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One-year follow-up study detects myocardial changes with cardiovascular magnetic resonance tagging in active rheumatoid arthritis

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One-year follow-up study detects myocardial changes with cardiovascular magnetic resonance tagging in active rheumatoid arthritis

ABSTRACT

Rationale and objectives: To evaluate the effects of one-year of medical treatment on myocardial function in active rheumatoid arthritis (RA).

Materials and methods: Thirty-nine female RA patients without any known cardiovascular disease underwent a cardiovascular magnetic resonance (CMR) examination before and after one-year of antirheumatic treatment. The population comprised untreated active early RA (ERA) and chronic RA (CRA) patients, which were grouped accordingly. The CMR protocol included volumetric determinations, late gadolinium enhancement imaging, myocardial tagging and native T1 mapping. DAS28-CRP disease activity scores were calculated before and after the treatment.

Results: Results are reported as median (quartile 1 - quartile 3). Time to peak diastolic filling rate improved in ERA (495 (443 - 561) ms vs 441 (340 - 518) ms, $p = 0.018$). Peak diastolic mean mid short-axis circumferential strain rate of all six segments was improved (82 (74 - 91) %/s vs 91 (77 - 100) %/s, $p = 0.05$, particularly in the anterior segment (82 (63 - 98) %/s vs 86 (77 - 109) %/s, $p = 0.013$). DAS28-CRP decreased in ERA (3.8 (3.2 - 4.1) vs 1.6 (1.4 - 2.2), $p < 0.001$). In CRA, no statistically significant improvement was detected.

Conclusion: Early treatment of active RA is important, as myocardial function detected with CMR tagging improved in ERA in parallel with decreasing inflammatory activity.

Keywords: cardiovascular magnetic resonance imaging, tagging, strain, rheumatoid arthritis.

Introduction

Rheumatoid arthritis (RA) is a chronic systemic autoimmune disease with common and often subclinical cardiovascular involvement [1]. The mechanisms of myocardial disease in RA are not fully understood but higher prevalence of myocardial fibrosis, diastolic dysfunction or heart failure with normal ejection fraction

have been documented [2,3]. The prevalence of heart failure with normal ejection fraction in RA patients has been reported to be as high as 23% [4] and the prevalence of predominant diastolic dysfunction to be even higher (31-66%) [5,6]. Cardiac involvement is assumed to result from a combination of processes, such as chronic inflammation leading to endothelial dysfunction, and increased levels of inflammatory cytokines that lead to the development of myocardial dysfunction [7]. A major contributor to reduced life expectancy in RA patients is coronary heart disease and heart failure [7]. Therefore, early detection of myocardial changes in RA is crucial to ensure early therapeutic intervention.

Global left ventricular ejection fraction (LVEF) and left ventricular filling parameters measured with cardiovascular magnetic resonance (CMR) imaging can be insensitive for the detection and assessment of early changes in myocardial contractility and relaxation [8]. The myocardial contractility and relaxation use strain as a measure of myocardial deformation, and this approach can be assessed with strain echocardiography or CMR tagging. Tagging is considered as the gold standard for non-invasive deformation imaging [9,10]. Global circumferential strain assessed by CMR can identify myocardial dysfunction for several conditions that are independent of LVEF [11,12]. Recently, global circumferential strain has been shown to have an independent prognostic value in both asymptomatic patients and those with heart failure [13]. For non-invasive evaluation of diffuse myocardial inflammation and fibrosis, native T1 mapping has become a promising CMR tool. Decreased native T1 values have been identified in myocardial iron overload states or glycosphingolipid accumulation in Anderson-Fabry disease, whereas high native T1 values have been related to myocardial inflammation, fibrosis, amyloid accumulation, and other conditions [14]. The influence of active RA and the effects of medical treatment with synthetic and biological disease modifying drugs (DMARDs) were our area of interest in this one-year follow-up study.

Materials and methods

Study population

The 39 patients of this study (Table 1) were selected from a previous study population of 60 patients that had active RA [2]. To minimize the risk of a patient having any other disorder than RA that could damage the myocardium, the study population comprised non-smoking, non-diabetic females under the age of 70 who had no history of heart disease, renal failure, thyrotoxicosis or untreated hypertension and who had no severe obesity. There were two patient groups: patients with untreated active early RA (ERA) who started conventional synthetic disease modifying antirheumatic drugs (csDMARDs) and patients with chronic RA (CRA) who had had inadequate response to csDMARDs and were candidates for biological treatment (bDMARDs). The 39 RA patients had successfully undergone CMR examinations with sufficient image quality for reliable analyses of tagging and native T1 images before and after the one-year DMARD treatment period. RA disease activity score DAS28-CRP was assessed before and after the treatment period. All 60 patients had two CMR examinations (total of 120) out of which 21 had insufficient image quality for quantitative analysis. These studies had severe cardiac gating and breathing induced image artefacts in either the native T1 images or strain tagging images. Thus, these studies were excluded from analysis and only patients with all T1 and strain results were included in the study.

The study was approved by the local ethics review board and a written consent was obtained from each participating patient before the study commenced.

Table 1

CMR examination

The CMR protocol was identical for each patient before and after the one-year treatment period. The CMR studies were performed using either 3T (23 patients) or 1.5T (16 patients) systems (Verio and Avanto^{fit},

Siemens Healthcare, Germany, respectively) with a 32-channel cardiac coil. The use of two scanner systems was due to the availability of the T1 mapping sequence at our institution (before 2014: 3T; after: 1.5T). Each patient was imaged using the same scanner before and after the treatment. The imaging protocol included complete stacks of long-axis (4-chamber view) and short-axis cine images, strain tagging, conventional late gadolinium enhancement (LGE) imaging and native mid-ventricular short-axis T1 mapping. The complete acquisition and analysis procedure excluding the strain tagging sequences has been described in a previous study [2]. Tagging analysis was performed only recently and thus not described before.

The strain tagging sequences were performed at the mid-ventricular levels for both long-axis and short-axis directions using prospective cardiac gating and breath hold to minimize motion artefacts. The sequence used was a typical spatial modulation of magnetization sequence with TR/TE = 33.7/4.1 ms, flip angle of 14°, matrix size of 256 x 256, slice thickness of 6 mm and the number of phases 20-25.

Image analysis

The volumetric studies and LGE images were read in consensus by two experienced radiologists each of whom had over 10 years of experience. The T1 analysis was performed by a qualified medical physicist and, the strain tagging segmentation in consensus by a physicist and a radiologist in training. Additionally, the strain image segmentation was verified by a radiologist with over 10 years of experience. The volumetric studies and T1 mapping analyses were performed using QMass MR Software (version 7.6., Medis Medical Imaging Systems, Leiden, Netherlands) and the strain tagging analysis using Segment software v.2.0 R5030 (<http://segment.heiberg.se>) [15,16]. The T1 mapping and short-axis strain tagging analyses were both performed for each of six segments in the mid short-axis level of the left ventricle. The boundaries of the tagged mid short-axis left ventricle were drawn using the manual segmentation tools of Segment for the strain tagging analysis. The segmentation was performed in one of the first five images of the image sequence (Fig. 1) and the software analyzed the rest of the images semi-automatically. The strain tagging analysis resulted in calculation of segmental circumferential and longitudinal strain (%) curves as a function

of time (ms), which covered the whole cardiac cycle. We focused on the analysis of segmental circumferential peak mid short-axis and peak mean long-axis strain parameters.

Fig. 1

The strain data of each segment was used to derive the mean time derivative, i.e. the strain rate of the corresponding strain. The derivatives were computed using a custom function that utilizes the “diff-function” in MATLAB R2016A (The MathWorks, Inc., Natick, MA, USA). The segmental peak short-axis systolic strain and diastolic strain rate were then determined as the momentary maximum value of the curves (Fig. 2). In the long-axis direction, the peak mean systolic strain and diastolic strain rate were calculated as the mean value across all seven long-axis segments. Strain values were analyzed per segment in the short-axis direction and as a mean in the long-axis direction. This difference in approach was because short-axis systolic strain and diastolic strain rates were compared with the corresponding T1 relaxation times to find correlations, whereas no long-axis T1 values were available. The values of peak systolic strain were negative, thus, a change was considered positive when the value of strain was more negative after the treatment than before the treatment.

Fig. 2

Statistical analysis

All the acquired results were compared separately for ERA and CRA patients and were presented as median and quartile 1 - quartile 3 (Q1 - Q3). Continuous variables were compared before and after one-year of DMARD treatment using the Wilcoxon signed-rank test. Pearson and Spearman correlations were used to estimate statistical correlations between the changes in T1 relaxation times and the changes in peak diastolic strain rate for both groups in the short-axis direction. Pearson and Spearman correlations were also used to test correlations between the changes in DAS28-CRP and the changes in peak diastolic strain rates for the short-axis and long-axis directions for both groups. The peak mean systolic strain was additionally compared

with the peak mean diastolic strain rate. The statistical tests used were two-sided and p-values < 0.05 were considered statistically significant. Statistical analyses were performed using MATLAB R2016A.

Results

Volumetric findings

The median time to peak filling rate shortened (495 (443 - 561) ms vs 441 (340 - 518) ms, $p = 0.018$) and DAS28-CRP improved ERA (3.8 (3.2 - 4.1) vs 1.6 (1.4 - 2.2), $p < 0.001$) for the ERA patients (Table 2). Left ventricle end-diastolic volume decreased among CRA patients (81 (74 - 92) ml/m² vs 77 (72 - 87) ml/m², $p = 0.031$) (Table 3). No other significant changes were found in either group.

Table 2

Table 3

Strain tagging findings

The peak diastolic short-axis strain rate for ERA patients (Table 4) improved (82 (74 - 91) %/s vs 91 (77 - 100) %/s, $p = 0.05$), particularly in the anterior segment (82 (63 - 98) %/s vs 85 (77 - 109) %/s, $p = 0.013$). The mean long-axis diastolic strain rate did not improve significantly for either group. The systolic strain changes were statistically not significant in either group (Table 5).

Table 4

Table 5

LGE findings

Before starting the DMARD treatment, LGE was detected in 17 out of 25 (68%) ERA patients and in 8 out of 14 (57%) CRA patients. After one-year of DMARD treatment, LGE was observed in 19 out of the 25 (76%) ERA patients and 8 out of 14 (57%) CRA patients. Fig. 3 shows the distribution of the LGE detected in both groups following the 17-segment model of the left ventricle by the American Heart Association [17].

Fig. 3

LGE was detected mainly in the septal, inferior and inferolateral segments in basal and mid-ventricular levels of the left ventricle in both groups. No LGE was detected in apical segments in any of the patients. LGE was typically subepicardial, midmyocardial or patchy in both groups. LGE did not change significantly in either group during treatment.

T1 findings and correlation

Median changes in the T1 relaxation times varied from +25 to -53 ms in ERA and from +33 to -47 ms in CRA (appendix Tables A1 and A2). The T1 relaxation times, segmental or mean, did not change significantly in either group. Changes in T1 relaxation showed no correlation with changes in short-axis or long-axis peak diastolic strain rate in either group.

Correlation with DAS28-CRP

Changes in DAS28-CRP correlated with the changes in mean mid short-axis peak diastolic strain rate in ERA (Fig. 4) but not for the CRA group (data not shown). The correlation was negative ($R = -0.46$, $p = 0.026$) and thus, the DAS28-CRP decreased as the peak mean mid short-axis diastolic strain rate improved. The change in DAS28-CRP did not correlate with the change in peak diastolic long-axis strain rate or peak systolic short-axis strain in either group.

Fig. 4

Correlation of the changes in peak systolic strain and peak diastolic strain rate

Statistically strong correlations were detected between the changes in peak mean short-axis systolic strain and peak mean short-axis diastolic strain rate in the entire study population of 39 RA patients. A similar correlation was also found in the long-axis direction (Fig. 5).

Fig 5

Discussion

The current work is the first prospective follow-up study that assesses the effects of active RA and DMARD treatment targeting to remission on myocardial function that has been evaluated with CMR tagging. We found statistically significant improvement in diastolic myocardial function in the newly diagnosed group after one-year csDMARD treatment. Time to peak diastolic filling rate and peak diastolic circumferential short-axis strain rate improved in this group. Systolic strain did not change significantly in either group, regardless, changes in peak systolic strain correlated with the changes in diastolic strain rate in the entire study population (Fig 5). Myocardial involvement and diastolic dysfunction have been reported to be common in RA patients free of any clinical cardiovascular disease [2,4,5]. Increased prevalence of diastolic heart failure in patients with RA is suggested to correlate with RA disease activity but not with the treatment type [18]. Generally, changes in the LV function and structure are known to correlate with a higher risk of cardiovascular mortality [19]. However, an active antirheumatic treatment and thus a decrease in RA disease activity may also inhibit the progression of myocardial involvement [20].

Left ventricle end-diastolic volume decreased slightly in chronic patients. Although diastolic strain rate decreased in all segments no significant changes or any improvement in the myocardial function was found in CRA after one-year treatment with bDMARDs. On the other hand, evidence does exist that reduced

systolic tissue velocities occur in diastolic heart failure, as systole and diastole are closely interdependent [21]. Several physiological variables simultaneously affect left ventricular filling and may thus have confounding effects on the ventricular inflow [22]. CMR tagging and ultrasonography-based speckle tracking are less sensitive to these pre- and afterload changes [23]. Therefore, CMR tagging might be an accurate method in the detection of early myocardial changes in diastolic dysfunction. In the present study, the peak systolic circumferential mid short-axis strain was within normal range in both ERA and CRA while the peak systolic longitudinal strain was normal in ERA and slightly reduced in CRA [24,25]. RA disease activity of the ERA patients as measured by DAS28-CRP score, was reduced after the one-year treatment with csDMARD. This change in disease activity associated with the changes in mean short-axis diastolic strain rate (Fig. 4) is in line with previous studies [18,26]. Contrary to ERA patients, disease activity did not improve in the CRA group. It is plausible that this lack of improvement is partly due to this group having had the chronic active disease for a mean of 17.3 years.

Native T1 values showed no statistically significant change within the follow-up period. Furthermore, individual T1 values showed no correlation to circumferential peak diastolic strain rate in either group. We found a correlation between the mid-ventricular short-axis strain and T1 relaxation time at 1.5T in both ERA ($n = 14$, $R = 0.61$, $p = 0.03$) and CRA ($n = 18$, $R = 0.55$, $p = 0.04$) patients' studies. These correlations are in line with the previous results reported by Ntusi et al [24]. Comparing with recent studies of healthy myocardial T1 relaxation times [27,28] our patients imaged at 1.5T ($n = 16$) had elevated T1 relaxation times whereas patients imaged at 3T ($n = 23$) did not. An increase of native T1 relaxation time is reported to associate with myocardial inflammation or fibrosis. T1 mapping, therefore, seems to be a good method for detecting diffuse myocardial fibrosis, whereas conventional LGE imaging is useful for assessing local scarring [26]. A higher prevalence of myocardial fibrosis, inflammation and positive LGE findings in RA patients have been reported and all these parameters may contribute to higher native T1 values [29]. LGE was found in 64% before and in 69% of our patient population after the one-year follow-up period. Accurate distinction of the underlying causes of elevated T1 levels is not possible using native T1 myocardial relaxation times without post-contrast T1 mapping and extracellular volume calculations [14]. The local scarring areas may affect T1 relaxation times directly, whereas acute inflammation may convert into fibrosis

over time. Both these explanations may contribute to the fact that we found no statistically significant changes in T1 relaxation times during the one-year follow-up in our patients.

Both 3T and 1.5T MRI scanners were used in this study for image acquisition. Native T1 relaxation time is prolonged in higher magnetic fields so the absolute T1 values are not comparable for the two MRI systems used in our study. The strength of the magnetic field may also have impact on the changes of T1 values as T1 relaxation time increases in non-linear fashion as the magnetic field strength increases [30]. At 3T, we found no correlation between T1 and mid-ventricular short-axis strain. This could indicate that myocardial strain might also be nonlinearly affected by the increasing magnetic field strength similarly to T1 relaxation. Recently, variations of global circumferential strain with CMR feature tracking in different studies were specifically associated to differences in magnetic field strength [31]. Strain values have also been shown to differ at 1.5T and 3T [32].

Limitations

The study groups for this work were part of a larger group of patients that had been selected on image quality grounds, to enable reliable quantitative analysis. This reduced our group of ERA patients to 25 individuals and CRA patients to only 14 subjects. Myocardial function is known to depend on age, sex and physical activity [33], the small sample size of CRA patients may therefore explain our inability to find statistically significant changes. The size of our study population also prevented us from dividing ERA and CRA patients into subgroups based on magnetic field strength of the MRI system used.

Conclusion

Diastolic myocardial function is affected in the course of RA. Therefore, early antirheumatic treatment in the targeting of active RA to remission can maintain or improve diastolic myocardial function. These findings may emphasize the importance of effective treatment of RA not only for preventing joint destruction, but also for preventing concomitant myocardial damage.

Conflict of interest: None.

Informed consent: Written informed consent was obtained from all individual participants included in the study.

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Table 1 Baseline clinical features of RA patients. Data expressed as mean $\pm$ standard deviation. *RA = rheumatoid arthritis, RF = rheumatoid factor, ACPA = anti-citrullinated peptide antibody, DAS28-CRP = disease activity score, CRP = C-reactive protein, LDL = low density lipoprotein, BMI = body mass index.

Fig. 1 Mid- ventricular short-axis (left) and long-axis (right) tagging images with endocardial and epicardial segmentation

Fig. 2 Example curves demonstrating the mid short-axis strain (left) and strain rate (right). The bold arrow depicts peak systolic strain and the dashed arrow peak diastolic strain rate.

Table 2 Volumetric results for ERA patients (n = 25). Results are expressed as median (Q1 - Q3). *BSA = body surface area, LVESV = left ventricle end-systolic volume, LVEF = left ventricle ejection fraction, PFR = peak filling rate, TPFR = time to peak filling rate, DAS28-CRP = RA disease activity score, *statistically significant difference

Table 3 Volumetric results for CRA patients (n = 14). Results are expressed as median (Q1 - Q3). *Abbreviations are as in table 2.

Table 4 Results of strain tagging analysis for ERA patients (n = 25). Results are expressed as median (Q1 - Q3) *SA = short-axis, LA = long-axis, *statistically significant change

Table 5 Results of strain tagging analysis for CRA patients (n = 14). Results are expressed as median (Q1 - Q3). *SA = short-axis, LA = long-axis.

Fig. 3 Results for LGE for both groups. Numbers indicate the number of patients with LGE in the segment in question. Upper row: ERA (n = 25). Bottom row: CRA (n = 14)

Fig. 4 Correlation with the change in DAS28-CRP and mean mid short-axis diastolic strain rate for ERA (n = 25), SA = short axis

Fig 5 Correlations between the changes in peak mean systolic strain and peak mean diastolic strain rate in short-axis (SA) (left) and long-axis (LA) (right) directions in the entire study population (n = 39)

Appendix

Table A1 Results of mid short-axis T1 analysis for 25 ERA patients (n = 7 for 1.5T and n = 18 for 3T). Results are expressed as median (Q1 - Q3).

Table A2 Results of mid short-axis T1 analysis for 14 CRA patients (n = 9 for 1.5T and n = 5 for 3T). Results are expressed as median (Q1 - Q3).

Figure1_left

Figure1_right

Figure2_left

Figure2_right

Figure3

ERA

CRA

Figure4

Figure5_left

Figure5_right

Table1

Clinical feature	Patients with early RA (n = 25)	Patients with chronic RA (n = 14)	p-value (t-test)
Age (years)	48 ± 14	49 ± 15	0.921
RF positivity; n (%)	22 (88%)	13 (93%)	1.000
ACPA positivity; n (%)	22 (88%)	13 (93%)	1.000
Swollen joints	8 ± 6	6 ± 5	0.296
Tender joints	8 ± 8	7 ± 4	0.549
DAS28-CRP	3.7 ± 0.9	3.2 ± 1.1	0.356
Extra-articular manifestations; n (%)	4 (16%)	7 (50%)	0.033*
Erosions on radiographs; n (%)	3 (13%)	11 (85%)	< 0.001*
Duration of RA symptoms (months)	11 ± 15	207 ± 133	< 0.001*
CRP (mg/l)	12 ± 14	6 ± 6	0.058
LDL (mmol/l)	2.9 ± 0.7	3.2 ± 1.0	0.434
BMI (kg/m ²)	23 ± 4	24 ± 4	0.518
Waist circumference (cm)	79 ± 10	81 ± 11	0.668
Mean blood pressure (mmHg)	109 ± 13	111 ± 19	0.779

Table2

Volumetric studies	Before treatment	After treatment	Change	p-value
BSA (m ²)	1.7 (1.7 - 1.8)	1.7 (1.7 - 1.8)	0.0	0.742
Mean heart rate (bpm)	70 (66 - 77)	71 (65 - 79)	2.0 (-1.5 - 5.5)	0.577
LVEDV (ml/m ²)	81 (76 - 90)	83 (76 - 94)	2.0 (-4.5 - 4.0)	0.639
LVESV (ml/m ²)	35 (31 - 40)	33 (30 - 40)	0.0 (-3.0 - 2.0)	0.704
LVEF (%)	57 (56 - 60)	57 (55 - 62)	0.0 (-1.0 - 2.0)	0.978
LV mass (mg/m ²)	51 (46 - 57)	54 (50 - 58)	1.0 (-2.5 - 7.5)	0.211
PFR (1/s)	1.5 (1.3 - 1.9)	1.7 (1.5 - 2.1)	0.1 (0.0 - 0.2)	0.646
TPFR (ms)	495 (443 - 561)	441 (340 - 518)	-64 (-91 - (-33))	0.018*
DAS28-CRP	3.8 (3.2 - 4.1)	1.6 (1.4 - 2.2)	-1.7 (-2.4 - (-1.2))	< 0.001*

Table3

Volumetric studies	Before treatment	After treatment	Change	p-value
BSA (m ²)	1.7 (1.6 - 1.7)	1.7 (1.6 - 1.7)	0.0	0.971
Mean heart rate (bpm)	75 (68 - 89)	75 (67 - 81)	-2.0 (-9.0 - 5)	0.730
LVEDV (ml/m ²)	81 (74 - 92)	77 (72 - 87)	-2.5 (-10.0 - 0.0)	0.031*
LVESV (ml/m ²)	32 (28 - 40)	32 (25 - 35)	-1.0 (-5.0 - 0.0)	0.307
LVEF (%)	60 (58 - 62)	59 (58 - 64)	0.0 (-2.0 - 2.0)	0.791
LV mass (mg/m ²)	52 (45 - 56)	51 (45 - 56)	0.0 (-7.0 - 4.0)	0.441
PFR (1/s)	1.8 (1.4 - 2.2)	1.8 (1.5 - 2.0)	-0.1 (-0.4 - 0.2)	0.952
TPFR (ms)	433 (326 - 516)	433 (393 - 504)	2.8 (-27.8 - 60.1)	0.670
DAS28-CRP	3.4 (2.3 - 4.2)	3.0 (2.3 - 3.4)	-0.2 (-1.3 - 0.6)	0.296

Table4

Segment	Before treatment	After treatment	Change	p-value
Peak systolic SA strain (%)				
Anterior	-21.6 (-24.2 - (-19.8))	-22.0 (-24.8 - (-19.4))	0.1 (-2.1 - 1.6)	0.775
Anteroseptal	-17.0 (-19.8 - (-15.4))	-17.6 (-21.1 - (-16.5))	-0.2 (-2.6 - 1.2)	0.753
Inferoseptal	-15.0 (-17.6 - (-12.2))	-16.2 (-18.5 - (-14.4))	-1.1 (-2.7 - 1.2)	0.076
Inferior	-18.7 (-19.9 - (-16.4))	-17.5 (-22.6 - (-15.4))	0.4 (-2.2 - 2.2)	0.886
Inferolateral	-20.8 (-23.9 - (-18.7))	-21.6 (-23.6 - (-15.4))	-0.7 (-2.8 - 1.0)	0.391
Anterolateral	-19.8 (-20.8 - (-17.3))	-20.5 (-21.9 - (-17.1))	0.7 (-0.7 - 2.1)	0.932
Mean	-18.9 (-20.8 - (-16.6))	-19.3 (-21.3 - (-17.0))	-0.4 (-1.6 - 0.8)	0.199
Peak diastolic SA strain rate (%/s)				
Anterior	82.2 (63.3 - 98.4)	85.5 (76.5 - 109.2)	18.7 (3.1 - 26.4)	0.013*
Anteroseptal	82.0 (75.8 - 97.0)	95.8 (78.1 - 102.7)	5.5 (-6.7 - 22.7)	0.159
Inferoseptal	71.0 (64.7 - 81.3)	79.0 (64.6 - 92.8)	2.2 (-7.8 - 11.5)	0.394
Inferior	77.2 (65.9 - 97.4)	84.7 (67.6 - 92.8)	2.6 (-13.0 - 21.4)	0.434
Inferolateral	89.3 (83.8 - 120.8)	103.4 (75.6 - 133.6)	8.0 (-21.9 - 33.3)	0.664
Anterolateral	76.6 (61.3 - 90.6)	88.7 (73.1 - 105.6)	14.6 (-10.1 - 36.4)	0.092
Mean	82.3 (73.9 - 90.7)	91.1 (77.0 - 100.1)	7.7 (-8.2 - 23.4)	0.050*
Peak systolic LA strain (%)				
Mean	-15.0 (-16.4 - (-13.1))	-14.1 (-15.6 - (-12.6))	0.5 (-0.8 - 1.6)	0.549
Peak diastolic LA strain rate (%/s)				
Mean	42.0 (32.7 - 49.1)	43.2 (34.9 - 49.7)	-0.1 (-9.1 - 9.9)	0.670

Table5

Segment	Before treatment	After treatment	Change	p-value
Peak systolic SA strain (%)				
Anterior	-21.3 (-24.5 - (-18.8))	-20.5 (-23.0 - (-18.4))	-0.1 (-1.6 - 4.4)	0.380
Anteroseptal	-16.6 (-18.5 - (-13.4))	-17.5 (-19.2 - (-15.2))	-1.1 (-3.0 - 0.7)	0.204
Inferoseptal	-14.1 (-16.9 - (-13.1))	-14.7 (-19.6 - (-12.2))	-1.4 (-2.5 - 2.9)	0.733
Inferior	-17.9 (-19.7 - (-17.0))	-18.3 (-20.0 - (-16.1))	-0.5 (-1.4 - 1.0)	0.622
Inferolateral	-20.0 (-23.5 - (-18.5))	-22.8 (-24.1 - (-16.5))	-0.1 (-3.3 - 1.6)	0.791
Anterolateral	-19.6 (-21.2 - (-17.2))	-17.5 (-19.2 - (-15.5))	1.8 (-2.4 - 5.8)	0.204
Mean	-18.1 (-19.5 - (-17.2))	-19.1 (-20.1 - (-15.7))	-0.7 (-1.9 - 2.5)	0.733
Peak diastolic SA strain rate (%/s)				
Anterior	87.0 (56.0 - 104.4)	80.3 (65.2 - 94.7)	-17.7 (-24.9 - 14.2)	0.519
Anteroseptal	85.7 (66.6 - 101.8)	75.2 (63.0 - 87.7)	-15.0 (-32.4 - 6.5)	0.266
Inferoseptal	79.5 (66.5 - 99.7)	84.8 (53.1 - 96.6)	-18.4 (-35.1 - 11.8)	0.266
Inferior	91.4 (77.8 - 97.8)	83.7 (76.8 - 110.6)	-5.8 (-13.6 - 21.4)	0.910
Inferolateral	91.1 (72.3 - 112.8)	77.5 (61.7 - 92.8)	-10.3 (-31.8 - 7.6)	0.233
Anterolateral	87.5 (68.0 - 93.7)	81.5 (50.8 - 94.7)	-5.5 (-24.4 - 10.8)	0.622
Mean	86.7 (76.3 - 94.7)	83.3 (61.1 - 97.8)	-7.2 (-17.3 - 1.3)	0.176
Peak systolic LA strain (%)				
Mean	-11.1 (-15.6 - (-9.9))	-12.7 (-16.4 - (-8.7))	0.5 (-1.8 - 1.3)	0.776
Peak diastolic LA strain rate (%/s)				
Mean	34.3 (27.5 - 38.7)	35.2 (28.5 - 48.3)	2.3 (-6.0 - 22.9)	0.380

Table A1

Segment		Before treatment	After treatment	Change	p-value
T1 relaxation (ms)					
Anterior	1.5T	980 (949 - 1011)	969 (946 - 996)	-15 (-16 - (-14))	0.844
	3T	1126 (1116 - 1139)	1135 (1109 - 1196)	7 (-77 - 35)	0.084
Anteroseptal	1.5T	968 (950 - 1031)	1019 (966 - 1033)	-11 (-49 - 28)	0.219
	3T	1172 (1161 - 1175)	1146 (1109 - 1196)	-15 (-82 - 49)	0.417
Inferoseptal	1.5T	978 (956 - 1043)	1010 (991 - 1023)	-21 (-66 - 24)	0.578
	3T	1162 (1148 - 1182)	1147 (1109 - 1200)	-23 (-66 - 11)	0.815
Inferior	1.5T	971 (938 - 1038)	1004 (997 - 1016)	4 (-54 - 62)	0.469
	3T	1160 (1153 - 1165)	1148 (1112 - 1198)	-16 (-81 - 29)	0.532
Inferolateral	1.5T	964 (948 - 1010)	958 (945 - 992)	-9 (-26 - 9)	1
	3T	1165 (1110 - 1185)	1153 (1140 - 1179)	-53 (-69 - (-34))	0.148
Anterolateral	1.5T	944 (934 - 983)	991 (985 - 998)	25 (-25 - 74)	0.219
	3T	1130 (1116 - 1149)	1137 (1105 - 1170)	1 (-50 - 37)	0.833
Mean	1.5T	963 (953 - 1011)	989 (977 - 1003)	-4 (-39 - 30)	0.375
	3T	1159 (1143 - 1166)	1147 (1117 - 1181)	-15 (-71 - 21)	0.669

Table A2

Segment		Before treatment	After treatment	Change	p-value
T1 relaxation (ms)					
Anterior	1.5T	1000 (977 - 1019)	982 (977 - 1047)	-20 (-24 - (-2))	0.906
	3T	1164 (1127 - 1175)	1096 (1084 - 1108)	-47 (-56 - (-37))	0.313
Anteroseptal	1.5T	1005 (970 - 1042)	1028 (1026 - 1048)	31 (29 - 35)	1
	3T	1187 (1159 - 1189)	1163 (1135 - 1191)	-10 (-52 - 32)	0.813
Inferoseptal	1.5T	1007 (973 - 1028)	997 (980 - 1000)	-7 (-28 - (-6))	0.570
	3T	1148 (1147 - 1163)	1154 (1138 - 1171)	7 (-9 - 23)	0.750
Inferior	1.5T	1001 (996 - 1010)	1000 (987 - 1010)	-6 (-16 - (-3))	0.382
	3T	1178 (1139 - 1192)	1165 (1116 - 1213)	6 (-62 - 74)	1
Inferolateral	1.5T	980 (976 - 999)	992 (989 - 995)	33 (-8 - 48)	0.938
	3T	1168 (1147 - 1197)	1147 (1114 - 1179)	-11 (-33 - 11)	1
Anterolateral	1.5T	987 (955 - 996)	999 (989 - 1011)	24 (14 - 29)	0.469
	3T	1146 (1135 - 1190)	1108 (1095 - 1121)	-16 (-25 - (-7))	0.813
Mean	1.5T	1000 (991 - 1008)	990 (989 - 1014)	6 (-2 - 12)	0.570
	3T	1154 (1147 - 1184)	1139 (1114 - 1163)	-12 (-33 - 10)	1

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Abbreviations List

ACPA	anti-citrullinated peptide antibody
ERA	early rheumatoid arthritis
BMI	body mass index
BSA	body surface area
CMR	cardiovascular magnetic resonance
CRA	chronic rheumatoid arthritis
CRP	C-reactive protein
bDMARD	biological disease modifying antirheumatic drug
csDMARD	conventional synthetic disease modifying antirheumatic drug
DAS28-CRP	disease activity score
DMARD	disease modifying antirheumatic drug
LA	long-axis
LDL	low density lipoprotein
LGE	late gadolinium enhancement
LVEF	left ventricle ejection fraction
LVESV	left ventricle end systolic volume
PFR	peak filling rate
Q1	first quartile
Q3	third quartile
RA	rheumatoid arthritis
RF	rheumatoid factor
SA	short-axis
TPFR	time to peak filling rate