



Comparison of Cardiac Magnetic Resonance Imaging Findings and Outcome in Different Types of Cardiomyopathy

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ABSTRACT:

Introduction: Nondilated left ventricular cardiomyopathy (NDLVC) is a recently recognized subtype of cardiomyopathy. This study aimed to evaluate and compare the phenotypic characteristics of dilated cardiomyopathy (DCM) and NDLVC using cardiac magnetic resonance imaging (CMR), and to investigate the prognostic implications associated with these conditions.

Methods: A total of 144 patients were enrolled and categorized into three groups. Group 1 included patients with left ventricular ejection fraction (LVEF) < 40%, corresponding to NDLVC with reduced ejection fraction (NDLVC-REF). Group 2 comprised those with LVEF between 40% and 50%, classified as NDLVC with mildly reduced ejection fraction (NDLVC-MREF). Group 3 consisted of patients diagnosed with DCM. All participants were followed for a median duration of 12 months to assess a composite cardiac endpoint.

Results: During the follow-up period, atrial fibrillation was more commonly observed in the NDLVC groups. In contrast, the DCM group exhibited a higher burden of myocardial late gadolinium enhancement (LGE). Most patients in the NDLVC groups did not present with LGE. The septal wall was the most frequently involved region of the left ventricle, and the midwall pattern was the most common LGE distribution across all groups. Notably, patients who experienced a composite cardiac event (CCE) demonstrated a higher prevalence of myocardial replacement fibrosis.

Conclusion: The prognosis of NDLVC has shown recent improvements. It may be appropriate to consider NDLVC as part of a spectrum that includes DCM. However, further research is required to elucidate the prognostic risk factors associated with this condition.

Introduction

Cardiomyopathies represent a significant cause of heart failure, with a prevalence of conditions such as hypertrophic cardiomyopathy and dilated cardiomyopathy (DCM) estimated at approximately 1 in 500 individuals in the general adult population [1]. Based on etiology, cardiomyopathic heart failure is broadly classified into ischemic and nonischemic

cardiomyopathies (NICMs). Ischemic cardiomyopathy is attributable to coronary artery disease, whereas NICMs, including DCM, typically occur in the absence of ischemia or overt structural heart disease [1]. Despite similarities in clinical manifestations—such as peripheral venous congestion, exercise intolerance, and dyspnea—the underlying pathophysiology differs



substantially, warranting distinct applications of cardiac magnetic resonance imaging (CMR) in each group.

The European Society of Cardiology has introduced a new classification termed nondilated left ventricular cardiomyopathy (NDLVC), characterized by left ventricular (LV) dysfunction or scarring without chamber dilatation and often accompanied by regional wall motion abnormalities [2]. NDLVC is defined by a left ventricular ejection fraction (LVEF) of less than 45% and is considered an early manifestation of DCM, with no significant difference in mortality between the two entities [3]. However, CMR findings indicate that some patients meeting similar clinical and structural criteria exhibit mildly reduced LVEF ($45\% < \text{LVEF} < 50\%$), suggesting that the current definition of non-DCM may not adequately encompass all cases of nondilated ventricles with subtle systolic impairment [4].

Both dilated and nondilated cardiomyopathies can culminate in heart failure syndrome, yet they differ in anatomical and functional attributes. Accurate differentiation between these forms is crucial for diagnosis and therapeutic management. Based on our review of clinical data and CMR studies, NDLVC does not merely represent a milder or incipient stage of DCM. Rather, it warrants recognition as a distinct clinical entity, necessitating refinement of its diagnostic criteria and a reevaluation of its prognostic and outcome measures.

This study employed CMR imaging to evaluate and compare the phenotypic characteristics of NDLVC—stratified by reduced and mildly reduced LVEF—with those of DCM, and to explore the prognostic significance of these cardiomyopathies in patients referred to a tertiary cardiovascular center.

Materials and Methods

This prospective study was conducted in the Department of Cardiology between January 2022 and January 2023. A total of 144 patients with newly diagnosed heart failure, suspected of having cardiomyopathy and undergoing imaging evaluation, were enrolled. Dilated cardiomyopathy (DCM) was defined as a left ventricular ejection fraction (LVEF) of less than 50% accompanied by an increased left ventricular end-diastolic volume indexed (LVEDVI) to body surface area (BSA). Nondilated left ventricular cardiomyopathy (NDLVC) was defined based on the following criteria: (1) LVEF <

50% as measured by cardiac magnetic resonance (CMR) imaging, and (2) no increase in LVEDVI compared to published reference values that are age- and sex-specific.

The inclusion criteria for the study comprised a minimum patient age of 18 years and the absence of coronary artery disease, which was confirmed either through invasive selective coronary angiography or coronary CT angiography. Additional exclusion criteria included abnormal loading conditions such as significant primary valvular heart disease, severe systemic hypertension, or congenital heart disease; active inflammatory conditions like acute myocarditis; infiltrative cardiac diseases; and chronic systemic illnesses such as diabetes mellitus, chronic kidney disease, or chronic pulmonary disease. Patients with known supraventricular arrhythmias, persistent atrial fibrillation, peripartum cardiomyopathy, tachycardia-induced cardiomyopathy, or arrhythmogenic right ventricular cardiomyopathy were also excluded.

Patients with DCM who fulfilled these same eligibility criteria were selected for comparative analysis. Relevant data, including the indication for CMR and its final interpretation, demographic details, clinical history and diagnosis, signs and symptoms, and medication history at the time of CMR referral, were collected from hospital records and, when necessary, through follow-up telephone communication.

Cardiac magnetic resonance imaging was performed using a standardized protocol on a 1.5 Tesla system. Ten minutes after intravenous administration of gadoterate meglumine at a dose of 0.15 mmol/kg, late gadolinium enhancement (LGE) imaging was conducted using an inversion recovery gradient echo sequence. Images were obtained in standard long-axis planes and sequential short-axis slices with an 8 mm thickness and 2 mm interslice gap, using two-phase encoding directions. The myocardium was appropriately nulled by optimizing inversion time. Ventricular volumes and masses were assessed using dedicated software (CMR42, Circle Cardiovascular Imaging Inc., Calgary, Canada) and indexed to BSA.

Assessment of nonischemic LGE was independently performed by two investigators, with a third investigator consulted in cases of disagreement. LGE was considered present if it was identified in both short- and long-axis planes, in both phase encoding directions, and outside localized insertion points of the ventricles.



The primary endpoint of the study was a composite cardiac event (CCE), defined as death and/or hospitalization for cardiovascular causes. Secondary endpoints included the occurrence of atrial fibrillation or flutter, persistent ventricular arrhythmias, and implantation of an implantable cardioverter-defibrillator (ICD). Based on LVEF and morphological criteria, patients were categorized into three groups. Group 1 included patients with LVEF < 40%, classified as NDLCV with reduced ejection fraction (NDLCV-REF). Group 2 comprised patients with LVEF between 40% and 50%, designated as NDLCV with mildly reduced ejection fraction (NDLCV-MREF). Group 3 consisted of patients with DCM.

Statistical analysis: The normality of variable distributions was assessed using the one-sample Kolmogorov–Smirnov test. Descriptive statistics were expressed as mean with standard deviation (SD), median with interquartile range (IQR), or frequency and percentage, as appropriate. Comparative analyses and associations were evaluated using the Chi-square test, Student’s t-test, analysis of variance (ANOVA), or the Mann–Whitney U test, depending on the nature and distribution of the data. Multivariate analysis was conducted using binary logistic regression to determine adjusted associations between composite cardiac events (CCE) and relevant clinical variables. Survival analysis over the follow-up period was performed using the Kaplan–Meier method. All statistical analyses were carried out using IBM SPSS Statistics for Windows, version 25.0. A p-value of ≤ 0.05 was considered statistically significant.

Results

The clinical and demographic profiles of the three patient groups—NDLCV-REF, NDLCV-MREF, and DCM—were broadly comparable in terms of age (mean ranging from 40.1 to 44.8 years, $p = 0.426$), sex distribution (male proportion 53.2%–63.8%, $p = 0.23$), NYHA class, and family history of cardiomyopathy. Atrial flutter/fibrillation was significantly more prevalent in the NDLCV-REF group (44.7%) compared to the other groups ($p = 0.041$). The use of sodium-glucose cotransporter-2 inhibitors (SGLT2I) was notably highest in DCM patients (85.1%), with lower usage in NDLCV-REF (42.5%) and NDLCV-MREF (28%) groups ($p = 0.048$). Mineralocorticoid receptor antagonist (MRA)

use differed significantly across groups ($p = 0.015$), being highest in NDLCV-REF (83%). Diuretic use was markedly more common in DCM patients (66%) compared to very low use in NDLCV groups ($p < 0.001$). Guideline-directed medical therapy (GDMT) at follow-up also showed significant variation, highest in NDLCV-REF (95.7%) and lowest in NDLCV-MREF (82%) ($p < 0.001$). While the rates of composite cardiac events and sustained VT/ICD use were not statistically different across groups, all-cause mortality was observed only in NDLCV-REF (8.5%) and DCM (6.4%) groups, with a statistically significant difference ($p = 0.043$).

Cardiac magnetic resonance (CMR) imaging parameters revealed significant structural and functional differences between the three groups. Patients with DCM exhibited markedly higher left ventricular (LV) mass index (63.1 vs. 45.0 and 42.2 g/m²), LV end-diastolic volume index (LVEDVI: 131.5 vs. 75.1 and 73.0 mL/m²), and LV end-systolic volume index (LVESVI: 90.7 vs. 47.8 and 39.0 mL/m²), with all comparisons yielding $p < 0.001$. LVEF was lowest in DCM (32.8%) and highest in NDLCV-MREF (46.3%), also statistically significant ($p < 0.001$). Right ventricular indices including RVEDVI and RVESVI were significantly elevated in DCM ($p < 0.001$), though right ventricular ejection fraction (RVEF) did not differ significantly across groups ($p = 0.295$). Valvular regurgitation was most prevalent in DCM (89.3%) compared to approximately 53% in both NDLCV subgroups ($p = 0.005$). Myocardial late gadolinium enhancement (LGE) was also significantly more frequent in DCM (83%) than in NDLCV-REF (51.1%) and NDLCV-MREF (36%) patients ($p = 0.004$). Left atrial area was similar across all groups ($p = 0.88$).

Discussion

The objective of this study was to compare the cardiac magnetic resonance (CMR) findings and clinical outcomes between individuals with nondilated left ventricular cardiomyopathy (NDLCV) and those with dilated cardiomyopathy (DCM). Although NDLCV is traditionally defined as having a left ventricular ejection fraction (LVEF) below 45%, we observed that several patients referred for CMR with suspected cardiomyopathy had nondilated, hypokinetic ventricles with LVEF values exceeding this threshold. Therefore, we stratified our study population based on heart failure



classification in terms of LVEF to capture a broader spectrum of phenotypes.

To ensure diagnostic precision, we focused on selecting idiopathic cases and excluded patients with known comorbidities or abnormal loading conditions that could potentially alter cardiac function. The final cohort comprised patients with recently diagnosed cardiomyopathy referred specifically for advanced CMR evaluation. All participants received management from a multidisciplinary cardiomyopathy team and were treated in accordance with contemporary heart failure guidelines.

NDLVC is characterized by abnormalities in LVEF, wall motion, or myocardial scarring in the absence of ventricular dilatation. Despite being subsumed under the broader DCM phenotype due to overlapping features, the classification of NDLVC remains debated due to morphological variability and heterogeneity in clinical presentation [1–7]. We propose that the discordant findings across studies largely stem from reliance on morphological parameters alone for defining cardiomyopathy, coupled with differences in study populations and baseline characteristics.

Our study identified both similarities and divergences when compared to prior investigations on DCM and NDLVC. While retrospective studies have suggested poorer long-term outcomes in DCM relative to NDLVC [8], other research indicates that, even after adjusting for LVEF and comorbidities, midterm prognoses may be comparable among patients with DCM and those with normal or mildly dilated ventricles [9].

A critical feature in CMR studies of cardiomyopathy is the presence and extent of late gadolinium enhancement (LGE), which reflects myocardial replacement fibrosis and holds significant prognostic implications. Consistent with previous literature, LGE burden was higher in DCM, signifying more advanced myocardial fibrosis. For instance, Eda et al. reported that LGE was more frequently observed in DCM compared to NDLVC-REF, highlighting the greater fibrotic load in DCM [9].

Numerous studies have shown that the presence of multiple LGE lesions is an independent predictor of adverse cardiovascular outcomes—including all-cause mortality, ventricular arrhythmias, sudden cardiac death, hospitalizations for heart failure, and the need for

transplantation—in patients with nonischemic cardiomyopathy. Furthermore, among individuals with NDLVC-MREF, those with higher LVEF tended to have lower LGE burden and correspondingly better clinical outcomes.

However, the prognostic significance of LGE remains contested due to the absence of a uniform definition and variable composite endpoints across studies. For example, some investigations have included non-life-threatening arrhythmias such as premature ventricular contractions (PVCs) and nonsustained ventricular tachycardia (NSVT) in their outcome measures [10], limiting the comparability of results.

Notably, the high incidence of atrial arrhythmias observed in the NDLVC group—particularly in those without LGE—raises the possibility of tachycardia-induced cardiomyopathy [11]. Therefore, classification as a nondilated variant of DCM alone may not adequately predict the risk of atrial fibrillation (AF) or its sequelae. These patients warrant closer monitoring, comprehensive CMR evaluation for LGE detection, and proactive screening for atrial arrhythmias [12]. As highlighted by Eda et al., increased left ventricular filling pressures and the presence of AF may be significant predictors of adverse events, thereby equating the risk of mortality between patients with DCM and those with NDLVC-REF [9].

The principal limitation of this study is its relatively small sample size. Secondly, as a single-center investigation, the findings may not be generalizable to wider populations. Moreover, by excluding individuals with comorbid conditions, the applicability of our results may be limited, especially for patients with NDLVC coexisting with systemic diseases such as diabetes mellitus or connective tissue disorders.

Conclusion

In conclusion, the prognosis for NDLVC appears relatively favorable. It may be appropriate to consider NDLVC as part of a continuum within the broader spectrum of DCM. Within this spectrum, certain NDLVC patients with mildly reduced ejection fraction may exhibit better clinical outcomes and should not be overlooked. Nonetheless, the conflicting results reported across various studies highlight the need for further



research to clarify the prognostic implications and risk factors associated with this cardiomyopathy subtype.

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Table 1: Comparison of Baseline Characteristics and Clinical Outcomes

Variables	NDLVC-REF (N=47)	NDLVC-MREF (N=50)	DCM (N=47)	p-value
Age (in years), Mean (SD)	42.7 (12.9)	40.1 (12.3)	44.8 (15.2)	0.426
Male, n (%)	25 (53.2)	27 (54)	30 (63.8)	0.23
NYHA class I/II/III, n	14/27/6	17/25/8	13/26/8	0.13
Family history of cardiomyopathy, n (%)	9 (19.1)	9 (18)	8 (17)	0.71
Atrial flutter/fibrillation, n (%)	21 (44.7)	12 (24)	8 (17)	0.041
Sustained VT/ICD, n (%)	7 (14.9)	5 (10)	9 (19.1)	0.19
Beta blocker, n (%)	45 (95.7)	45 (90)	46 (97.8)	0.21
ACEI/ARB/ARNI, n (%)	45 (95.7)	41 (82)	45 (95.7)	0.27
SGLT2I, n (%)	20 (42.5)	14 (28)	40 (85.1)	0.048
MRA, n (%)	39 (83)	29 (58)	36 (76.6)	0.015
Diuretics, n (%)	3 (6.4)	2 (4)	31 (66)	<0.001
GDMT at follow-up, n (%)	45 (95.7)	41 (82)	43 (91.5)	<0.001
Composite cardiac event, n (%)	18 (38.3)	13 (26)	19 (40.4)	0.21
All-cause mortality, n (%)	4 (8.5)	0	3 (6.4)	0.043

ACEI, angiotensin-converting enzyme; ARB, angiotensin receptor blockers; ARNI, angiotensin neprilysin inhibitors; DCM, dilated cardiomyopathy; GDMT, guideline directed medical therapy; MRA, mineralocorticoid receptor antagonists; NDLVC-MREF, nondilated left ventricular cardiomyopathy-mildly reduced ejection fraction; NDLVC-REF, nondilated left ventricular cardiomyopathy-reduced ejection fraction; NYHA, New York Heart Association; SGLT2I, sodium-glucose transport protein 2 inhibitors

Table 2: Comparison of Cardiac MRI Parameters

Variables	NDLVC-REF	NDLVC-MREF	DCM	p-value
LV Mass Index	45.0 (11.3)	42.2 (9.1)	63.1 (22.2)	<0.001
LA Area	17.0 (5.7)	16.0 (4.3)	17.2 (8.4)	0.88
LV EDVI (Left ventricular end-diastolic volume index)	75.1 (9.0)	73.0 (9.3)	131.5 (35.2)	<0.001



LV ESVI (Left ventricular end-systolic volume index)	47.8 (7.2)	39.0 (5.0)	90.7 (40.8)	<0.001
LVEF (Left ventricular ejection fraction)	35.9 (5.5)	46.3 (1.8)	32.8 (13.1)	<0.001
RV EDVI (Right ventricular end-diastolic volume index)	64.0 (1.5)	69.8 (10.0)	92.4 (29.3)	<0.001
RV ESVI (Right ventricular end-systolic volume index)	34.9 (8.6)	36.0 (6.0)	53.4 (23.2)	<0.001
RVEF (Right ventricular ejection fraction)	44.8 (7.8)	47.6 (5.2)	44.0 (13.7)	0.295
Valvular Regurgitation, n (%)	25 (53.2)	27 (54)	42 (89.3)	0.005
Myocardial LGE, n (%)	24 (51.1)	18 (36)	39 (83)	0.004
CMR, cardiac magnetic resonance imaging; DCM, dilated cardiomyopathy; NDLCV-MREF, nondilated left ventricular cardiomyopathy-mildly reduced ejection fraction; NDLCV-REF, nondilated left ventricular cardiomyopathy-reduced ejection fraction; Myocardial late gadolinium enhancement (LGE)				