REVISTA ESPAÑOLA DE
ENFERMEDADES DIGESTIVAS
The Spanish Journal of Gastroenterology

Title:
The use of serum calprotectin as a biomarker for inflammatory activity in inflammatory bowel disease

Authors:
Cristina Suárez Ferrer, Marta Abadía Barno, Eduardo Martín Arranz, Andrea Jochems, Laura García Ramírez, Joaquín Poza Cordón, Marta Jaquotot Herranz, Alberto Cerpa Arencibia, María Dolores Martín Arranz

DOI: 10.17235/reed.2019.5797/2018
Link: PubMed (Epub ahead of print)

Please cite this article as:
Suárez Ferrer Cristina, Abadía Barno Marta, Martín Arranz Eduardo, Jochems Andrea, García Ramírez Laura, Poza Cordón Joaquín, Jaquotot Herranz Marta, Cerpa Arencibia Alberto, Martín Arranz María Dolores. The use of serum calprotectin as a biomarker for inflammatory activity in inflammatory bowel disease. Rev Esp Enferm Dig 2019. doi: 10.17235/reed.2019.5797/2018.

REVISTA ESPAÑOLA DE
ENFERMEDADES DIGESTIVAS
The Spanish Journal of Gastroenterology

OR 5797 inglés

The use of serum calprotectin as a biomarker for inflammatory activity in inflammatory bowel disease

Cristina Suárez Ferrer[1], Marta Abadía Barno[1], Eduardo Martín Arranz[1], Andrea Jochems[2], Laura García Ramírez[1], Joaquín Poza Cordón[1], Marta Jaquotot Herranz[1], Alberto Cerpa Arencibia[1] and María Dolores Martín Arranz[1]

Departments of [1]Digestive Diseases and [2]Immunology. Hospital Universitario La Paz. Madrid, Spain

Received: 02/07/2018

Accepted: 17/03/2019

Correspondence: Cristina Suárez Ferrer. Department of Digestive Diseases. Hospital Universitario La Paz. Paseo de la Castellana, 261. 28046 Madrid, Spain
e-mail: cristinajsuarezferrer@gmail.com

ABSTRACT

Introduction: simple, reliable and non-invasive biomarkers are needed to enable the early detection of inflammatory activity for the correct management of inflammatory bowel disease (IBD). One of these biomarkers may be serum calprotectin (SC).

Material and methods: a prospective study was performed of patients with IBD due to undergo a colonoscopy as part of the common clinical practice. The study parameters included SC, fecal calprotectin (FC) and conventional blood test parameters. Clinical indices (Harvey and Walmsley) and relevant endoscopic scores were completed for each scenario (Simple Endoscopic Score Crohn Disease [SES-CD] and Mayo).

Results: fifty-three patients were included in the study, 51% (27 patients) with ulcerative colitis (UC) and 49% (26 patients) with Crohn's disease (CD). The CS values in UC were significantly higher with an endoscopic Mayo score 2/3 (median score 10.39 mg/ml [IQR: 7.4-12.2]) compared to those with a Mayo score of 0/1 (median 4.07 mg/ml [IQR: 2.9-7.2]) (p = 0.01). The area under the ROC curve (AUCROC) was 0.85 and

REVISTA ESPAÑOLA DE
ENFERMEDADES DIGESTIVAS
The Spanish Journal of Gastroenterology

the sensitivity and specificity were 83.3% and 81.25%, respectively, for a SC cut-off point of 4.4 mg/dl. Furthermore, a higher AUCROC was obtained in comparison with other serological markers for activity (C-reactive protein [CRP], erythrocyte sedimentation rate [ESR], hemoglobin [Hb] and platelets). There were no statistically significant differences in the comparison between SC and endoscopic findings in CD (SES CD > 3: 20.1 [IQR: 16.8-23.4] *vs* SESC ≤ 3:6.25 [IQR: 5.4-7.1]) (p = 0.8).

Conclusions: SC is a good indirect marker of inflammatory activity and there was a correlation with endoscopic findings in UC. However, there were no statistically significant differences in the case of CD.

Key words: Inflammatory bowel disease. Fecal calprotectin. Serum calprotectin. IBD biomarker.

INTRODUCTION

The classic treatment approach for inflammatory bowel disease (IBD) was based on controlling symptoms and scaling treatment up and down, mainly based on the clinical condition (1,2). In the long term, this approach does not alter the natural course of the disease and does not prevent the appearance of complications and/or development into more aggressive forms of the condition. Furthermore, a high percentage of patients, around 40% in the case of Crohn's disease (CD) and 30% in ulcerative colitis (UC), may have inflammatory activity despite remaining asymptomatic (3,4). Thus, the condition needs to be managed using therapeutic targets other than those based exclusively on clinical practice, including analytical markers and image testing. Although ileocolonoscopy is the gold standard, it is an invasive and expensive procedure with possible complications (3-5).

There are biological markers for the assessment of inflammatory activity. In general, biological markers are more specific than clinical indices, less expensive and more comfortable than endoscopic monitoring. The most commonly used serum marker is C-reactive protein (CRP) in the current clinical practice. However, its sensitivity for the detection of intestinal inflammation is low and it can increase in other extra-intestinal inflammatory processes (6).

Inflammatory markers in feces have the advantage of being more specific than plasma markers as they would not increase in processes outside the digestive system (7). Thus, they would be more efficient than plasma markers and may even reduce the need for endoscopic examinations in certain clinical situations. Fecal calprotectin (FC) is currently the most commonly used fecal biomarker used in the clinical practice (8,9). Calprotectin is a 36kDa protein that binds with calcium and zinc and is found in plasma, some bodily fluids and inflamed mucosa, but not in healthy intestinal mucosa. It constitutes 60% of the cytosolic proteins in neutrophils, monocytes and activated macrophages. Due to the inflammatory activity in intestinal mucosa, it is habitually accompanied by exudate from these cells into the intestinal lumen. The presence of this protein in feces is directly proportional to the migration of neutrophils into the gastrointestinal tract (10).

FC has an excellent stability in feces due to its resistance to breakdown by bacteria in the colon and it can also be quantified using ELISA techniques with a small stool sample (5 g). It has been proven to be a highly sensitive marker for organic intestinal pathology, insofar that it is found in high quantities in different processes such as neoplasms, infections and the consumption of NSAIDs. However, it is not affected by functional conditions such as irritable bowel syndrome (7,11).

Several studies have assessed the use of plasma and fecal markers as objective indicators of inflammatory activity in CD. FC may be useful for differentiating patients with active CD and in remission (12-15) and also shows a good correlation with the level of inflammatory activity assessed using clinical indices (12-17). Other studies have demonstrated that FC levels are associated with the presence of tissue alterations in endoscopic biopsies and are lower in the absence of anatomopathological inflammation (18,19). Consequently, existing data suggest that FC would be more sensitive than current serum markers for identifying inflammatory activity (20,21).

Despite the advantages of fecal markers, there are some disadvantages with regard to their use in the clinical practice, such as patient resistance to collecting stool samples or the handling of fecal material in the laboratory. Thus, this study addressed the possibility of using serum calprotectin (SC) as a marker of intestinal inflammation, attempting to verify its correlation with current endoscopic, analytical and clinical

parameters.

MATERIAL AND METHODS

The patients included had an established diagnosis of UC, CD or non-specific colitis and were under treatment at the IBD Unit at Hospital Universitario La Paz; in addition, they were due to undergo an endoscopy as part of the monitoring of their condition for any reason. All patients provided informed consent. The inflammatory activity observed during the endoscopic study was classified bearing in mind the contrasted indices for each scenario, the Simple Endoscopic Score Crohn's Disease (SES-CD) for CD and the Mayo endoscopic score for UC.

A blood test was performed in all patients during the colonoscopy. This included acute-stage reactants such as CRP and SC as well as the conventional parameters. SC levels were measured using the PhiCal®Calprotectin ELISA Kit, Inmundiagnostik. This consists of a sandwich ELISA using two selected monoclonal antibodies that bind human calprotectin. The test was performed using plasma, with duplicate dilutions of 1:50 (40 samples per kit). The sample was applied to the coated capture antibody plate, incubated and washed. The amount of bound calprotectin was detected using the second monoclonal layer marked with biotin. A biotin-streptavidin reagent with a TMB substrate was used to reveal the reaction. Normal levels of calprotectin in serum of healthy subjects are > 3 mg/ml. FC levels were also tested, using the sample provided on the day of the endoscopy. Stool samples were collected by the patient at home prior to starting intestinal preparation in order to prevent any interference with results; these were kept refrigerated until the day of the colonoscopy.

Patient baseline data was collected such as age, sex and date of birth, as well as the nature of their IBD (IBD type, area affected, phenotype, current treatment, prior surgery, etc.). Finally, the clinical indices were drawn up. This was the Harvey Index (remission at ≤ 4 points) in the case of CD and the Walmsley Index (remission at ≤ 3 points) for UC.

Statistical analysis

A descriptive analysis was performed on the data obtained, both for patient baseline data and specific IBD data. The median and interquartile range (IQR) were calculated for continuous variables and percentages were calculated for categorical variables. The quantitative variables were compared using the applicable non-parametric test. The Mann-Whitney U test was used for the mean comparison.

ROC curves were also completed to study the sensitivity and specificity of the test. A multivariate analysis was performed via logistic regression, using the presence of categorical endoscopic inflammatory activity as the dependent variable. The Spearman correlation coefficient for quantitative variables was used to study the SC:FC ratio. A value of $p < 0.05$ was considered as statistically significant. The statistical analysis was performed using the Stata software for Mac.

RESULTS

A total of 53 patients were included in the study, with a median age of 50 years (IQR 39-61 years) and 53% (28 patients) were male. All the patients had an established prior diagnosis of IBD, 51% (27 patients) had UC and 49% (26 patients) had CD. The activity of biomarkers (including SC) and their relationship with endoscopic findings are shown in table 1. There were no statistically significant differences between the FC values in UC patients (median 47.2, IQR: 15-171) and CD (median 83.2, IQR: 38.3-217) ($p = 0.3$). Similarly, no significant differences between UC and CD were found in the analysis of SC values, 10.73 mg/mg (IQR: 2.97-16.0) *vs* 10.82 mg/ml (IQR: 3.73-11.9) ($p = 0.98$).

The association between the severity of the endoscopic affectation and SC was studied in UC patients, which was significantly higher with an endoscopic Mayo score of 2/3 (median 10.39 mg/ml [IQR: 7.4-12.2]) compared with those with a Mayo score of 0/1 (median 4.07 mg/ml [IQR: 2.9-7.2]) ($p = 0.01$). A ROC curve was used to determine the sensitivity and specificity of SC in UC in comparison with endoscopic findings. An area under the curve of 0.85 was obtained, with a cut-off point for SC of 4.4 mg/ml. The sensitivity and specificity obtained were 83.3% and 81.25%, respectively, for the identification of an endoscopic Mayo score of 2/3.

ROC curves were also drawn for the different serum activity markers most commonly used in the clinical practice for UC such as CRP, erythrocyte sedimentation rate (ESR),

hemoglobin and platelets. When plotted together with SC, larger areas under the curve were obtained and therefore, higher sensitivity and specificity values. The results are shown in figure 1. In addition, the median of FC was higher in patients with endoscopic activity, Mayo 0/1 81.5 (IQR: 20.1-160) *vs* Mayo 2/3 141 (IQR: 45-527). However, this did not reach statistical significance (p = 0.5).

A multivariate analysis using logistic regression was performed to study the connection between the different biochemical parameters and the endoscopic findings in UC. A statistical significant association was not obtained for any variable. Furthermore, no association was observed between the activity measured using this scale and SC, according to the analysis of the clinical indices for UC (Walmsley) (p = 0.37). However, there were statistically significant differences when we compared SC with the endoscopic findings for CD, between patients with SES-CD ≤ 3 compared to those with a higher score (p = 0.8). Nevertheless, the median SC was higher in patients with greater endoscopic activity, SES-CD ≤ 3: 6.25 (IQR: 5.4-7.1) *vs* SESCD > 3: 20.1 (IQR: 16.8-23.4).

The sensitivity and specificity for SC was determined depending on endoscopic findings in CD), which were low at 62.50% and 42.86%, respectively (CS cut-off point: 3.2 mg/ml). ROC curves were also drawn for the different serum activity markers most commonly used in the clinical practice for CD (CRP, VSG, hemoglobin and platelets). When potted together with SC, there was no good correlation between any of the biomarkers studied and endoscopic activity. The results are shown in figure 2. In CD, the median FC was higher in patients with greater endoscopic activity, SES-CD ≤ 3: 48.2 (IQR: 8.6-86.4) *vs* > 3: 136 (IQR: 47.2-280). These results were not statistically significant (p = 0.8)

A multivariate analysis was also performed to study the association between the different biochemical parameters and the endoscopic findings in patients with CD. There were no statistically significant variables according to this analysis. With regard to the clinical parameters, there was no significant association between SC levels and the Harvey scale (p = 0.39) in CD patients. When we compared SC with FC for both UC and CD patients, there was a poor linear correlation between the two (*Spearman rho = 0.11*, p = 0.46).

DISCUSSION

Previous studies have demonstrated the usefulness of SC as a marker of inflammation in rheumatoid diseases such as rheumatoid arthritis. Furthermore, it is also considered as a useful biomarker for monitoring the response to anti-TNF treatment (22-25). However, there are few studies to date that examine the use of SC to assess intestinal inflammatory activity in IBD patients compared with endoscopic findings (26,27).

The study of a Belgium group (26) included patients in the STORI study and selected those patients with CD under treatment with infliximab for comparison with healthy controls. The levels of SC were higher in patients with CD compared with the control group ($p < 0.0001$) (28). Furthermore, SC was significantly greater when there was CD activity (mean 19.5 ng/ml *vs* 8,353 ng/ml, $p < 0.0001$). There was also a good correlation with CRP ($r = 0.4092$, $p < 0.0001$) and CDAI ($r = 0.4442$, $p < 0.0001$) but not with endoscopic findings (CDEIS). Mao et al. recently completed a study to assess the usefulness of SC for the detection of inflammatory activity in both UC and CD. They identified a positive connection between SC and other biomarkers such as CRP or fecal calprotectin, as well as with clinical activity indices such as CDAI or Mayo score for each scenario. However, SC was not compared with endoscopic findings.

In our experience, SC has a good correlation with endoscopic activity in UC (sensitivity of 83.3% and specificity of 81.25%) and there were also statistically significant differences between SC levels in patients with a Mayo score of 0/1 *vs* 2/3. However, the correlation with endoscopic findings in our CD sample was weaker. It is possible that these results are affected by the fact that the endoscopically accessible sections of bowel are not always the total affected segments. However, it is of note that although statistical significance was not reached, the levels of SC were higher in our study when endoscopic activity was present (median 20.1 [16.8-23.4] *vs* 6.25 [5.4-7.1]). In order to find statistically significant differences, the sample size would likely need to be increased.

In general, the clinical indices for IBD do not have a good correlation with endoscopic findings, both in UC and CD (1-5). In our experience, no statistically significant differences were found with the Harvey scale for CD or the Walmsley scale for UC

when these clinical scores were correlated with SC.

Finally, FC is used in the daily clinical practice for the management of IBD, although it has been used categorically as high or normal, without setting any validated cut-off points for the association with the severity of endoscopic lesions. However, several studies have observed a good correlation between FC and endoscopic activity (18-20). In our study, we aimed to assess whether there was a good linear correlation between FC and SC, with poor results (*Spearman rho* 0.11, p = 0.46)

It should be noted that in our sample, SC was higher than other serum parameters such as CRP or VSG for the quantification of inflammatory activity in UC. In this case, the sensitivity and specificity of SC was considerably higher than other serum estimates, 83.3% and 81.25%, respectively, as shown in figure 1. Although further studies are needed with a larger number of patients, our experience suggests that SC is higher than other analytical markers for the detection of activity in UC (29-31). In our experience, SC is a good indirect marker for inflammatory activity and correlates with endoscopic findings in UC, although there were no statistically significant differences for CD. Further studies are needed with a larger number of patients in order to increase the statistical potential and to make definitive conclusions.

REFERENCES

1. Gomollon F, Dignass A, Annese V, et al. Third European Evidence-based Consensus on the Diagnosis and Management of Crohn's Disease 2016. Part 1: Diagnosis and Medical Management. J Crohns Colitis 2017;11(1):3-25. DOI: 10.1093/ecco-jcc/jjw168

2. Gionchetti P, Dignass A, Danese S, et al. Third European Evidence-based Consensus on the Diagnosis and Management of Crohn's Disease 2016. Part 2: Surgical Management and Special Situations. J Crohns Colitis 2017;11(2):135-49. DOI: 10.1093/ecco-jcc/jjw169

3. Magro F, Gionchetti P, Eliakim R, et al. Third European Evidence-based Consensus on Diagnosis and Management of Ulcerative Colitis. Part 1: Definitions, Diagnosis, Extra-intestinal Manifestations, Pregnancy, Cancer Surveillance, Surgery and Ileo-anal Pouch Disorders. J Crohns Colitis 2017;11(6):649-70. DOI: 10.1093/ecco-

jcc/jjx008

4. Harbord M, Eliakim R, Bettenwoth D, et al. Third European Evidence-based Consensus on Diagnosis and Management of Ulcerative Colitis. Part 2: Current Management. J Crohns Colitis 2017;11(7):769-84. DOI: 10.1093/ecco-jcc/jjx009

5. Stange EF, Travis SP, Vermeire S, et al. European evidence based consensus on the diagnosis and management of Crohn's disease: definitions and diagnosis. Gut 2006;55(Suppl 1):1-15. DOI: 10.1136/gut.2005.081950a

6. Vermeire S, Van Assche G, Rutgeerts P. C-reactive protein as a marker for inflammatory bowel disease. Inflamm Bowel Dis 2004;10:661-5. DOI: 10.1097/00054725-200409000-00026

7. Guardiola J, Lobatón T, Cerrillo E, et al.; en representación de GETECCU. Recommendations of the Spanish Working Group on Crohn's Disease and Ulcerative Colitis (GETECCU) on the utility of the determination of faecal calprotectin in inflammatory bowel disease. Gastroenterol Hepatol 2018;41(8):514-29. DOI: 10.1016/j.gastrohep.2018.05.029

8. Sipponen T, Savilahti E, Kohlo K, et al. Crohn's disease activity assessed by fecal calprotectin and lactoferrin: correlation with Crohn's disease activity index and endoscopic findings. Inflamm Bowel Dis 2008;14:40-6. DOI: 10.1002/ibd.20312

9. Manolakis AC, Kapsoritakis AN, Tiaka EK, et al. Calprotectin, calgranulin C, and other members of the S100 protein family in inflammatory bowel disease. Dig Dis Sci 2011;56:1601-11. DOI: 10.1007/s10620-010-1494-9

10. D'Haens G, Ferrante M, Vermeire S, et al. Fecal calprotectin is a surrogate marker for endoscopic lesions in inflammatory bowel disease. Inflamm Bowel Dis 2012;18:2218-24. DOI: 10.1002/ibd.22917

11. Judd TA, Day AS, Lemberq DA, et al. Updates of fecal markers of inflammation in inflammatory bowel disease. J Gastroenterol Hepatol 2011;26:1493-9. DOI: 10.1111/j.1440-1746.2011.06846.x

12. Lobatón T, Rodríguez-Moranta F, López A, et al. A new rapid quantitative test for fecal calprotectin predicts endoscopic activity in ulcerative colitis. Inflamm Bowel Dis 2013;19(5):1034-42. DOI: 10.1097/MIB.0b013e3182802b6e

13. Lobatón T, López-García A, Rodríguez-Moranta F, et al. A new rapid test for fecal calprotectin predicts endoscopic remission and postoperative recurrence in Crohn's disease. J Crohns Colitis 2013;7(12):e641-51. E-pub Jul 1st, 2013. DOI: 10.1016/j.crohns.2013.05.005

14. D'Haens G, Ferrante M, Vermeire S, et al. Fecal calprotectin is a surrogate marker for endoscopic lesions in inflammatory bowel disease. Inflamm Bowel Dis 2012;18(12):2218-24. E-pub Feb 16th, 2012. DOI: 10.1002/ibd.22917

15. Kawashima K, Ishihara S, Yuki T, et al. Fecal calprotectin level correlated with both endoscopic severity and disease extent in ulcerative colitis. BMC Gastroenterol 2016;16:47. DOI: 10.1186/s12876-016-0462-z

16. Schoepfer AM, Beglinger C, Straumann A, et al. Fecal calprotectin more accurately reflects endoscopic activity of ulcerative colitis than the Lichtiger Index, C-reactive protein, platelets, hemoglobin, and blood leukocytes. Inflamm Bowel Dis 2013;19(2):332-41. DOI: 10.1097/MIB.0b013e3182810066

17. Vázquez Morón JM, Pallarés Manrique H, Machancoses FH, et al. Accurate cut-offs for predicting endoscopic activity and mucosal healing in Crohn's disease with fecal calprotectin. Rev Esp Enferm Dig 2017:130-6. DOI: 10.17235/reed.2017.4542/2016

18. Laharie D, Mesli S, El Hajbi F, et al. Prediction of Crohn's disease relapse with faecal calprotectin in infliximab responders: a prospective study. Aliment Pharmacol Ther 2011;34:462-9. DOI: 10.1111/j.1365-2036.2011.04743.x

19. Jusué V, Chaparro M, Gisbert JP. Accuracy of fecal calprotectin for the prediction of endoscopic activity in patients with inflammatory bowel disease. Dig Liver Dis 2018;50(4):353-9. DOI: 10.1016/j.dld.2017.12.022

20. Molander P, af Björkesten CG, Mustonen H, et al. Fecal calprotectin concentration predicts outcome in inflammatory bowel disease after induction therapy with TNFα blocking agents. Inflamm Bowel Dis 2012;18:2011-17. DOI: 10.1002/ibd.22863

21. Pardi DS, Sandborn WJ. Predicting relapse in patients with inflammatory bowel disease: what is the role of biomarkers? Gut 2005;54:321-2.

22. Nordal HH, Brokstad KA, Solheim M, et al. Calprotectin (S100A8/A9) has the strongest association with ultrasound-detected synovitis and predicts response to biologic treatment: results from a longitudinal study of patients with established rheumatoid arthritis. Arthritis Res Ther 2017;19(1):3. DOI: 10.1186/s13075-016-1201-0

23. Hurnakova J, Zavada J, Hanova P, et al. Serum calprotectin (S100A8/9): an independent predictor of ultrasound synovitis in patients with rheumatoid arthritis. Arthritis Res Ther 2015;17:252. DOI: 10.1186/s13075-015-0764-5

24. Nielsen UB, Bruhn LV, Ellingsen T, et al. Calprotectin in patients with chronic rheumatoid arthritis correlates with disease activity and responsiveness to methotrexate. Scand J Clin Lab Invest 2018;78(1-2):62-7. DOI: 10.1080/00365513.2017.1413591

25. Kopec-Medrek M, Kucharz EJ. Fibulin-3 and other cartilage metabolism biomarkers in relationship to calprotectin (MRP8/14) and disease activity in rheumatoid arthritis patients treated with anti-TNF therapy. Adv Clin Exp Med 2018;27(3):383-9. DOI: 10.17219/acem/68362

26. Meuwis MA, Vernier-Massouille G, Grimaud JC, et al. Serum calprotectin as a biomarker for Crohn's disease. Crohns Colitis 2013;7(12):e678-83. E-pub Jul 9th, 2013. DOI: 10.1016/j.crohns.2013.06.008

27. Mao JY, Li L, Pang Z. Significance of serum calprotectin in assessing inflammatory bowel disease activity. Zhonghua Yi Xue Za Zhi 2017;97(38):3001-4. DOI: 10.3760/cma.j.issn.0376-2491.2017.38.011

28. Louis E, Mary JY, Vernier-Massouille G, et al. Maintenance of remission among patients with Crohn's disease on antimetabolite therapy after infliximab therapy is stopped. Gastroenterology 2012;142(1):63-70.e5;quiz e31. DOI: 10.1053/j.gastro.2011.09.034

29. Fukunaga S, Kuwaki K, Mitsuyama K, et al. Detection of calprotectin in inflammatory bowel disease: fecal and serum levels and immunohistochemical localization. Int J Mol Med 2018;41(1):107-18. E-pub Nov 7th, 2017. DOI: 10.3892/ijmm.2017.3244

30. Nancey S, Boschetti G, Moussata D, et al. Neopterin is a novel reliable fecal marker as accurate as calprotectin for predicting endoscopic disease activity in

patients with inflammatory bowel diseases. Inflamm Bowel Dis 2013;19(5):1043-52. DOI: 10.1097/MIB.0b013e3182807577

31. Buderus S, Boone J, Lyerly D, et al. Fecal lactoferrin: a new parameter to monitor infliximab therapy. Dig Dis Sci 2004;49:1036-9. DOI: 10.1023/B:DDAS.0000034568.69407.47

	Ulcerative colitis n = 27 (%) Mayo 0/1: 17 patients Mayo 2/3: 10 patients		**Crohn´s disease** n = 26 (%) SESCD ≤ 3: 10 patients SESCD>3: 16 patients	
Montreal classification	E1: 2 (7.4%) E2: 11 (40.7%) E3: 14 (51.8%) S0: 12 (44.4%) S1: 7 (25.9%) S2: 8 (29.7%) S3: 0		A1 4 (15.4%) A2 15 (57.7%) A3 7 (26.9%) L1 7 (26.9%) L2 7 (26.9%) L3 12 (46.2%) B1 10 (38.5%) B2 9 (34.6%) B3 7 (26.9%) Perianal: 6 (23%)	
CRP (mg/dl) median/IQR	**Mayo 0/1:** 2.34 (0.93-14.56) **Mayo 2/3:** 1.86 (1-14-4.9)	p = 0,52	**SESCD ≤ 3:** 7 (3.23-15.8) **SESCD > 3**: 17.5 (14.9-20.1)	p = 0,68
ESR median/IQR	**Mayo 0/1:** 14.5 (9-25) **Mayo 2/3:** 10 (6-12)	p = 0,27	**SESCD ≤ 3:** 42 (30-50) **SESCD > 3:** 44.5 (41-48)	p = 0,31
Hemoglobin (g/dl) median/IQR	**Mayo 0/1:** 13.8 (13.2-15.3) **Mayo 2/3:** 13.5 (12.9-16.1)	p = 0,88	**SESCD ≤ 3:** 13.3 (12.8-13.7) **SESCD > 3:** 12.4 (11.7-13.2)	p = 0,67
Platelets (x10^6/l) median/IQR	**Mayo 0/1:** 254000 (219000-268000) **Mayo 2/3:** 260700 (75746-271000)	p = 0,52	**SESCD ≤ 3:** 207500 (150000-239000) **SESCD > 3:** 317500 (232000-403000)	p = 0,68
Albumin (g/dl) median/IQR	**Mayo 0/1:** 4.1 (3.4-4.5) **Mayo 2/3:** 4 (3.6-4.3)	p = 0,49	**SESCD ≤ 3:** 4.5 (4.5-4.5) **SESCD > 3:** 3.9 (3.9-3.9)	p = 0,47
Serum calprotectin (mg/ml) median/IQR	**Mayo 0/1:** 4.07 (2.9-7.19) **Mayo 2/3:** 10.39 (7.4-12.2)	p = 0,01	**SES-CD ≤ 3:** 6.25 (5.4-7.09) **SES-CD > 3:** 20.1 (16.8-23.4)	p = 0,8
Fecal calprotectin (µg/g) mediana/IQR	**Mayo 0/1**: 81.5 (20.1-160) **Mayo 2/3:** 141 (45-527)	p = 0,5	**SES-CD ≤ 3 :** 48.2 (8.6-86.4) **SES-CD > 3:** 136 (47.2-280)	p = 0,8

REVISTA ESPAÑOLA DE
ENFERMEDADES DIGESTIVAS
The Spanish Journal of Gastroenterology

REVISTA ESPAÑOLA DE
ENFERMEDADES DIGESTIVAS
The Spanish Journal of Gastroenterology

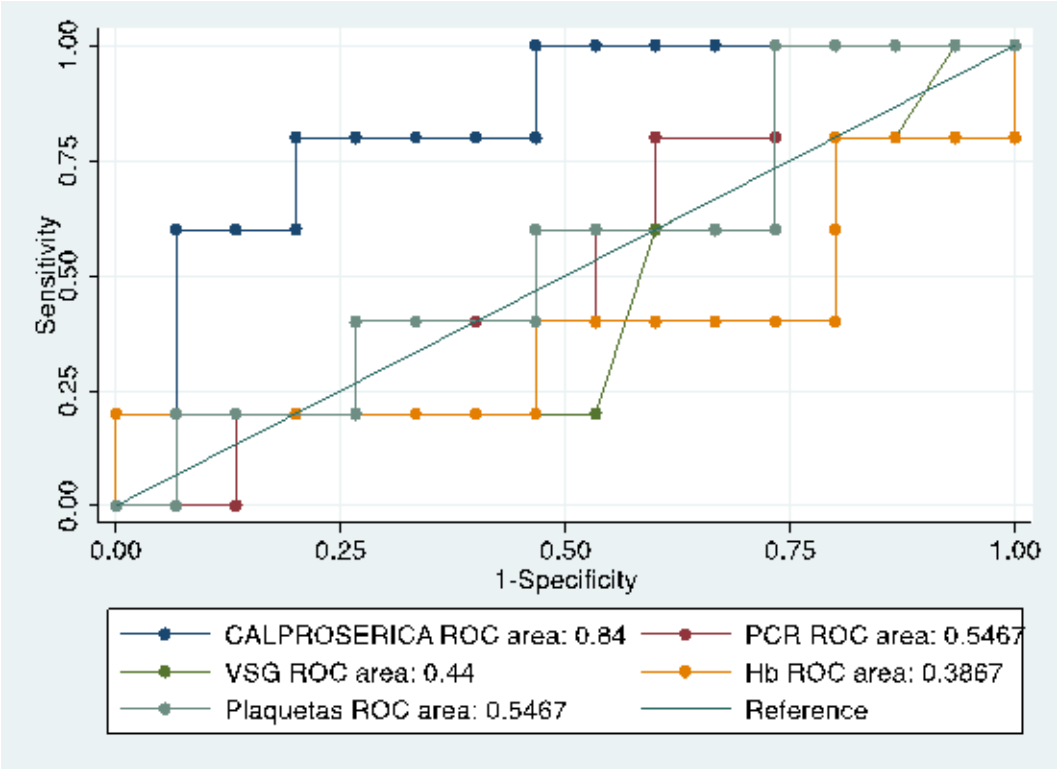

Fig. 1. Area under the curve (ROC curve) for different serum markers of activity in ulcerative colitis.

REVISTA ESPAÑOLA DE
ENFERMEDADES DIGESTIVAS
The Spanish Journal of Gastroenterology

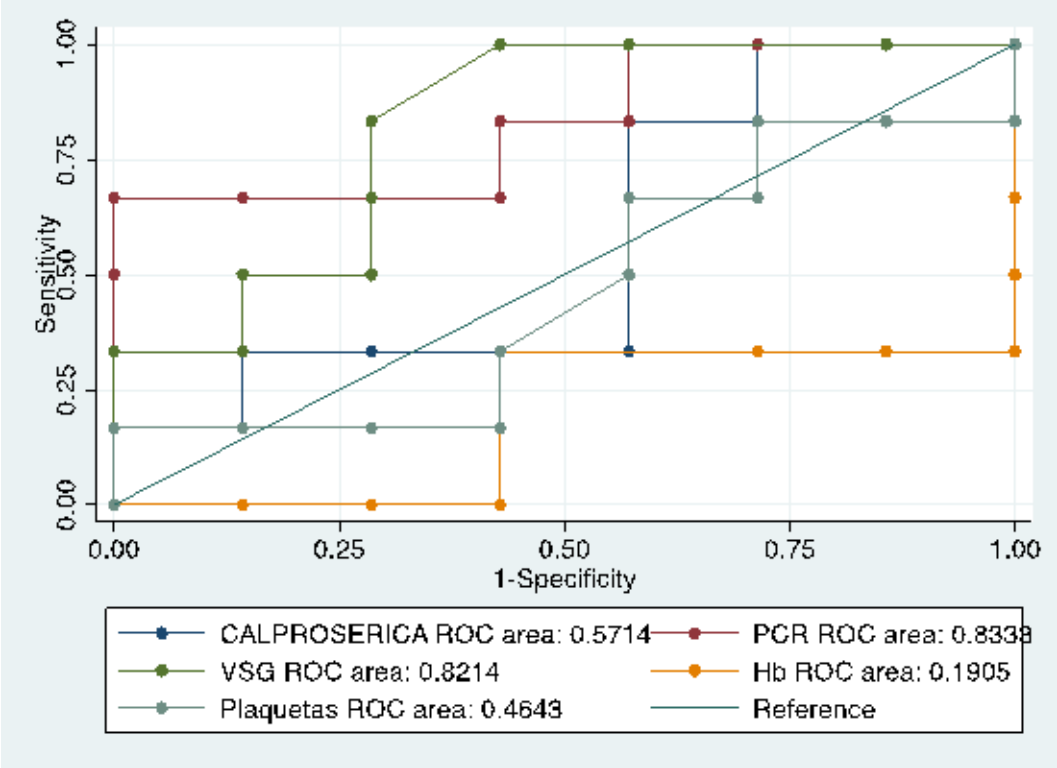

Fig. 2. Area under the curve (ROC curve) for different serum markers of activity in Crohn's disease.