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ORIGINAL ARTICLE

Cardiac MRI findings in patients with Crohn's disease

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Abstract

Background Early cardiac death is more common in patients with Crohn's disease (CD) than in healthy adults, but the exact cause is unknown.

Aims The aim of this study is to investigate the cardiac magnetic resonance imaging (MRI) findings in patients with CD and compare the MRI findings with healthy controls (HCs). This study also aimed to demonstrate the possible cardiac involvement in patients with CD using MRI.

Methods In this prospective study, participants with CD ($n=20$) and HC ($n=20$) underwent cardiac MRI. Erythrocyte sedimentation rate (ESR) and hematocrit levels were investigated before MRI in both groups. Two observers evaluated the ventricular functional and morphological parameters in consensus. Myocardial T1/T2-relaxation times were calculated by two observers independently using two different software, and hematocrit-corrected left ventricle extracellular volume (LV-ECV) was calculated. Observer-2 also performed histogram analysis for T1/T2-mapping images.

Results Patients with CD had a significantly higher LV-ECV, mildly decreased right ventricle ejection fraction, and prolonged T2-relaxation time than HC. Moreover, histogram analysis showed that the maximum and mean T2-relaxation times were higher in patients with CD. There was an excellent agreement between observers for the assessment of mean native and post-contrast T1-relaxation time (intraclass correlation coefficient (ICC) of 0.991 and ICC of 0.941, respectively) and mean T2-relaxation time measurements (ICC of 0.983). Moreover, mean T2-relaxation time was found to be significantly correlated with ESR.

Conclusions This study suggests visually undetectable myocardial involvement due to chronic systemic inflammation in patients with Crohn's disease. Cardiac MRI can help assess and monitor cardiac involvement in patients with CD.

Keywords Cardiac edema · Crohn's disease · Magnetic resonance imaging · Myocardial diseases · Parametric mapping

Ibrahim Hasbey and Furkan Ufuk contributed equally and share the first authorship.

Key points
- Patients with Crohn's disease (CD) had a higher myocardial ECV, mildly decreased RV-EF, and prolonged mean T2-relaxation time than healthy participants. There was an excellent agreement between observers for mean native T1, contrast enhanced T1-relaxation time, and mean T2-relaxation time measurements.
- Histogram analysis of T1/T2-mapping images demonstrated the maximum and mean T2-relaxation times were found to be higher in patients with CD, and mean T2-time was significantly correlated with ESR values in the measurements made by both observers with different software.
- The present study results suggest visually undetectable myocardial involvement due to systemic inflammation in patients with CD.

Extended author information available on the last page of the article

Abbreviations

MRI	Magnetic resonance imaging
LV	Left ventricle
RV	Right ventricle
LVEF	Left ventricular ejection fraction
WBC	White blood cell
CRP	C-reactive protein
ESR	Erythrocyte sedimentation rate
BTFE	Balanced turbo field echo
sBTFE	Sine balanced turbo field echo
BBSSh	Black blood single shot
T2 STIR	T2-short tau inversion recovery
PSIR	Phase-sensitive inversion recovery
TF	Turbo factor
FA	Flip angle
FOV	Field of view
Slice Thic.	Slice thickness.
ECV	Extracellular volume

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Min	Minimum
Max	Maximum
Skew	Skewness
Kurt	Kurtosis
AUC	Area under the curve
CI	Confidence interval
CD	Crohn's disease

Introduction

Crohn's disease (CD) is an inflammatory disorder that mainly affects the gastrointestinal system (GIS), and all segments of the GIS can be involved [1]. Moreover, CD can cause extra-intestinal involvement in approximately 25–40% of the patients [2]. The most commonly affected organs and systems are the musculoskeletal system, liver, pancreas, bile ducts, eye, and heart. Extra-intestinal involvement in patients with CD significantly increases morbidity and mortality [2, 3]. It has been shown that the risk of early cardiac death is increased in patients with CD. Although the exact cause is unknown, this situation may be due to chronic systemic inflammation, accelerated atherosclerosis, hypercoagulability, peri-myocarditis, myocardial fibrosis, or drug-related cardiotoxicity [4–7]. Moreover, myocardial amyloid accumulation, impaired myocardial functions, and myocardial atrophy due to malnutrition and malabsorption rarely reported in patients with CD. The cardiac involvement is a relatively rare but important complication in CD, and early detection is of great importance [8–12].

Cardiac magnetic resonance imaging (MRI) is the gold standard method for evaluating cardiac morphology, myocardial volumes, and functions. Moreover, myocardial edema and fibrosis can be quantitatively evaluated with recently developed MRI (T1/T2-mapping) techniques [13]. Cardiac MRI with a T1 mapping technique can objectively reveal extracellular volume (ECV) and diffuse myocardial disorders in the early and asymptomatic period [14, 15].

This study aims to investigate the cardiac MRI findings in patients with CD and demonstrate the possible cardiac involvement in patients with CD using MRI.

Material and methods

The Clinical Research Ethics Committee of Pamukkale University has approved this HIPAA-compliant prospective study (decision number 60116787–020/41759), and written informed consent was obtained from all cases. The present study was achieved following the Declaration of Helsinki. Participants with CD and healthy control (HC) were consecutively included during the recruitment period between June 2018 and June 2019.

Study population

Patients with a diagnosis of CD, no active cardiac or respiratory complaints, and who agreed to participate were included as the patient group. Patients < 18 years, patients with contraindications for MRI (such as claustrophobia, pregnancy, and presence of metallic foreign body or pacemaker), and patients with a prior history of cardiac problems such as heart failure, congenital heart disease, myocardial infarction, arrhythmia, valvular heart disease, or myocarditis were excluded from the study.

Participants with a similar demographic characteristic to the patient group without chronic disease or cardiac/respiratory complaints were included in the study to form the healthy control group. Those with a prior history of cardiac pathologies such as myocardial infarction, congenital heart disease, or myocarditis were excluded from the study.

Laboratory and clinical examinations

Serum creatinine, white blood cell (WBC) count, hematocrit, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) values were examined in all cases just before MRI examination. In addition, the patients with CD were examined in terms of disease activity using the "Crohn's Disease Activity Index (CDAI)" [16]. According to these criteria, those with CD were divided into four classes: asymptomatic remission, mildly moderately active CD, moderately severely active CD, and severely fulminant CD [16]. The presence of comorbidities and the medical therapy used in patients with CD were also noted.

Cardiac MRI examination

MRI examinations were performed with a 1.5-T MRI system (Philips Ingenia; Best, The Netherlands) using electrocardiogram (ECG) gating and a 32-channel anterior torso coil, a 44-channel posterior coil located in the table while the patient was in the supine position. Imaging was performed while holding a breath at the end of expiration. MRI examinations were obtained with appropriate parameters in accordance with the recently published guideline [17]. Imaging protocol included electrocardiogram (ECG)-gated steady-state free-precession (SSFP), two-chamber, short-axis, and four-chamber cine images, and a short-axis SSFP cine stack covering both ventricles. T2-weighted short-tau inversion-recovery (STIR) sequences were performed to assess the myocardial edema (apical, midventricular, and basal short-axis). Late gadolinium enhancement (LGE) images were obtained based on phase-sensitive inversion-recovery (PSIR) gradient-echo sequence in four-chamber, two-chamber, and short-axis views.

Native T1-, post-contrast T1-, and T2-mapping images were obtained in the mid-diastolic phase in the mid-ventricular short-axis view, as previously described [18–20]. In the case of respiratory artifacts in the acquisition of T1/T2-mapping images, the image acquisition was repeated. T1-mapping images were obtained with a modified Look-Locker inversion recovery (MOLLI) technique with 5-(3)-3 sampling scheme, and T2-mapping images were obtained with a T2-prepared balanced-SSFP sequence. For contrast-enhancement, a single bolus of 0.2 mmol/kg of gadoteric acid (Dotarem; Guerbet, Aulnay Sous Bois, France) was administrated. T1-mapping images were acquired 15 min after the injection of contrast medium. Cardiac MRI acquisition parameters are defined in Table 1. Moreover, ECV values were calculated using blood hematocrit levels as follows:

$$ECV = [1 - hematocrit]x\frac{\left(\frac{1}{post} - contrastT1myocardium\right) - \left(\frac{1}{native}T1myocardium\right)\left(\frac{1}{post} - contrastT1myocardium\right) - (1/nativeT1myocardium}{\left(\frac{1}{post} - contrastT1blood\right) - (1/nativeT1blood)}$$

Cardiac MRI analysis

The cardiac functional and morphological analyses were performed with consensus among two observers in a workstation (Extended MR Workspace, Philips Medical Systems, Best, Holland) who were blinded to the clinical information of the participants. The presence of high-signal intensities on T2 STIR and on LGE images was assessed visually by the two observers' consensus agreement. Endocardial and epicardial borders were automatically defined by the software and corrected with minimal user intervention if necessary. Papillary muscles were excluded from the volumes. Ventricular parameters were calculated on short-axis cine stack images. Moreover, the presence of left ventricular non-compaction (LVNC) was assessed by observers, and a ratio of non-compacted to compacted myocardial thickness > 2.2 in at least two left ventricular segments was accepted as LVNC.

Myocardial T1- and T2-relaxation times were calculated by two observers independently using two different software. Measurements were made by applying 10% offset from the epicardial and endocardial borders to minimize the partial volume effect. Observer-1 calculated the myocardial T1- and T2-relaxation times using dedicated software (IntelliSpace Portal, Philips Medical Systems, Best, The Netherlands), which automatically define the endocardial and epicardial borders. Minimal user intervention was performed when necessary to correct endocardial–epicardial contours of the LV. The mid-ventricular short-axis, T1/T2-mapping images were divided into six segments according to the standardized myocardial segmentation [21]. T1/T2 values were calculated for each myocardial segment, and also global LV T1/T2-relaxation times were calculated. Moreover, using an oval region of interest (ROI), the blood pool T1-relaxation times were manually measured before and after contrast material administration to calculate the hematocrit-corrected ECV values (Fig. 1). Then, Observer-2 calculated the myocardial T1/T2-relaxation times by a manual ROI placement on T1- and T2-mapping images using commercially available software (Osirix MD, Pixmeo, Bernex, Switzerland). The global T1/T2-relaxation times were calculated with the largest range of interest (ROI) covering the left ventricle myocardium as much as possible (Fig. 2). In these measurements, in addition to the global T1/T2-relaxation times, histogram analysis was also performed, and minimum (Min), mean, maximum (Max), skewness (Skew), and kurtosis (Kurt) values (for T1/T2 relaxation times) were noted. Observer-2 was unaware of the first observer's measurements.

Statistical analysis

MedCalc (version 19.2; MedCalc Software, Ostend, Belgium) and SPSS Statistics (version 24; IBM, Armonk, NY) were used for statistical analyses. The characteristics of the cases

Table 1 Cardiac magnetic resonance imaging parameters

	TR (ms)	TE (ms)	PP TI (ms)	TF	EPI factor	FOV (mm)	FA	Matrix	Slice Thic	Inter-slice gap
BTFE	2,5	1,2		70	1	300		120×256	8	0
sBTFE	2,4	1,2		18	1	300	60°	176×240	8	0
BBC	1791	31		46	1	300		130×288	8	0,8
STIR	1714	70		30	1	300		172×352	8	0
PSIR	6.1	3	450	20	1	300	25°	158×336	10	0
T1	2,3	1	350	92	1	300	35°	150×256	10	0

BTFE balanced turbo field echo, *sBTFE* sine balanced turbo field echo, *BBSSh* black blood single shot, *T2 STIR* T2 short tau inversion recovery, *PSIR* phase-sensitive inversion recovery, *TF* turbo factor, *FA* flip angle, *FOV* field of view, *Slice Thic.* slice thickness

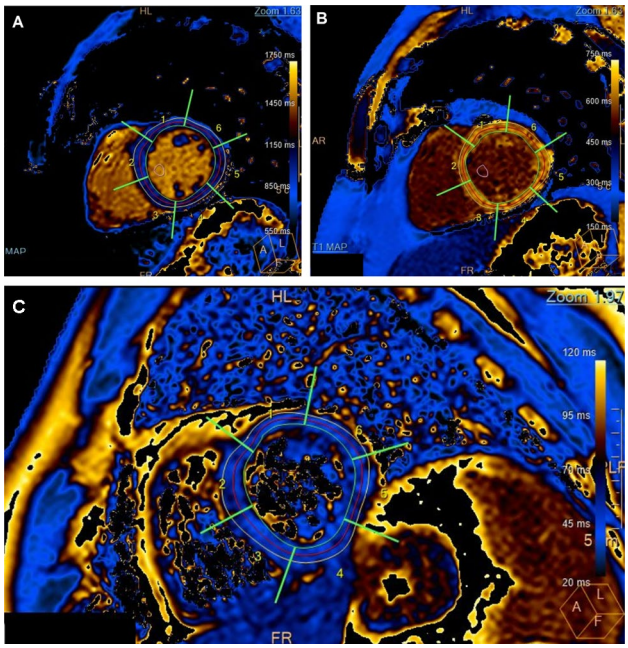

Fig. 1 Presentation of **A**) native T1-, **B**) post-contrast T1-, and **C**) T2-parametric mapping image analysis by Observer-1 using dedicated software (IntelliSpace Portal, Philips Medical Systems, Best, The Netherlands)

are presented as mean with standard deviation (mean ± SD) or absolute frequency percentage. The mean values of continuous variables were compared using Student's *t* test. Associations between two categorical variables were assessed using the Fisher's exact test or chi-square (X^2) test. Spearman correlation coefficients were used to test the correlations between

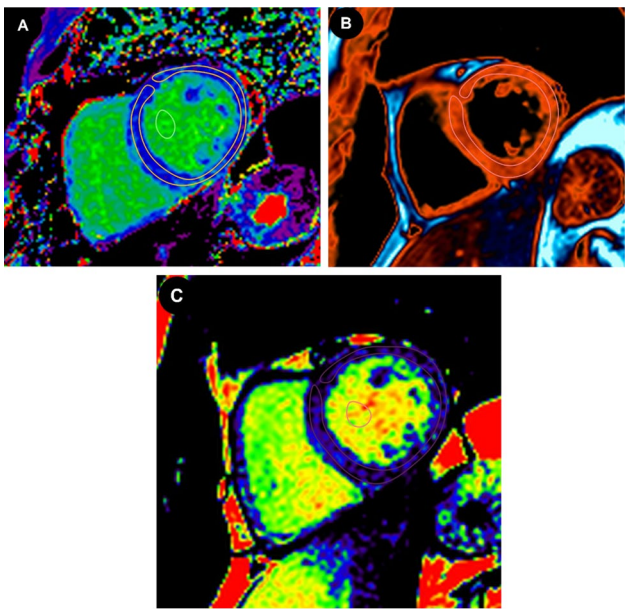

Fig. 2 Presentation of **A**) native T1-, **B**) post-contrast T1-, and **C**) T2-parametric mapping image histogram analysis by Observer-2 using commercially available software (Osirix MD, Pixmeo, Bernex, Switzerland)

continuous variables. The cardiac MRI–based cutoff values for Crohn's disease (CD) were investigated using the receiver operating characteristic (ROC) curve. To determine the optimal cutoff values, Youden index was used. Confidence intervals were calculated at 95% confidence level. The consistency between the two methods (automatic and manual segmentation methods) in the measurements of parametric mapping times were investigated using the intraclass correlation coefficient (ICC) and Bland–Altman analysis. Statistical significance level was accepted as $p < 0.05$.

Results

Study population characteristic

A total of 40 participants were included in this prospective study, including 20 patients with CD (mean age ± standard deviation, 40.5 ± 7.7 years, 10 females), and 20 HCs (mean age ± standard deviation, 35.8 ± 13.3 years, 11 females). There was no significant difference between the CD and HC groups in gender ($p = 0.632$), age ($p = 0.188$), weight ($p = 0.112$), height ($p = 0.779$), and body mass index ($p = 0.063$) (Table 2).

The clinical findings of the patients were represented in Supplementary document. There was no significant difference between the CD and HC groups in hematocrit ($p = 0.341$) and serum creatinine ($p = 0.506$) levels. However, patients with CD had significantly higher WBC count ($p = 0.015$), CRP values (0.009), and ESR in 1 h ($p = 0.004$) (Table 2).

Analysis of ventricular functions, morphology, and LGE

No significant difference was found in LV morphological and functional parameters (end-diastolic volume [EDV], end-sistolic volume [ESV], ejection fraction [EF], cardiac output [CO], cardiac index [CI], and myocardial mass) between CD and HC. While patients with CD had significantly lower RV-EF than HC ($p = 0.010$), there was no significant difference in other RV functional parameters (EDV and ESV) between the CD and HC groups (Table 3). No LGE or high-signal intensities on T2 STIR were detected in participants with CD and HC. There was no pleural or pericardial effusion in any of the participants in the patient and control groups. Two patients (10%) with Crohn's disease had left ventricular non-compaction (LVNC), but none of the healthy controls had LVNC (Fig. 3). Analysis results for global LV/RV functional parameters are shown in Table 3.

Analysis of T1/T2-mapping and ECV

There was an excellent agreement between observers for mean native and contrast-enhanced myocardial T1 relaxation time (ICC of 0.991; 95% CI 0.983 to 0.995 and ICC of

Table 2 The characteristics of the study population and laboratory test results

Characteristics	Healthy controls	Crohn's disease	*p* value
Age (years)	35.8 ± 13.3	40.5 ± 7.7	0.188
Male sex (*n*)	9	10	0.632
Height (cm)	168.2 ± 10.7	167.3 ± 9.4	0.779
Weight (kg)	76 ± 11.7	69.6 ± 13	0.112
Body mass index (kg/m^2)	26.8 ± 3	24.8 ± 3.6	0.063
Heart rate (bpm)	69.5 ± 9.9	67.1 ± 11.9	0.495
Systolic blood pressure (mmHg)	117.5 ± 12.1	118.9 ± 17.2	0.532
Diastolic blood pressure (mmHg)	80.3 ± 9.8	81.1 ± 9.9	0.667
Hematocrit (%)	40.9 ± 5.6	39.2 ± 5.9	0.341
Creatinine (mg/dL)	0.8 ± 0.25	0.9 ± 0.4	0.448
WBC Count (× 10^3/dL)	7 ± 1.3	7.8 ± 2.7	0.150
CRP (mg/L)	0.38 ± 0.18	1.87 ± 2.3	0.009
ESR (mm/h)	9.9 ± 5.5	28.3 ± 24.6	0.004

Values are presented as mean ± standard deviation

bpm beats per minute, *WBC* white blood cell, *CRP* C-reactive protein, *ESR* erythrocyte sedimentation rate

0.941; 95% CI, 0.887 to 0.969, respectively), and mean T2 relaxation time measurements (ICC of 0.983; 95% CI, 0.949 to 0.994) (Fig. 4).

Parametric mapping and ECV values were reported in Table 4. No significant difference was found between myocardial segments (six segments in mid-ventricular short-axis image) in native T1-, post-contrast T1-, and T2-relaxation times of the LV (*p* values ranges from 0.298 to 0.946). There was no statistically significant difference between the CD and HC groups in terms of LV native and contrast-enhanced mean T1-relaxation time in measurements made by different software by both observers. However, mean myocardial T2-time and ECV values were significantly higher in patients with CD group than the HC in the measurements made by both observers. In the histogram analysis of the measurements of the Observer-2, a statistically significant difference was found between the CD and HC in native T1 Min, native T1 Skew, and T2 Max values. There was no significant difference between the CD and HC groups regarding other histogram parameters (Table 4).

The mean and maximum T2 relaxation time values showed the best diagnostic performance to distinguish patients with CD and HC. The diagnostic performances of T1/T2-mapping and histogram parameters are reported in Table 5.

Mean T2-relaxation time was found to be significantly correlated with ESR values in the measurements made by both observers ($p = 0.020$, $r = 0.504$ for Observer-1 and $p = 0.047$, $r = 0.429$ for Observer-2). Serum CRP levels were significantly correlated with T2 Kurt ($p = 0.010$, $r = 0.573$) and contrast-enhanced T1 Min ($p = 0.019$, $r = -0.389$) values. There was no significant correlation between laboratory values and other histogram parameters.

Table 3 Results of ventricular assessment

	Healthy controls	Crohn's disease	*p* value
Left ventricular assessment			
Ejection fraction [%]	63 ± 5.9	60.3 ± 6.2	0.180
Mass [g]	75.8 ± 14.7	78.2 ± 12.3	0.594
End-diastolic volume [ml]	100.1 ± 21.1	95.6 ± 23.5	0.532
End-systolic volume [ml]	37.4 ± 10.2	38.6 ± 10.9	0.718
Right ventricular assessment			
Ejection Fraction [%]	54.6 ± 7.9	47 ± 5.8	0.010
End-diastolic volume [ml]	91.6 ± 12.6	86.2 ± 13.9	0.202
End-systolic volume [ml]	42.4 ± 12.3	39.3 ± 11.7	0.198

Values are presented as mean ± standard deviation

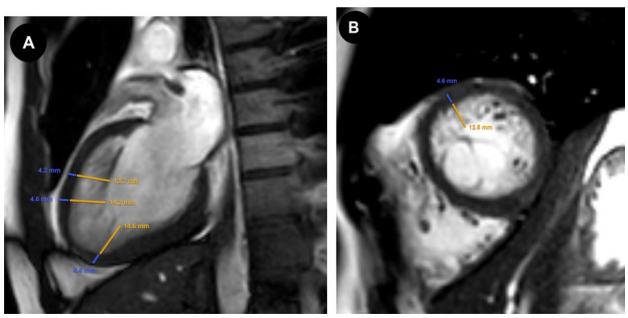

Fig. 3 A 44-year-old asymptomatic male with left ventricular non-compaction (LVNC). **A)** Two-chamber and **B)** short-axis steady-state free precession (SSFP) images show a mean ratio of non-compacted (yellow line) to compacted (blue line) myocardial thickness (calculated as 3.2)

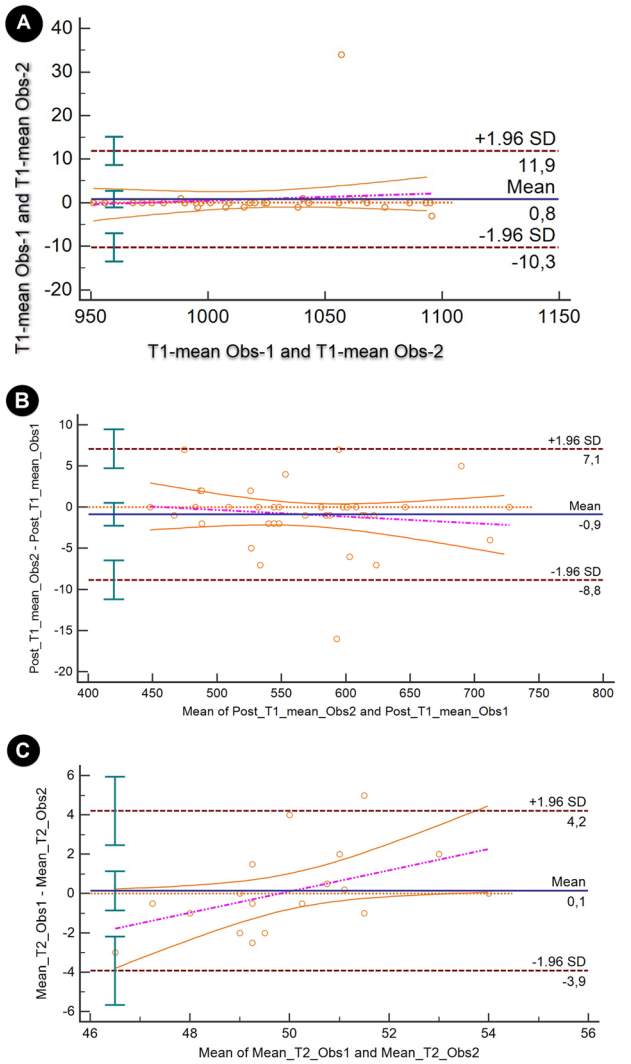

Fig. 4 Bland–Altman plots of **A**) mean native T1-, **B**) mean post-contrast T1-, and **C**) mean T2-time measurements for agreement between observers

Discussion

The present prospective study in patients with CD without active cardiac or respiratory complaints reveals that Crohn's patients had a higher myocardial ECV, mildly decreased RV-EF, and prolonged myocardial T2-relaxation time than HCs. Moreover, histogram analysis performed on mapping images confirmed these findings, and the minimum, maximum, and mean T2-relaxation times were found to be higher in patients with CD than HC. The present study results suggest affected myocardium due to systemic inflammation in patients with CD.

Extra-intestinal involvement in CD is observed in approximately 25–40% of the patients, and patients with CD have an increased incidence of early cardiac death compared to the healthy population. The exact cause of this condition has not been fully elucidated. It is thought to be associated with coronary atherosclerosis due to systemic inflammation, hypercoagulability, myocarditis/pericarditis due to increased immune response, or cardiotoxicity due to drugs used in treatment [4–6]. Besides, it has been rarely shown that patients with CD may experience myocardial amyloidosis, myocardial fibrosis, or myocardial atrophy [8–11]. Feng et al. [22] showed that the risk of ischemic heart disease (IHD) is increased in patients with CD (relative risk ratio of 1.243; 95% CI, 1.042 to 1.482) compared to the healthy adults. Runge et al. [23] demonstrated the mildly increased risk of IHD in patients with CD compared to the HC (11.6% vs. 8.4%), and they showed that the risk of IHD was lower in patients with CD who used 5-aminosalicylic acid compared to those who did not.

Bracamonte-Baran et al. [24] reported that mediators such as TNF-a, IL-1, and IL-6, which are increased in the blood during the ongoing systemic inflammatory process, may cause cytotoxic damage in myocytes and oxidative stress. If the systemic inflammatory processes are not detected early, and inflammation is not suppressed, it may cause myocardial fibrosis and early cardiac death [25, 26]. Cardiac MRI is a valuable method for evaluating inflammatory processes affecting the heart and can detect myocardial pathologies such as myocarditis in the early (subclinical) period [27]. In the present study, the myocardial T2-relaxation times were significantly prolonged in the patients' group, consistent with visually undetectable myocardial edema. Moreover, the increase in extracellular volume in the Crohn's patient group suggests an increase in the distance between myocytes due to ongoing systemic inflammation rather than myocyte loss.

Aarestrup et al. [28] showed that the patients with inflammatory bowel disease (IBD) have significantly higher serum inflammatory marker levels than healthy adults, independent of disease activity. Therefore, they suggested that the increased risk of cardiovascular disease in patients with IBD might be caused by prolonged systemic inflammation rather than traditional risk factors, such as hyperlipidemia, hypertension, obesity, smoking, and alcohol use [28]. Similarly, in the present study, patients with CD had significantly higher serum inflammatory levels than HC.

Kıvrak et al. [29] were found that preserved LV functions in patients with CD without active cardiac complaints using speckle tracking echocardiography (STE). In line with Kıvrak et al.'s study [29], no significant difference was found in the present study in LV functions between the patients with CD and HC. However, Kıvrak et al. [29] showed decreased left ventricular global longitudinal strain values in patients with CD ($p=0.014$) and were inversely correlated to CD severity score ($r=-0.703$, $p<0.001$) (131). Hensel et al. [30] showed decreased LV circumferential strain ratios in pediatric patients with IBD both during rest ($p=0.001$)

Table 4 Parametric mapping measurement results and extracellular volume

Characteristics	Healthy controls	Crohn's disease	*P* value
Observer-1			
Mean native T1-time [ms]	1018.5 ± 45	1021.6 ± 39.3	0.820
Mean contrast-enhanced T1-time [ms]	582.6 ± 69.2	556.4 ± 63.3	0.247
ECV [%]	27.2 ± 1.5	30.1 ± 2.8	0.001
Mean T2-time [ms]	47.7 ± 2.4	50.8 ± 2.2	0.009
Observer-2			
Mean native T1-time [ms]	1018.4 ± 44.9	1023.2 ± 40.6	0.736
Min native T1-time [ms]	910.8 ± 46.6	945.6 ± 43.8	0.025
Max native T1-time [ms]	1133.6 ± 60.2	1147.1 ± 63.9	0.517
Skew native T1-time [ms]	0.19 ± 0.38	0.59 ± 0.48	0.010
Kurt native T1-time [ms]	− 0.28 ± 0.75	− 0.06 ± 0.9	0.432
Mean contrast-enhanced T1-time [ms]	578.2 ± 70.1	550.5 ± 64.8	0.225
Min contrast-enhanced T1-time [ms]	509.1 ± 77.3	494.2 ± 72.5	0.553
Max contrast-enhanced T1-time [ms]	642.5 ± 69	605.7 ± 60.4	0.097
Skew contrast-enhanced T1-time [ms]	− 0.13 ± 0.55	− 0.06 ± 0.51	0.703
Kurt contrast-enhanced T1-time [ms]	− 0.02 ± 1.04	− 0.13 ± 1.45	0.367
ECV [%]	27.1 ± 1.4	29.9 ± 2.5	0.004
Mean T2-time [ms]	47.1 ± 1.9	50.6 ± 1.4	0.001
Min T2-time [ms]	41.2 ± 4.2	42.3 ± 3.6	0.561
Max T2-time [ms]	55.6 ± 4.1	62.5 ± 6.6	0.041
Skew T2-time [ms]	0.34 ± 0.2	0.38 ± 0.44	0.871
Kurt T2-time [ms]	0.85 ± 0.2	0.84 ± 0.25	0.375

Values are presented as mean ± standard deviation

ECV extracellular volume, *Min* minimum, *Max* maximum, *Skew* skewness, *Kurt* kurtosis

and exercise ($p = 0.022$). To the best of our knowledge, the present study is the first study to investigate RV functions in patients with CD, and the RV-EF was significantly decreased in patients with CD compared to the HC.

Pericarditis has been frequently reported in patients with IBD, with a prevalence of 0.19% among Crohn's patients [28, 31]. Although the number of participants was low in the present study, there were no cases that had pericarditis (pericardial effusion, thickening, or gadolinium enhancement) on cardiac MRI. This may be due to the fact that the majority of patients are in remission or under immunosuppressive therapy.

CD is the fourth most common cause of secondary amyloidosis and amyloidosis develops in approximately 1% of patients with CD [8]. Cardiac amyloidosis is a rare condition that results from the accumulation of amyloid protein in the interstitial (extracellular) area and causes an increase in ECV [32]. Myocardial T1-mapping with ECV calculation is an invaluable investigation technique in identifying myocardial amyloidosis and the quantitative evaluation of myocardial amyloid burden [32]. In the present study, ECV in patients with CD was significantly higher than the HC. This may be due to the presence of subclinical (visually undetectable) myocardial

Table 5 Diagnostic performances of T1/T2-mapping parameters with histogram analysis and extracellular volume (ECV)

Parameters	AUC	Cutoff value	Sensitivity	Specificity
Observer-1				
ECV [%]	0.823 (95% CI; 0.665–0.927)	> 28.2	73.7 (48.8–90.9)	84.2 (95% CI; 60.4–96.6)
Mean T2-time [ms]	0.837 (95% CI; 0.612–0.960)	> 47.5	100 (76.8–100)	71.4 (95% CI; 29–96.3)
Observer-2				
Min native T1-time [ms]	0.709 (95% CI; 0.537–0.846)	> 913	75 (50.9–91.3)	64.7 (95% CI; 38.3–85.8)
Skew native T1-time [ms]	0.762 (95% CI; 0.593–0.886)	> 0.325	75 (50.9–91.3)	70.6 (95% CI; 44–89.7)
ECV [%]	0.823 (95% CI; 0.634–0.982)	> 27.6	78.6 (52.4–91.8)	66.7 (95% CI; 52–86.4)
Mean T2-time [ms]	0.966 (95% CI; 0.905–1)	> 49	85.7 (57.2–98.2)	100 (95% CI; 47.8–100)
Max T2-time [ms]	0.940 (95% CI; 0.812–1)	> 59	78.6 (49.2–95.3)	100 (95% CI; 47.8–100)

AUC area under the curve, *ECV* extracellular volume, *Min* minimum, *Max* maximum, *Skew* skewness, *CI* confidence interval

amyloidosis due to chronic inflammation. Since the number of participants in the present study is low, these findings need to be confirmed in studies with larger patient groups.

This study has several limitations. Although the small population is an essential limitation of the present study, this is the first study in the literature investigating possible cardiac involvement in Crohn's patients with MRI and mapping techniques. Another limitation of this study is that most of the patients included in the study had a short duration of illness, and most patients were in asymptomatic remission. Therefore, our study does not reflect the full spectrum of CD, and the findings may differ in patients with longer disease duration, severe-fulminant disease, and patients not under treatment. Another limitation is that we did not compare the MRI findings with histopathological examination, since myocardial biopsy was not performed on the patients with CD. In addition, since the patients were under medical therapy, the medical treatment's possible cardiac effects could not be evaluated in this study. For these reasons, studies with the more extensive patient and control groups are needed. Moreover, longitudinal cardiac MRI studies to evaluate the outcomes in patients with Crohn's disease are required.

In conclusion, patients with CD had a higher myocardial ECV, mildly decreased RV-EF, and prolonged myocardial T2-relaxation time (minimum, maximum, and mean) than HC. Mean T2-relaxation time was significantly correlated with ESR values in the patients with CD. These results could suggest myocardial affection due to chronic systemic inflammation in patients with CD, and cardiac MRI can help evaluate and monitor cardiac involvement in these patients. Successful management of systemic inflammatory processes in patients with CD can prevent cardiac involvement.

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Declarations

Conflict of interest The authors declare no competing interests.
The Institutional Review Board statement.
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