Updating the Risk Stratification for Sudden Cardiac Death in Cardiomyopathies: The Evolving Role of Cardiac Magnetic Resonance Imaging. An Approach for the Electrophysiologist

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Abstract: The prevention of sudden cardiac death (SCD) in cardiomyopathies (CM) remains a challenge. The current guidelines still favor the implantation of devices for the primary prevention of SCD only in patients with severely reduced left ventricular ejection fraction (LVEF) and heart failure (HF) symptoms. The implantation of an implantable cardioverter-defibrillator (ICD) is a protective barrier against arrhythmic events in CMs, but the benefit does not outweigh the cost in low risk patients. The identification of high risk patients is the key to an individualized prevention strategy. Cardiac magnetic resonance (CMR) provides reliable and reproducible information about biventricular function and tissue characterization. Furthermore, late gadolinium enhancement (LGE) quantification and pattern of distribution, as well as abnormal T1 mapping and extracellular volume (ECV), representing indices of diffuse fibrosis, can enhance our ability to detect high risk patients. CMR can also complement electro-anatomical mapping (EAM), a technique already applied in the risk evaluation and in the ventricular arrhythmias ablation therapy of CM patients, providing a more accurate assessment of fibrosis and arrhythmic corridors. As a result, CMR provides a new insight into the pathological substrate of CM. CMR may help identify high risk CM patients and, combined with EAM, can provide an integrated evaluation of scar and arrhythmic corridors in the ablative therapy of ventricular arrhythmias.

Keywords: cardiomyopathy; sudden cardiac death; implantable cardiac defibrillators; ventricular tachycardia; ventricular fibrillation; cardiac magnetic resonance; electroanatomic mapping

1. Introduction

Cardiac plasticity permits the heart to adjust its function and structure in response to environmental stimuli such as the increase in the wall thickness or the dilatation of the ventricles due to pressure or volume overload conditions [1]. The term cardiomyopathy (CM) is used to describe an inhomogeneous group of disorders affecting the function and the structure of the myocardial wall without an obvious triggering factor such as arterial hypertension, coronary artery disease, valvular disease or congenital heart disease. The European Society of Cardiology (ESC) in 2008 classified CMs in five groups according to their functional and morphological characteristics (hypertrophic cardiomyopathy (HCM), dilated cardiomyopathy (DCM), arrhythmogenic right ventricular cardiomyopathy (ARVC), restricted cardiomyopathy (RCM) and an unclassified group) [2]. The prevalence of CMs differs

significantly among these groups, with HCM and DCM being the most common (1:250/500) and ARVC (1:2000/5000) and RCM (unknown prevalence) being the rarest [3]. It is worth noting that although the term of ischemic cardiomyopathy (ICM) is used to describe patients with myocardial dysfunction caused by severe coronary disease, it is, by definition, not considered to be a "real" CM according to the ESC since myocardial hypoperfusion is the cause of the dysfunction.

Patients diagnosed with any kind of CM are threatened by a variety of complications including progressive heart failure, need for cardiac transplantation or sudden cardiac death (SCD). Even if manifestations such as an episode of heart failure decompensation give time to seek medical help and are manageable, SCD leaves no room for reaction. SCD can be divided into two major categories—deaths that occur as a consequence of a mechanical complication, for instance, myocardial rupture or left ventricular outflow tract obstruction in HCM and deaths that have a malignant arrhythmic origin [4]. The latter cases are more likely to have an autopsy negative SCD since the post-mortem analysis of the cardiac conduction system is not routinely feasible given that it is technically demanding [5]. As an epidemiological hint, in the United States, up to 300,000 cardiac deaths occur suddenly every year. The majority of them have an ischemic etiology (75%) followed by CMs (15%) [6]. More precisely, in DCM, studies suggest that 30% of deaths occur unexpectedly. Among them, patients with preserved functional status (NYHA class I and II) are more prone to SCD (50–60% of their overall mortality) than patients in a worse clinical status who mainly die due to heart failure complications [7]. Undoubtedly, the primary prevention of SCD demands that medical teams are a step forward in patients' therapeutic management.

Accurate and straightforward arrhythmic risk stratification algorithms for the primary prevention of major arrhythmic events (MAEs)—including, in this article, SCD and both sustained ventricular tachycardia (VT) and fibrillation (Vf)—constitute the holy grail of clinical electrophysiology. An effective and efficient approach allows for the rational targeted allocation of life-saving implantable cardioverter defibrillators (ICDs), with the expected benefit outweighing any device related complication and adverse events (e.g., infections and inappropriate shocks) [8]. Based on results from seminal trials, most of which were published approximately 15 years ago [9–17], left ventricular function, assessed in terms of ejection fraction (LVEF), and functional status (NYHA classification), dominate American [18] and European [19] primary prevention guidelines regarding both ischemic (ICM) and nonischemic dilated cardiomyopathy (NIDCM).

The aforementioned studies were not designed to stratify patients according to arrhythmic risk but rather, based on their LVEF; consequently, they only demonstrated that moderately-to-severely impaired LVEFs were associated with high arrhythmic risk, without including patients with mildly-to-moderately impaired contractility. Not unexpectedly, a two-fold disparity between ICD allocation and MAE occurrence in the primary prevention population has been noted, with an ever increasing trend, given that the majority of sudden deaths in the community occurs in people with mildly impaired LVEF [20,21], and in modern ICD registries [22], the rates of appropriate ICD activation are low (2.6% at 30 months), even at low LVEFs.

As contemporary studies [20–22] raise skepticism about the true role of LVEF in the prediction of malignant arrhythmias, the introduction of new parameters in the daily practice for the risk stratification of patients is a necessity for the near future. Cardiac magnetic resonance (CMR) is a highly effective imaging modality for the characterization of myocardial tissue as well as for the anatomical and the functional evaluation of the heart [23]. Several CMR findings are associated with arrhythmogenic substrates in CMs, with the late gadolinium enhancement (LGE) quantification and distribution pattern being the most well established [24–34]. The addition of CMR in the field of risk stratification for SCD of the CM patients is promising.

The aim of this review is to present the CMR imaging patterns of the arrhythmogenic substrate, studied up to date in CMs, and examine the role of CMR findings in the clinical decision making of the electrophysiologist.

2. CMR Basics

The diagnostic imaging of the human body, independently of the modality used, enables the creation of contrast between tissues. The signal source that serves as contrast for magnetic resonance imaging (MRI) is the response of hydrogen atoms to the magnetic field. Each hydrogen atom is composed of a proton which carries its own spin. The human body does not spontaneously create magnetic signal since spins are oriented randomly [35]. By placing the human body in a strong uniform magnetic field, the spins are forced to align in a parallel or anti-parallel way along the field, creating a new equilibrium with slightly more atoms choosing the parallel orientation. The next step is the interruption of this provoked equilibrium by a radiofrequency pulse (RF) applied in the magnetic field for a specific amount of time. Hydrogen atoms absorb and reemit the radiofrequency received in a different manner that depends on their surroundings. After the appliance of the pulse, as the spins return to the previous equilibrium, the phenomenon of "relaxation" begins. T1 relaxation, or spin-lattice relaxation time, is the recovery of the longitudinal net magnetization vector, and it occurs due to the exchange of energy between the spins and the lattice. T2 relaxation time or spin–spin relaxation is the recovery of the transverse net magnetization vector, and it occurs due to spin–spin interactions and their progressive dephasing [36].

The heart, as a constantly beating organ, which is also affected by respiration movements, makes CMR measurements challenging because of multiple artifacts. Techniques such as the Look Locker (LL) sequence, the Modified Look Locker Inversion Recovery Sequence (MOLLI), the shortened MOLLI (shMOLLI) and the Saturation recovery single-shot acquisition sequence (SASHA) overcome these difficulties by using protocols of supplement excitation RF pulses to extract T1 measurements and have significantly improved the reproducibility of the method [37].

Regarding T1 mapping, it is created by the accumulation of multiple T1 measurements from many heart beats, all at the same phase of the cardiac cycle. Each T1 value is represented by a pixel in the map. T1 mapping images the entire myocardium and does not separate extracellular from cellular environments. The deposition of lipids, water, proteins or iron change T1 measurements and reveal early histological changes [38,39]. Native T1 is a CMR parameter that does not require the use of contrast and, subsequently, is suitable for patients with renal impairment.

When CMR imaging is being supplemented with intravenous contrast agents, the information derived is multiplied. Gadolinium-based contrast agents (GBCAs) are the most widely used agents approved for use [40].They are well-tolerated with extremely low allergic reactions and side effects (0.01%) and have a minimum impact on renal function. Nephrogenic Systemic Sclerosis (NSF), is a rare side effect of GBCAs and has only been reported in patients with renal impairment [41]. Although deposits of gadolinium have been identified in the brains of patients without renal disease who received multiple doses, the clinical relevance of this finding remains to be clarified [42,43]. GBCAs cannot insert the intracellular compartment due to their high molecular weight. Consequently, their distribution is possible only to the extracellular space-intravascular compartment and interstitial space.

The paramagnetic properties of gadolinium lead to a shorten T1 relaxation time in these areas. The most valuable information extracted by the use of GBCA is its pattern of removal from tissues. Normally, after its first distribution, a GBCA is progressively washed out. In areas of myocardial fibrosis, the wash out is delayed since the extracellular space is expanded, the capillary density is reduced and the distance between myocardial cells is augmented. Imaging the heart "late" after the gadolinium has been washed out from healthy tissue can identify these areas with pathological response indicative of replacement fibrosis. It is noticeable that, by definition, late gadolinium enhancement (LGE) (Figure 1) expresses the difference between two areas and is not useful in diffuse myocardial disease, where the entire myocardium is affected and no healthy areas exist to serve as a control [44].

Last but not least, extracellular volume (ECV) is another useful parameter reflecting histological changes early in the CMs' course, independently of their cause. It is measured by the native and postcontrast T1 mapping also including the hematocrit level [45,46] (Figure 2).
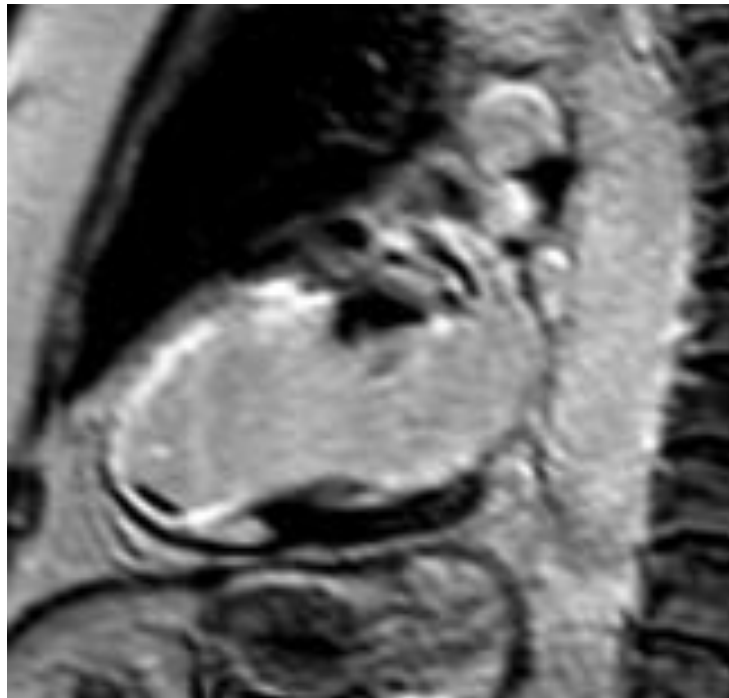
Figure 1. ''Bright is dead''. Inversion recovery image showing extensive LGE area due to anterior myocardial infarction. During late imaging, a gadolinium-based contrast agent (GBCA) is present in areas of fibrosis, as mentioned in the text. The bright area in the anterior and apical wall represents scar tissue.
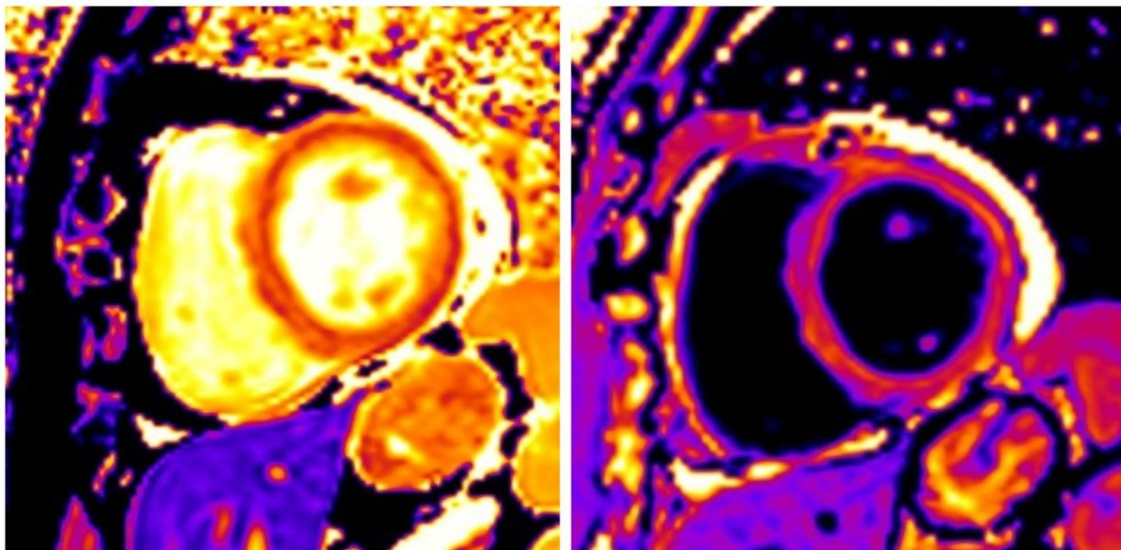

Figure 2. Native and postcontrast T1 mapping in the midventricular short axis level of the left ventricle (LV) in a patient with inflammatory cardiomyopathy. The left image was derived before the administration of a GBCA. The myocardial wall is shown in an inhomogeneous deep orange color which corresponds to pathologically elevated native T1 values. The right one was taken after the administration of the agent. It is worth noting that postcontrast T1 values are influenced by factors other than tissue characteristics such as the agent's dosage and the time of the imaging. An algorithm that combines native and postcontrast T1 values allows us to calculate a more tissue specific parameter, the ECV, in areas of interest.

The quantification of ECV by CMR is an excellent noninvasive method as the measurements are highly correlated with the results of biopsies [47,48]. ECV is useful when the myocardium is being infiltrated by diffuse diseases such as amyloidosis or diffuse fibrosis that cannot be evaluated with LGE distribution, demanding areas of healthy tissue for comparison and also thicker areas of collagen deposition in order to be visible [38,49].

A common issue affecting all contrast-based scar detection lies in the definition of scar and its subtypes, given that it hinges on relative signal intensity. There is not a universal cutoff over which the high signal intensity in LGE-CMR reflects scar tissue. Subsequently, the definition of scar varies between different studies and researchers. Two major approaches have been pursued, one defining scars based on increased signal intensity (versus a healthy remote area) and the other defining healthy tissue based on less pronounced signal intensity (versus the maximal intensity observed at a dense scar region). A few of the most popular scar definitions in studies are the followings: areas with signal intensity >6 standard deviations (SD) higher than the average intensity of remote areas [50], or with signal intensity ≥50% of the maximal within infarct zone value [51–53], or signal intensity >2SDs above the value for normal myocardium [54]. At the same time, border scars (grey zone) can be defined as having an intensity of either 35% to 50% [53] or <60% [55] of the above value.

3. CMR Imaging Patterns Reveal the Arrhythmogenic Burden in Cardiomyopathies

3.1. Nonischemic Dilated Cardiomyopathy

The most well established parameter of an arrhythmogenic substrate in NIDCM is the LGE imaging [24–31]. The existence, the localization but not the quantification of LGE are all strong independent predictors for ventricular arrhythmias, SCD and hospitalization in all ranges of LVEF [56–58]. Precisely, septal LGE carries the worst prognosis even if the fibrotic area is restricted. Moreover, the coexistence of septal with free wall LGE as well as a subepicardial pattern of LGE are all additive risk factors for fatal arrhythmias [56–59]. Interestingly, concerning the inducibility of ventricular arrhythmias during programmed ventricular stimulation (PVS), the absence of LGE is an excellent predictor of noninducibility of monomorphic but not polymorphic VT/VF [29,50,60].

Furthermore, T1 mapping and ECV are also valuable tools in the arrhythmic risk stratification of NIDCM [46,61–64]. ECV and postcontrast T1 mapping correlate with the severity of systolic dysfunction [61]. An increase in ECV is detected early, even before the systolic impairment, reflecting the pathological substrate of the myocardium. Except from the early reveal of the disease, ECV measurements serve also as an independent prognostic factor for cardiovascular death, heart failure hospitalization and appropriate ICD firing [46,47]. However, in patients who cannot receive intravenous contrast agents, ECV measurements can be successfully replaced by native T1 mapping which is a strong independent predictor of an adverse outcome such as all cause mortality, heart failure death and hospitalization in NIDCM [62,64].

Finally, CMR derived left ventricular longitudinal strain is a newly proposed marker of prognosis in patients with NIDCM with conflicting results [65,66]. In one study, the prognostic value of longitudinal strain was even superior to other markers such as LVEF, NT-proBNP and LGE mass [65]. However, other studies failed to confirm this finding [67].

3.2. Ischemic Cardiomyopathy

The scar tissue following an acute coronary syndrome (ACS) constitutes the most common arrhythmogenic substrate in ICM [68–70]. Although malignant arrhythmias occurring early after an ACS are caused by abnormal automaticity and triggered activity of hypoperfused myocardial cells, after the formation of the scar, mechanisms of reentry dominate [71].

Focal myocardial fibrosis detected by LGE imaging substantially increases the risk for life threatening arrhythmias in ICM [32–34,72]. Histologically, a myocardial scar is not always a uniform lesion. In the dense core of the scar, areas of fibrosis are interrupted by viable fibers that serve as

slow conduction pathways. In addition, the tissue surrounding the core of the scar is a 'grey zone' of hypoperfused myocardium with arrhythmogenic properties [73–75]. The heterogeneity of the scar as well as the size of the border zone assessed by CMR parameters are all predictors of malignant arrhythmias and appropriate ICD firings in ICM [76–78].

Regarding the role of T1 mapping and ECV measurements in the arrhythmic risk stratification of ICM, there are a few studies, including both ischemic and nonischemic CM patients, suggesting a correlation between their pathological values and an increased arrhythmic burden [79,80].

Here, it should be highlighted that another highly effective risk stratification approach with absolute negative predictive value, and a positive predictive one of 22% over a mean follow up of 32 months, is that of PVS response in post-myocardial infarction (MI) patients with a LVEF ≥ 40% having at least one out of seven noninvasive risk factors (NIRFs) present on ambulatory and signal averaged electrocardiography [81]. This approach did not incorporate any abnormal CMR data of the corresponding post-MI population although a probable association can coexist in these patients [82]. Such a two step combined noninvasive/invasive risk stratification approach holds promise for a significant, yet until recently unrecognized post MI patient population at risk, to be addressed through cost effective and readily available algorithm [83].

3.3. Hypertrophic Cardiomyopathy

In a rare divergence between American and European guidelines [84,85], primary prevention in hypertrophic cardiomyopathy (HCM) is based either on the presence of 1 out of 3 major clinical risk factors (SCD history, marked left ventricular (LV) hypertrophy, unexplained syncope) with the presence of LGE upon CMR and outflow tract obstruction acting as risk modifiers in cases of nonsustained VT and abnormal blood pressure response to exercise (AHA) or on the calculated 5-year risk of MAEs (ESC–ICD strongly indicated when ≥6%). Notably, there is considerable debate on the value of the latter approach, with contradictory evidence published [86,87].

Indeed, there has been considerable debate concerning the value of the latest European risk score [84,88] regarding arrhythmic events in HCM, as exhibiting high specificity but low sensitivity [89]. This is a population where protection from arrhythmic death has been claimed to lead to an almost normal life expectancy [90], although recent surveys [91] cast doubt on this, reporting an increased mortality even among such well protected patient cohorts. The reverse is true for the currently undergoing major reshaping [92] American criteria, that have excellent sensitivity yet rather low specificity [89], with patients experiencing more inappropriate shocks and complications than receiving appropriate therapies [93,94]. Thus, CMR has long been thought as a potential tie-breaker in the clinical decision-making process [95,96].

The presence of scar, imaged by LGE in HCM patients is considered to be a strong independent predictor for ventricular arrhythmias, ventricular remodeling, all-cause mortality and cardiac death [72,97–100]. The extent of myocardial LGE involvement has been proposed as a better risk stratifier, with cutoffs oscillating from as low as 10% [101], to as high as 20%, with the mean value of 15% attaining wider acceptance [96]. The pattern of LGE distribution, patchy with multiple foci or diffuse, does not carry an additional risk [100]. However, diffuse myocardial fibrosis identified by pathological postcontrast T1 mapping is correlated with episodes of NSVT on Holter monitoring of HCM patients [102].

A relatively common finding during CMR imaging of HCM patients is the appearance of areas of T2-high signal spotted within LGE. Although its clinical significance is not well established, a study of 81 HCM patients concluded that high T2 signal is another parameter for VT manifestation in this group [103]. Concerning the role of ECV, a study incorporating the measured global ECV in the already suggested HCM risk-SCD score of the European society of cardiology (ESC) was associated with a significant improvement in the diagnostic accuracy of the score offering a better risk stratification in this disease [104].

3.4. Inflammatory Cardiomyopathy

Inflammatory CM is the result of an inflammatory process due either to infective or autoimmune causes. Myocardial oedema and fibrosis as a result of macro-, micro-vascular coronary artery disease, vasculitis and autoimmune myocarditis may lead to SCD in patients with autoimmune diseases, even if the left ventricular ejection fraction (LVEF) is preserved [105]. These changes in the myocardial substrate of patients with autoimmune rheumatic diseases (ARDs), imaged in CMR as elevated median T1 mapping values, pathological T2 mapping and increased ECV values, were all predictors for malignant arrhythmias in a study of 61 patients with ARDs and preserved LVEF [105].

Between various ARDs, polymyalgia rheumatica, the commonest rheumaticdisease in elderly people, may present with SCD, as a result of chronic inflammation. Several studies demonstrated that besides promoting structural heart disease, inflammatory activation may also be per se arrhythmogenic, via cytokine-mediated effects on cardiac electrophysiologic properties. Furthermore, there is increasing evidence that inflammation is a risk factor for QTc prolongation and associated life-threatening arrhythmias, specifically torsade de pointes (TdP) [106]. Additionally, rheumatoid arthritis (RA) patients have twice the risk of SCD, compared with non-RA patients, due to an increased incidence of VT/VF. Although the pathophysiologic background of the proarrhythmic substrate in RA is rather complicated, it seems that chronic systemic inflammation can introduce arrhythmias either by promoting the development of ICM or by altering the electrophysiological properties of the heart. Therefore, the tight control of the inflammatory process is probably the most effective intervention to decrease the arrhythmic risk in RA patients.

Autonomic dysfunction, potentially leading to SCD, even in the absence of relevant symptoms or reduced LVEF, was documented in systemic lupus erythematosus, idiopathic juvenile arthritis patients and children with type 1 diabetes mellitus [107–109]. Sporadic VT/VF has also been observed in dermato-, poly-, and inclusion body myositis patients [110]. Finally, SCD was observed in various infiltrative diseases such as sarcoidosis and systemic sclerosis [111]. Specifically, in systemic sclerosis, the presence of oedema and LGE are predictive factors for arrhythmia development [112].

4. The Complementary Role of CMR and Electroanatomical Mapping in Ventricular Tachycardia Ablation

A significant limitation of VT ablation is its variable success rate. The HELP-VT study evaluated VT ablation outcomes among patients with ICM and NIDCM, demonstrating similar success rates in the short term, but with significant reappearance of the arrhythmia in the long term in the latter [113]. The absolute VT noninducibility has been claimed as a prerequisite for long term success [113]. The differences in the arrhythmia substrate are a major determinant of this failure in NIDCM, since the isthmus and critical parts of the circuit are located in regions difficult to map and ablate such as the epicardium [114].

Electroanatomic mapping (EAM) is the currently used approach to identify the arrhythmiologic substrate. However, in EAM the arrhythmogenic substrate is identified indirectly by collecting local voltage amplitudes of the myocardium. This method has some drawbacks: (a) it is time consuming, (b) it lacks sensitivity for scar substrates deep in the mapped surface and (c) it lacks specificity for scar detection in the case of poor catheter contact or thin myocardium. Therefore, the need for new strategies to define arrhythmogenic scar substrates is relevant [115]. CMR examination before or during EAM could reveal these difficult areas and potentially enhance the ablation's success rate. An example of the complementary approach to the incorporation of CMR in interventional electrophysiology is depicted in Figure 3.
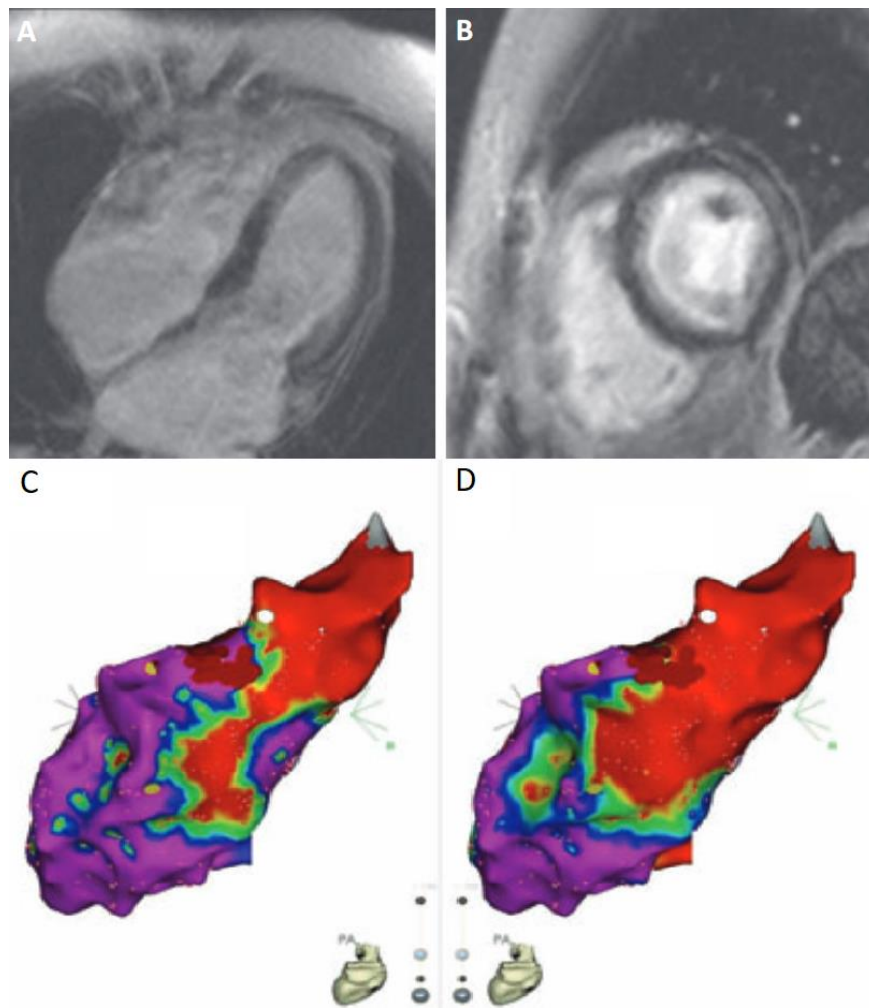
Figure 3. Joint application of cardiac magnetic resonance (CMR) and electro-anatomical mapping (EAM) in the case of a 43 year old female diagnosed with Behçet's disease and high burden of symptomatic ventricular extrasystoles (≈20,000 on 24 h ambulatory electrocardiography), without LV dysfunction. (**A,B**) T1-weighted sequence CMR with obvious LGE both at the left ventricular lateral wall (midmyocardial) and subendocardially (diffuse pattern, not corresponding to coronary artery territory). Four chamber (**A**) and short axis (**B**) views. (**C,D**) Electroanatomical map of the LV using the CARTO3® system (Biosense-Webster, Diamond Bar, CA, USA) depicting a low voltage area (non-purple color) in the same segments, using both bipolar (**C**) and unipolar (**D**) settings. Successful ablation of the arrhythmia was achieved following radiofrequency energy application at the basal lateral wall, an area with abnormal unipolar but not bipolar voltage values, suggesting a nonsubendocardial arrhythmogenic focus [116].

The first necessary step in this algorithm is to incorporate CMR into 3D-EAM in order to transfer anatomical data from one software environment to the other. Potential causes of a mismatch include different rhythms during different image acquisition timings, as well as different loading conditions, leading to slight geometric alterations in chamber geometry [117], as it has been shown in several studies [55,118,119]. Regarding the association between scar features and measured voltages, a correlation between both bipolar and unipolar values with scar nature (dense/border, transmurality) has been reported [118]. However, it is worth noting that a bipolar voltage threshold of <1.5mV (usual threshold for border-zone tissue) did miss dense scars with <75% transmurality and nontransmural border scars, potentially explaining why some VT isthmuses were not detected by substrate 3D-EAM and were not ablated [118].

In one of the first studies, to evaluate the integration of CMR to achieve the demanding task of scar definition in a clinical setting [120], this imaging technique facilitated conducting channel characterization and demarcation of possible entrance sites, allowing for a more targeted and comprehensive isolation. The ability of CMR to accurately detect subendocardial conducting channels was also confirmed in another study [55], where 81% of them could be identified by CMR prior to 3D-EAM. Similar results have been reported [54] with an impressive 92.2% of 3D-EAM points lying within a 5mm distance of the imported CMR-formed shell. Additionally, all critical sites for premature ventricular contractions (PVCs) and VT isthmuses were detected within the LGE-defined scar.

In a more radical approach, the field of magnetic resonance electrophysiology (MR-EP) [119], alternatively known as interventional CMR (iCMR), has been developed with the CMR scanner now forming an integral, rather than a complementary/auxiliary, part of the 3D-EAM. The approach is still theoretic, with proof of concept animal studies having been carried out to validate the functionality of prototype integrated MR-EP systems [121,122] with no currently existing human studies [117]. More precisely, a scanner can be used, virtually in lieu of a fluoroscopy machine [123] to:

I.　　Generate anatomic images during the procedure. Consequently, any registration mismatch errors are avoided. The operator uses the CMR scanner virtually in the same manner as a fluoroscope, with an attached pedalfor image acquisition whenever e.g., tissue characterization is needed [117].

II.　　Locate indwelling ablation catheters [121–124].

III.　　Produce substrate maps to be compared with those derived from the "classical" EAM module and improve area of interest targeting.

IV.　　Evaluate the formation of permanent, irreversible lesions [124–126] prior to catheter withdrawal. Regarding real-time lesion formation assessment, acute LGE grossly overestimates the effect (ECV expansion), while thenoncontrast method, using fast T1- and T2-weighted imaging [127–130] has only been able to acutely detect a minority (~30%) of lesions. CMR thermography is a newly introduced parameter with promising results [42,131,132].

5. Future Perspectives in the Arrhythmic Risk Stratification in Cardiomyopathies

A multidisciplinary approach for the risk stratification of ICM and NIDCM patients seems to be more suitable than the proposed oversimplified one based on LVEF so far, in order to better define their complex substrate and support individualization. Towards this direction, several efforts have been made to update primary prevention arrhythmic risk stratification in ICM and NIDCM with rather well maintained LVEF, either by assessing the presence of an arrhythmogenic substrate through a two-step approach with noninvasive risk factor presence leading to PVSin both diseases [81,89,133] or by the use of imaging [56,59,134–136] in the latter. Such preliminary combinational approaches are associated with encouraging results [81,133,137] for the detection of a high risk NIDCM cohort with low LVEF and 3year event rates similar to that of a secondary prevention population based on the ESTIMATED score, a score derived from the combination of abnormal CMR findings with various clinical and electrocardiographic NIRFs.

In this direction, two prospective observational studies are currently underway: The CMR-Guide trial [138] (NCT01918215) will define the role of CMR in the primary prevention of SCD in ICM and NIDCM patients with well maintained LVEF>35%. After assessing the presence of either an ischemic or nonischemic LGE pattern, patients will be randomized to receive either an implantable loop recorder or an ICD. The ReCONSIDER study [139] (NCT04246450) will incorporate CMR findings, namely LGE presence along with a variety of other NIRFs, leading to invasive PVS in NIDCM patients across the LVEF spectrum in a two step approach.

The question of which is the best risk stratification approach among HCM patients with a low European risk score and/or a single conventional noninvasive risk factor present, remains a highly debatable issue. On the contrary, there is solid evidence that, in the presence of multiple NIRFs and/or a high European risk score, the justification of ICD insertion is well supported [89].

Although electrophysiology testing (ET) has received a class III recommendation for the risk stratification of HCM patients [19], it has an excellent predictive ability for HCM patients with a single NIRF, such as the presence of nonsustained VT or unexplained syncope, by revealing either a potentially malignant ventricular arrhythmogenic substrate and/or an underlying conduction system disease [89]. Whether a combinational multifactorial, CMR and ET-inclusive, approach is appropriately suited for this rather large subgroup of HCM patients is currently unknown [140].

6. Conclusions

There is an urgent need to update our risk stratification criteria for the appropriate and timely selection of the ICD candidates among CM patients at all LVEF spectrum values. In this direction, CMR imaging may play a significant role. Indeed, LGE quantification and pattern of distribution, as well as abnormal T1 mapping and ECV, can further enhance our ability to identify patients susceptible to life threatening arrhythmogenesis. Currently, more sophisticated approaches combining a variety of noninvasive and invasive modalities are underway in the new era of the arrhythmic risk stratification among CM patients even at early heart failure stages with less impaired LV function. Furthermore, CMR in combination with EAM may assist in the effectiveness of demanding interventional EP procedures not uncommonly applied among such seriously affected high risk patients.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Pitoulis, F.G.; Terracciano, C.M. Heart plasticity in response to pressure- and volume-overload: A review of findings in compensated and decompensated phenotypes. *Front. Physiol.* **2020**, *11*, 92. [CrossRef] [PubMed]

2. Elliott, P.; Andersson, B.; Arbustini, E.; Bilinska, Z.; Cecchi, F.; Charron, P.; Dubourg, O.; Kühl, U.; Maisch, B.; McKenna, W.J.; et al. Classification of the cardiomyopathies: A position statement from the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases. *Eur. Heart. J.* **2008**, *29*, 270–276. [CrossRef] [PubMed]

3. McKenna, W.J.; Maron, B.J.; Thiene, G. Classification, epidemiology, and global burden of cardiomyopathies. *Circ. Res.* **2017**, *121*, 722–730. [CrossRef] [PubMed]

4. Buja, L.M.; Ottaviani, G.; Mitchell, R.N. Pathobiology of cardiovascular diseases: An update. *Cardiovasc. Pathol.* **2019**, *42*, 44–53. [CrossRef]

5. Ottaviani, G.; Buja, L.M. Anatomopathological changes of the cardiac conduction system in sudden cardiac death, particularly in infants: Advances over the last 25 years. *Cardiovasc.Pathol.* **2016**, *25*, 489–499. [CrossRef]

6. Srinivasan, N.T.; Schilling, R.J. Sudden cardiac death and arrhythmias. *Arrhythm. Electrophysiol. Rev.* **2018**, *7*, 111–117. [CrossRef]

7. Sen-Chowdhry, S.; McKenna, W.J. Sudden death from genetic and acquired cardiomyopathies. *Circulation* **2012**, *125*, 1563–1576. [CrossRef]

8. Gatzoulis, K.A.; Sideris, A.; Kanoupakis, E.; Sideris, S.; Nikolaou, N.; Antoniou, C.K.; Kolettis, T.M. Arrhythmic risk stratification in heart failure: Time for the next step? *Ann. Noninvasive. Electrocardiol.* **2017**, *22*, e12430. [CrossRef]

9. Moss, A.J.; Zareba, W.; Hall, W.J.; Klein, H.; Wilber, D.J.; Cannom, D.S.; Daubert, J.P.; Higgins, S.L.; Brown, M.W.; Andrews, M.L.; et al. Prophylactic implantation of a defibrillator in patients with myocardial infarction and reduced ejection fraction. *N. Engl. J. Med.* **2002**, *346*, 877–883. [CrossRef]

10. Bänsch, D.; Antz, M.; Boczor, S.; Volkmer, M.; Tebbenjohanns, J.; Seidl, K.; Block, M.; Gietzen, F.; Berger, J.; Kuck, K.H. Primary prevention of sudden cardiac death in idiopathic dilated cardiomyopathy: The Cardiomyopathy Trial (CAT). *Circulation* **2002**, *105*, 1453–1458. [CrossRef]

11. Bardy, G.H.; Lee, K.L.; Mark, D.B.; Poole, J.E.; Packer, D.L.; Boineau, R.; Domanski, M.; Troutman, C.; Anderson, J.; Johnson, G.; et al. Amiodarone or an implantable cardioverter-defibrillator for congestive heart failure. *N. Engl. J. Med.* **2005**, *352*, 225–237. [CrossRef] [PubMed]

12. Bristow, M.R.; Saxon, L.A.; Boehmer, J.; Krueger, S.; Kass, D.A.; De Marco, T.; Carson, P.; DiCarlo, L.; DeMets, D.; White, B.G.; et al. Cardiac-resynchronization therapy with or without an implantable defibrillator in advanced chronic heart failure. *N. Engl. J. Med.* **2004**, *350*, 2140–2150. [CrossRef] [PubMed]

13. Desai, A.S.; Fang, J.C.; Maisel, W.H.; Baughman, K.L. Implantable defibrillators for the prevention of mortality in patients with nonischemic cardiomyopathy: A meta-analysis of randomized controlled trials. *JAMA* **2004**, *292*, 2874–2879. [CrossRef] [PubMed]

14. Kadish, A.; Dyer, A.; Daubert, J.P.; Quigg, R.; Estes, N.A.; Anderson, K.P.; Calkins, H.; Hoch, D.; Goldberger, J.; Shalaby, A.; et al. Prophylactic defibrillator implantation in patients with nonischemic dilated cardiomyopathy. *N. Engl. J. Med.* **2004**, *350*, 2151–2158. [CrossRef]

15. Køber, L.; Thune, J.J.; Nielsen, J.C.; Haarbo, J.; Videbæk, L.; Korup, E.; Jensen, G.; Hildebrandt, P.; Steffensen, F.H.; Bruun, N.E.; et al. Defibrillator implantation in patients with nonischemic systolic heart failure. *N. Engl. J. Med.* **2016**, *375*, 1221–1230. [CrossRef]

16. Strickberger, S.A.; Hummel, J.D.; Bartlett, T.G.; Frumin, H.I.; Schuger, C.D.; Beau, S.L.; Bitar, C.; Morady, F.; AMIOVIRT Investigators. Amiodarone versus implantable cardioverter-defibrillator: Randomized trial in patients with nonischemic dilated cardiomyopathy and asymptomatic nonsustained ventricular tachycardia—AMIOVIRT. *J. Am. Coll. Cardiol.* **2003**, *41*, 1707–1712. [CrossRef]

17. Marwick, T.H. Ejection fraction pros and cons: JACC state-of-the-art review. *J. Am. Coll. Cardiol.* **2018**, *72*, 2360–2379. [CrossRef]

18. Al-Khatib, S.M.; Stevenson, W.G.; Ackerman, M.J.; Bryant, W.J.; Callans, D.J.; Curtis, A.B.; Deal, B.J.; Dickfeld, T.; Field, M.E.; Fonarow, G.C.; et al. 2017 AHA/ACC/HRS guideline for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: Executive summary: A report of the American College of Cardiology/American Heart Association task force on clinical practice guidelines and the Heart Rhythm Society. *J. Am. Coll. Cardiol.* **2018**, *72*, 1677–1749. [CrossRef]

19. Priori, S.G.; Blomström-Lundqvist, C.; Mazzanti, A.; Blom, N.; Borggrefe, M.; Camm, J.; Elliott, P.M.; Fitzsimons, D.; Hatala, R.; Hindricks, G.; et al. 2015 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: The task force for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death of the European Society of Cardiology (ESC). Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC). *Eur. Heart J.* **2015**, *36*, 2793–2867. [CrossRef]

20. Gorgels, A.P.; Gijsbers, C.; de Vreede-Swagemakers, J.; Lousberg, A.; Wellens, H.J. Out-of-hospital cardiac arrest—The relevance of heart failure. The Maastricht Circulatory Arrest Registry. *Eur. Heart, J.* **2003**, *24*, 1204–1209. [CrossRef]

21. Stecker, E.C.; Vickers, C.; Waltz, J.; Socoteanu, C.; John, B.T.; Mariani, R.; McAnulty, J.H.; Gunson, K.; Jui, J.; Chugh, S.S. Population-based analysis of sudden cardiac death with and without left ventricular systolic dysfunction: Two-year findings from the Oregon sudden unexpected death study. *J. Am. Coll. Cardiol.* **2006**, *47*, 1161–1166. [CrossRef]

22. Sabbag, A.; Suleiman, M.; Laish-Farkash, A.; Samania, N.; Kazatsker, M.; Goldenberg, I.; Glikson, M.; Beinart, R.; Israeli Working Group of Pacing and Electrophysiology. Contemporary rates of appropriate shock therapy in patients who receive implantable device therapy in a real-world setting: From the Israeli ICD Registry. *Heart Rhythm* **2015**, *12*, 2426–2433. [CrossRef] [PubMed]

23. Pattanayak, P.; Bleumke, D.A. Tissue characterization of the myocardium: State of the art characterization by magnetic resonance and computed tomography imaging. *Radiol. Clin.* **2015**, *53*, 413–423. [CrossRef] [PubMed]

24. Assomull, R.G.; Prasad, S.K.; Lyne, J.; Smith, G.; Burman, E.D.; Khan, M.; Sheppard, M.N.; Poole-Wilson, P.A.; Pennell, D.J. Cardiovascular magnetic resonance, fibrosis, and prognosis in dilated cardiomyopathy. *J. Am. Coll. Cardiol.* **2006**, *48*, 1977–1985. [CrossRef]

25. Wu, K.C.; Weiss, R.G.; Thiemann, D.R.; Kitagawa, K.; Schmidt, A.; Dalal, D.; Lai, S.; Bluemke, D.A.; Gerstenblith, G.; Marbán, E.; et al. Late gadolinium enhancement by cardiovascular magnetic resonance heralds an adverse prognosis in nonischemic cardiomyopathy. *J. Am. Coll. Cardiol.* **2008**, *51*, 2414–2421. [CrossRef] [PubMed]

26. Iles, L.; Pfluger, H.; Lefkovits, L.; Butler, M.J.; Kistler, P.M.; Kaye, D.M.; Taylor, A.J. Myocardial fibrosis predicts appropriate device therapy in patients with implantable cardioverter-defibrillators for primary prevention of sudden cardiac death. *J. Am. Coll. Cardiol.* **2011**, *57*, 821–828. [CrossRef]

27. PerazzoloMarra, M.; De Lazzari, M.; Zorzi, A.; Migliore, F.; Zilio, F.; Calore, C.; Vettor, G.; Tona, F.; Tarantini, G.; Cacciavillani, L.; 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. *Heart Rhythm* **2014**, *11*, 856–863. [CrossRef] [PubMed]

28. Masci, P.G.; Doulaptsis, C.; Bertella, E.; Del Torto, A.; Symons, R.; Pontone, G.; Barison, A.; Droogné, W.; Andreini, D.; Lorenzoni, V.; et al. Incremental prognostic value of myocardial fibrosis in patients with non-ischemic cardiomyopathy without congestive heart failure. *Circ. Heart Fail.* **2014**, *7*, 448–456. [CrossRef]

29. Piers, S.R.; Everaerts, K.; van der Geest, R.J.; Hazebroek, M.R.; Siebelink, H.M.; Pison, L.A.; Schalij, M.J.; Bekkers, S.C.; Heymans, S.; Zeppenfeld, K. Myocardial scar predicts monomorphic ventricular tachycardia but not polymorphic ventricular tachycardia or ventricular fibrillation in nonischemic dilated cardiomyopathy. *Heart Rhythm* **2015**, *12*, 2106–2114. [CrossRef]

30. Shin, D.G.; Lee, H.J.; Park, J.; Uhm, J.S.; Pak, H.N.; Lee, M.H.; Kim, Y.J.; Joung, B. Pattern of late gadolinium enhancement predicts arrhythmic events in patients with non-ischemic cardiomyopathy. *Int. J. Cardiol.* **2016**, *222*, 9–15. [CrossRef]

31. Lehrke, S.; Lossnitzer, D.; Schöb, M.; Steen, H.; Merten, C.; Kemmling, H.; Pribe, R.; Ehlermann, P.; Zugck, C.; Korosoglou, G.; et al. Use of cardiovascular magnetic resonance for risk stratification in chronic heart failure: Prognostic value of late gadolinium enhancement in patients with non-ischaemic dilated cardiomyopathy. *Heart* **2011**, *97*, 727–732. [CrossRef] [PubMed]

32. Zhang, Y.; Guallar, E.; Weiss, R.G.; Stillabower, M.; Gerstenblith, G.; Tomaselli, G.F.; Wu, K.C. Associations between scar characteristics by cardiac magnetic resonance and changes in left ventricular ejection fraction in primary prevention defibrillator recipients. *Heart Rhythm* **2016**, *13*, 1661–1666. [CrossRef]

33. Scott, P.A.; Rosengarten, J.A.; Curzen, N.P.; Morgan, J.M. Late gadolinium enhancement cardiac magnetic resonance imaging for the prediction of ventricular tachyarrhythmic events: A meta-analysis. *Eur. J. Heart Fail.* **2013**, *15*, 1019–1027. [CrossRef] [PubMed]

34. Van der Bijl, P.; Delgado, V.; Bax, J.J. Noninvasive imaging markers associated with sudden cardiac death. *Trends Cardiovasc. Med.* **2016**, *26*, 348–360. [CrossRef]

35. Pohost, G.M.; Nayak, K.S. *Handbook of Cardiovascular Magnetic Resonance Imaging*, 1st ed.; CRC Press: New York, NY, USA, 2006; pp. 1–30.

36. Kwong, R.Y. *Cardiovascular Magnetic Resonance Imaging*; Humana Press Inc.: Totowa, NJ, USA, 2008.

37. Kim, P.K.; Hong, Y.J.; Im, D.J.; Suh, Y.J.; Park, C.H.; Kim, J.Y.; Chang, S.; Lee, H.J.; Hur, J.; Kim, Y.J.; et al. Myocardial T1 and T2 mapping: Techniques and clinical applications. *Korean J. Radiol.* **2017**, *18*, 113–131. [CrossRef] [PubMed]

38. Mavrogeni, S.; Apostolou, D.; Argyriou, P.; Velitsista, S.; Papa, L.; Efentakis, S.; Vernardos, E.; Kanoupaki, M.; Kanoupakis, G.; Manginas, A. T1 and T2 mapping in cardiology: "Mapping the obscure object of desire". *Cardiology* **2017**, *138*, 207–217. [CrossRef]

39. Moon, J.C.; Messroghli, D.R.; Kellman, P.; Piechnik, S.K.; Robson, M.D.; Ugander, M.; Gatehouse, P.D.; Arai, A.E.; Friedrich, M.G.; Neubauer, S.; et al. Myocardial T1 mapping and extracellular volume quantification: A Society for Cardiovascular Magnetic Resonance (SCMR) and CMR Working Group of the European Society of Cardiology consensus statement. *J. Cardiovasc. Magn. Reson.* **2013**, *15*, 92. [CrossRef]

40. Xiao, Y.D.; Paudel, R.; Liu, J.; Ma, C.; Zhang, Z.S.; Zhou, S.K. MRI contrast agents: Classification and application (Review). *Int. J. Mol. Med.* **2016**, *38*, 1319–1326. [CrossRef]

41. Ranga, A.; Agarwal, Y.; Garg, K.J. Gadolinium based contrast agents in current practice: Risks of accumulation and toxicity in patients with normal renal function. *Indian, J. Radiol. Imaging* **2017**, *27*, 141–147. [CrossRef]

42. Choi, J.W.; Moon, W.J. Gadolinium deposition in the brain: Current updates. *Korean, J. Radiol.* **2019**, *20*, 134–147. [CrossRef]

43. Gulani, V.; Calamante, F.; Shellock, F.G.; Kanal, E.; Reeder, S.B.; International Society for Magnetic Resonance in Medicine. Gadolinium deposition in the brain: Summary of evidence and recommendations. *Lancet Neurol.* **2017**, *16*, 564–570. [CrossRef]

44. Mewton, N.; Liu, C.Y.; Croisille, P.; Bluemke, D.; Lima, J.A. Assessment of myocardial fibrosis with cardiovascular magnetic resonance. *J. Am. Coll. Cardiol.* **2011**, *57*, 891–903. [CrossRef] [PubMed]

45. Haaf, P.; Garg, P.; Messroghli, D.R.; Broadbent, D.A.; Greenwood, J.P.; Plein, S. Cardiac T1 mapping and Extracellular Volume (ECV) in clinical practice: A comprehensive review. *J. Cardiovasc. Magn. Reson.* **2016**, *18*, 89. [CrossRef] [PubMed]

46.   Barison, A.; Del Torto, A.; Chiappino, S.; Aquaro, G.D.; Todiere, G.; Vergaro, G.; Passino, C.; Lombardi, M.; Emdin, M.; Masci, P.G. Prognostic significance of myocardial extracellular volume fraction in nonischaemic dilated cardiomyopathy. *J. Cardiovasc. Med.* **2015**, *16*, 681–687. [CrossRef] [PubMed]

47.   Aus dem Siepen, F.; Buss, S.J.; Messroghli, D.; Andre, F.; Lossnitzer, D.; Seitz, S.; Keller, M.; Schnabel, P.A.; Giannitsis, E.; Korosoglou, G.; et al. T1 mapping in dilated cardiomyopathy with cardiac magnetic resonance: Quantification of diffuse myocardial fibrosis and comparison with endomyocardial biopsy. *Eur. Heart J. Cardiovasc. Imaging* **2015**, *16*, 210–216. [CrossRef]

48.   Kammerlander, A.A.; Marzluf, B.A.; Zotter-Tufaro, C.; Aschauer, S.; Duca, F.; Bachmann, A.; Knechtelsdorfer, K.; Wiesinger, M.; Pfaffenberger, S.; Greiser, A.; et al. T1 mapping by CMR imaging: From histological validation to clinical implication. *JACC Cardiovasc. Imaging* **2016**, *9*, 14–23. [CrossRef]

49.   Taylor, A.J.; Salerno, M.; Dharmakumar, R.; Jerosch-Herold, M. T1 mapping: Basic techniques and clinical applications. *JACC Cardiovasc. Imaging* **2016**, *9*, 67–81. [CrossRef]

50.   Nazarian, S.; Bluemke, D.A.; Lardo, A.C.; Zviman, M.M.; Watkins, S.P.; Dickfeld, T.L.; Meininger, G.R.; Roguin, A.; Calkins, H.; Tomaselli, G.F.; et al. Magnetic resonance assessment of the substrate for inducible ventricular tachycardia in nonischemic cardiomyopathy. *Circulation* **2005**, *112*, 2821–2825. [CrossRef]

51.   Dawson, D.K.; Hawlisch, K.; Prescott, G.; Roussin, I.; Di Pietro, E.; Deac, M.; Wong, J.; Frenneaux, M.P.; Pennell, D.J.; Prasad, S.K. Prognostic role of CMR in patients presenting with ventricular arrhythmias. *JACC Cardiovasc. Imaging* **2013**, *6*, 335–344. [CrossRef]

52.   Gulati, A.; Jabbour, A.; Ismail, T.F.; Guha, K.; Khwaja, J.; Raza, S.; Morarji, K.; Brown, T.D.; Ismail, N.A.; Dweck, M.R.; et al. Association of fibrosis with mortality and sudden cardiac death in patients with nonischemic dilated cardiomyopathy. *JAMA* **2013**, *309*, 896–908. [CrossRef]

53.   Demirel, F.; Adiyaman, A.; Timmer, J.R.; Dambrink, J.H.; Kok, M.; Boeve, W.J.; Elvan, A. Myocardial scar characteristics based on cardiac magnetic resonance imaging is associated with ventricular tachyarrhythmia in patients with ischemic cardiomyopathy. *Int. J. Cardiol.* **2014**, *177*, 392–399. [CrossRef] [PubMed]

54.   Gupta, S.; Desjardins, B.; Baman, T.; Ilg, K.; Good, E.; Crawford, T.; Oral, H.; Pelosi, F.; Chugh, A.; Morady, F.; et al. Delayed-enhanced MR scar imaging and intraprocedural registration into an electroanatomical mapping system in post-infarction patients. *JACC Cardiovasc. Imaging* **2012**, *5*, 207–210. [CrossRef] [PubMed]

55.   Andreu, D.; Berruezo, A.; Ortiz-Pérez, J.T.; Silva, E.; Mont, L.; Borràs, R.; de Caralt, T.M.; Perea, R.J.; Fernández-Armenta, J.; Zeljko, H.; et al. Integration of 3D electroanatomic maps and magnetic resonance scar characterization into the navigation system to guide ventricular tachycardia ablation. *Circ. Arrhythmia Electrophysiol.* **2011**, *4*, 674–683. [CrossRef]

56.   Halliday, B.P.; Gulati, A.; Ali, A.; Guha, K.; Newsome, S.; Arzanauskaite, M.; Vassiliou, V.S.; Lota, A.; Izgi, C.; Tayal, U.; et al. Association between midwall late gadolinium enhancement and sudden cardiac death in patients with dilated cardiomyopathy and mild and moderate left ventricular systolic dysfunction. *Circulation* **2017**, *135*, 2106–2115. [CrossRef] [PubMed]

57.   Becker, M.A.J.; Cornel, J.H.; van de Ven, P.M.; van Rossum, A.C.; Allaart, C.P.; Germans, T. The prognostic value of late gadolinium-enhanced cardiac magnetic resonance imaging in nonischemic dilated cardiomyopathy: A review and meta-analysis. *JACC Cardiovasc. Imaging* **2018**, *11*, 1274–1284. [CrossRef] [PubMed]

58.   Di Marco, A.; Anguera, I.; Schmitt, M.; Klem, I.; Neilan, T.G.; White, J.A.; Sramko, M.; Masci, P.G.; Barison, A.; Mckenna, P.; et al. Late gadolinium enhancement and the risk for ventricular arrhythmias or sudden death in dilated cardiomyopathy: Systematic review and meta-analysis. *JACC Heart Fail.* **2017**, *5*, 28–38. [CrossRef]

59.   Halliday, B.P.; Baksi, A.J.; Gulati, A.; Ali, A.; Newsome, S.; Izgi, C.; Arzanauskaite, M.; Lota, A.; Tayal, U.; Vassiliou, V.S.; et al. Outcome in dilated cardiomyopathy related to the extent, location, and pattern of late gadolinium enhancement. *JACC Cardiovasc. Imaging* **2019**, *(Pt 2)*, 1645–1655. [CrossRef]

60.   Mueller, K.A.; Heck, C.; Heinzmann, D.; Schwille, J.; Klingel, K.; Kandolf, R.; Kramer, U.; Gramlich, M.; Geisler, T.; Gawaz, M.P.; et al. Comparison of ventricular inducibility with late gadolinium enhancement and myocardial inflammation in endomyocardial biopsy in patients with dilated cardiomyopathy. *PLoS ONE* **2016**, *11*, e0167616. [CrossRef] [PubMed]

61.   Tachi, M.; Amano, Y.; Inui, K.; Takeda, M.; Yamada, F.; Asai, K.; Kumita, S. Relationship of postcontrast myocardial T1 value and delayed enhancement to reduced cardiac function and serious arrhythmia in dilated cardiomyopathy with left ventricular ejection fraction less than 35. *Acta Radiol.* **2016**, *57*, 430–436. [CrossRef] [PubMed]

62. Puntmann, V.O.; Carr-White, G.; Jabbour, A.; Yu, C.Y.; Gebker, R.; Kelle, S.; Hinojar, R.; Doltra, A.; Varma, N.; Child, N.; et al. T1-Mapping and Outcome in Nonischemic Cardiomyopathy: All-Cause Mortality and Heart Failure. *JACC Cardiovasc. Imaging* **2016**, *9*, 40–50. [CrossRef]

63. Hong, Y.J.; Park, C.H.; Kim, Y.J.; Hur, J.; Lee, H.J.; Hong, S.R.; Suh, Y.J.; Greiser, A.; Paek, M.Y.; Choi, B.W.; et al. Extracellular volume fraction in dilated cardiomyopathy patients without obvious late gadolinium enhancement: Comparison with healthy control subjects. *Int. J. Cardiovasc. Imaging* **2015**, *31* (Suppl. 1), 115–122. [CrossRef] [PubMed]

64. Nakamori, S.; Dohi, K.; Ishida, M.; Goto, Y.; Imanaka-Yoshida, K.; Omori, T.; Goto, I.; Kumagai, N.; Fujimoto, N.; Ichikawa, Y.; et al. Native T1 mapping and extracellular volume mapping for the assessment of diffuse myocardial fibrosis in dilated cardiomyopathy. *JACC Cardiovasc. Imaging* **2018**, *11*, 48–59. [CrossRef] [PubMed]

65. Buss, S.J.; Breuninger, K.; Lehrke, S.; Voss, A.; Galuschky, C.; Lossnitzer, D.; Andre, F.; Ehlermann, P.; Franke, J.; Taeger, T.; et al. Assessment of myocardial deformation with cardiac magnetic resonance strain imaging improves risk stratification in patients with dilated cardiomyopathy. *Eur. Heart J. Cardiovasc. Imaging* **2015**, *16*, 307–315. [CrossRef]

66. Riffel, J.H.; Keller, M.G.; Rost, F.; Arenja, N.; Andre, F.; Aus dem Siepen, F.; Fritz, T.; Ehlermann, P.; Taeger, T.; Frankenstein, L.; et al. Left ventricular long axis strain: A new prognosticator in non-ischemic dilated cardiomyopathy? *J. Cardiovasc. Magn. Reson.* **2016**, *18*, 36. [CrossRef] [PubMed]

67. Pi, S.H.; Kim, S.M.; Choi, J.O.; Kim, E.K.; Chang, S.A.; Choe, Y.H.; Lee, S.C.; Jeon, E.S. Prognostic value of myocardial strain and late gadolinium enhancement on cardiovascular magnetic resonance imaging in patients with idiopathic dilated cardiomyopathy with moderate to severely reduced ejection fraction. *J. Cardiovasc. Magn. Reson.* **2018**, *20*, 36. [CrossRef] [PubMed]

68. Kron, I.L.; DiMarco, J.P.; Lerman, B.B.; Nolan, S.P. Resection of scarred papillary muscles improves outcome after surgery for ventricular tachycardia. *Ann. Surg.* **1986**, *203*, 685–690. [CrossRef]

69. Josephson, M.E.; Harken, A.H.; Horowitz, L.N. Endocardial excision: A new surgical technique for the treatment of recurrent ventricular tachycardia. *Circulation* **1979**, *60*, 1430–1439. [CrossRef]

70. Moran, J.M.; Kehoe, R.F.; Loeb, J.M.; Lichtenthal, P.R.; Sanders, J.H., Jr.; Michaelis, L.L. Extended endocardial resection for the treatment of ventricular tachycardia and ventricular fibrillation. *Ann. Thorac. Surg.* **1982**, *34*, 538–552. [CrossRef]

71. Kalarus, Z.; Svendsen, J.H.; Capodanno, D.; Dan, G.A.; De Maria, E.; Gorenek, B.; Jędrzejczyk-Patej, E.; Mazurek, M.; Podolecki, T.; Sticherling, C.; et al. Cardiac arrhythmias in the emergency settings of acute coronary syndrome and revascularization: An European Heart Rhythm Association (EHRA) consensus document, endorsed by the European Association of Percutaneous Cardiovascular Interventions (EAPCI), and European Acute Cardiovascular Care Association (ACCA). *Europace* **2019**, *21*, 1603–1604. [CrossRef]

72. Mavrogeni, S.; Petrou, E.; Kolovou, G.; Theodorakis, G.; Iliodromitis, E. Prediction of ventricular arrhythmias using cardiovascular magnetic resonance. *Eur. Heart, J. Cardiovasc. Imaging* **2013**, *14*, 518–525. [CrossRef]

73. Stevenson, W.G. Ventricular scars and ventricular tachycardia. *Trans. Am. Clin. Climatol. Assoc.* **2009**, *120*, 403–412. [PubMed]

74. Martin, R.; Maury, P.; Bisceglia, C.; Wong, T.; Estner, H.; Meyer, C.; Dallet, C.; Martin, C.A.; Shi, R.; Takigawa, M.; et al. Characteristics of scar-related ventricular tachycardia circuits using ultra-high-density mapping: A multi-center study. *Circ. Arrhythmia Electrophysiol.* **2018**, *11*, e006569. [CrossRef]

75. Fenoglio, J.J., Jr.; Pham, T.D.; Harken, A.H.; Horowitz, L.N.; Josephson, M.E.; Wit, A.L. Recurrent sustained ventricular tachycardia: Structure and ultrastructure of subendocardial regions in which tachycardia originates. *Circulation* **1983**, *68*, 518–533. [CrossRef] [PubMed]

76. Schmidt, A.; Azevedo, C.F.; Cheng, A.; Gupta, S.N.; Bluemke, D.A.; Foo, T.K.; Gerstenblith, G.; Weiss, R.G.; Marbán, E.; Tomaselli, G.F.; et al. Infarct tissue heterogeneity by magnetic resonance imaging identifies enhanced cardiac arrhythmia susceptibility in patients with left ventricular dysfunction. *Circulation* **2007**, *115*, 2006–2014. [CrossRef] [PubMed]

77. Jablonowski, R.; Chaudhry, U.; van der Pals, J.; Engblom, H.; Arheden, H.; Heiberg, E.; Wu, K.C.; Borgquist, R.; Carlsson, M. Cardiovascular magnetic resonance to predict appropriate implantable cardioverter defibrillator therapy in ischemic and nonischemic cardiomyopathy patients using late gadolinium enhancement border zone: Comparison of four analysis methods. *Circ. Cardiovasc. Imaging* **2017**, *10*, e006105. [CrossRef]

78. Roes, S.D.; Borleffs, C.J.; van der Geest, R.J.; Westenberg, J.J.; Marsan, N.A.; Kaandorp, T.A.; Reiber, J.H.; Zeppenfeld, K.; Lamb, H.J.; de Roos, A.; et al. Infarct tissue heterogeneity assessed with contrast-enhanced MRI predicts spontaneous ventricular arrhythmia in patients with ischemic cardiomyopathy and implantable cardioverter-defibrillator. *Circ. Cardiovasc. Imaging* **2009**, *2*, 183–190. [CrossRef]

79. Olausson, E.; Fröjdh, F.; Maanja, M.; Niklasson, L.; Fridman, Y.; Bering, P.; Wertz, J.; Wong, T.; Kellman, P.; Miller, C.; et al. Diffuse myocardial fibrosis measured by extracellular volume associates with incident ventricular arrhythmia in implantable cardioverter defibrillator recipients more than focal fibrosis. *J. Am. Coll. Cardiol.* **2018**, *71*, A1454. [CrossRef]

80. Chen, Z.; Sohal, M.; Voigt, T.; Sammut, E.; Tobon-Gomez, C.; Child, N.; Jackson, T.; Shetty, A.; Bostock, J.; Cooklin, M.; et al. Myocardial tissue characterization by cardiac magnetic resonance imaging using T1 mapping predicts ventricular arrhythmia in ischemic and non-ischemic cardiomyopathy patients with implantable cardioverter-defibrillators. *Heart Rhythm* **2015**, *12*, 792–801. [CrossRef]

81. Gatzoulis, K.A.; Tsiachris, D.; Arsenos, P.; Antoniou, C.K.; Dilaveris, P.; Sideris, S.; Kanoupakis, E.; Simantirakis, E.; Korantzopoulos, P.; Goudevenos, I.; et al. Arrhythmic risk stratification in post-myocardial infarction patients with preserved ejection fraction: The PRESERVE EF study. *Eur. Heart. J.* **2019**, *40*, 2940–2949. [CrossRef]

82. Gatzoulis, K.A.; Antoniou, C.K.; Dilaveris, P.; Chrysohoou, C.; Arsenos, P.; Trachanas, K.; Tousoulis, D. Ventricular arrhythmogenic potential assessment in an asymptomatic ischemic cardiomyopathy patient with a normal ejection fraction. *Hell. J. Cardiol.* **2017**, *58*, 443–445. [CrossRef]

83. Velasquez, A.; Goldberger, J.J. Risk stratification for sudden cardiac death: Show me the money! *Eur. Heart, J.* **2019**, *40*, 2950–2952. [CrossRef]

84. Elliott, P.M.; Anastasakis, A.; Borger, M.A.; Borggrefe, M.; Cecchi, F.; Charron, P.; Hagege, A.A.; Lafont, A.; Limongelli, G.; Mahrholdt, H.; et al. 2014 ESC Guidelines on diagnosis and management of hypertrophic cardiomyopathy: The task force for the diagnosis and management of hypertrophic cardiomyopathy of the European Society of Cardiology (ESC). *Eur. Heart J.* **2014**, *35*, 2733–2779. [CrossRef]

85. Gersh, B.J.; Maron, B.J.; Bonow, R.O.; Dearani, J.A.; Fifer, M.A.; Link, M.S.; Naidu, S.S.; Nishimura, R.A.; Ommen, S.R.; Rakowski, H.; et al. 2011 ACCF/AHA guideline for the diagnosis and treatment of hypertrophic cardiomyopathy: A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation* **2011**, *124*, 2761–2796. [CrossRef] [PubMed]

86. Maron, B.J.; Casey, S.A.; Chan, R.H.; Garberich, R.F.; Rowin, E.J.; Maron, M.S. Independent assessment of the european society of cardiology sudden death risk model for hypertrophic cardiomyopathy. *Am. J. Cardiol.* **2015**, *116*, 757–764. [CrossRef] [PubMed]

87. Vriesendorp, P.A.; Schinkel, A.F.; Liebregts, M.; Theuns, D.A.; van Cleemput, J.; Ten Cate, F.J.; Willems, R.; Michels, M. Validation of the 2014 European Society of Cardiology guidelines risk prediction model for the primary prevention of sudden cardiac death in hypertrophic cardiomyopathy. *Circ. Arrhythmia Electrophysiol.* **2015**, *8*, 829–835. [CrossRef] [PubMed]

88. O'Mahony, C.; Jichi, F.; Pavlou, M.; Monserrat, L.; Anastasakis, A.; Rapezzi, C.; Biagini, E.; Gimeno, J.R.; Limongelli, G.; McKenna, W.J.; et al. A novel clinical risk prediction model for sudden cardiac death in hypertrophic cardiomyopathy (HCM risk-SCD). *Eur. Heart J.* **2014**, *35*, 2010–2020. [CrossRef]

89. Gatzoulis, K.A.; Georgopoulos, S.; Antoniou, C.K.; Anastasakis, A.; Dilaveris, P.; Arsenos, P.; Sideris, S.; Tsiachris, D.; Archontakis, S.; Sotiropoulos, E.; et al. Programmed ventricular stimulation predicts arrhythmic events and survival in hypertrophic cardiomyopathy. *Int. J. Cardiol.* **2018**, *254*, 175–181. [CrossRef]

90. Maron, B.J.; Rowin, E.J.; Casey, S.A.; Link, M.S.; Lesser, J.R.; Chan, R.H.; Garberich, R.F.; Udelson, J.E.; Maron, M.S. Hypertrophic cardiomyopathy in adulthood associated with low cardiovascular mortality with contemporary management strategies. *J. Am. Coll. Cardiol.* **2015**, *65*, 1915–1928. [CrossRef] [PubMed]

91. Lorenzini, M.; Anastasiou, Z.; O'Mahony, C.; Guttman, O.P.; Gimeno, J.R.; Monserrat, L.; Anastasakis, A.; Rapezzi, C.; Biagini, E.; Garcia-Pavia, P.; et al. Mortality among referral patients with hypertrophic cardiomyopathy vs the general European population. *JAMA Cardiol.* **2019**, *27*, e194534. [CrossRef]

92. Maron, M.S.; Rowin, E.J.; Wessler, B.S.; Mooney, P.J.; Fatima, A.; Patel, P.; Koethe, B.C.; Romashko, M.; Link, M.S.; Maron, B.J. Enhanced American College of Cardiology/American Heart Association strategy for prevention of sudden cardiac death in high-risk patients with hypertrophic cardiomyopathy. *JAMA Cardiol.* **2019**, *4*, 644–657. [CrossRef]

93. Schinkel, A.F.; Vriesendorp, P.A.; Sijbrands, E.J.; Jordaens, L.J.; ten Cate, F.J.; Michels, M. Outcome and complications after implantable cardioverter defibrillator therapy in hypertrophic cardiomyopathy: Systematic review and meta-analysis. *Circ. Heart Fail.* **2012**, *5*, 552–559. [CrossRef] [PubMed]

94. Maron, B.J.; Maron, M.S. LGE means better selection of HCM patients for primary prevention implantable defibrillators. *JACC Cardiovasc. Imaging* **2016**, *9*, 1403–1406. [CrossRef] [PubMed]

95. Ismail, T.F.; Jabbour, A.; Gulati, A.; Mallorie, A.; Raza, S.; Cowling, T.E.; Das, B.; Khwaja, J.; Alpendurada, F.D.; Wage, R.; et al. Role of late gadolinium enhancement cardiovascular magnetic resonance in the risk stratification of hypertrophic cardiomyopathy. *Heart* **2014**, *100*, 1851–1858. [CrossRef] [PubMed]

96. Chan, R.H.; Maron, B.J.; Olivotto, I.; Pencina, M.J.; Assenza, G.E.; Haas, T.; Lesser, J.R.; Gruner, C.; Crean, A.M.; Rakowski, H.; et al. Prognostic value of quantitative contrast-enhanced cardiovascular magnetic resonance for the evaluation of sudden death risk in patients with hypertrophic cardiomyopathy. *Circulation* **2014**, *130*, 484–495. [CrossRef] [PubMed]

97. Adabag, A.S.; Maron, B.J.; Appelbaum, E.; Harrigan, C.J.; Buros, J.L.; Gibson, C.M.; Lesser, J.R.; Hanna, C.A.; Udelson, J.E.; Manning, W.J.; et al. Occurrence and frequency of arrhythmias in hypertrophic cardiomyopathy in relation to delayed enhancement on cardiovascular magnetic resonance. *J. Am. Coll. Cardiol.* **2008**, *51*, 1369–1374. [CrossRef]

98. Leonardi, S.; Raineri, C.; De Ferrari, G.M.; Ghio, S.; Scelsi, L.; Pasotti, M.; Tagliani, M.; Valentini, A.; Dore, R.; Raisaro, A.; et al. Usefulness of cardiac magnetic resonance in assessing the risk of ventricular arrhythmias and sudden death in patients with hypertrophic cardiomyopathy. *Eur. Heart J.* **2009**, *30*, 2003–2010. [CrossRef]

99. Moon, J.C.; McKenna, W.J.; McCrohon, J.A.; Elliott, P.M.; Smith, G.C.; Pennell, D.J. Toward clinical risk assessment in hypertrophic cardiomyopathy with gadolinium cardiovascular magnetic resonance. *J. Am. Coll. Cardiol.* **2003**, *41*, 1561–1567. [CrossRef]

100. Bruder, O.; Wagner, A.; Jensen, C.J.; Schneider, S.; Ong, P.; Kispert, E.M.; Nassenstein, K.; Schlosser, T.; Sabin, G.V.; Sechtem, U.; et al. Myocardial scar visualized by cardiovascular magnetic resonance imaging predicts major adverse events in patients with hypertrophic cardiomyopathy. *J. Am. Coll. Cardiol.* **2010**, *56*, 875–887. [CrossRef]

101. Todiere, G.; Nugara, C.; Gentile, G.; Negri, F.; Bianco, F.; Falletta, C.; Novo, G.; Di Bella, G.; De Caterina, R.; Zachara, E.; et al. Prognostic role of late gadolinium enhancement in patients with hypertrophic cardiomyopathy and low-to-intermediate sudden cardiac death risk score. *Am. J. Cardiol.* **2019**, *124*, 1286–1292. [CrossRef]

102. McLELLAN, A.J.; Ellims, A.H.; Prabhu, S.; Voskoboinik, A.; Iles, L.M.; Hare, J.L.; Kaye, D.M.; Macciocca, I.; Mariani, J.A.; Kalman, J.M.; et al. Diffuse ventricular fibrosis on cardiac magnetic resonance imaging associates with ventricular tachycardia in patients with hypertrophic cardiomyopathy. *J. Cardiovasc. Electrophysiol.* **2016**, *27*, 571–580. [CrossRef]

103. Hen, Y.; Iguchi, N.; Machida, H.; Takada, K.; Utanohara, Y.; Sumiyoshi, T. High signal intensity on T2-weighted cardiac magnetic resonance imaging correlates with the ventricular tachyarrhythmia in hypertrophic cardiomyopathy. *Heart Vessel.* **2013**, *28*, 742–749. [CrossRef] [PubMed]

104. Avanesov, M.; Münch, J.; Weinrich, J.; Well, L.; Säring, D.; Stehning, C.; Tahir, E.; Bohnen, S.; Radunski, U.K.; Muellerleile, K.; et al. Prediction of the estimated 5-year risk of sudden cardiac death and syncope or non-sustained ventricular tachycardia in patients with hypertrophic cardiomyopathy using late gadolinium enhancement and extracellular volume CMR. *Eur. Radiol.* **2017**, *27*, 5136–5145. [CrossRef] [PubMed]

105. Mavrogeni, S.I.; Sfikakis, P.P.; Markousis-Mavrogenis, G.; Bournia, V.K.; Poulos, G.; Koutsogeorgopoulou, L.; Karabela, G.; Stavropoulos, E.; Katsifis, G.; Boki, K.; et al. Cardiovascular magnetic resonance imaging pattern in patients with autoimmune rheumatic diseases and ventricular tachycardia with preserved ejection fraction. *Int. J. Cardiol.* **2019**, *284*, 105–109. [CrossRef] [PubMed]

106. Lazzerini, P.E.; Bertolozzi, I.; Acampa, M.; Fulceri, R.; Laghi-Pasini, F.; Capecchi, P.L. Torsades de pointes in patients with polymyalgia rheumatica. *Curr. Pharm. Des.* **2018**, *24*, 323–340. [CrossRef] [PubMed]

107. Lazzerini, P.E.; Capecchi, P.L.; Laghi-Pasini, F. Systemic inflammation and arrhythmic risk: Lessons from rheumatoid arthritis. *Eur. Heart J.* **2017**, *38*, 1717–1727. [CrossRef]

108. El-Sayed, Z.A.; Mostafa, G.A.; Aly, G.S.; El-Shahed, G.S.; El-Aziz, M.M.; El-Emam, S.M. Cardiovascular autonomic function assessed by autonomic function tests and serum autonomic neuropeptides in Egyptian children and adolescents with rheumatic diseases. *Rheumatology* **2009**, *48*, 843–848. [CrossRef]

109. Metwalley, K.A.; Hamed, S.A.; Farghaly, H.S. Cardiac autonomic function in children with type 1 diabetes. *Eur. J. Pediatr.* **2018**, *177*, 805–813. [CrossRef]

110. Dilaveris, P.; Pietri, P.; Tsiachris, D.; Gatzoulis, K.; Stefanadis, C. Inducible ventricular tachycardia due to dermatomyositis-related cardiomyopathy in the era of implantable cardioverter-defibrillator therapy. *Circulation* **2012**, *125*, 967–969. [CrossRef]

111. Lubitz, S.A.; Goldbarg, S.H.; Mehta, D. Sudden cardiac death in infiltrative cardiomyopathies: Sarcoidosis, scleroderma, amyloidosis, hemachromatosis. *Prog. Cardiovasc. Dis.* **2008**, *51*, 58–73. [CrossRef]

112. Mavrogeni, S.; Gargani, L.; Pepe, A.; Monti, L.; Markousis-Mavrogenis, G.; De Santis, M.; Marchi, D.; Koutsogeorgopoulou, L.; Karabela, G.; Stavropoulos, E.; et al. Cardiac magnetic resonance predicts ventricular arrhythmias in scleroderma: The Scleroderma Arrhythmia Clinical Utility Study (SAnCtUS). *Rheumatology* **2019**, kez494. [CrossRef]

113. Dinov, B.; Fiedler, L.; Schönbauer, R.; Bollmann, A.; Rolf, S.; Piorkowski, C.; Hindricks, G.; Arya, A. Outcomes in catheter ablation of ventricular tachycardia in dilated nonischemic cardiomyopathy compared with ischemic cardiomyopathy: Results from the Prospective Heart Centre of Leipzig VT (HELP-VT) Study. *Circulation* **2014**, *129*, 728–736. [CrossRef] [PubMed]

114. Shirai, Y.; Liang, J.J.; Santangeli, P.; Arkles, J.S.; Schaller, R.D.; Supple, G.E.; Nazarian, S.; Garcia, F.C.; Lin, D.; Dixit, S.; et al. Comparison of the ventricular tachycardia circuit between patients with ischemic and nonischemic cardiomyopathies: Detailed characterization by entrainment. *Circ. Arrhythmia Electrophysiol.* **2019**, *12*, e007249. [CrossRef] [PubMed]

115. Koplan, B.A.; Stevenson, W.G. Ventricular tachycardia and sudden cardiac death. *Mayo Clin. Proc.* **2009**, *84*, 289–297. [CrossRef] [PubMed]

116. Antonopoulos, A.S.; Tsiachris, D.; Economou, E.K.; Alexopoulos, N.; Goliopoulou, A.; Gatzoulis, K.A. Behçet's disease cardiomyopathy: The role of magnetic resonance imaging and electroanatomical mapping in diagnosis and treatment. *Case report. Curr. Cardiol.* **2017**, *1*, 42–45.

117. Mukherjee, R.K.; Chubb, H.; Roujol, S.; Razavi, R.; O'Neill, M.D. Advances in real-time MRI-guided electrophysiology. Version 2. *Curr. Cardiovasc. Imaging Rep.* **2019**, *12*, 6. [CrossRef]

118. Wijnmaalen, A.P.; van der Geest, R.J.; van Huls van Taxis, C.F.; Siebelink, H.M.; Kroft, L.J.; Bax, J.J.; Reiber, J.H.; Schalij, M.J.; Zeppenfeld, K. Head-to-head comparison of contrast-enhanced magnetic resonance imaging and electroanatomical voltage mapping to assess post-infarct scar characteristics in patients with ventricular tachycardias: Real-time image integration and reversed registration. *Eur. Heart J.* **2011**, *32*, 104–114. [CrossRef]

119. Fernández-Armenta, J.; Berruezo, A.; Andreu, D.; Camara, O.; Silva, E.; Serra, L.; Barbarito, V.; Carotenutto, L.; Evertz, R.; Ortiz-Pérez, J.T.; et al. Three-dimensional architecture of scar and conducting channels based on high resolution ce-CMR: Insights for ventricular tachycardia ablation. *Circ. Arrhythmia Electrophysiol.* **2013**, *6*, 528–537. [CrossRef]

120. Andreu, D.; Penela, D.; Acosta, J.; Fernández-Armenta, J.; Perea, R.J.; Soto-Iglesias, D.; de Caralt, T.M.; Ortiz-Perez, J.T.; Prat-González, S.; Borràs, R.; et al. Cardiac magnetic resonance-aided scar dechanneling: Influence on acute and long-term outcomes. *Heart Rhythm* **2017**, *14*, 1121–1128. [CrossRef]

121. Chubb, H.; Harrison, J.L.; Weiss, S.; Krueger, S.; Koken, P.; Bloch, L.Ø.; Kim, W.Y.; Stenzel, G.S.; Wedan, S.R.; Weisz, J.L.; et al. Development, preclinical validation, and clinical translation of a cardiac magnetic resonance—Electrophysiology system with active catheter tracking for ablation of cardiac arrhythmia. *JACC Clin. Electrophysiol.* **2017**, *3*, 89–103. [CrossRef]

122. Mukherjee, R.K.; Costa, C.M.; Neji, R.; Harrison, J.L.; Sim, I.; Williams, S.E.; Whitaker, J.; Chubb, H.; O'Neill, L.; Schneider, R.; et al. Evaluation of a real-time magnetic resonance imaging-guided electrophysiology system for structural and electrophysiological ventricular tachycardia substrate assessment. *Europace* **2019**, *21*, 1432–1441. [CrossRef]

123. Chubb, H.; Williams, S.E.; Whitaker, J.; Harrison, J.L.; Razavi, R.; O'Neill, M. Cardiac electrophysiology under MRI guidance: An Emerging technology. *Arrhythmia Electrophysiol. Rev.* **2017**, *6*, 85–93. [CrossRef]

124. Ranjan, R.; Kholmovski, E.G.; Blauer, J.; Vijayakumar, S.; Volland, N.A.; Salama, M.E.; Parker, D.L.; MacLeod, R.; Marrouche, N.F. Identification and acute targeting of gaps in atrial ablation lesion sets using a real-time magnetic resonance imaging system. *Circ. Arrhythmia Electrophysiol.* **2012**, *5*, 1130–1135. [CrossRef] [PubMed]

125. Celik, H.; Ramanan, V.; Barry, J.; Ghate, S.; Leber, V.; Oduneye, S.; Gu, Y.; Jamali, M.; Ghugre, N.; Stainsby, J.A.; et al. Intrinsic contrast for characterization of acute radiofrequency ablation lesions. *Circ. Arrhythmia Electrophysiol.* **2014**, *7*, 718–727. [CrossRef] [PubMed]

126. Dickfeld, T.; Kato, R.; Zviman, M.; Nazarian, S.; Dong, J.; Ashikaga, H.; Lardo, A.C.; Berger, R.D.; Calkins, H.; Halperin, H. Characterization of acute and subacute radiofrequency ablation lesions with nonenhanced magnetic resonance imaging. *Heart Rhythm* **2007**, *4*, 208–214. [CrossRef] [PubMed]

127. Arujuna, A.; Karim, R.; Caulfield, D.; Knowles, B.; Rhode, K.; Schaeffter, T.; Kato, B.; Rinaldi, C.A.; Cooklin, M.; Razavi, R.; et al. Acute pulmonary vein isolation is achieved by a combination of reversible and irreversible atrial injury after catheter ablation: Evidence from magnetic resonance imaging. *Circ. Arrhythmia Electrophysiol.* **2012**, *5*, 691–700. [CrossRef] [PubMed]

128. Harrison, J.L.; Jensen, H.K.; Peel, S.A.; Chiribiri, A.; Grøndal, A.K.; Bloch, L.Ø.; Pedersen, S.F.; Bentzon, J.F.; Kolbitsch, C.; Karim, R.; et al. Cardiac magnetic resonance and electroanatomical mapping of acute and chronic atrial ablation injury: A histological validation study. *Eur. Heart J.* **2014**, *35*, 1486–1495. [CrossRef]

129. Vergara, G.R.; Vijayakumar, S.; Kholmovski, E.G.; Blauer, J.J.; Guttman, M.A.; Gloschat, C.; Payne, G.; Vij, K.; Akoum, N.W.; Daccarett, M.; et al. Real-time magnetic resonance imaging-guided radiofrequency atrial ablation and visualization of lesion formation at 3 Tesla. *Heart Rhythm* **2011**, *8*, 295–303. [CrossRef]

130. Tao, S.; Guttman, M.A.; Fink, S.; Elahi, H.; Patil, K.D.; Ashikaga, H.; Kolandaivelu, A.D.; Berger, R.D.; Halushka, M.K.; Schmidt, E.J.; et al. Ablation lesion characterization in scarred substrate assessed using cardiac magnetic resonance. *JACC Clin. Electrophysiol.* **2019**, *5*, 91–100. [CrossRef]

131. Toupin, S.; Bour, P.; Lepetit-Coiffé, M.; Ozenne, V.; Denis de Senneville, B.; Schneider, R.; Vaussy, A.; Chaumeil, A.; Cochet, H.; Sacher, F.; et al. Feasibility of real-time MR thermal dose mapping for predicting radiofrequency ablation outcome in the myocardium in vivo. *J. Cardiovasc. Magn. Reson.* **2017**, *19*, 14. [CrossRef]

132. Wang, P. Evaluation of MR thermometry with proton resonance frequency method at 7T. *Quant. Imaging Med. Surg.* **2017**, *7*, 259–266. [CrossRef]

133. Gatzoulis, K.A.; Vouliotis, A.I.; Tsiachris, D.; Salourou, M.; Archontakis, S.; Dilaveris, P.; Gialernios, T.; Arsenos, P.; Karystinos, G.; Sideris, S.; et al. Primary prevention of sudden cardiac death in a nonischemic dilated cardiomyopathy population: Reappraisal of the role of programmed ventricular stimulation. *Circ. Arrhythmia Electrophysiol.* **2013**, *6*, 504–512. [CrossRef] [PubMed]

134. Haugaa, K.H.; Goebel, B.; Dahlslett, T.; Meyer, K.; Jung, C.; Lauten, A.; Figulla, H.R.; Poerner, T.C.; Edvardsen, T. Risk assessment of ventricular arrhythmias in patients with nonischemic dilated cardiomyopathy by strain echocardiography. *J. Am. Soc. Echocardiogr.* **2012**, *25*, 667–673. [CrossRef] [PubMed]

135. Haugaa, K.H.; Grenne, B.L.; Eek, C.H.; Ersbøll, M.; Valeur, N.; Svendsen, J.H.; Florian, A.; Sjøli, B.; Brunvand, H.; Køber, L.; et al. Strain echocardiography improves risk prediction of ventricular arrhythmias after myocardial infarction. *JACC Cardiovasc. Imaging* **2013**, *6*, 841–850. [CrossRef] [PubMed]

136. Travin, M.I.; Feng, D.; Taub, C.C. Novel imaging approaches for predicting arrhythmic risk. *Circ. Cardiovasc. Imaging* **2015**, *8*, e003019. [CrossRef]

137. Li, X.; Fan, X.; Li, S.; Sun, W.; Shivkumar, K.; Zhao, S.; Lu, M.; Yao, Y. A novel risk stratification score for sudden cardiac death prediction in middle-aged, nonischemic dilated cardiomyopathy patients: The ESTIMATED score. *Can. J. Cardiol.* **2020**, *36*, 1121–1129. [CrossRef]

138. Selvanayagam, J.B.; Hartshorne, T.; Billot, L.; Grover, S.; Hillis, G.S.; Jung, W.; Krum, H.; Prasad, S.; McGavigan, A.D. Cardiovascular magnetic resonance-GUIDEd management of mild to moderate left ventricular systolic dysfunction (CMR GUIDE): Study protocol for a randomized controlled trial. *Ann. Noninvasive Electrocardiol.* **2017**, *22*, e12420. [CrossRef]

139. Gatzoulis, K.A.; Dilaveris, P.; Arsenos, P.; Tsiachris, D.; Antoniou, C.K.; Sideris, S.; Kolettis, T.; Kanoupakis, E.; Sideris, A.; Flevari, P.; et al. Arrhythmic risk stratification in nonischemic dilated cardiomyopathy: The ReCONSIDER study design—A two-step, multifactorial, electrophysiology-inclusive approach. *Hell. J. Cardiol.* **2020**, *21*, S1109-9666(20)30075-0. [CrossRef]

140. Monfredi, O.; Calkins, H. Was a mistake made when programmed electrical stimulation was eliminated as a sudden death risk marker in hypertrophic cardiomyopathy? *Int. J. Cardiol.* **2018**, *254*, 238–239. [CrossRef]