

Cardiovascular magnetic resonance in autoimmune rheumatic diseases: a clinical consensus document by the European Association of Cardiovascular Imaging

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Autoimmune rheumatic diseases (ARDs) involve multiple organs including the heart and vasculature. Despite novel treatments, patients with ARDs still experience a reduced life expectancy, partly caused by the higher prevalence of cardiovascular disease (CVD). This includes CV inflammation, rhythm disturbances, perfusion abnormalities (ischaemia/infarction), dysregulation of vasoreactivity, myocardial fibrosis, coagulation abnormalities, pulmonary hypertension, valvular disease, and side-effects of immunomodulatory therapy.

Currently, the evaluation of CV involvement in patients with ARDs is based on the assessment of cardiac symptoms, coupled with electrocardiography, blood testing, and echocardiography. However, CVD may not become overt until late in the course of the disease, thus potentially limiting the therapeutic window for intervention. More recently, cardiovascular magnetic resonance (CMR) has allowed for the early identification of pathophysiologic structural/functional alterations that take place before the onset of clinically overt CVD. CMR allows for detailed evalu-

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ation of biventricular function together with tissue characterization of vessels/myocardium in the same examination, yielding a reliable assessment of disease activity that might not be mirrored by blood biomarkers and other imaging modalities. Therefore, CMR provides diagnostic information that enables timely clinical decision-making and facilitates the tailoring of treatment to individual patients.

Here we review the role of CMR in the early and accurate diagnosis of CVD in patients with ARDs compared with other non-invasive imaging modalities. Furthermore, we present a consensus-based decision algorithm for when a CMR study could be considered in patients with ARDs, together with a standardized study protocol. Lastly, we discuss the clinical implications of findings from a CMR examination.

Keywords

echocardiography • coronary artery disease • inflammatory myocardial disease • inflammatory vascular disease • valvular heart disease • pulmonary hypertension • myocardial fibrosis • vessel fibrosis

Introduction

Autoimmune rheumatic diseases (ARDs) represent a heterogeneous group of disorders in which tolerance to self-antigens and/or immunoregulation are compromised, leading to inappropriate immune reactivity against diverse body tissues. Although novel targeted treatments for the management of ARDs have produced significant reduction of disease-associated mortality, patients with ARDs still experience a lower average life expectancy compared with the general population.¹ This is partly due to the increased incidence of cardiovascular disease (CVD) in this population, which has variable but clearly demonstrated adverse effects on prognosis.² The average 5-year survival rate in patients with inflammatory arthritis under treatment is currently comparable with that of the general population,³ but long-term life expectancy remains significantly lower by comparison.¹ Similarly, all-cause mortality in patients with systemic lupus erythematosus (SLE) and systemic sclerosis (SSc) is 2-fold and 4-fold higher, respectively, while being even higher for males and younger patients.³ Irrespective of aetiology, CVD in patients with ARDs may remain asymptomatic or cause few symptoms for considerable periods of time. As a result, clinically overt CVD often presents at a late stage, and carries a poor prognosis.⁴ The main types of CVD seen in patients with ARDs are summarized in *Table 1*.

Aim of the consensus

Non-invasive cardiovascular imaging is being increasingly utilized for the early identification and evaluation of CVD in patients with ARDs, with cardiovascular magnetic resonance (CMR) in particular playing an important role in this regard. The aims of this consensus document are as follows:

- (1) to place CMR in context compared with other non-invasive cardiovascular imaging modalities for use in patients with ARDs,
- (2) to propose a decision algorithm for the evaluation of suspected CVD in patients with ARDs, including specific indications for when a CMR examination might be considered,
- (3) to propose a standardized CMR study protocol for the evaluation of CVD in patients with ARDs, and
- (4) to present the clinical implications of potential findings in a CMR examination.

Methods

Development process

The document begins with a narrative review of the literature on the use of CMR in patients with ARDs composed by an expert panel of

cardiologists and cardiovascular imaging experts specialized in ARDs, as well as rheumatologists. In addition, CMR applications in patients with ARDs are reviewed in the context of other imaging modalities, to delineate in which cases CMR should be performed, and how study interpretation can be optimized to assess cardiac structural and functional alterations in patients with ARDs. The review was performed to add relevant statements, eliminate redundancies, and improve overall quality in the utilization of CMR to benefit patients with ARDs, as per the European Society of Cardiology guidelines for position papers.

Pathophysiology of cardiovascular involvement in ARDs

The most prevalent ARDs presenting with significant CVD are illustrated in **Key point 1** and are summarized in the following sections.

Key point 1. Autoimmune rheumatic diseases with cardiovascular involvement.

- (1) Rheumatoid arthritis and spondyloarthropathies
- (2) Systemic lupus erythematosus
- (3) Systemic vasculitides
- (4) Inflammatory myopathies
- (5) Mixed connective tissue diseases
- (6) Systemic sclerosis
- (7) Sarcoidosis (autoimmune but not considered an ARD)

Rheumatoid arthritis and the spondyloarthropathies

Accelerated atherosclerosis in patients with rheumatoid arthritis (RA) leads to a 2-fold greater incidence of coronary artery disease (CAD), stroke, heart failure (HF), and peripheral arterial disease compared with the general population.⁴ Valvular heart disease (VHD) is also an often-overlooked disease manifestation in patients with RA.⁵ Spondyloarthropathies (SpA) is associated with VHD, myocardial involvement may manifest as myocarditis, and/or HF, while pericardial disease is rarer.⁶ In addition, CAD, myocardial infarction (MI), and stroke may also occur in the setting of SpA.^{6,7} After accounting for cardiovascular risk factors, age, sex, and disease duration, the incidence of CVD in patients with SpA does not differ significantly from the incidence of CVD in patients with RA.⁸

Table 1 Manifestations of CVD in patients with ARDs

| Affected tissue | Responsible structure | Pathology | Clinical presentation |
|---------------------------------|--|--|---|
| Heart | Coronary arteries: | Vasculitis (see also 'Blood Vessels'), | Myocardial ischaemia, myocardial infarction, endothelial dysfunction-HF |
| | (a) Epicardial disease | vascular spasm, atherosclerosis, ectasia/aneurysm | |
| | (b) Microvascular disease | | |
| | Left and/or right ventricular myocardium | Systolic/diastolic dysfunction, inflammation, infarction, oedema, replacement/diffuse fibrosis | Myocarditis, HFpEF, HFrEF, cardiac rhythm disturbances |
| | Any heart valves | Valvular dysfunction | Valvular regurgitation and/or stenosis, Valvular thickening |
| | Conduction system, cardiomyocytes | Cardiac conduction abnormalities | Arrhythmias: (a) Supraventricular (b) Ventricular/sudden cardiac death |
| | Pericardium | Inflammation | Pericarditis: (a) Without effusion (b) With effusion (c) Constrictive |
| Lungs/ pulmonary arteries | Pulmonary arterial circulation | Inflammation, vasoconstriction, endothelial proliferation, chronic thromboembolic disease | Pulmonary hypertension Types 4 and 5 |
| | Lung parenchyma | Inflammation, fibrosis | Pulmonary hypertension Type 3 |
| Blood vessels | Small vessels | Inflammation | Myocarditis, myocardial ischaemia/infarction, HF, peripheral arterial disease, hypertension, mesenteric angina, retinopathy, aortic regurgitation |
| | Medium vessels | | |
| | Great vessels | | |

HF, heart failure; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction.

SLE/antiphospholipid syndrome

CVD is a major cause of morbidity/mortality in patients with SLE mainly due to the development of CAD, vasculitis, and myocarditis.⁹ The prevalence of CAD has been reported at ~6–10%, and the risk of developing CAD is 4–8-fold higher in patients with SLE, compared with the general population.⁹ Clinically overt myocarditis appears in 3–15% of patients with SLE, usually in association with pericarditis; however, it is more common at autopsy, suggesting an important subclinical component.⁹ Antiphospholipid syndrome (APS) may co-occur in patients with SLE (secondary APS) or may manifest independently. In the setting of APS, microvascular CAD constitutes a disease-specific manifestation.¹⁰ CMR has been successfully used to diagnose CVD in both SLE and APS, and to detect active clinical and subclinical myocardial disease.^{11–13} Autoimmune valvular disease may either accompany SLE or may result from secondary APS,¹¹ and constitutes an important risk factor for stroke.¹⁴ Immunoglobulin and complement deposition on valvular structures may result in Libman-Sacks vegetations with valvular regurgitation, while stenosis is rare. In most patients VHD is asymptomatic, but in those with severe mitral regurgitation, HF may impair quality of life and may also negatively affect prognosis.⁵

Systemic vasculitides

Typical lesions in patients with vasculitides include inflammation and fibrinoid necrosis of the blood vessel wall. The classification of systemic necrotizing vasculitides depends on the predominant calibre

of vessels affected.¹⁵ Based on endomyocardial biopsy (EMB) findings, myocardial inflammation and small vessel involvement may lead to ischaemia and HF.¹⁶ Vasculitis in patients with SLE, SSc, and RA may affect the small vessels and can be life-threatening.¹⁵ CMR has been successfully used in the diagnosis and follow-up of patients with systemic vasculitides¹⁷ (Figure 1).

Inflammatory myopathies

The prevalence of CVD in patients with polymyositis (PM)/dermatomyositis (DM) varies between 6 and 75% and may be clinically overt at diagnosis or may become clinically overt after initiation of treatment, or even during remission; it is usually clinically silent but may lead to fatal arrhythmias or HF.¹⁸ CMR may detect early myocardial involvement in asymptomatic patients with PM/DM without overt left ventricular (LV) dysfunction¹⁹ (Figure 2).

SSc (scleroderma)

In patients with SSc, the myocardium is affected by inflammation followed by diffuse interstitial myocardial fibrosis, while in parallel, an epicardial vasculopathy predominantly involving the media and intima vascular layers takes place.²⁰ CVD is responsible for 15% of all deaths in patients with SSc, either due to primary myocardial inflammation–fibrosis, or secondary pulmonary arterial hypertension.^{20,21} Myocarditis may rapidly lead to the development of myocardial fibrosis together with parallel involvement of the microvasculature.²¹ CMR can provide additional information compared with

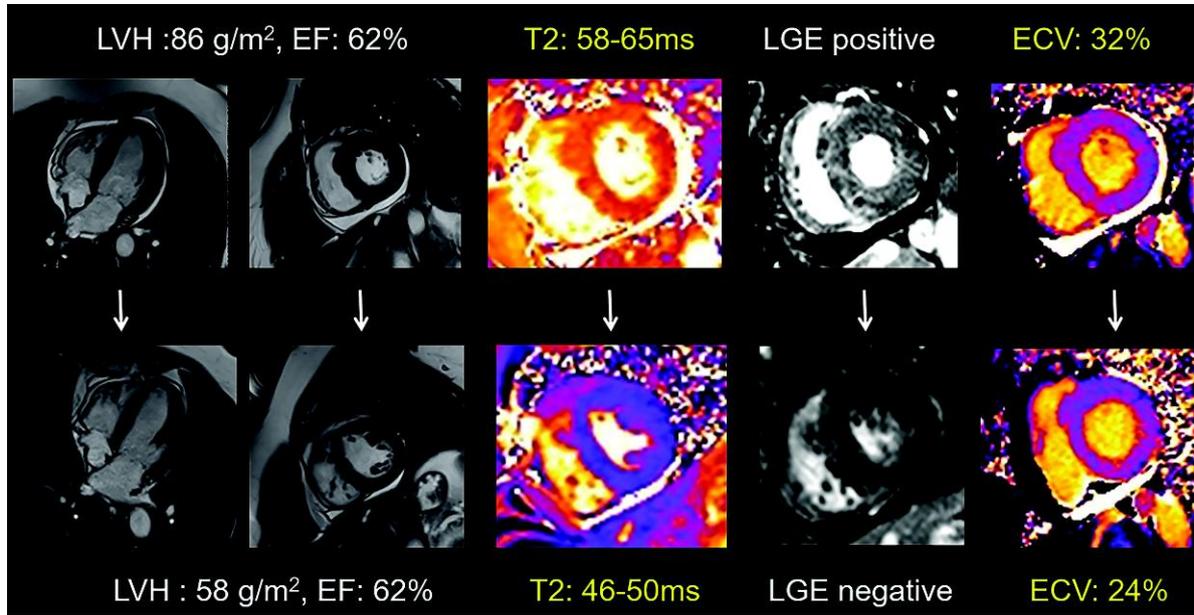


Figure 1 CMR imaging of a patient with eosinophilic granulomatosis with polyangiitis (Churg-Strauss syndrome) at diagnosis (first row) and 10 days thereafter (second row). > First and second columns: Cine imaging demonstrating left ventricular hypertrophy and initially oedematous appearance of the myocardium (upper picture). Reduction of the measured LV mass and LV wall thickness can be observed over time. > Third column: T₂-weighted imaging. The uppermost image was from a study performed on a system not allowing T₂ mapping. Nevertheless, a higher T₂ signal intensity is observed in the myocardium. In the next MRI study, quantitative T₂ mapping was performed, demonstrating progressive normalization of the T₂ values ($N \leq 50$ ms) suggesting the resolution of oedema. > Fourth column: Inversion recovery sequence demonstrating diffuse late gadolinium enhancement (LGE) with an abnormal grey and oedematous appearance of the myocardium. At 10 days, LGE signal is prominent at the level of the mid septum. > Fifth column: T₁ mapping with quantification of the ECV.

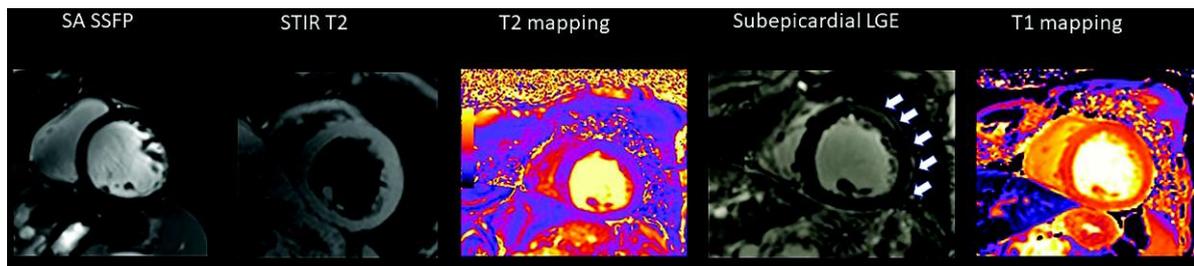


Figure 2 CMR imaging of a patient with DM and acute shortness of breath. > First image: short axis SSFP for function assessment (LVEF = 21%). > Second image: STIR-T₂ short axis image showing diffuse oedema (T₂ ratio of myocardium over skeletal muscle is 2.3). > Third image: T₂ mapping showing abnormally elevated values (60 ms), due to myocardial oedema. > Fourth image: Inversion recovery short axis image showing extensive subepicardial fibrosis in the antero-lateral and inferior wall of LV (arrows). > Fifth image: native T₁ mapping with abnormally elevated values (1330 ms), due to myocardial oedema.

echocardiography in patients with SSC,²² and may identify subclinical myocardial involvement in asymptomatic patients.²³ The main pathologic mechanisms in SSC are chronic myocardial inflammation and focal/diffuse myocardial fibrosis²³ (Figure 3). CMR also has prognostic implications in patients with SSC.^{24,25}

Mixed connective tissue diseases

Raynaud's phenomenon of the epicardial vasculature, similar to that observed in the fingers, and development of pulmonary arterial

hypertension, are the most important cardiac pathologies in mixed connective tissue disease (MCTD).²⁶ In these patients, CMR can reveal MI, inflammation, diffuse subendocardial fibrosis, and diffuse perfusion defects, that may necessitate further investigation and specific treatment.²⁷

Sarcoidosis

Sarcoidosis (SRC) is not officially considered an ARD. However, due to its inflammatory nature and pathologic similarities to ARDs, as

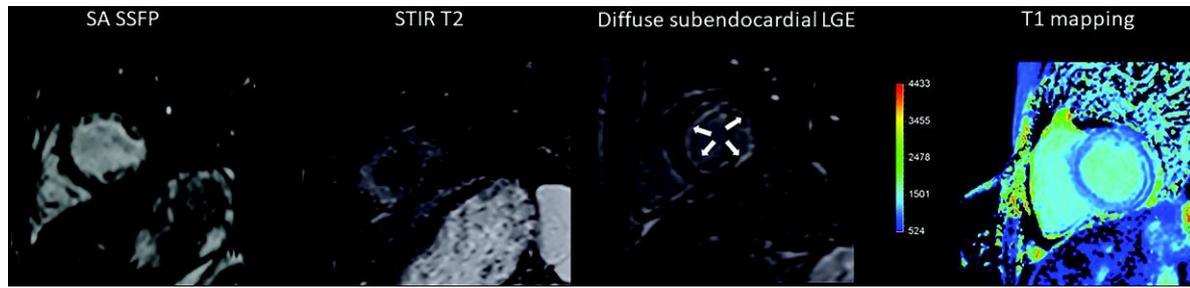


Figure 3 CMR imaging of a young patient with diffuse SSc and multifocal ventricular arrhythmias. The patient died suddenly, due to ventricular tachycardia. > First image: short axis SSFP sequence to assess ventricular function (LVEF = 57%). > Second image: STIR-T₂ short axis image showing extensive, diffuse oedema (T₂ ratio of myocardium over skeletal muscle is 2.5). > Third image: inversion recovery short axis image showing diffuse subendocardial fibrosis of LV (arrows). > Fourth image: Short axis T₁ mapping showing abnormally elevated values (1320 ms) due to severe myocardial oedema.

well as the crucial role of CMR in the diagnosis and follow-up monitoring of its cardiac manifestations, SRC is included in this consensus document. Autopsy studies have shown that CVD occurs in ~25% of patients with SRC and carries a poor prognosis.²⁸ Autopsy confirmed myocardial granulomas occur in up to 50% of fatal SRC, and cardiac dysfunction with sudden death in up to 67% of cardiac SRC.²⁹ Despite the high prevalence of cardiac SRC at autopsy, only 5% of patients present with clinically overt CVD and only 40–50% of them are correctly diagnosed during their lifetime.²⁹ CMR and fluorodeoxyglucose-positron emission tomography (FDG-PET) can detect early CVD in SRC and predict cardiac death.³⁰

Large CMR outcome studies are available today,^{31,32} while prospectively designed diagnostic accuracy studies in comparison with histology are still lacking. Similar to FDG-PET, the diagnostic accuracy of CMR in cardiac SRC is hampered by the lack of a gold standard. The first report on the diagnostic accuracy of CMR for cardiac SRC showed a sensitivity of 100% and specificity of 78% vs. the clinically used Japanese Criteria (JMHW).³⁰ The relatively low specificity can be explained by the low diagnostic sensitivity of JMHW.³⁰ While evidence of CMR performance vs. EMB is scarce, large outcome studies have demonstrated the excellent prognostic value of late gadolinium enhancement (LGE) for predicting malignant arrhythmias and sudden cardiac death in patients with SRC.^{31,32} Promising results have been reported for *in silico* modelling of CMR and FDG-PET to predict ventricular tachycardia, with LGE showing strong predictive power.³³

Potential cardiotoxicity of immunomodulatory treatments

A number of immunomodulatory treatments used in clinical practice for the management of various ARDs are known to be associated with cardiotoxic effects. These are discussed in detail elsewhere.^{34,35} CMR has already shown clinical utility in patients with cardiotoxicity cause by immune checkpoint inhibitors³⁶ and can similarly provide important diagnostic information in cases where such cardiotoxicity manifests as myopericarditis or HF.³⁷ However, studies specifically investigating the utility of CMR for the evaluation of cardiotoxicity in patients with ARDs are currently lacking.

Non-invasive cardiovascular imaging modalities for the evaluation of patients with ARDs

Echocardiography

Echocardiography is the cornerstone imaging modality for assessing cardiac morphology/function. Speckle tracking echocardiography has been successfully used for the assessment of subclinical LV dysfunction,³⁸ specifically in patients with SSc.^{39,40} Moreover, stress echocardiography has similar diagnostic/prognostic accuracy to radionuclide stress testing, but at a lower cost and without the need for exposure to ionizing radiation. Coronary flow reserve assessed by Doppler echocardiography can reveal microvascular disease in patients with ARDs⁴¹ and in patients with subclinical epicardial CAD,⁴² although this is not routinely employed in clinical practice. Stress echocardiography can also detect exercise-induced pulmonary hypertension (PH) in patients with SSc, but routine clinical implementation is also not yet established.⁴³

Stress myocardial perfusion scintigraphy

Myocardial perfusion scintigraphy (MPS) can assess patients with suspected CAD, as occurs often in patients with ARDs.¹ We should acknowledge its wide use across Europe and therefore its high availability as well as the strong prognostic data that support the use of this technique in the evaluation of epicardial coronary artery disease in ARDs.¹ However, MPS has certain limitations including the need for exposure to ionizing radiation, as well as the presence of imaging artefacts and low spatial resolution which do not allow for quantification of subendocardial ischaemia and small scars.^{44–46} The MR-IMPACT trial⁴⁵ and the CE-MARC study⁴⁶ support the wider adoption of CMR for the assessment of CAD rather than SPECT, owing to the higher diagnostic accuracy of CMR combined with concerns about ionizing radiation exposure, particularly in young women.⁴⁶ In a meta-analysis comparing myocardial perfusion assessments with single photon emission tomography (SPECT), PET, and CMR, all modalities yielded a high sensitivity (between 88 and 91% on a patient basis), but with significant differences in specificity.⁴⁷ SPECT had the lowest specificity, while PET and CMR

achieved the highest diagnostic performance, with stress CMR providing an important alternative without ionizing radiation.⁴⁷ In current European⁴⁸ and American⁴⁹ guidelines, all non-invasive modalities are recommended at similar level.^{49,50}

PET and PET/computed tomography

PET/computed tomography (CT) is routinely used in oncology but less often in cardiology. In addition to accumulation of FDG in tumour cells, macrophages also demonstrate increased FDG uptake, which is relevant in the context of vascular inflammation. As such, ascending aortic FDG uptake has been identified in patients with RA without clinical CVD.⁵¹ Although there are currently no guidelines regarding PET imaging for large vessel vasculitis (LVV) and polymyalgia rheumatica (PMR), FDG-PET/CT may be of synergistic value for optimal disease monitoring in LVV.⁵² Lastly, the higher sensitivity of FDG-PET is important in capturing cardiac SRC at earlier stage, which may improve responsiveness to immunosuppressive therapy and guide treatment follow-up.⁵³ Yet, its routine use in clinical practice is limited by the lack of availability, high costs, the use of ionizing radiation, and the lack of expertise.

Computed tomography angiography

Computed tomography angiography (CTA) is routinely used for the non-invasive assessment of the coronary arteries and large vessels. Compared with age-matched controls, patients with RA had a greater prevalence of asymptomatic CAD, with higher mean coronary calcium score, more frequent multivessel disease, as well as more high-risk plaques.⁵⁴ Furthermore, the use of biologic disease modifying anti-rheumatic drugs has been associated with reduced CVD risk based on CTA findings.⁵⁵ Lastly, in patients with Takayasu arteritis there is a high prevalence of great vessel and coronary arterial abnormalities, regardless of disease activity or symptoms.⁵⁶ Therefore, CTA is widely used for the diagnosis of both LVV and CAD.⁵⁶ In patients with Kawasaki disease, CTA is not indicated for serial evaluation, because patients are most commonly children or young adults. Radiation and nephrotoxic contrast agents may also limit its routine use in serial evaluation.

Cardiovascular magnetic resonance

CMR can analyse a multitude of important characteristics of cardiovascular tissues, many of which may be perturbed in various ARDs. In this regard, CMR can provide considerable diagnostic information.⁵⁷ Specifically, CMR can assess:

- (5) Cardiac structure/anatomy and function using T₁-weighted (T₁-W) imaging and balanced steady-state free precession (bSSFP), respectively.
- (6) Myocardial perfusion and replacement fibrosis using first-pass T₁-W imaging and late gadolinium T₁-enhanced imaging (LGE), respectively.
- (7) Myocardial oedema using short-tau inversion recovery T₂-weighted images (STIR-T₂), as well as native T₁ and T₂ mapping.
- (8) Diffuse myocardial fibrosis using native T₁ mapping and extracellular volume fraction (ECV) quantification.
- (9) Myocardial inflammation using STIR-T₂, early gadolinium enhancement (EGE), LGE,⁵⁸ as well as native T₁ mapping, T₂ mapping and ECV.⁵⁹
- (10) Valvular disease (mainly mitral regurgitation) using LV planimetry and phase-contrast imaging of the aortic root.

- (11) Vascular disease with or without contrast agents with T₁-W imaging.
- (12) PH using bSSFP, LGE, and 4D-flow.

The individual sequences as well as the suggested imaging protocols for each domain are described in detail in the following sections. The immediately following section focuses specifically on clinical scenarios where CMR could potentially be considered, as well as what information it could provide in the corresponding context.

Summary

The performance of different imaging modalities in the evaluation of the various clinical scenarios that are pertinent to ARDs are outlined in **Key point 2**.

Key point 2. Performance of cardiovascular imaging modalities in various manifestations of CVD in patients with autoimmune rheumatic diseases.⁶¹

| CVD manifestation | Echo | SPECT | PET | CT | CMR |
|---------------------------|------|-------|------|-----|------|
| Myocardial ischaemia | ++ | +++ | ++++ | – | ++++ |
| Coronary anatomy | – | – | + | +++ | +++* |
| Pericarditis** | +++ | – | – | ++ | ++++ |
| Myocarditis | +/- | – | +/- | – | ++++ |
| Heart failure*** | +++ | ++ | ++ | ++ | ++++ |
| Pulmonary hypertension | ++++ | – | – | – | +++ |
| Valvular disease | ++++ | – | – | – | +++ |
| Vascular inflammation**** | +/- | – | +++ | ++ | +++ |

CVD, cardiovascular disease; Echo, echocardiography; SPECT, single photon emission computed tomography; PET, positron emission tomography; CT, computed tomography, CMR, cardiovascular magnetic resonance.
 *Paediatric patients.
 **Particularly, pericarditis without effusion can be detected by CMR by positive LGE of the pericardium.
 ***CMR is particularly useful for identifying the aetiology of heart failure (e.g. case of scleroderma patient with infarction, pericarditis, interstitial myocardial fibrosis but no myocarditis; see also Figure 4).
 ****Both CT and CMR do not assess vascular inflammation per se, but they can assess the structural consequences of inflammation in large vessels (vessel thickening). In this regard, both CT and CMR are of equal value.

Clinical scenarios for CMR in the evaluation of cardiovascular involvement in ARDs

Pericardial disease

Pericardial inflammation

Pericarditis is the most frequent and often neglected cardiac manifestation of ARDs. Approximately 30–50% of patients with RA have clinically silent pericarditis at autopsy.⁶⁰ In most cases, it is detected incidentally during routine echocardiography.⁶⁰ CMR using

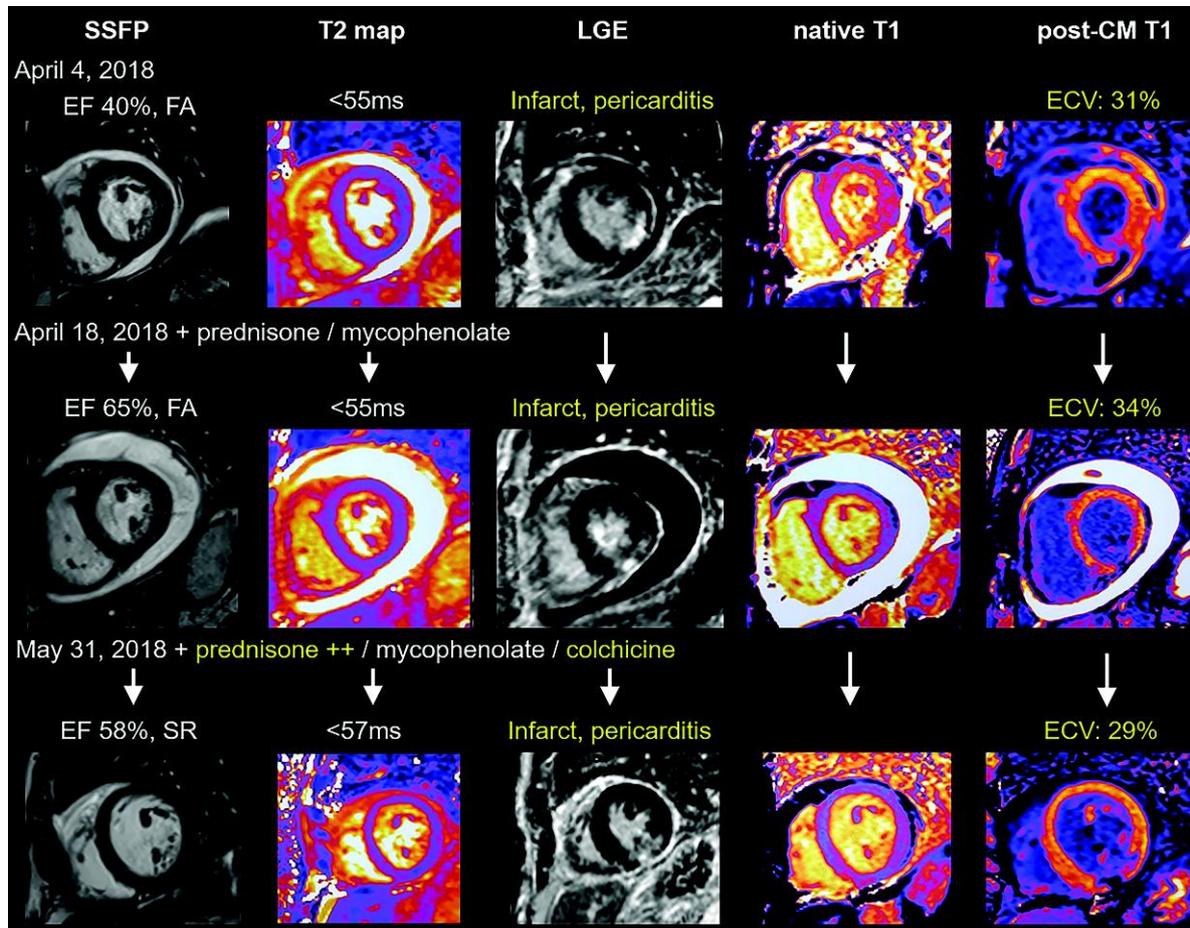


Figure 4 CMR images of a female patient, 78-years old, with SSc, who developed increasing dyspnoea and heart failure symptoms. CMR revealed a lateral infarction (subendocardial LGE) and the follow-up coronary angiogram showed diffuse severe disease of the small epicardial vessels of the circumflex coronary artery and no major occlusions. The CMR also showed acute pericarditis (LGE pos) and minor effusion, no myocarditis (T₂ in the upper normal range) and interstitial fibrosis (ECV >28%). The immunosuppressive treatment was continued with mycophenolate, and prednisone dosing was slightly increased. A follow-up CMR showed progressive pericarditis (LGE pos and increase of effusion). To control this and prevent further infarctions, prednisone was given in high doses and colchicine was added. Another follow-up CMR showed almost complete resolution of pericardial effusion, but still slightly persisting pericarditis (LGE pos). Prednisone was reduced to maintenance dose. The patient improved clinically. > First column: SSFP cine images demonstrating the evolution of left ventricular function at diagnosis and during treatment. > Second column: T₂ mapping at diagnosis and during treatment showing no evidence of oedema. > Third column: inversion recovery sequence demonstrating subendocardial LGE in the lateral wall of the LV with concurrent pericarditis. > Fourth columns: T₁ mapping quantification at diagnosis and during treatment. > Fifth columns: quantification of ECV at diagnosis and during treatment.

T₁-weighted black blood and bSSFP sequences, allows for anatomical characterization of the pericardium. Native T₁ and T₂ mapping provide additional information on pericardial inflammation and oedema. The inflamed pericardium is enhanced after the injection of gadolinium-based paramagnetic contrast agent, which constitutes a key marker of pericardial inflammation.⁶¹ The persistence of pericardial enhancement despite standard medical treatment in symptomatic patients, should prompt enhanced and/or prolonged treatment.⁶¹

Pericardial effusion

CMR criteria for pericardial effusion are based on the total amount of fluid in the pericardial sac. If the intrapericardial space anterior to right ventricular (RV) on bSSFP is <4 mm, the effusion is considered small; ≥ 5 and ≤10–15 mm as moderate (100–500 mL) and >10–

15 mm as large. Native T₁ mapping of the pericardial fluid provides information on its composition. A native T₁ mapping cut-off value of 3013 ms can differentiate transudates from exudates with a sensitivity of 94% and a specificity of 79%,⁶² with lower values suggesting exudative pericardial effusions.⁶² In addition, native T₁ mapping and T₂ mapping may reveal coexisting myocardial inflammation/fibrosis (myopericarditis). Finally, CMR can reliably quantify pericardial thickening.

Cardiac tamponade

Echocardiography is the modality of choice in the evaluation of tamponade and CMR is rarely used to assess haemodynamic compromise.⁶³

Constrictive pericarditis

In a patient with suggestive history and physical examination for constrictive pericarditis, a thickened pericardium (>4 mm), visualized with bSSFP or LGE, is a potential indicator of constriction.⁶⁴ However, constriction is characterized by both anatomic and haemodynamic alterations and therefore, the diagnosis of constrictive pericarditis should be ultimately confirmed by cardiac catheterization. In this context, CMR can assess the characteristic S-shaped interventricular septal bounce using bSSFP and can identify dilation of the inferior or superior vena cava and/or coronary sinus. Real time cine may demonstrate the effect of free breathing on ventricular interdependence, a unique marker of constrictive pericarditis.^{64–66} Importantly, in symptomatic patients with thickened pericardia, pericardial enhancement on LGE combined with either high signal intensity on T₂-W and/or elevated T₁/T₂ mapping reflect active inflammation and could be used for preferential initiation of anti-inflammatory treatment as opposed to surgery.⁶³

Myocardial disease

Functional abnormalities

Functional abnormalities are aspecific characteristics of various clinical abnormalities including myocarditis, myocardial ischaemia, MI, Takotsubo cardiomyopathy, cardiac trauma, and others, and may manifest as wall motion abnormalities (hypo-/akinesia), reduced ventricular systolic function, and diastolic dysfunction.⁶⁷ The aforementioned abnormalities can be evaluated using bSSFP.

Myocardial inflammation

Autoimmune myocardial inflammation is primarily observed in patients with SLE, RA, SpA, and SSc.⁶⁸ CMR can identify the presence of myocardial oedema using STIR-T₂ and native T₁ mapping and T₂ mapping, as well expansion of the extracellular space due to oedema or fibrosis using LGE, native T₁ mapping, and ECV. The previously developed Lake Louise criteria⁵⁸ as well the more recently updated criteria that also include all T₁- and T₂-based indices,⁵⁹ can serve as a summary score for confirming the diagnosis of myocardial inflammation.

Myocardial infarction

MI may be the consequence of either epicardial CAD or microvascular CAD, with each causative pathophysiologic background being associated with a distinct pattern of myocardial fibrosis.⁶⁹ Namely, MI secondary to epicardial CAD may present with either transmural or subendocardial fibrosis, while MI due to microvascular CAD exclusively presents as subendocardial lesions.⁶⁹ CMR can also characterize the acuity of MI, as newer lesions will manifest with concomitant myocardial oedema, which can be assessed using T₂-based sequences, while potential endomyocardial haemorrhage, which confers an ominous prognosis, can be detected using T₂*.⁷⁰ Older lesions in contrast, exhibit normal values in T₂-based imaging, with the additional presence of replacement fibrosis, as identified using LGE. T₁ mapping and ECV may become abnormally elevated at the infarct site both in the acute and chronic phase, as they reflect both myocardial oedema and fibrosis. Elevations of these indices in remote myocardial tissue confer a poor prognosis.⁷¹

Vascular abnormalities

Great vessel disease

Non-contrast MR angiography (MRA) can provide pivotal information regarding large vessel aneurysm/stenosis without the need for contrast administration, while black blood images depicting increased wall thickness in a circumferential pattern characterize LVV.⁷² Contrast-enhanced (CE) MRA is also frequently used to establish large vessel patency and identify mural inflammation in large vessel vasculitides.⁷² In patients with suspected TA, CMR and PET-CT are the best modalities to detect mural inflammation or luminal changes. In young patients with TA, CMR is preferred to limit radiation exposure.⁷³ PET-CT can be considered as a first-line imaging modality in patients with chronic peri-aortitis and may aid in detecting other affected organs when peri-aortitis is part of a systemic disorder.⁷⁴ Combined PET-CMR may become the imaging modality of choice for patients with LVV in the future.⁷⁴

Coronary artery anatomy

Coronary artery vasculitis imaging is feasible using CMR methods that are presently at the investigational level but are nonetheless important specifically for the evaluation of children with Kawasaki disease and coronary artery aneurysms.⁷⁵ Moreover, stress CMR can be used to assess myocardial ischaemia in Kawasaki disease.⁷⁶

Pulmonary hypertension

Echocardiography remains the standard imaging modality for non-invasively estimating pulmonary artery pressure (PAP), with CMR playing an important complementary role.⁷⁷ Namely, CMR can uniquely provide important structural and functional information on the pulmonary artery and RV, which is of significant prognostic value.⁷⁷ bSSFP allows for accurate quantification of RV mass, volumes, and wall motion abnormalities with high reproducibility.⁷⁷ LGE at the RV insertion points is commonly found in PH and is not associated with disease severity.⁷⁷ A previously proposed CMR-based model using the interventricular septum angle, RV-LV mass ratio, and PA anatomy, was documented to have a sensitivity of 93% and specificity of 79% to detect PH non-invasively.⁷⁸ Lastly, abnormal flow patterns in the main pulmonary artery (MPA) have been identified using 4D-flow CMR and have been associated with PH. 4D-flow CMR can also be used to estimate mean PAP (mPAP) and MPA wall shear stress (WSS), with reliable quantification of tricuspid regurgitation.⁷⁹

Valvular heart disease

Echocardiography remains the main imaging modality used for the initial assessment and long-term follow-up of patients with ARD-induced VHD. However, CMR is also an excellent modality for serial assessment of VHD in this population, considering its low inter-study variability.⁸⁰ In patients with mitral regurgitation, total LV stroke volume is equivalent to the total aortic forward stroke volume (total anterograde flow) plus the mitral regurgitant volume (retrograde mitral flow), all of which can be calculated with CMR using LV planimetry and phase-contrast imaging of the aortic root.

In aortic stenosis, phase-contrast velocity mapping can measure peak velocity across the valve. However, this approach is reserved for patients with poor acoustic windows because the lower

temporal resolution of CMR compared with Doppler echocardiography may lead to underestimation of disease severity. Aortic valve area (AVA) can be measured with CMR using planimetry,⁸⁰ although this technique remains inferior to AVA assessment by Doppler echocardiography. Conversely, the reproducibility of CMR in quantifying the severity of valvular regurgitation is superior to TTE and provides powerful prognostic information.⁸¹

CMR sequences for the investigation of CVD in patients with ARDs

Cardiac function assessment using bSSFP

The CMR pulse sequence used for functional evaluation is bSSFP. It is the gold standard for the assessment of cardiac anatomy, mass, wall motion, atrial and ventricular function.⁶⁸ CMR is also ideal for the assessment of RV function, which is of special interest in patients with ARDs, and difficult to quantify using echocardiography.⁶¹

T₁-based sequences

T₁-W imaging is ideal for anatomical and morphological assessment by CMR.

Late gadolinium enhancement

LGE using T₁-W inversion recovery pulse sequences 10–15 min after gadolinium-based intravenous contrast administration, allows for the detection and quantification of myocardial replacement fibrosis (scar).⁶⁸ LGE may also detect marked expansion of the extracellular space in amyloidosis (amyloid deposition and fibrosis), and in PH (myocardial disarray with increased collagen content without focal replacement fibrosis). In myocarditis, LGE predominantly reflects inflammation with or without fibrosis, depending on the timing of post-contrast imaging.⁶⁸ In the acute phase of myocarditis, LGE correlates with myocardial necrosis (associated with oedema as assessed by T₂ mapping), while in the chronic phase, it predominantly corresponds to fibrosis (with less or no oedema).⁶⁸ Thrombi (if not organized) do not accumulate contrast, making LGE ideal in detecting/excluding the presence of recent thrombi.⁸² Moreover, contrast accumulation within adherent organized thrombi is typically slower than in more vascularized scar, allowing for its distinction.⁸²

MI is characterized by subendocardial or transmural LGE along the distribution of epicardial coronary arteries. Subepicardial or patchy LGE usually in the inferolateral wall is characteristically associated with myocarditis. Finally, diffuse subendocardial LGE that does not follow the typical distribution of coronary myocardial territories is often associated with small vessel vasculitides, severe cases of SSc, APS, or RA.⁶⁸

Stress CMR

First-pass T₁-W imaging after pharmacologic hyperaemic stress with adenosine (or dipyridamole, adenosine triphosphate, or regadenoson) and bolus injection of paramagnetic gadolinium-based contrast agent can reliably and reproducibly assess myocardial perfusion during stress.^{45,68} This approach allowed the detection of perfusion

defects in patients with SSc and APS without cardiac symptoms.^{10,83} Unlike other imaging modalities, stress CMR is not limited by body habitus, acoustic windows, or operator expertise, and is the modality of choice for the assessment of CAD and particularly microvascular disease. Stress CMR is also especially useful for the evaluation of patients with ARDs that are unable to exercise adequately due to arthritic lesions.⁴⁵

T₁ mapping and ECV

Although LGE is well-validated for the detection of replacement fibrosis, it has inherent disadvantages when assessing diffuse myocardial fibrosis, as it is based on signal intensity differences between the scarred and normal myocardium.^{68,84} To overcome this limitation, T₁ mapping and ECV were developed. T₁ mapping [native (pre-contrast) T₁ mapping and post-contrast T₁] provides a quantitative assessment of tissue T₁ values and enables identification of diffuse myocardial fibrosis, which may be undetectable by currently used circulating biomarkers.⁷⁷ Furthermore, native T₁ mapping is also sensitive to myocardial oedema and iron overload.⁶⁸ Normal values of T₁ mapping are 995.8 ± 30.9 ms at 1.5T⁸⁵ and 1183.8 ± 37.5 ms at 3.0 T.⁸⁶ However, field strength and the types of pulse sequence used influence T₁ mapping measurements. Therefore, normal values should be generated specifically for each MR unit for use in clinical practice.⁸⁴

Post-contrast T₁ mapping is used for ECV calculation in combination with native T₁ mapping. ECV estimation requires measurement of myocardial and blood T₁ mapping, before and after the intravenous administration of gadolinium-based contrast agents; ECV is calculated using the following formula:

$$ECV = (1 - \text{hematocrit}) \times \frac{(1/T1_{(\text{myo post-contrast})}) - (1/T1_{(\text{myo pre-contrast})})}{(1/T1_{(\text{blood post-contrast})}) - (1/T1_{(\text{blood pre-contrast})})}$$

Normal ECV values of 25.3 ± 3.5% have been reported in healthy individuals at 1.5 T⁸⁴ and 26.6 ± 3.2% at 3.0 T.⁸⁷ Increased ECV is most often due to excessive collagen deposition as in diffuse fibrosis accompanying SSc,⁸⁴ but may also occur due to amyloid deposition in amyloidosis, or disease processes leading to myocardial oedema/inflammation and subsequent expansion of the extracellular space.⁸⁴ Specifically in the setting of myocardial inflammation, ECV is more likely to represent the presence of oedema, rather than diffuse fibrosis.⁸⁸ ECV also exhibits good agreement with histology.⁸⁴ ECV is more reproducible than native and post-contrast T₁ mapping at different field strengths and with different acquisition techniques and shows less variability between vendors.⁷⁷ As such, at the time of writing, ECV is the only parametric CMR index that is comparable between MR units of different field strengths. Patients with ARDs often have higher values of T₁ mapping, T₂ mapping, and ECV compared with healthy controls,⁸⁵ with greater differences in native T₁ and T₂ mapping, which seem to be independent of LGE presence.⁸⁶

T₂-based sequences

T₂-weighted imaging

T₂-W imaging visualizes myocardial accumulation of extracellular water due to oedema,⁵⁸ reflecting acute myocardial response to

damage of either ischaemic aetiology (MI) or inflammatory aetiology (myocarditis). Myocardial oedema may be localized or diffuse, subendocardial, or transmural, following the territory of coronary arteries as in CAD, or subepicardial as in myocarditis. It can also be diffuse subendocardial as in vasculitides.⁶⁸ Pathological areas in T_2 -W imaging appear as a high signal intensity area on STIR- T_2 images, where the signal contrast between oedema, normal myocardium and the LV cavity is optimized. However, STIR- T_2 images have limitations due to low signal to noise ratio,⁶⁸ stemming from poor contrast between healthy and oedematous areas, magnetic field inhomogeneities, and greater susceptibility to motion artefacts due to slow flow hyperintensity.⁶⁸

T_2 mapping

In T_2 mapping, a parametric image of each voxel is reconstructed to overcome the aforementioned limitations of STIR- T_2 . Normal myocardial T_2 values range between 55.8 ± 2.8 ms at 1.5 T and 51.6 ± 3 ms at 3.0 T.⁷⁰ T_2 measures are independent of body surface area and/or heart rate and have good reproducibility; however, they may vary with different scanner types or field strengths.⁸⁹ Normal values are also dependent on topographical LV location with increasing values from base to apex.⁸⁹ Increased signal on T_2 mapping indicates myocardial oedema due to recent myocardial injury.^{68,90} However, T_2 mapping has the same limitations with regards to standardization as T_1 mapping.⁸⁹

T_2^* relaxation time

Myocardial iron quantification is important for the management of patients at risk of iron overload cardiomyopathy, as well as for the evaluation of intramyocardial haemorrhage secondary to extensive acute MI.⁹¹ Myocardial iron cannot be reliably predicted using serum ferritin or liver iron, and incremental abnormalities in cardiac function manifest only in advanced disease.⁹¹ Cardiac T_2^* is the most widely accepted MRI-based method for assessing cardiac iron overload.⁹¹ Iron overload results in faster T_2^* relaxation due to susceptibility-induced field distortions, which reduces signal intensity more rapidly and can be visualized as darkening of the myocardium proportional to the iron concentration. A strong correlation was observed between T_2^* and tissue iron concentration in post-mortem human hearts of transfusion-dependent patients.⁹¹ T_2^* CMR can be used to evaluate myocardial iron, which in turn can characterize the efficacy of chelation treatment.

Assessment of vascular/transvalvular flow

Angiography using T_1 -w imaging and four-dimensional flow

MRA comprises the combination of various techniques based on two general concepts: (i) methods relying on natural flow effects such as time-of-flight and phase-contrast techniques, either in two- or three-dimensional acquisition modes and (ii) more recently developed CE MRA methods. MRA is as accurate as X-ray angiography in detecting abnormalities of the great vessels, with important applications in ARDs.⁷² Four-dimensional flow (4D flow) is a new CMR method that allows 3D visualization of vascular flow over time (hence four

dimensions) and quantitative assessment of transvalvular or intracavity flow.⁷²

Valvular disease

bSSFP is the most widely used CMR sequence for assessing valve anatomy and function, due to its excellent blood-to-myocardium contrast and a high signal-to-noise ratio.⁹² Non-cine pulse sequences (spin echo T_1 -W, T_2 -W) may aid in tissue characterization of valvular masses.⁹² Phase-contrast pulse sequences (velocity-encoded cine, Q flow, or velocity mapping) are used for flow velocity measurements. Velocity mapping produces two sets of images: a magnitude image and phase velocity maps. The magnitude image is used for anatomic orientation and identification of the boundaries of the imaged valve. The phase map encodes the velocities within each pixel. Using both images, a region of interest can be traced on each timeframe. Within each region of interest, the peak instantaneous velocity (V_{max}) for each timeframe can be obtained. Using the simplified Bernoulli equation ($4V_{max}^2$), the peak instantaneous gradient per frame can be estimated by substituting the peak instantaneous velocity with the corresponding obtained value. Mean pressure gradients are obtained by averaging all of the instantaneous velocities during systole.⁹²

Limitations of CMR

- (1) Low availability. However, CMR availability has increased since the beginning of the coronavirus disease-2019 pandemic.
- (2) CMR is contra-indicated in patients with metal fragments in the eyes and devices that are not MR-conditional and metallic fragments in the eyes.⁹³
- (3) Gadolinium-based contrast agents should be used with caution in patients with impaired renal function (glomerular filtration rate <30 mL/min).⁶⁸ Importantly, several non-contrast sequences can also provide valuable information in this context.⁶⁸
- (4) There is no cost-effectiveness analysis of CMR use in patients with ARDs. However, a cost-minimization analysis for cardiac revascularization showed the clear benefit of using CMR in decision-making.⁹⁴ Furthermore, the high costs of novel immunomodulatory treatment should be taken into account when combined with the high prevalence of CVD in patients with ARDs.

CMR implementation, site preparation, study procedure

Close monitoring of patient vital signs is necessary during CMR scanning. Standardized CMR protocols have been previously published and are currently used internationally.⁹⁵ SSFP sequences can be used in both 1.5 and 3.0 T systems. Normal values for volumes, ejection fractions, aortic dimensions, and valvular function have been reported previously.⁶⁸ T_1/T_2 mapping and ECV can also be performed in both 1.5 and 3.0 T MR systems. For the purposes of clinical utilization of mapping studies, commercial pulse sequences are preferable. For native T_1 and T_2 mapping, local results should be benchmarked against published reported ranges, but a local reference range should primarily be used. Scan planning and reporting guidelines have been published previously.⁶⁸

CMR protocols for patients with ARDs

CMR yields comprehensive information on cardiac structure, function, and tissue composition and has a prominent place in current cardiology practice guidelines.⁹⁶ Specifically in patients with ARDs, a CMR protocol including biventricular functional assessment, LGE, STIR-T₂, T₁ mapping, T₂ mapping, and ECV, which can be performed in <60 min, is proposed as the standard clinical tool for everyday clinical practice. For addressing additional clinical questions, such as the need for valvular disease quantification or specific vascular assessment, more sophisticated approaches including MRA should be added. Each CMR examination should be individually tailored to the clinical needs of the corresponding patient instead of relying on a uniform implementation in all patients. A standardized CMR protocol for the evaluation of patients with ARDs is presented in **Key point 3**.

Key point 3. CMR protocol for ARDs.

- (a) Biventricular function using bSSFP (the gold standard for **function** evaluation).
- (b) EGE ratio between myocardium and skeletal muscle in gadolinium-enhanced T1-weighted images (to detect myocardial **hyperaemia** during inflammation).
- (c) LGE using inversion recovery sequence (gold standard to detect **replacement fibrosis**).
- (d) STIR T2 (**oedema** index, widely available, but limited by artefacts).
- (e) T2 mapping (**quantification of oedema**).
- (f) Native T1 mapping (**quantification of oedema/diffuse fibrosis, ideal in reduced GFR**).
- (g) Post-contrast T1 mapping (**necessary to calculate ECV**).
- (h) ECV (**index of diffuse fibrosis, independent of magnetic field strength**).

Inter-modality comparison in the evaluation of CVD in ARDs

All imaging modalities provide useful information regarding biventricular function. Stress echocardiography has greater specificity for detecting wall motion abnormalities associated with myocardial replacement fibrosis, while SPECT, and PET have higher sensitivities.⁴⁷ The presence of myocardial replacement fibrosis >5% of the LV mass is associated with a 3-fold increase in the risk of future CV events.⁶⁸ Importantly, CMR is the preferred method to detect diffuse myocardial fibrosis, even in the absence of LGE, as in SSc and other ARDs.⁹⁷

All imaging modalities can be used to detect myocardial ischaemia due to epicardial CAD. A negative stress CMR confers an excellent prognosis in patients with CAD.⁴⁴ However, there is no study so far that has specifically investigated the utility of stress CMR in patients with ARDs. Lastly, only CMR and PET can detect coronary microvascular disease non-invasively,⁹⁸ which is important in patients with ARDs (**Key point 4**).

Severe oedema can be inferred indirectly with echocardiography in selected clinical situations. However, only CMR can provide quantification of myocardial oedema.⁵⁹ This information can potentially be used to modify or initiate immunomodulatory and/or cardioprotective treatment.⁹⁹

Key point 4. Comparison of imaging modalities for the evaluation of CVD in patients with ARDs.

- (a) All imaging modalities can provide information on biventricular function.⁶⁸
- (b) Stress echo has greater specificity for detecting wall motion abnormalities associated with myocardial replacement fibrosis, while SPECT and PET have higher sensitivities.⁴⁷
- (c) CMR detects myocardial replacement fibrosis directly.⁶⁸
- (d) CMR can be used to detect oedema indicative of acute cardiac disease.⁶⁸
- (e) Replacement/diffuse fibrosis, assessed by CMR, correlates well with histology.⁶⁸
- (f) All stress imaging modalities can detect myocardial ischaemia secondary to epicardial CAD, but only CMR and PET can detect microvascular disease, frequently pivotal in ARDs.⁴⁷

Consensus on clinical indications of CMR in patients with ARDs

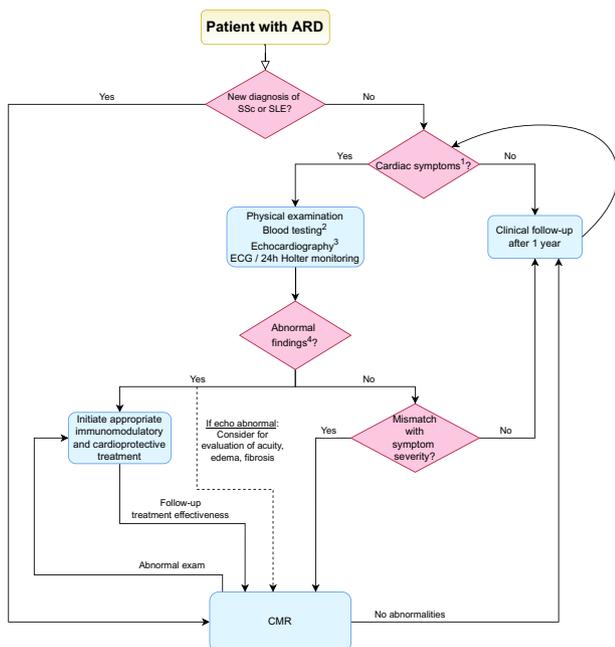
Currently, the first-line imaging modality of choice for evaluating CVD in patients with ARDs is echocardiography. Although a CMR examination is not routinely carried out in all patients with ARDs, it should be noted that echocardiography cannot provide direct information on tissue characterization (disease acuity and/or myocardial oedema/fibrosis), which can have important implications for clinical decision-making in these patients.⁶⁸ At the time of writing, there are no established guidelines regarding the clinical application of CMR in patients with ARDs. Based on consensus agreement of all authors, the conditions where a CMR examination can be considered in patients with ARDs are the following:

- (1) Suspected cardiac involvement at the time of diagnosis in patients with SSc or SLE. Cardiac involvement in these patients may precede the clinical diagnosis.⁹⁰
- (2) In patients with cardiac symptoms (chest pain at rest or on exertion, dyspnoea at rest or on exertion, palpitations or unexplained fatigue), an initial evaluation including physical examination, blood testing, electrocardiography/24 h Holter monitoring, and echocardiography should be performed. In the case of an abnormal echocardiogram, CMR can be considered if more accurate disease activity and oedema/fibrosis characterization are thought to be clinically indicated.⁶⁸ In case of normal findings in the aforementioned diagnostic testing (i.e. mismatch between cardiac symptoms and findings),⁶⁸ CMR can be considered to rule out potentially occult cardiac pathology; notably also if the underlying ARD seems clinically quiescent.
- (3) To evaluate the effectiveness of immunomodulatory/cardioprotective treatment.⁹⁰

- (4) If extracardiac manifestations of the corresponding ARD do not respond adequately to immunomodulatory therapy even if no cardiac symptoms are present. For example, in patients with RA without cardiac symptoms or CVD risk factors and inadequate disease response to methotrexate, treatment with tocilizumab led to increases in LVEF, and decreases in LV mass index.¹⁰⁰

Lastly, it is important to note that treating physicians should remain vigilant as to the development of new CVD in patients with ARDs, who should be followed-up clinically at 1-year intervals. The consensus agreement is schematically represented as a clinical decision flowchart in **Key point 5**.

Key point 5. Consensus clinical practice algorithm for the evaluation of CVD in patients with ARDs.



¹Chest pain at rest or on exertion, dyspnea at rest or on exertion, palpitations, unexplained fatigue

²Complete blood count, CRP, ESR, high-sensitivity cardiac troponin T or I, BNP or NT-proBNP

³Biventricular systolic function, wall motion, diastolic function, valvular function, LV strain / strain rate, pulmonary pressures

⁴Any of the following: leukocytosis, abnormally elevated CRP/ESR or cardiac troponins, any echocardiographic abnormalities other than valvular disease, any ventricular or supraventricular arrhythmias, new atrioventricular block

SSc, systemic sclerosis; SLE, systemic lupus erythematosus; ECG, electrocardiogram; CMR, cardiovascular magnetic resonance; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; BNP, brain natriuretic peptide; NT-proBNP, N-terminal brain natriuretic peptide; CK, creatine kinase; LV, left ventricular; CVD, cardiovascular disease; ARD, autoimmune rheumatic disease.

Clinical implications of CMR findings in patients with ARDs

CMR has important clinical implications which can also potentially prompt changes in therapeutic decision-making. These clinical implications are summarized in **Key point 6**:

Key point 6. Clinical implications of CMR in ARDs.

- Early identification of asymptomatic CVD** (oedema, diffuse and/or replacement fibrosis).
- Elucidation of CVD acuity** (oedema with concurrent replacement fibrosis in acute CVD, diffuse and/or replacement fibrosis without concurrent oedema in chronic CVD).
- Elucidation of HF aetiology** (ischaemic/non-ischaemic CVD, acute inflammation).
- Identification of arrhythmogenic substrates** (diffuse/replacement fibrosis with/without oedema).

Unmet needs and future research avenues

Although the field of CMR has seen rapid growth in the preceding years, much remains to be learned in the special population of patients with ARDs. Some of the currently unmet needs and related future research avenues are presented below:

- Large, multi-centre observational studies with sufficient population size and long-term follow-up are necessary to delineate the exact prognostic significance of CMR findings in patients with ARDs.
- Studies that directly evaluate the role of CMR as a guide for immunomodulatory/cardioprotective treatment initiation in patients with ARDs are severely lacking. Such studies will pave the way for more concrete recommendations for implantation in the future.
- Little is known regarding the potential of co-existent occult CVD in patients with ARDs in whom extracardiac disease activity is not optimally controlled. Further research using CMR is required to elucidate the prevalence and prognostic significance of cardiovascular abnormalities in this subgroup of patients with ARDs.
- Current literature is limited with regard to the exact relationship between CMR indices and circulating levels of biomarkers of inflammation, cardiac damage, and cardiac stretch, as well as ARD-associated autoantibodies. In addition, multi-omics technologies are being used more frequently and constitute an additional source of information regarding circulating or organ-specific mediators. Studies relating the probability of having CMR abnormalities with circulating mediator/autoantibody profiles may lead to the identification of patients with a higher a priori chance for a pathologic CMR examination. As such they could optimize the decision-making process presented in **Key point 5**.
- Large studies with consecutive patients with ARDs are necessary in order to perform head-to-head comparisons of CMR with other non-invasive cardiovascular imaging modalities, as well as EMB.
- Targeted therapies against pathologic myocardial fibrosis, as in the case of as nintentanib,¹⁰¹ may constitute a potential therapeutic option in patients with ARDs. CMR is the only imaging modality that can adequately quantify myocardial fibrosis and could thus be used for patient selection for such treatments in the future.
- The integration of cardiac electro-mechanical modelling in CMR examinations may allow for the identification of patients at risk for malignant arrhythmias.¹⁰² However, this promising application needs to be research further.

Conclusions

Currently, the evaluation of CVD in patients with ARDs is based on the presence of cardiac symptoms and the identification of cardiac functional changes, which are usually clinically overt in the late stages of the disease. CMR can provide cardiac tissue characterization and biventricular functional assessment in the same examination, allowing for the early and accurate identification of important subclinical abnormalities before clinically overt CVD. CMR tissue characterization by T₁ mapping, T₂ mapping, and ECV can provide reliable assessment of CVD activity beyond blood biomarkers, facilitating early clinical consideration of appropriate immunomodulatory, and cardioprotective therapies. The quality and extent of information provided by CMR may permit a personalized medicine approach to patients with ARDs, enabling better disease- and patient-oriented choices of diagnostic, therapeutic, and monitoring strategies to prolong survival and enhance quality of life.

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