

## Cardiovascular magnetic resonance as a treatment guide for cardiac involvement in autoimmune rheumatic diseases.

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### Abstract

**Ventricular tachycardia is not unusual during the course of cardiac involvement in Autoimmune Rheumatic Diseases (ARDs). It may be the result of myocardial inflammation/ischemia, or in rare cases the result of immunosuppressive medication. Our aim in this mini review is to present the existing literature about the role of Cardiovascular Magnetic Resonance (CMR) as a guide for arrhythmia prediction/treatment in ARDs.**

CMR has been successfully used for diagnosis and follow up of cardiac involvement. Furthermore, its role in the identification of arrhythmogenic substrate has been extensively studied in non ARDs patients. However, there are only few data about its role in the detection of arrhythmogenic substrate in ARDs. In a recent study, T1/T2-mapping and Extracellular Volume Fraction (ECV) was found to offer incremental value as identifiers of arrhythmogenic substrates in ARD patients, beyond traditionally used indices and can thus guide Implantable Cardiac Defibrillator (ICD) implantation. Additionally, a recent multicenter CMR study showed that T2 ratio and % LGE had the greatest utility as independent predictors of rhythm disturbances in SSc patients. Finally, in a population of sarcoid patients with nonspecific symptoms, the presence of myocardial scar, assessed by LGE, was the best independent predictor of potentially lethal events, as well as other adverse events.

All previous mentioned studies showed that CMR has a great potential as a tool for arrhythmogenic substrate diagnosis and treatment guide in ARDs. However, multicenter studies are still needed to establish its role as a guide for arrhythmogenic substrate detection/treatment in ARDs.

**Keywords:** Autoimmune rheumatic diseases, Cardiovascular magnetic resonance imaging, Arrhythmia, Cardiovascular disease.

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### About the Study

Ventricular Tachycardia (VT) is not unusual during the course of cardiac disease in Autoimmune Rheumatic Diseases (ARDs). In Rheumatoid Arthritis (RA), atherosclerotic Coronary Artery Disease (CAD) may lead to acute coronary syndrome and VT [1]. Additionally, VT was detected after low dose methotrexate [2] and intravenous infusion of infliximab [3]. Giant Cell Myocarditis (GCM) can be also presented as VT with or without Congestive Heart Failure (CHF), during the course of RA, with poor prognosis, despite partial responsiveness to immunosuppressive medications [4]. In Systemic Lupus Erythematosus (SLE), although supraventricular tachycardia is the commonest finding, VT is not unusual and is mainly the result of CAD. Chloroquine plays a protective role in cardiac arrhythmias and conduction disturbances, observed in SLE [5]. Acute myocarditis and VT can be also found at the initial presentation of SLE in children and a combination treatment for heart failure, arrhythmias and immunosuppression

may lead to a favorable prognosis [6]. Acute myocarditis in SLE may present with VT as a first clinical sign [7]. Long QT syndrome with atrioventricular block and VT can be also developed in neonates of mothers with SLE. Finally, the chronic use of antimalarial drugs may also lead to VT [8]. In Systemic Sclerosis (SSc), the most frequent arrhythmias are Premature Ventricular Contractions (PVCs), appearing as monomorphic, single PVCs, bigeminy, trigeminy or pairs. Non-sustained VT was described in 7%-13%, while SCD was reported in 5%-21% of unselected SSc patients. VT and SCD can be also assessed during Polymyositis (PM) and Dermato-Myositis (DM), although their incidence has been poorly defined [9-12]. In our days, an implantable defibrillator represents a valuable adjunct to medical treatment in ARDs with lethal arrhythmias [13].

Cardiovascular Magnetic Resonance (CMR) is a non-invasive imaging modality without ionizing radiation with excellent performance in the evaluation of patients with and without ARDs.

Specifically, CMR can assess right/left ventricular function and also tissue characterization with regard to the presence of oedema/fibrosis [14]. In the case of VT evaluation, the role of CMR is indispensable. More specifically, it can diagnose myocardial inflammation, as a result of the systemic inflammatory process of the underlying disease that cannot be detected by echocardiography, before serious deterioration of cardiac function occurs. Additionally, diffuse, subendocardial vasculitis, small scars, due to inflammation or myocardial infarction, heart disease acuity and vascular inflammation can be diagnosed neither by echocardiography nor by nuclear techniques/cardiac CT, but can be potential foci of arrhythmia [15].

Our aim in this mini review is to present the existing literature regarding the role of CMR as a guide for arrhythmia prediction/treatment in ARDs.

The literature about the role of CMR in the evaluation of cardiac involvement in ARDs is rather scarce. CMR, as diagnostic and treatment guide, was first applied in Kawasaki disease and small vessel vasculitis [16-19]. The results of these CMR studies were used to start or modify anti-rheumatic and/or cardiac treatment [20]. Furthermore, in a population of treatment naive ARDs, it was identified the presence of various cardiovascular pathologies at the time of the ARD diagnosis that were not detected by echocardiography and needed immediate anti-rheumatic and cardiac treatment.

In the field of inflammatory arthritis, Kobayashi et al. showed that tocilizumab (TCZ) was associated with left ventricular dysfunction in RA patients, which correlated with a reduction in RA disease activity [21]. Additionally, Yokoe et al. showed that Global Circumferential Strain (GCS), Global Longitudinal Strain (GLS) and Global Radial Strain (GRS) assessed by Feature Tracking Cardiac Magnetic Resonance (FTCMR) can reveal subclinical LV dysfunction in patients with RA and can be used to determine the normalization of LV regional dysfunction induced by biologic disease-modifying anti-rheumatic drugs (bDMARDs) [22]. Additionally, early treatment of active RA is important, as myocardial function, detected with CMR tagging, was improved in Early Rheumatoid Arthritis (ERA) in parallel with decreasing inflammatory activity [23]. Ntusi et al. showed that anti-TNF therapy reduces subclinical myocardial inflammation and improves cardiovascular function in RA, AS and PsA and therefore, CMR can be used to track disease progression and response to therapy [24]. Finally, a recent paper reported the first evidence of vascular and myocardial abnormalities in an ERA randomized controlled trial cohort using CMR and showed improvement with DMARD therapy [25].

In the field of vasculitides, other investigators showed that although TCZ resulted in complete clinical and laboratory remission of Giant Cell Arthritis (GCA) over 52 weeks, Magnetic Resonance Angiography (MRA) signals in vessel walls normalized in only one-third of patients [26].

Regarding Systemic Lupus Erythematosus (SLE) patients with atypical cardiac symptoms/signs and normal echocardiography,

CMR assessed occult cardiac lesions including myocarditis, myocardial infarction and vasculitis that influenced both anti-rheumatic and cardiac treatment [27]. Another study showed that cardiac involvement, as observed by CMR, was frequent in SLE and not necessarily associated with typical symptoms. In these cases, CMR may help to detect subclinical cardiac involvement leading to earlier treatment [28]. Recently, native T1 and T2 mapping were found to facilitate the recognition of lupus myocarditis, reflect the response to anti-inflammatory treatment and were proposed as an effective, noninvasive, radiation and gadolinium contrast-free screening tool for lupus myocarditis evaluation [29].

In sarcoidosis, of all cardiac tests to detect cardiac sarcoidosis, CMR was the most valuable in the diagnosis and prognosis in a general sarcoidosis cohort. It was shown that echocardiography had an overall limited diagnostic value as a screening test, and an abnormal study, despite a high positive predictive value, may still need confirmation with CMR [30]. Furthermore, a large-extent LGE correlates with lack of LV functional improvement and high incidence of adverse outcomes in patients with cardiac sarcoidosis after steroid therapy [31].

In Systemic Sclerosis (SSc), CMR proved that fourteen days of treatment with nifedipine improves both myocardial perfusion and function [32]. Additionally, treatment with intravenous methylprednisolone, followed by prednisone and immunosuppressive therapy was evaluated using CMR and proved to be effective for treating myocardial involvement in SSc patients with idiopathic inflammatory myopathies, either alone or presenting as overlap syndromes [33]. Furthermore, a combination therapy with ambrisentan and tadalafil, was evaluated using CMR and found that significantly improved hemodynamics, RV structure/function/functional status in treatment-naive patients with pulmonary hypertension, due to systemic sclerosis (SSc-PAH) [34].

CMR has been successfully used for diagnosis and follow up of cardiac involvement, although multicenter studies are still missing. Furthermore, the role of CMR in the identification of arrhythmogenic substrate has been extensively studied in non ARDs patients [35]. However, there are only few data about its role in the detection of arrhythmogenic substrate in ARDs. In a recent study, T1/T2-mapping and ECV was found to offer incremental value as identifiers of arrhythmogenic substrates in ARD patients, beyond traditionally used indices and can thus guide Implantable Cardiac Defibrillator (ICD) implantation [36]. Additionally, a recent multicenter CMR study showed that T2 ratio and % LGE had the greatest utility as independent predictors of rhythm disturbances in SSc patients [37]. In another study, LGE among others was independent predictor of all events. Additionally, in a population of sarcoid patients with nonspecific symptoms, the presence of myocardial scar, assessed by LGE, was the best independent predictor of potentially lethal events, as well as other adverse events [38].

All previous mentioned studies showed that CMR has a great potential as a tool for arrhythmogenic substrate and treatment guide in ARDs. However, multicenter studies are needed in order to

establish its role as a guide for arrhythmogenic substrate detection/treatment in ARDs.

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