Assessment of inflammation activity in the small and large bowel using the MaRIAs index for Crohn's disease

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ABSTRACT *AIM: to evaluate diagnostic value of magnetic resonance enterocolonography (MR-enterocolonography) with the use of the segmental index MaRIAs (Simplified Magnetic Resonance Index of Activity) for inflammation activity in small and large intestine colon compared with ileocolonoscopy.*

PATIENTS AND METHODS: the prospective cohort study included 58 patients with Crohn's disease aged 19–45 years. All patients underwent MR-enterocolonography with intravenous contrast and ileocolonoscopy. MR-enterocolonography assessed inflammatory activity in the large and small intestine (406 segments) using the MaRIAs index (segmental). MRI data were compared with ileocolonoscopy.

RESULTS: ileocolonoscopy showed no signs of inflammatory activity in 71 (71/406, 17.5%) segments. In 168 (168/406, 41.3%) segments endoscopic signs of low or moderate inflammatory activity were detected, in 167 (167/406, 41.2%) segments inflammatory activity with the presence of ulcers were detected. MR-enterocolonography did not detect any activity in 121 (121/406, 29.8%) segments (0 points by MaRIAs index), in 285 (285/406, 70.2%) segments, the inflammation activity was revealed by MaRIAs index from 1 to 5 points. There was a moderate agreement (Cohen's Kappa: 0.57) between the data of MR-enterocolonography and ileocolonoscopy in detection of affected segments. ROC analysis revealed that with the value of the MaRIAs index (segmental) of 1 point or more with sensitivity of 82.0% and specificity of 92.0% (AUC 0.85), it is possible to consider the presence of inflammatory activity of any severity, and with index value of 2 points or more with sensitivity of 75.0% and specificity of 91.0% (AUC 0.91) can diagnose the severe inflammation with ulcers.

CONCLUSION: the results obtained revealed the value of MaRIAs index and the further study to evaluate the effectiveness of conservative treatment of Crohn's disease is needed.

KEYWORDS: *MR-enterocolonography, intravenous contrast, MaRIAs, ileocolonoscopy, Crohn's disease*

CONFLICT OF INTEREST: *the authors declare no conflict of interest*

INTRODUCTION

MR enterocolonography is a medical imaging technique that is used in patients with Crohn's disease to evaluate both the small and large intestine. The method allows you to determine the site and extent of changes, to assess the activity of inflammation, to identify fibrous changes in the intestinal wall, and to reveal complications [1–5]. An important diagnostic aim is to estimate the activity of the inflammatory process, which is currently assessed by most radiologists on the basis of a set of qualitative signs, such as thickening of the intestinal wall with increased accumulation of contrast agent, swelling of the submucosal layer, infiltration of surrounding tissue, hyper vascularization of altered sections [6,7]. Various quantitative indices have also been proposed. The most famous of them: MARIA (Magnetic Resonance Index of Activity), Clermont score (DWI-MaRIA scoring system), CDMI (Crohn's Disease Magnetic Resonance Imaging Index), MEGS (Magnetic Resonance Enterography Global Score) [8–13]. Each of the presented indices requires rather

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complex calculations and, as the authors themselves admit, this makes them of little use in everyday practical work. The most studied to date is the MARIA index, which is calculated using the formula:

1.5 × bowel wall thickness (mm) + 0.02 × relative contrast enhancement + 5 × edema + 10 × ulcers [1,13].

The most labor-intensive parameter to calculate in this formula is the parameter of relative contrast enhancement, which requires estimation of the MR signal intensity, as well as the noise-to-signal ratio before and after intravenous contrast. According to Ordas I. et al., the mean time to calculate the total MARIA index, even for an experienced radiologist, is 17 minutes [14]. In 2019, Ordas I. et al. published a work in which they proposed a simplified MARIA index, the so-called MaRIAs (Simplified Magnetic Resonance Index of Activity), in which such signs as thickening of the intestinal wall more than 3 mm, swelling of the submucosal layer and the absence of a clear margins between the intestinal wall and paracolic tissue are assigned one point, and the presence of ulcers — two points [14]. Segmental and general indices are calculated. The general index is the sum of all segmental indices and is used to determine the activity of inflammation before the start of conservative therapy and during treatment to assess its effectiveness.

Recently, only a few papers have been published on diagnostic effectiveness of the MaRIAs index, and it seems that it is relevant to research it [14–16]. At the first stage, we set the goal of assessing the diagnostic effectiveness of the segmental MaRIAs index for the activity of inflammation in the small and large intestine when compared with data from endoscopy (ileocolonoscopy).

PATIENTS AND METHODS

The study included 58 patients (36 females) aged 32 ± 8 (19–45) years, which were treated (steroid, immunosuppressive, biological therapy) in 2020–2022 for Crohn's disease in forms of colitis, ileocolitis, terminal ileitis.

Inclusion criteria: all patients underwent MR enterocolonography with intravenous contrast and ileocolonoscopy. The interval between two diagnostic procedures did not exceed five days and was two days on the average. The study did not include patients with inflammatory diseases of the small and large intestine of a non-granulomatous origin and patients with Crohn's disease who had previously undergone resection of the colon, including the ileocecal area.

Exclusion criteria were: the absence of inflammatory activity during endoscopy, as well as the impossibility of endoscopic assessment of all parts of the colon and terminal ileum.

MR enterocolonography was performed on an Achieva 1.5 T MR tomograph (Philips). Two-three days before the test, patients were prescribed a fiber-free diet. On the day of the test, 60 minutes before the procedure, patients took a Lavacol solution or water *per os* in a volume of 500–1500 ml, in small portions every 15–20 minutes to contrast the small and large bowel.

For intravenous contrast, a solution of gadopentetate adimeglumine was used at a dosage of 0.1 mmol/kg. The MR scanning protocol included T1-weighted (T1-weighted) and T2-weighted (T2-weighted) images, including fat-suppressed, diffusion-weighted images (DWI) and T1-weighted images with intravenous contrast. Analysis of the obtained MR images included assessment of the following parameters: thickness of the intestinal wall; increased accumulation of contrast agent by the intestinal wall during intravenous contrasting; swelling of the intestinal wall; infiltration of fiber (lack of a clear margins between the intestinal wall and fiber due to the spread of the inflammatory process beyond the intestinal wall); presence of ulcers; increased MR signal on DWI (diffusion limitation).

With MR enterocolonography and ileocolonoscopy, the activity of the inflammatory process

was assessed segment by segment. Seven segments were identified: terminal ileum, cecum, ascending colon, transverse colon, descending colon, sigmoid colon, rectum. A total of 406 segments were assessed using each method.

The activity of the inflammatory process by MR enterocolonography was determined using the MaRIAs index (segmental), which was calculated using the formula:

MaRIAs (segmental) = (1 × thickening of the bowel wall > 3 mm) + (1 × bowel wall edema) + (1 × paraintestinal infiltration) + (2 × ulcers).

The range of index values was from 0 to 5 points. During endoscopy, the activity of inflammation was assessed in each segment, and depending on the detected changes, three groups of segments were identified: 1st group — no changes/activity; Group 2 — minor/moderate activity (aphthae, erosions, hemorrhages, infiltration of the mucous layer); Group 3 — severe activity (ulcers).

Statistical data processing was performed using the SPSS and Microsoft Excel 2020 software package.

RESULTS

Endoscopy did not reveal any changes or signs of inflammatory activity in 71 (71/406, 17.5%) segments. In 168 (168/406, 41.3%) segments, endoscopic signs of slight or moderate activity were found, and in 167 (167/406, 41.2%) segments, severe activity of the inflammatory process with ulcers was detected (Fig. 1). With MR enterocolonography, we did not detect any changes in 121 (121/406, 29.8%) segments (0 points on the MaRIAs index (segmental)). In the remaining 285 (285/406, 70.2%) segments the activity of the inflammatory process by the MaRIAs index (segmental) varied from 1 to 5 points (Fig. 2, 3, 4, 5, 6). There was a moderate degree of agreement (Cohen's Kappa: 0.57) between the data of MR enterocolonography and ileocolonoscopy in identifying the affected segments.
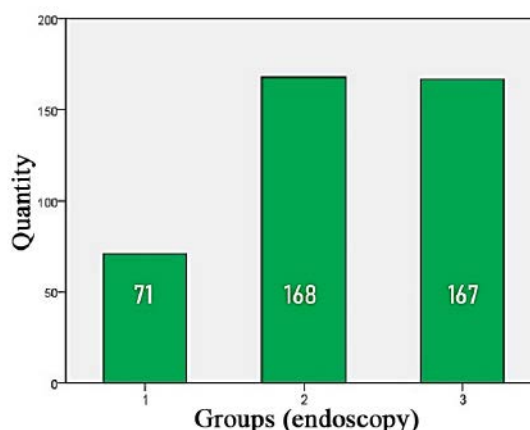
Figure 1. *The distribution of segments according to the severity of inflammatory process activity in patients with Crohn's disease according to ileocolonoscopy: group 1 — no changes/activity; group 2 — minor/moderate activity; group 3 — high activity*
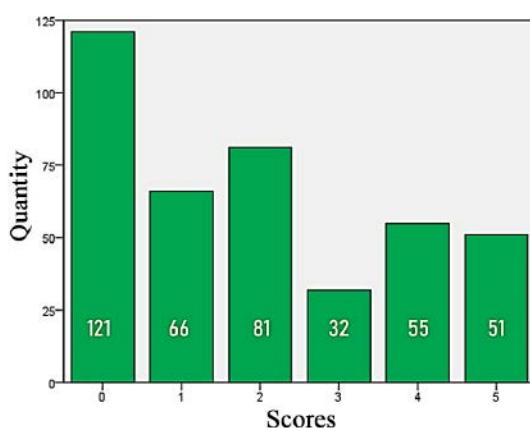
Figure 2. *The distribution of segments according to the severity of the inflammatory process activity, estimated using the MaRIAs index (segmental) from 0 to 5 points in patients with Crohn's disease*
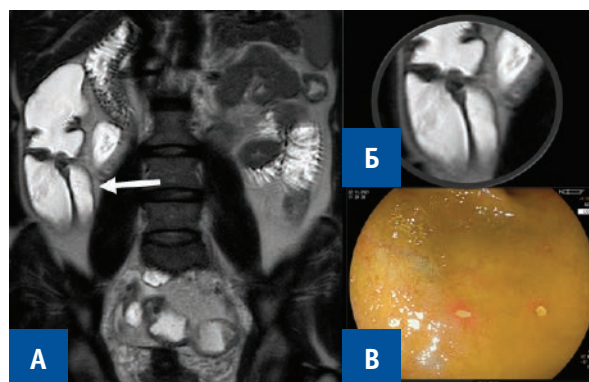
Figure 3. *А, Б — MR-enterocolonography, coronal scan, T2-WI. Unchanged terminal ileum (arrow). MaRIAs index (segmental) = 0. В — Endophoto. Crohn's disease in the form of terminal ileitis, infiltration phase: against the background of an unchanged mucous membrane, single rounded aphthae up to 0.2–0.3 cm in diameter are determined, with a fibrin and hyperemia around*
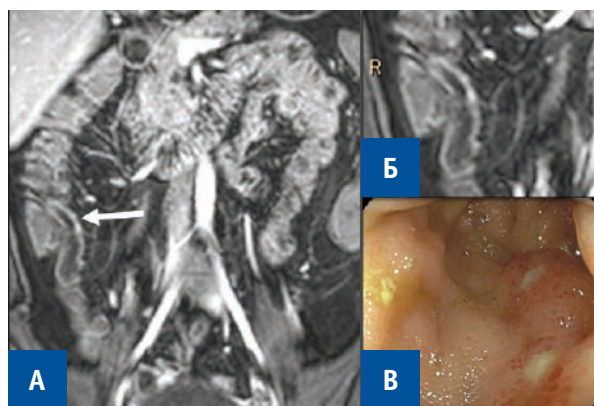
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We analyzed the distribution of the main MR signs of the inflammatory process depending on the severity of inflammatory activity according to endoscopic examination. It was found that thickening and edema of the intestinal wall, the presence of ulcers, infiltration of paraintestinal tissue and increased accumulation of contrast in the intestinal wall were more often detected with endoscopic signs of severe activity. The identified differences were statistically significant ($p < 0.05$) (Table 1).

ROC analysis showed that with a MaRIAs (segmental) index value of 1 point or more, with a sensitivity of 82% and a specificity of 92%, one can reveal the presence of inflammatory activity of any severity, and with an index value of 2 points or more with a sensitivity of 75% and a specificity of 91%, we can talk about severe inflammation with the presence of ulcers (Fig. 7). When determining the activity of inflammation of any severity with MaRIAs (segmental) index values ≥ 1, 61 discrepancies with ileocolonoscopy were noted (55 false-negative and 6 false-positive results). When assessing the severe activity of the inflammatory process with ulcers with MaRIAs (segmental) index values ≥ 2, discrepancies were identified in 46 cases (41
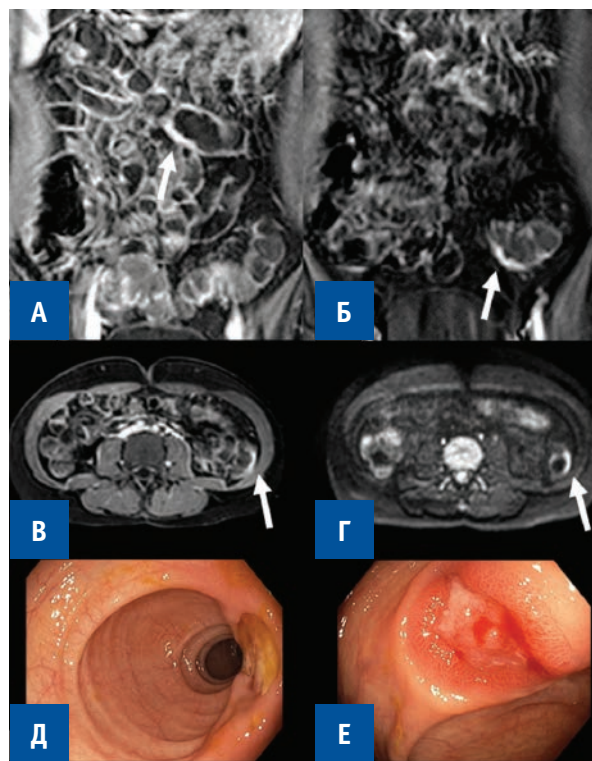
false-negative results and 5 false-positive results).

DISCUSSION

Ileocolonoscopy is considered as a standard for objective assessment of the activity of the inflammatory process in Crohn's disease [17,18]. Endoscopic indices for assessing the severity of the disease CDEIS (The Crohn's Disease Endoscopic Index of Severity) and SES-CD (Simple Endoscopic Score for Crohn's disease) are validated and reproducible methods for quantitative endoscopic assessment of the activity of the inflammatory process in the colon and small

Figure 5. *А, Б, В, Г — MR-enterocolonography. Crohn's disease of the colon with the presence of ulcers. MaRIAs index (segmental) = 3. А, Б — coronalscan, T1-WI with intravenous contrast and fat suppression; В — axial projection, T1-WI with intravenous contrast and fat suppression; Г- axial scan, DWI. Local (up to 1.5–2.0 cm) areas of thickening of intestinal wall up to 4 mm with a high accumulation of IV contrast (А,Б,В) and limited diffusion (hyperintensive MR signal) (Г) (arrows) are determined. Д, Е — Endophoto. Crohn's disease of the colon, ulcers phase: against the background of an unchanged mucous membrane, a deep stamped ulcer up to 1.2 cm in diameter with slightly hyperemic and hyperplastic edges is determined, the bottom is covered with a coating of fibrin*

Figure 4. *А, Б — MR-enterocolonography, coronal scan, T1-WI with intravenous contrast and fat suppression. Crohn's disease. Terminal ileitis. MaRIAs index (segmental) = 1. The wall of the terminal ileum is thickened to 4 mm and to3 cm long, with a moderately increased accumulation of contrast agent (arrow). В — Endophoto. Crohn's disease in the form of terminal ileitis: the lumen of the small intestine is deformed, slightly unevenly narrowed, ulceration with a diameter of 0.3–0.4 cm with a fibrin located on the infiltrated base is visible*
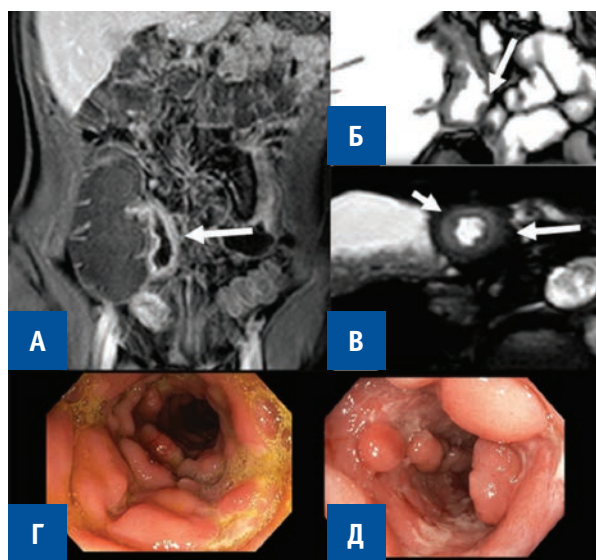
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intestine in patients with Crohn's disease [10, 19]. At the same time, endoscopy makes it possible to assess only the surface of the intestinal mucosa, not allowing the necessary assessment of the severity of transmural inflammation, the presence or absence of extraluminal complications of Crohn's disease, and the condition of the proximal parts of the small intestine. The use of MR enterography/MR enterocolonography makes it possible to overcome these limitations to a certain extent due to the ability to evaluate the entire length of the large and small intestine and visualize all layers of the intestinal wall and surrounding tissues. To quantitatively characterize the activity of inflammation, various MR indices have been proposed, developed and verified based on comparison with endoscopic data, accepted as the "gold standard"

Figure 6. *A, Б, В — MR-enterocolonography. Crohn's disease, terminal ileitis with ulcers. MaRIAs index (segmental) = 5. A — coronalscan, T1-WI with intravenous contrast and fat suppression; the wall of the terminal ileum is thickened to 6 mm, with a pronounced accumulation of contrast agent (arrow); Б — coronal scan TrueFISP: a transmural ulcer is detected in the form of a linear defect of the intestinal wall (arrow); В — axial scan, T2-WI with fat suppression: a moderately hyperintensive submucosal layer due to edema (short arrow) and an uneven, fuzzy outer border of the intestinal wall due to infiltration of fiber (long arrow) are determined. Г, Д — Endophoto. Crohn's disease in the form of terminal ileitis, the phase of ulcerscracks: the lumen of the intestine is moderately narrowed due to inflammatory changes, extended deep ulcers of longitudinal orientation are detected on all walls, the surrounding mucous membrane is hyperemic and infiltrated*

[8–13]. However, rather complex calculations of quantitative indicators make these indices of little use in common clinical practice. The recently proposed simplified MaRIAs index is considered by some authors as an alternative to the most popular MaRIA index, which is usually used in scientific studies [14–16]. In a paper by Ordas I. et al., when studying 588 segments in 98 patients with Crohn's disease, a high level of correlation was observed between the MaRIAs and MaRIA indices ($r = 0.93$), as well as MaRIAs and CDEIS ($r = 0.83$) [14].

At the first stage of our study, we compared the segmental MaRIAs index with the severity of inflammatory activity according to ileocolonoscopy. At the same time, when determining segments with inflammatory changes of any activity (MaRIAs segmental ≥ 1) and with severe inflammation with ulcers (MaRIAs segmental ≥ 2), rather high specificity rates were noted — 92% and 91%, respectively. False-positive results were due to the fact that in non-expanded sections of the intestine we could not always distinguish inflammatory thickening of the intestinal wall from physiological thickening caused by contraction. In studies by Ordas I. et al. [14] and Capozzi N. et al. [15] obtained similar results: for MaRIAs segmental ≥ 1, the specificity was 81% and 93%, for MaRIAs segmental ≥ 2 — 90% and 92%, respectively. The main diagnostic problems in our study were associated with underestimation of changes, which was reflected in sensitivity rates: 83% for MaRIAs segmental ≥ 1 and 75% for MaRIAs segmental ≥ 2. Ordas I. et al. [14] and Capozzi N. et al. [15] give higher sensitivity: 89% and 90% for MaRIAs segmental $\geq 1.85%$ and 87% for MaRIAs segmental ≥ 2, respectively. We were unable to identify any MR signs of Crohn's disease in segments with the presence of single aphthae during endoscopy, and single, even deep ulcers detected during ileocolonoscopy could not always be visualized using MR enterocolonography. To a certain extent, the sensitivity of MR diagnostics was affected by insufficient

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Table 1. *Distribution of MR signs of the inflammatory process in patients with Crohn's disease depending on the severity of inflammation activity according to endoscopic examination*

MR symptom	Unchanged segments (endoscopy) n = 71	Segments with slight or moderate activity (endoscopy) n = 167	Segments with severe activity (endoscopy) n = 168	Total n = 406
Bowel wall thickening	5 (7%)* 4-5мм	115 (68.9%)* 4–6 mm	165 (98.2%)* 4–9 mm	285 (70.2%) 4–9 mm
Bowel wall edema	0	72 (43.1%)*	103 (61.3%)*	175 (43.1%)
Ulcers	0	5 (3.0%)*	105 (62.5%)*	108 (26.6%)
Paraintestinal infiltration	0	2 (1.0%)*	55 (32.7%)*	57 (14.0%)
Enhanced contrast in bowel wall	2 (3%)*	118 (70.6%)*	164 (97.6%)*	284 (70.0%)

*Note: * the values are statistically significant, $P \leq 0.05$ (χ^2 criterion)*

stretching of all segments, since a number of patients, due to severe comorbidities, could not take the required amount of Lavacol solution orally, and some took only water *per os*, which is more quickly absorbed from the gastrointestinal tract and does not provide adequate stretching of the intestinal lumen. Thus, this factor was one of the limitations of our study.

Ordas I. et al. improved colonic distension by retrograde colon contrast with a neutral contrast agent [14]. Recently, this is not included in the standards for MR enterography/MR enterocolonography, and a number of publications report the high diagnostic accuracy of the method using only oral contrast of the gastrointestinal tract [20,21].

Another question that arose in the study is the feasibility of using intravenous contrast, since the MaRIAs index formula (unlike the MaRIA index) does not take into account the accumulation of the contrast agent in the intestinal wall during inflammatory changes. Capozzi N. et al. a study of 294 segments in 50 patients with Crohn's disease did not reveal any advantages of MR enterocolonography with intravenous

contrast compared to a study without the administration of gadolinium-containing drugs [15]. We did not make a statistical analysis of our data in this aspect, but it cannot be affirmed that in the study of 25 (25/406, 6%) segments, it was the increased accumulation of contrast agent in the intestinal wall that allowed us to asess the presence of minimal inflammatory changes, as well as to reveal ulcerative lesions with single, including "stamped" ulcers. Thus, intravenous contrast, as well as the use of DWI, helped us in identifying MR signs of inflammatory changes, which was indirectly reflected in the calculation of the MaRIAs index. This is consistent with the data of Ordas I. et al. [14].

The results of the first stage of the study assessing the diagnostic effectiveness of the MaRIAs segmental index seem to us to be quite encouraging. We plan to continue collecting cases to determine the activity of the inflammatory process in patients with Crohn's disease using segmental and general MaRIAs indices. The next aim will be to determine the diagnostic performance of the MaRIAs index when compared with the endoscopic SES-CD inflammatory

activity index. And at the final stage, we plan to compare the MaRIAs total index with the endoscopic SES-CD total index in patients with Crohn's disease before prescribing conservative therapy and during treatment to assess the effectiveness of the therapy.

CONCLUSION

The results obtained on determining the activity of inflammation in the small and large intestine using the MaRIAs index (segmental) in patients with Crohn's disease, make it advisable to continue the study with evaluation of the diagnostic effectiveness of the MaRIAs index (total) in order to use it to assess the effectiveness of conservative treatment of patients with Crohn's disease.

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AUTHORS CONTRIBUTION
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