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REVIEW ARTICLE

Review and critical appraisal of the indications for cardiac magnetic resonance imaging in the ESC guidelines

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ABSTRACT

Cardiac MRI has made significant advances in the past decade, becoming an important technique for the evaluation of various cardiac pathologies. The aim of this document is to review the current indications for performing cardiac MRI based on the current ESC guidelines for STEMI, NSTEMI, chronic coronary artery disease, heart failure, arrhythmias, sudden cardiac death, valvular heart disease, pericardial disease and congenital heart disease. The review discusses the diagnostic and prognostic value of cMR for numerous cardiac diseases, and its important value in assessing structural heart disease and predicting arrhythmia risk. Additionally, it reflects upon the appropriateness of the guidelines and points out areas where the indications should be revised in future editions, based on the author's personal opinion. It is suggested that guideline criteria for the use of cMR should be more explicit to promote its use and lead to more specific reimbursements. However, further studies are needed to even better document the value of cMR in the future.

Abbreviations: ARVC: Aryhthmogenic Right Ventricular Cardiomyopathy; CAD: Coronary Artery Disease; cMR: Cardiac Magnetic Resonance; DCM: Dilated Cardiomyopathy; EACVI: European Association for Cardiovascular Imaging; ECV: Extracellular Volume Fraction; EF: Ejection Fraction; ESC: European Society of Cardiology; LGE: Late Gadolinium Enhancement; LV: Left Ventricle; MINOCA: Myocardial Infarction with normal coronary arteries; NSTEMI: Non ST Elevation Myocardial Infarction; PET: Positron Emission Tomography; RV: Right Ventricle; STEMI: ST elevation Myocardial Infarction

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Introduction

Cardiac Magnetic Resonance (cMR) has experienced considerable development over the last decades, making it a versatile, non-invasive imaging technique for comprehensive evaluation of various cardiac conditions. It is particularly useful for analysing left and right ventricular volumes and function, measuring forward and regurgitant flow, examining the pericardium, great vessels. Its most prominent distinctive feature however is the ability to characterise tissue composition through T1 and T2 weighted imaging, T1, T2, T2* mapping, late Gadolinium Enhancement (LGE), and Extracellular Volume Fraction (ECV) measurement. Additionally, cMR is able to evaluate myocardial perfusion at rest and under stress, including quantifying stress myocardial perfusion and perfusion reserve. Due to these technological advances, cMR has increasingly been implemented in clinical practice, with numerous studies demonstrating its value in diagnosis and prognosis of various cardiac diseases. This has been acknowledged in the recent clinical practice guidelines of the European Society of Cardiology (ESC). This paper seeks to review the current indications for performing cMR according to the ESC guidelines (Table 1) and to appraise where the indications should be revised in future editions, based on the author's personal opinions.

Current recommendation for cMR in the ESC guidelines

Detection of myocardial infarction and use in acute coronary syndromes

The Fourth Universal Definition of Myocardial Infarction [5] identifies myocardial injury as the rise and fall of biomarkers (i.e. troponin) with clinical symptoms. Acute infarct is classified as myocardial injury in the setting of acute ischaemia, which is

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Table 1. Indications for cMR and for cMR guided interventions in the current ESC guidelines.

Indication	Guideline text	Indication/Level of Evidence		Guidelines published
Detection of infarct	Supportive technique for confirmation of myocardial infarction	None		4the Universal definition of MI
Evaluation of function after STEMI (during hospital stay and 6-12 weeks after discharge)	When echocardiography is suboptimal/inconclusive for evaluation of EF after acute MI, another method (preferably cMR) should be used	IIA	C	STEMI (2017)
Detection of ischaemia and viability after STEMI	Either stress echo, cMR, SPECT, or PET may be used to assess myocardial ischaemia and viability, including in multivessel CAD.	IIB	C	STEMI (2017)
Detection of MINOCA or myocarditis in NSTEMI	It is recommended to perform cMR in all MINOCA patients without an obvious underlying cause	I	C	NSTEMI (2020)
Detection of ischaemia in patients with angina	Non-invasive functional imaging for myocardial ischaemia using either Stress echocardiography, stress cardiac magnetic resonance, single-photon emission CT, or positron emission tomography or coronary CTA is recommended as the initial test to diagnose CAD in symptomatic patients in whom obstructive CAD cannot be excluded by clinical assessment alone	I	B	Chronic CAD (2019) [1]
Suspected microvascular angina	Transthoracic Doppler of the LAD, cMR, and PET may be considered for non-invasive assessment of CFR.	IIB	C	Chronic CAD (2019)
Detection of myocardial viability in chronic CAD	Either stress Echo, cMR SPECT or PET can be used for detection of myocardial ischaemia or viability	IIB	B	Chronic CAD (2019) [1] Heart Failure (2021) [2]
Evaluation of DCM	cMR is recommended for the assessment of myocardial structure and function in those with poor echocardiogram acoustic windows.	I	C	Heart Failure (2021)
	cMR is recommended for the characterisation of myocardial tissue in suspected infiltrative disease, Fabry disease, inflammatory disease (myocarditis), LV non-compaction, amyloid, sarcoidosis, iron overload/haemochromatosis.	I	C	Heart Failure (2021)
	cMR with LGE should be considered in DCM to distinguish between ischaemic and non-ischaemic myocardial damage.	IIA	C	Heart Failure (2021)
Risk for arrythmia stratification in DCM	cMR with LGE should be considered in DCM/HNDCM patients for assessing the aetiology and the risk of VA/SCD.	IIA	C	Ventricular arrythmias and SCD (2022) [3]
	ICD implantation should be considered in DCM/ HNDCM patients with a LVEF <50% and ≥2 risk factors (syncope, LGE on cMR, inducible SMVT at PES, pathogenic mutations in LMNA, PLN, FLNC, and RBM20 genes).	IIA	C	Ventricular arrythmias and SCD (2022)
"Non-Compaction"	In patients with a LVNC cardiomyopathy phenotype based on cMR or echocardiography, implantation of an ICD for primary prevention of SCD should be considered to follow DCM/ HNDCM recommendations.	IIA	C	Ventricular arrythmias and SCD (2022)
Cardiomyopathy	Contrast-enhanced cMR is recommended in patients with cardiomyopathy at initial evaluation	I	B	Cardiomyopathies (2023) [4]
	Contrast-enhanced cMR should be considered in patients with cardiomyopathy during follow-up to monitor disease progression and aid risk stratification and management.	IIa	C	
	Contrast-enhanced cMR should be considered for the serial follow-up and assessment of therapeutic response in patients with cardiac amyloidosis, Anderson–Fabry disease, sarcoidosis, inflammatory cardiomyopathies, and haemochromatosis with cardiac involvement	IIa	C	
	In families with cardiomyopathy in which a disease-causing variant has been identified, contrast-enhanced cMR should be considered in genotype-positive/phenotype-negative family members to aid diagnosis and detect early disease.	IIa	B	
	In cases of familial cardiomyopathy without a genetic diagnosis, contrast-enhanced cMR may be considered in phenotype-negative family members to aid diagnosis and detect early disease	IIb	C	
Evaluation of Hypertrophic cardiomyopathy	In Hypertrophic cardiomyopathies cMR with LGE is recommended in HCM patients for diagnostic work-up.	I	C	Ventricular arrythmias and SCD (2022)
	Contrast-enhanced cMR may be considered before ASA or myectomy to assess the extent and distribution of hypertrophy and myocardial fibrosis	IIb	C	Cardiomyopathies (2023)
Evaluation of risk for arrythmia in HCM	ICD implantation should be considered in HCM patients aged 16 years or more with an intermediate 5-year risk of SCD (≥4 to <6%), and with (a) significant LGE at cMR (usually ≥15% of LV mass) or (b) LVEF <50% or (c) abnormal BP response during exercise test; or (d) LV apical aneurysm; or (e) presence of sarcomeric pathogenic mutation	IIA	B	Ventricular arrythmias and SCD (2022)

(*continued*)

Table 1. Continued.

Indication	Guideline text	Indication	Level of Evidence	Guidelines published
	ICD implantation may be considered in HCM patients aged 16 years or more with a low estimated 5-year risk of SCD (>4%), and with (a) significant LGE at cMR (usually ≥15% of LV mass) or (b) LVEF <50% or (c) LV apical aneurysm	IIb	C	Ventricular arrythmias and SCD (2022)
Detection of ARVC	In patients with suspected ARVC, cMR is recommended	I	C	Ventricular arrythmias and SCD (2022)
Myotonic Dystrophy	Invasive electrophysiological evaluation should be considered in patients with myotonic dystrophy and a PR interval ≥240 ms or QRS duration ≥120 ms or who are older than 40 years and have supraventricular arrhythmias or who are older than 40 years and have significant LGE on cMR	IIA	C	Ventricular arrythmias and SCD (2022)
	Implantation of an ICD over a permanent pacemaker may be considered in myotonic dystrophy patients with additional risk factors for VAs and SCD (including structural abnormalities by cMR)	IIb	C	Ventricular arrythmias and SCD (2022)
Duchenne/Becker Disease	Implantation of an ICD may be considered in patients with Duchenne/Becker muscular dystrophy and significant LGE at cMR	IIb	C	Ventricular arrythmias and SCD (2022)
Sarcoidosis	In patients with cardiac sarcoidosis who have a LVEF >35% but significant LGE at cMR after resolution of acute inflammation, ICD implantation should be Considered	IIA	B	Ventricular arrythmias and SCD (2022)
	In patients with cardiac sarcoidosis who have a LVEF 35–50% and minor LGE at cMR, after resolution of acute inflammation, PES for risk stratification should be considered.	IIA	C	Ventricular arrythmias and SCD (2022)
Patients with ventricular tachycardiac or frequent PVC	In patients with newly documented VA (frequent PVCs, NSVT, SMVT) and suspicion of SHD other than CAD after initial evaluation, a cMR should be considered	IIA	B	Ventricular arrythmias and SCD (2022)
	In patients with PVCs/VT and a presentation not typical for an idiopathic origin, (older age, right bundle branch block morphology, SMVT consistent with re-entry). cMR should be considered, despite a normal echocardiogram	IIA	C	Ventricular arrythmias and SCD (2022)
Survivors of SCD	Coronary imaging and cMR with LGE are recommended for evaluation of cardiac structure and function in all SCA survivors without a clear underlying cause	I	B	Ventricular arrythmias and SCD (2022)
Pericardial disease	CT or cMR should be considered in suspected cases of loculated pericardial effusion, pericardial thickening and masses, as well as associated chest abnormalities	IIA	C	Pericardial diseases (2015)
Pericardial constriction	CT and/or cMR are indicated as second-level imaging techniques to assess calcifications (CT), pericardial thickness, degree and extension of pericardial involvement	I	C	Pericardial diseases (2015)
	Empiric anti-inflammatory therapy may be considered in cases with transient or new diagnosis of constriction with concomitant evidence of pericardial inflammation (i.e. CRP elevation or pericardial enhancement on CT/cMR)	IIB	C	Pericardial diseases (2015)
Suspicion of abnormal coronary arteries	Non-pharmacological functional imaging (e.g. nuclear study, echocardiography, or cMR with physical stress) is recommended in patients with coronary anomalies to confirm/exclude myocardial ischaemia	I	C	Congenital Heart diseases (2019)
Tetralogy of Fallot	All patients should undergo regular cMR.	No recommendation		Congenital Heart diseases (2019)
	ICD implantation should be considered in selected TOF patients with multiple risk factors for SCD, including LV dysfunction, non-sustained, symptomatic VT, QRS duration >_180 ms, extensive RV scarring on cMR, or inducible VT at programmed electrical stimulation.	IIa	C	Congenital Heart diseases (2019)
	PVRep should be considered in asymptomatic patients with severe PR and/or RVOTO when one of the following criteria is present. • Decrease in objective exercise capacity. • Progressive RV dilation to RVESVi >_80 mL/ m2, and/or RVEDVi >_160 mL/m2, and/or progression of TR to at least moderate. • Progressive RV systolic dysfunction. • RVOTO with RVSP >80 mmHg	IIA	C	Congenital Heart diseases (2019)

ARVC: Arrhythmogenic Right Ventricular Cardiopathy; ASA: Alcohol Septal Ablation; CAD: Coronary Artery Disease; CFR: Coronary Flow Reserve:; cMR: cardiac Magnetic Resonance; CTA: Computed Tomography Angiography; DCM: Dilated Cardiomyopathy; EDVi: Indexed End-diastolic Volume; ESVi: indexed End-Systolic Volume; HCM: Hypertrophic Cardiomyopathy; HNDCM: Hypokinetic Non-Dilated Cardiomyopathy; ICD: Implantable Cardiac Defibrillator; LAD: Left Anterior Descending Coronary artery; LV: Left Ventricle; LVNC: Left Ventricular Non-Compaction; NSVT: Non-Sustained Ventricular Tachycardia; PES: Programmed Electrical Stimulation; PR: Pulmonary Regurgitation; PVRep: Pulmonary Valve Reparation; RV: Right Ventricle; RVOTO: Right Ventricular Outflow Obstruction; RVSP: Right Ventricular Systolic Pressure; SCD: Sudden Cardiac Death; SHD: Structural Heart Disease; SMVT: Sustained monomorphic ventricular tachycardia; SPECT: Single Photon Emission Computed Tomography; TOF: Tetralogy of Fallot; TR: Tricuspid Regurgitation; VA: Ventricular Arrhythmia.

identified through electrocardiographic analysis, identification of wall motion abnormalities or coronary thrombus. The definition of chronic infarct for epidemiological studies and quality programs relies only on the ECG (i.e. Q waves). The guidelines recognise late-gadolinium enhanced (LGE) cMR as a reference method for detecting acute and chronic myocardial injuries as small as 1 g due to the ability of gadolinium-based contrast agents to accumulate in these areas and its high spatial resolution. They also acknowledge that the ECG is not sensitive and specific for chronic infarct detection. Nevertheless, cMR is only suggested as a supplementary technique for detection of chronic infarct, potentially due to its limited availability. We contend that cMR-based definitions would be more accurate for both epidemiological and clinical definitions of acute and chronic infarcts.

Given that the initial diagnosis of STEMI is based solely on ECG findings, and that fast revascularization is primordial, imaging plays primarily a role in a post-revascularization context for the purpose of risk stratification and providing treatment guidance. According to the 2017 ESC STEMI guidelines [6] echocardiography is recommended as a Class IC indication for evaluating resting left ventricular (LV) and right ventricular (RV) function, detecting early mechanical complications, and excluding LV thrombus at the time of hospitalisation. Additionally, echocardiography should be repeated 6-12 weeks post discharge if the pre-discharge LV ejection fraction is less than 40%. The evaluation of LVEF is indeed key for the initiation of heart failure therapy and also serves as basis of whether an implantable cardioverter-defibrillator (ICD) should be implanted for primary prevention of sudden cardiac death (SCD) [7]. Currently, the use of cardiac magnetic resonance (cMR) imaging in the STEMI guidelines is classified as a class IIa level C indication for evaluating left ventricular ejection fraction (LVEF) when echocardiography is suboptimal or inconclusive. However, such instances are relatively rare, given the current capabilities of echocardiography. In addition, cMR offers a more comprehensive tissue characterisation post STEMI patients than LVEF assessment alone. Specifically, cMR can be used to accurately assess infarct size and transmurality through late gadolinium enhancement (LGE) and retrospectively determine the area at risk through T2 weighted or T2 mapping sequences up to 48-72 h post-revascularization, thereby allowing for the evaluation of the proportion of salvaged myocardium. Furthermore, cMR allows to evaluate the quality of myocardial reperfusion at a microvascular level by detecting the so called no-reflow phenomenon on early gadolinium enhanced images as well as the detection of intramyocardial haemorrhage on unenhanced T2* weighted images. All these parameters have strong prognostic significance, exceeding those of peak troponin levels and ejection fraction in post-STEMI patients. They could potentially be a valuable tool for risk stratification and treatment guidance post myocardial infarction [8]. However, due to the lack of prospective randomised trials demonstrating such benefit clinically, this is currently not recognised in the guidelines. cMR also has clearly demonstrated superior sensitivity over echocardiography for detection of intraventricular thrombus post MI [7, 9]. Yet again, because of the lack of evidence supporting the value of thrombus detection on outcomes, this indication is not yet recognised in the guidelines. Therefore, prospective trials should be conducted to evaluate the potential of cMR in this regard. cMR has higher accuracy for the identification of cardiac complications such as right ventricular infarction, and for the distinction of free wall rupture and for the distinction of pseudoaneuvrysm vs true aneurysm. While these indications are recognised in the current guidelines, they do not have any recommendation class. Indeed, it is merely stated that RV infarcts are also well assessed by cMR, that cMR can complement the diagnosis of free wall rupture identifying the contained cardiac rupture and its anatomical features to guide surgical intervention and that patients without inflammatory signs in whom circumferential pericardial effusion $>$10 mm is detected or those who become symptomatic for suspected tamponade, should be investigated for a possible subacute rupture by echocardiography or by cMR if echocardiography is inconclusive. The authors believe that the utility of cMR in these regards should be more prominently reflected in future editions of the guidelines.

By contrast, the value of cMR is very well recognised for patients with NSTMI (Figure 1). Indeed the 2020 guidelines [10] explicitly acknowledged the significance of cMR in the differential diagnosis of acute coronary syndromes with troponin elevations in the absence of significant coronary artery disease. Through cMR, it is indeed possible to precisely differentiate MINOCA (i.e. ischaemic myocardial infarction without coronary artery disease due to coronary spasm, embolism, or type 2 myocardial infarction) from alternative diagnoses such as myocarditis [11], perimyocarditis, or Takotsubo syndrome, and from troponin elevations that are due to other causes (e.g. cardiomyopathies). A meta-analysis conducted on the topic revealed that cMR allowed the recognition of up

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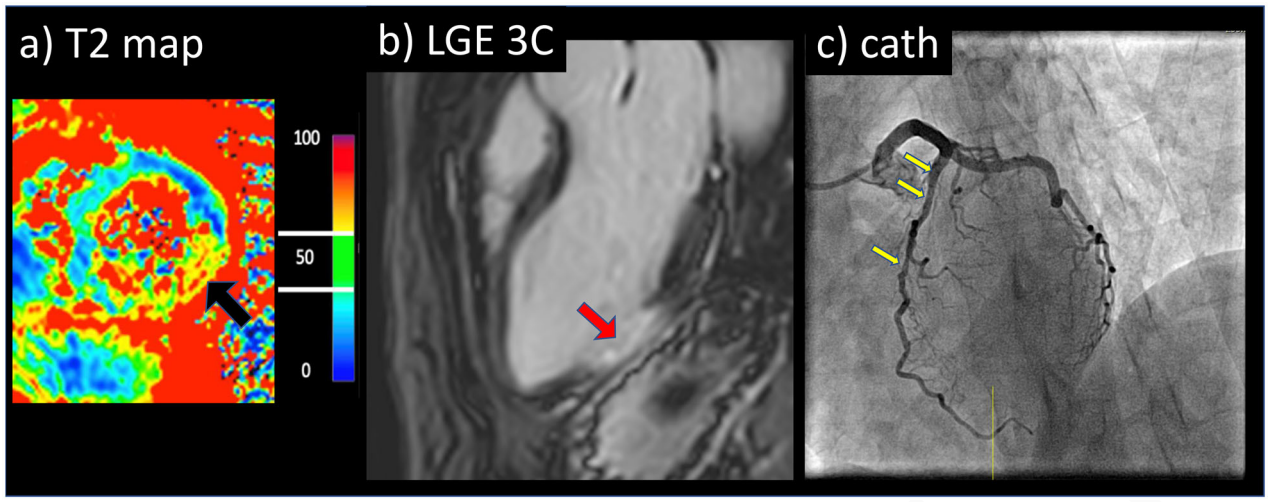

Figure 1. Example of a Class I indication of cMR: evaluation of MINOCA. A 37-year-old woman hospitalised with chest pain and troponin elevation. The initial coronary angiogram was considered normal. LGE-cMR showed increased T2 signal on T2 mapping (a) and transmural posterior infarction on LGE images (b). A repeat coronary angiogram post cMR allowed to detect spontaneous dissection of the LAD and marginal branch (c)

to 87% of the causes of MINOCA [12] and the reclassification of up to 68% of cases [13]. The 2020 NSTEMI guidelines now recommend the utilisation of cMR in all patients presenting with MINOCA without an obvious underlying cause as Class I-B indication. A potential concern is however that this could lead to an overuse of cMR in patients with minimal troponin elevation, as recent studies suggest a minimal troponin-I peak level of 200 pg/ml is needed for detectable myocardial damage by cMR [14]. Therefore, in future revisions of guidelines, it should probably be encouraged to limit cMR only to patients with significant troponin levels l greater than this cut-off value.

Evaluation of chronic coronary artery disease

In recent years stress perfusion cardiovascular magnetic resonance (cMR) with vasodilators such as adenosine, dipyridamole and regadenoson has become an established technique for the detection of coronary artery stenosis. Owing to its higher spatial resolution allowing visualisation of subendocardial perfusion defects it has higher sensitivity than SPECT [15], with accuracy matching that of PET, in particular in patients with 3 vessel disease. Furthermore, the prognostic value of cMR perfusion is now well-documented by numerous randomised trials, most notably in the CE-MARC-II study [16], which demonstrated that a cMR-perfusion-guided approach was as effective as one based on the National Institute for Health and Care Excellence (NICE) guidelines, and the MR INFORM Trial [17] which that a cMR-guided strategies was not inferior to fractional flow reserve (FFR)-guided strategy, while allowing for fewer revascularizations. Other large-scale studies have demonstrated that stress perfusion cMR is both safe and prognostically beneficial, not only in the general population, but also in specific subgroups, such in revascularized patients [18], in patients with heart failure [19], in patients with inconclusive stress tests [20] and even in patients with pacemakers [21]. Additionally, stress perfusion cMR offers certain advantages over other imaging modalities, including its lack of radiation exposure, short duration, and moderate cost. Nevertheless, current 2020 ESC guidelines for chronic coronary artery disease [1] indicate that all tests are similarly indicated for detection of ischaemia, despite differences in diagnostic accuracy [22], and cost-effectiveness. In our opinion, future guidelines should incorporate the higher diagnostic accuracy of cMR for its recommendation strength.

Angina is also often observed in individuals with non-obstructive epicardial coronary arteries (INOCA), which is postulated to arise from microvascular dysfunction. cMR is a highly beneficial diagnostic tool for confirming this diagnosis, as its high spatial resolution allows for the identification of subendocardial ischaemia, and particularly when quantitative stress perfusion techniques are utilised to calculate myocardial stress perfusion reserve [23,24]. Nevertheless, cMR has currently only a low-Class IIb indication for detection of microvascular angina in the 2017 guidelines similar to PET and transthoracic Doppler of the LAD, whereas the invasive approaches guidewire-based coronary flow reserve and microcirculatory resistance measurements have a Class IIa indication in patients with

persistent symptoms. We suggest that this be taken into consideration in future guidelines to prioritise non-invasive approaches for the evaluation of microvascular angina. Additionally, cMR also allows for the detection of myocardial scar by late gadolinium enhancement with higher sensitivity than other techniques. Detection of scar by cMR has been shown to possess prognostic value in multiple studies and is an important tool to assess the presence of myocardial viability. However, following the negative results of the STICH trial, the use of this technique for the detection of myocardial viability is only a class IIb indication. Since further negative results were seen in the REVASC trial, it is likely that the indication will be downgraded to a class III indication in the future. In our opinion myocardial viability detection nevertheless remain clinically useful in certain circumstances [25] such as when deciding to revascularize surgically vs using angioplasty, in evaluation of candidates for revascularization of chronic coronary occlusion, in potential candidates for resynchronisation therapy, as well as when trying to understand the underlying aetiology of myocardial dysfunction in patients with heart failure.

Heart failure and cardiomyopathies and their risk stratification for sudden cardiac death

The utility of cMR in the differential diagnosis of cardiomyopathies is widely acknowledged, as the combination of LGE patterns, morphological features, native tissue relaxation times, and extracellular volume measurements allows for a comprehensive approach for refined differential diagnosis of its aetiology [26] (Figure 2). This is now well recognised in the new 2023 guidelines for cardiomyopathies [4] which recommend contrast-enhance cMR as a class I level B indication for all patients at initial evaluation. cMR is also helpful and indicated to detect early disease in patents with familiar cardiomyopathies in which a disease-causing variant has been identified (Class IIa level of Evidence B) or even in phenotype-negative family members Class IIb level of Evidence C). Indeed, cMR LGE patterns allow to distinguish between ischaemic and non-ischaemic aetiologist of heart failure and also to differentiate several forms of distinct cardiomyopathies, and multiple studies have demonstrated that LGE-identified scarring is associated with unfavourable prognoses, not only in ischaemic cardiomyopathies, but also in a variety of non-ischaemic disorders [27]. The identification of LGE is not therefore only instrumental for differential diagnosis, but also for prognostication, and particular risk stratification of arrythmias in these diseases. It is hypothesised that scar tissue identified by LGE represents the anatomical substrate for potentially lethal ventricular arrythmias. Indeed, prognoses for ischaemic and non-ischaemic cardiomyopathies diverge, and the risk of death, particularly sudden cardiac death (SCD), is significantly higher in heart failure of ischaemic origin. Also as highlighted by the DANISH trial [28] the therapeutic benefits of prophylactic ICD implantation are less in HF of non-ischaemic aetiology. Therefore in the latest ESC 2022 guidelines for ventricular arrythmia and sudden

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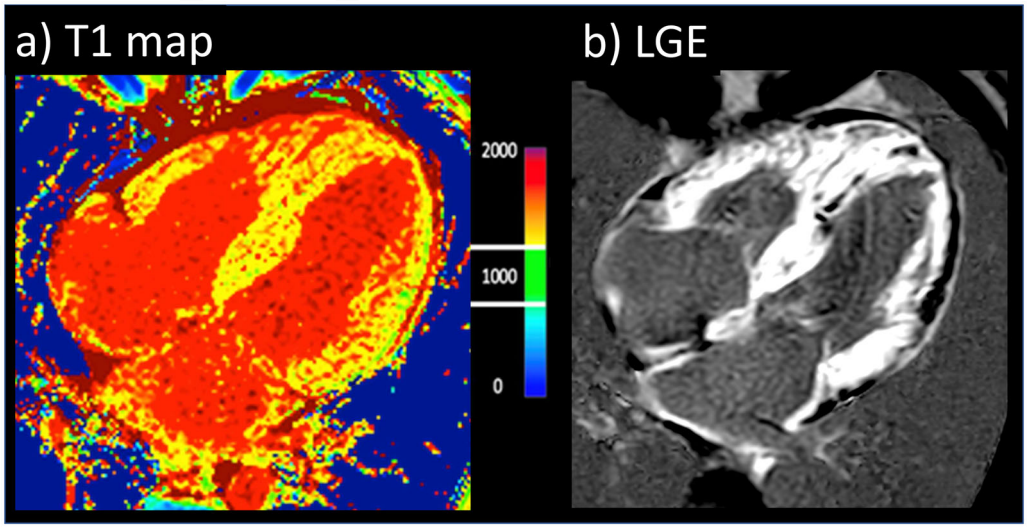

Figure 2. Example of a Class I indication of cMR: characterisation of infiltrative disease. 58-year-old man, with recently discovered hypertrophic cardiomyopathy complaining about chest-pain and dyspnoea. cMR showed markedly increased native T1 (1462 ms) on T1 mapping and diffuse LGE compatible with amyloidosis. ATTR amyloidosis was subsequently confirmed by absence of paraprotein and positive DPD scintigraphy.

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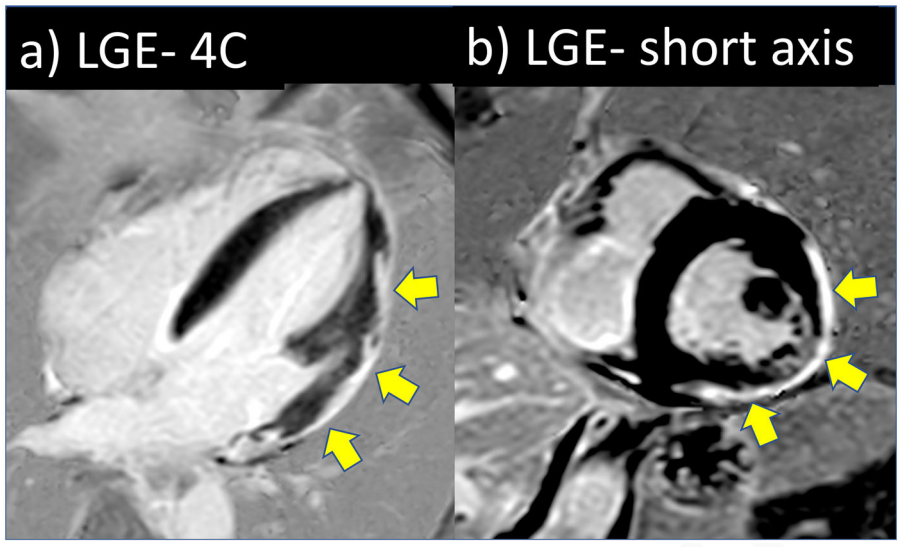

Figure 3. Example of a Class IIa indication of cMR: evaluation of DCM for risk stratification. A 53-year-old male with moderate alteration of LV function and premature ventricular beats. cMR demonstrated moderate alteration of LV function (40%) and diffuse epicardial LGE, suggesting either myocarditis or left sided arrhythmogenic cardiomyopathy. 3 months later the patients suffered cardiac arrest due to ventricular tachycardia and underwent ICD implantation.

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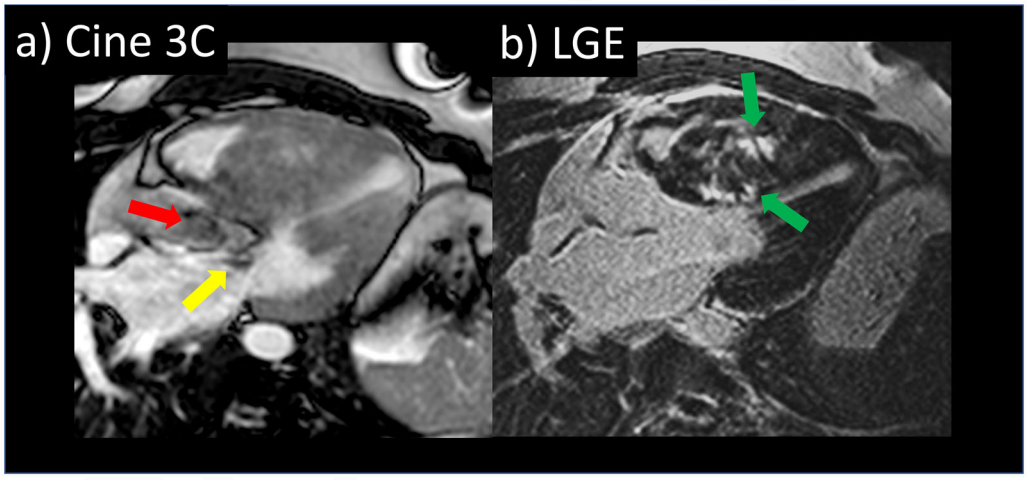

Figure 4. Example of a Class I indication of cMR: characterisation of LGE in HCM. A 22-year-old man with severe obstructive HCM. Cine images (a) showed important septal hypertrophy (40 mm), with SAM (red arrow) and mitral regurgitation (yellow arrow). LGE (b) images revealed diffuse LGE indicating fibrosis in the hypertrophic septum (green arrow)

cardiac death [3] the indication for prophylactic ICD implantation for non-ischaemic HF with LVEF $< 35\%$, was downgraded from a class I to a class IIa indication, while it remains a class I indication in heart-failure of ischaemic aetiology. Also, the usefulness of cMR for risk prediction of arrythmias are now well recognised in these latest guidelines. Indeed, systematic use of cMR imaging with late gadolinium enhancement (LGE) is now encouraged as a Class IIa-C indication for diagnosing the cause and assessing risk of ventricular arrhythmias/sudden cardiac death in patients with dilated and hypokinetic non dilated non-ischaemic cardiomyopathy (DCM/HNDCM) (Figure 3). Additionally, the presence of LGE in individuals with left ventricular ejection fraction (LVEF) between 35-50% has been established as a risk factor, warranting consideration of primary ICD implantation with a Class IIa-C indication. According to the same guidelines, the identification of LGE by cMR is also currently considered a modulating factor possibly indicting ICD implantation in patients with left ventricular 'non-compaction' phenotype (Class IIa-C). The existence of this type of cardiomyopathy as an entity remains however severely debated [29], and in our opinion the guidelines may have been excessively permissive for this indication without significant documented scientific evidence.

cMR is also particularly beneficial for differential diagnosis of hypertrophic cardiomyopathies from

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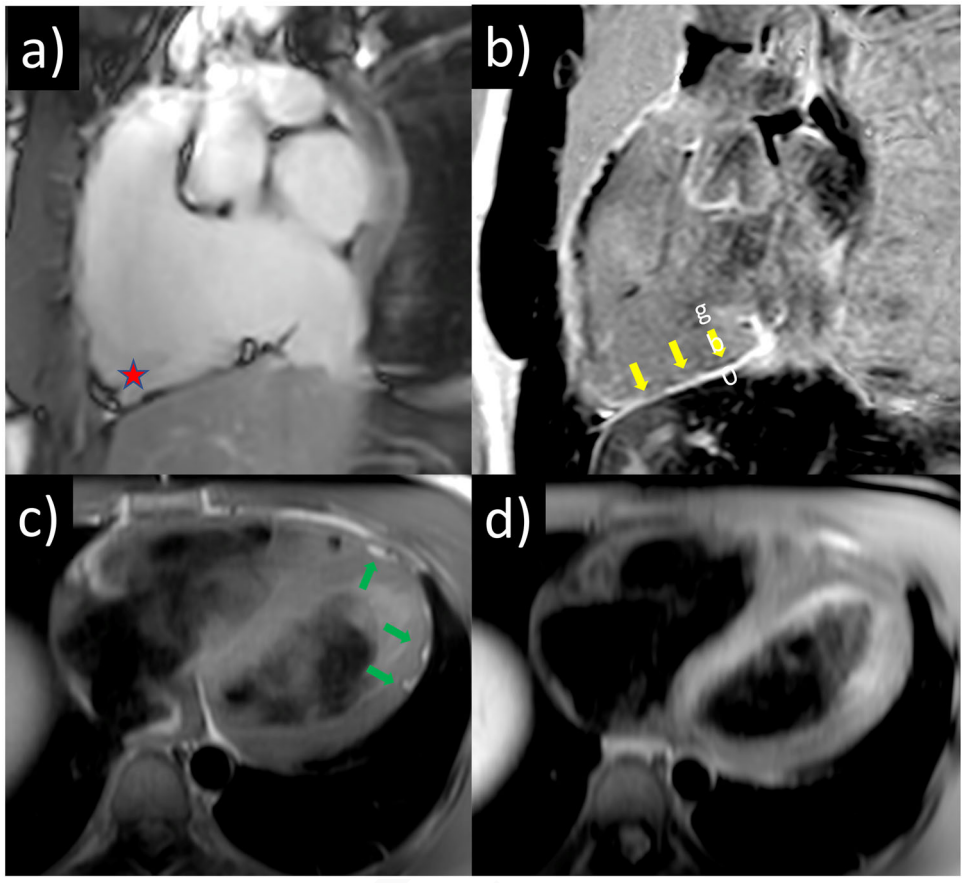

Figure 5. Example of a Class I indication of cMR: Diagnosis of ARVC. A 28-year-old male with cardiac arrest during sport. A) cine images of the RV showed dilatation (152 ml/m2) reduced EF (24%) and focal aneurysm (star). B) LGE showed fibrosis in the RV (yellow arrow) C) T1 weighted images demonstrated high signal corresponding to fat infiltration in the epicardium of the left ventricle (green arrow), confirmed by fat suppression (D)

phenocopies such as Fabry disease or amyloidosis through native T1 times and LGE patterns. The extent of LGE in hypertrophic has been associated by numerous studies with increased risk of arrhythmia and sudden cardiac death [30]. This is now well recognised in the latest 2022 guidelines for arrhythmia and SCD [3], which recommend systematic cMR with LGE in HCM patients (Figure 4) for diagnostic work-up as a class I-C indication. Also, they recognise a large extent of LGE (i.e. >15%) and the presence of left ventricular (LV) apical aneurysms and left ventricular ejection fraction (LVEF) < 50% (which can be better detected by cMR than echocardiography) as modulating risk factors for SCD. The new guidelines state that presence of either of these risk factors should warrant ICD implantation in patients with an intermediate ESC risk score for SCD (i.e. 4-6%) with a class IIa-C indication and may be even considered with a low (<4%) SCD ESC risk score with a class IIb-C indication. The newest guidelines for cardiomyopathies also

cMR is also instrumental for the diagnosis of ARVD/C (Figure 5), as it facilitates more precise assessment of right ventricular volume and function than echocardiography, which are essential components of the 2010 Task Force Criteria for ARVD/C diagnosis [31]. cMR can also detect other characteristic features of ARVD such as fatty infiltration and LGE in the right ventricle. These are however not currently included in the Task Force Criteria. The new 2022 ESC guidelines for ventricular arrhythmia and SCD [3] now recognise the importance of cMR in the diagnosis of ARVD, with a Class I-C indication. Unfortunately, the criteria for left sided ARVD remain ill-defined, requiring more precise delineation in future guidelines. Additionally, task force criteria or future guidelines should take into consideration identification of RV fat and late gadolinium enhancement (LGE) in the diagnosis of ARVD.

cMR LGE can also be present in numerous neuromuscular diseases. According to the 2022 guideline for ventricular arrhythmia and SCD [3] in myotonic dystrophy electrophysiological evaluation should be considered in patients who are older than 40 years and have supraventricular arrhythmias or who are older than 40 years and have significant LGE on cMR (Class

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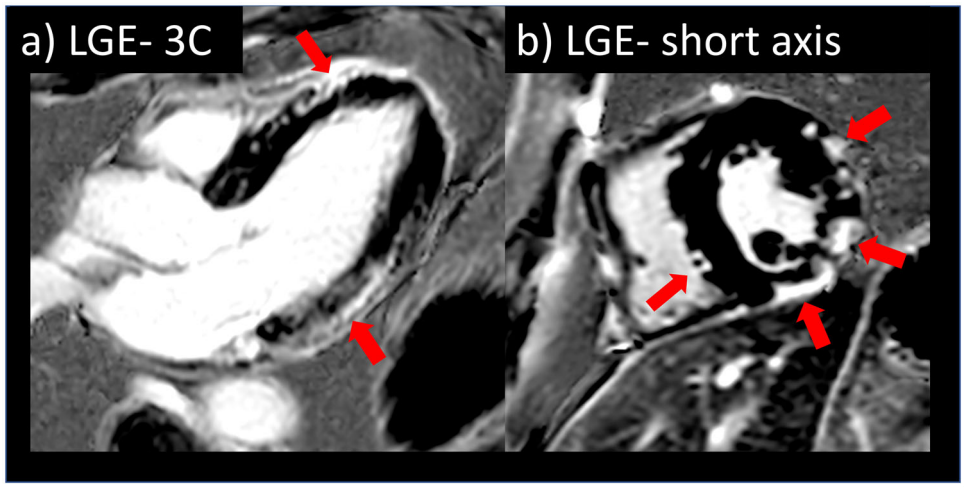

Figure 6. Example of a Class IIa indication for cMR: evaluation of becker cardiomyopathy. A 46-year-old male with Becker cardiomyopathy. Echocardiography was normal. cMR showed normal LV and RV function, but LGE images demonstrated diffuse epicardial LGE, considered as risk factor for arrythmia.

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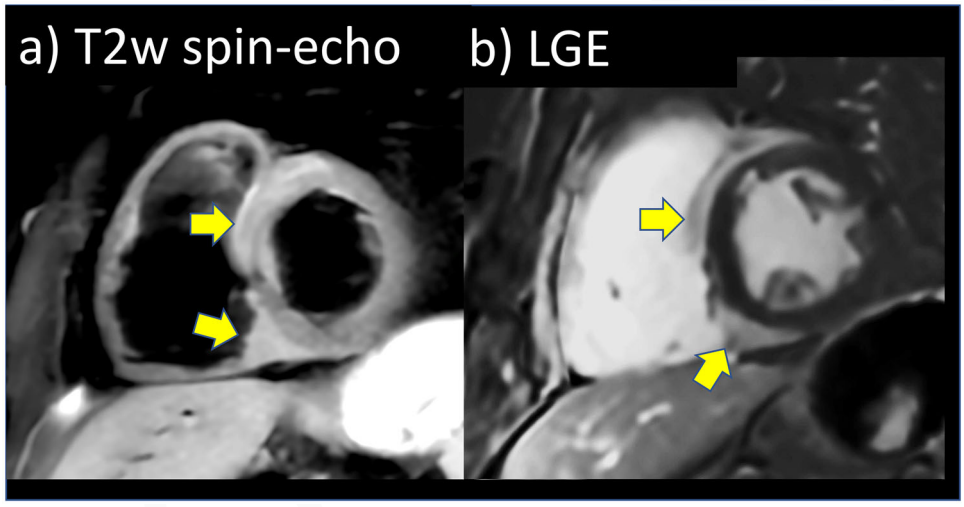

Figure 7. Example of a Class IIa indication for cMR: evaluation of suspected sarcoidosis. A 60-year-old man with pacemaker implantation 1 year ago (cMR normal at that time) for 2nd degree AV block. Patient presented progressive dyspnoea for 1 month. cMR shows oedema in the RV septum and inferior insertion point on T2 weighted images (a) and LGE in corresponding areas (b), suggesting sarcoidosis, which was subsequently confirmed by histopathology.

IIa-C), whereas implantation of an ICD over a permanent pacemaker may be considered in patients with additional risk factors for VAs and SCD such as structural abnormalities by LGE-cMR (Class IIb-C). In Duchene/Becker muscular dystrophy (Figure 6) the new guidelines also state that implantation of an ICD may be considered in the setting of significant LGE by cMR (Class IIb-C). However, both these indications are based on few scientific documentations. Also, the statements would actually imply that both patients with myotonic dystrophy or Becker/Duchenne's disease should be regularly followed using cMR. This is, however, not clearly written out. Additionally, the definition of 'significant LGE' remains ambiguous. Consequently, we believe that that these recommendations should be more explicit.

Finally, cMR is also highly useful for diagnosis of inflammatory myocardial diseases such as myocarditis [11]. Although this is recognised in current guidelines, they do not yet make any recommendations for its use in suspected cases (contrasting the Class I-C indication of cMR for suspected myocardial infarction in non-ST elevation myocardial infarction). cMR is also instrumental for the identification of cardiac sarcoidosis (Figure 7). Studies have demonstrated that cardiac sarcoidosis conformed by LGE is associated with a poor prognosis, including a high rate of ventricular arrhythmias and mortality. As a result the new 2022

guidelines for arrythmia and SCD now indicate that patients with cardiac sarcoidosis should (class IIa-C) undergo ICD implantation if they have significant LGE at cMR with LVEF ≤35% after resolution of acute inflammation, and may undergo positron emission tomography for risk stratification (class IIb-C) if they have LVEF 35–50% and minor LGE at cMR, after resolution of acute inflammation, In our opinion, the guidelines remain too vague on the definition of 'significant' and 'minor' LGE. Also given the extremely high risk of ventricular arrhythmia in patients with sarcoidosis irrespective of LVEF and inflammatory status, they are probably still not stringent enough. In our opinion, presence of LGE and confirmation of cardiac sarcoidosis should probably indicate ICD implantation irrespective of LVEF and inflammatory status.

Besides for diagnosis and risk stratification, the newest 2023 guidelines for cardiomyopathies [4] also recommend that it should be considered to repeat contrast-enhanced cMR (Class IIa – level C indication) every 2-5 years depending on the initial severity and clinical to follow disease progression and assessment of therapeutic response, particularly in patients with amyloidosis, Anderson Fabry disease, sarcoid, inflammatory cardiomyopathies and hemochromatosis with cardiac involvement. Indeed, the changes in LGE, and of native tissue times (such as T1 in amyloidosis, Fabry disease, T2* in hemochromatosis) and ECV (in amyloidosis) are correlated with the severity of disease and may allow to determine improvement and therapeutic response or, by contrast, progression of the disease.

Evaluation of patients with arrhythmias and SCD survivors

In patients with ventricular arrhythmia or those who have survived sudden cardiac death, cMR with LGE offers invaluable insights into the underlying cardiomyopathy. This not only enhances the comprehension of the pathophysiological mechanisms at play but also facilitates the judicious selection of an appropriate therapeutic approach, such as guiding ablation therapy to target re-entry circuits frequently localised within scarred cardiac tissue. This application is particularly advantageous in the evaluation of individuals with monomorphic sustained ventricular tachycardia, as cMR with LGE can identify previously undetected areas of myocardial scarring, discern inflammatory conditions such as myocarditis and sarcoidosis, and reveal potential arrhythmogenic cardiomyopathies affecting either the right or left ventricle, as well as scarring within the mitral annulus. In light of this, the new 2022 guidelines [3] offer a class IIa-B recommendation for the use of cMR in patients with newly documented VA (frequent PVCs, NSVT, SMVT) and suspicion of structural heart disease other than CAD after initial evaluation. They also recommend cMR as class IIa-C indication for patients with PVCs/VT and a presentation not typical for an idiopathic origin, (older age, right bundle branch block morphology, sustained monomorphic ventricular tachycardia consistent with re-entry) despite a normal echocardiogram. In our view, it is clearly appropriate to perform cMR in all patients with sustained or non-sustained ventricular tachycardia of unknown aetiology given the seriousness of the condition. However, cMR may not be necessary for all patients with frequent ventricular beats. While cMR is effective in detecting structural abnormalities and arrhythmogenic right ventricular dysplasia (ARVD) in this population [32], frequent premature ventricular beats are common and performing cMR may not be necessary in all cases, as many of these conditions are benign. We recommend reserving the use of cMR for patients exhibiting a substantial burden of premature ventricular beats (e.g. >10000/24 h) or those presenting with high-risk characteristics (e.g. syncope/presyncope, family history of sudden cardiac death, and abnormal resting ECG).

cMR is of great value in individuals who have survived SCD, as it may reveal the underlying cause in many cases and alter the suspected diagnosis in a considerable number of SCD survivors [33–35]. Consequently, the latest guidelines indicate cMR with LGE as a class I indication for evaluating cardiac structure and function in all SCA survivors in whom the origin of the disease is unclear. cMR could be likewise beneficial in some patients with implanted ICD who experience recurrent arrhythmias, as it could allow for the identification of the cause of the disorder if it is unknown, or for the detection of disease progression, mainly in inflammatory illnesses, such as sarcoidosis [36,37]. The identification of these lesions may also be of potential use for programming ablation therapy, although this is not yet addressed in the guidelines and may need to be included in future revisions.

Lastly, cMR has also emerged as a promising tool for the evaluation of atrial fibrosis in atrial fibrillation. Studies have indicated that the extent of fibrosis may predict the success rate of ablation therapy [38] although it was not able to guide the ablation strategy [39]. Unfortunately, the interpretability of fibrosis degree in the atria remains operator-dependent, which is likely why the use of this technique is not mentioned in the 2020 ESC guidelines for atrial fibrillation [40].

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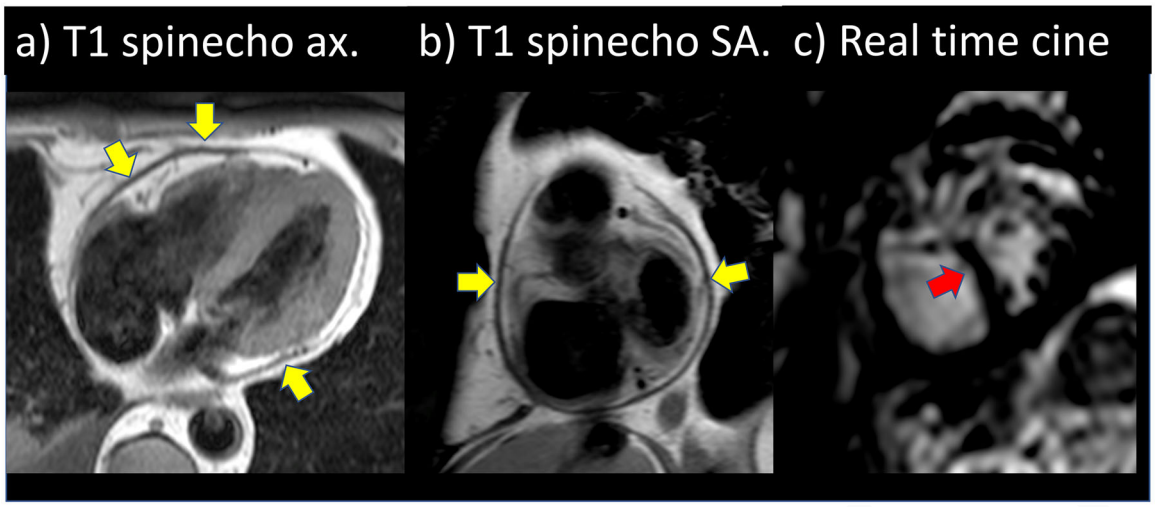

Figure 8. Example of a Class I indication for cMR: evaluation of pericardial constriction. A 56-year-old man complained of dyspnoea 3 months after acute pericarditis. Axial (a) and short axis (b) T1 weighted turbo-spin echo images showed diffuse pericardial thickening (yellow arrows). Real-time cine (c) showed important paradoxical septal movement (red arrow) during inspiration confirming constrictive physiology.

Valvular heart disease

Comprehensive cMR has also considerable potential for the assessment of valvular heart diseases. Its most advantageous features are its ability to accurately measure ventricular mass, systolic and diastolic volumes, and ejection fraction. Moreover, it allows for direct quantitative measurement of regurgitant volumes in the aorta and pulmonary artery through phase contrast imaging, as well as for the indirect estimation of regurgitant volumes of the mitral and tricuspid valves, using Simpson's method and the forward flow volume in either the aorta or pulmonary artery through phase contrast imaging. Additionally, cMR can identify late gadolinium enhancement in several advanced valvular disorders, such as aortic stenosis, aortic regurgitation, and mitral regurgitation, and this has been associated with outcomes. Finally, cMR can also provide a comprehensive evaluation of the aorta, which is advantageous in the evaluation of aortic and, particularly, bicuspid valve diseases. All in all, cMR is more useful for the assessment of regurgitant than stenotic valve diseases, and its primary utility lies in its ability to precisely quantify regurgitant volume as well as ventricular volumes in mitral and, especially, aortic regurgitation in cases where conventional echocardiography has difficulty or discordant results (e.g. in patients with multiple or highly eccentric jets, or in cases of poor echocardiographic windows). Therefore, cMR should be as a supplementary diagnostic modality in instances where echocardiographic findings yield inconclusive results. This recommendation is duly acknowledged in the position paper of the European Association for Cardiovascular Imaging (EACVI) for valvular heart disease [41]. Yet the current 2021 ESC guidelines on valvular heart disease fail to provide a recommendation for the use of cMR and solely state that 'In patients with inadequate echocardiographic quality or discrepant results, cMR should be used to assess the severity of valvular lesions, particularly regurgitant lesions, and to assess ventricular volumes, systolic function, abnormalities of the ascending aorta, and myocardial fibrosis'. In our opinion, given the considerable amount of recent evidence regarding the prognostic value of cMR for aortic [42] and mitral regurgitation [43] future revisions of the guidelines should include more explicit instructions for the utilisation of cMR in regurgitant valve disease.

Pericardial diseases

cMR also has substantial value in the evaluation of pericardial disease as it allows comprehensive examination of the pericardium on T1-weighted anatomical images with high resolution in multiple directions, enabling assessment of its thickness, regularity and the presence of tumoral invasion. Furthermore, cMR can detect pericardial effusion and cysts on SSFP cine images, and T1 and T2-weighted images may allow to clarify the nature of the effusion. Moreover, LGE imaging can not only identify inflammation linked to the response to anti-inflammatory treatment but also provide evidence of myocardial involvement, such as perimyocarditis or myopericarditis Cine and real-time images, as well as phase contrast measurements, can

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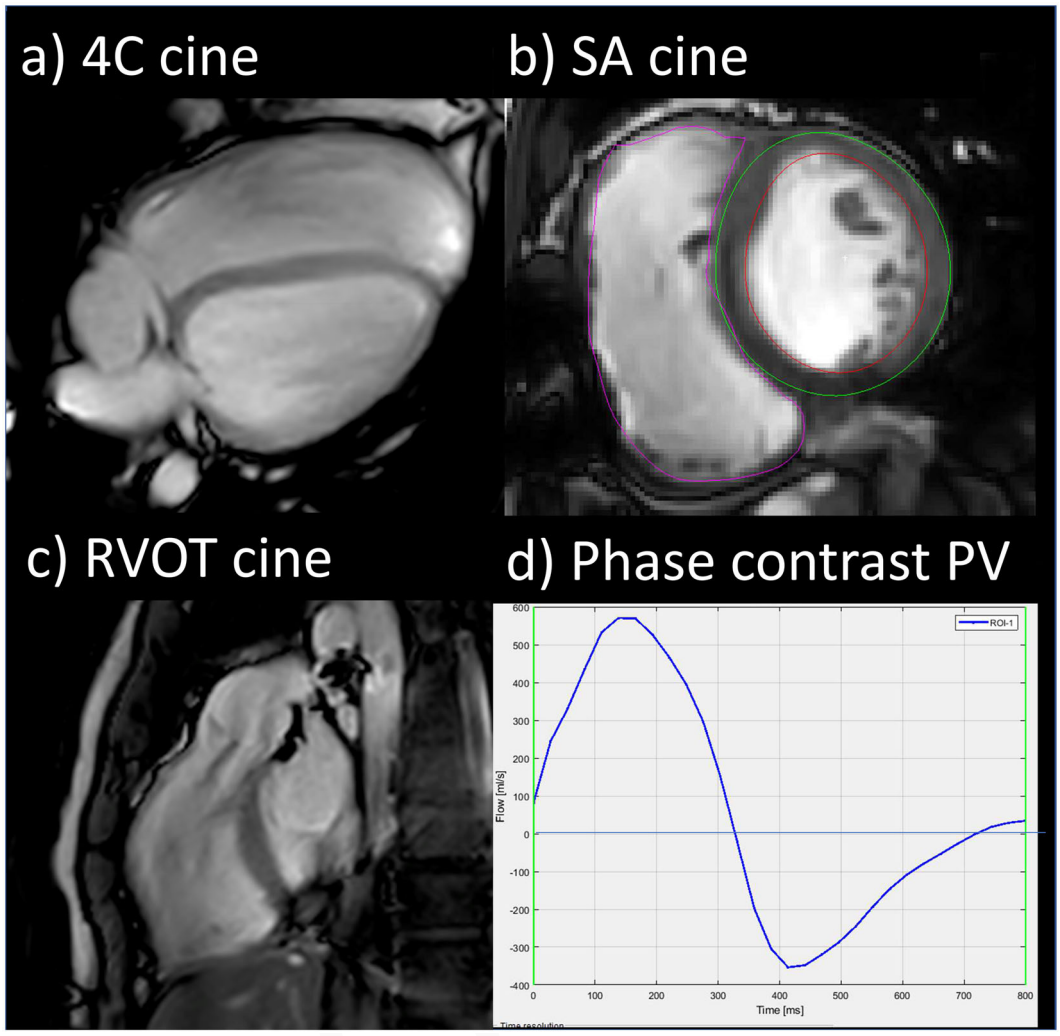

Figure 9. Example of indication for cMR: evaluation of tetralogy of Fallot. A 36-year-old male with repaired tetralogy of Fallot at 1 year age. cMR showed significantly dilated RVEDVi (160 ml/m2) with mildly altered RVEF (45%), normal LVEDVi (72 ml/m2) and LVEF (65%) and severe pulmonary regurgitation (RV 74 ml or 57% RF)

be used to evaluate the hemodynamic consequences and confirm constriction (Figure 8). Accordingly, the 2015 ESC guidelines on pericardial disease [44] recommend the use of CT or cMR in cases of suspected loculated pericardial effusion, pericardial thickening and masses, as well as associated chest abnormalities as a IIa level C recommendation. Also, CT and/or cMR are indicated with a level I-C recommendation as second-level imaging techniques to assess calcifications (CT), pericardial thickness, degree and extension of pericardial involvement in suspected pericardial constriction. cMR is also useful (Level IIB-C recommendation) in guiding empiric anti-inflammatory treatment, especially in cases where there is a transient or new diagnosis of constriction accompanied by evidence of pericardial inflammation (i.e. CRP elevation or pericardial enhancement on CT/cMR) with a level IIB-C recommendation.

Adult congenital heart disease

Finally, cMR is essential for the evaluation of patients with congenital heart disease due to its capacity to comprehensively evaluate cardiac anatomy, and particularly right ventricular volume and function, quantifying pulmonary regurgitation, and precisely characterising cardiac shunts with phase contrast imaging. Moreover, it enables 3D angiography of the aortic and pulmonary vessels, thereby allowing to evaluate the permeability of conduit repair surgery and detecting collateral pathways. Additionally, cMR can detect myocardial fibrosis through late gadolinium enhancement and identify ischaemia through stress perfusion imaging. The 2020 ESC guidelines for congenital heart disease [45] mention multiple recommendations regarding the use of cMR: They propose cMR to evaluate ventricular volumes and shunt severity in atrial septal defect, ventricular septal defect,

atrioventricular septal defect, or patent ductus arteriosus. They also mention CT or cMR for comprehensive evaluation of the aorta in congenital aortic stenosis and particular bicuspid valve disease, for supra or infraaortic stenosis, aortic coarctation and Marfans disease. Further, they propose evaluation of RV volumes and function by cMR for patients with right ventricular obstruction syndrome and for Ebstein's abnormality. In tetralogy of Fallot (Figure 9) they consider cMR the preferred modality for assessing RV volume and function, pulmonary regurgitation, size, shape and expansion of the pulmonary arteries and residual shunt (Qp/Qs ratio) and recommended that all tetralogy of Fallot patients have regular cMR examinations depending on the pathology identified. The guidelines also state that cMR provides more reliable and more robust quantitative assessment of systemic RV systolic function than echocardiography, and of patency of the conduits in patients with transposition of the great arteries repaired by atrial switch, or with the Rastelli operation and especially indicate cMR for quantification of ventricular volumes mass and EF in congenitally corrected TGV. Lastly, they also consider cMR as the imaging modality of choice for extracardiac anatomy, quantification of ventricular volumes, EF, and relative distribution of blood flow in the left and right lungs in univentricular hearts, particularly after Fontan operation and suggest using cMR at least once at adult age, and follow-up cMR on an individual basis according to baseline findings.

Unfortunately, all these cited indications lack a clear level of recommendation. The only clear recommendation specifically concerns patients with anomalous coronary artery vessels, where non-pharmacological functional imaging (e.g. nuclear study, echocardiography, or cMR with physical stress) is recommended with a Class I-C indication. The authors express concern about the absence of more specific guidelines for utilising cMR to evaluate right ventricular volumes and function in tetralogy of Fallot. This concern arises from the fact that the criteria for ventricular dilatation and right ventricular ejection fraction (RV-EF) are categorised as Class IIa-C criteria for pulmonary valve replacement or implantation of an implantable cardioverter-defibrillator (ICD). The same is true for patients with right ventricular to pulmonary valve conduits, where progressive right ventricular dilation to RV end-systolic volume index (RVESVi) >80 mL/m2, and/or right ventricular end-diastolic volume index (RVEDVi) >160 mL/m2, and/or progression of tricuspid regurgitation (TR) to at least moderate, are considered a Class IIa-C criteria for intervention. In our opinion the guidelines should also clearly recommend regular follow-up by cMR to track these endpoints with an indication class. We also advocate for the provision of more comprehensive guidelines delineating the appropriate use of cMR in assessing univentricular hearts and hearts affected by transposition of the ventricles.

Conclusion

The utility of cMR for the diagnosis and prognosis of many cardiac conditions is now well recognised in many of the latest ESC guidelines. In particular the important value of LGE by cMR for cardiomyopathies and for risk prediction of arrythmia in structural heart disease is now well acknowledged by the guidelines. However, in our opinion, some recommendations for use of cMR remain unclear. Indeed, it appears illogical that cMR parameters are recommended as criteria for interventions in conditions such as muscular dystrophy, Becker/Duchenne, or Tetralogy of Fallot without explicitly highlighting the importance of undergoing cMR imaging within these patient groups. Furthermore, we assert that the recommendations concerning the utilisation of cMR in the context of valvular heart disease and adult congenital heart disease should be further clarified and reinforced. Also, the Level of Evidence in guideline indications remains often low (C) due to a lack of large prospective studies. Hence, additional research is needed to substantiate the effectiveness of cMR in guiding treatment decisions and predicting clinical outcomes. This should allow subsequent enhancement of clarity within the guidelines pertaining to the criteria for cMR usage, and a more equitable reimbursement system linked to certification of imaging specialists in this field.

Disclosure statement

No potential conflict of interest was reported by the authors.

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