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**ABSTRACT
ON DISSERTATION PAPER
FOR THE AWARD OF THE SCIENTIFIC AND EDUCATIONAL
DEGREE "DOCTOR" ON THE TOPIC:**

**Role of CT and MR enterocolonography for
diagnosis and follow-up in Crohn's disease**

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Scientific specialty: Medical Radiology

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The dissertation contains 141 pages, including 9 tables and 49 figures. 190 literary sources are cited, of which 4 are in Cyrillic and 186 are in Latin

The dissertation work was discussed and proposed for defense to the departmental council of the Department of "Diagnostic imaging, interventional radiology and radioteraphy " at the medical university "Prof. Paraskev Stoyanov" - Varna

The official defense of the dissertation work will take place on 30.05.2023 at 11:00 a.m. in the hall "Prof. Dr. Luka Pranchev, MD" of UMBAL "St. Marina" at open sessions of the Scientific Jury. The defense materials are available in the library of the MU "Prof. Paraskev Stoyanov" – Varna

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Most commonly used abbreviations:

ADC	Apparent diffusion coefficient maps
Ax T1 VIBE dix	Axial T1 Volumetric interpolated breath-hold examination with Dixon after contrast material
Ax DWI	Axial Diffusion-weighted imaging
Ax FIESTA	Axial fast imaging employing steady state acquisition
Ax HASTE fat sat	Axial Half-Fourier Acquisition Single-shot Turbo spin Echo imaging with fat saturation
Ax LAVA	Axial Liver acceleration volume acquisition
Ax LAVA +C	Axial liver acceleration volume acquisition after contrast material
Ax T1 VIBE fat sat	Axial T1 Volumetric interpolated breath-hold examination with fat saturation
Ax T2 FRFSE	Axial t2 fast relaxation fast spin echo
Ax T2 FS FRFSE	Axial T2 fat saturation Fast Relaxation Fast Spin Echo
Ax T2 HASTE	Axial T2 Half-Fourier Acquisition Single-shot Turbo spin Echo imaging
CDAI	Crohn's disease activity index
CM	Contrast material
Cor FIESTA	Coronary fast imaging employing steady state acquisition
Cor LAVA	Coronary Liver acceleration volume acquisition
Cor LAVA +C	Coronary Liver acceleration volume acquisition after contrast material
Cor T1 VIBE fat sat +C	Coronary T1 Volumetric interpolated breath-hold examination with fat saturation after contrast material
Cor T2 HAST fat sat	Coronary T2 Half-Fourier Acquisition Single-shot Turbo spin Echo imaging with fat saturation
Cor T2 HASTE	Coronary T2 Half-Fourier Acquisition Single-shot Turbo spin Echo imaging
Cor T2 SSFSE	Coronary T2 Single shot fast spin echo
Cor T2 SSFSE FS	Coronary T2 Single shot fast spin echo with fat saturation
Cor T2 TRUFI	Coronary T2 True Fast Imaging with steady-state-free precession
CRP	C reactive protein
CT	Computed tomography
CTE	Computerized enterocolonography
DCE MR	Dynamic contrast enhanced magnetic resonance
DWI	Diffusion-weighted imaging

ESR	Erythrocyte sedimentation rate
FCP	Fecal calprotectin
GIT	Gastrointestinal tract
HASTE	Half-Fourier acquisition single-shot turbo spin-echo
IBDQ	Inflammatory bowel disease questionnaire
MaRIA	Magnetic Resonance Index of Activity
MEGS	Magnetic resonance enterography global score
MR	Magnetic resonance
MR	Magnetic resonance
MRE	Magnetic resonance enterocolography
Sag VIBE +C	Sagittal Volumetric interpolated breath-hold examination with fat saturation after contrast material after contrast material
True FISP	Fast imaging with steady-state free precession
VMC	Virtual monochromatic images
VMI	Virtual monoenergetic imaging

1. Introduction

Inflammatory bowel disease are bowel diseases with a chronically relapsing course. This group also includes Crohn's disease. Crohn's disease mainly affects young patients between the ages of 20 and 40. The chronic relapsing and destructive course of can really lead to temporary or permanent disruption of normal physical activity and work capacity. That is why it is defined as socially significant.

Although it was described 90 years ago, there are still many questions surrounding the disease. Etiology, pathogenesis and risk factors are not fully understood. Different tools are used to make the diagnosis - clinical, laboratory, imaging, endoscopic. No medication or remedy that leads to a cure has been found, but different medications and therapeutic regimens are used depending on the severity and stage of the disease. Image diagnostics has an extremely large role, both for the diagnosis and for the follow-up of a disease. The most commonly used methods are computed tomographic enterography and magnetic resonance enterography. Crohn's disease can involve the entire gastrointestinal tract. In 50% there is simultaneous involvement of both the small and large intestinal loops. When performing and especially when interpreting the performed research, changes are interpreted both in the small intestinal loops and in the colon, and therefore in the present work we will use the broad terms computerized enterocolonography (CTE) and magnetic resonance enterocolonography (MPE), and not only enterography.

The correct recognition and interpretation of imaging findings has a key role, both for the correct diagnosis and for the follow-up of patients.

2. Purpose of the dissertation work

To investigate changes in CTE and MRE in Crohn's disease and to determine their role in the diagnosis and follow-up of the disease.

3. Tasks of the dissertation work

1. To determine the most common CT and MR enterocolonography changes in Crohn's disease.

2. To evaluate the frequency of the most common CT and MR enterocolonography changes in Crohn's disease patients with histological evidence of activity.

3. To determine whether there is a dependence between Lemann index and quality of life (IBDQ).

4. To establish whether there is a correlation between the changes found on CT and MR enterocolonography and paraclinical and laboratory tests in patients with Crohn's disease.

5. To evaluate the role of CT and MR enterocolonography in the follow-up of patients with Crohn's disease.

6. Development of an exemplary protocol for the preparation, examination and follow-up of patients with Crohn's disease by CT and MR enterocolonography.

4. Research methodology and organization:

4.1. Subject of the study:

Analysis of imaging findings of CTE and MPE in patients with Crohn's disease. Determination of their frequency and localization in GIT. Correlation between imaging

changes and the most commonly used clinical and paraclinical tests for the diagnosis and follow-up of patients with Crohn's disease. Calculation of the MEGS score and Lemann score in these patients, as well as the follow-up of the Lemann score over a period of two years.

4.2. Objects of the study are:

194 patients examined in the imaging clinic at the "St. Marina" UMBAL, Varna for the period 2017-2022.

The study is retrospective and prospective. In both the retrospective and prospective analysis, only information from the database of the "Sveta Marina" UMHAT, Varna, is used. The information from laboratory, imaging studies and data recorded in the patient's medical history were used.

Inclusion criteria

- Patients hospitalized in UMHAT "Sveta Marina", Varna
- Period of hospitalization – between 2017-2022 year.
- Patients with histologically proven Crohn's disease
- Patients who have undergone CTE and/or MRE
- An oral solution of mannitol with water was used

Exclusion criteria

- Patients who are not hospitalized in UMHAT "Sveta Marina", Varna
- Patients whose Crohn's disease is not histologically confirmed
- Patients without CTE and/or MRE
- Patients in whom x-ray positive oral contrast was used

Specific studies - to achieve the research goals and to solve the previously formulated tasks, the data of patients with histologically proven Crohn's disease were studied and analyzed. The imaging studies of all patients - CTE and/or MRE, were reviewed and

summarized. The values from the performed laboratory tests (CRP, FCP), as well as calculated index of disease activity (CDAI) and quality of life (IBDQ) were used.

Conducting and organizing the survey

- Study period: 2017-2022
- The study was carried out in UMHAT "Sveta Marina", Varna
- After reading the imaging studies, processing the results, determining the highlights, the actual research was carried out by processing the data with the mathematical and statistical program SPSS v 20 and Jamovi 2.3.24

4.3. Methods applied to realize the purpose and tasks of the study:

4.3.1. Laboratory exams

In the present study, only laboratory tests, performed during the hospitalization of the patients in UMHAT "Sveta Marina", Varna were used. The included exams are:

- C-reactive protein (CRP)
- Fecal calprotectin (FCP)

A clinical laboratory scale was also used to determine disease activity:

- Crohn's Disease Activity Index (CDAI)

Clinical research to determine the quality of life of patients:

- Inflammatory Bowel Disease Questionnaire (IBDQ).

Imaging studies

Imaging tests performed in the Department of Radiology UMHAT "Sveta Marina", Varna during the hospitalization of the patients, were considered.

Computed tomographic enterocolonography (CTE)

188 patients underwent CTE. The examinations were performed on a Siemens Dual Source 64-slice computed tomograph and a Siemens Somatom Force.

The same protocol of preparation and performance was used in the study of all patients. Patients should not take food, 4-6 hours before the examination. Intake of oral contrast begins 40-50 minutes before the examination. The contrast material is a 3-5% solution of mannitol in a volume of 1500 ml in patients with a body weight over 50 kg, and those whose body weight is less than 50 kg take 20 ml/kg body weight. It is taken evenly until the very beginning of the study. In the computer tomography room, immediately before the start of the scan, 1 ml of 20 mg/ml buscolysin is injected. Three scanning phases are performed, in the same volume, from the upper edge of the diaphragmatic cupola to the lower edge of the symphysis pubis. The patient's position is supine. The first phase is a native scan. After the native series, intravenous contrast Omnipaque 350 mg/ml was administered by automatic injector at a speed of 3 mml/sec in an amount of 1.2 ml/sec body weight. Two postcontrast series are performed. The beginning of the first is determined by bolus tracking placed in the abdominal aorta, where a value of 100 HE is set. The start starts 20s after reaching this value. The second phase is standard for all patients, starting 70 seconds after the start of contrast material injection. All patients in all phases underwent reconstruction of the images in the three planes (axial, coronal and sagittal) in a collimation of 3 mm.

When processing the images, the following parameters are used for the respective scanner:

Siemens Dual Source 64

- Window – Window width 300 Window Center 40
- Kernel - B30f

Siemens Vario

- Window - Window width 300 Window Center 40
- Kernel – Br40.d1n



Figure 1 CTE coronary plane optimal bowel extention.

Magnetic resonance enterocolonography (MRE)

47 patients underwent MRE. The examinations were performed on a Siemens Magnetom Verio 3T or GE Signa 1.5T magnetic resonance imaging machine. The same protocol of preparation and performance was used in the study of all patients. Patients should not take food, 4-6 hours before the examination. Intake of oral contrast begins 40-50 minutes before the examination. The contrast material is a 3-5% solution of mannitol in a volume of 1500 ml in patients with a body weight over 50 kg, and those whose body weight is less than 50 kg take 20 ml/kg body weight. It is taken evenly until the very beginning of the study. Half of 1 ml of 2 mg/ml buscolysin is injected into the MRI room immediately before the start of the scan, the remaining ½ is injected before the post-contrast series. An abdominal coil was used in all patients. The patient's position is supine. The studied volume is from the diaphragmatic cupola to the symphysis pubis. At the beginning, native series are performed - axial and coronary T2 with and without fat suppression, axial T1 with and without fat suppression, axial DWI. A postcontrast

study is then performed. Contrast material is injected using an automatic injector. Two post-contrast series are performed at 35 sec coronary T1, at 70 sec axial T1.

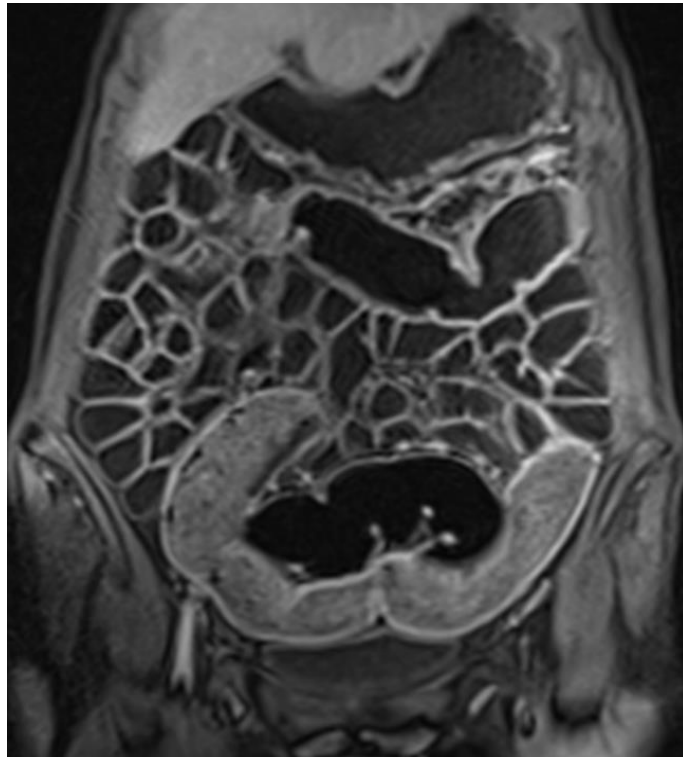


Figure 2 MRE coronary plane, T1 contrast enhancement, optimal bowel extension

The following sequences are used for the respective device:

Simens Magnetom Verio 3T

- Coronary T2 Half-Fourier Acquisition Single-shot Turbo spin Echo imaging (Cor T2 HASTE)
- Coronary T2 Half-Fourier Acquisition Single-shot Turbo spin Echo imaging with fat saturation (Cor T2 HAST fat sat)
- Axial T2 Half-Fourier Acquisition Single-shot Turbo spin Echo imaging (Ax T2 HASTE)
- Axial Half-Fourier Acquisition Single-shot Turbo spin Echo imaging with fat saturation (Ax HASTE fat sat)
- Coronary T2 True Fast Imaging with steady-state-free precession (Cor T2 TRUFI)

- Axial T1 Volumetric interpolated breath-hold examination with fat saturation (Ax T1 VIBE fat sat)
- Axial Diffusion-weighted imaging (Ax DWI)
- Coronary T1 Volumetric interpolated breath-hold examination with fat saturation after contrast material (Cor T1 VIBE fat sat +C)
- Axial T1 Volumetric interpolated breath-hold examination with Dixon after contrast material (Ax T1 VIBE dix)
- Sagittal Volumetric interpolated breath-hold examination with fat saturation after contrast material after contrast material (Sag VIBE +C)

General Electric Signa 1.5T

- Axial T2 fat saturation Fast Relaxation Fast Spin Echo (Ax T2 FS FRFSE)
- Axial T2 Fast Relaxation Fast Spin Echo (Ax T2 FRFSE)
- Coronary Fast Imaging Employing Steady State Acquisition (Cor FIESTA)
- Axial Fast Imaging Employing Steady State Acquisition (Ax FIESTA)
- Coronary T2 Single shot fast spin echo with fat saturation (Cor T2 SSFSE FS)
- Coronary T2 Single shot fast spin echo (Cor T2 SSFSE)
- Axial Diffusion-weighted imaging (Ax DWI)
- Axial Liver acceleration volume acquisition (Ax LAVA)
- Coronary Liver acceleration volume acquisition (Cor LAVA)
- Coronary Liver acceleration volume acquisition after contrast material (Cor LAVA +C)
- Axial liver acceleration volume acquisition after contrast material (Ax LAVA +C)
-

Scores to determine disease activity and severity

Leman index

Leman index was calculated for all patients. The gastrointestinal tract (GIT) is divided into four parts (organs): upper GIT, small intestine, colon and anus. The upper GIT includes the esophagus, stomach, and duodenum. The small intestine is divided into separate segments, with one segment being up to 20 cm long. Colon is considered in six segments - cecum, ascending, descending, transverse, sigmoid part and rectum.

$$2 \times \text{sum upper GIT} + 5 \times \text{sum small intestine} + 3,5 \times \text{sum colon} + 3,5 \times \text{sum anus} = \text{Lemann index}$$

Table 1 Lemann index

	Grade	Upper GT	Small bowel	Colon/rectum	Anus
Surgical	1				Reconstruction of the fistula
	2	By pass Stricture operative correction	By pass Stricture operative correction	Stomy,by pass, Stricture operative correction	Large surgery leading to sphincter damaging
	3	Resection	Resection	Resection	Resection
Stricture/ulceration	1	MR/CT wall thick more than 3mm/ bowel narrowing without pre-stenotic dilation	MR/CT wall thick more than 3mm/ bowel narrowing without pre-stenotic dilation	MR/CT wall thick more than 3mm/ bowel narrowing without pre-stenotic dilation	Clinical examination Moderate stricture
	2	Endoscopy: narrowing bowel,but pervious MR/CT: wall thick more than 3mm/mural stratification	MR/CT wall thick more than 3mm/ mural stratification without pre-stenotic dilation	Colonoscopy: narrowing bowel,but pervious MR/CT: wall thick more than 3mm / segment enhacemant	Clinical examination Pervious stricture

		without pre-stenotic dilation		without pre-stenotic dilation < 50% of the lumen	
	3	Endoscopy: nonpervious stricture MR/CT: stricture with dilation	MP/KT: stricture with dilation	Colonoscopy: nonpervious stricture MR/CT: stricture with pre-stenotic dilation, > 50% of the lumen	Clinical examination Frank, nonpervious stricture
Penetrating lesion	1	Endoscopy: Superficial ulceration	-	Colonoscopy Superficial ulceration	Clinical examination Anal ulceration MP/KT Simple fistula
	2	Endoscopy Deep ulceration MR/CT: deep transmural ulceration	MR/CT: deep transmural ulceration	Colonoscopy: Deep ulceration MR/CT: transmural ulceration	Clinical examination Multiple fistula MR/CT: Branching fistula, multiple fistula or any type of abscess > 1 cm
	3	Endoscopy: Fistula MR/CT: Phlegmon or any type of fistula	MR/CT: Phlegmon or any type of fistula	Colonoscopy fistula MR/CT Phlegmon or any type of fistula	Clinical examination Multiple fistula MR/CT Multiple fistula with extensive anal and perianal suppuration, horseshoe abscess, or fistula involving or extending above the levator plate

Each individual segment is evaluated according to three parameters: penetration, stricture, and underlying surgical intervention, scoring 0, 1, 2, and 3 depending on its involvement. Then the values of all segments for each individual part (organ) are summed. The resulting value of the individual parts is multiplied by the corresponding organ coefficient and then the result of all parts is added. [60, 121] Table 2 shows the calculation method.

Magnetic Resonance Index of Activity (MEGS)

The MEGS score was calculated for all patients who underwent MRE. To calculate this score, the GIT is divided into nine segments: jejunum, proximal ileum, terminal ileum, cecum, ascending, transverse, descending, sigmoid colon and rectum. Each individual segment is evaluated according to several parameters: mural thickness, mural T2 signal, perimural T2 signal, T1 enhancement, mural enhancement pattern, haustral loss. Each segment is scored according changes with 1, 2 or 3 points. Each segment is then multiplied by the score for the corresponding segment and an additional score is added for each patient. The additional score for each patient is the sum of four indicators: lymph nodes over 10 mm, comb sign, abscess and fistulas, and each indicator is evaluated with five points. The table below shows how it is calculated.

$$\left[(A+B+C+D+F) \times \text{segment length} + \text{extraluminal score} \right] = \text{MEGS}$$

Calculated for
each segment

Table 2 MEGS

Imaging finding	0	1	2	3	5
Mural thickness	< 3mm	3-5 mm	5-7 mm	> 7 mm	A
Mural T2 signal	normal	Minimal increase	Moderate increase	Large increase	B
Perimural T2 signal	normal	Increase signal, (-) fluid	Small fluid < 2mm	large fluid > 2mm	C
T1 enhancement	normal	Minimum enhancement	moderate enhancement	Severe enhancement	D
Mural enhancement pattern	None/ homogeneous	Mucosal	Layered		E
Haustral loss	none	<1/3 segment	1/3 -2/3 segment	> 2/3 segment	F
Length of the affected segment	1- < 5cm; 1,5 – 5- 15 cm; 2 > 15 cm				
Екстралумени промени					
Abscess	absent				present
Fistula	absent				present
Lymph nodes > 1sm	absent				present
Comb sign	absent				present

4.3.6. Statistical methods – Various statistical methods were used in the preparation of the present study:

- **Correlation analysis** shows the strength and direction of a relationship between two metrics. This statistical method calculates whether the influence of a given factor is random or not. The influence of both indicators is significant when the null hypothesis is rejected. Significance was determined by the p value – strong statistical significance $p < 0.01$ and moderate $p < 0.05$. The strength and direction of the relationship is based on the Pearson (r) and Spierman (rs) coefficient results
- **Analysis of variance (ANOVA)** was used to determine a relationship between the studied phenomena. It assesses to what extent the influence of a factor is statistically significant or not
- **ROC curve analysis** allows to distinguish low and high value of the indicator and to determine the cut-off value. Graphically, the results are represented by a Roc curve
- **Descriptive statistics** are used to summarize data through quantitative representation. Presents information about absolute count, arithmetic mean, median, standard deviation (SD), and more.

Different programs were used for data processing and calculation: IBM SPSS v.25 and Jamovi 2.3.24 current. Microsoft Office Excel 2013 for Windows 10 was used to create a graphical and tabular presentation of the results.

5. Results and Discussion

Characteristics of the studied patients

For a period of five years (2017-2022), 194 patients with Crohn's disease were examined, in which 446 imaging studies were performed during the specified period - 386 CTE and 60 MRE. Due to the chronic-recurring nature of the disease, the patients were hospitalized several times in UMHAT "Sveta Marina" Varna. For the purposes of the dissertation, only hospitalizations with CTE and/or MRE were considered. The

corresponding hospitalization is considered a separate visit. The maximum number of visits for the specified period is six.

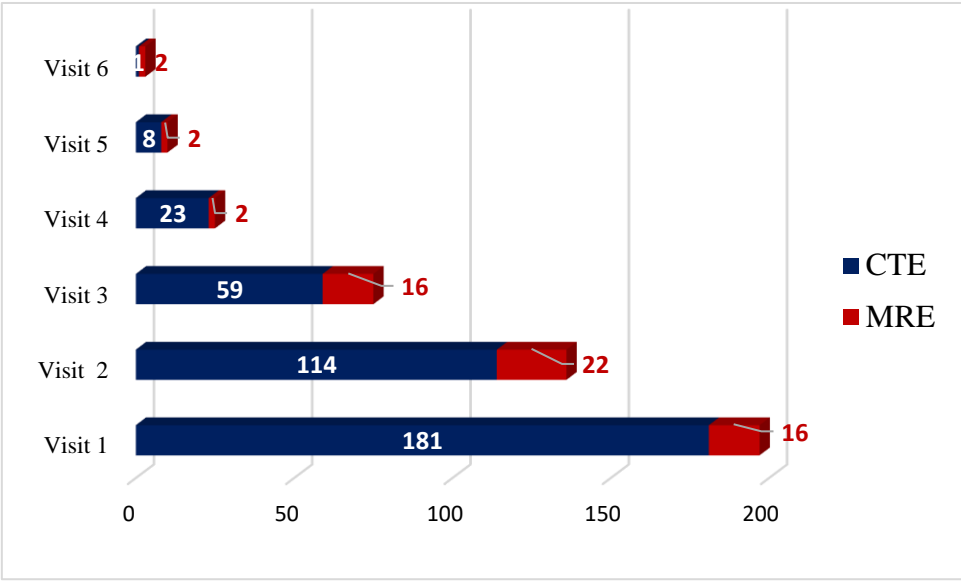
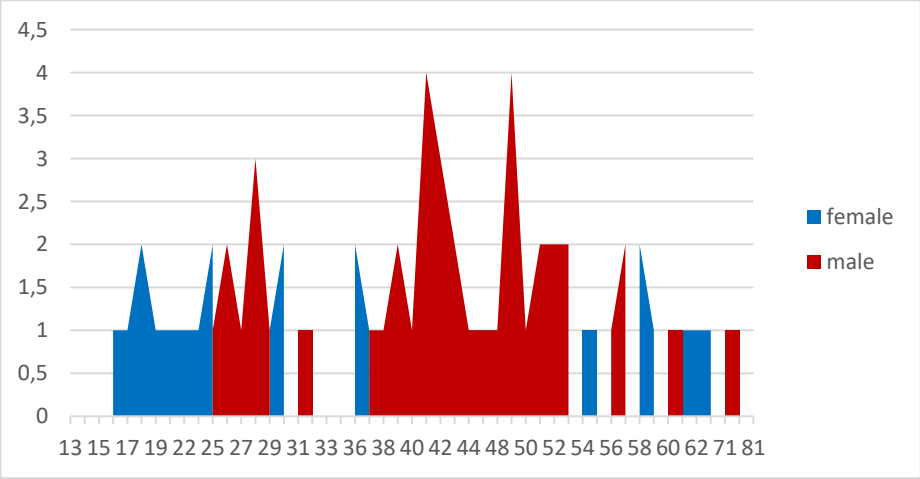


Figure 3 Distribution of CTE and MRE by visits

Table 3 presents the characteristics of the considered group. The gender distribution is as follows – 47.9% (93) women, 52.1% (101) men. The average age of patients at diagnosis is 36.93 ± 16.15 , the youngest individual diagnosed with the disease



is 9 years old, the oldest is 71 years old. Figure 4 shows the distribution of the studied patients by age and gender.

Figure 4 Distribution of the patients by age and gender

Table 3 Characteristics of the studied group of patients.

Sign		Count/%
Age	mean±SD (range)	36,93±16,15 (9-81)
Gender	Men	101/52,1%
	Women	93/47,9%
Image studies		
CTE	Number of patients	188/96,9%
MRE	Number of patients	47/24,2%
CTE+MRE	Number of patients	9/4.63%
Image findings		
thickened wall >3mm	count	155/79,89%
bilaminar hyperenhancement	count	62/32%
trilaminar hyperenhancement	count	106/54,62%
homogeneous late hyperenhancement	count	54/27,83%
thickened mesenteric adipose tissue	count	57/29,38%
Comb sign	count	108/55,67%
lymph nodes > 1cm	count	132/68,04%
fistulas	count	48/24,74%
abscesses	count	116/59,79%
Laboratory exams		
CRP	mean±SD (range)	36.37 ± 50.25 (0.57-324)
	< 5	51/26.3 %
FCP	mean±SD (range)	562.76 ± 1023.25 (0-10001)

	< 50	21/ 10.8%
CDAI	mean±SD (range)	263.95 ± 98.62 (37-622)
	<150	10/ 5.2 %
Scores		
Lemann index	count	194/100%
MEGS score	count	46/23,7%
Extraintestinal manifestations		
sacroileitis	count	42/30,9%
cholelithiasis	count	36/25,4%

At the time of diagnosis and during the follow-up in order to assess the effect of the treatment/progression of the disease in the patients, CTE is performed in 188 patients and MRE in 47 patients, and in 9 patients both tests are performed. When performing imaging studies, a thickened wall > 3mm was observed in 79.89% (155). Pathological contrasting observed in patients is divided into 3 groups: trilaminar hyperenhancement, bilaminar hyperenhancement, homogeneous late hyperenhancement. Thickened mesenteric adipose tissue is observed in 29.38%. A comb sign is observed in 55.68%, lymph nodes > 1 cm are found in the examination of imaging studies in 68.04% of patients. The distribution of findings according the number of patients is presented graphically in Figure 5.

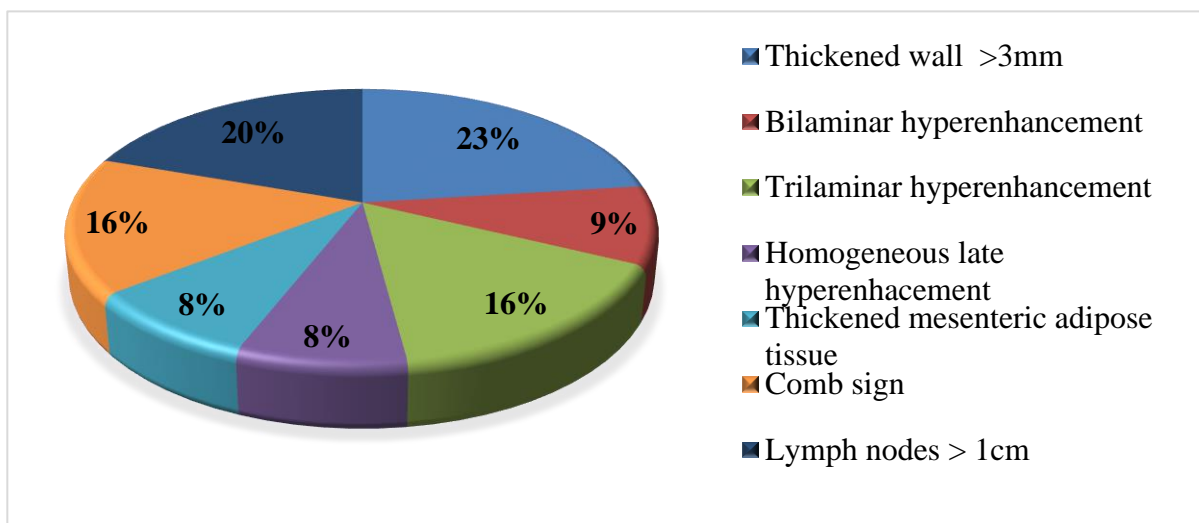


Figure 5 Distribution of imaging findings according the number of patients

Abscesses and fistulas are also detected by the performed imaging studies, in 59.79% and 24.74%, respectively.

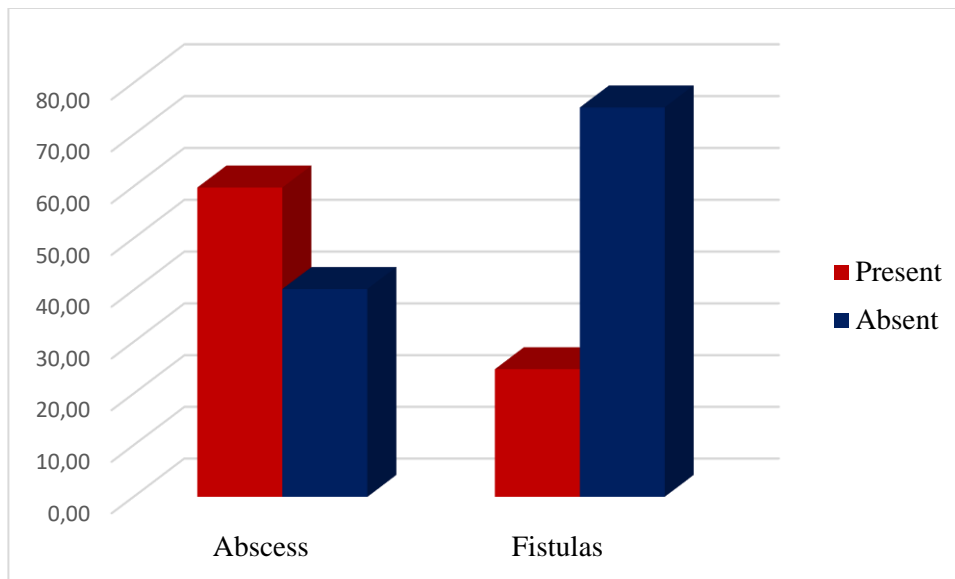


Figure 6 Ddistribution of the patients with abscess and fistulas

During the hospitalization of the patients, laboratory tests were performed. The tests we have used in the disertation are CRP and FCP. The average value of CRP in our study is 36.37 ± 50.25 , with the highest measured value being 324. In 26.3% of the examined persons, CRP has normal values.

During hospitalization, the patients also presented FCP, with the average value 562.76 ± 1023.25 . This marker is specific and increases in intestinal inflammation. Its high average value, as well as the fact that the majority of patients have an elevated (>50) values, shows that at the time of hospitalization and imaging studies, patients are in an active phase. This is also confirmed by the fact that only 5.2% of patients are with $CDAI < 150$. Increased values of $CDAI > 150$ were observed in the active phase of the disease. Figure 5 shows a box-plot of the mean CDAI values of the patients at the different visits. It shows that the main part are patients with $CDAI > 150$, i.e. with active inflammation.

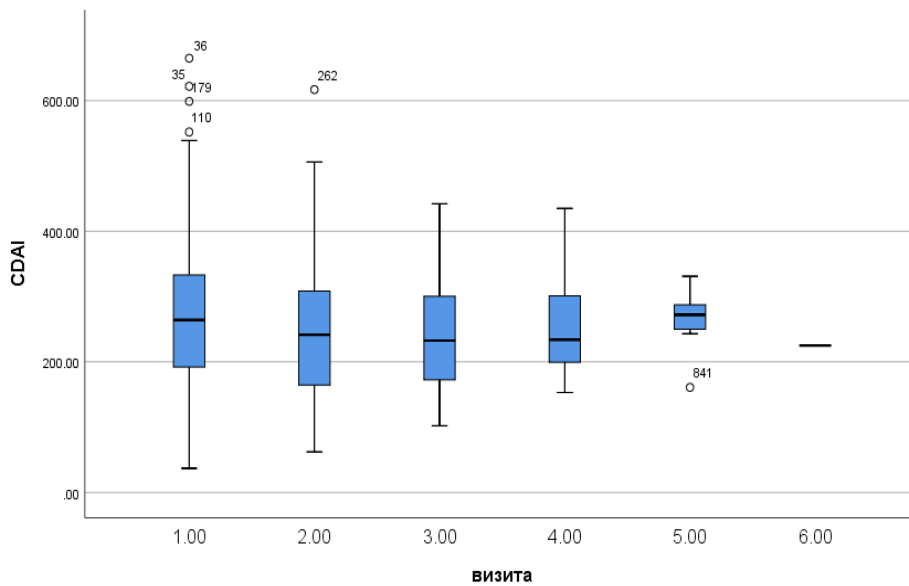


Figure 7 Box-plot graphics of mean CDAI values at each patient visit

The Lemann index is calculated for all patients, and the MEGS score was also calculated for 46 patients with MRE.

In the interpretation of imaging studies in patients with Crohn's disease, the number of the following extraintestinal manifestations of the disease are determined: sacroileitis and cholelithiasis. Sacroiliitis was found in 42 (30.9%) patients, and cholelithiasis in 36 (25.4%). The distribution is shown graphically in Figure 8.

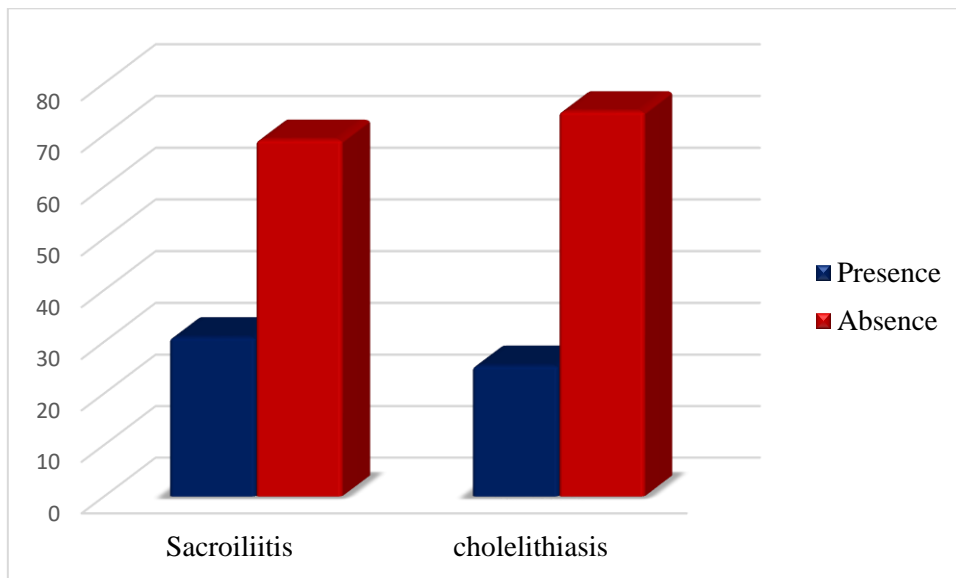


Figure 8 Number of patients with and without corresponding extraintestinal manifestation

5.1. Assessment of which are the most common CTE and MRE changes in patients with Crohn's disease.

All 194 patients underwent imaging studies at diagnosis and/or follow-up. Patients with Crohn's disease underwent CTE and/or MPE, for which several imaging studies were performed in each patient. In the sample, 386 KTE and 60 MRE were examined. Imaging findings that show enhancement from those shown are: bowel wall thickening >3 mm, comb sign, bilaminar contrast enhancement, trilaminar contrast enhancement, homogeneous late contrast enhancement, thickened mesenteric fat, enlarged lymph nodes >1 cm, fistula and abscess.

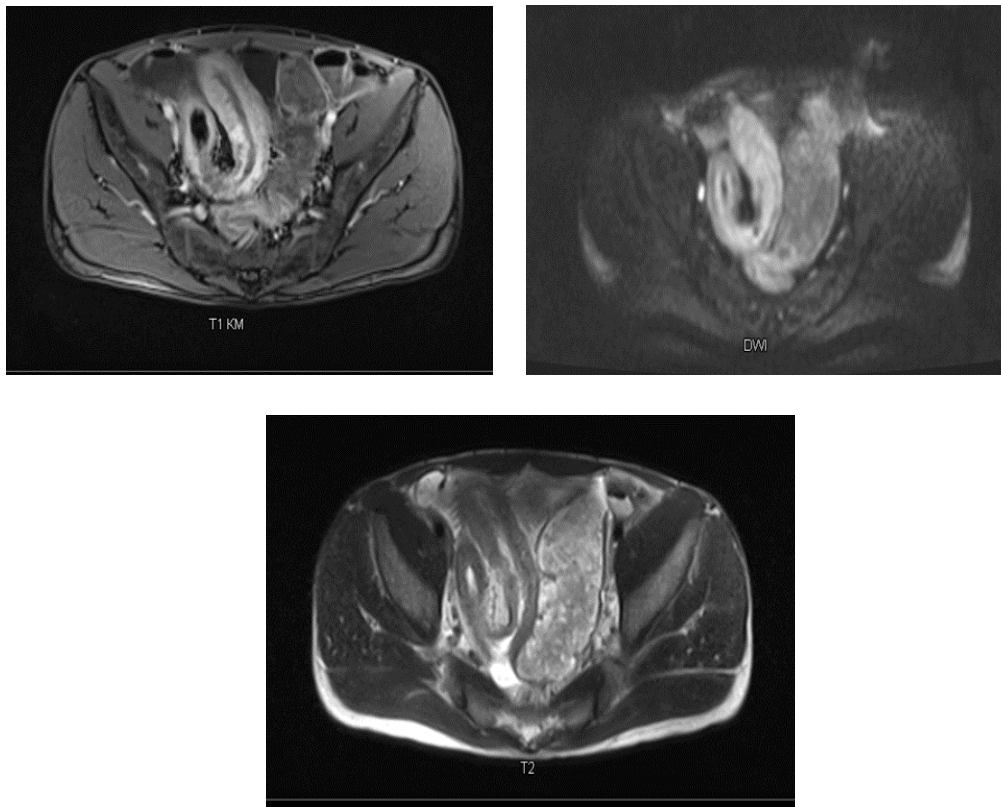


Figure 9 MPE showing wall thickening, postcontrast enhancement, DWI restriction, and free fluid around a T1 postcoel bowel loop. A T1 with contrast; B DW; C T2.

Different areas of the GI tract can be affected in Crohn's disease. Figure 10 shows the percentage distribution of affected segments. Most often, the disease affects the terminal ileum (56%) and small intestine (35%). The third most frequently affected area is the colon. The sigmoid and colon transversum are the most frequently involved sections of the colon - 29% and 24%, respectively

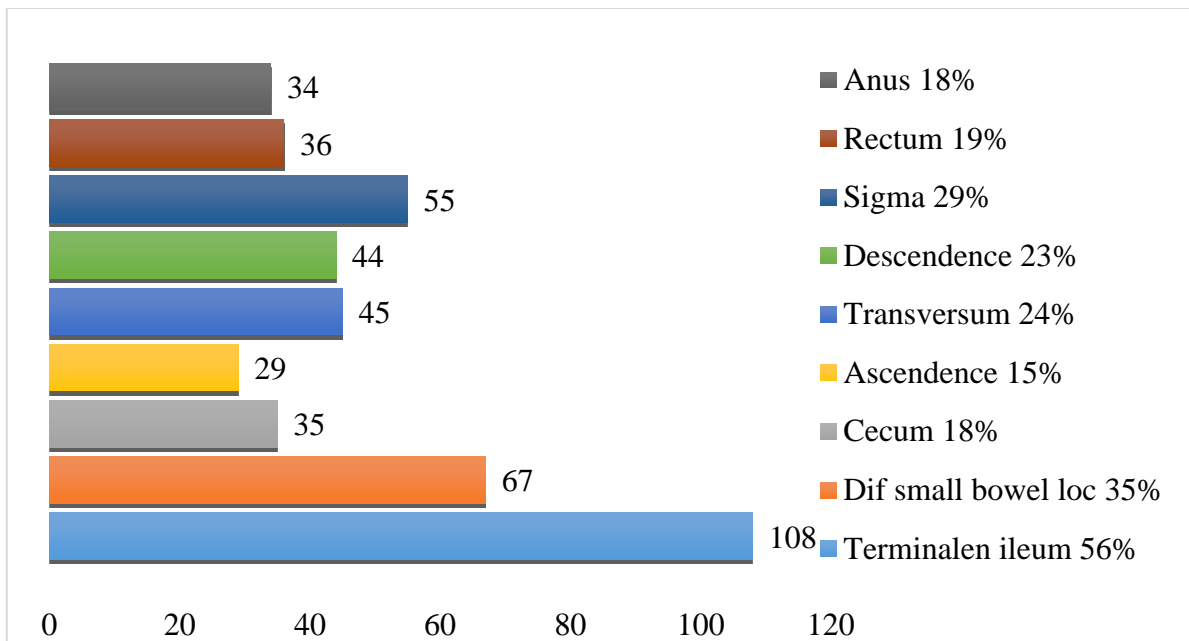


Figure 10 intestinal segments affected by Crohn's disease

. Figure 11 shows the distribution of findings against their frequency in percentages. The most common imaging findings in Crohn's disease patients in our study were bowel wall thickening > 3 mm – 84%, and trilaminar hyperenhancement – 78.90%, followed by enlarged lymph nodes > 1 cm – 69%. Comb sign is the next most frequent imaging finding observed in patients with Crohn's disease - 61.60%.

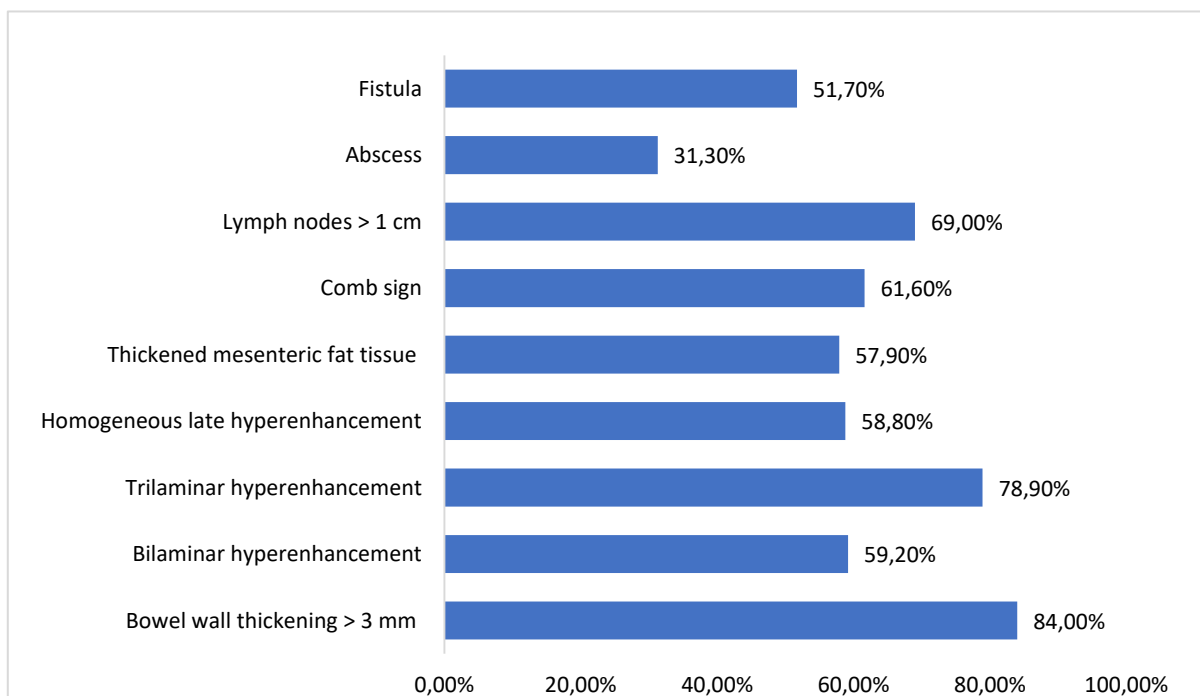


Figure 11 Frequency of CTE and MPE changes

Bilaminar contrast, homogeneous late contrast, and thickened mesenteric fat tissue were of similar frequency – 59.20%, 58.80%, and 57.90%, respectively.

Other authors describe similar results. In his study, Carlos Santosa, 2015 reported the highest incidence of contrast enhancement at 67%. [25] The author combined pathological contrast enhancement in one indicator, therefore this parameter has the highest frequency. If our study also considers pathological contrast, which includes bilaminar hyperenhancement, trilaminar hyperenhancement, and homogeneous late contrast, as one indicator, it will also have a higher percentage. The thickened wall is also of high frequency in the Carlos Santosa sample – 64%.

Table 4 Frequency of imaging findings, comparison with other authors [25]

Imaging findings	Own research, 2022 (n=194)	Carlos Santosa, 2015 (n=42)
Bowel wall thickening > 3 mm	84%	64%
Thickened mesenteric fat tissue	57,90%	58%
Lymph nodes > 1 cm	69%	50%
Comb sign	61,60%	59%
Fistula	51,70%	14%
Abscess	31,30%	11%

As seen in Table 4, the thickened frequent mesenteric adipose tissue and comb sign is similar to the study in our study - 57.90% and 61.60% for the study and 58% and 59% for the study of Carlos Santosa, respectively. Enlarged lymph nodes >1 cm in both samples have a high frequency - 69% for our study and 50% according to the data from 2015.

Figure 12 shows a coronary CTE section of diseased terminal ileum. There is wall thickening with trilaminar contrast, increased mesenteric blood flow (comb sign), thickened mesenteric fatty tissue.

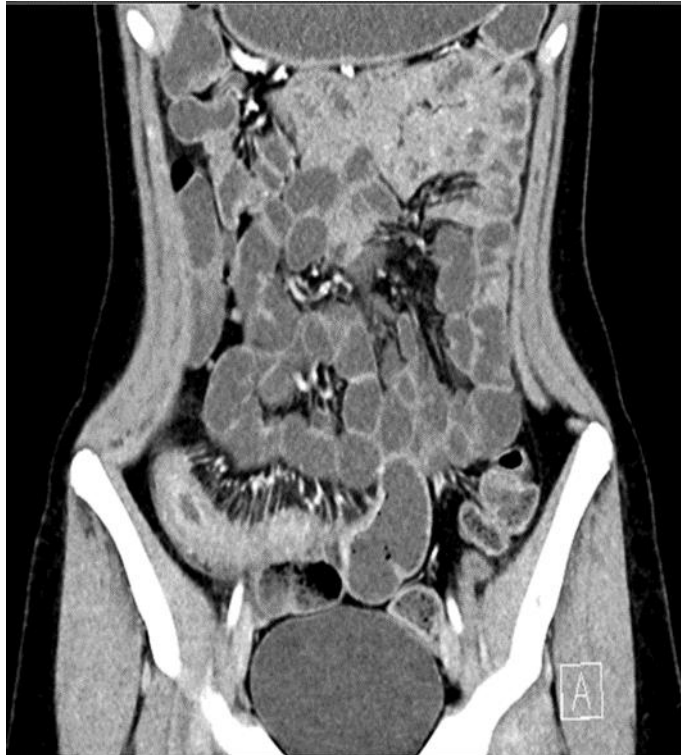


Figure 12 KTE coronal section, thickened intestinal wall with trilaminar hyperenhancement is visualized, as well as comb sign with fatty tissue compaction

Abscesses and fistulas have the lowest frequency, both in our sample and in Carlos Santosa's study – 51.70% and 31.30% according to our results, 14% and 11% according to other authors' data.

Fig. 13 visualizes fistula courses between small intestinal loops. In the follow-up of the same patient after 1 year and 4 months, disease progression was observed, in which the fistula courses involved m. psoas (Figure 14).



Figure 13 CTE axial section demonstrates fistula courses between small bowel loops

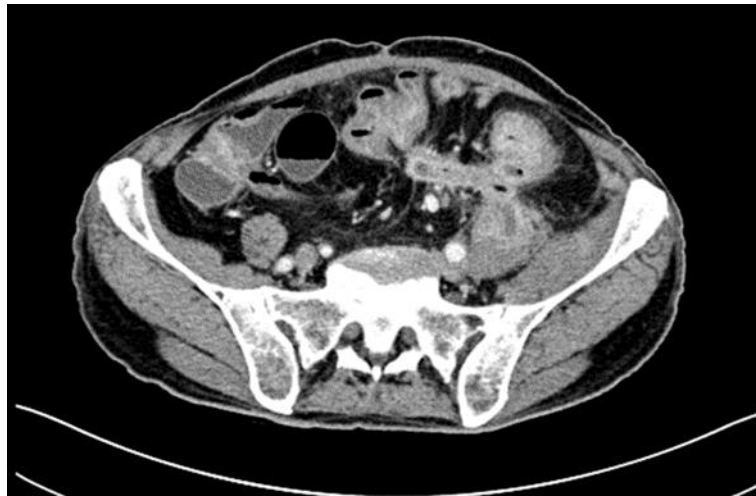


Figure 14 CTE axial section after 1 year and 4 months, the fistula courses involve and m. psoas

The average number of findings that were observed using imaging methods was 4, ranging from 1 to 8. The histogram presented in Figure 15 shows the distribution of the number of findings. Using both methods separately CTE and MPE resulted in an average of 4 findings, while using both imaging methods simultaneously resulted in between 5 and 6 findings.

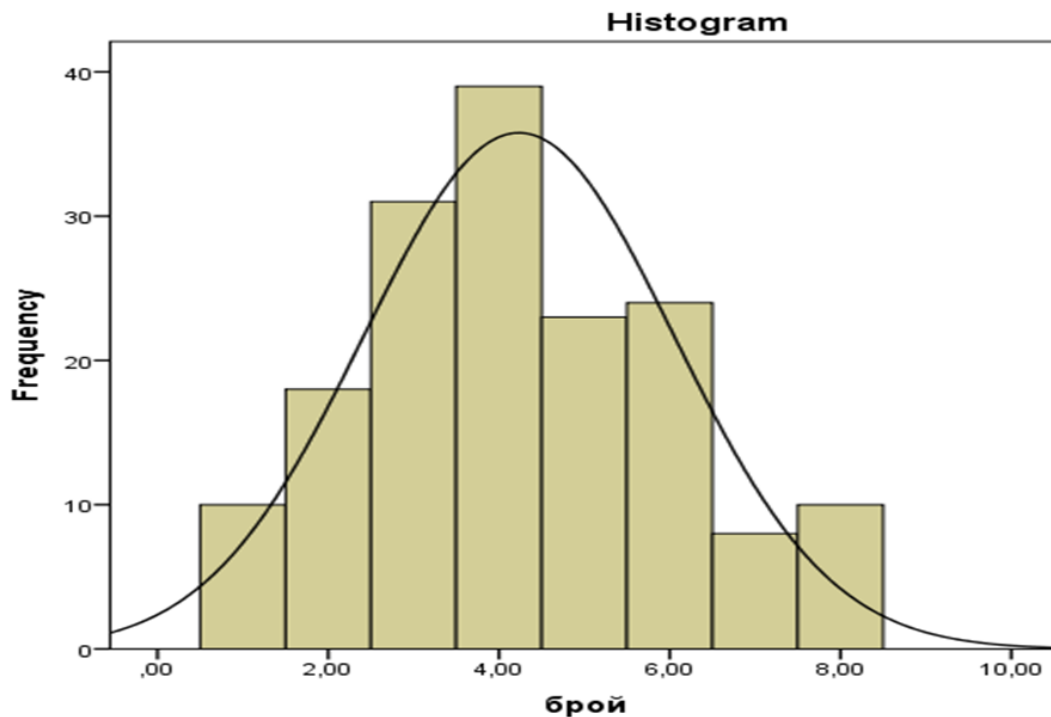


Figure 15 Histogram - number of CTE and MPE findings

This shows that the use of the combination of the two imaging methods (CTE and MPE) increases the informativeness of the studies.

The most common combination of findings was wall thickening >3mm, trilaminar enhancement, thickened mesenteric fat, comb sign, enlarged lymph nodes >1cm (9.8%), followed by wall thickening >3mm and trilaminar enhancement (5.2%).

5.2. To evaluate the frequency of the most common CT and MR enterocolonography changes in Crohn's disease patients with histological evidence of activity.

To assess the specificity of the most common CTE and MPE changes in patients with Crohn's disease, we compared imaging findings in patients who had evidence of histological activity. These are the patients in whom, during the hospitalization (visit), imaging studies and endoscopy are performed, during which a biopsy is taken. From the material taken for research, there are histological data on the activity of the successful. In 31 (16%) patients, there was evidence of hytological activity of the test at the time of performing the relevant imaging study.

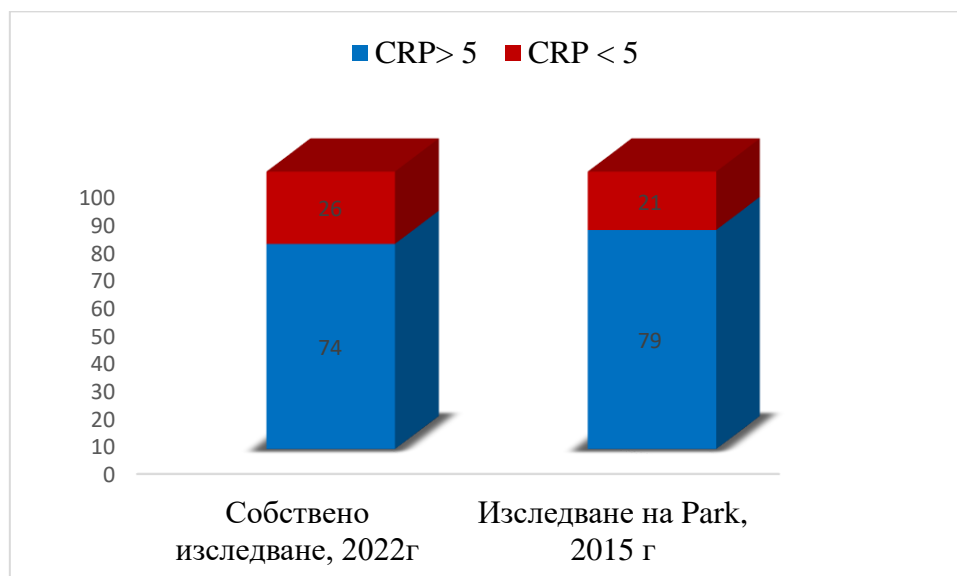


Figure 16 Ratio of patients with elevated CRP values to patients with normal values of the indicator compared with Park's data

Table 5 Characteristics of patients with histological activity

Parameter		Own research, 2022r n=31	Park`s research, 2015 n=39
Age		34	27
Sex	Male	15	26
	Female	16	13
CRP median		51.85	
CRP normal		8 (26%)	8 (21%)
CRP high		23 (74%)	31 (79%)
CDAI mediana		268,5	128,8
CDAI < 150		3 (9%)	29 (58%)
CDAI >150		22 (71%)	21 (42%)
Lymph nodes > 1 cm		13(42%)	14(28%)
Abscess		3(9%)	3 (6%)
Fistula		5(16%)	4 (8%)

Table 5 presents the characteristics of these 31 patients, compared with the characteristics of patients included in Park's study, 2016 [122] In our sample, patients with histological evidence of activity had a mean age of 34 years at diagnosis, with the distribution by gender it is evenly 15 men, 16 women. The average age of the patients in Park's sample was 27 years, and the distribution by gender was not even - there were more men. Both in our study and in that of the other authors, patients with elevated

values of the inflammatory marker CRP predominate - 74% for our study and 79% in Park's sample. The mean CRP in our sample is 51.85.

In the patients with Crohn's disease with histological data of activity, CDAI > 150 was in 22 patients (71%), 2 had CDAI < 150, in 7 patients we did not have a calculated CDAI. In Park's sample, patients with no evidence of disease activity ie. CDAI < 150 were more 58% (29), compared to our group. The CDAI mean in our sample was a significantly higher 268.5 compared to Park's pool mean of 128.8. There were 5 patients with fistulas in our study, 4 in Park's study, and three patients with abscesses in both studies. In the CTE and MPE conducted in our study, enlarged lymph nodes > 1 cm were found in 42%. In patients included in the research of the other authors, this percentage is significantly lower - 28%.

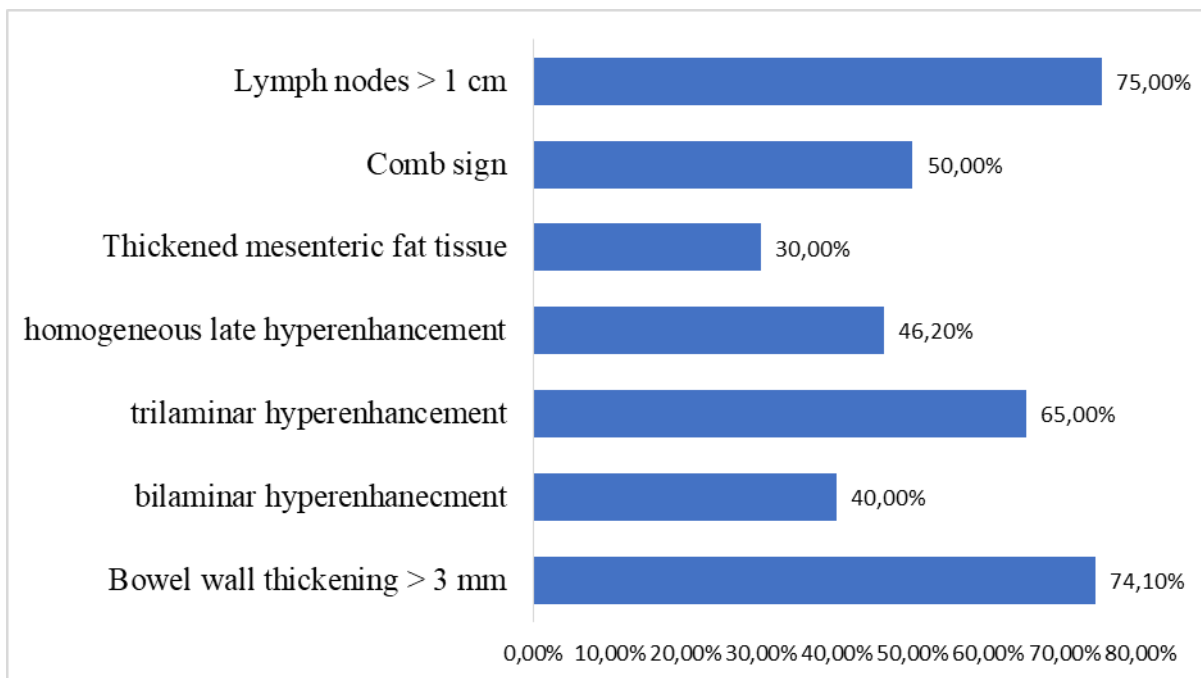


Figure 17 Frequency of CTE and MPE changes in patients with histologic activity data.

During the CTE and MPE examinations, the following imaging findings were observed in the patients: thickened wall >3mm; bilaminar enhancement, trilaminar enhancement, homogeneous late contrast, thickened mesenteric fat, cComb sign. The distribution of imaging findings, by frequency, of these patients for our study is presented in Figure 17. The figure shows that the most common imaging findings in patients with histological activity are enlarged lymph nodes and thickened wall > 3 mm – 75%, respectively and 74.10%.

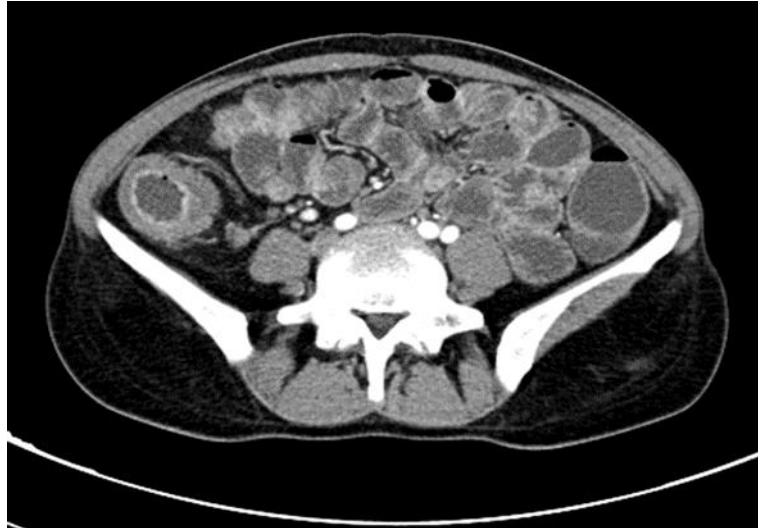


Figure 18 CTE Axial ileal slice bilaminar contrast enhancement with thickened wall and mesenteric lymph nodes

Figure 18 shows an axial section CT image of a patient with Crohn's disease showing bilaminar enhancement and thickened bowel wall and mesenteric lymph nodes.

Trilaminar enhancement is the third most frequent imaging finding in patients with Crohn's disease - 65%. Comb sign is found in half of the tests performed.

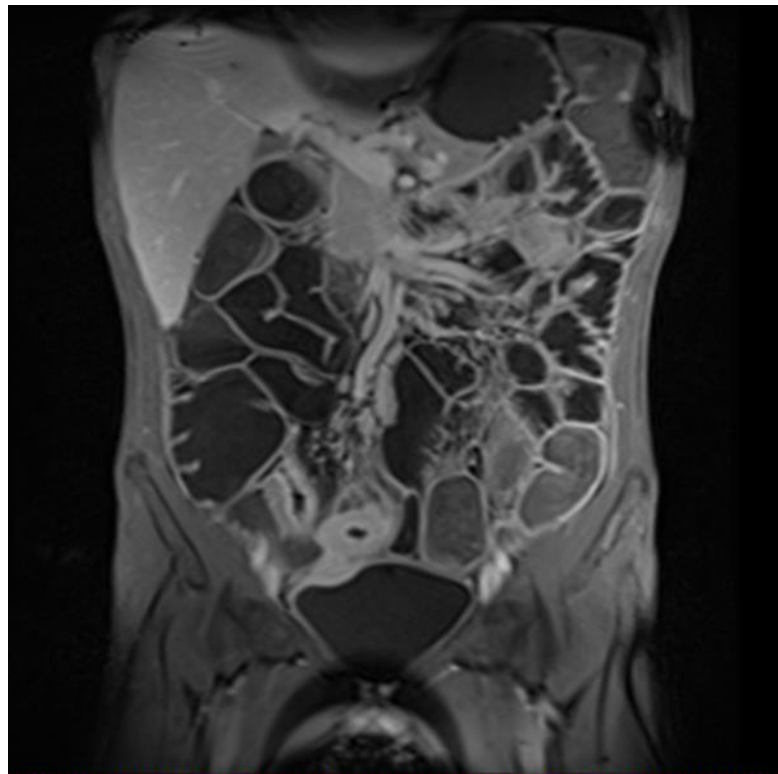


Figure 19 MPE T1 CM terminus ileum, thickened wall with pathological contrast

Homogeneous late contrast was observed in 46.2%. Bilaminar enhancement is the next most common imaging finding – found in 40% of cases. The lowest percentage is the mesenteric adipose tissue - 30%.

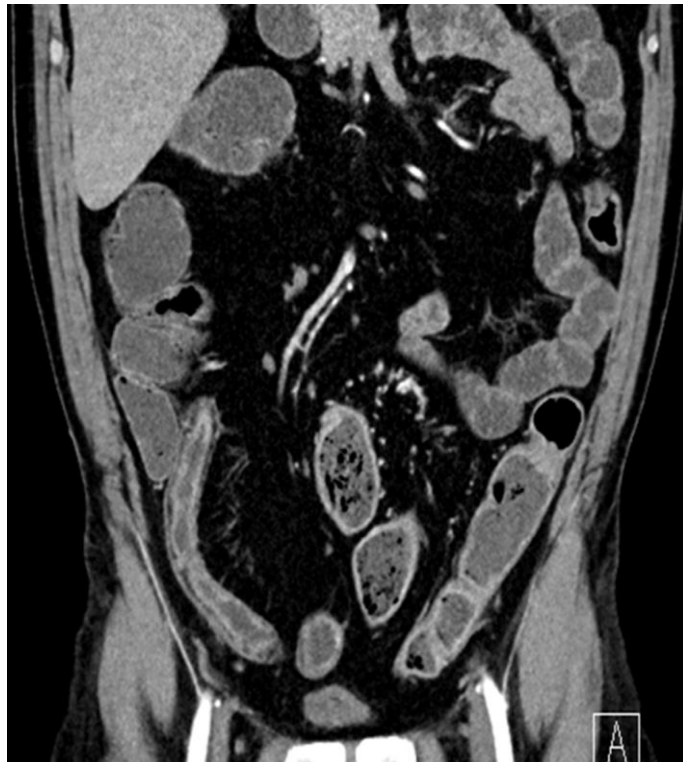


Figure 20 KTE coronary plane, bowel thickened, trilaminar enhancement

5.3. To establish the correlation between the Lemann index and quality of life (IBDQ).

Crohn's disease is chronically caused, which affects the impact of everyday life on the patient, affects his physical and mental state. A valid for the test questionnaire called IBDQ (Inflammatory Bowel Disease Questionnaire) is used to assess the quality of life of patients with Crohn's disease. The index that is used to assess the degree of damage from software in imaging is the Lemann index. It assesses penetration, stricture and surgery performed. 96.9% (188) of patients underwent CTE and 24.2% (47) underwent MPE. In all patients, the Lemann index was calculated in 101 (52.1%) men and 93 (47.9%) women, respectively. The highest value of the indicator for men is 31.75 and for women the highest value is 26.33. The average value of the Lemann index in our sample was 4.2 ± 4.93 (0 – 31.75). (figure 21)

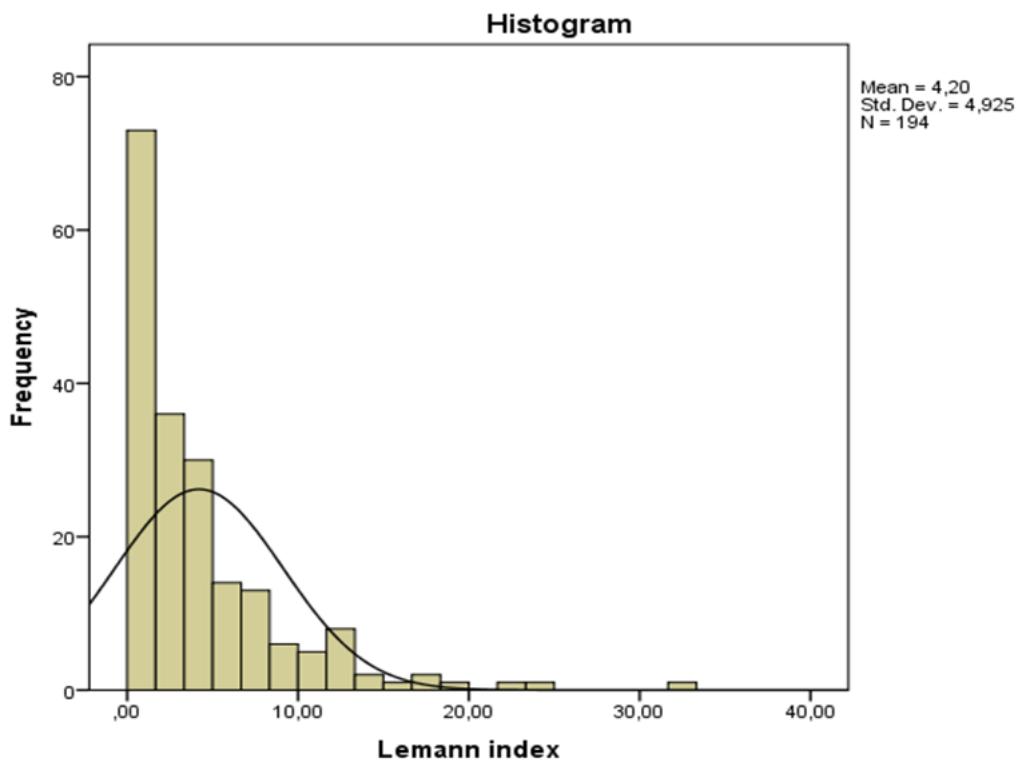


Figure 21 Histograma of average value of Lemann index

In our sample, the IBDQ questionnaire was used in 47 patients over the age of 18 years. The change in the indicator was tracked in three visits. In 10 patients, the IBDQ value was calculated in two consecutive visits. IBDQ scores can range from 32 – 224,

with the highest score correlating with good quality of life. The values found in our sample are presented graphically, by means of a histogram in figure 18. It shows that the main part of the patients has a low to average quality of life. The mean IBDQ in our sample was 134.09 ± 37.29 (41-203).

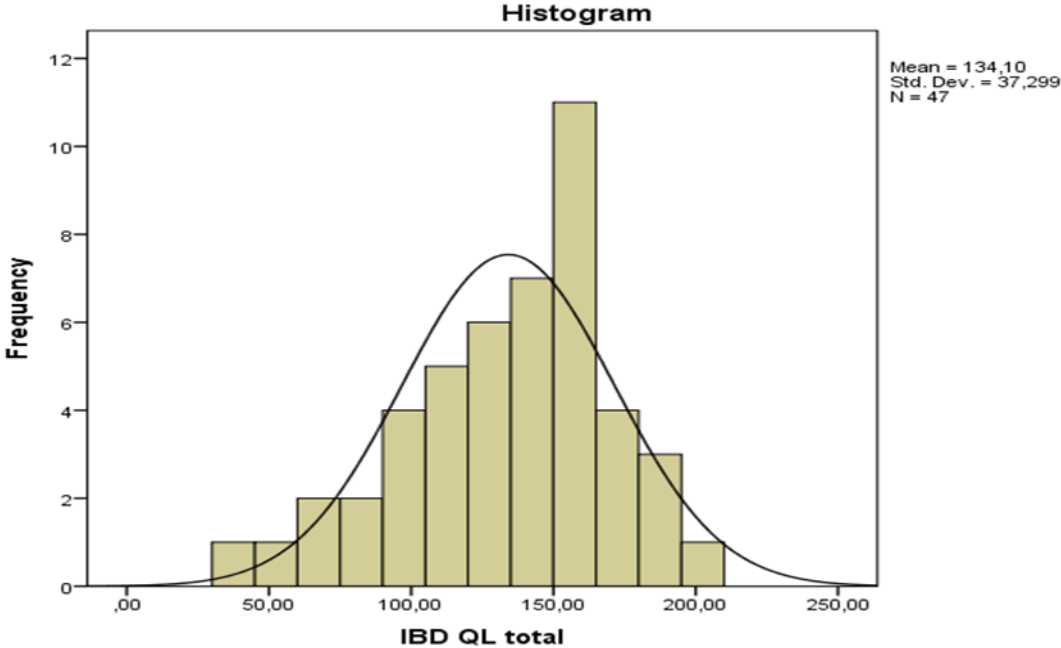


Figure 22 Histogram of IBDQ

The analysis showed a decrease in the values of the indicator with the progression of the disease over time, the difference is significant - at the first visit the average value of the IBDQ was 139.2, and at 2 visits - 122.6. **We also found a statistically significant relationship between the Lemann values index on 1 year and after 2 years, with average values of 3.9 and 7, respectively.**

Table 6 presents the characteristics of patients with calculated IBDQ in our sample and compared with those of other authors. The mean age of the patients followed was 39.87 ± 14.80 , which is close to the mean age in the Straksyte sample, 2019.[164] Male gender predominated in both samples 61.7% for our study and 60.4% in the Straksyte study, 2019. Crohn's disease mainly affected the colon and terminal ileum in our group, while Straksyte predominated. In our sample, as well as according to the data of other authors, the non-penetrating and non-stricturing form of the disease prevails. The mean CRP value in our sample was significantly lower than the mean inflammatory

marker value in the Straksyte study. In the other study, there were no patients with operative treatment, whereas in our sample, operative examination was performed in 10 patients. Straksyte found a strong negative inverse relationship between the two indicators ($r = -0.812$, $P < 0.01$).

Table 6 Characteristics of patients with calculated IBDQ followed up at 2-year intervals, with data compared with those of other authors [164]

Indicator	Own research, 2022 n=47	Straksyte`s research, 2019 n=53	P value
Male	29/61,7%	32 (60,4%)	
Female	18/38,2%	21(39,6%)	
Average age at diagnosis	39,87±14,80	37±14,4	
Affected segments			
L1 Terminal ileum	22/50%	23/43,4%	<0,443
L2 colon	28/59,57%	7/13.2%	
L3 ileum/colon	19/40,42%	23/43,4%	
L4 upper GIT	0	0	
B1	22/50%	31/58,5%	<0,367
B2	19/40,4%	11/20,75%	
B3	11/23,40%	11/20,75%	
CRP (mean ±SD)	44,57±57,1	305,33±76,66	
Surgery (none)	40/85,10%	53/100%	

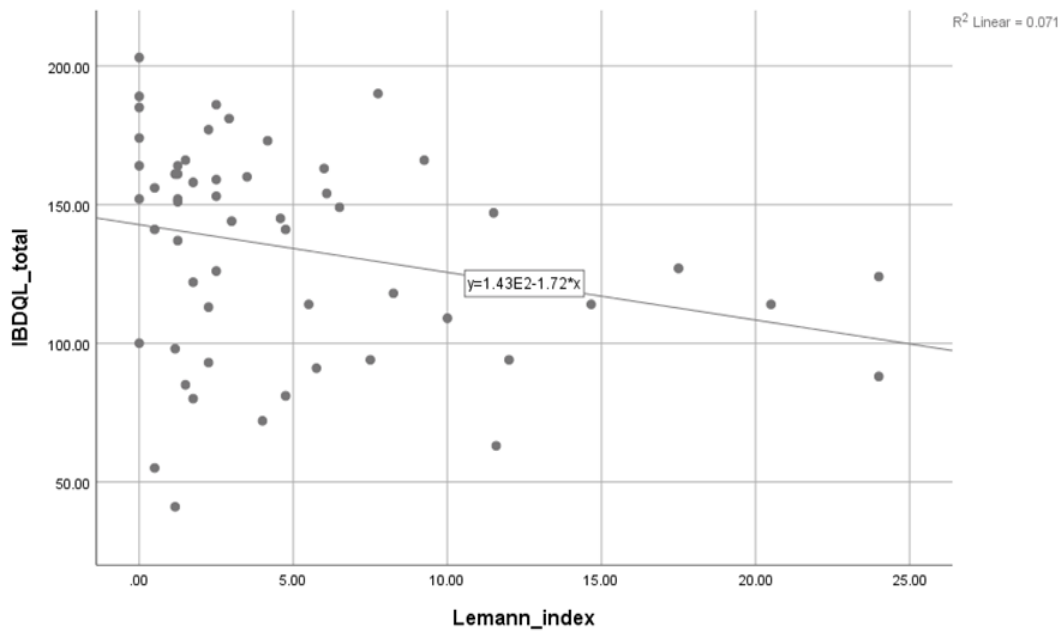


Figure 23 Correlation between Lemann index and IBDQ

In our study, we also found an inverse, statistically significant moderate correlation between Lemann index and IBDQ, by correlation analysis using the Pierson method, namely, with increasing index values, quality of life decreases ($r = -0.266$, $p = 0.045$). Graphically, the dependence is expressed on a scatterplot graph - figure 23.

In our study, we looked for an association between thickened wall > 3 mm, pathological contrast enhancement, thickened mesenteric fat, comb sign, and enlarged lymph nodes > 1 cm, which are the most common imaging findings found in patients with Crohn's disease.

An inverse correlation was observed in all of them, showing that with lower IBDQ values, there are high Lemann index values, there are higher IBDQ values, with the dependence being strongest for Comb sign, enlarged lymph nodes > 1 cm, thickened wall > 3 mm and the bilaminar contrast. The dependence is presented graphically in figures 24, 25 and 26.

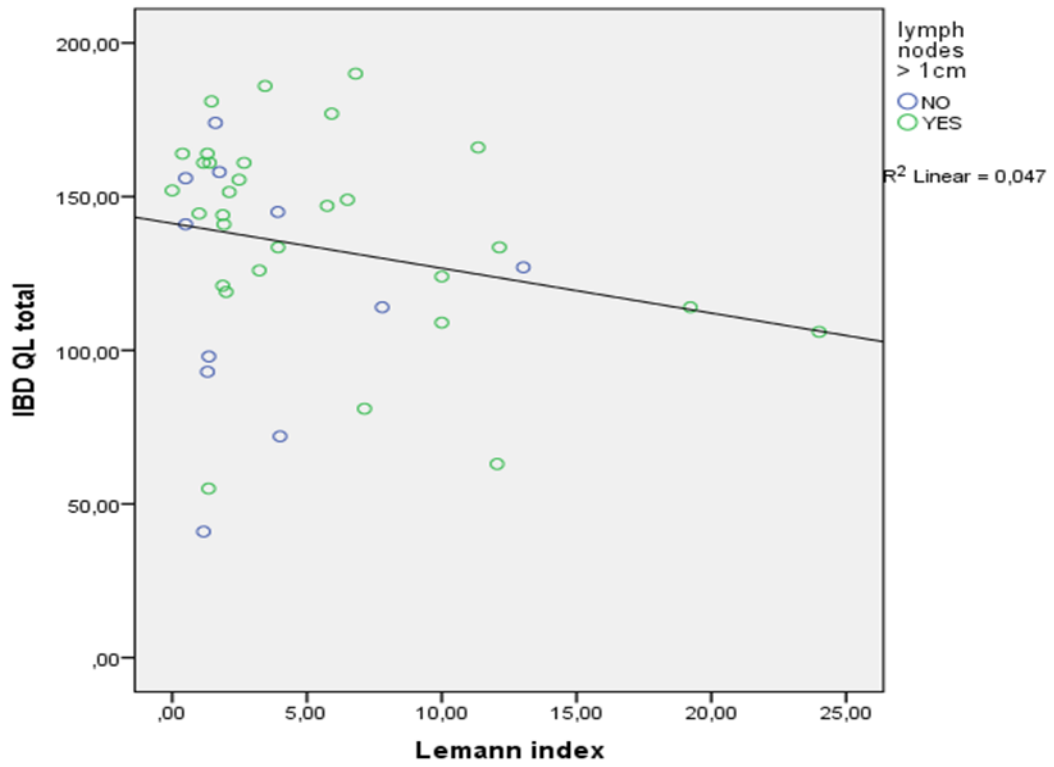


Figure 24 Correlation between enlarged lymph nodes > 1cm and IBDQ and Lemann index

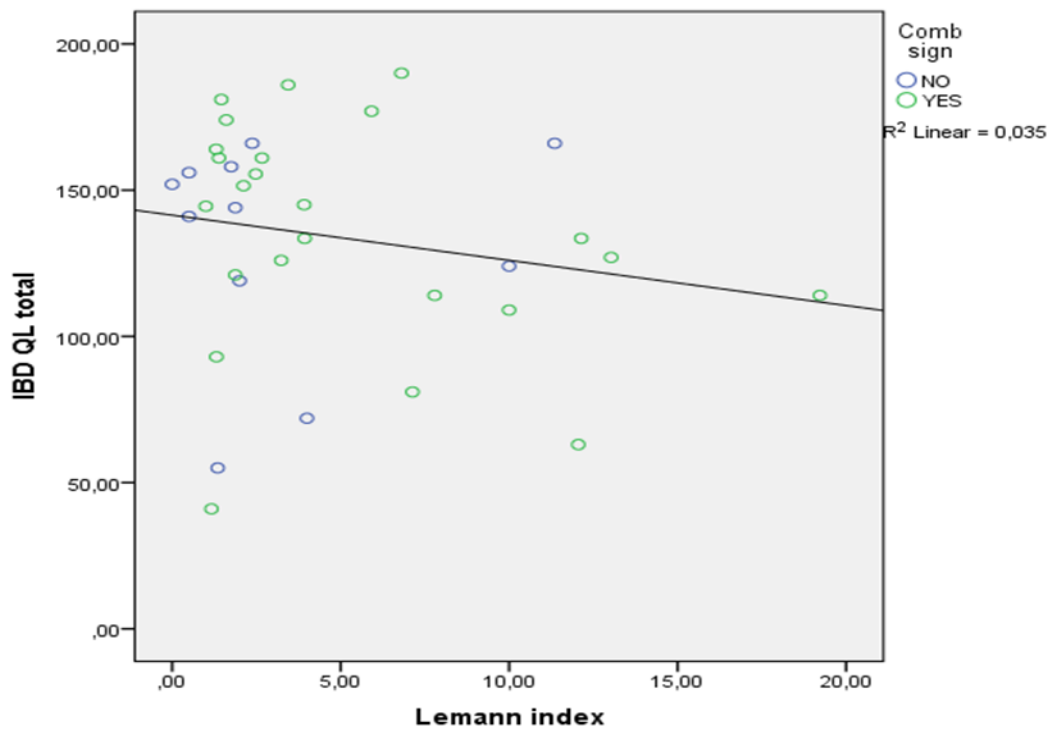


Figure 25 Correlation between Comb sign and IBDQ and Lemann index

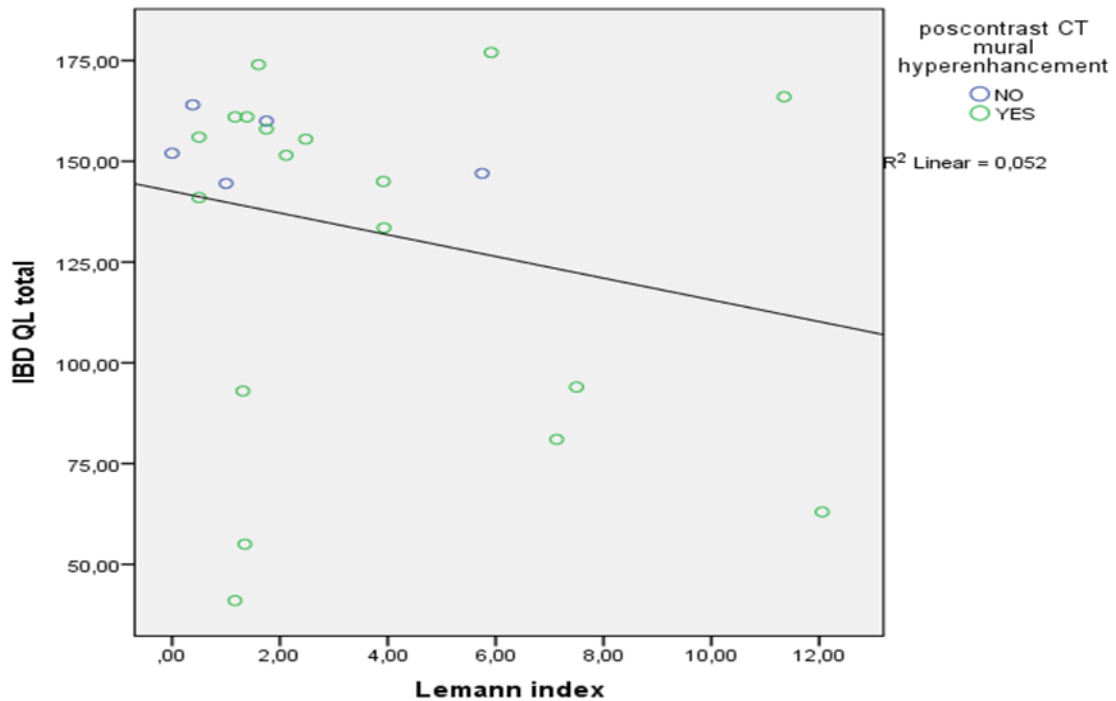


Figure 26 Correlation between bilamillary enhancement and IBDQ and Lemann index

Despite the small study group, we found a correlation between Lemann index and IBDQ. This relationship gives us reason to argue that CTE and MPE can be used to assess patients' quality of life. Unlike the IBDQ self-assessment questionnaire, which is somewhat subjective, the Lemann index is a much more objective method. Lemann index is calculated only by professionals, specialists in imaging diagnostics.

5.4. To determine whether there is a correlation between changes detected on CT and MRI enterocolonography and paraclinical and laboratory tests in patients with Crohn's disease.

The chronic-relapsing course of Crohn's disease requires long-term follow-up of patients, repeated evaluation and reevaluation of the therapeutic approach. In our study, we compared the imaging data established in them with the most commonly used laboratory and paraclinical indicators. Imaging findings in the Crohn's disease patients found on CT and MPI in our sample were thickened wall > 3mm, bilaminar hyperenhancement, trilaminar hyperenhancement, homogeneous late hyperenhancement, thickened mesenteric fat, Comb sign, lymph nodes >1cm. Complications of Crohn's disease that we have seen on imaging studies are abscesses and fistulas. We have compared these findings with the values of CRP, FCP, CDAI. We looked for a correlation between the laboratory and paraclinical indicators with the imaging Scores - Lemann index and MEGS.

C reactive protein

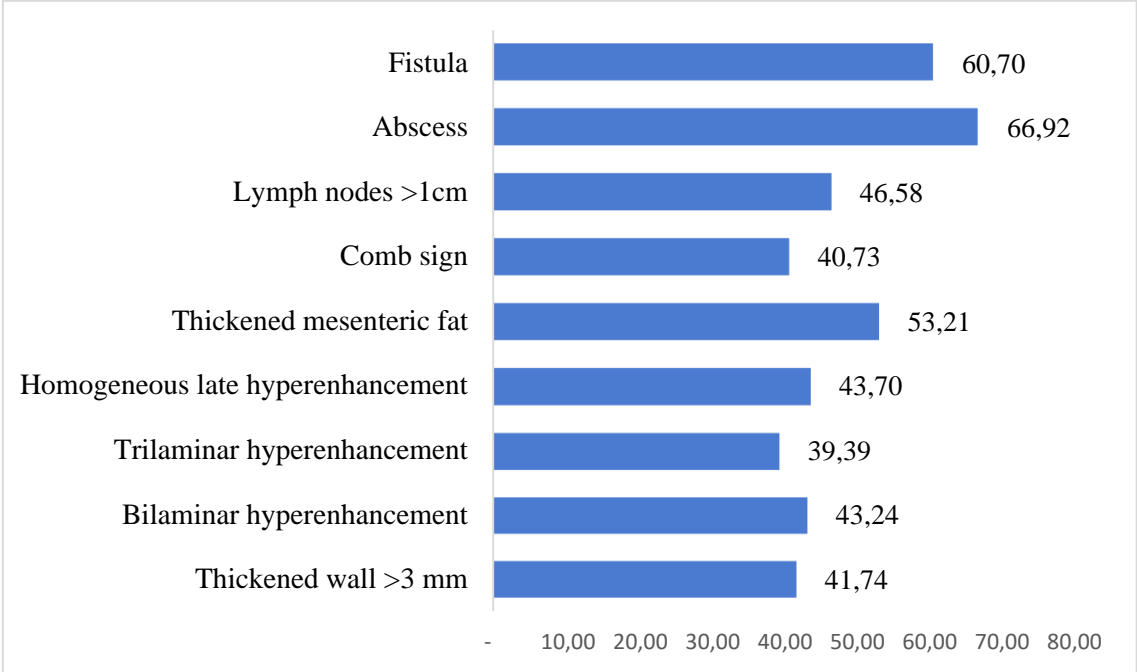


Figure 27 Average CRP levels according to CT and MPI changes

Figure 27 shows mean CRP values and imaging findings. The highest values of the indicator correlate with abscess and fistula, which is explained by the fact that CRP

is an inflammatory marker. The average inflammatory marker values for thickened wall > 3 mm was 41.74. A statistically significant weak correlation was found between serum CRP levels and thickened wall > 3 mm (r=0.198; p=0.001). A thickened wall is established with increased CRP values, as an expression of the active inflammatory process of the intestinal wall.(figure 28)

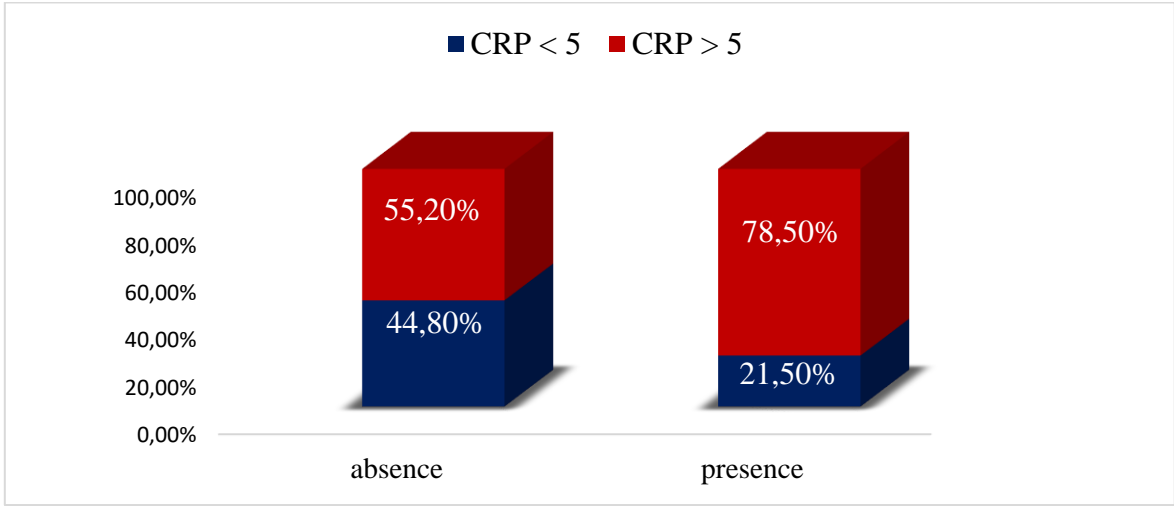


Figure 28 Correlation between the presence of a thickened wall > 3 mm and CRP levels

The mean CRP values in established thickened mesenteric adipose tissue was 52.21. We found a statistically significant moderate correlation between serum CRP levels and thickened mesenteric adipose tissue (r=0.419; p<0.001). This indicates that thickened mesenteric adipose tissue correlates with active inflammation in Crohn's disease. (figure 29)

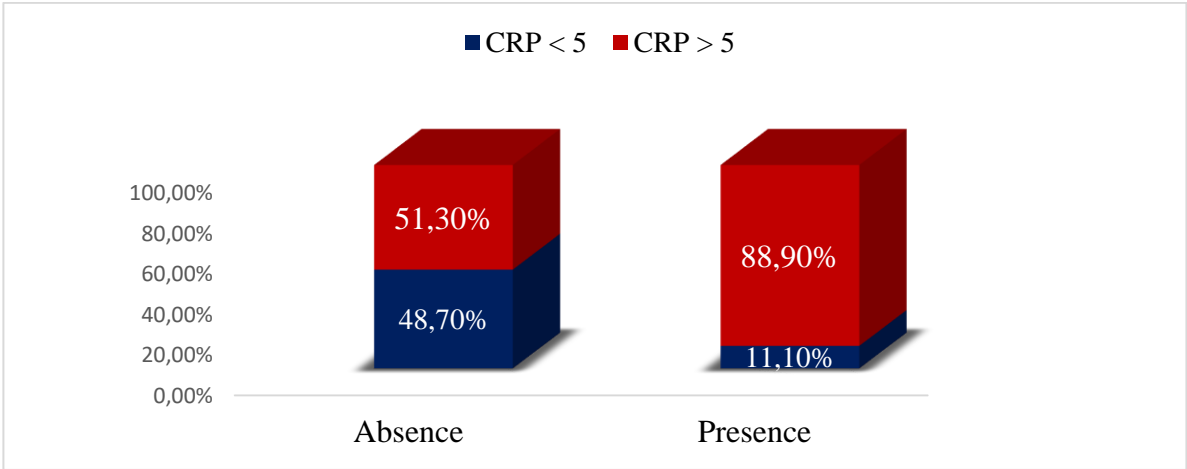


Figure 29 Correlation between the presence of dense mesenteric adipose tissue and CRP levels

The average value of CRP in Comb sign was 40.73. We found that elevated levels of CRP correlated with the presence of the Comb sign, and the relationship was statistically significant. ($r=0.355$; $p<0.001$) (figure 30)

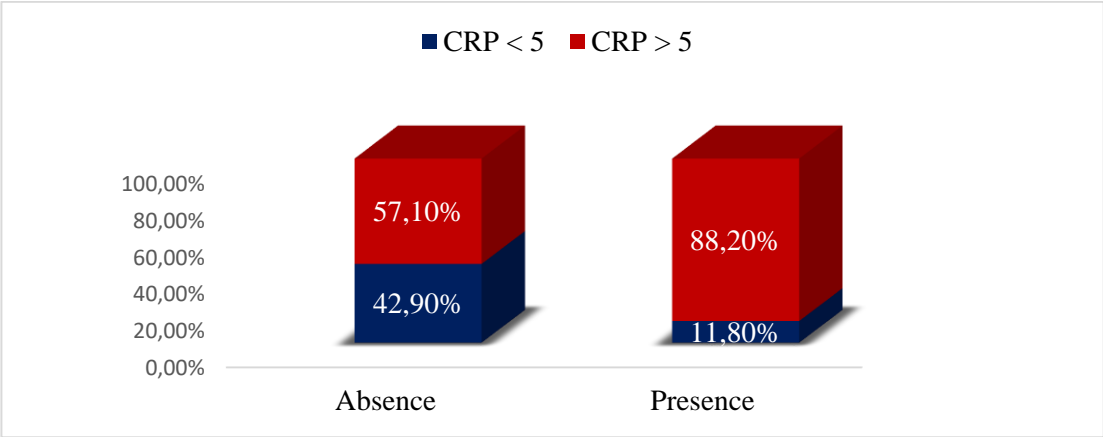


Figure 30 Correlation between the presence of Comb sign and CRP levels

The mean CRP on trilaminar hyperenhancement was 39.39. A statistically significant moderate correlation was found between serum levels of CRP and trilaminar contrast enhancement ($r=0.292$; $p=0.001$) and trilaminar hyperenhancement was observed with increased values of the inflammatory marker. This correlation is shown on figure 31.

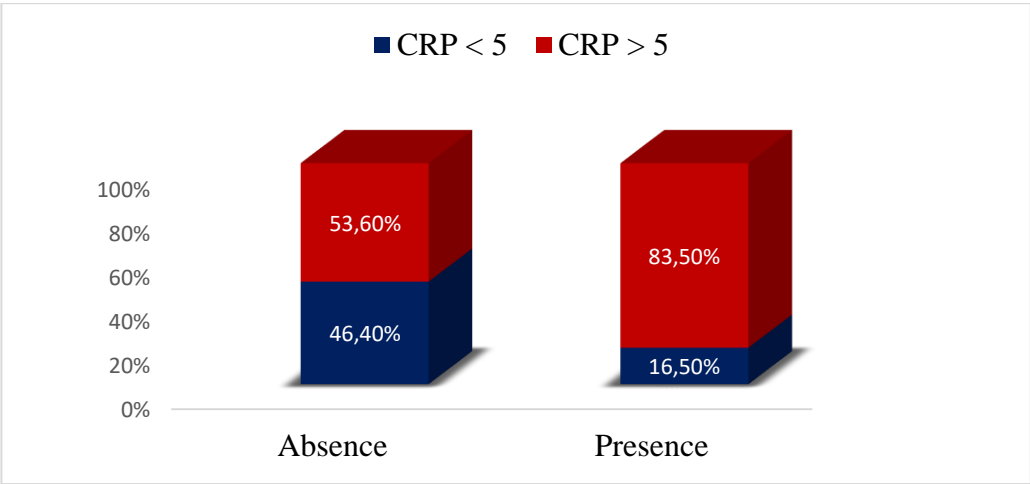


Figure 31 Correlation between the presence of trilaminar homogeneous contrast and CRP levels

The average value of CRP found in observed homogeneous late hyperenhancement imaging studies of patients with Crohn's disease was 43.70. The

correlation that was established between serum levels of CRP and homogeneous late contrast was a statistically significant moderate dependence ($r=0.270$; $p=0.013$). (fig 31)

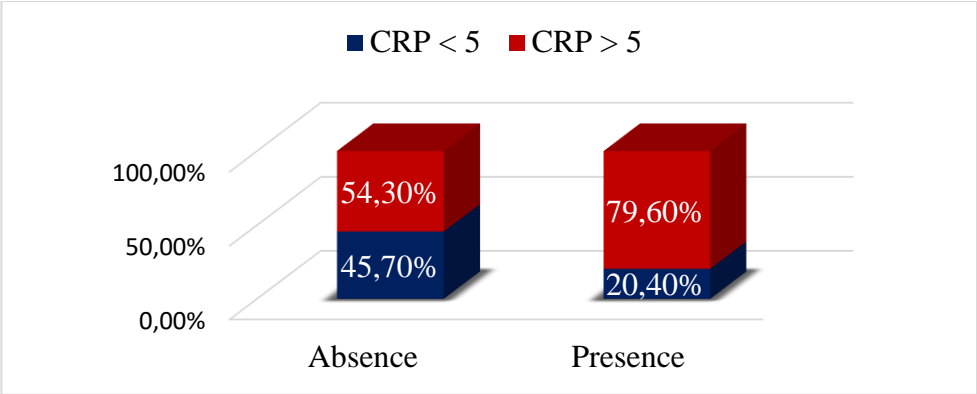


Figure 32 Correlation between the presence of homogeneous late contrast and CRP levels

No correlation was found between CRP and bilaminar contrast enhancement, but we found a statistically significant weak correlation between serum CRP levels and enlarged lymph nodes > 1cm ($r=0.275$; $p=0.001$). (figure 32)

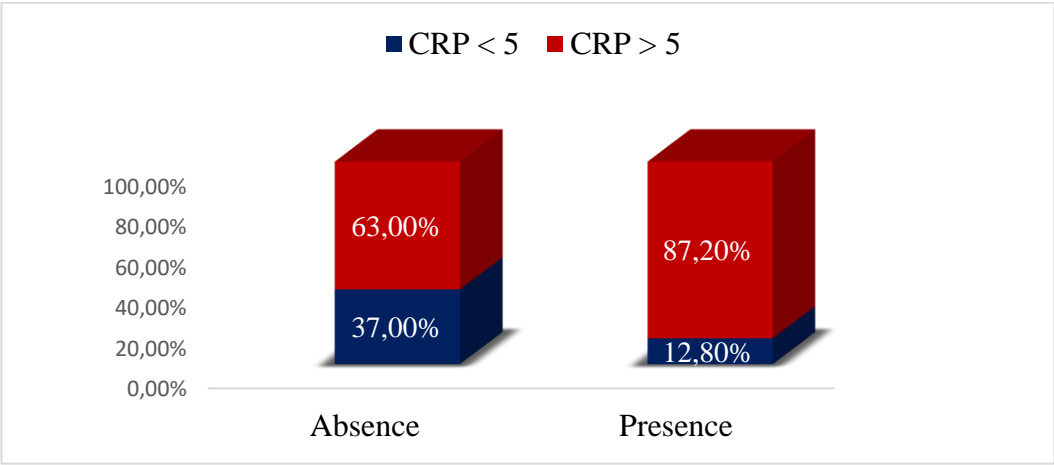


Figure 33 Correlation between the presence of enlarged lymph nodes > 1 cm and CRP levels

We looked for a correlation between CT/MPI complications of Crohn's disease - abscess and fistula - and elevated CRP values. Using Pierson's correlation analysis, we found a statistically significant weak correlation between serum CRP levels and abscess. ($r=0.221$; $p=0.05$)

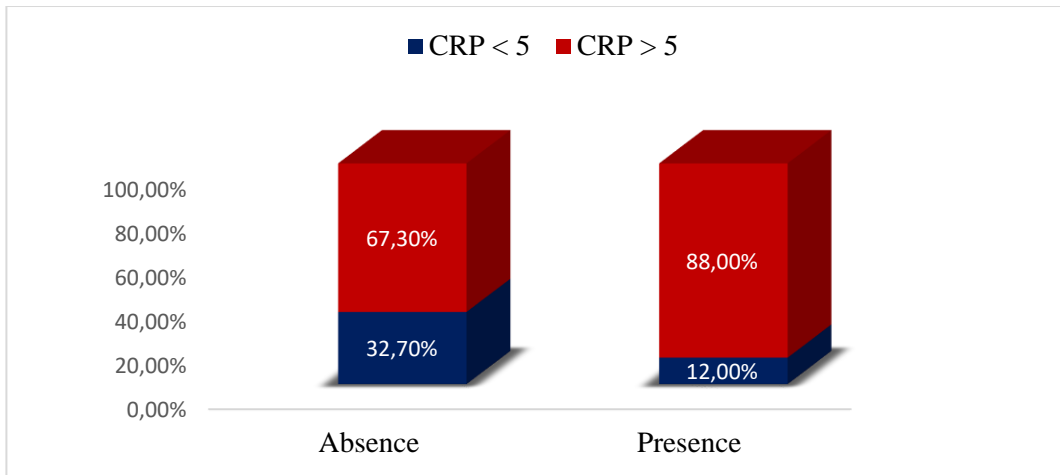


Figure 34 Correlation between presence of abscess and CRP levels

Using the same method, a significant difference ($p=0.004$) and a moderate correlation between serum CRP levels and fistula ($r=0.311$; $p=0.004$) were also found. The result is presents on figure 35.

The results show that the imaging findings observed in the performed CT and MPI of the studied group of patients with Crohn's disease correlate the values of the inflammatory marker CRP, i.e. higher values are observed in the presence of a characteristic imaging finding, and the correlation is statistically significant.

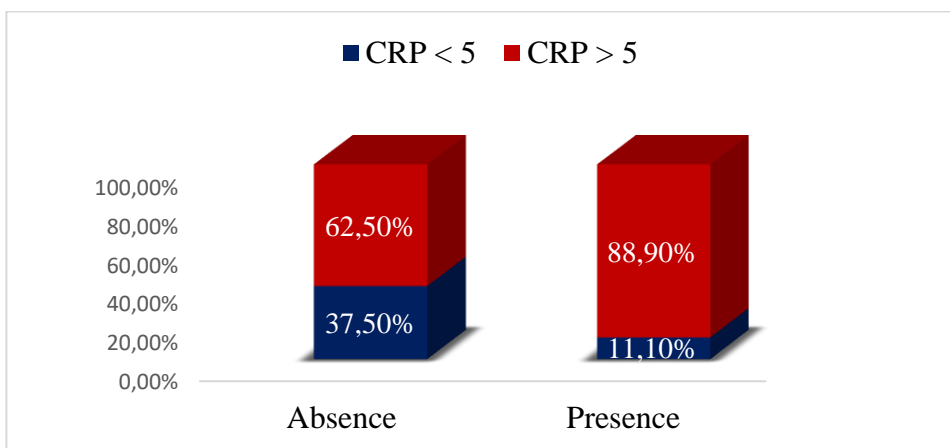


Figure 35 Correlation between fistula presence and CRP levels

When reading CT and MPI, the Lemann index was also calculated. When comparing the index with the values of one of the most commonly used inflammatory markers – CRP, a positive correlation was found between the indicators – the index

increases in parallel with the increasing CRP values. The correlation is statistically significant. ($r=0.102$, $p=0.0001$) (figure 36)

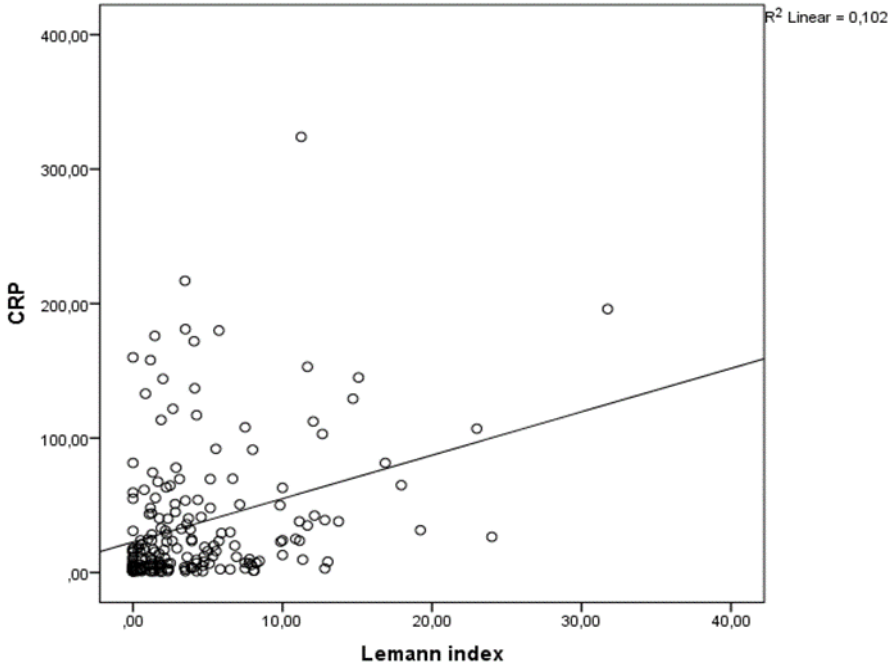


Figure 36 Correlation between CRP and Lemann index values.

MEGS is a score for determining inflammatory activity of the patient based on changes of the intestinal wall and adjacent mesenteric fatty tissue diagnosed on MRE.

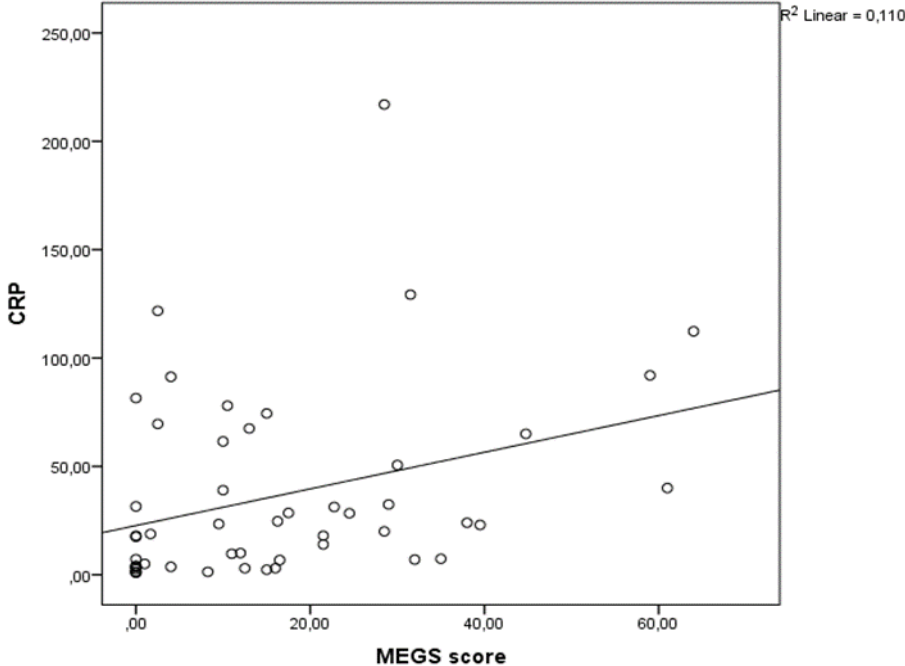


Figure 37 Correlation between CRP and MEGS values

MEGS is a score for determining inflammatory activity of the patient based on changes of the intestinal wall and adjacent mesenteric fatty tissue diagnosed on MRE.

A statistically significant correlation was also found between the inflammatory marker and MEGS, namely, with an increase in CRP, the score increases. ($r=0.110$, $p=0.001$)

Fecal calprotectin

FCP is the index which was examined. Figure 38 presents the mean levels of the indicator against the observed imaging findings. The highest values of the indicator were recorded in the patients with dense mesenteric fat tissue established during the interpretation of CT/MPI. The FCP values in patients with established bilaminar hyperenhancement, lymph nodes and Comb sign are the findings with reported average levels of the indicator, respectively – 796.38; 710.31 and 706.56

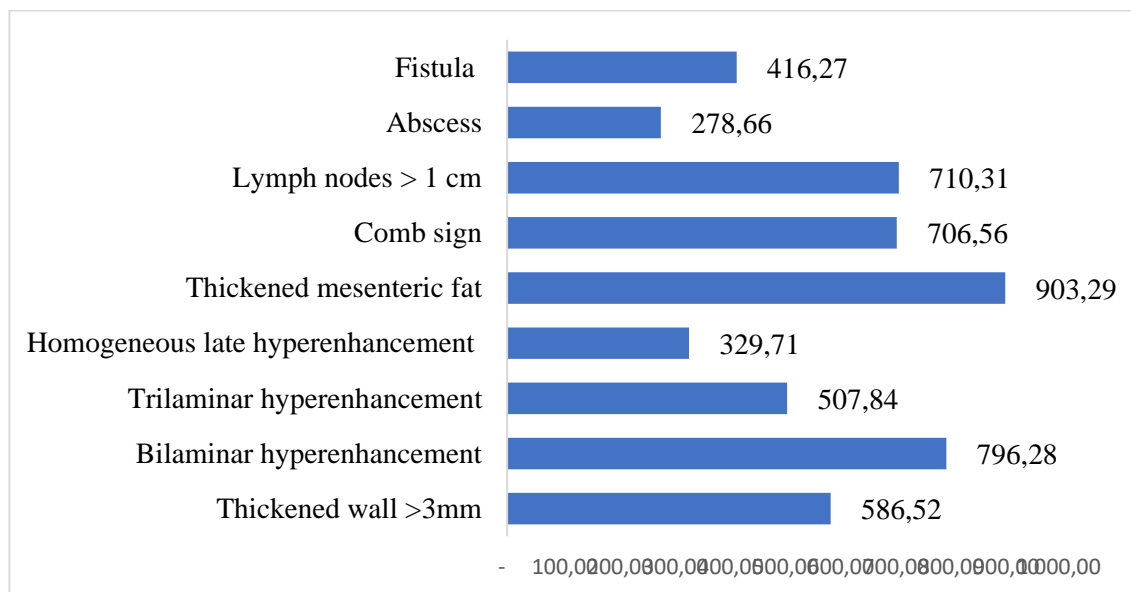


Figure 38 Average levels of PCF in the different imaging findings

The lowest levels of PCF were reported for abscess and homogeneous late hyperenhancement - 329.71 and 278.66. No correlation was found between the serum levels of PCP and the findings established by the imaging methods.

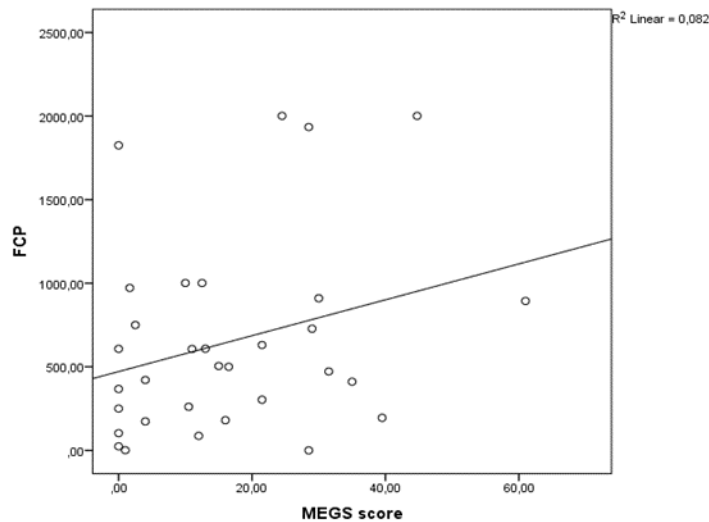


Figure 39 Correlation between FCP and MEGS values

A strong correlation was found between the increasing values of FCP and MEGS, namely the increase in the score is directly proportional to the increasing FCP.

We looked for a correlation between imaging findings and the most widely used score to determine disease activity in patients with Crohn's disease - the CDAI. The average levels of the indicator for the different findings are presented in figure 40. It shows that the highest score values are reported in patients with imaging data for abscess and fistula, namely – 325.82 and 319.31. The value of CDAI in the patients with the other imaging findings were similar and ranged from 264.34 to 295.04.

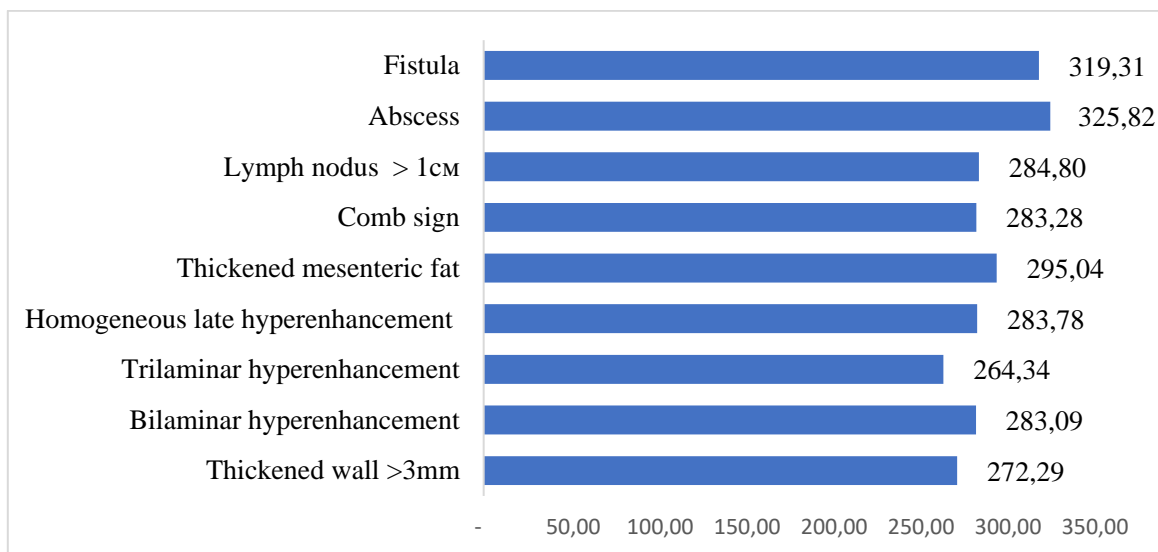


Figure 40 Average CDAI levels according to CTE and MPE changes

When analyzing the collected data, we found a statistically significant moderate correlation between CDAI and Comb sign ($r=0.303$; $p=0.001$). Comb sign was observed in all patients in the active phase of the disease, i.e. with $CDAI > 150$. (figure 41)

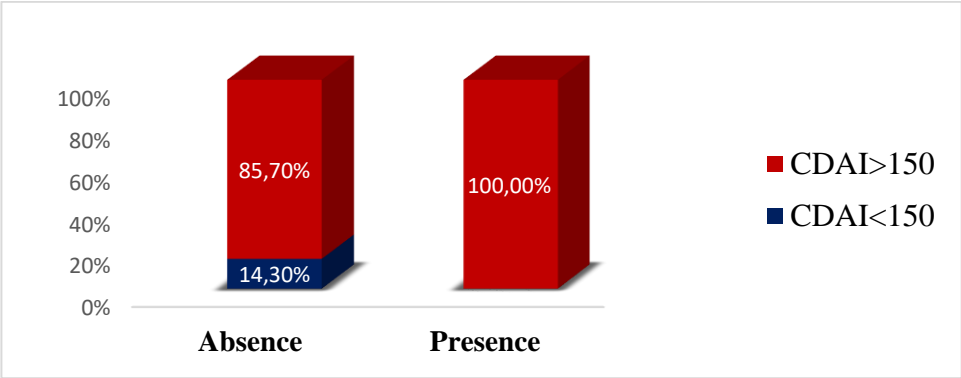


Figure 41 Correlation between Comb sign and CDAI

Our study shows that in all patients with established fistulas on imaging studies, CDAI is increased - a statistically significant weak correlation. ($r=0.295$; $p=0.015$). (figure 42)

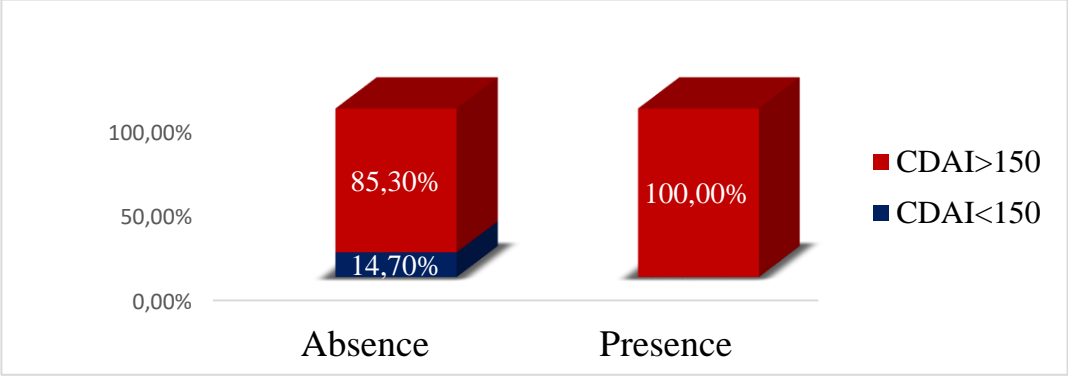


Figure 42 Correlation between the presence of fistulas and CDAI.

In almost all patients with imaging data of lymph nodes > 1cm per CT/MPI CDAI > 150, and the established relationship was weak but statistically significant. ($r=0.248$; $p=0.005$) (Figure 43)

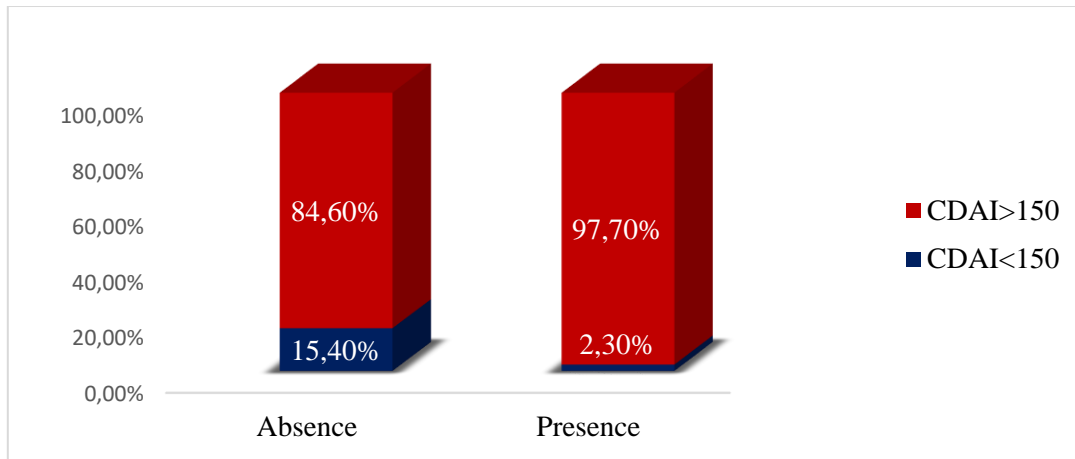


Figure 43 Correlation between the presence of lymph nodes > 1 cm and CDAI

The imaging scores considered in the study – Lemann index and MEGS also correlate reliably with increasing CDAI values. The results of the performed correlations show us that the changes visualized on the imaging studies, CT and MPI, are comparable to the widely used laboratory indicators.

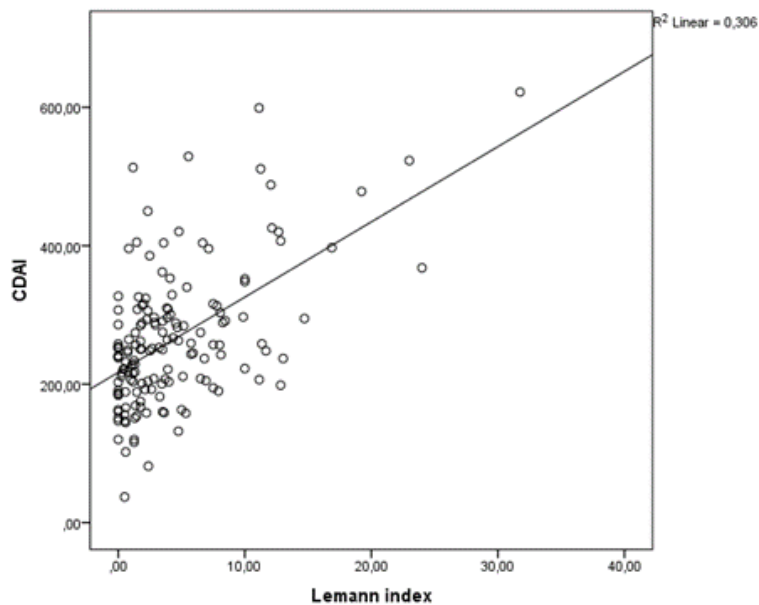


Figure 44 Correlation between CDAI values and Lemann index

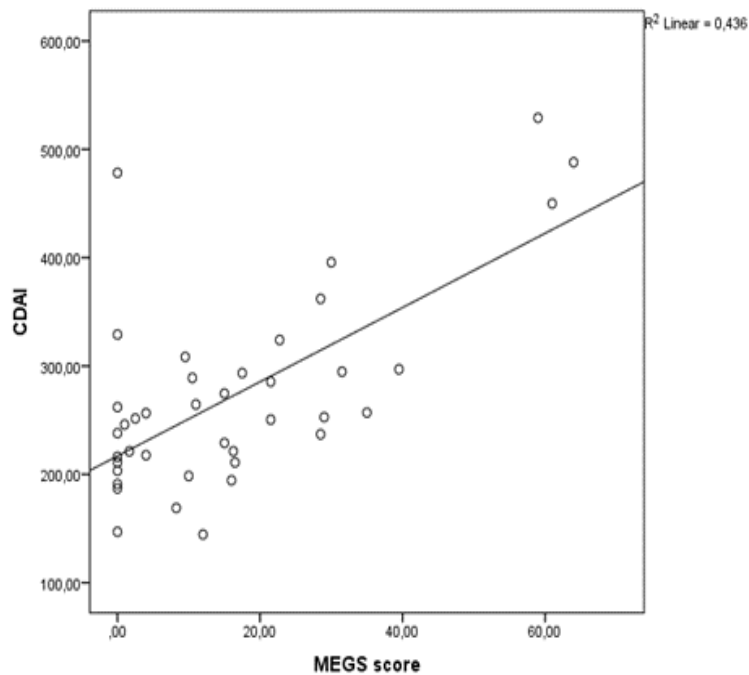


Figure 45 Correlation between CDAI values and Lemann index

We should note that CT and MPI also have their advantages. Unlike CRP, which is a non-specific inflammatory marker, the changes registered with them visualize directly whether or not there is a change in the intestinal wall and adjacent fatty tissue. It is possible to determine not only the presence or absence of an involved segment, but also to determine the number of affected, information that cannot be obtained through laboratory indicators.

5.5. To evaluate the role of CT and MR enterocolonography in the follow-up of patients with Crohn's disease.

Crohn's disease is an inflammatory process of the GI tract, which has a destructive course. The disease lasts throughout the patient's life. In order to avoid complications and slow down its progression, it is necessary to hospitalize patients and reassess the stage of the disease and, if necessary, reassess the therapeutic approach. In our study, we aimed to evaluate the extent of GIT damage due to Crohn's disease using the Lemann index. The index was studied in all patients, and 57 of the patients were followed up at an interval of two years. When comparing the values of the index at the beginning and in the second year, it was found that it increases with the progression of the disease, and the change is statistically significant ($p < 0.001$) (table 7). The table shows that the average value in the first year is 2.65 ± 3.83 and in the second year is 4.3260 ± 5.18 . In their study in 2015, Gilletta reported similar mean scores at month 0 and between 18-24 months of 2.3 and 3.5 respectively. A similar dependence was described by Rozendorn in his research in 2018, with the Lemann index calculated on the first, second and tenth years and the average value is 6.3; 14.3 and 19.0. **Figure 18** compares our data with those of other authors.

Table 7 Correlation between Lemann 1 and Lemann 2 values

		Lemann1	Lemann2
Lemann	Pearson Correlation (r)	1	.614**
	P		.000
	N	57	57

	N	Minimum	Maximum	Mean	Std. Deviation
Lemann1	57	.00	24.00	2.6511	3.82988
Lemann2	57	.00	24.00	4.3260	5.18720

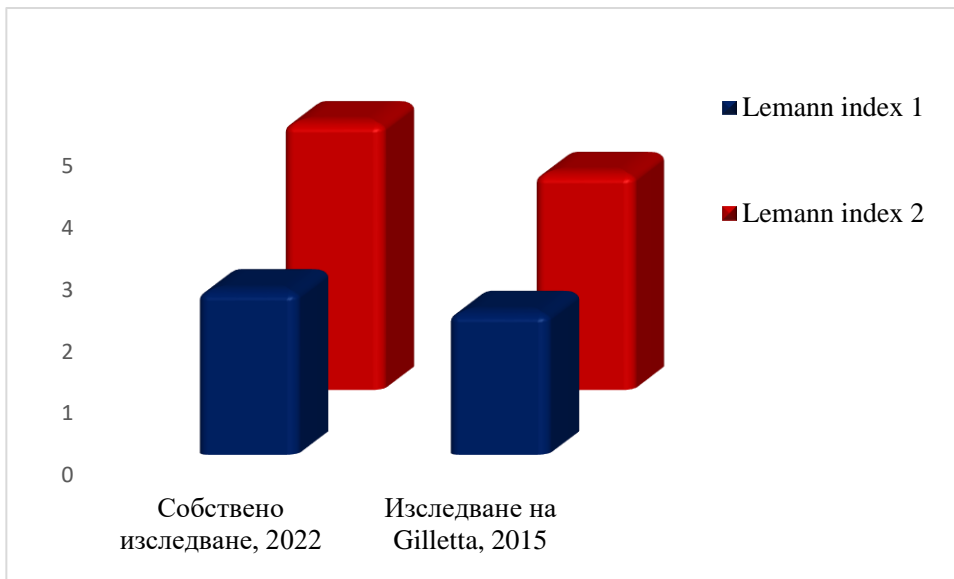


Figure 46 Comparison between the average values of Lemann index 1 and Lemann index 2

The change of the Lemann index is also presented graphically in figure47

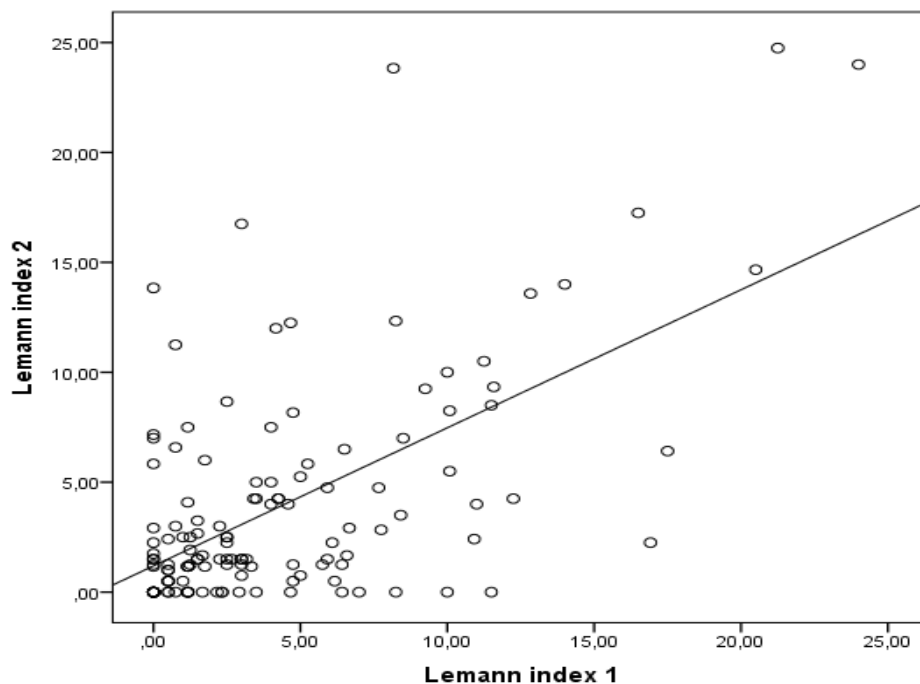


Figure 47 Lemann index 1 и 2

We looked separately at the patients in whom the Lemann index was examined at an interval of 2 years, comparing them with the patients included in the Gilletta study in 2015. We divided the patients into 2 groups. The first group consists of patients in whom the Lemann index increases, and the second group - patients in whom the Lemann

index decreases or does not change. The characteristics of these 57 patients are presented in table 8, comparing our data with Gilletta's data.

Table 8 Characteristics of the patients with an increasing Lemann index and the patients with an unchanged/decreasing Lemann index, compared with the data of other authors.

Index	Our study, 2022		P value	Study of Gilletta, 2015		P value
	Increasing Lemann index (26)	Decreasing Lemann index (31)		Increasing Lemann index (126)	Decreasing Lemann index (95)	
Mean age	36,93±16,37	36,9±16,17	0,36	25	23	0,36
Man	15	16		66	43	0,31
Woman	11	15		60	52	0,19
Localisation of the disease						
L1	14	12	0,05	82(65)	33(35)	<0,001
L2	19	13		15(12)	22(23)	
L3	14	7		29(23)	38(40)	
L4	0	0		21(17)	15(16)	
Perianal involvement	12	3		28(22)	20(21)	
Extraintestinal involvement	6 (23)	8 (26)		31(25)	24 (25)	
Increased CRP	19	17	0,17	82(75)	57(63)	
CDAI> 150	17	14	0,26			
Surgical treatment	11	3	<0,01	86(68)	1(1)	<0,01

The mean age of the two groups was 36 years, significantly higher than that of the Gilletta group, 25 years for the group with increasing Lemann index and 23 years for the other group. Regarding the localization of the disease, our results confirm the results of other authors, precisely in the group with increasing Lemann index at second year, the disease affects the ileum and ileocolon. In our study, a moderate statistical dependence was found, while Gilletta's study described the same dependence, but in his study the values were statistically significant.

This is probably related to the larger number of studied patients included in his pool. In the group of patients with an increasing Lemann index, patients with perianal disease predominated, as our research and Gilletta's show, and the difference in our study is significant.[49] No significant difference was found in CRP and faecal calprotectin values. We examined the dynamics of the Lemann index in patients with CDAI>150. We found that the index had a reliable prognostic value of 67.5% in these patients. The result was calculated by rock-curve analysis, which is shown in figure 48.

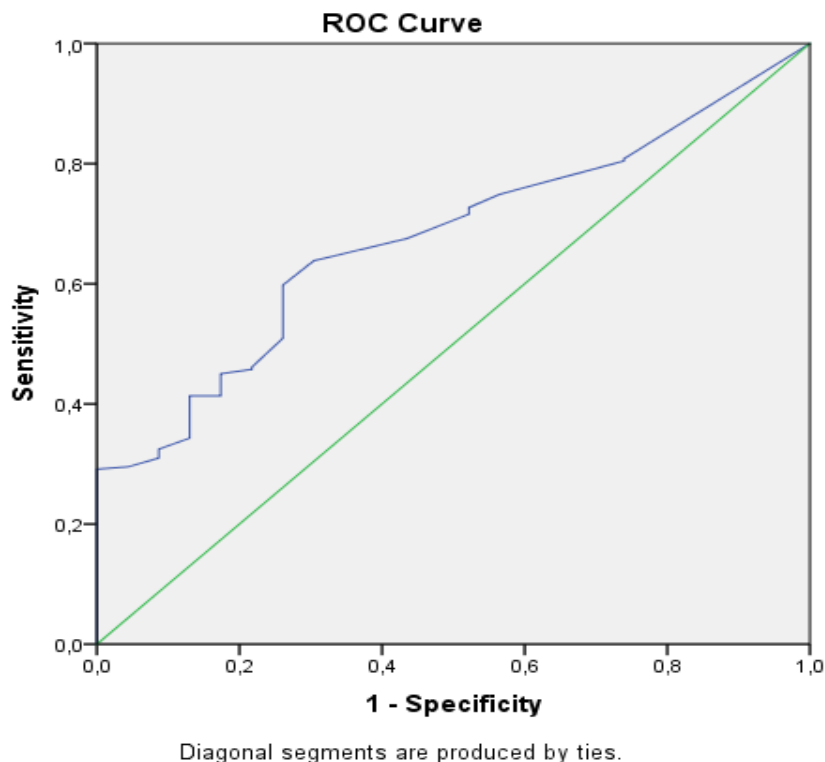


Figure 48 Calculation of Cut off point for Lemann Index by ROC curve analysis (AUC=0.675, p=0.005, 95% CI: 0.584;0.767)

The cut off point for the Lemann Index in our sample is in the range between 1.37-1.20 with index sensitivity between 63.8%-67.5% and specificity between 67%-70%.

The frequency of extraintestinal manifestations in both groups of patients in our study was similar. In both our group and Gilletta's group, extraintestinal manifestations occurred in ¼ of patients with Crohn's disease. Dependence was found regarding the surgical treatment performed – patients with increasing values more often reached surgical treatment than those in which the value of the Lemann index decreased or did not change. In our pool, the dependence is moderate, while in the other author's it is statistically significant. We found a moderate directly proportional relationship between the Lemann index and the subsequent operation ($r=0.404$; $p<0.001$). **The difference in Lemann index in patients with and without subsequent surgical treatment is shown in the box-plot graphic 49. The difference between the index values is statistically significant ($p<0.001$).**

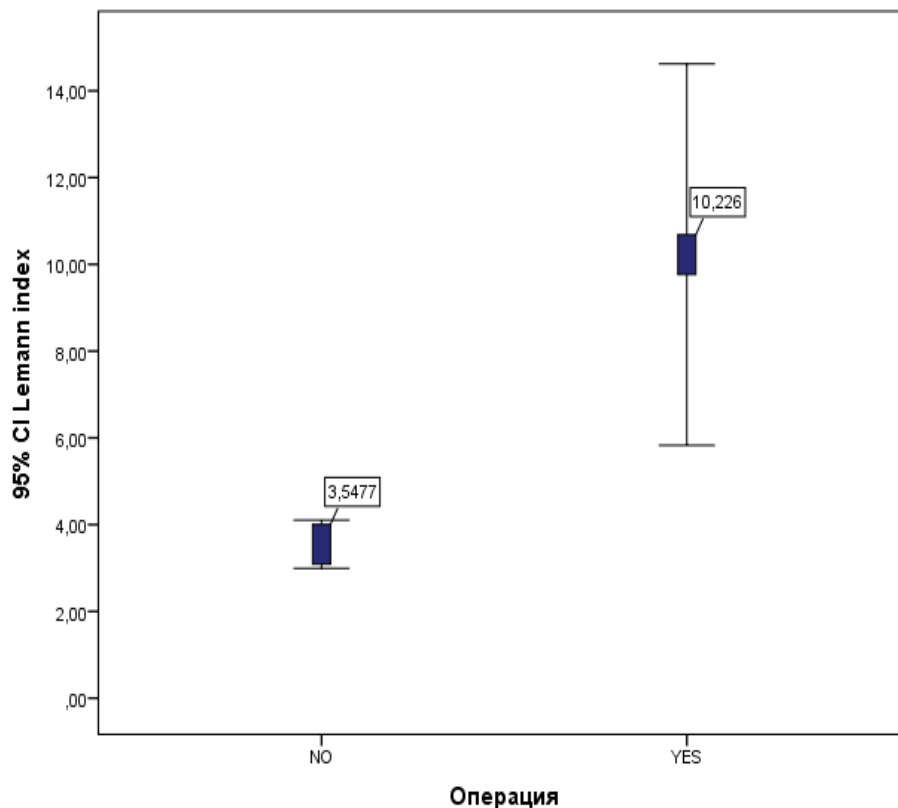


Figure 49 Box plot graphics of Lemann index in patients with subsequent surgery and those without surgery

The results of our study confirm the opinion of other authors that the increase of the Lemann index predicts the progression of the disease, as well as the risk of recent surgical treatment. It can be used to follow up patients in order to define at-risk patients who should be followed for a shorter period of time or to switch to a more aggressive therapeutic approach to avoid a complication or delay progression of the disease.

5.6. Development of an exemplary protocol for the preparation, examination and follow-up of patients with Crohn's disease by CT and MR enterocolonography.

Based on literature data and the obtained results of our research, we created an algorithm for examination by CT or MPI of patients with Crohn's disease, according to their age, neuropsychiatric condition, accompanying diseases, previous operative interventions and possibility of administration of intravenous contrast material.

To achieve optimal results from the examination, patients must be properly prepared for it. Only with optimal extension of the intestinal tract and its filling with appropriate contents can changes in the wall be interpreted. It is appropriate that the last meal should be of liquid or mushy food. 4-6 hours before the examination itself, the patient should not take food, there is no restriction on fluid intake. Optimal intestinal extension is achieved by taking a 3% to 5% solution of mannitol with water. The amount to be taken depends on the patient's weight. With a body weight below 50 kg. the dosage is 20 ml. per kilogram of body mass, and with a weight over 50 kg - 1500 ml. Drinking the solution should be done in 10-12 equal doses every 5 minutes for an interval of 45-60 minutes, immediately before the beginning of the study.

The next important step is to determine the most appropriate modality - CT and MRI. Each of the modalities has its advantages. MPI is recommended as the first choice of investigation in young patients, in pregnant women who have multiple complications of the disease and are expected to perform controls at small time intervals. In case of suspected or proven penetrating form of Crohn's disease with involvement of the anus and perianal space, it is also recommended to perform MPE, because in them a more

dilated duct can be performed, namely to combine MPI and magnetic resonance examination of the small pelvis. So with a single visit of the patient to the magnetic resonance, the imaging clinic will be able to assess the overall condition of the patient.

When there are contraindications to the administration of intravenous contrast material, it is also recommended to perform MPI. T2 and DWI images, even without contrast material, are sufficient to distinguish pathological changes along the intestinal wall and peritoneal space. (While) performing a native CT will not adequately determine changes in the intestinal wall.

CT also has numerous advantages over MPI. For example, in patients with a penetrating form of the disease, in which the fistula moves involve muscles or the abdominal wall. As a result, lying on the back or stomach is impossible or greatly reduced in time. Computed tomographic examination is significantly faster, new devices allow each separate phase to be performed in less than 5 seconds. The short examination time reduces the possibility of motion artifacts that would make interpretation impossible.

In elderly patients, due to a natural decline in lung volumes, CT is recommended as the first diagnostic method. CT testing is also recommended for claustrophobic sufferers. The presence of implants that can be affected by the magnetic field is also a contraindication for performing MPI.

The technical parameters for performing CTE and MPE are described in detail in Appendix 4

Based on the results of our study, as well as literature data, we recommend that in patients with a high Lemann index, due to the risk of developing complications in the next two years, the follow-up should be performed at shorter intervals - the study should be before the second year.

6. CONCLUSION

Crohn's disease is an inflammatory disease of the gastrointestinal tract, with a chronic-relapsing nature. It can involve all segments - from the mouth to the anus inclusive. The inflammation has a destructive course, all layers of the intestinal wall may be involved. The initial appearance in most cases is at a young age of 10-40 years. The etiology, pathogenesis and risk factors are still not fully understood.

A characteristic feature of the disease is that it can involve either one segment of the GIT or several, with a normal healthy section between them. Another important feature of Crohn's disease is the involvement of the intestinal wall, that is, only the innermost layer or the entire thickness of the wall may be affected, even extending beyond it. Fistulas and/or abscesses may form.

In the therapy of the disease, conservative and surgical methods are used. Surgery is required both in the case of a complication of the penetrating form, such as perforation, abscess, fistula, and in the case of a stricturing form with the formation of a permanent, insurmountable stricture.

A diverse set of methods is used in the diagnosis and follow-up of the disease: clinical, laboratory, endoscopic, histological, imaging. Crohn's Disease Activity Index (CDAI) is a clinico-laboratory index for determining activity and exacerbation of Crohn's disease. Given that the disease affects both the physical and mental state of patients, a special questionnaire was created to assess their quality of life - Inflammatory Bowel Disease Questionnaire (IBDQ).

In our study, we determined the most frequently affected intestinal segments. The type of changes of the involved segments are distinguished using CT and MRI scans. We calculated the Lemann index of all patients, and for those with MRI, we also determined the MEGS. We looked for a relationship between the detected changes of CT and MRI, Lemann index, MEGS and the most commonly used studies to determine disease activity (CRP, PCP, CDAI). We also looked for a relationship between the Lemann index and patients' quality of life as determined by the IBDQ. We determined

whether there was and what was the change in the Lemann index in patients in the second year after determining the initial value.

Crohn's disease can affect the entire gastrointestinal tract, from the mouth to the anus. In the studied group, the colon and ileocolon were most often involved, while the mouth, esophagus, stomach and duodenum were not affected. The segmental distribution of the areas affected by the disease confirms the data of other authors.

The CT and MRI changes can differ, such as: thickened wall over 3 mm, bilaminar hyperenhancement, trilaminar hyperenhancement, thickened mesenteric fatty tissue, enhanced mesenteric blood flow (Comb sign), enlarged mesenteric lymph nodes and others. Due to the chronic-relapsing nature of the disease and the tendency to involve more than one segment, the described findings may occur differently distributed, in different segments in the same patient or in different stages of the disease. The most common findings when interpreting patients' imaging studies are wall thickening > 3 mm, enlarged lymph nodes > 1 cm, and Comb sign-a. Furthermore, a different combination of changes can be found in some patients. The most common combination of findings is wall thickening > 3 mm, trilaminar hyperenhancement, thickened mesenteric adipose tissue, Comb sign, enlarged lymph nodes > 1 cm. In patients with histological evidence of disease activity, the most frequent imaging findings are enlarged lymph nodes and a thickened wall > 3 mm – 75% and 74.10%, respectively.

We found statistical significance between quality of life and detected imaging changes calculated by Lemann index - there is an inverse correlation to IBDQ. When the Lemann index increases, the quality of life of patients with Crohn's disease worsens. This means that CT and MRI methods can be used not only for diagnosis and therapy monitoring, but also for determining the general health status of the patient.

CRP, FCP, and CDAI are some of the main clinical laboratory parameters that are used to diagnose and determine exacerbations of Crohn's disease. But they are not specific to the disease itself. The findings that are visualized on CT and MRI are an expression of changes related to the intestinal wall and the surrounding fatty tissue. I.e. to a lesser extent, they are affected by diseases of the other systems. We found a

statistically significant correlation between CRP and imaging findings of thickened wall > 3 mm, thickened mesenteric fatty tissue, Comb sign, trilaminar hyperenhancement.

In the analysis of the data from our study, no association was found between increasing PCP values and imaging findings.

Imaging findings observed in patients with CDAI>150 are Comb sign and enlarged lymph nodes>1cm.

The values of the Lemann index and MEGS correlate with the clinical and laboratory parameters. Image Scores increase in direct proportion with the increase in the value of CRP, FCP and CDAI, and the dependence is statistically significant.

In the majority of cases, patients with Crohn's disease endure a disease progression. We tried to find a correlation between the duration of the disease and imaging changes. A significant difference was demonstrated, an increase in the Lemann index at follow-up over a two-year period. We also found a correlation between the Lemann index calculated for patients whose disease progressed and necessitated surgery and those who did not. These data show that the Lemann index can be used to define risk groups of patients, those in whom progression is expected. In these groups, a change in therapeutic agents may be considered to avoid or delay this progression.

In conclusion, we can say that CT and MRI can be used both for the diagnosis and follow-up of patients with Crohn's disease, as well as for determining the risk of disease progression.

7. FINDINGS

1. The most common changes seen on CT and MRI in patients with Crohn's disease are a thickened red wall greater than 3 mm and trilaminar hyperenhancement. (p<0.001)

2. In patients with histological evidence of activity, the most common changes are enlarged mesenteric lymph nodes greater than 10 mm, thickened red wall greater than 3 mm, and trilaminar hyperenhancement.

3. High Lehman index values are inversely correlated with quality of life in patients with Crohn's disease.

4. Elevated CRP values have a directly proportional relationship with thickened wall over 3mm, thickened mesenteric fat tissue, Comb sign, trilaminar hyperenhancement, homogeneous late hyperenhancement of the intestinal wall and enlarged mesenteric lymph nodes over 10mm.

5. There is a direct correlation between CRP, Lemann index and MEGS.

6. When increasing the values of FCP, the value of MEGS also increases.

7. Comb sign, enlarged mesenteric lymph nodes and high MEGS values correlate with increasing CDAI value.

8. When following up the patients at an interval of two years, the Lemann index increases.

9. High Lemann index values can be used as a protector for subsequent surgery.

8. CONTRIBUTIONS

Scientific contributions of an original nature

- For the first time in Bulgaria, the results of CT and MRI of such a large group of patients with Crohn's disease are examined and summarized
- Lemann index was calculated for all patients, and MEGS was also calculated for patients with MRI
- An analysis of the most frequent changes as well as the most frequently affected segments of CT and MRI in patients with Crohn's disease was performed
- Looked for a correlation between Lemann index and IBDQ

Scientific contributions of a confirmatory nature

- A statistical relationship was found between serum CRP levels and thickened wall over 3mm, thickened mesenteric fatty tissue, Comb sign, trilaminar hyperenhancement, homogeneous late hyperenhancement and enlarged mesenteric lymph nodes.
- A positive correlation was found between CRP and imaging scores, Lemann index and MEGS
- A positive correlation was observed between PCP levels and MEGS value
- A statistically significant relationship between CDAI and Comb sign, enlarged mesenteric lymph nodes and MEGS was demonstrated
- A significant difference was found in the Lemann index values of patients with subsequent surgical intervention and those without

Scientific contributions of practical value

- An inverse relationship between Lemann index and IBDQ was proven
- A statistically significant difference was found in the values of the Lemann index calculated at an interval of two years
- An example protocol was developed for the preparation and examination of patients with Crohn's disease with CT and MRI

9. Publications and participation in scientific forums related to the topic of the dissertation work

1. Chakarov St. Abscesses in patients with Crohn's disease - the radiologist's perspective. Varna Medical Forum, Item 11, 2022, Issue 1;
2. Chakarov St., Georgiev R., Valchev G., Atanasova An., Yordanova M., Mavrodinova St., Kostova E. Crohn's disease - latest diagnostic techniques. Varna Medical Forum, Item 11, 2022, Appendix 2;
3. Chakarov St., Georgiev R., Valchev G, Balve B, Banova S., Crohn's disease - changes in the intestinal wall at CT enterography and MR enterography. Rentgenology and Radiology;

Scientific announcements related to the dissertation work

1. VI National Pediatric Conference 2022 - lecturer on the topic Severe inflammatory bowel diseases in childhood, a field for interdisciplinary medical activity
2. Tenth scientific session for teachers and students 2022 - lecturer on Crohn's disease - latest diagnostic techniques

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