The Role of Cardiac MRI in the Management of Ventricular Arrhythmias in Ischaemic and Non-ischaemic Dilated Cardiomyopathy

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Abstract

Ventricular tachycardia (VT) and VF account for the majority of sudden cardiac deaths worldwide. Treatments for VT/VF include anti-arrhythmic drugs, ICDs and catheter ablation, but these treatments vary in effectiveness and carry substantial risks and/or expense. Current methods of selecting patients for ICD implantation are imprecise and fail to identify some at-risk patients, while leading to others being overtreated. In this article, the authors discuss the current role and future direction of cardiac MRI (CMRI) in refining diagnosis and personalising ventricular arrhythmia management. The capability of CMRI with gadolinium contrast delayed-enhancement patterns and, more recently, T1 mapping to determine the aetiology of patients presenting with heart failure is well established. Although CMRI imaging in patients with ICDs can be challenging, recent technical developments have started to overcome this. CMRI can contribute to risk stratification, with precise and reproducible assessment of ejection fraction, quantification of scar and “border zone” volumes, and other indices. Detailed tissue characterisation has begun to enable creation of personalised computer models to predict an individual patient’s arrhythmia risk. When patients require VT ablation, a substrate-based approach is frequently employed as haemodynamic instability may limit electrophysiological activation mapping. Beyond accurate localisation of substrate, CMRI could be used to predict the location of re-entrant circuits within the scar to guide ablation.

Keywords

Cardiac MRI, risk stratification, cardiomyopathy, ventricular tachycardia ablation

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Ventricular tachycardia (VT) and VF occur mainly in people with impaired cardiac function and/or ischaemic heart disease, and account for the majority of sudden cardiac deaths worldwide.1 Treatment with anti-arrhythmic drugs such as amiodarone may be at best neutral in terms of mortality and carries significant long-term risks.2 While ICDs significantly improve survival for patients with significantly impaired left ventricular ejection fraction (LVEF), the devices also carry risks of infection and inappropriate shocks being given.3,4

Some patients may present with a ‘secondary prevention’ ICD indication such as sustained VT or VF arrest, but, in the primary prevention setting, the risk of arrhythmia is based on the presence and severity of structural heart disease. Selection of patients in this way lacks precision and fails to identify some at-risk patients while leading to overtreatment in others. Current guidelines recommend echocardiography as the first-line investigation for cardiac function due to ease of access, because the echocardiographic equipment is usually available in heart clinics, whereas cardiac MRI (CMRI) services currently tend to only be available in specialist (tertiary) centres.4 However, CMRI is superior in terms of both accuracy and reproducibility when quantifying LVEF and myocardial mass, and can overcome limitations of inadequate echocardiographic windows. CMRI offers a one-stop investigation for accurately establishing cardiac structure, function and myocardial tissue characterisation.

Understanding the Substrate for Ventricular Arrhythmia

Ischaemic Cardiomyopathy

Studies of cardiac tissue obtained before transplantation or following left ventricular (LV) aneurysm surgery, as well as more recent human and animal CMRI studies, have confirmed our understanding of the structural changes that occur in ischaemic cardiomyopathy (ICM). Strands of surviving tissue within and at the periphery of the infarct region form tortuous and slowly-conducting channels which support re-entry, so the infarct border zone frequently has a heterogeneous appearance on CMRI.5–10 Fenoglio et al. demonstrated there were bundles of surviving myocytes in endocardial resection samples; some of these had a diameter of <100 μm, but it was not known which of these channels were mechanistically important.11 De Bakker et al. showed that differential slow conduction occurs with multiple tracts <200 μm.9 Recently, ultra-
high (submillimetre) resolution ex vivo CMRI of infarcted porcine hearts showed conducting pathways were mainly subendocardial. However, in this study, a significant minority of pathways were observed to be entirely epicardial and would be inaccessible for endocardial catheter ablation.

Urgent reperfusion (by either thrombolysis or angioplasty) for MI reduces infarct size and the incidence of subsequent chronic VT. In observational studies, VT cycle lengths were shorter, possibly suggesting a smaller circuit, in patients who had received revascularisation than in those who had not been revascularised. This would suggest that reperfusion strategies can introduce greater substrate heterogeneity within the infarcted area.

Techniques that characterise and quantify the scar border zone or identify channels could improve risk stratification and treatment planning. However, while larger conducting channels may be identified using CMRI, it is likely that others are missed because of the limited spatial resolution of current clinical imaging. Where channels are too small to be visualised, measures of tissue heterogeneity may act as surrogates for the presence of ‘sub-resolution’ channels.

Non-ischaemic cardiomyopathy

The aetiology of VT in patients with non-ischaemic cardiomyopathy (NICM) is less well understood, partly because of the heterogeneity of underlying pathological processes in NICM. When regional fibrosis is detectable, it is often midwall or subepicardial, making access for catheter ablation challenging. These factors may explain why outcomes from NICM VT ablation are worse than those in ischaemic cardiomyopathy.

In contrast to macro re-entrant VT, polymorphic VT or VF may occur due to distinct (but related) mechanisms. Replacement fibrosis can be patchy and/or diffuse, with disruption of the left ventricular microarchitecture. This diffuse fibrosis provides the substrate for conduction block and micro re-entry resulting in VF. This substrate is often dynamic with progressive fibrosis, reducing the long-term efficacy of targeted substrate modification.

Cardiac MRI Tissue Characterisation

Late Gadolinium Enhancement

Late gadolinium enhanced (LGE) CMRI imaging has become the de facto standard for imaging myocardial fibrosis. This approach uses gadolinium as a contrast agent to highlight areas of heterogeneity within the myocardium, giving insights into the aetiology of NICM. T1 values are rapidly after myocardial infarction, and T2-weighted CMRI sequences, Acute myocardial injury results in interstitial oedema. This occurs though a map can be generated showing the native T1 values across an imaging slice. The T1 map may highlight focal areas of oedema as seen in acute myocarditis, acute myocardial infarction or takotsubo cardiomyopathy.

T1 Mapping

Conditions with diffuse tissue fibrosis are more challenging to detect with LGE if there are no unaffected myocardial segments. Measurement of absolute T1 relaxation values sidesteps the requirement for tissue inhomogeneity in LGE imaging. Spatial resolution is inferior to LGE imaging at approximately 1.4 × 1.9 × 6 mm and is challenging at higher heart rates, though native T1 mapping does not require the use of a contrast agent. As imaging protocols, field strength and acquisition parameters vary, reference T1 values are specific to the vendor/manufacturer.

Unlike LGE, native T1 values are frequently abnormal in diffuse diseases of the myocardium, giving insights into the aetiology of NICM. T1 values are increased by tissue oedema and fibrosis, and are reduced by lipid overload (e.g. in Anderson-Fabry disease) and iron overload. For clinical use, mid-myocardial septal values for T1 are reported, though a map can be generated showing the native T1 values across an imaging slice. The T1 map may highlight focal areas of oedema as seen in acute myocarditis, acute myocardial infarction or takotsubo cardiomyopathy.

Extracellular Volume

Contrast-enhanced T1 mapping allows the extracellular volume (ECV) to be estimated. By comparing pre- and post-contrast T1 values (referencing the T1 values of the blood pool and the patient’s haematocrit, a value for ECV is obtained. This is expressed as a fraction of the tissue volume; published normal values for ECV are approximately 25%. While native T1 values examine entire tissues, ECV characterises only the extracellular matrix and is therefore less affected by acute oedema. Higher ECV values are seen with expansion of the interstitium due to fibrosis or deposition and therefore correlate well with fibrotic changes at endomyocardial biopsy.

As with native T1, ECV can be expressed as a global value or as a map highlighting regional variation. While ECV is raised in areas of chronic infarction, its main advantage over LGE for arrhythmic risk stratification is its potential to identify diffuse myocardial fibrosis in NICM.

T2 Imaging

Acute myocardial injury results in interstitial oedema. This occurs rapidly after myocardial infarction, and T2-weighted CMRI sequences, which identify oedema, can predict final infarct size. In chronic conditions such as cardiac sarcoidosis, myocarditis, transplant rejection and toxic cardiomyopathies, T2-weighted imaging accurately...
Ischaemic and Non-ischaemic Dilated Cardiomyopathy

Comparison of Techniques
LGE CMRI identifies the aetiology of left ventricular systolic dysfunction (LVSD), and permits the identification and quantification of myocardial fibrosis. As a semi-quantitative technique, LGE can demonstrate only relative differences between fibrotic and non-fibrotic myocardium. As a result, diffuse diseases of the myocardium may be missed with this technique. Newer techniques such as T1 and ECV mapping have the advantage of being quantitative and, as such, can be used to identify such diffuse myocardial fibrosis seen in some forms of NICM. Table 1 demonstrates these differences. Examples of these techniques are shown in Figure 1 and Figure 2.

Current Clinical Application of Cardiac MRI
Current guidelines recommend echocardiography as the firstline investigation in patients presenting with heart failure or VT, although CMRI gains a class I recommendation if an infiltrative cause is suspected. With echocardiography or CMRI, regional wall motion abnormalities and wall thinning suggest an ischaemic aetiology, while global hypokinesis supports a non-ischaemic cause. However, assessment is highly dependent on image quality and CMRI can overcome inadequate echocardiographic windows. In patients presenting with VT, CMRI is particularly useful for identifying inflammatory or infiltrative aetiology as well as ischaemic and non-ischaemic cardiomyopathies. In one series, CMRI changed the working diagnosis in 50% of patients presenting with VT/VF. Myocardial infarction shows a subendocardial to full thickness pattern of LGE, which will conform to one or more coronary territories. Conversely, non-ischaemic dilated cardiomyopathy often has a more diffuse pattern of fibrosis. As a result, the location of regions highlighted by LGE in such patients is variable, but it is more commonly located in the midwall or epicardial regions of anteroseptal or inferolateral segments.

Revascularisation of hypokinetic non-infarcted chronically ischaemic tissues may result in functional recovery. Hyperenhancement transmurality in LGE CMRI correlates well with myocardial recovery after revascularisation. In a series of 50 patients, regions with <25% transmurality were likely to demonstrate improved contractility, while those with >50% transmurality showed poor functional recovery after revascularisation.

When myocardial ischaemia causes polymorphic VT/VF, revascularisation is indicated. However, in patients with sustained monomorphic VT, revascularisation is more contentious, since monomorphic VT usually reflects established substrate that may not be altered by revascularisation.

Indeed, in a case series of 65 patients with coronary disease and VT/VF, surgical revascularisation did not appear to affect inducibility of
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Non-ischaemic Cardiomyopathy

As in ICM, the presence of LGE on CMRI in patients with NICM strongly predicts mortality and arrhythmic events across the spectrum of LV impairment. Patients with fibrosis identified by LGE are also less likely to achieve reverse remodelling with medical therapy. The spatial distribution of fibrosis is also important, with septal scarring conferring a higher risk of sudden cardiac death (SCD) than inferolateral variants, and subepicardial scarring conferring a higher risk than linear mid-wall fibrosis.

Although patients with a low LVEF (<35%) have the highest individualised risk of SCD, this accounts for only ~20% of all cardiac arrests. The majority of cardiac arrests occur outside this high-risk category. Patients with fibrosis identified by LGE have worse outcomes than those without and risk stratification of individuals based on the presence or absence of LGE rather than on LVEF alone may aid patient selection for ICDs. For example, compared with all those with LVEF <35% (i.e. using echocardiographic risk stratification alone), those with an LVEF >35% and LGE have similar risks of SCD. Moreover, these selected patients with preservation of pump function will often have a lower competing risk of non-arrhythmic death.

In contrast with ICM, where scar-related monomorphic VT predominates, patients with NICM are more likely to experience polymorphic VT and VF. On a review of the literature, most studies examining CMRI for risk stratification in NICM do not differentiate between VT and VF (Table 2). This practical approach is helpful for treatment decisions. However, Piers et al. found that imaging activity predicts monomorphic VT but not polymorphic VT or VF, suggesting that factors other than macroscopic anatomical substrate may be important in arrhythmogenesis in NICM.

Patients with NICM with no evidence of fibrosis on CMRI have fewer arrhythmic events, a lower risk of death and a higher likelihood of reverse remodelling. Careful patient selection for prophylactic ICD implantation in this population is required, and it therefore seems logical that identification of fibrosis using CMRI could more accurately identify those who would benefit, particularly patients with NICM and those with an LVEF >35%. However, no trial data exist to supports this approach.

Ischaemic Cardiomyopathy

The presence of LGE with CMRI imaging strongly predicts mortality in patients with ischaemic cardiomyopathy, independently of LVEF, including in patients without detectable LVSD. Total scar burden correlates with mortality and ICD discharges, even in multivariate models including LVSD (Table 2). Quantification of the scar border zone (rather than scar core) or quantifying the number of peri-infarct channels are alternative approaches to predicting VT/VF events.

Cardiac MRI Risk Stratification

Current European Society of Cardiology guidelines for ICD implantation (in both ICM and NICM) are based upon LVEF and New York Heart Association class but not formal scar quantification. The more recent 2017 American Heart Association guidelines differ slightly, with a class IIa recommendation given for the use of CMRI imaging to aid risk stratification in patients with suspected NICM. To investigate the role of CMRI as a tool for risk stratification, PubMed was searched using the terms ‘Risk Assessment’ OR ‘Prognosis’ OR ‘Predictive Value of Tests’ AND ‘Myocardial Ischemia’ OR ‘Dilated Cardiomyopathy’ AND ‘Magnetic Resonance Imaging’ OR ‘Gadolinium’ to identify studies using CMRI to guide risk stratification. These studies are summarised in Table 2.

Late Enhancement

There is now persuasive evidence that quantification of the scar and/or border zone burden can be used to help risk stratify patients with both ICM and NICM, in addition to measures of LVEF. The fact that this relationship exists across the range of LVSD suggests that fibrosis itself is an important determinant of arrhythmic risk, rather than being simply a marker of end-stage disease.

While the presence of any degree of LGE predicts risk in both NICM and ICM, quantification of scar extent only appears to add substantial incremental risk prediction benefit in patients with ICM. However, the clinical applicability of fibrosis quantification is limited by a lack of consensus over which scar metrics and thresholds are the best predictors of outcomes, or how to apply these metrics to individuals.
| Author                  | n   | Method for Scar Quantification | HR for Adverse Outcome (95% CI) | Result                                                                                     |
|------------------------|-----|--------------------------------|---------------------------------|-------------------------------------------------------------------------------------------|
| **Ischaemic Cardiomyopathy** |     |                                |                                 |                                                                                           |
| Bello et al. 2005<sup>11</sup> | 48  | ≥2 SD above remote normal myocardium | Not given, p=0.02              | Greater infarct mass and infarct surface area predicts inducible VT at EPS                 |
| Yan et al. 2006<sup>12</sup> | 144 | ≥2 SD above remote normal myocardium | 1.45 (1.15–1.84) per 10% increase in scar border zone | Extent of the peri-infarct zone defined by delayed-enhancement CMRI is an independent predictor of post-myocardial infarction all-cause and cardiovascular mortality, after adjusting for LV volumes or LVEF |
| Schmidt et al. 2007<sup>13</sup> | 47  | FWHM                           | Not given, p=0.02              | Border zone mass was higher in those with inducible VT than those with no inducibility, but there was no difference in scar core mass |
| Roes et al. 2009<sup>14</sup> | 91  | FWHM (35-50%)                  | 1.49 1.01–2.20 per 10 g increase in scar border zone | Extent of infarct border zone is the strongest predictor of subsequent ICD therapy          |
| Kwon et al. 2009<sup>15</sup> | 349 | ≥2 SDs above remote normal myocardium | 1.02 (1.003–1.03) per 1% increase in LV scar | Scar mass predicts mortality or transplantation                                              |
| Kelle et al. 2009<sup>16</sup> | 177 | Number of AHA 17 segment model with enhancement | 1.27 (1.064–1.518) per additional enhanced segment | Number of AHA segments involved predicts death and non-fatal myocardial infarction.          |
| Heidary et al. 2010<sup>17</sup> | 70  | FWHM border zone (remote max to 50%), FWHM scar core (>50%) | Not given, p=0.03 | Total scar mass and border zone mass (but not scar core mass) predict adverse outcomes     |
| Scott et al. 2011<sup>18</sup> | 64  | The number of transmural scar segments (using AHA 17 segment model) | 1.48 (1.18–1.84) in multivariate analysis | The number of transmural scar segments predicts subsequent ICD therapies                   |
| Krittayaphong et al. 2011<sup>19</sup> | 1,148 | Visual presence of LGE | 3.92 (1.98–7.6) in multivariate analysis | LGE predicts MACE in a cohort with normal wall motion.                                      |
| Boyé et al. 2011<sup>20</sup> | 52  | ≥5 SD                          | Not given, p=0.02              | Infarct mass expressed as a percentage of LV mass predicts appropriate device therapy       |
| Rubenstein et al. 2013<sup>21</sup> | 47  | Between 2 and 3 SD above remote normal myocardium | 1.97 (1.04–3.73) per 1% increase in multivariate analysis | Border zone mass higher in those with VT inducibility (2.64% of LV mass) than those without (1.35%) |
| Alexandre et al. 2013<sup>22</sup> | 49  | Scar mass by manual planimetry | 1.08 (1.04–1.12) unadjusted, 3.15 (1.35-7.33) in multivariate analysis (per 1g extra scar mass) | Scar mass predicts appropriate device therapy                                               |
| Kwon et al. 2014<sup>23</sup> | 450 | ≥2 SD above remote normal myocardium | 1.34 (1.15–1.55) in multivariate analysis | Scar percentage strongly predicts mortality                                                  |
| Demirel et al. 2014<sup>24</sup> | 99  | FWHM                           | 2.01 (1.17–3.44) in multivariate analysis | Ratio of peri-infarct border zone to scar core is associated with appropriate ICD therapy |
| Rijnierse et al. 2016<sup>25</sup> | 52  | FWHM (>50%)                    | Not given, p=0.07              | Trend towards higher scar burden in those with inducible VT (not significant)              |
| **Non-ischaemic Cardiomyopathy** |     |                                |                                 |                                                                                           |
| Assomull et al. 2006<sup>26</sup> | 101 | Visual presence of midwall LGE | 3.4 (1.4–8.7) for presence of LGE | Presence of midwall fibrosis predicts death or hospitalisation                             |
| Wu et al. 2008<sup>11</sup> | 65  | Visual presence of LGE          | 8.2 (2.2–30.9) in multivariate analysis | Presence of LGE predicts cardiovascular death, ICD therapy and HF hospitalisation          |
| Iles et al. 2011<sup>27</sup> | 61  | Visual presence of LGE          | Not given, p=0.01              | Patients with LGE had significantly higher rates of appropriate ICD therapy                |
| Lehke et al. 2011<sup>28</sup> | 184 | Visual presence of LGE, SD >2 for quantification | 3.5 for presence of scar: 5.28 using threshold of scar >4.4% total LV mass | Presence of LGE predicts cardiac death, ICD therapy or HF hospitalisation                   |
| Nellán et al. 2013<sup>29</sup> | 162 | Both FWHM and SD methods used   | 14.5 (6.1–32.6) for LGE presence, 1.15 (1.12–1.18) for each 1% increase in scar volume | Presence and volume of LGE predicts cardiovascular death or ICD therapy                     |
| Gulati et al. 2013<sup>30</sup> | 472 | Visual presence, FWHM           | 2.96 (1.87–4.69) for presence of LGE, 1.1 (1.06–1.17) per 1% extra LVGE | LGE presence, extent predicts mortality, independently of LVEF                             |
| Machii et al. 2014<sup>31</sup> | 72  | Visual presence of LGE          | Not given, p=0.02 for extensive LGE versus no LGE | Lower event-free survival in patients with extensive LGE                                  |

(Continued)
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Table 2: Cont.

| Authors            | n   | Metric                          | Hazard Ratio (95% CI)            |
|--------------------|-----|--------------------------------|---------------------------------|
| Perazzolo-Marra et al. 2014a | 137 | Visual presence of LGE          | 3.8 (1.3–10.4) in multivariate analysis |
| Masci et al. 2014a | 228 | Visual presence of LGE          | 4.02 (2.08–7.76) in multivariate analysis |
| Piers et al. 2015a | 87  | Visual presence, FWHM           | 2.71 (1.10–6.69) for LGE presence |
| Shin et al. 2016a  | 365 | FWHM                           | 8.45 (2.91–24.6) for LGE extent ≥ 8%, increasing to 6.98 (1.74–28.0) for those with subepicardial pattern of disease |
| Mueller et al. 2016a | 56  | Visual presence of LGE          | 1.9 (1.1–3.4) of LGE presence VT inducibility |
| Puntmann et al. 2016a | 637 | T1 mapping                      | 1.1 (1.07–1.17) per 10 ms change in T1 time, multivariate analysis |
| Halliday et al. 2017a | 399 | Visual presence of LGE, FWHM for quantification | 9.2 (3.9–21.8) in patients with LVEF > 40% A 17.8% event rate (median follow-up 4.6 years) in patients with LGE |
| Halliday et al. 2016a | 874 | FWHM                           | LGE extent of 0 to 2.55%, 2.55% to 5.10%, and >5.10%, respectively, were 1.12 per 5% extra LGE mortality |

Studies showing the prognostic effect of CMRI data in ischaemic cardiomyopathy and non-ischaemic cardiomyopathy. AHA = American Heart Association; CMRI = cardiac MRI; EPS = electrophysiology study; ECV = extracellular volume; FWHM = full width at half maximum; HF = heart failure; LGE = late gadolinium enhancement; LV = left ventricle; LVEF = left ventricular ejection fraction; MACE = major adverse cardiac event; VT = ventricular tachycardia.

Extracellular Volume and T1 Mapping for Risk Stratification

Alternative metrics, such as native T1 values and ECV, measure diffuse myocardial fibrosis. In patients with both ICM and NICM, myocardial T1 values (at sites spatially discrete from areas of LGE) incrementally improved risk stratification in a model that already included LVEF, QRS duration, and metrics of scar core and border zone (using LGE). In a similar study using ECV rather than T1, high ECV values correlated with mortality. In two small case series, high ECV values correlated with ICD therapies. These studies suggest that, when dense scar is surrounded by diffusely fibrotic myocardium, VT/VF is more likely than if the scar is encompassed by normal myocardium.

ECV and T1 mapping techniques have a sound physiological basis for identifying diffusely abnormal myocardium not identified with LGE imaging. ECV is of particular interest as a marker of risk in patients with NICM who do not have identifiable LGE, since it offers the ability to identify diffuse interstitial fibrosis. Complementary assessment of diffuse and regional disease by ECV mapping and LGE respectively may provide incremental benefit for risk stratification in both ICM and NICM. ECV may also have value in further characterising the density of discrete scars, although data to support this use are limited.

Ablation for Ventricular Tachycardia

For patients with a high burden of VT, catheter ablation can successfully reduce ICD shocks. These procedures can be challenging, with significant morbidity and mortality, since VT is frequently poorly tolerated and precise localisation of re-entrant circuits using traditional electrophysiological techniques is often challenging. VT ablation therefore often targets the myocardial scar substrate. Differing approaches to substrate ablation have been described – linear transection, core isolation, scar homogenisation or abolition of late...
potentials. Often, this requires extensive, time-consuming ablation in haemodynamically fragile individuals, which could be streamlined with a more detailed appreciation of the underlying substrate. CMRI can be used to predict the location of re-entrant circuits and channels within the scar to guide ablation lesions, the success of which can be predicted by computer modelling.

Planning
The configuration of LGE on CMRI allows the operator to estimate the likelihood of successful ablation and identify whether epicardial access is required. Predominantly subendocardial ischaemic scar-related VT is usually treatable with endocardial ablation. Conversely, VT ablation in NICM may be hampered by inaccessibility of the substrate, and epicardial access may be required for patients with inferolateral and/or subepicardial scarring. Epicardial access is typically not required for patients with VT originating from a septal intramural scar, although outcomes from ablation of ‘deep’ substrate are poorer, as might be expected.

Image Fusion
Conventional 3D electroanatomical maps (EAMs) generated during ablation procedures may be inaccurate because of poor catheter contact or reach, and contact mapping of entire cardiac chambers is time consuming.

Clinical CMRI studies can be reconstructed into 3D geometries demonstrating the distribution of a scar (Figure 3). With further refinement using 3D acquisition and image-processing methods, channels that might facilitate re-entry can be identified in advance (Figure 4). These geometries can be used simply as a road map for the operator during ablation procedures. Alternatively, fusion of these 3D geometries with the EAM system can leverage the accurate and high resolution anatomical detail of clinical imaging, allowing the operator to observe CMRI (and/or CT) images directly in the mapping software to reduce the time spent generating EAMs. Contact mapping can be focused on regions of interest determined in advance, e.g. by using algorithms for localising the VT origin based on 12-lead ECG morphology or by non-invasive mapping (ECGI) techniques. While image fusion has the potential to streamline ablation procedures, as yet, the benefits of such an approach have not been formally evaluated, and widespread applicability is not assured since it requires significant clinical and imaging expertise.

Future Directions
Overcoming Technical Limitations of Cardiac MRI
Many patients at risk of VT/VF have cardiac implantable electronic devices (CIEDs). Historically, MRI has been contraindicated in patients with CIEDs due to safety concerns. However, with advances in CIED technology such as MRI-conditional devices, growing experience and appropriate precautions and monitoring, CMRI can often be performed safely even in patients with historic non-conditional devices. Nevertheless, images may be significantly degraded by the presence of CIEDs, particularly the anteroseptal regions of the left ventricle in patients with left-sided pulse generators that lie in close proximity to the heart. Wideband sequences are described which can reduce these artefacts.

LGE imaging is usually obtained by multiple short axis planes through the heart. This results in excellent in-plane resolution, but a large slice width (approximately 10 mm) between images. Reconstructions of the heart can suffer with a ‘partial volume’ artefact that can overestimate the infarct border zone. This effect can be mitigated by evolving techniques such as 3D image acquisition or super-resolution image reconstruction. Histological studies have demonstrated myocyte fibre disarray at the border zone of a chronic infarction. Due to anisotropic conduction of myocytes, knowledge of fibre orientation is potentially important to understand propensity to arrhythmia. Diffusion tensor imaging can demonstrate fibre direction and may thereby inform computer models of arrhythmia, although this use of CMRI is in its infancy.

Ventricular Tachycardia Stimulation and Modelling
Inducibility of VT during an electrophysiology study (EPS) by programmed ventricular stimulation (PVS) pacing from a right ventricular site predicts arrhythmic events in ICM. This meta-analysis demonstrated PVS had the power to predict subsequent arrhythmic events (pooled OR 4.00, 95% CI [2.30–6.96]). Depending on patient selection and the number of extrastimuli used, the sensitivity, specificity and predictive value of this test varies, although it is not commonly used clinically due to its invasiveness, cost and insufficient negative predictive value. In NICM, assessment with PVS is less well studied and probably less effective than with ICM.
Scar-related re-entry often relies upon functional block as well as anatomical barriers to conduction. Scar quantification methods do not account for these complex mechanisms, but computer modelling has the potential to improve risk stratification by combining a personalised anatomical model with simulation of tissue electrophysiology. This method allows simulated PVS performed from multiple sites in both ventricles. In a retrospective study of 41 patients with severe LVSD, by comparing these patient-specific simulations with clinical outcomes, a positive ‘virtual-heart arrhythmia risk predictor’ simulation was associated with adverse outcomes (OR 4.05 (95% CI [1.20–13.8]), which is similar to published results from invasive PVS. Work is ongoing to determine the utility of such simulations in preserved LVFS.108

Simulated PVS methods are computationally significantly more challenging in NICM where myocardial fibrosis is less confluent and more heterogeneous, and the microscopic nature of the substrate is difficult to fully characterise with clinical imaging. Moreover, the substrate in NICM is often progressive and, as such, risk stratification at a single time point may fail to accurately estimate lifetime risk.

These methods are promising but are potentially limited by simplifications and assumptions in models of cell and tissue electrophysiology, the computational resources required, and the resolution of currently available clinical imaging. Despite encouraging preliminary studies, there are significant obstacles to be overcome before these approaches can be used routinely in clinical practice.110 Constructing a personalised computational model of anatomy and electrophysiology requires calibration from clinical images and data that are often noisy and incomplete, so methods for embedding uncertainties and variability into computational models are an area of active research.111 Whether these approaches can be used to guide ICD implantation in the future remains to be seen. Technological advances in imaging and modelling, along with clinical studies of their utility, will help advance this promising concept.

Future Clinical Studies

Tissue characterisation to determine who needs and, perhaps more importantly, who does not need an ICD is a complex but evolving field. Estimates of risk currently do not allow for disease progression, and it is unclear how frequently investigations should be repeated, particularly for the dynamic substrate that occurs in some forms of NICM. The effect of dynamic conditions such as electrolyte disturbance, volume overload and myocardial ischaemia on arrhythmic risk remains unknown.

In the DANish Randomized, Controlled, Multicenter Study to Assess the Efficacy of Implantable Cardioverter Defibrillator in Patients With Non-ischemic Systolic Heart Failure on Mortality (DANISH) trial (NCT00542945), investigators found no overall mortality benefit for primary prevention ICD implantation in patients with NICM.112 However, outcomes were improved by ICD implantation for those in prespecified subgroups – namely younger patients and those with lower levels of N-terminal pro-brain natriuretic peptide (NT-proBNP) – who, presumably, had a lower risk of non-sudden death. Since CMRI studies have consistently demonstrated a higher arrhythmic burden in those with evidence of LGE, a clinical trial that used CMRI-based risk stratification in NICM patients with LVEF <35% would provide clinically useful information.

Similarly, the Cardiac Magnetic Resonance GUIDEd Management of Mild-moderate Left Ventricular Systolic Dysfunction (CMR_GUIDE) trial (NCT01918215) will identify patients who have evidence of LGE but do not qualify for ICD treatment under current guidelines (LVEF 35–50%), to determine whether prophylactic ICD implantation is beneficial.113 The Programmed Ventricular Stimulation to Risk Stratify for Early Cardioverter-Defibrillator (ICD) Implantation to Prevent Tachyarrhythmias Following Acute Myocardial Infarction (PROTECT-ICD) trial will examine whether a multiparametric risk stratification algorithm (including echocardiography, CMRI and PVS) used post-infarction will identify those who may benefit from early ICD implantation.114

Contribution to Novel Therapies

Recent developments in CMRI and electrophysiology mapping systems have shown real-time tracking and visualisation of catheter position during ablation procedures to be feasible and safe for an ‘anatomical’ ablation of the cavo-tricuspid isthmus.115,116 Advantages of such a system include 3D visualisation of catheter position within complex anatomical structures (including the ability to see surrounding structures) and real-time lesion evaluation. This technology has the potential to improve outcomes in ablation procedures, but significant technological challenges remain for its use in ventricular arrhythmia.

Stereotactic body radiotherapy has recently been reported as a novel, non-invasive treatment for VT.117,118 It is dependent on accurate anatomical localisation of arrhythmic substrate to determine the radiotherapy target. CMRI imaging is the ideal modality for treatment planning.

Conclusion

CMRI imaging can accurately quantify cardiac function, and characterise the myocardial substrate to refine risk stratification to identify people who may benefit from ICD implantation and revascularisation. Although large-scale trials in this area are required, it is likely that measures of scar quantification will become increasingly recognised by guidelines in future.

A multiparametric approach using imaging and other criteria may provide the most accurate risk assessment in the future, although the interaction between each of the metrics discussed is complex and requires careful study. Advanced techniques such as automated image segmentation and channel detection, or computer simulation of electrophysiology, offer significant potential, but are still in the early stages of development.

Significant challenges remain in overcoming technological barriers and understanding how best to use the considerable information gained from a CMRI study. Nevertheless, CMRI offers clinicians and researchers an increasingly comprehensive way to diagnose, risk stratify and tailor the treatment of patients with cardiomyopathy.
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11. Fenoglio JJ, Pham TD, Harken AH, et al. Recurrent sustained ventricular tachycardia: structure and ultrastructure of sites of ischemic ventricular tachycardia are in zones of tissue heterogeneity, visualized by magnetic resonance imaging in the infarcted human heart. 'Zigzag' course of activation. Circulation 1993;88:915–26. https://doi.org/10.1161/01. Cir.88.3.915; PMID: 8353918.

12. Pashakhanloo F, Herzka DA, Halperin H, et al. Role of myocardial fibrosis in ventricular arrhythmias in porcine models. Circ Arrhythm Electrophysiol 2011;4:324–30. https://doi.org/10.1161/CIRCEP.110.959544; PMID: 22038750.

13. Wijnmaalen A, Schalij MJ, von der Thüsen JH, et al. Accurate objective indexing by contrast-enhanced magnetic resonance imaging in a canine myocardial infarction model. J Am Coll Cardiol 2004;44:2383–9; PMID: 15640702.

14. Khan JH, Aronson NW, Hildreth MA, et al. Comparison of semi-automated methods to quantify infarct size and area at risk by cardiac magnetic resonance imaging at 1.5 and 3.0 T field strengths. J Magn Reson Imaging 2015;41:479–86. https://doi.org/10.1002/jmri.24955; PMID: 25887957.

15. Arntz UC, Gavilán JM, Gindea N, et al. Evidence for the hibernating myocardium. J Am Coll Cardiol 2008;52:1169–77. https://doi.org/10.1016/j.jacc.2008.07.070; PMID: 18559509.

16. Kottkamp H, An V, Vahakes LA, et al. Clinical coronary revascularization in survivors of prehospital cardiac arrest: its influence on inducible ventricular arrhythmias and left ventricular function. J Am Coll Cardiol 1995;25:267–73. https://doi.org/10.1016/0735-1097(95)00308-3; PMID: 7612974.

17. Holmgren P, Deger WJ, Wilkins E, Brugada P. Coronary artery bypass grafting and defibrillator implantation in patients with ventricular tachycardia/myocarditis and ischaemic heart disease. Pacing Clin Electrophysiol 1999;22:1129–35. https://doi.org/10.1111/j.1540-8199.1999.tb00387.x; PMID: 10562467.

18. Wu TJ, Ong JJ, Hwang C, et al. Characteristics of wave front propagation during ventricular fibrillation in human hearts. Circulation 2010;121:1887–95. https://doi.org/10.1161/CIRCULATIONAHA.105.602870; PMID: 16880326.

19. Nash MP, Mourad A, Clayton RH, et al. Evidence for the ‘hibernating myocardium’. J Am Coll Cardiol 2000;2:271–8. https://doi.org/10.1016/s0735-1097(00)00436-7; PMID: 10593597.
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**ARRHYTHMIA & ELECTROPHYSIOLOGY REVIEW**

69. Messroghli DR, Moon JC, Ferreira VM, et al. Clinical tools to predict ventricular tachycardia substrate in nonischaemic dilated cardiomyopathy. JACC Cardiovasc Imaging 2015;12:2106–14. https://doi.org/10.1016/j.jcmg.2018.03.006; PMID: 29640351.

70. Piers SRD, Everaerts K, van der Geest RJ, et al. Myocardial tissue characterization by cardiac magnetic resonance imaging using wideband sequences in patients with scar-related ventricular tachycardia. Circ Cardiovasc Imaging 2016;9:933–46. https://doi.org/10.1161/CIRCIMAGING.115.002965; PMID: 27388666.

71. Chem Z, Sohal M, Voigt T, et al. Myocardial tissue voltage mapping to assess post-infarct scar characteristics in patients with ventricular tachycardia: real-time image integration and review of the literature. Eur Heart J 2011;32:104–14. https://doi.org/10.1093/eurheartj/ehq343; PMID: 20944484.

72. Andreu D, Penela D, Alocia D, et al. Cardiac magnetic resonance–aided scar denoising: influence on acute and long-term outcomes. J Magn Reson Imaging 2017;46:1121–4. https://doi.org/10.1002/jmri.25208; PMID: 28705325.

73. Nieder T, Sibilia S, Maccabello G, et al. Catheter ablation of ventricular arrhythmia in nonischaemic cardiomyopathy: anteroseptal versus intercalated scar sub-types. J Am Coll Cardiol 2014;64:1418–33. https://doi.org/10.1016/j.jacc.2014.03.051; PMID: 24675607.

74. Gökoglu Y, Mohanty S, Gianni C, et al. Scar homogenization for Cardiovascular Imaging (EACVI). Circulation 2015;131:2787–93. https://doi.org/10.1016/j.circlevas.2015.05.026; PMID: 26090916.

75. Chen Z, Sohal M, Voigt T, et al. Myocardial tissue voltage mapping to assess post-infarct scar characteristics in patients with ventricular tachycardia: real-time image integration and review of the literature. Eur Heart J 2011;32:104–14. https://doi.org/10.1093/eurheartj/ehq343; PMID: 20944484.

76. Segal OR, Chow AWC, Wong T, et al. A novel algorithm for determining endocardial VT exit site from 12-lead surface ECG characteristics in human, infarct-related ventricular tachycardia. Circ Arrhythm Electrophysiol 2016;9:933–46. https://doi.org/10.1161/CIRCEP.115.002965; PMID: 27388666.

77. Oloriz T, Silberbauer J, Maccabelli G, et al. Catheter ablation in patients with ventricular tachycardias: real-time image integration and review of the literature. Eur Heart J 2011;32:104–14. https://doi.org/10.1093/eurheartj/ehq343; PMID: 20944484.

78. Keijmen AM van der Geest RJ, van Huis van Tsela CF, et al. Head-to-head comparison of contrast-enhanced magnetic resonance imaging and intracoronary electrophysiology-guided EP ablation procedures. JACC Cardiovasc Imaging 2017;10:717–27. https://doi.org/10.1016/j.jcmg.2018.03.006; PMID: 29680351.

79. Kelle S, Roes SD, Klein C, et al. Prognostic value of myocardial collagen organization within the fibrotic scar after myocardial infarction and preserved ejection fraction. J Am Coll Cardiol 2018;11:1274–84. https://doi.org/10.1016/j.jcmg.2018.03.006; PMID: 29680351.

80. León DG, López-Yunta M, Alfonso-Almazán JM, et al. Defibrillator implantation for guiding EP ablation procedures. JACC Cardiovasc Imaging 2017;10:717–27. https://doi.org/10.1016/j.jcmg.2018.03.006; PMID: 29680351.

81. Mirams GR, Pathmanathan P, Gray RA, et al. Uncertainty and background and significance. JACC Clin Electrophysiol 2017;3:851–61. https://doi.org/10.1016/j.jcledp.2017.04.007; PMID: 28760258.

82. Andreu D, Fernández-Armenta J, Acosta J, et al. A QRS Association model. J Cardiovasc Electrophysiol 2017;28:75–81. https://doi.org/10.1111/jce.13264; PMID: 28012052.

83. Cano O, Hutchinson M, Lin D, et al. Electroanatomic substrate modification in patients with coronary heart disease (VTACH): a randomized double-blind trial. Circulation 2005;111:233–8. https://doi.org/10.1161/01.CIR.101.111288-721083; PMID: 16018884.

84. Njeim M, Desjardins B, Bogun F. Multimodality imaging technology. J Am Coll Cardiol 2011;57:2056–64. https://doi.org/10.1016/j.jacc.2011.03.031; PMID: 21885406.

85. Køber L, Thune JJ, Nielsen JC, et al. Defibrillator implantation for guiding EP ablation procedures. JACC Cardiovasc Imaging 2017;10:717–27. https://doi.org/10.1016/j.jcmg.2018.03.006; PMID: 29680351.

86. Oloriz T, Silberbauer J, Maccabelli G, et al. Catheter ablation in patients with ventricular tachycardias: real-time image integration and review of the literature. Eur Heart J 2011;32:104–14. https://doi.org/10.1093/eurheartj/ehq343; PMID: 20944484.

87. Andreu D, Penela D, Alocia D, et al. Cardiac magnetic resonance–aided scar denoising: influence on acute and long-term outcomes. J Magn Reson Imaging 2017;46:1121–4. https://doi.org/10.1002/jmri.25208; PMID: 28705325.

88. Nieder T, Sibilia S, Maccabello G, et al. Catheter ablation of ventricular arrhythmia in nonischaemic cardiomyopathy: anteroseptal versus intercalated scar sub-types. J Am Coll Cardiol 2014;64:1418–33. https://doi.org/10.1016/j.jacc.2014.03.051; PMID: 24675607.

89. Gökoglu Y, Mohanty S, Gianni C, et al. Scar homogenization for Cardiovascular Imaging (EACVI). Circulation 2015;131:2787–93. https://doi.org/10.1016/j.circlevas.2015.05.026; PMID: 26090916.

90. Segal OR, Chow AWC, Wong T, et al. A novel algorithm for determining endocardial VT exit site from 12-lead surface ECG characteristics in human, infarct-related ventricular tachycardia. Circ Arrhythm Electrophysiol 2016;9:933–46. https://doi.org/10.1016/j.jcmg.2018.03.006; PMID: 29680351.

91. Andreu D, Penela D, Alocia D, et al. Cardiac magnetic resonance–aided scar denoising: influence on acute and long-term outcomes. J Magn Reson Imaging 2017;46:1121–4. https://doi.org/10.1002/jmri.25208; PMID: 28705325.
Ischaemic and Non-ischaemic Dilated Cardiomyopathy

126. Demirel F, Adiyaman A, Timmer JR, et al. Myocardial scar with ischemic cardiomyopathy. JACC Cardiovasc Imaging 2011;4:871–9. https://doi.org/10.1016/j.jcmg.2011.04.014; PMID: 21836379.

127. Iles L, Pfluger H, Lefkovits L, et al. Myocardial fibrosis predicts long term appropriate ICD therapy in patients with dilated cardiomyopathy. JACC Cardiovasc Imaging 2011;4:864–8. https://doi.org/10.1016/j.jcmg.2011.05.013; PMID: 23932642.

128. Neilan TG, Casillo-Filho OR, Dank SB, et al. CMR quantification of myocardial scar provides additional prognostic information in nonischemic cardiomyopathy. JACC Cardiovasc Imaging 2013;6:944–54. https://doi.org/10.1016/j.jcmg.2013.05.011; PMID: 23622786.

129. Shin DG, Lee H-J, Park J, et al. Pattern of late gadolinium enhancement predicts arrhythmic events in patients with non-ischaemic dilated cardiomyopathy. JACC Cardiovasc Imaging 2014;7:593–600. https://doi.org/10.1016/j.jcmg.2015.02.005; PMID: 24926567.

130. Sohn DG, Lee H-I, Park J, et al. Pattern of late gadolinium enhancement predicts arrhythmic events in patients with non-ischaemic cardiomyopathy. JACC Cardiovasc Imaging 2016;9:40–50. https://doi.org/10.1016/j.jcmg.2015.12.001; PMID: 26762873.

131. Machi M, Sabih H, Shrivat K, et al. Distribution of late gadolinium enhancement predicts arrhythmic outcome. Magn Reson Imaging 2014;32:118–24. https://doi.org/10.1016/j.mri.2013.10.011; PMID: 24315193.

132. Peruzzo Maria M, De Lazzeri M, Zorzi A, et al. Impact of the presence and amount of myocardial fibrosis by cardiac magnetic resonance on arrhythmic outcome and sudden cardiac death in nonischemic dilated cardiomyopathy: a powerful predictor of mortality and sudden cardiac death in patients with non-ischaemic dilated cardiomyopathy. JACC Cardiovasc Imaging 2014;7:448–56. https://doi.org/10.1016/j.jcmg.2015.12.005; PMID: 26762873.

133. Kwon DH, Hachamovitch R, Adeniyi A, et al. Myocardial scar burden predicts survival benefit with implantable cardioverter-defibrillator implantation in patients with severe ischaemic cardiomyopathy. Int J Cardiol 2016;222:9–15. https://doi.org/10.1016/j.ijcard.2016.07.122; PMID: 27458824.

134. Masci PG, Doulaptsis C, Bertella E, et al. Incremental prognostic value of myocardial fibrosis by cardiac magnetic resonance imaging on event-free survival in patients presenting with signs or symptoms of coronary artery disease. Circ Cardiovasc Imaging 2016;9:1337–43. https://doi.org/10.1161/CIRCIMAGING.115.002663; PMID: 26843532.

135. Kim SY, Chan AK, Brown KA, et al. Impact of unrecognized myocardial scar detected by cardiac magnetic resonance imaging on event-free survival in patients presenting with signs or symptoms of coronary artery disease. Circ Cardiovasc Imaging 2011;4:864–8. https://doi.org/10.1161/CIRCIMAGING.111.101765; PMID: 21097819.

136. Almehmadi F, Joncas SX, Nevis I, et al. Prognostic role of CMR in patients presenting with ventricular arrhythmias. JACC Cardiovasc Imaging 2013;6:335–44. https://doi.org/10.1016/j.jcmg.2012.09.012; PMID: 23433931.

137. Kwon DH, Hachamovitch R, Adeniyi A, et al. Prognostic value of myocardial fibrosis by cardiac magnetic resonance imaging on mortality and heart failure in patients presenting with signs or symptoms of coronary artery disease. JACC Cardiovasc Imaging 2014;7:593–600. https://doi.org/10.1016/j.jcmg.2015.02.005; PMID: 25890580.

138. Puntmann VO, Carr-White G, Jabbour A, et al. T1-mapping and outcome in non-ischemic-cardiomyopathy: all-cause mortality and heart failure. JACC Cardiovasc Imaging 2011;4:860–9. https://doi.org/10.1016/j.jcmg.2011.12.001; PMID: 226762873.

139. Kwon DH, Hachamovitch R, Adeniyi A, et al. Prognostic value of myocardial fibrosis by cardiac magnetic resonance imaging on mortality and heart failure in patients presenting with signs or symptoms of coronary artery disease. JACC Cardiovasc Imaging 2011;4:860–9. https://doi.org/10.1016/j.jcmg.2011.12.001; PMID: 226762873.

140. Almehmadi F, Joncas SX, Nevis I, et al. Prognostic role of CMR in patients presenting with ventricular arrhythmias. JACC Cardiovasc Imaging 2013;6:335–44. https://doi.org/10.1016/j.jcmg.2012.09.012; PMID: 23433931.