last few years, possibly due to the use of less traumatic needles and the progressive changes in the patient's skin flora (8). The use of the 1990 International Study Group (ISG) criteria for BD is helpful in clinical practice (9); however, the absence of severe manifestations of BD such as neurological or vascular involvement of BD in these criteria is a limitation of its application. Later, the 2014 International Criteria for Behçet's Disease (ICBD) did not include oral ulcers as a mandatory criterion, whereas novel BD severe manifestations were added to the scoring items for BD diagnosis (10). However, the ICBD criteria may lead to overdiagnosis of BD, and it lacks specificity in non-endemic areas for BD (11).

It is postulated that chronic and smouldering inflammation may occur in the large veins of BD patients regardless of the development of venous thrombosis (4). The first evidence of this smouldering venous inflammation in BD came from a study published in 2014, in which increased thickness of the popliteal veins was observed by magnetic resonance imaging of lower limbs in BD patients (12), while another study found that one-third of BD patients had venous insufficiency despite no history of venous thrombosis (13). Afterward, a group from Turkey evaluated the common femoral vein thickness (CFVT) as a possible diagnostic test for BD and found that BD patients had a considerably higher CFVT than patients with ankylosing spondylitis and healthy controls (14). Further studies performed in Turkey analysed CFVT for BD diagnosis and confirmed the good results originally described (15-19). In contrast, despite the increased CFVT in BD patients compared to controls, in one of the studies no differences were observed between BD patients with and without vascular involvement, whereas vascular involvement had a relation with increased portal vein thickness (20).

Therefore, this study aims to evaluate the measurement of the CFVT and the diameter of all lower limb veins by venous Doppler ultrasound as a possible diagnostic test for BD in a non-endemic area for BD.

Materials and methods

Patients and controls

A cross-sectional study was conducted at the Outpatient Clinic of Vasculitis at the Rheumatology Division of Universidade Federal de São Paulo, Escola Paulista de Medicina (Unifesp-EPM). The inclusion criteria were age above 18 years, fulfilment of the 1990 International Study Group (ISG) criteria for BD (9) and written informed consent. Patients were excluded if they presented other systemic inflammatory or autoimmune diseases overlapping with BD. The control group comprised healthy individuals who were non-consanguineous companions of the patients and hospital staff. The inclusion criteria in the control group were age above 18 years, the absence of systemic inflammatory or autoimmune diseases, and written informed consent. The study protocol was approved by the Institutional Ethics Committee (CAAE: 22272819.7.0000.5505) and was performed in accordance with the Declaration of Helsinki.

Data collection and disease activity

We collected information about demographics, body mass index, and comorbidities in both BD patients and controls. Data about previous disease manifestations, current therapy, and laboratory tests such as *HLA-B*51* positivity, C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR) were retrieved from medical records. Patients with BD were assessed for current disease manifestations and disease activity was evaluated by the Brazilian version of Behcet's Disease Current Activity Short Form (BR-BDCAFs) (21).

Venous Doppler ultrasound

Venous Doppler ultrasound of the lower limbs was performed by a blinded vascular surgeon with more than 30 years of experience (FHM). A high-resolution GE (General Electric Inc., Boston, MA, United States) system equipped with a high-resolution linear transducer (7–13 MHz) was used for venous Doppler assessment. The protocol of the venous Doppler ultrasound was performed as previously described (15). Briefly, in the supine position, the thickness of the right and left CFV was analysed in the posterior wall of the CFV at 2 cm distal to saphenofemoral junction and above the confluence of deep and superficial femoral veins, where two measurements were made (Fig. 1). Then, the mean value of these measurements was recorded for further analysis. The diameters of the right and left great saphenous veins (GSV), and small saphenous veins (SSV) were also evaluated. In addition, all lower limb veins, such as external iliac veins, common/superficial and deep femoral veins, GSV, SSV, popliteal veins, anterior and posterior tibial veins, peroneal veins, and perforating veins were evaluated for the presence of signs of insufficiency, thrombosis, recanalisation, and collateral circulation. Venous insufficiency was evaluated after Valsalva's manoeuvre in supine and prone positions.

To analyse the reproducibility of the CFVT measurement, two different sonographers (FHM and EN) performed repeated venous Doppler ultrasound tests on ten volunteers on the same day. The intraclass correlation coefficient (ICC) was calculated and results were displayed with a 95% confidence interval (95% CI). The intra-rater ICC were 0.931 (95% CI: 0.712–0.983) and 0.934 (95% CI: 0.717–0.894) for the right and left CFVT, respectively. The inter-rater ICC was 1.0 and 0.968 (95% CI: 0.874–0.992) for the right and left CFVT, respectively.

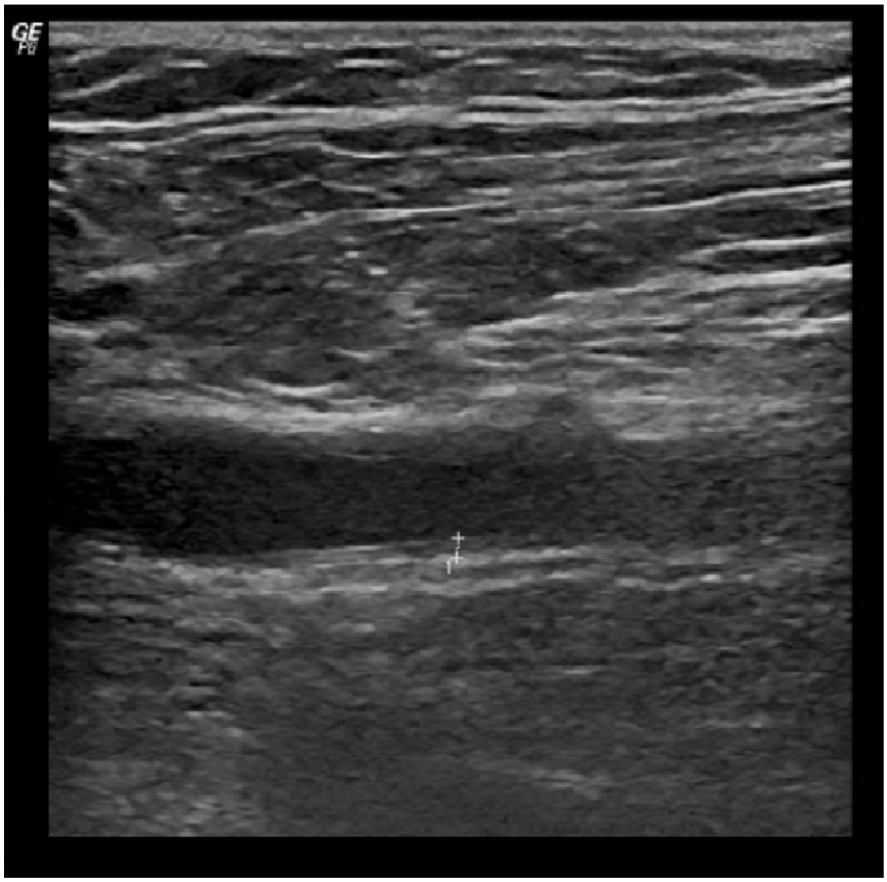

Fig. 1. A representative picture of the venous Doppler ultrasound in a patient with Behçet's disease. B-mode imaging on the longitudinal plane showing the measurement of the posterior vein wall of the left common femoral vein in a patient with Behçet's disease.

Statistical analysis

Categorical variables were presented as numbers and percentages. The Kolmogorov-Smirnov test was used as a normality test and continuous variables were presented as mean and standard deviation or as median and interquartile range (IQR). Comparisons between two groups regarding continuous variables were performed by the Student's *t*-test or by the Mann-Whitney U-test, while comparisons for three groups were performed by the Kruskal-Wallis test, followed by the Mann-Whitney U-test as a *post-hoc* test. Categorical variables were assessed by the Chi-square or by Fisher's exact tests. The Receiver operating characteristic (ROC) curves were built and the Youden test was used to find the best cut-off point of the CFVT for BD diagnosis. Then, 2x2 tables were created to analyse the accuracy, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV), positive and negative likelihood ratio (LR+ and LR-) of CFVT as a BD diagnostic tool. Spearman's test was used to analyse correlations between continuous variables. The significance level accepted was 5% (p-value <0.05) and for multiple comparisons in the *post-hoc* analysis by the Mann-Whitney U-test, the level of significance of the p-value was adjusted to 0.016 by the Bonferroni correction. The statistical analysis was carried out by the IBM SPSS Statistics for Windows v. 21.0 (Armonk, NY, USA) and the GraphPad Prism for Windows v. 9.0 (San Diego, CA, USA).

Results

BD patients and controls

One hundred BD patients and 100 controls were included, they had similar mean age (43.9±12.9 years *vs*. 46.4±12.6 years; *p*=0.166), proportion of females (64% *vs*. 69%; *p*=0.454) and BMI in the study (27.7±5.6 kg/m^2 *vs*. 27.7±5.2 kg/m^2; *p*=0.941). A detailed description of disease features and therapy for BD can be found in Table I. Although almost half of BD patients presented at least one manifestation of active disease in the study, median levels of acute phase reactants were low. The following disease manifestations were found in 46 patients presenting active disease: oral ulcers (58.7%), cutaneous manifestations (43.5%), joint complaints (37.0%), genital ulcers (21.7%), ocular inflammation (6.5%), neuro-Behçet (2.2%) and gastrointestinal involvement (2.2%).

No BD patient presented active vascular involvement in the study.

Most BD patients (87%) were under therapy to control disease manifestations or to prevent relapses, but only a few of them used prednisone at a relatively low median daily dose. Immunosuppressives were the most common therapy prescribed for BD, mostly azathioprine (78.3%). TNF inhibitors were the only biological agents prescribed for BD patients in the study (Table I).

In BD patients with previous vascular involvement, venous, arterial, and both arterial and venous manifestations were found in 71.4%, 14.3%, and 14.3%, respectively. Amongst BD patients with venous involvement (n=18), eleven had deep venous thrombosis (DVT) in the lower limbs. Other sites affected by venous thrombosis were the cerebral sinus (n=3), superior vena cava (n=2), inferior vena cava (n=2), internal jugular vein (n=1), basilic vein (n=1), right hepatic vein (n=1), left subclavian vein (n=1), and left brachiocephalic vein (n=1). In addition to DVT, four patients with BD had superficial thrombophlebitis, and four presented pulmonary thromboembolisms.

Recurrence of venous thrombotic events was observed in 10 (62.5%) cases and the median number of events was 1.0 (1.0–3.0).

Table I. Clinical and laboratory features of BD patients.

Variables	Results (n=100)
Previous manifestations	
Oral ulcers	100%
Genital ulcers	83%
Cutaneous involvement	72%
Joint complaints	52%
Ocular inflammation	56%
Neuro-Behçet	31%
Vascular involvement	21%
Gastrointestinal manifestations	3%
Disease activity	
Active disease during the study	46%
Median BR-BDCAFs	1.0 (1.0-3.0)
Median physician's VAS	3.0 (2.0-5.0)
Laboratory tests	
*HLA-B*51* positivity*	31%
CRP levels, mg/L	2.4 (0.6-5.2)
ESR, mm/hour	9.0 (5.0-20.0)
Current therapy	
Colchicine	39%
Prednisone	24%
Prednisone daily dose, mg	10.0 (5.0-20.0)
Immunosuppressive agents	60%
TNF inhibitors	27%

*HLA-B*51 was tested in 58 patients.
Continuous variables are presented as median and interquartile range.
BD: Behçet's disease; BR-BDCAFs: Brazilian version of the Behçet's disease Current Activity Form; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; n: number of patients; TNF: tumour necrosis factor.

Venous Doppler ultrasound in BD patients and controls

BD patients presented a significantly higher median CFVT on both sides ($p<0.05$) compared to controls, while no differences were found between BD patients and controls regarding the diameter of the GSV and SSV on both sides (Table II). Moreover, no significant differences were observed between BD patients and controls related to venous insufficiency and reflux in lower limb veins (Supplementary Table S1).

We compared BD patients with past vascular manifestations to BD patients without vascular manifestations and controls, we found significantly higher CFVT in those with past vascular manifestations than BD patients without vascular manifestations and controls on the right [0.70 mm (0.55-0.90) *vs*. 0.55mm (0.50–0.65) *vs*. 0.52mm (0.45-0.64); *p*=0.002] and left [0.70 mm (0.55–1.02) *vs*. 0.50mm (0.45-0.60) *vs*. 0.50mm (0.45–0.55); *p*=0.0001] sides, respectively (Fig. 2A and 2B). When only BD patients presenting or not DVT were analysed against controls, BD patients with DVT had increased CFVT compared to BD patients without previous DVT and to controls on the right side [0.80mm (0.55–1.30) *vs*. 0.55mm (0.50–0.65) *vs*. 0.52mm (0.45–0.64); *p*=0.002] and on the left side [0.90mm (0.55–1.75) *vs*. 0.55mm (0.45–0.65) *vs*. 0.50mm (0.45–0.55); *p*<0.0001], respectively (Fig. 2C-D).

CFVT as a diagnostic test for BD

The best cut-off point for BD diagnosis by the Youden test was 0.575mm for both sides. The AUC was 0.602 (95% CI: 0.524–0.680) and 0.615 (95% CI: 0.537–0.693) in the right and left CFVT, respectively (Fig. 3). For the diagnosis of BD, this right and left CFVT cut-off value had accuracy of 58.0% and 60.0%, sensitivity of 52.0% and 43.0%, specificity of 64.0% and 77.0%, PPV of 59.0% and 65.1% and NPV of 57.1% and 57.4%, respectively. The CFVT of the right and left sides had an LR+ of 1.44 and 1.87, and LR- of 0.75 and 0.74, respectively. The false negative rate of this test was as high as 48.0% and 57.0% for the CFVT on the right and left sides.

In the next step, Fagan nomograms were built to assess how much the post-test probability for BD diagnosis increases after a positive and negative CFVT test, according to the LR+ and LR-, respectively. For the right CFVT, a positive test increased the probability of diagnosing BD from 50.0% (*i.e*. the prevalence of BD in the study) to 59.0% (95% CI: 51.0–67.0%), while a negative test reduced the chance of diagnosing BD to 43.0% (95% CI: 37.0–49.0%). For left CFVT, a positive test increased the probability of a diagnosis of BD from 50% to 65.0% (95% CI: 55.0–74.0%), while a negative test reduced the chance of a diagnosis of BD to 43.0% (95% CI: 38.0–47.0%) (Suppl. Fig. S1).

CFVT and clinical variables in BD

We tested the impact of acute phase reactants, disease activity score by the BR-BDCAFs, time since diagnosis,

Table II. Comparisons between BD patients and controls regarding CFVT and the diameters of saphenous veins.

Variables	Behçet's disease (n=100)	Controls (n=100)	*p*
Right CFVT, mm	0.600 (0.500-0.700)	0.525 (0.450-0.637)	0.012*
Left CFVT, mm	0.550 (0.450-0.650)	0.500 (0.450-0.550)	0.004*
Right GSV diameter, mm	4.000 (3.275-5.025)	4.100 (3.400-5.450)	0.591
Left GSV diameter, mm	3.750 (3.150-4.650)	4.050 (3.400-5.000)	0.266
Right SSV diameter, mm	2.750 (2.150-3.437)	2.575 (2.212-3.075)	0.306
Left SSV diameter, mm	2.600 (2.275-3.550)	2.650 (2.112-3.537)	0.259

Results are presented as median and interquartile range. *Significant results.
CFVT: common femoral vein thickness; GSV: great saphenous vein; n: number of participants; SSV: small saphenous vein.

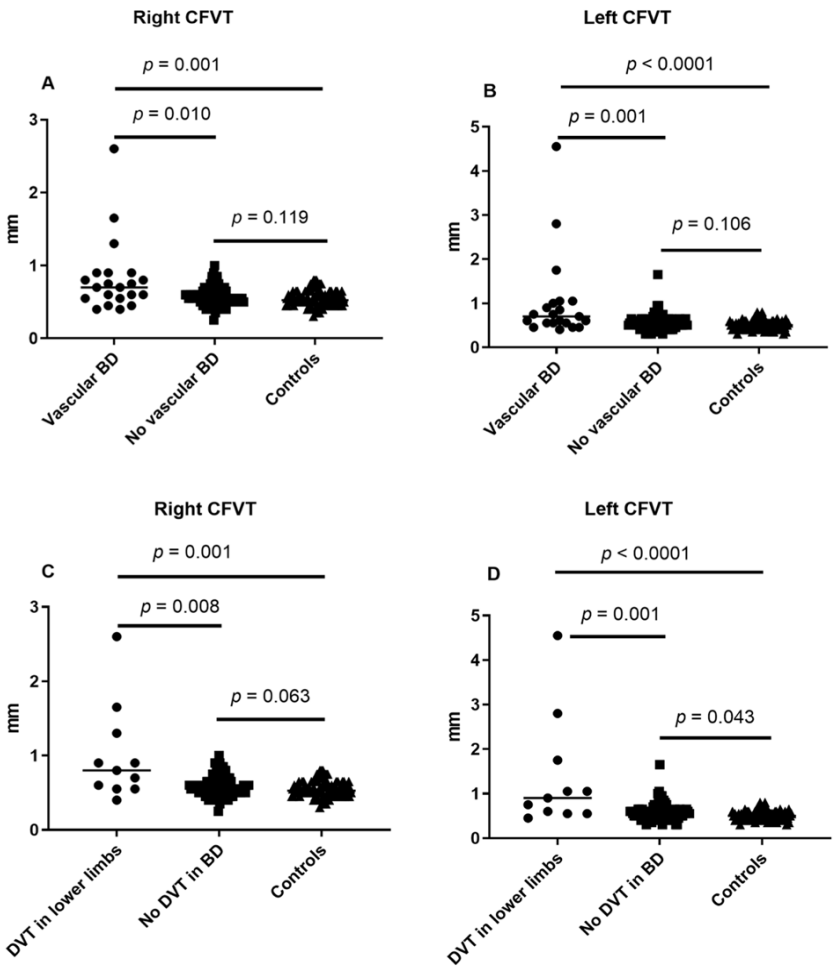

Fig. 2. CFVT in BD patients with and without vascular events or DVT in comparison to controls. The crossbars represent the median values of the CFVT. Comparisons between patients with vascular-Behçet's, without vascular-Behçet's and controls for right CFVT (**A**) and left CFVT (**B**). Comparison between BD patients with and without lower limb DVT and controls for right CFVT (**C**) and left CFVT (**D**). The significance level was adjusted to $p<0.016$ for post hoc analysis, by Bonferroni correction.
BD: Behçet's disease; CFVT: common femoral vein thickness; DVT: deep venous thrombosis.

and the number of thrombotic events on CFVT in BD patients. The number of thrombotic events correlated significantly with the right CFVT (Rho = 0.475; *p*=0.030), whereas a tendency for a positive correlation was found for the left CFVT (Rho = 0.429; *p*=0.052). No other significant correlations were observed between CFVT, and the other continuous variables analysed such as ESR levels, serum CRP levels, BR-BDCAFs, and time since BD diagnosis (Suppl. Table S2). In addition, the carriage of *HLA-B*51* was not related to higher CFVT at the right [0.625 (0.587–0.762) *vs*. 0.575 (0.500–0.687); *p*=0.139] or left side [0.600 (0.487–0.762) *vs*. 0.500 (0.412–0.637); *p*=0.102].

Regarding therapy for BD, no significant correlations were found between daily prednisone dose and right or left CFVT (Rho=0.279; *p*=0.186 and Rho=0.264; *p*=0.213). The comparisons between BD patients with or without prednisone, immunosuppressants, or biological agents for the right and left CFVT yielded no significant differences (Suppl. Table S3). Furthermore, no impact on the right [0.55mm (0.50–0.70) *vs*. 0.60 (0.50–0.67); *p*=0.853] or left [0.55 (0.50–0.65) *vs*. 0.55 (0.45–0.65); *p*=0.299] CFVT was observed related to colchicine use in BD patients, respectively.

Discussion

This cross-sectional study carried out in Brazilian individuals was the largest one performed outside Turkey to evaluate CFVT as a diagnostic method for BD. Patients with BD had significantly higher median right and left CFVT than controls. These differences were pronounced in patients with BD who had a history of vascular involvement or venous thrombosis of the lower limbs. The best cut-off point for the CFVT was 0.575 mm on both sides for the diagnosis of BD. However, with this cut-off point, we obtained relatively low values for sensitivity, specificity, PPV, and NPV. Moreover, the diameters of the right and left great and small saphenous veins were also analysed, but no differences were found between patients and controls.

Since 2019, different studies have analysed CFVT as a diagnostic test for BD, and all of them were performed in Turkey (14-20). In most of these studies, CFVT was shown to be a good tool for BD diagnosis (14-19). Our study was the first to evaluate CFVT in a large number of BD patients outside Turkey. Despite the CFVT being significantly higher in BD patients compared to controls, its usefulness as a diagnostic test was not confirmed by our data. In one

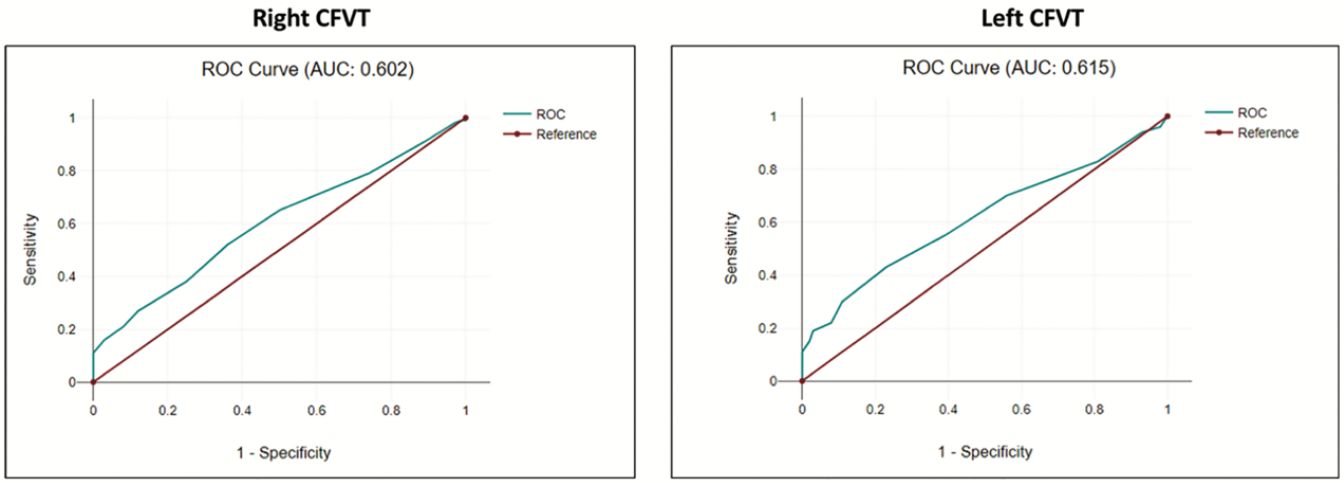

Fig. 3. ROC curve analysing CFVT for BD diagnosis.
AUC: area under the curve; CFVT: common femoral vein thickness; ROC: receiver operating characteristics.

study carried out in Turkey, despite the higher CFVT in BD patients than controls, patients with previous vascular involvement had higher portal vein wall thickness than patients without vascular involvement, but no differences were found regarding CFVT (20). The poorer performance of the CFVT measurement for the diagnosis of BD in Brazilian patients may be related to the low prevalence of the disease in our country since it is estimated to be 0.259 cases/100,000 (*i.e.* much lower than that reported for Turkey) (22). Indeed, diagnostic tests usually perform worse when evaluated in places with a low prevalence for a given disease. On the other hand, as a diagnostic test for BD, it is necessary to assess the CFVT measurement in other countries besides Turkey.

In the first study evaluating CFVT in BD, patients were compared to ankylosing spondylitis patients and healthy controls. The best cut-off points of CFVT found was 0.49mm and 0.48mm for the right and left sides, respectively (14). Although these cut-off points were lower than that observed in our study (*i.e.* 0.575mm for both sides), the AUC values (0.801–0.858), sensitivity (78.4–81.0%), specificity (78.4-81.1%), PPV (78.6–87.5%) and NPV (68.2–75.0%) were much higher, respectively.

A subsequent study carried out by the same group in Turkey evaluated the diagnostic performance of the 0.5mm CFVT cut-off point bilaterally for BD (15). They included patients with ankylosing spondylitis, other systemic vasculitis, venous insufficiency, antiphospholipid syndrome, non-inflammatory DVT, and controls as comparators. The sensitivity for BD diagnosis was also higher than that observed in this study. However, the specificity was variable in different control groups (46.5–96.3%) and it was lower when BD patients were compared to patients with antiphospholipid syndrome (46.5–51.2%). The low specificity to differentiate BD from antiphospholipid syndrome may be due to the inflammatory nature of venous thrombosis in both conditions since the specificity for diagnosing BD remained high when the BD cases were compared to patients with previous DVT of non-inflammatory cause (*i.e.* 84–96%) (15). In our study, CFVT was significantly higher in BD patients with previous vascular manifestations and in those with lower limb DVT compared to controls, and the number of venous thrombotic events was correlated with CFVT. Our findings are in line with two other studies carried out in Turkey, in which vascular manifestations of BD led to higher CFVT compared to controls (18, 19). Possibly, chronic venous inflammation and consequent endothelial dysfunction may be associated with a higher risk of thrombotic events in BD. Conversely, the recurrence of thrombotic events may have contributed to higher CFVT in BD patients with previous DVT due to ongoing vein wall remodelling as reported by Seyahi *et al.* who showed that the mean CFVT was significantly increased on the thrombotic leg vein side compared with the contralateral unaffected side (19, 23). Hence, the higher CFVT in our BD patients compared to controls was mostly related to Behçet's vascular involvement. Nonetheless, the high specificity of CFVT for BD diagnosis found when BD patients were compared to patients with non-inflammatory causes of DVT and venous insufficiency highlights the influence of venous wall inflammation and/or remodelling as the cause of increased CFVT (15, 23).

Most studies carried out in Turkey showed excellent results in terms of sensitivity, and specificity, as well as PPV and NPV of CFVT measurement for the diagnosis of BD (14-16). Only one study performed in that country found different results for CFVT as a diagnostic test for BD (20). In this study, the best CFVT cut-off point was 0.75mm for the right side and 0.65mm for the left side, and the diagnostic parameters of CFVT on the right and left sides were worse than that reported by other studies, with sensitivities of 66.7% and 70.8% and specificities of 56.9% and 57.4%, respectively (20). Nonetheless, the portal vein thickness showed higher diagnostic accuracy for BD than the CFVT measurement (20).

Another study carried out in Turkey found a different cut-off point for CFVT (*i.e.* 0.617mm) as a diagnosis

marker for BD with AUC, sensitivity, specificity, PPV, and NPV of 0.833, 72%, 90%, 87.8%, and 76.3%, respectively. In addition, superficial femoral and great saphenous vein wall thickness had also good parameters for the diagnosis of BD in this study (19).

Based on the studies performed in Turkey and on the results from our study, we still need more evidence before adding CFVT assessment as a diagnostic test for BD in clinical practice. The main reasons for precluding its widespread use include the variability of the CFVT measurement by different sonographers, the different cut-off points for BD diagnosis described in studies carried out in Turkey, and the lack of data analysing this diagnostic method in other countries. In Turkey, the method was initially tested outside the context of investigating patients with suspected BD, as only patients with an established diagnosis of the disease were evaluated in comparison to other diseases that are not mimics of BD, which overestimates the diagnostic power of the test (24). Nonetheless, a recent report from that country analysed individuals with suspected BD who did not meet the ISG and Japan Research Committee Criteria. They found that the mean CFVT was significantly higher in this suspected BD group than in controls. In addition, 94.1% of these individuals had CFVT ≥0.5mm (*i.e.* the cut-off point previously described for BD diagnosis) and no differences were found regarding vascular manifestations (25).

One study observed independent correlations between CFVT and acute phase reactants in multivariate analyses (18). However, in our study, we found no relations between laboratory parameters, including inflammatory tests, *HLA-B*51* positivity, or drug therapy in use with CFVT. Our results may indicate that the inflammatory process or fibrotic repair in the venous wall may occur regardless of current systemic inflammation.

In addition to the vein wall thickness, recent studies have evaluated the intimal medial thickness (IMT) of the venous wall, excluding the adventitial layer from the assessment of the venous Doppler ultrasound image. Two studies were performed, one in Turkey and another in Spain, and they found higher mean values of both CFVT and the IMT of the venous wall in BD patients compared to controls (26, 27). In the former study, BD patients with a history of vascular events had a significantly higher mean IMT of the common femoral vein than BD patients without vascular involvement of BD (26). None of these two studies analysed the IMT of the common femoral vein as a diagnostic test for BD.

Some limitations can be attributed to our study. Firstly, vascular ultrasound is an operator-dependent imaging technique and may be influenced by potential method variability. Other potential limitations include the evaluation of patients with a previously established diagnosis of BD, as well as the inclusion of apparently healthy individuals in the control group, rather than mimics of BD as a control group.

In conclusion, Brazilian BD patients present higher CFVT than controls, especially those with previous vascular events. However, CFVT was not shown to be a good diagnostic tool for BD in this country far from the Silk Route. In addition, no correlations were found between CFVT and acute phase reactants, *HLA-B*51* positivity, or therapy.

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