Kobayashi et al. Int J Immunol Immunother 2016, 3:019
Volume 3 | Issue 1
ISSN: 2378-3672

International Journal of
Immunology and Immunotherapy

Mini Review: Open Access

The Diagnostic Role of Cardiac Magnetic Resonance Imaging in Rheumatoid Arthritis

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Abstract

In patients with rheumatoid arthritis (RA), cardiac involvement such as myocarditis and myocardial infarction is common. This cardiac involvement may have serious consequences and can contribute to worsening of a patient's cardiac-related morbidity and mortality. Importantly, cardiac involvement is typically clinically silent, only manifesting as cardiac dysfunction after an extended preclinical phase. Cardiovascular magnetic resonance (CMR) is a sensitive noninvasive diagnostic technique that can identify subclinical cardiac structural and functional abnormalities. MRI can be performed with repeatedly for diagnosis and follow-up in collagen-vascular diseases, which mostly affect relatively young individuals. We present a short review of the diagnostic role of CMR in patients with RA.

Keywords

Rheumatoid arthritis, Cardiac magnetic resonance imaging, Cardiac involvement

Introduction

Rheumatoid arthritis (RA) is a multi-organ disease that presents with not only articular symptoms but also various other clinical manifestations. In Western countries, life expectancy is approximately 10 years shorter in patients with RA than in healthy individuals, and cardiac involvement is the leading cause of death in those with RA [1-3]. However, even in the presence of cardiac involvement, RA is more likely to be asymptomatic, and compromises the vital prognosis [4]. Recently, cardiac involvement has also become a major cause of death in patients with RA in Japan [5].

With advances in cardiac magnetic resonance imaging (CMR), the assessment of regional or global cardiac function (contractility and diastolic function), myocardial ischemia, the condition of the myocardium, the coronary arteries and before myocardial ischemia can be performed in clinical settings; the detection of cardiac lesions can be performed with noninvasive manner, and the severity of the lesions can be quantified [6]. Furthermore, CMR provides better detection capability than nuclear testing for small myocardial infarctions and myocardial ischemia due to lesions in the three main coronary artery branches [7]. Furthermore, contrast-enhanced CMR is recognized as a valuable tool for the diagnosis of myocardial diseases. Unlike nuclear tests and computed tomography (CT), MRI causes no radiation exposure; therefore, MRI can be performed with repeatedly for diagnosis and follow-up in collagen-vascular diseases, which mostly affect relatively young individuals. Compared to echocardiography, this test has high reproducibility, with stable measurements [8,9]. It is particularly useful for measuring left ventricular (LV) mass in CMR. Because the entire LV volume is evaluated by measuring the LV mass and the volume of the cardiac chamber in CMR, CMR might be a better option to precisely measure the LV geometry [10,11].

Its detection and histological confirmation are often difficult because of a lack of symptoms in RA. CMR might be considered a useful and less invasive diagnostic method for assessing cardiac involvement in asymptomatic patients with RA. This paper provides a short review focused on the role of CMR in RA patients.

The Basics of Cardiac MRI

Alone among diagnostic imaging modalities, MRI allows not only morphological evaluation, but also enables simultaneous functional diagnosis and noninvasive assessment of myocardial properties. CMR has several positive features. (1) The test is minimally invasive and causes no radiation exposure. (2) In addition to allowing cardiac morphological diagnosis, the test also uses various sequences and enables functional diagnosis of cardiac motion and myocardial ischemia. (3) Allergic reactions to gadolinium-based MRI contrast agents are believed to be less common than those due to iodinated contrast agents used in CT and angiography [12]. However, CMR also has problematic features. (1) The tests are time-consuming. (2) Artifacts often occur when the tests are conducted on arrhythmia patients. (3) Experience is needed to interpret the results. (4) A contrast agent is often needed, and patients with allergies or impaired renal function are at risk of developing nephrogenic systemic fibrosis [13].

CMR utilizes various sequences as described below, and the choice of sequence depends on the purpose.

Cine MRI and tagging MRI

Global function: This enables evaluation of ejection fraction, end-

Citation: Kobayashi H, Kobayashi Y, Ode S, Sugiyama K, Kitamura N, et al. (2016) The Diagnostic Role of Cardiac Magnetic Resonance Imaging in Rheumatoid Arthritis. Int J Immunol Immunother 3:019

Received: June 19, 2016: **Accepted:** June 28, 2016: **Published:** June 30, 2016

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diastolic volume, and end-systolic volume, as well as measurement of myocardial mass

Regional function: This enables quantitative evaluation as well as visual assessment. Tagging MRI or feature tracking MRI, permit measurement of the local strain value of myocardium. With recent software development, feature tracking analysis also enables strain measurement using cine MRI.

Black-blood T2-weighted imaging (BB T2-WI): This visualizes myocardial edema as a high-signal area, and can assess myocarditis and acute myocardial infarction. BB T2-WI shows active inflammation in the myocardium.

Late gadolinium enhancement (LGE): In this phenomenon, the contrast effect can be observed in the myocardium approximately 10-15 minutes after intravenous injection of gadolinium-based contrast agent. In the early stages after administration, the contrast agent is distributed in the myocardial vascular bed, but later leaks into the interstitium and fills the extracellular space, results in delayed wash-out. The LGE indicates myocardial fibrosis, myocardial infarction and severe myocarditis.

ECV and T1 mapping: With recent advance of cardiac MRI, myocardial inflammation and diffuse fibrosis can be detected noninvasively by using native T1 mapping and extracellular volume (ECV) quantification on CMR.

Proper Combination of Sequences in RA

If the findings show pathological features (myocarditis and fibrosis) that are assumed to be associated with cardiac lesions in RA patients, further evaluation can include a combination of cine MRI + BB T2-WI + LGE (if possible, + T1 mapping) when there are no clear symptoms of ischemia; with this combination, CMR can be included among routine laboratory tests.

Research Study on CMR in RA

Until now, CMR has been successfully used for the evaluation of myocardial inflammation in different types of vasculitis [14,15], myositis [16], and SLE [17,18]. Giles et al. demonstrated the evaluation of left ventricular structure and function in patients with RA, as assessed by CMR [19]. They suggest that the progression to heart failure in RA may occur through reduced myocardial mass rather than hypertrophy.

We demonstrated that CMR was performed in RA patients without known heart disease, and the findings showed potential cardiac lesions in a pilot study [20]. LGE was observed in seven patients (38.9%). Perfusion defects under pharmacologic stress were observed in two patients. Mean DAS28 was significantly higher in the group with LGE compared to the group without by an average of 1.32 DAS28 units. Myocardial abnormalities, as detected by CMR were frequent in RA patients without known cardiac disease. Abnormal CMR findings were associated with higher RA disease activity, suggesting a role for inflammation in the pathogenesis of myocardial involvement in RA. Furthermore, we also demonstrated that regional function in RA patients was apparently lower than that found in healthy subjects assessed using CMR [21]. In addition, global cardiac function and left ventricular mass (LVM) and geometry were examined by using CMR in healthy subjects and RA patients without cardiac symptoms, matched according to age and sex; in comparison with healthy subjects, RA patients had a lower ejection fraction, increase LVM, and altered geometry [22]. When the patients were administered the biological product tocilizumab for one year, cardiac function improved, and LVM and geometry also showed improvement. Multivariate analyses revealed that disease activity in RA contributed the most to the improvements. Our study also showed improvement in regional function, associated with disease activity in RA, after a biological product was administered for one year [21]. This suggested that cardiac function and geometry associated with RA might be caused by RA itself (through inflammatory pathways mediated by cytokines). The findings also suggested that when RA was in the highly active phase, the resulting cardiac involvement remained subclinical, but had an impact on cardiac function, and could be diagnosed by CMR.

However, LGE relies on the comparison of focal myocardial damage against unaffected normal myocardium. Therefore, it is difficult to detect diffuse myocardial fibrosis. ECV and T1 mapping has proved to be a robust tool for the noninvasive assessment of diffuse myocardial fibrosis. Ntsui et al. reports that patients with RA had larger areas of focal myocardial edema, higher native T1 values and expansion of ECV compared with control subjects, and myocardial T1 and ECV were correlated with myocardial strain and RA disease activity [23]. Recently, Holmström M et al. demonstrated that myocardial T1 relaxation times are prolonged suggesting diffuse inflammation or fibrosis in RA and local myocardial scars and inflammation, visible as LGE, are also common, as are impairments of LV systo-diastolic function [24]. Miszalski-Jamka T et al. showed that cardiac involvement are common in Churg-Strauss syndrome and granulomatosis with polyangiitis (Wegener's) patients with normal electrocardiograms and transthoracic echocardiography, evaluating by using standard and feature tracking magnetic resonance [25]. Further studies of this diagnostic tool should be evaluated to discuss its utility.

Clinical Use of CMR in CVD due to RA

In general, cardiac involvement due to RA has features that are different from cardiac involvement caused by other diseases. RA patients reportedly have fewer typical cardiac symptoms. Kremers et al. showed that RA patients have a significantly higher risk of cardiac involvement when compared with non-RA subjects. They also indicated that RA patients are less likely to report symptoms of cardiac involvement and sudden cardiac death [4]. This evidence showed the importance of early assessment for subclinical heart disease in RA patients. Research studies on the stratification of high-risk patients with subclinical heart disease will be needed even more in the future; if heart disease could be diagnosed at an early stage with CMR, the prevention and treatment of CVD associated with RA would be followed. Rheumatologists should always consider the possibility of CVD as a complication of RA, in order to advance the diagnosis of subclinical heart disease.

*All authors attest that they have no financial conflicts of interest pertaining to this investigation

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