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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 | (a) Supraventricular |
| | | (b) Ventricular/sudden cardiac death | (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

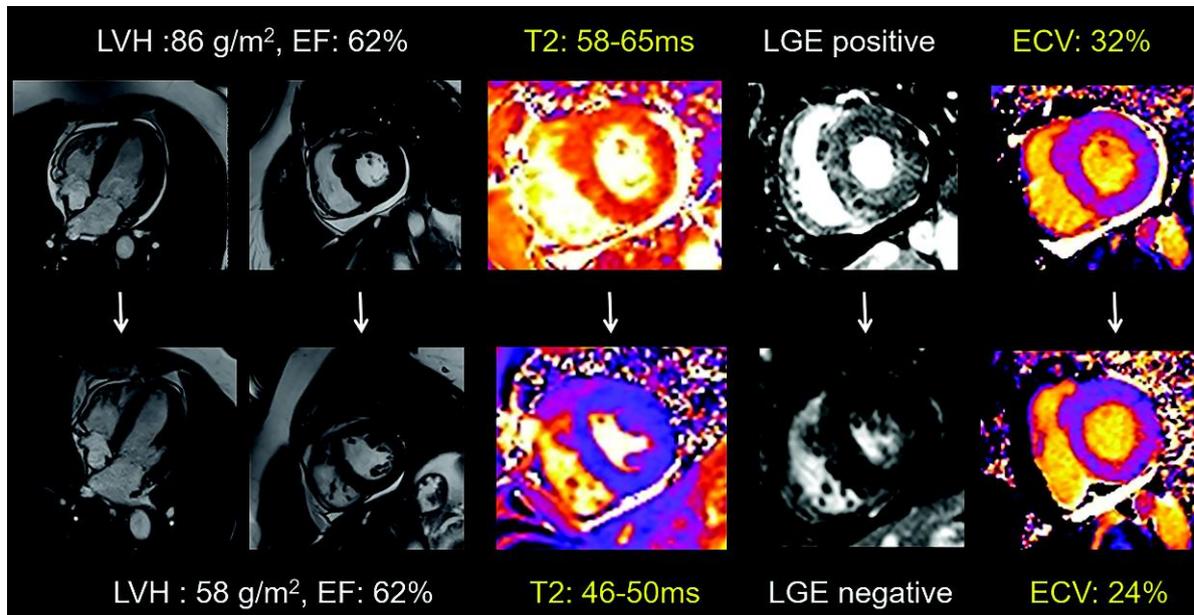


Figure 1 CMR imaging of a patient with eosinophilic granulomatosis with polyangiitis (Churg-Strauss syndrome) at diagnosis (first row) and 10 days thereafter (second row). > First and second columns: Cine imaging demonstrating left ventricular hypertrophy and initially oedematous appearance of the myocardium (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.

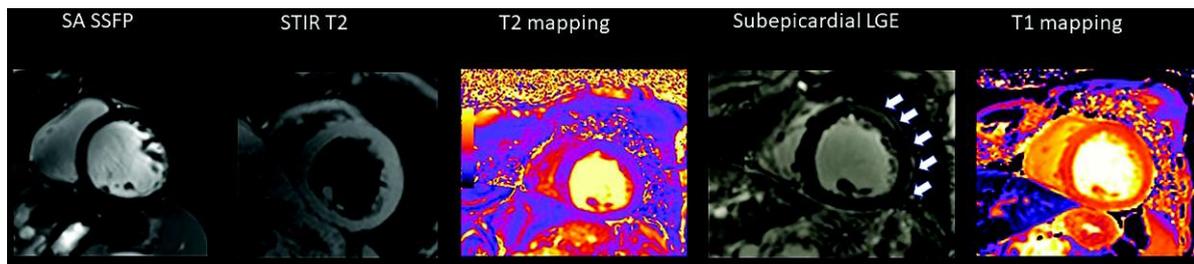


Figure 2 CMR imaging of a patient with DM and acute shortness of breath. > First image: short axis SSFP for function assessment (LVEF = 21%). > Second image: STIR-T₂ short axis image showing diffuse oedema (T₂ ratio of myocardium over skeletal muscle is 2.3). > Third image: T₂ mapping showing abnormally 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

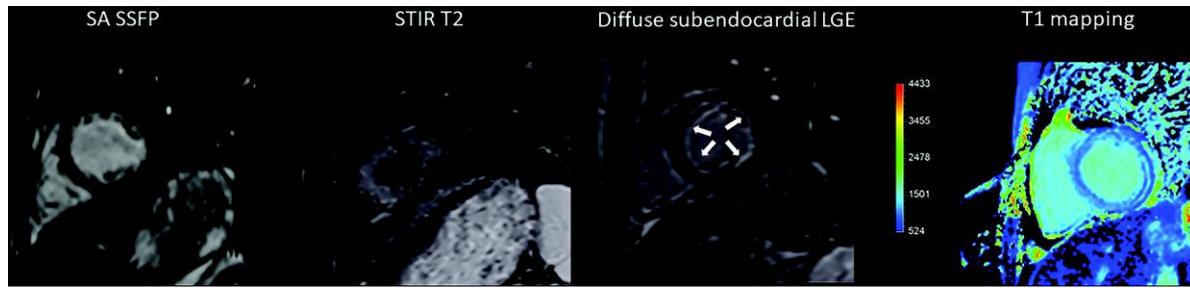


Figure 3 CMR imaging of a young patient with diffuse SSc and multifocal ventricular arrhythmias. The patient died suddenly, due to ventricular tachycardia. > First image: short axis SSFP sequence to assess ventricular function (LVEF = 57%). > Second image: STIR-T₂ short axis image showing extensive, 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

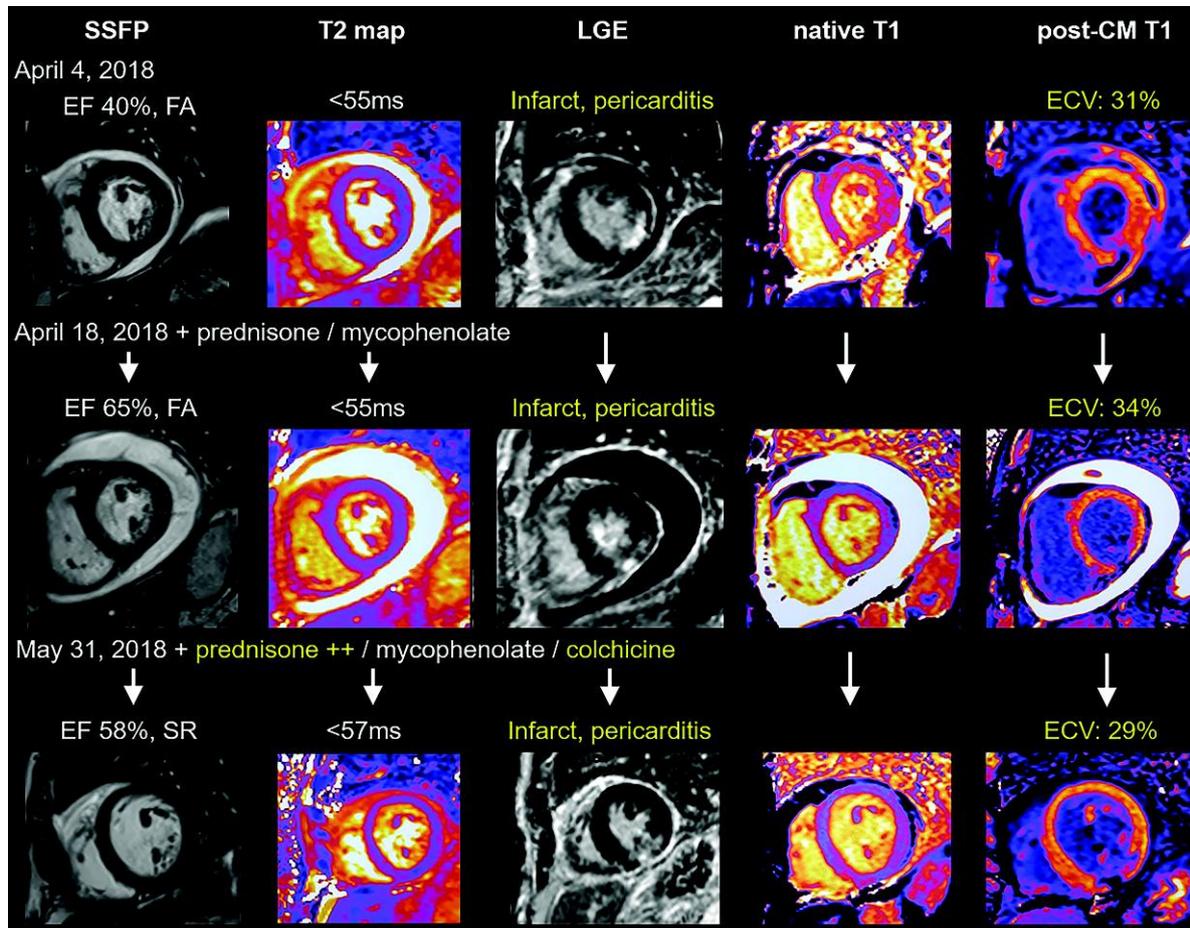


Figure 4 CMR images of a female patient, 78-years old, with SSc, who developed increasing dyspnoea and heart failure symptoms. CMR revealed a lateral infarction (subendocardial LGE) and the follow-up coronary angiogram showed diffuse severe disease of the small epicardial vessels of the circumflex coronary artery and no major occlusions. The CMR also showed acute pericarditis (LGE pos) and minor effusion, no myocarditis (T_2 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: T_2 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: T_1 mapping quantification at diagnosis and during treatment. > Fifth columns: quantification of ECV at diagnosis and during treatment.

T_1 -weighted black blood and bSSFP sequences, allows for anatomical characterization of the pericardium. Native T_1 and T_2 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 T_1 mapping of the pericardial fluid provides information on its composition. A native T_1 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 T_1 mapping and T_2 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

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

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