CARDIOLOGIE TUNISIENNE

ARTICLE ORIGINAL

Beyond Ejection Fraction: The Role of Cardiac MRI in Stratifying Risk in Dilated and Non-Dilated Cardiomyopathies

Au-delà de la fraction d'éjection : Apport de l'IRM cardiaque dans la stratification du risque dans les cardiomyopathies dilatées et non dilatées

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Summary

Introduction: Dilated cardiomyopathy (DCM) and non-dilated left ventricular cardiomyopathy (NDLVC) are associated with a high risk of major cardiovascular events. Traditional risk assessment relies heavily on LVEF, yet growing evidence highlights the prognostic value of CMR, particularly late gadolinium enhancement (LGE).

Objectives: Investigate the associations between CMR-derived parameters (LV volumes, LVEF, LGE patterns) and clinical outcomes, including dyspnea severity, arrhythmic events, and major hemodynamic events.

Determine the prognostic value of LGE in predicting arrhythmic risk compared with traditional LVEF-based assessment.

Methods: A retrospective, single-center study was conducted on patients diagnosed with DCM or NDLVC who underwent CMR at our institution and followed up between June 2021 and October 2024.

Results: Among 60 patients (65% with DCM, 35% with NDLVC), LGE was present in 45% of cases, with intramural and subepicardial distributions being the most common. A significant correlation was found between LV end-diastolic and end-systolic volumes and dyspnea (NYHA ≥ 3). Similarly, larger LV volumes and lower LVEF were strongly associated with the occurrence of major hemodynamic events. LGE was not significantly correlated with major hemodynamic events but was associated with a higher risk of arrhythmias. Two patients with LVEF >35% experienced life-threatening arrhythmia, underscoring the limitations of LVEF as the sole criterion for ICD eligibility.

Conclusions: CMR, particularly LGE assessment, provides critical insights into myocardial tissue characterization and arrhythmic risk stratification. Our findings support the need for an updated ICD implantation strategy incorporating CMR-derived risk factors.

Keywords

Magnetic resonance imaging, Dilated cardiomyopathy, non-dilated cardiomyopathy, Late enhancement, Prognosis

Résumé

Introduction : La cardiomyopathie dilatée (CMD) et la cardiomyopathie non dilatée ventriculaire gauche

(CNDVG) sont associées à un risque élevé d'événements cardiovasculaires majeurs. L'évaluation traditionnelle des risques repose largement sur la FEVG, mais de plus en plus de données soulignent la valeur pronostique de l'IRM cardiaque, en particulier du rehaussement tardif au gadolinium (RT).

Méthodes : Une étude rétrospective monocentrique a été menée sur des patients diagnostiqués avec une CMD ou une CNDVG qui ont subi une IRM cardiaque dans notre établissement et ont été suivis entre juin 2021 et octobre 2024.

Résultats : Parmi les 60 patients (65 % atteints de DCM, 35 % atteints de NDLVC), un LGE était présent dans 45 % des cas, les distributions intramurales et sous-épicardiques étant les plus fréquentes. Une

corrélation significative a été observée entre les volumes télédiastolique et télésystolique du VG

et la dyspnée (NYHA ≥ 3). De même, des volumes ventriculaires gauches plus importants et une FEVG plus faible étaient fortement associés à la survenue d'événements hémodynamiques majeurs. Le RT n'était pas significativement corrélé aux événements hémodynamiques majeurs, mais était associé à un risque plus élevé d'arythmies. Deux patients présentant une FEVG > 35 % ont souffert d'une arythmie potentiellement mortelle, soulignant les limites de la FEVG comme seul critère d'éligibilité à un DAI.

Conclusions : L'IRM cardiaque, en particulier l'évaluation du RT fournit des informations essentielles sur la caractérisation du tissu myocardique et la stratification du risque arythmique. Nos résultats confirment la nécessité d'une stratégie actualisée d'implantation d'un DAI intégrant les facteurs de risque dérivés de l'IRM cardiaque.

Mots-clés

Mort subite d'origine cardiaque ; Dépistage cardiovasculaire ; Aptitude militaire ; Échocardiographie transthoracique ; Électrocardiogramme

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INTRODUCTION

Dilated cardiomyopathy (DCM) is defined by left ventricular (LV) dilation with global or regional systolic dysfunction that cannot be explained by volume or pressure overload (such as hypertension, valvular disease, or congenital cardiomyopathy) or by significant coronary artery disease (CAD) [1, 2]. DCM is the most common cardiomyopathy, with a prevalence ranging from 1 in 2,500 to 1 in 250, depending on evolving diagnostic criteria and geographical variations [3], highlighting its significance as a public health issue. Its complexity also lies in its multiple and heterogeneous etiologies. Up to 40% of DCM cases are hereditary, with mutations in more than 40 genes implicated in its pathogenesis [4].

Non-dilated left ventricular cardiomyopathy (NDLVC) is a newly recognized entity that represents intermediate phenotypes. It is defined by the presence of non-ischemic scarring or fatty replacement of the LV myocardium, regardless of LV wall motion abnormalities, or by isolated global hypokinesia of the LV without scarring [1].

Cardiovascular complications of these two cardiomyopathies, particularly major ventricular arrhythmias and heart failure, remain the leading causes of morbidity and mortality despite advances in therapeutic strategies, with sudden cardiac death accounting for 30% of fatalities [5]. One of the key measures to reduce the risk of ventricular arrhythmias and sudden death is the implantation of an implantable cardioverter-defibrillator (ICD). For primary prevention, a left ventricular ejection fraction (LVEF) ≤ 35% remains the primary selection criterion for ICD implantation. However, an increasing number of studies over the past 15 years have demonstrated significant limitations of LVEF as a predictive marker [6]. As a result, LVEF ≤ 35% as an indication for primary prevention ICD implantation has been downgraded from a Class I to a Class IIa recommendation in the latest guidelines of the European Society of Cardiology (ESC) [7, 8].

Cardiac magnetic resonance imaging (CMR) with late gadolinium enhancement (LGE) sequences allows for precise diagnosis and identification of myocardial fibrosis, which serves as the substrate for ventricular arrhythmias. This study aims to describe the role of CMR in the initial evaluation of DCM and NDLVC and to assess the prognostic value of LGE and quantitative CMR parameters.

METHODS

Study Population

This is a single-centre, retrospective, descriptive, and prognostic study. All patients diagnosed with DCM or NDLVC at the cardiology department of University Hospital (UH) Hédi Chaker Sfax, Tunisia, between June 2021 and October 2024 who underwent CMR at the same institution were included. The diagnosis of DCM was based on the ESC criteria, defined as LV dilatation with systolic dysfunction characterized by LVEF<50%, in the absence of volume overload conditions or significant CAD. Left ventricular dilation was determined by an indexed left ventricular end-diastolic volume (LVEDVi)> 96 mL/m² for women and 106 mL/m² for men, as per the recommendations of the European Association of Cardiovascular Imaging [9]. NDLVC was defined as the presence of non-ischemic left ventricular scar (subepicardial or intramyocardial LGE distribution), in the absence of LV dilation, with or without regional or global systolic dysfunction. Additionally, patients with isolated global LV hypokinesia without evidence of myocardial scarring were also included.

Patients with a history of myocardial infarction or significant CAD, defined as >50% stenosis in major coronary arteries on coronary angiography, were excluded. Other exclusion criteria included cardiomyopathy secondary to valvular disease, any form of cardiomyopathy other than DCM or NDLVC, and age below 18 years. Patients lost during follow-up or with incomplete medical records were not included in the final analysis. Demographic, clinical data and coronarography data were collected at baseline evaluation.

CMR Acquisition Protocol and Image Analysis

All imaging studies were performed using a Siemens 1.5 Tesla at the radiology department of UH Hédi Chaker Sfax. Before the examination, oral consent was obtained from each patient, and contraindications to MRI and gadolinium administration were systematically assessed. For patients with cardiac electronic implantable devices (CEID), a pre-scan checklist was completed by the referring cardiologist, electrophysiologist, and radiologist, in accordance with international guidelines for CMR safety in device carriers [10].

Cine imaging was performed using balanced steady-state free precession (bSSFP) sequences (TrueFISP, Siemens) to evaluate global and segmental LV function. Late gadolinium enhancement imaging was conducted approximately 10 minutes after intravenous injection of 0.2 mL/kg of gadoteric acid (Dotarem®, Guerbet, France). Post-processing was performed using a dedicated imaging workstation. LV volumes, mass, and ejection fraction were quantified using Simpson's method.

Study Endpoints

The primary endpoint was the occurrence of sudden cardiac death (SCD) or major ventricular arrhythmias. Sudden cardiac death was defined as an unexpected cardiac death occurring within one hour of symptom onset or during sleep without preceding signs of deterioration. Major ventricular arrhythmias included sustained ventricular tachycardia lasting more than 30 seconds with hemodynamic instability, documented ventricular fibrillation, or appropriate ICD interventions.

The secondary endpoint included major hemodynamic events, comprising death due to end-stage heart failure, hospitalization for acute heart failure requiring inotropic support or mechanical circulatory assistance, and listing for heart transplantation. The date of the enrollment CMR scan was considered as the baseline evaluation. The end of follow-up was on October 2024 or the date of the primary endpoint.

Statistical Analysis

Statistical analyses were conducted using IBM SPSS 20, with a p-value of <0.05 considered statistically significant. Continuous variables were assessed for normality using the Shapiro-Wilk test and were presented as mean ± standard deviation or median with interquartile range, as appropriate. Categorical variables were compared using the chi-square test or Fisher's exact test. Comparisons of continuous variables were performed using independent t-tests or the Mann-Whitney U test. Survival analysis was performed using the Kaplan-Meier method, with differences between survival curves assessed by the log-rank (Mantel-Cox) test.

RESULTS

Clinical and Demographic Characteristics

A total of 60 patients were included in this study, with 39 (65%) diagnosed with DCM and 21 (35%) with NDLVC. The mean age of the cohort was 57 ± 14.5 years, ranging from 18 to 83 years and 68% (n=41) of patients were male.

Among the included patients, 53% (n=32) had at least one cardiovascular risk factor. The most frequently observed risk factors were hypertension (43%), diabetes mellitus (36%), smoking (33%), and dyslipidemia (25%). In contrast, 12 patients (20%) had no identifiable cardiovascular risk factors (Table 1).

Table 1. Baseline Demographic and Clinical Characteristics

Characteristic	Value
Demographics	
Age (years), mean ± SD [range]	57 ± 14.5 [18–83]
Male sex, n (%)	41 (68%)
Cardiovascular Risk Factors, n (%)	
Hypertension	26 (43%)
Diabetes mellitus	22 (36%)
Smoking	20 (33%)
Dyslipidemia	15 (25%)
None	12 (20%)
Clinical Symptoms, n (%)	
Dyspnea	46 (76%)
NYHA class:	
- II	30 (50%)
- III	10 (16%)
- IV	6 (10%)
Syncope	5 (8%)
Chest pain	8 (13%)
Coronary Angiography (n=54 performed)	
Normal	18 (30%)
Atherosclerosis without significant stenosis	36 (60%)
Not performed	6 (10%)

Dyspnea was the most common symptom, present in 76% (n=46) of patients, with 50% (n=30) classified as NYHA II, 16% (n=10) as NYHA III, and 10% (n=6) as NYHA IV. Other symptoms included chest pain (13%) and syncope (8%).

Coronary angiography was performed in 90% (n=54) of patients, while 6 patients (10%) did not undergo the procedure (aged under 35 and free of cardiovascular risk factors). The majority of patients, 60% (n=36), exhibited coronary atherosclerosis without significant stenosis, and 30% (n=18) had normal coronary arteries.

Four patients had implanted cardiac devices. One patient underwent primary prevention implantable cardioverter-defibrillator (ICD) placement, while two patients had a CRT-D (cardiac resynchronization therapy-defibrillator) and one patient received a CRT-P (cardiac resynchronization therapy pacemaker).

Morphologic and Quantitative Cardiac CMR Findings

The mean LVEF was 33% (range 13-65%). Global systolic dysfunction was observed in 85% (n=51) of patients, with segmental wall motion abnormalities identified in 15% (n=9).

Late Gadolinium Enhancement Analysis

Late gadolinium enhancement was present in 45% (n=27) of patients, with no significant difference between DCM (46%) and NDLVC (42%) groups (Table 2). Among patients with LGE, the most common location was the lateral wall (48%), followed by the septum (33%), and combined septal and lateral wall involvement (19%). The most frequent LGE pattern was intramural fibrosis (44%), followed by subepicardial (19%), mixed (subepicardial and intramural) (19%), subendocardial (11%), and transmural fibrosis (7%) (Figures 1, 2). Analysis of LGE localization and pattern did not reveal significant differences between DCM and NDLVC.

Table 2. Late Gadolinium Enhancement Characteristics

LGE Presence by Cardiomyopathy Type	LGE (+)	LGE (-)	Total
DCM (n=39)	18 (46%)	21 (54%)	39 (100%)
NDLVC (n=21)	9 (42%)	12 (58%)	21 (100%)
Total (n=60)	27 (45%)	33 (55%)	60 (100%)
LGE Localization and Patterns (among LGE+, n=27)	**DCM (n=18)**	**NDLVC (n=9)**	**Total (%)**
Location			
Lateral wall	7	6	13 (48%)
Septum	7	2	9 (33%)
Combined (septal and lateral)	4	1	5 (19%)
Pattern			
Intramural	8	4	12 (44%)
Subepicardial	4	1	5 (19%)
Mixed (subepicardial and intramural)	2	3	5 (19%)
Subendocardial	2	1	3 (11%)
Transmural	2	0	2 (7%)

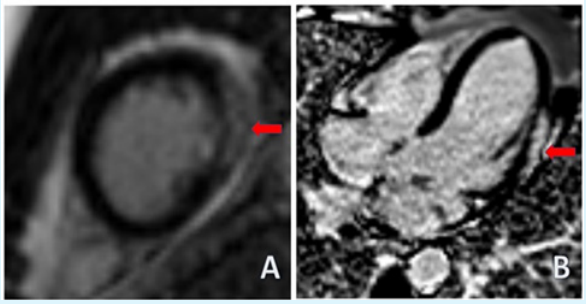

Figure 1. Short-axis LGE sequence of the left ventricle (a) and four-chamber view (b) showing subendocardial enhancement of the lateral-apical segment.

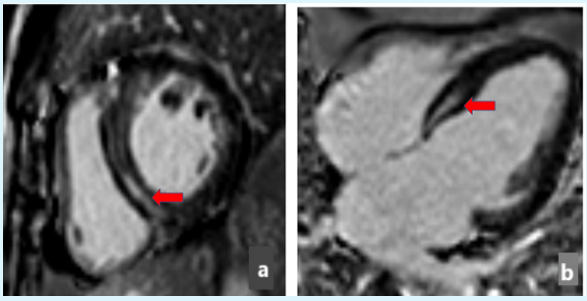

Figure 2. Short-axis LGE sequence of the left ventricle (a) and four-chamber view (b) showing intramural enhancement of the septum.

Follow-Up and Outcomes

Over a mean follow-up of 19 ± 8 months (range 10–41 months), major arrhythmic events occurred in 3% (n=2) of patients, both presenting with sustained ventricular tachycardia and hemodynamic instability. Major hemodynamic events were observed in 20% (n=12) of patients, including 10 cases of acute heart failure hospitalization, 1 death due to end-stage heart failure, and 1 patient listed for heart transplantation.

Correlation between CMR Findings, Dyspnea, and Clinical Events

No significant correlation was found between the presence of LGE and dyspnea severity (p=0.602). However, a statistically significant correlation was observed between left ventricular volumes and dyspnea severity, with both LVEDVi (p=0.016) and LVESVi (p<0.001) being significantly higher in patients with NYHA III–IV symptoms (Table 3).

No statistically significant correlation was found between the presence of LGE and left ventricular ejection fraction or volumetric parameters.

Patients who experienced major hemodynamic events had significantly larger LVEDVi and LVESVi and lower LVEF ($p<0.05$ for all). However, LGE presence was not significantly associated with hemodynamic events (Table III).

No statistically significant correlation was found between LVEDVi, LVESVi, or LVEF and arrhythmic events ($p>0.05$). However, both patients who developed sustained ventricular tachycardia exhibited a mixed-type LGE pattern involving the septum. A summary of significant correlations is provided in Table 3.

Table 3. Summary of Correlations and Outcomess

Correlation/Outcome	p-value
LVEF and NYHA ≥ III	0.162
LVEF and hemodynamic events	0.001
LGE presence and NYHA ≥ III	0.331
LGE presence and hemodynamic events	**0.741**
LGE presence and arrhythmias	OR undefined (both events in LGE+; n=2)
Overall Outcomes	
Major arrhythmic events, n (%)	2 (3%)
Major hemodynamic events, n (%)	12 (20%)
Mean follow-up (months)	19 ± 8

Survival Analysis

Kaplan-Meier survival analysis did not show a significant difference in event-free survival between DCM and NDLVC ($p=0.300$, log-rank test) (Figure 3).

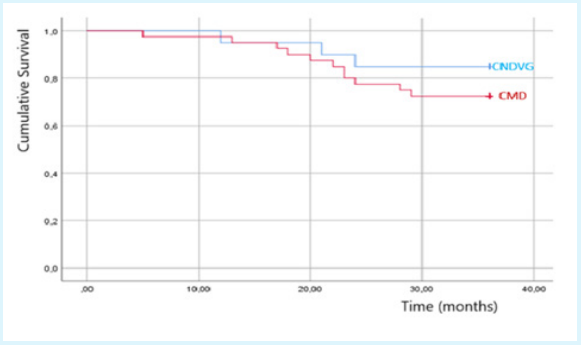

Figure 3. Kaplan-Meier survival curve comparing DCM and NDLVC

DISCUSSION

To prevent sudden cardiac death, European guidelines recommend ICD implantation in symptomatic patients with an LVEF below 35% despite optimal medical therapy [1, 8]. These recommendations are based on clinical trials conducted over two decades ago, which exclusively included patients with an LVEF ≤ 35% [11–14]. Since then, advancements in heart failure pharmacotherapy have significantly reduced both all-cause and sudden cardiac mortality [15]. The observed decline in sudden cardiac death has reignited debate over ICD eligibility, particularly in patients with dilated cardiomyopathy. The results of the DANISH trial have further contributed to this discussion [16].

Halliday et al. [17] were the first to demonstrate an association between LGE and arrhythmic events in patients with an LVEF >40%. They showed that patients with dilated cardiomyopathy and mild to moderate LVEF reduction with LGE had an annual arrhythmic event rate comparable to cohorts with severely reduced LVEF without LGE (approximately 3.6% per year). Another study further confirmed that patients with an LVEF >35% and myocardial fibrosis were at a higher risk for arrhythmic events than those with an LVEF of 21–35% without myocardial fibrosis [18]. As a result, the indication for primary prevention ICD implantation based on LVEF ≤ 35% has been downgraded from class I to class IIa in recent ESC guidelines [1]. In our study, both patients who developed sustained ventricular tachycardia had an LVEF >35%, meaning they would not have been eligible for an ICD under current guidelines.

Prevalence of late gadolinium enhancement

The most recent meta-analysis by Theerasuwipakorn et al. [19], which included 60 studies and 15,217 patients, reported the presence of LGE in 46% of cases, with a prevalence ranging from 25% to 82%. In our study, LGE was assessed using visual analysis and was present in 27 patients, representing 45% of the study population, which is concordant with the average prevalence reported in the latest meta-analysis (Table 4).

Table 4. Prevalence and Interpretation Method of LGE Across Studies

First author	Year	Study type	N	Age	LVEF (%)	LGE assessment	LGE (%)	Follow-up (years)
Infante [20]	2021	Retrospective	86	44.9 ± 16.1	36.9 ± 2.2	Visual	55 (64%)	4.9 ± 3.2
Kolluru [21]	2021	Prospective	61	54 ± 13	33	Visual	21 (34.4%)	2 ± 0.3
Kim [22]	2021	Retrospective	78	54.9 ± 13.6	25.4	Intensity>5 SD	63 (80.8%)	3.1
Klem [23]	2021	Prospective	1020	54	33	Visual, intensity >2 SD	461 (45.2%)	2.3
Xu [24]	2021	Prospective	412	48 ± 14.4	23.7 ± 9.8	Visual	201 (48.8%)	4.2
Li [25]	2022	Retrospective	659	45 ± 15	29.6 ± 9.3	FWHM	355 (55.9%)	5.4 ± 1.8
Theerasuwipakorn [19]	2023	Meta-analysis	15,217	-	-	Various methods	7061 (46%)	-
Castrichini [26]	2024	Retrospective	462	43 ± 15	44 ± 14	Visual	237 (59%)	6.75
Our study	2024	Retrospective	60	57 ± 14.5	33 ± 9	Visual	27 (45%)	1.6

Presence of late gadolinium enhancement and arrhythmic risk

Myocardial fibrosis is recognized as the primary substrate for ventricular tachycardia, as it provides the necessary components for the maintenance of reentrant circuits. This has been well established in ischemic cardiomyopathy and has also been confirmed in non-ischemic dilated cardiomyopathy [27]. Liuba et al. [28] demonstrated that in patients with dilated cardiomyopathy, electroanatomic mapping revealed delayed and asynchronous electrical activation between the epicardium and endocardium due to the presence of subepicardial or intramyocardial fibrosis. The largest and most recent meta-analysis [18] reported that 10.7% of patients experienced major arrhythmic events. The presence of LGE was a strong predictor of ventricular arrhythmic events, with a combined odds ratio of 3.99. These findings were consistent with the earlier meta-analysis by Di Marco et al. [29], which included a smaller sample size but reported a similar odds ratio of 4.3 (Table 5). In our study, both patients who developed major arrhythmic events had LGE.

Table 5. Number of Major Arrhythmic Events and Odds Ratio (OR) Across Studies

Study	Year	Sample size	Arrhythmic events wit LGE (+)	Arrhythmic events wit LGE (-)
Di Marco et al.	2017	2948	272	78
Barison et al.	2020	183	18	2
Guaricci et al.	2021	1000	66	27
Di Marco et al.	2021	1165	68	6
Theerasuwipakon et al.	2023	7541	-	-
Our study	2024	60	2	0

Type of late gadolinium enhancement and occurrence of major arrhythmic events Halliday et al. [17] demonstrated that the presence of intramural LGE was associated with a ninefold increased risk of sudden cardiac death in patients with DCM and an LVEF >40%. De Frutos et al. [33] analyzed LGE distribution in relation to genotype and arrhythmic risk in a large multicenter cohort of patients with DCM. Their findings indicated a significantly increased risk of arrhythmic events in patients with mixed-pattern LGE distribution. In our study, both patients who developed major arrhythmic events exhibited a mixed-pattern LGE.

Location of late gadolinium enhancement and occurrence of major arrhythmic events

Di Marco et al. [31] reported that the combination of septal and lateral wall LGE was associated with a higher risk of major ventricular arrhythmias compared to isolated septal or lateral involvement. Barison et al. [29] further demonstrated that septal and inferior wall LGE were linked to an increased risk of ICD interventions. A more recent study involving patients with DCM and NDLVC confirmed that not only the presence of LGE but also its septal localization was associated with a higher prevalence of major arrhythmic events compared to isolated lateral wall involvement [26]. In our study, both patients who developed major arrhythmic events exhibited septal LGE. Among the 11 patients with septal LGE, five had an LVEF >35%. Additionally, five patients had both septal and lateral wall LGE, including two with an LVEF >35%. These patients remain at increased risk for arrhythmic events despite being ineligible for ICD implantation according to the latest ESC guidelines [1].

Extent of late gadolinium enhancement and major arrhythmic events

Although a quantitative relationship between LGE burden and arrhythmic risk has been reported [23], an optimal cutoff value for LGE extent has not yet been established. Halliday et al. [16] and Behera et al. [34] demonstrated that the correlation between LGE burden and clinical outcomes appear nonlinear, as even a slight increase in LGE extent can significantly elevate the risk of adverse events.

Late gadolinium enhancement and major hemodynamic events

Previous meta-analyses [18, 34] have reported an association between LGE and the occurrence of major hemodynamic events. However, these studies indicate that the correlation between LGE and arrhythmic events is stronger than its association with heart failure-related complications. Di Marco et al. [32] demonstrated that while LVEF exhibited a similar predictive value for both arrhythmic and hemodynamic events, LGE was not an independent predictor of MHEs. In our study, no statistically significant correlation was found between LGE and the occurrence of major hemodynamic events.

Role of cardiac MRI in the differential diagnosis of ischemic cardiomyopathy

In our study, patients with significant CAD identified on coronary angiography or those presenting with ischemic-pattern LGE were excluded. Cardiac MRI has proven useful in reclassifying patients initially diagnosed with non-ischemic cardiomyopathy. Soriano et al. [35] found that 81% of patients with angiographically proven coronary occlusion and 9% of those with non-occlusive coronary atherosclerosis exhibited subendocardial or transmural enhancement consistent with prior infarction. McCrohon et al. [36] reported that in a cohort of 90 heart failure patients, 13% exhibited ischemic-pattern LGE suggestive of underlying CAD, despite being initially classified as non-ischemic.

CONCLUSION

Dilated and non-dilated left ventricular cardiomyopathies represent complex and multifactorial conditions. The integration of MRI findings into clinical decision-making algorithms has further emphasized the limitations of LVEF as the sole criterion for primary prevention ICD implantation. While LVEF remains an essential parameter, the presence of LGE in specific myocardial locations appears to be a more sensitive marker for identifying patients at high risk for ventricular arrhythmias.

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