Original Investigation

One-Year Follow-up Study Detects Myocardial Changes with Cardiovascular Magnetic Resonance Tagging in Active Rheumatoid Arthritis

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Rationale and Objectives: To evaluate the effects of 1 year of medical treatment on myocardial function in active rheumatoid arthritis (RA).

Materials and Methods: Thirty-nine female patients with RA without any known cardiovascular disease underwent a cardiovascular magnetic resonance (CMR) examination before and after 1 year of antirheumatic treatment. The population comprised untreated active early RA (ERA) and chronic RA patients, who 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, $P = .018$). Peak diastolic mean mid short-axis circumferential strain rate of all six segments was improved (82 [74–91] %/s vs 91 [77–100] %/s, $P = .05$), particularly in the anterior segment (82 [63–98] %/s vs 86 [77–109] %/s, $P = .013$). DAS28-CRP decreased in ERA (3.8 [3.2–4.1] vs 1.6 [1.4–2.2], $P < .001$). In chronic RA, no statistically significant improvement was detected.

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

Key Words: 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 has been documented (2,3). The prevalence of heart failure with normal ejection fraction in patients with RA 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 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

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CMR tagging. Tagging is considered as the gold standard for noninvasive deformation imaging (9,10). Global circumferential strain assessed by CMR can identify myocardial dysfunction for several conditions that are independent of left ventricular ejection fraction (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 noninvasive 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 1-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 who 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 nonsmoking, nondiabetic 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. The 39 patients with RA had successfully undergone CMR examinations with sufficient image quality for reliable analyses of tagging and native T1 images before and after the 1-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 artifacts in either the native T1 images or the 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.

CMR Examination

The CMR protocol was identical for each patient before and after the 1-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 because of 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 proce-

TABLE 1. Baseline Clinical Features of Patients with RA

Clinical Feature	Patients with Early RA ($n = 25$)	Patients with Chronic RA ($n = 14$)	P Value (t test)
Age (y)	48 ± 14	49 ± 15	.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	.296
Tender joints	8 ± 8	7 ± 4	.549
DAS28-CRP	3.7 ± 0.9	3.2 ± 1.1	.356
Extra-articular manifestations; n (%)	4 (16%)	7 (50%)	.033
Erosions on radiographs; n (%)	3 (13%)	11 (85%)	<.001
Duration of RA symptoms (mo)	11 ± 15	207 ± 133	<.001
CRP (mg/L)	12 ± 14	6 ± 6	.058
LDL (mmol/L)	2.9 ± 0.7	3.2 ± 1.0	.434
BMI (kg/m^2)	23 ± 4	24 ± 4	.518
Waist circumference (cm)	79 ± 10	81 ± 11	.668
Mean blood pressure (mm Hg)	109 ± 13	111 ± 19	.779

ACPA, anti-citrullinated peptide antibody; BMI, body mass index; CRP, C-reactive protein; DAS28-CRP, disease activity score; LDL, low density lipoprotein; RA, rheumatoid arthritis; RF, rheumatoid factor.
Data expressed as mean ± standard deviation.