Optimal use of serum leucine-rich alpha-2 glycoprotein as a biomarker for small bowel lesions of Crohn's disease

Kunio Asonuma
Kitasato University Kitasato Institute Hospital

Taku Kobayashi (drkobataku@gmail.com)
Kitasato University Kitasato Institute Hospital

Nao Kikkawa
National Cancer Center Hospital

Masaru Nakano
Kitasato University Kitasato Institute Hospital

Shintaro Sagami
Kitasato University Kitasato Institute Hospital

Hiromu Morikubo
Kitasato University Kitasato Institute Hospital

Yusuke Miyatani
Kitasato University Kitasato Institute Hospital

Aya Hojo
Kitasato University Kitasato Institute Hospital

Tomohiro Fukuda
Kitasato University Kitasato Institute Hospital

Toshifumi Hibi
Kitasato University Kitasato Institute Hospital

Article

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Abstract

A large proportion of small bowel lesions in Crohn's disease (CD) may exist beyond the scope of ileocolonoscopy, suggesting the need for optimal biomarkers. This cross-sectional observational study prospectively measured C-reactive protein (CRP), faecal calprotectin (FC), and leucine-rich alpha-2 glycoprotein (LRG) in patients with quiescent CD who underwent imaging examinations (capsule or balloon-assisted endoscopy, magnetic resonance enterography, or intestinal ultrasound). Mucosal healing (MH) of the small bowel was defined as a lack of ulcers. Patients with a Crohn's disease activity index of >220 and active colonic lesions were excluded. Seventy patients (29, MH; 41, small bowel inflammation) were analysed. The area under the curve (AUC) of CRP, FC, and LRG was 0.74 (95% confidence interval 0.60-0.86), 0.68 (0.52-0.80), and 0.75 (0.58-0.84), respectively. A cut-off of 16 μg/ml of LRG showed the highest positive predictive value of 0.95 with a specificity of 0.96, while the negative predictive value was the highest (0.71) with a sensitivity of 0.90 at a cut-off of 9 μg/ml. This suggests that LRG can accurately detect and/or exclude the small bowel lesions using two cut-off values.

Introduction

Crohn's disease (CD) is a chronic refractory inflammatory bowel disease that can cause strictures and fistulas, which may require bowel surgery [1]. Small bowel lesions are seen in 70% of CD patients [2], and patients with small bowel or ileocecal disease have a higher risk of undergoing surgery than those with colonic disease [3]. Therefore, the evaluation of small bowel lesions is important for the management of CD.

A large proportion of small bowel lesions exist beyond the reach of ileocolonoscopy (CS); therefore, various modalities are used, such as balloon-assisted enteroscopy (BAE) [4, 5], capsule endoscopy (CE) [6], magnetic resonance enterography (MRE) [7-9], and intestinal ultrasound (IUS) [10, 11]. Overall, the diagnostic accuracy of these modalities seems to be comparable for small bowel CD [12-14]. However, potential differences in their optimal use for various types and locations of lesions still exist. For example, MRE/IUS is suitable for evaluation of extraluminal and transmural inflammation such as abscesses and fistulas, whereas CS/BAE/CE is reliable for luminal inflammation but may not be used in patients with strictures. Furthermore, availability and access may vary for each facility. Therefore, there is no single gold standard in clinical practice, and the optimal diagnostic modality must be selected on a case-by-case basis by the treating physician.

The complexity of the small bowel imaging strategy highlights the importance of biomarkers. C-reactive protein (CRP) and faecal calprotectin (FC) have been widely used as biomarkers for inflammatory bowel disease (IBD) and have been reported as treatment targets [15, 16]. Recently, leucine-rich alpha-2 glycoprotein (LRG) was discovered as a novel biomarker [17], and its usefulness in CD has been suggested [18, 19]. However, it is unclear whether LRG is more useful than CRP and/or FC, specifically for small bowel lesions. Therefore, in this study, we directly compared the diagnostic accuracy of LRG with that of CRP and FC and attempted to optimise the use of LRG in determining small bowel lesions of CD.
Results

Patients

Small bowel evaluations and biomarker measurements were conducted in 107 CD patients who underwent small bowel evaluation between 1 June 2019 and 30 November 2021. Among them, 17 patients with Crohn’s disease activity index (CDAI) ≥ 220, 17 patients with active colonic inflammation, 2 patients with abdominal or perianal abscess, and one patient who only had CS for the surveillance of small bowel inflammation were excluded.

A total of 70 patients (29 with MH and 41 with small bowel inflammation) were included in the analysis for small bowel lesions (Figure 1), and the median (interquartile range [IQR]) CDAI was 65 (46 – 89). A total of 38 patients (57.8%) had ileal CD and 32 patients (42.2%) had ileocolonic CD. The imaging examinations performed included CS (n=16), BAE (n=27), CE (n=1), MRE (n=31), and IUS (n=26).

The baseline characteristics of the patients are presented in Table 1. There were no statistically significant differences in age, sex, disease duration, CDAI, perianal involvement, history of intestinal resection, treatment, or imaging examinations between patients with small bowel inflammation and those with MH. Nine patients (12.9%) had missing data on CDAI, 11 patients (15.7%) had missing data on FC, and 2 patients (2.9%) had missing data on LRG.

Accuracy of each biomarker for predicting MH

In the overall patient population, the median (IQR) CRP, FC, and LRG were 0.5 mg/l (0.2-1.4), 208 μg/g (83-389), and 11.9 μg/ml (9.4-16.6), respectively. All biomarkers were significantly higher in patients with small bowel inflammation than in those with MH (Figure 2). Furthermore, the receiver operating characteristic (ROC) curve analysis showed that the area under the curve (AUC) of CRP, FC, and LRG were 0.74 (95% confidence interval (CI) 0.60-0.86)), 0.68 (95% CI 0.52-0.80), and 0.75 (95% CI 0.58-0.84), with LRG being the highest among the three biomarkers. (Figure 3).

Accuracy of FC and LRG in patients with negative CRP < 3 mg/dl

Because LRG is reported to be more sensitive than CRP because of the presence of interleukin (IL)-6-independent production [17], we investigated the diagnostic accuracy of LRG in patients with negative CRP (< 3 mg/dl) (n=61; 27, MH; 34, small bowel inflammation). The ROC curve analysis showed that the AUC of FC and LRG were 0.68 (95% CI 0.50-0.80), and 0.72 (95% CI 0.53-0.82), respectively (Figure 4).

Accuracy of each biomarker using two cut-offs in detecting and/or excluding small bowel inflammation

Next, we examined the accuracy of CRP and FC using two previously validated cut-offs for detecting and/or excluding small bowel inflammation (Table 2). High specificity and positive predictive value (PPV) were obtained when the cut-off value of CRP was set as 3 mg/l (0.93 and 0.78, respectively), but
sensitivity and negative predictive value (NPV) were low (0.17 and 0.44, respectively). Sensitivity and NPV were insufficient (0.54 and 0.57, respectively), even when the cut-off value was lowered to 1 mg/l.

The specificity and PPV of FC were 0.68 and 0.69 (cut-off of 250 μg/g), and the sensitivity and NPV were 0.82 and 0.65 (cut-off of 100 μg/g), respectively. Interestingly, the specificity and PPV of LRG with the cut-off of 16 μg/ml were 0.96 and 0.95, comparable to CRP (cut-off 3 mg/l) and better than FC (cut-off 250 μg/g). In addition, we attempted to determine the cut-off value that demonstrates high sensitivity and NPV to exclude the presence of small bowel inflammation and found that a cut-off of 9 μg/ml showed the highest NPV in all cases (0.71) with a high sensitivity of 0.90. This was also true for CRP-negative cases (NPV, 0.71 and sensitivity, 0.88) (Table 3).

Discussion

To the best of our knowledge, this is the first study to directly compare the usefulness of CRP, FC, and LRG in the evaluation of small bowel lesions in CD. Our results demonstrated that LRG is a useful biomarker for small bowel CD and can more efficiently determine the presence or absence of small bowel inflammation by utilising two different cut-offs.

MH in CD is associated with a higher steroid-free remission rate and lower risk of hospitalisation and surgery [20]. Recently, deep remission (MH + clinical remission) has been suggested as more important in the long-term course of the disease [21]. Biomarkers have traditionally been used to predict mucosal healing, but the CALM trial reported that treatment escalation based on biomarkers could improve the long-term outcomes of CD [16]. STRIDE-II defines normalisation of CRP and reduction of FC as intermediate targets, while endoscopic mucosal healing is the long-term target [15]. Thus, the importance of biomarkers has been reinforced in the management of CD.

CRP is an inexpensive and widely used serum biomarker that is produced via an IL-6-dependent inflammatory pathway. However, despite its high specificity, its sensitivity is low for active CD, despite its high specificity [22]. In this study, a validated cut-off of 3 mg/l had a very high specificity of 0.96. Therefore, other biomarkers seem to have no additive benefits when CRP levels are positive. However, it had a low sensitivity of 0.28, which was consistent with a previous study that also reported a considerable proportion of patients (CRP < 3 mg/l) with active disease as assessed by conventional CS [22]. In addition, its sensitivity was not sufficiently high, even when a lower cut-off (1 mg/l) was adopted. These results suggest that monitoring with CRP could miss active small bowel lesions due to false-negative results.

FC is a calcium-binding protein which accounts for approximately 60% of the cytosolic proteins in neutrophils and has been reported to be useful in the evaluation of small bowel inflammation in CD [5, 9, 23]. In evaluations using BAE, FC demonstrated a moderate correlation with the simple endoscopic score for Crohn's disease (SES-CD) [5, 23]. Kawashima et al. reported that the AUC for MH was 0.86 (sensitivity 0.92, specificity 0.82) [23], although the colonic disease was also included. Moreover, Jones et al.
reported that FC had an AUC of 0.91 (sensitivity 0.9, specificity 0.74), and demonstrated a moderate correlation with the magnetic resonance index of activity (MaRIA) score [9]. Reenaers et al. reported that FC < 100 μg/g suggested endoscopic and histological remission, while patients with FC > 250 μg/g were likely to have significant inflammation, even in asymptomatic IBD patients, which is consistent with the results of our study [24]. Overall, FC is more sensitive than CRP, and is thus widely used in clinical practice.

LRG has been identified as a novel serum biomarker for rheumatoid arthritis induced by IL-22, tumour necrosis factor-alpha (TNF-α), and IL-1β, independent of IL-6. Additionally, it was reported to be upregulated in CD and correlates better with CDAI than with CRP [17]. However, its usefulness for small bowel lesions in comparison with other biomarkers is not clear. Our results demonstrated that the diagnostic value of LRG for small intestinal lesions was numerically better than that of CRP and FC in the overall population, as examined using ROC analysis. Using two cut-offs, LRG by itself was able to obtain extremely high specificity/PPV comparable to CRP, as well as excellent sensitivity/NPV equivalent to FC. LRG ≥ 16 strongly suggests that patients may have active inflammation in the small intestine, which may be used as a criterion for intensifying treatment in a treat-to-target (T2T) strategy [25]. Importantly, its specificity and PPV remained very high, even in patients negative for CRP, probably because of its IL-6 independent production pathways. In contrast, if the LRG is < 9, the possibility of active inflammation could be excluded, and continued monitoring without additional imaging seems to be sufficient based on the high NPV.

Another strength of this study is that we not only directly compared the accuracy of biomarkers by AUC, but also took advantage of two previously validated cut-off values to seek optimal clinical implications. The diagnostic utility of LRG has been maximised by considering two cut-off values and can be more accurate than FC, despite similar overall AUC. Furthermore, FC may be less convenient in clinical practice than serum biomarkers in terms of patient acceptability, adherence, and sample storage [26]. Therefore, a combination of two cut-off values of a single serum biomarker would not only be accurate but also more convenient.

Our study has some limitations. First, MH was defined using five different modalities (CS, CE, BAE, MRE, and IUS). Previous studies have used only one imaging examination to assess their correlation with biomarkers [9, 23]. Two recent studies reported the usefulness of LRG in predicting the presence of small bowel lesions in CD, as assessed by BAE alone [18, 19]. However, BAE may not be the most appropriate modality for a considerable proportion of patients because it cannot detect transmural inflammation or lesions beyond its reach. In clinical practice, the optimal modality is selected depending on the type and location of the lesion for each patient. Therefore, our results are more clinically relevant than those of studies that performed only a single imaging examination in all patients. Second, we were unable to analyse the correlation of the severity indices of each imaging examination because of the relatively small sample size. Third, we were unable to compare the usefulness of biomarkers in determining treatment response and predicting relapse in small bowel lesions. Based on our findings, prospective studies are needed to understand whether LRG in combination with CRP is sufficient for T2T without
imaging examinations. Finally, the external validity of the LRG cut-off obtained in our study needs to be examined.

In conclusion, our study suggests that combining two LRG cut-off values is a useful strategy for detecting and/or excluding small bowel lesions of CD in clinical remission.

Materials And Methods

Patients and data collection

This was a single-centre cross-sectional observational study. Consecutive patients diagnosed with CD who were scheduled for imaging examinations such as BAE, CS, CE, MRE, and IUS to evaluate small bowel lesions from 1st June 2019 to 30 November 2021 at Kitasato University Kitasato Institute Hospital, were enrolled in this study. All patients were diagnosed according to established diagnostic criteria [27]. The selection of optimal imaging examinations (alone or in combination) for each patient was performed based on the judgment of IBD experts.

Because the aim of the present study was to detect small bowel lesions during clinical remission, the following patients were excluded: 1) patients with CDAI [28] > 220; 2) patients with active colonic inflammation detected by imaging examinations; 3) patients with abdominal or perianal abscess; and 4) patients who underwent conventional CS alone for surveillance of small bowel inflammation. All other data were retrospectively collected from patients’ electronic medical records.

Endoscopic procedure and evaluation

BAE was performed using a single-balloon enteroscope (SIF-Q260; Olympus Medical Systems, Tokyo, Japan). An expert endoscopist performed BAE and inserted it into the small bowel as deep as possible. When insertion was difficult owing to stenosis, imaging with a contrast medium injected from the scope was used to assess the lesions in the deeper parts. CS was performed using a conventional colonoscope (PCF-290ZI; PCF-PQ260L; Olympus Medical Systems, Tokyo, Japan). CE was performed using PillCam Small Bowel Capsule 3 (Medtronic, Minneapolis, MN, USA). All segments were retrospectively and separately scored using SES-CD [29] by endoscopists who were blinded to the biomarker results.

MRE procedure and evaluation

All patients were instructed to ingest 1000 mL of polyethylene glycol (PEG) orally within 45–60 min before MRE. MRE was performed using a 1.5-T magnetic resonance imaging unit (Signa HDx; GE Healthcare, Tokyo, Japan). The patients were placed in a supine position on a magnetic resonance imaging table using a previously described protocol [30].

The images were retrospectively evaluated by a radiologist with more than 10 years of experience who was blinded to the clinical information and results of the endoscopic examination and biomarkers. The
severity in six segments (distal ileum, ascending, transverse, descending, sigmoid colon, and rectum) was evaluated using the MaRIA score [31].

**IUS procedure and evaluation**

Ultrasound examinations were performed by a gastroenterologist with 10 years of sonographic experience or trained sonographers with > 5 years of experience who were blinded to the clinical information and results of the endoscopic examination and biomarkers. Examinations were performed using an Aplio 500 Ultrasound System (Canon Medical Systems Corporation, Tokyo, Japan) via convex (4 MHz), microconvex (6–8 MHz), and/or linear probes (10 MHz) with harmonic imaging, as previously reported [32].

The entire abdomen was systematically scanned starting from the rectum. The following ultrasonographic parameters were assessed: bowel wall thickness, colour Doppler signal [colour Doppler gain: 3-5 MHz, typical flow 4.6-6.0 m/s] according to the Limberg score, and bowel wall stratification [33].

**Definition of mucosal healing (MH)**

The composite panel definition of MH was defined as the lack of ulceration on a single or combination of imaging examinations that met the following criteria: 1) CS/BAE/CE: SES-CD ulcer subscores of 0 or 1; 2) segment MaRIA score < 11 [7]; and 3) Limberg score of 0 or 1 [11].

To rule out the influence of colorectal lesions, the criteria for MH of the colon were defined as no mucosal activity with the following scores: 1) CS/BAE/CE: SES-CD ulcer subscores of 0; 2) segment MaRIA score < 7 [7]; and 3) Limberg score of 0 or 1 [11] in the colorectum. Cases that did not meet the definition of MH were considered to have small-bowel inflammation.

**Biomarkers**

Stool samples were collected from patients within 3 days prior to the imaging examinations on the day of the procedure, and FC was measured immediately or within 1 week of storage at 4°C [32]. FC was assayed based on the colloidal gold aggregation method using an NS-Prime automatic analyser (Alfresa Pharma Corporation, Osaka, Japan). Serum LRG levels were measured using enzyme-linked immunosorbent assay (Sekisui Medical, Tokyo, Japan) on the day of the procedure. Serum CRP levels were measured within one month before and after the procedure. We used previously validated cut-offs (CRP, 1 mg/l and 3 mg/l; FC, 100 μg/g and 250 μg/g) [22, 23, 34, 35].

**Statistical analysis**

All numerical values are presented as mean ± standard deviation (SD) or median (IQR), and dichotomous variables are presented as proportions. Dichotomous variables were analysed using Fisher’s exact test and continuous variables were analysed using the Wilcoxon rank-sum test. ROC analysis was performed to determine the optimal cut-off value of the biomarkers with sensitivity and specificity based on MH.
AUC was also calculated. Missing data were declared in the results tables and ignored in the statistical analysis. This was a pilot study, and no predefined sample size calculations were performed. All statistical analyses were performed using JMP software (version 14.0; SAS Institute, Cary, NC, USA). For all tests, a $P$-value $< 0.05$ was considered statistically significant, and variables pertaining to accuracy were calculated with a 95% CI.

**Ethical considerations**

The study was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines. The study protocol and all documents were approved by the Research Ethics Committees of Kitasato University Kitasato Institute Hospital (Kitasato University Kitasato Institute Hospital approval number: 19003 (13 May 2019)) and were registered publicly on the UMIN (number: 000036944). Written informed consent was obtained from all patients.

**Data Availability Statement**

Data supporting the results are available from the corresponding author (TK) upon reasonable request.

**Abbreviations**

AUC, area under the curve; BAE, balloon-assisted enteroscopy; CD, Crohn's disease; CDAI, Crohn's disease activity index; CE, capsule endoscopy; CI, confidence interval;

CRP, C-reactive protein; CS, colonoscopy; FC, faecal calprotectin;

IBD, inflammatory bowel disease; IL, interleukin; IQR, interquartile range;

IUS, intestinal ultrasound; LRG, leucine-rich alpha-2 glycoprotein;

MaRIA, magnetic resonance index of activity; MH, mucosal healing;

MRE, magnetic resonance enterography; NPV, negative predictive value;

PEG, polyethylene glycol; PPV, positive predictive value;

ROC, receiver operating characteristic; SD, standard deviation;

SES-CD, simple endoscopic score for Crohn's disease;

STRIDE, the selecting therapeutic targets in inflammatory bowel disease;

T2T, treat-to-target; TNF-α, tumour necrosis factor-alpha.

**Declarations**
Acknowledgments:

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Authors’ Contributions

Study concept and design; Kunio Asonuma, Taku Kobayashi,

acquisition of data; Kunio Asonuma,

analysis and interpretation of data; Kunio Asonuma, Taku Kobayashi,

drafting of the manuscript; Kunio Asonuma, Taku Kobayashi,

critical revision of the manuscript for important intellectual content; all authors, statistical analysis; Kunio Asonuma,

administrative, technical or material support; Taku Kobayashi,

study supervision; Taku Kobayashi.

All authors read and approved the final manuscript.

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Competing interest Statement

speaker or a consultant in Covidien, Mochida Pharmaceutical, Takeda Pharmaceutical, Zeria Pharmaceutical, Kyorin Pharmaceutical, and Nippon Kayaku; received research funding from Mitsubishi Tanabe Pharma and Japanese foundation for research and promotion of endoscopy. SS has served as a speaker for AbbVie, Takeda Pharmaceutical, Mitsubishi Tanabe Pharma, Nippon Kayaku, and Zeria Pharmaceutical and as an endowed chair for AbbVie, JIMRO, Zeria Pharmaceutical, Kyorin Pharmaceutical, Mochida Pharmaceutical, and EA Pharma. HM has received research grant from Takeda Pharmaceutical. YM Has an endowed chair from AbbVie, JIMRO, Zeria Pharmaceutical, Kyorin Pharmaceutical, Mochida Pharmaceutical, EA Pharma. TF has received research funding from Mitsubishi Tanabe Pharma. TH has received lecture fees from Aspen Japan K.K, Abbvie GK , Ferring, Gilead Sciences, Janssen, JIMRO, Mitsubishi-Tanabe Pharma, Mochida Pharmaceutical, Pfizer, Takeda Pharmaceutical, Advisory/consultancy fees from Apo Puls Station, Abbvie GK, Bristol-Myers Squibb, Celltrion, EA Pharma, Eli Lilly, Gilead Sciences, Janssen, Kyorin, Mitsubishi-Tanabe Pharma, Nichi-Iko Pharmaceutical, Pfizer, Takeda Pharmaceutical, Zeria Pharmaceutical and research grants from Abbvie GK, Activaid, Al fresca Pharma Corporation, JMDC Inc., Gilead Sciences, Inc., Nippon Kayaku Co., Ltd., Eli Lilly Japan K.K., Mochida Pharmaceutical Co., Ltd., Janssen Pharmaceutical K.K., Pfizer Japan Inc., Takeda Pharmaceutical Co., Ltd., Ferring Pharmaceuticals and Bristol-Myers Squibb; received scholarship contributions from Mitsubishi Tanabe Pharma Corporation, Zeria Pharmaceutical Co., Ltd., Nippon Kayaku Co., Ltd.; and belonged to study group sponsorship by Otsuka Holdings, Abbvie GK, EA Pharma Co., Ltd., Zeria Pharmaceutical Co., Ltd., JIMRO Co., Ltd., Kyorin Pharmaceutical Co., Ltd., and Mochida Pharmaceutical Co., Ltd.

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**Tables**

Table 1. Baseline characteristics of patients enrolled in the study.
<table>
<thead>
<tr>
<th></th>
<th>Mucosal healing n=29</th>
<th>Small bowel inflammation n=41</th>
<th>P-value</th>
</tr>
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<tr>
<td>Age, y</td>
<td>37.8 (33.5-52.1)</td>
<td>46.4 (30.6-60.4)</td>
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<tr>
<td>Gender: male/female, n</td>
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<td>26/15</td>
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<td>Disease duration, y</td>
<td>15 (7.5-17.5)</td>
<td>10 (5-21)</td>
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<td>CDAI</td>
<td>66 (44-91)</td>
<td>64 (47-88)</td>
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<td>Age of diagnosis, n</td>
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<tr>
<td>A1 (below 16y)</td>
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<tr>
<td>A2 (between 17 - 40y)</td>
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<td>A3 (above 40y)</td>
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<td>L3 (ileocolonic)</td>
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<td>Behavior, n</td>
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<tr>
<td>B2 (structuring)</td>
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<td>B3 (penetrating)</td>
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</table>
Table 2. Sensitivity, specificity, and predictive values of C-reactive protein (CRP) and faecal calprotectin (FC) using two cut-offs for determining small bowel lesions.

<table>
<thead>
<tr>
<th>Cut-off value</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
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<tr>
<td>CRP 3 mg/l</td>
<td>0.17</td>
<td>0.93</td>
<td>0.78</td>
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<td>1 mg/l</td>
<td>0.54</td>
<td>0.86</td>
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<td>FC 250 μg/g</td>
<td>0.53</td>
<td>0.68</td>
<td>0.69</td>
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<td>100 μg/g</td>
<td>0.82</td>
<td>0.44</td>
<td>0.67</td>
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CRP, C-reactive protein; FC, faecal calprotectin; LRG, leucine-rich alpha-2 glycoprotein;
NPV, negative predict value; PPV, positive predict value;

Table 3. Sensitivity, specificity, and predictive value of leucine-rich alpha-2 glycoprotein (LRG) for determining small bowel lesions at detail cut-offs in entire patients and patients with negative C-reactive protein (CRP) < 3 mg/dl.
<table>
<thead>
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<th>Cut-off value (μg/ml)</th>
<th>Sensitivity</th>
<th>Specificity</th>
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<td>0.91</td>
<td>0.12</td>
<td>0.58</td>
<td>0.50</td>
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</tbody>
</table>

CRP, C-reactive protein; LRG, leucine-rich alpha-2 glycoprotein;

NPV, negative predict value; PPV, positive predict value;

**Figures**
Figure 1

Patient disposition enrolled in the study.

A total of 70 patients (29, MH; 41, small bowel inflammation) were included in the analysis.
Figure 2

Comparison of biomarkers between patients with small bowel inflammation and those with mucosal healing (Wilcoxon rank-sum test).

CRP, C-reactive protein; FC, faecal calprotectin; LRG, leucine-rich alpha-2 glycoprotein.
Figure 3

Receiver operating characteristic (ROC) analysis of each biomarker for determining the absence or presence of small bowel lesions.

AUC, area under the curve; CI, confidence interval; CRP, C-reactive protein; FC, faecal calprotectin; LRG, leucine-rich alpha-2 glycoprotein.

<table>
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<tr>
<th>Biomarker</th>
<th>AUC</th>
<th>95% CI</th>
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<tr>
<td>CRP</td>
<td>0.74</td>
<td>0.60-0.86</td>
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<tr>
<td>FC</td>
<td>0.68</td>
<td>0.52-0.80</td>
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<tr>
<td>LRG</td>
<td>0.75</td>
<td>0.58-0.84</td>
</tr>
</tbody>
</table>
Figure 4

Receiver operating characteristic (ROC) analysis of faecal calprotectin (FC) and leucine-rich alpha-2 glycoprotein (LRG) for determining the absence or presence of small bowel lesions in patients with negative C-reactive protein (CRP) < 3 mg/dl.

AUC, area under the curve; CI, confidence interval; FC, faecal calprotectin

LRG, leucine-rich alpha-2 glycoprotein