

Role of Doppler ultrasonography evaluation of superior mesenteric artery flow volume in the assessment of Crohn's disease activity*

Contribuição da medida do volume de fluxo da artéria mesentérica superior pelo Doppler na caracterização da atividade inflamatória em pacientes com doença de Crohn

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Abstract Objective: To investigate superior mesenteric artery flow measurement by Doppler ultrasonography as a means of characterizing inflammatory activity in Crohn's disease. **Materials and Methods:** Forty patients were examined and divided into two groups – disease activity and remission – according to their Crohn's disease activity index score. Mean superior mesenteric artery flow volume was calculated for each group and correlated with Crohn's disease activity index score. **Results:** The mean superior mesenteric artery flow volume was significantly greater in the patients with active disease (626 ml/min \pm 236 \times 376 ml/min \pm 190; $p = 0.001$). As a cut off corresponding to 500 ml/min was utilized, the superior mesenteric artery flow volume demonstrated sensitivity of 83% and specificity of 82% for the diagnosis of Crohn's disease activity. **Conclusion:** The present results suggest that patients with active Crohn's disease have increased superior mesenteric artery flow volume as compared with patients in remission. Superior mesenteric artery flow measurement had a good performance in the assessment of disease activity in this study sample. **Keywords:** Doppler ultrasonography; Superior mesenteric artery flow; Crohn's disease; Inflammatory activity.

Resumo Objetivo: Avaliar a medida do volume de fluxo da artéria mesentérica superior pelo Doppler como método para caracterizar a atividade inflamatória em pacientes com doença de Crohn. **Materiais e Métodos:** Quarenta pacientes foram submetidos ao exame e divididos em dois grupos – doença em atividade e remissão –, de acordo com o índice de atividade da doença de Crohn. Foram estabelecidas as médias do volume de fluxo da artéria mesentérica superior e feita a correlação com o escore do índice de atividade da doença de Crohn. **Resultados:** A média do volume de fluxo da artéria mesentérica superior foi significativamente maior nos pacientes com doença em atividade (626 ml/min \pm 236 \times 376 ml/min \pm 190; $p = 0,001$). Utilizando-se o ponto de corte de 500 ml/min, a medida apresentou sensibilidade de 83% e especificidade de 82% para o diagnóstico de atividade inflamatória. **Conclusão:** Os resultados sugerem que pacientes com doença de Crohn em atividade apresentam um aumento do volume de fluxo da artéria mesentérica superior. O teste apresentou bom desempenho na avaliação da atividade inflamatória nesta amostra de pacientes. **Unitermos:** Ultrassom Doppler; Fluxo da artéria mesentérica superior; Doença de Crohn; Atividade inflamatória.

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INTRODUCTION

Crohn's disease (CD) is a chronic recurrent inflammatory disorder which affects the gastrointestinal tract. Its treatment, al-

though effective in relieving symptoms and in improving the quality of life, is not curative. The evaluation of the inflammatory activity is of paramount importance, as the delay in instituting the treatment may lead to complications.

The ideal marker of inflammatory activity at CD is still to be determined. The available clinical indices rely on subjective symptoms such as abdominal pain and

well-being sensation, and present poor correlation with endoscopic and histopathological signs of disease activity. Biochemical tests may be more objective, but are not more specific than clinical indices. Endoscopic methods are invasive, costly and time consuming, so their utilization as a routine for all patients is not feasible, particularly in cases where serial examinations are necessary^(1,2). Computed tomography enterography has demonstrated to be efficient in the evaluation of inflammatory activity, but, as this method relies on ionizing radiation, its indication is limited in the context of frequent recurrences^(3,4).

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Magnetic resonance enterography provides results comparable to those of computed tomography enterography⁽¹⁾, however it is still scarcely available in our country.

Microvascular changes characterized by vascular injuries or infarct are observed in small bowel resection specimens from patients with CD, and vary according to the inflammatory reaction intensity, resulting in neovascularization^(5,6), which could also be observed in angiographic studies^(7,8), probably reflecting an increase in blood flow to the affected bowel segments. With the publication of studies demonstrating the viability of Doppler ultrasonography (US) for the evaluation of the superior mesenteric artery (SMA) flow⁽⁹⁻¹¹⁾, there has been an increasing interest in the splanchnic hemodynamics evaluation in CD by means of Doppler US, considering its noninvasiveness, safety, low-cost and capability for quantitative analysis.

MATERIALS AND METHODS

Patients

A group of 42 patients previously diagnosed with CD with small bowel involvement, defined according to clinical, endoscopic, radiological, surgical and histopathological⁽¹²⁾ criteria, were prospectively evaluated. All the patients originated from the Bowel Clinic of Instituto Alfa de Gas-

troenterologia – Hospital das Clínicas da Universidade Federal de Minas Gerais (UFMG), recruited between October 2006 and November 2009. The study was approved by the Committee for Ethics in Research of UFMG (ETIC 87/08). All patients signed a term of free and informed consent before their inclusion in the study.

The patients were divided into two groups on the basis of the score from the Crohn's disease activity index – CDAI (Table 1) as a reference standard⁽¹³⁾: group 1 – comprising patients with CDAI < 150, characterizing disease in remission; group 2 – comprising patients with CDAI > 150, characterizing active disease. Pregnant patients and those with severe coexisting disorders of cardiopulmonary or renal origin were excluded from the study.

The patients were clinically evaluated according to the routine of the outpatient clinic and underwent Doppler US before any change of the medical approach. The scans were blindly performed, with the observer being unaware of the patients' clinical history/classification.

Once the patients had undergone the scan, their records were reviewed for clinical and laboratory data collection. The patients were classified according to their ages at the time of the diagnosis, site and form of disease according to the Vienna classification⁽¹⁴⁾ (Table 2).

Doppler US of SMA

The scans were performed by an experienced radiologist specialized in Doppler US, utilizing a duplex Doppler US ATL 5000 Sono-CT model apparatus (Philips Medical Systems; Best, The Netherlands), equipped with a 2–5 MHz multi-frequency convex transducer.

The patients were examined in the morning, after fasting for eight hours. The SMA was sagittal scanned, with high definition zooming and 5 kHz pulse repetition. The Doppler sampling volume was positioned 2–3 cm distally from the vessel origin, before the emergence of its branches and adjusted to comprise the vascular lumen, but without touching its walls. A spectrum of at least five cardiac cycles was obtained during breath hold, and the mean flow velocity was automatically determined by the equipment. The insonation angle was determined on the real time B-mode image and always maintained below 60°. The measurement of the SMA diameter was utilized by the equipment for determining the vessel area and automatically calculating the SMA flow volume (Figure 1). With the objective of reducing random errors, each measurement was repeated for three times, and the mean value was considered as the final result⁽¹⁵⁾.

After Doppler US, the patients were submitted to total abdominal US studies,

Table 1 Crohn's disease activity index (CDAI).

Variable	Multiplier factor	Subtotal
1) Number of liquid or liquid-pasty stools in the last seven days.....	2	= _____
2) Classification of abdominal pain/colic in the last seven days (0 = no pain; 1 = mild pain; 2 = moderate pain; 3 = intense pain).....	5	= _____
3) Well-being sensation in the last seven days (0 = well; 1 = regular; 2 = bad; 3 = very bad; 4 = lousy).....	7	= _____
4) Afecções relacionadas com a DC.....	20	= _____
– arthritis or arthralgia		
– iritis/uveitis		
– erythema nodosum or pyoderma gangrenosum or aphthous stomatitis		
– anal fissure or fistula or perianal abscess		
– other bowel-related fistulae		
– fever above 37.8°C during the last seven days		
5) Antidiarrheal therapy (0 = none; 1 = yes).....	30	= _____
6) Abdominal mass (0 = none; 2 = questionable; 5 = unquestionable).....	10	= _____
7) Hematocrit.....	6	= _____
– male: 47 – Hct		Add or subtract
– female: 42 – Hct		
8) Weight.....	1	= _____
– standard weight – actual body weight × 100/standard weight		Add or subtract
		Total =

Table 2 Vienna classification in the patient groups with CD in remission (group 1) and active disease (group 2).

Vienna classification (%)	Group 1 N	Group 2 N	Statistical test	<i>p</i>
Age			Fisher's exact test	0.41
A1 (82.5%)	24	9		
A2 (17.5%)	4	3		
Site			Fisher's exact test	0.74
L1 (45%)	12	6		
L3 (55%)	16	6		
Behavior			Fisher's exact test	0.118
B1 (27.5%)	10	1		
B2 (30%)	6	6		
B3 (17.5%)	6	1		
B2/3 (25%)	6	4		

A1: < 40 years; A2: > 40 years; L1: terminal ileum; L3: ileocolon; B1: non-stenosing, non-penetrating; B2: stenosing; B3: penetrating.

with special attention to the evaluation of thickening of small bowel walls (> 4 mm) and to the presence of fistulas and abscesses^(16,17).

Statistical analysis

The comparison between the two groups was carried out with the by utilizing the chi-squared test and the Fisher's exact test for dichotomous variables and the Student's *t*-test for continuous variables. The considered significance level was 5% ($p < 0.05$). The evaluation of the test performance for characterization of inflammatory activity in CD was carried out by obtaining the receiver operating characteristic curve (ROC) and selection of a cut-

off point, with determination of sensitivity, specificity, positive and negative predictive values in relation to the reference standard.

RESULTS

Two patients were excluded from the analysis for not presenting with satisfactory technical conditions to be submitted to Doppler US of SMA, because of excessive abdominal distension. Thus, group 1 comprised 28 patients (70%) with CD in remission, and group 2 comprised 12 patients (30%) with active disease evaluated according to the CDAI score.

Abdominal US demonstrated alterations characterized by ileum wall thickening,

presence of entero-ental fistula and cavitary collection in 16 patients (40%), which were the changes most frequently observed in group 2 ($p = 0.037$). On average, the SMA flow volume was significantly greater in group 2 (626 ml/min \pm 236) as compared with group 1 (376 ml/min \pm 190), with $p = 0.001$ (Figure 2).

The area under the ROC curve for the SMA flow volume was 0.833 ($p = 0.001$). The value of 500 ml/min was adopted as the cutoff point, since such value is considered in literature as the upper limit of normality for healthy individuals⁽¹⁸⁻²⁰⁾ and is also utilized for evaluation of the test performance. In the present study, the measurement of the SMA flow volume at Doppler US presented a sensitivity of 83% and specificity of 82% for the diagnosis of inflammatory activity. There was also statistically significant association between altered result of SMA flow volume measurement and the presence of inflammatory activity in CD ($p = 0.0001$).

DISCUSSION

The presence of hemodynamic changes in patients with CD has already been previously demonstrated by angiography^(7,8) and studies with radionuclides⁽²¹⁾, characterized by a hyperdynamic state, probably caused by vascular congestion, stasis and neovascularization. From the physiopathological point-of-view, it would be reasonable to assume that such changes imply an increase in the SMA flow volume at Doppler US, a hypothesis already admitted in other studies.

Although some authors assert that results in the literature are conflicting as regards the association between changes observed at Doppler US of SMA and presence of inflammatory activity in CD^(22,23), the present study authors believe that such discrepancies are mostly due to crucial differences in the utilized method, notably in the parameters adopted for Doppler US of SMA. Undoubtedly, among the already evaluated parameters, the SMA flow volume stands out as that with best correlation with inflammatory activity^(24,25).

As previously observed by other authors⁽²⁴⁻²⁶⁾, the present study demonstrates that patients with active CD presented sig-

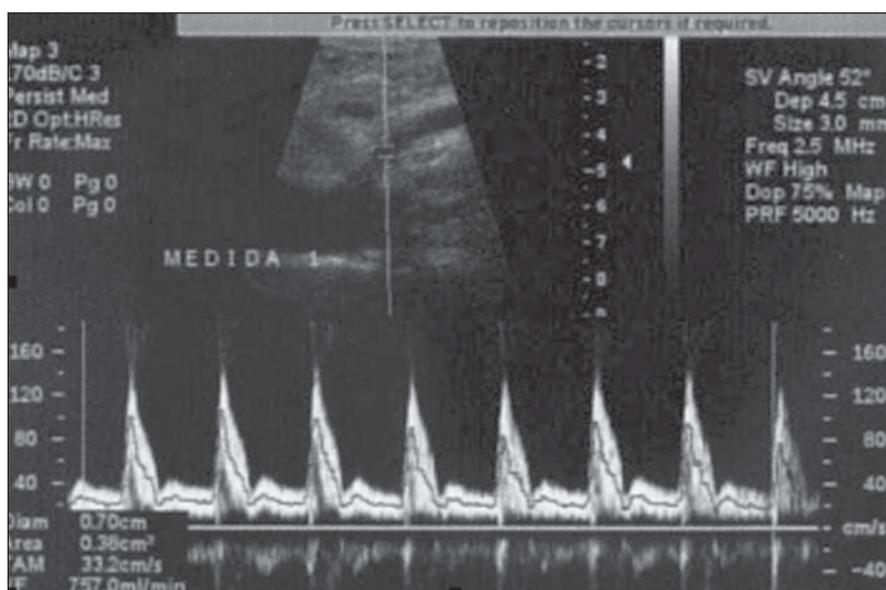


Figure 1. Spectrum of superior mesenteric artery flow at Doppler US in patient with active Crohn's disease.

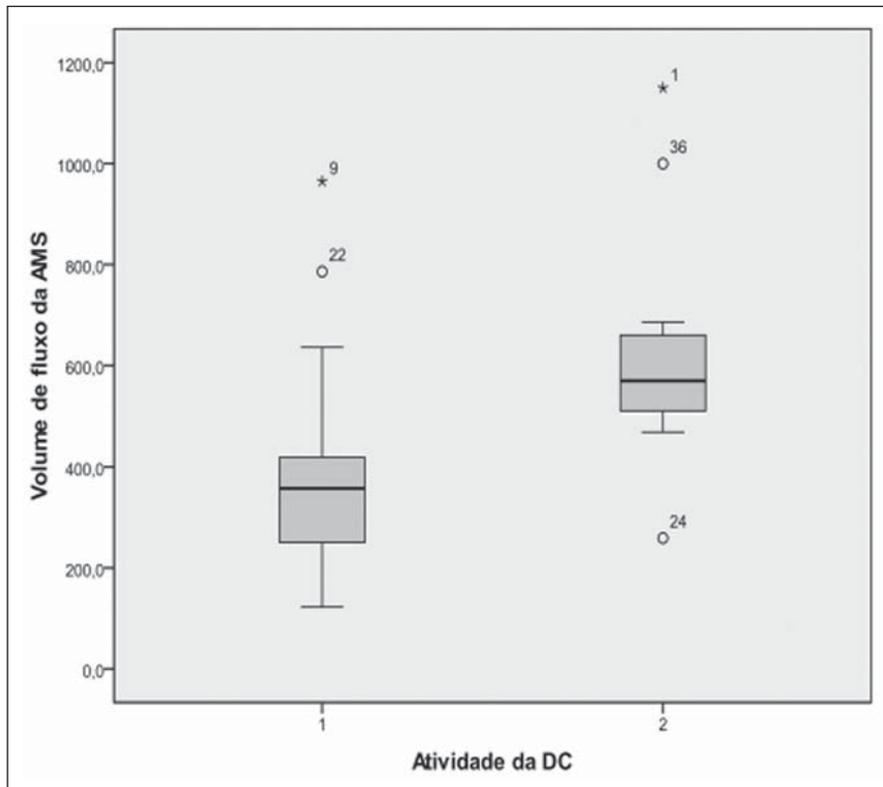


Figure 2. Boxplot of the comparison of the SMA flow volume in patients with CD in remission (group 1) and in activity (group 2).

nificantly greater SMA flow volume than patients with disease in remission. Additionally, as the value of 500 ml/min is considered as the cutoff point, the authors of the present study observed sensitivity of 83% and specificity of 82% in the diagnosis of inflammatory activity, values which are similar to those reported by other studies.

Some authors^(25,27) question the usefulness of the SMA flow volume measurement for characterizing inflammatory activity in CD, even after finding significant association between increased flow and clinical and laboratory signs of activity, due to the existence of an overlapping range of flow volume values between the patients with active CD and patients with the disease in remission, close to the cutoff point of 500 ml/min. Such range was observed by van Oostayen et al.^(28,29) and defined as a “gray zone” of values between 450 and 600 ml/min, where the test would be less useful.

In the present study, the authors observed seven patients with the flow volume within such “gray zone” of values. One might assume that patients presenting with less intense inflammatory activity or those

who normally have a greater flow volume would be in such zone; it is important to remind that CDAI, although being widely utilized, presents many limitations in the evaluation of inflammatory activity⁽¹³⁾. In the present study, there were two patients with false-negative results. One of them had a CDAI score of 180 and flow volume of 469 ml/min (therefore within the “gray zone”) and had been previously submitted to partial ileocolic enterectomy, which can explain the absence of increased SMA flow volume. The other patient had a CDAI score of 206 and the flow volume of 259 ml/min; despite the absence of an explanation for such a discrepancy, the patient presented normal C-reactive protein levels, a fact which allows the authors to assume that perhaps the increased CDAI might result from subjective symptoms and not related to inflammatory activity, an influence which is recognized in the literature⁽¹³⁾.

The main limitation of the present study was the sample size, which led to wide confidence intervals in the measurement of the test performance. Additionally, further studies with prospective evaluation of pa-

tients before and after treatment may be useful to elucidate some of the assumptions raised in the discussion.

CONCLUSION

The mean values for SMA flow volume were higher in patients with active CD, and a statistically significant association was observed between the altered results of the test and the inflammatory activity evaluated by the CDAI score. Because of its noninvasiveness, safety and low-cost, Doppler US of SMA can be useful in the evaluation of the inflammatory activity in patients with CD.

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