



## Original Article

# Prognostic value of late gadolinium enhancement in cardiac MRI of non-ischemic dilated cardiomyopathy patients

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## ABSTRACT

**Background:** The role of late gadolinium enhancement (LGE) in cardiac MRI (CMR) as prognostic marker in non-ischemic dilated cardiomyopathy (NIDCM) is evolving.

**Objective:** To study the effect of LGE in the prognosis of NIDCM patients.

**Methods:** 112 consecutive NIDCM patients, who underwent CMR, were prospectively followed up for 745 ± 320 days. Primary end point was occurrence of MACE {composite of all-cause mortality, resuscitated cardiac arrest, sustained ventricular tachycardia (VT)/appropriate ICD shock, heart failure (HF) hospitalization}.

**Results:** LGE was present in 44 out of 112 patients (39%). The primary end point (MACE) was significantly higher in LGE + ve group compared to the LGE –ve group (72.7% vs. 29.4%;  $p < 0.0001$ ). Similarly, cardiac mortality (9.1% vs 2.9%;  $p < 0.049$ ), VT (13.6% vs. 2.9%;  $p < 0.031$ ), HF hospitalization (63.6% vs. 30.9%;  $p < 0.001$ ) were significantly more in LGE + ve group. In univariate model, LGE demonstrated the strongest association with MACE (Hazard ratio [HR] = 2.96 [95% CI 1.685 to 5.201;  $p < 0.0001$ ]). LGE extent of >14% of LV predicted MACE with 90.6% sensitivity and 86% specificity. HR of LGE extent >14% of LV for MACE is 6.12;  $p < 0.01$ . LGE was associated with MACE irrespective of its location, pattern or distribution. Multivariate model showed LGE and its extent >14% of LV volume were strongest predictor of MACE.

**Conclusion:** LGE and its extent >14% predicts adverse cardiac events in NIDCM irrespective of LVEF and LGE location, pattern or distribution. This study emphasises the role of CMR in risk stratification of NIDCM patients and guiding therapy.

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**Abbreviations:** 95% CI, 95% confidence interval; ACEI/ARB, Angiotensin converting enzyme inhibitor/ angiotensin receptor blocker; AF/AT, Atrial fibrillation/ atrial tachycardia; BMI, Body mass index; CHB, Complete heart block; CMR, Cardiac MRI; CRT(P/D), Cardiac resynchronization therapy (pacing /defibrillator); CXR, Chest X ray; DEFINITE, Defibrillators in Non-Ischemic Cardiomyopathy Treatment Evaluation; EDV (I), End diastolic volume (index); ESV(I), End systolic volume (index); HR, Hazard ratio; ICD, Implantable cardioverter defibrillator; IQR, Inter quartile range; LBBB, Left bundle branch block; LGE, Late gadolinium enhancement; LV, Left ventricle; LVEF, Left ventricular ejection fraction; MACE, Major adverse cardiac events; NIDCM, Non ischemic dilated cardiomyopathy; NT pro BNP, N terminal pro brain natriuretic Peptide; NYHA, New York Heart association; OR, Odds ratio; RV, Right ventricle; SCD, Sudden cardiac death; SCTIMST, Sree Chitra Institute for Medical Science and Technology; SEM, Standard error of mean; SV (I), Stroke volume (index); VT, Ventricular tachycardia; WHO, World health organization.

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## 1. Introduction

Risk stratification in non-ischemic dilated cardiomyopathy (NIDCM) patients is still evolving. In NIDCM, a series of factors is associated with adverse prognosis, such as age, gender, LVEF (left ventricular ejection fraction), QRS duration and cardiac biomarkers.<sup>1</sup> Although late gadolinium enhancement (LGE) in cardiac MRI (CMR) is emerging as a poor prognostic marker in this group of patients, still this remains controversial.<sup>2</sup> The aim of the study was to know whether LGE was associated with poor prognosis in NIDCM patients and to find whether extent of LGE also helps in further prognostication.

## 2. Methods

This study was done at the Sree Chitra Institute for Medical Science and Technology (SCTIMST), Trivandrum, a tertiary care

cardiac referral centre in South India. Informed consent was obtained from all patients. This study was approved by the institute ethics committee (IEC No. SCT/IEC/944/August –2016).

### 2.1. Study design

It was a retrospective observational study. All the included patients were divided into two groups based on presence or absence of LGE in cardiac MRI, i.e., LGE +ve group and LGE –ve group (Fig. 1). They were followed prospectively up to June 2017 for clinical end points. Primary end point was defined as occurrence of major adverse cardiac end points (MACE). MACE was defined as composite of all-cause mortality, sustained ventricular tachycardia (VT)/appropriate ICD shock, resuscitated cardiac arrest, and heart failure (HF) hospitalization. Secondary end points were defined as occurrence of all-cause mortality, cardiac mortality, sudden cardiac death (SCD), sustained VT/ICD shock and HF hospitalization. Mean follow up period was  $745 \pm 320$  days (mean  $\pm$  SEM). The data was collected from medical records and follow up data was obtained from their follow up visits in cardiology outpatient clinics or by telephonic enquiry if there was no follow up visit in the last six months.

### 2.2. CMR protocol

Cardiac MRI was done with SIEMENS 1.5 T machine or a 3 Tesla system (Discovery 750w; General Electric GE healthcare; USA). Late Gadolinium enhancement was assessed using PSIR (Phase sensitive Inversion Recovery) sequences with an inversion time of 200 ms, a repetition time of 8.5 ms, and an echo time of 3.5 ms, after 20–30 min of intravenous injection of Gadolinium based contrast agent (0.2 mmol/kg body weight). LGE was analysed in two orthogonal planes, by two independent observers. LGE was defined as signal intensity  $>2$  SD from the remote reference myocardium. LGE was quantified by visual scoring method.<sup>3</sup> In a left ventricular 17-segment model, each segment was scored according to the percentage of enhancement estimated visually. Score 0 was given for no enhancement, score 1 for 0%–25% enhancement, score 2 for 26%–50% enhancement, score 3 for 51%–75% enhancement and

score 4 for 76%–100% enhancement. The global extent of LGE, “LGE score” was calculated by adding scores from all 17 segments. LGE extent (volume) of LGE was calculated as a percentage of the total score ( $4 \times 17 = 68$ ). So, LGE volume =  $100 \times (\text{LGE score})/68$ . It was expressed as % of LV volume.

### 2.3. Inclusion criteria

All patients of NIDCM who underwent CMR from 1/1/2012 to 31/12/2016 were included in the study. NIDCM was defined as decreased systolic function, i.e., left ventricle ejection fraction (LVEF)  $< 50\%$  in non-CMR study in the absence of significant coronary artery disease, valvular disease, hypertensive heart disease and congenital heart disease. It was based on the 1995 WHO/International Society and Federation of Cardiology criteria.<sup>4</sup>

### 2.4. Exclusion criteria

Patients with coronary artery disease were excluded. Coronary artery disease was defined  $>50\%$  luminal stenosis on coronary angiography and/or a history of coronary revascularisation or acute coronary syndrome. Other exclusion criteria were age  $< 18$  years; pregnancy; active myocarditis; standard contraindications for MRI (estimated glomerular filtration rate  $< 30$  ml/min/1.73 m<sup>2</sup>, cardiac pacemaker/ICD/CRT implants, other MRI non compatible metallic implants in heart, severe claustrophobia) and those who refused to give consent.

### 2.5. Statistical methods

The data was analysed by the principal investigator with advice from a statistician. Descriptive data were analysed by frequencies and categorical data by percentages, and continuous variables by means and standard deviations. Continuous variables were compared using Student's *t* test (for parametric test) or Mann–Whitney *U* test (for non-parametric test) as appropriate. Group comparisons were done by  $\chi^2$  tests. All statistical analyses were done by the SPSS statistical software (release 23.0, SPSS Inc.; Chicago).

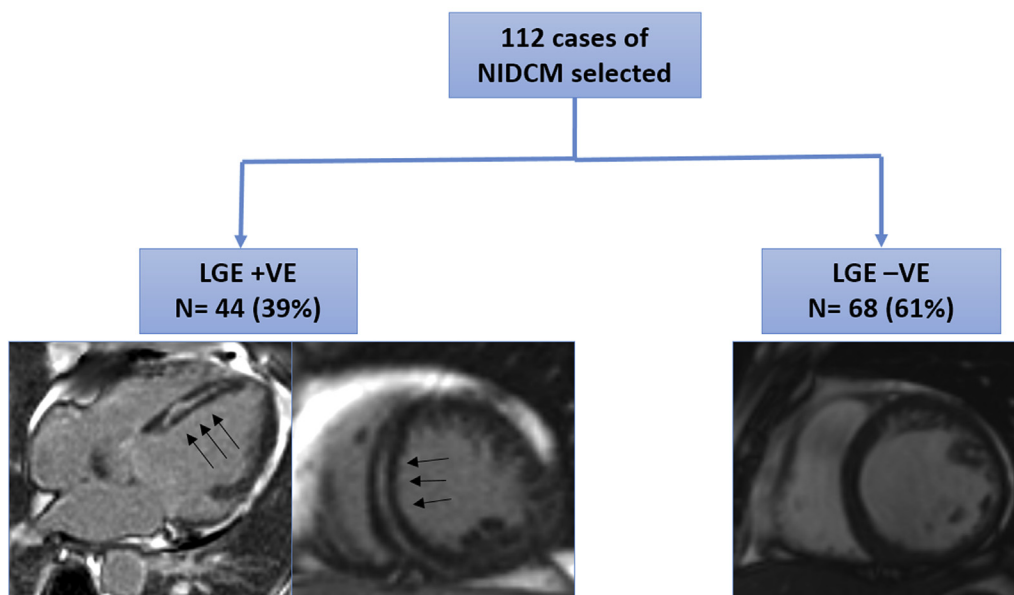


Fig. 1. Study flow chart. Arrow marks show the mid myocardial LGE.

### 3. Results

A total of 112 patients were selected for this study. Cardiac MRI showed 44 patients (39%) had LGE while 68 patients (71%) had no evidence of LGE. The various types of NIDCM were given in [Supplementary Table 1](#). Idiopathic DCM was the most common variety. The location, distribution, and pattern of LGE was shown in [Supplementary Table 2](#). Inter ventricular septum was the most common location and mid myocardial is the most common pattern of LGE distribution.

#### 3.1. Baseline characters

All the base line features were similar in both groups except NT pro BNP values at the time of admission ([Table 1](#)). Median NT pro BNP was significantly higher in LGE + ve group (2934.0 pg/ml) compared to LGE –ve group (1095.0 pg/ml),  $p < 0.023$ . Similarly, NT pro BNP values  $> 1000$  pg/ml was seen more in LGE + ve group than LGE–ve group (91.7% vs 52.5%,  $p = 0.018$ ). Treatment received by each group was not significantly different except antiarrhythmic medications such as amiodarone, which was more prescribed in LGE + ve group compared to LGE–ve group ( $p = 0.039$ ). All functional and volumetric parameters in CMR were similar in both the groups.

#### 3.2. Follow up

The mean follow up period was  $745 \pm 320$  days. There was no loss to follow up. The primary end point, combined major adverse cardiac event (MACE) was significantly more in LGE + ve group than the LGE –ve group (72.7% vs 29.4%,  $p < 0.0001$ ), ([Table 2](#)).

**Table 2**

Incidence of outcomes between LGE + ve group and LGE –ve group during follow up.

	LGE + VE <i>n</i> = 44	LGE –VE <i>n</i> = 68	<i>p</i> value
Primary End Point			
MACE	32 (72.7)	20 (29.4)	0.0001
Secondary End Points			
All-cause mortality	4 (9.1)	2 (2.9)	0.209
Cardiac mortality	4 (9.1)	1 (1.5)	0.048
HF hospitalization	28 (63.6)	21 (30.9)	0.001
Sudden cardiac death (SCD)	3 (6.8)	0 (0)	0.023
VT	6 (13.6)	2 (2.9)	0.031
CRT	7 (15.9)	9 (13.2)	0.784
CRT P	2 (4.4)	9 (13.2)	0.195
CRT D	5 (11.3)	0	0.008

Values are no (%) or mean  $\pm$  SEM or median (IQR).

The secondary end points were also significantly higher in LGE + ve group. The all-cause mortality was higher in LGE + ve group than the LGE –ve group. Cardiac mortality was statistically more in LGE + ve group than the other (9.1% vs 1.5%,  $p = 0.048$ ). SCD occurred in 3 patients (6.8%) in LGE + ve group compared to none in the LGE–ve group ( $p = 0.023$ ). Sustained VT was significantly more common in LGE + ve group than LGE –ve group (13.6% vs 2.9%,  $p = 0.031$ ). HF hospitalization was significantly more common in LGE + ve group than LGE–ve group (63.6% vs 30.4%,  $p < 0.001$ ). Sixteen patients received cardiac resynchronisation therapy (CRT). Among these, 5 patients received CRT-D and 11 received CRT-P. All patients who received CRT-D were LGE + ve. None had ICD implantation.

**Table 1**

Comparison of baseline characteristics and volumetric as well as functional parameters assessed by CMR between LGE + ve and LGE –ve groups.

Baseline characteristics	LGE + VE <i>n</i> = 44	LGE –VE <i>n</i> = 68	<i>p</i> value
Age (year)*	40.0 (24.5–54.5)	45.5 (33.0–58.7)	0.285
BMI (Kg/m <sup>2</sup> )	23.6 ( $\pm$ 4.1)	24.3 ( $\pm$ 5.0)	0.549
Gender, Male	30 (68.2)	42 (61.8)	0.548
DM	10 (22.7)	19 (27.9)	0.660
Alcoholic	1 (2.3)	6 (8.8)	0.242
F/H DCM	2 (4.5)	2 (2.9)	0.645
F/H SCD	2 (4.5)	2 (2.9)	0.645
NYHA	3 (2–3)	3 (2–3)	0.365
NYHA II	27 (61.4)	38 (56.7)	0.695
NYHA III	16 (36.4)	28 (41.8)	0.694
NYHA IV	0 (0.0)	1 (1.5)	1.000
NT proBNP (pg/ml)	2937.0 (361.5–3345.0)	1095 (352.2–3392.5)	0.023
Cardiomegaly in CXR	29 (65.9)	45 (67.2)	1.000
LBBB	11 (25.4)	28 (42.4)	0.105
QRS duration (ms)	100.0 (90–150)	110 (98.5–160)	0.417
LVEF	32.5 (27.0–41.0)	31.5 (28.0–36.2)	0.507
Treatment received			
ACEI/ARB	43 (97.7)	64 (94.1)	0.647
Beta blocker	43 (97.7)	66 (97.1)	1.000
Spironolactone	42 (95.5)	64 (94.1)	1.000
Diuretics	37 (84.1)	63 (92.6)	0.532
Digoxin	29 (65.9)	49 (72.1)	0.532
Antiarrhythmic drugs	10 (22.7)	6 (8.8)	0.039
Oral anticoagulant	4 (9.1)	6 (8.8)	1.000
CMR Parameters			
LVEDVI(ml/m <sup>2</sup> )	137.0 (87.5–225.2)	104.0 (77.0–125.0)	0.677
LVESVI (ml/m <sup>2</sup> )	102.0 (63.7–183.7)	79 (58.0–91.0)	0.857
LVSVI (ml/m <sup>2</sup> )	26.5 (21.2–50.7)	29.0 (22.0–34.0)	0.539
LVEF (%)	21.0 (13.2–34.2)	27 (21.0–32.0)	0.342
RVEDVI (ml/m <sup>2</sup> )	49.5 (31.5–86.0)	74.0 (57.0–92.0)	0.307
RVESVI (ml/m <sup>2</sup> )	37.0 (17.7–51.2)	30.0 (18.0–35.0)	0.087
RVSVI (ml/m <sup>2</sup> )	17.0 (10.0–34.7)	17.0 (13.0–19.0)	0.511
RVEF (%)	39.0 (31.2–47.5)	38.0 (36.0–46.0)	0.321

Values are no (%) or mean  $\pm$  SEM or median (IQR).

Kaplan–Meier survival curve were created for MACE and all individual out comes (Fig. 2). It showed significantly worst event free survival rate in LGE + ve group in comparison to LGE –ve group (Log rank 15.64;  $p < 0.0001$ ).

The median LGE extent in LGE + ve patients was 12% (4%–32%). ROC curve was created to know the best discriminator value of LGE extent for highest sensitivity and specificity for event free survival (Fig. 3A). The area under curve (AUC) of ROC curve was 0.889 with  $p = 0.0001$ . From this we got value of LGE extent >14% of LV volume, which was having 90.6% sensitivity and 84% specificity for predicting MACE.

LGE + ve group then subdivided into LGE >14% and LGE <14% of LV volume. Thirteen patients (30%) had LGE < 14% and 31 (70%) had LGE > 14% of LV volume. Three out of 13 (23%) had MACE in patients with LGE <14% while 29 out of 31 (93%) had MACE in patients with LGE >14% of LV volume which was statistically significant (OR 48.3,  $p < 0.0001$ ). Kaplan–Meier survival curve was plotted between patients with LGE > 14% and LGE <14% for occurrence of MACE (Fig. 3B). It showed significant event rate with LGE >14% group compared to the other group (Log rank 11.4,  $p < 0.001$ ).

### 3.3. Subgroup analysis

In a subgroup analysis the whole cohort is divided into 2 groups based upon the severity of LV dysfunction, i.e., severe LV dysfunction (LVEF <35%) and mild to moderate LV dysfunction (LVEF >35%–50%). Kaplan–Meier survival curves plotted to know the MACE free survival in each group amongst patients with no LGE, LGE volume <14% and LGE volume >14%. In the group with severe LV dysfunction (Fig. 3C), there was no statistically significant difference in MACE free survival between patients with no LGE and LGE volume <14% whereas there was significantly worse outcome if LGE volume was >14%. In contrast, in the group with mild to moderate LV dysfunction (Fig. 3D), there was statistically significant difference in survival between no LGE vs. LGE volume <14% and LGE volume <14% vs >14%. This implies that in patients with milder LV dysfunction any amount of LGE is significant.

### 3.4. Cox regression analysis

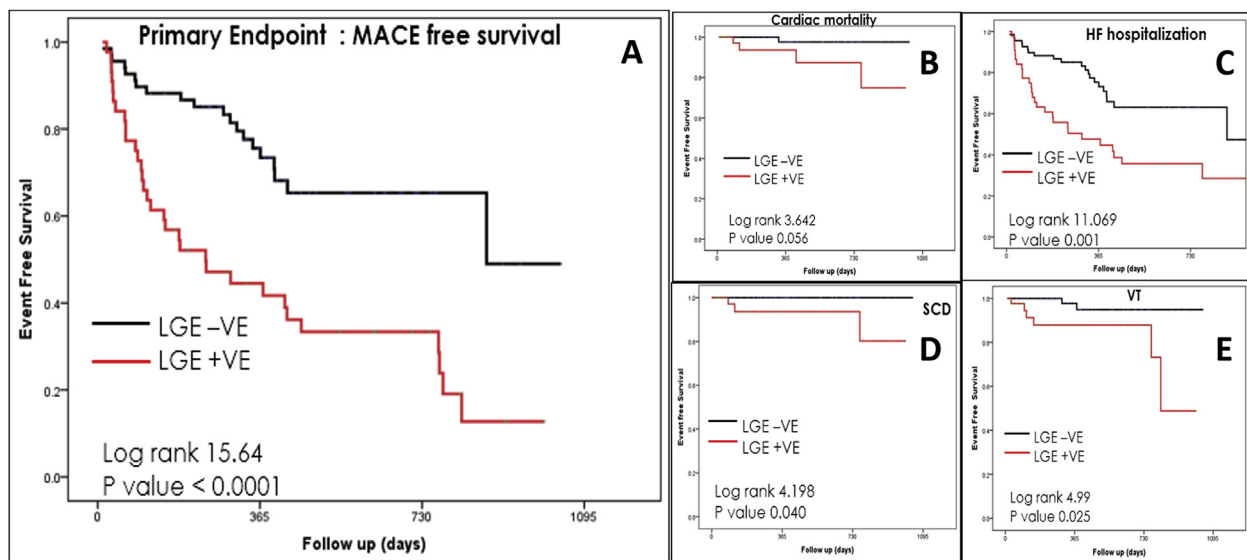
Univariate Cox regression analysis was performed for detecting significant unadjusted predictors of MACE (Table 3). Significant predictors of MACE were cardiomegaly by chest X-ray, NT pro BNP >1000 pg/ml at the time of admission, LVEF, RV SVI, presence of LGE and LGE >14% of LV volume. Among these LGE extent >14% of LV volume was the strongest predictor of MACE (HR 6.17, CI: 1.87–20.37,  $p = 0.003$ ). Multivariate Cox regression analysis was performed for detecting the adjusted predictors of MACE. The best overall predictors of MACE were LGE >14% of LV volume and presence of LGE.

The individual hazard ratio for having MACE for each location, distribution and pattern of LGE were compared with LGE –ve patients (Table 4). All location, pattern and distribution of LGE found to be significant. Amongst them septal LGE had highest hazard ratio (HR 3.046, CI: 1.726–5.376,  $p < 0.0001$ ) compared to those without LGE.

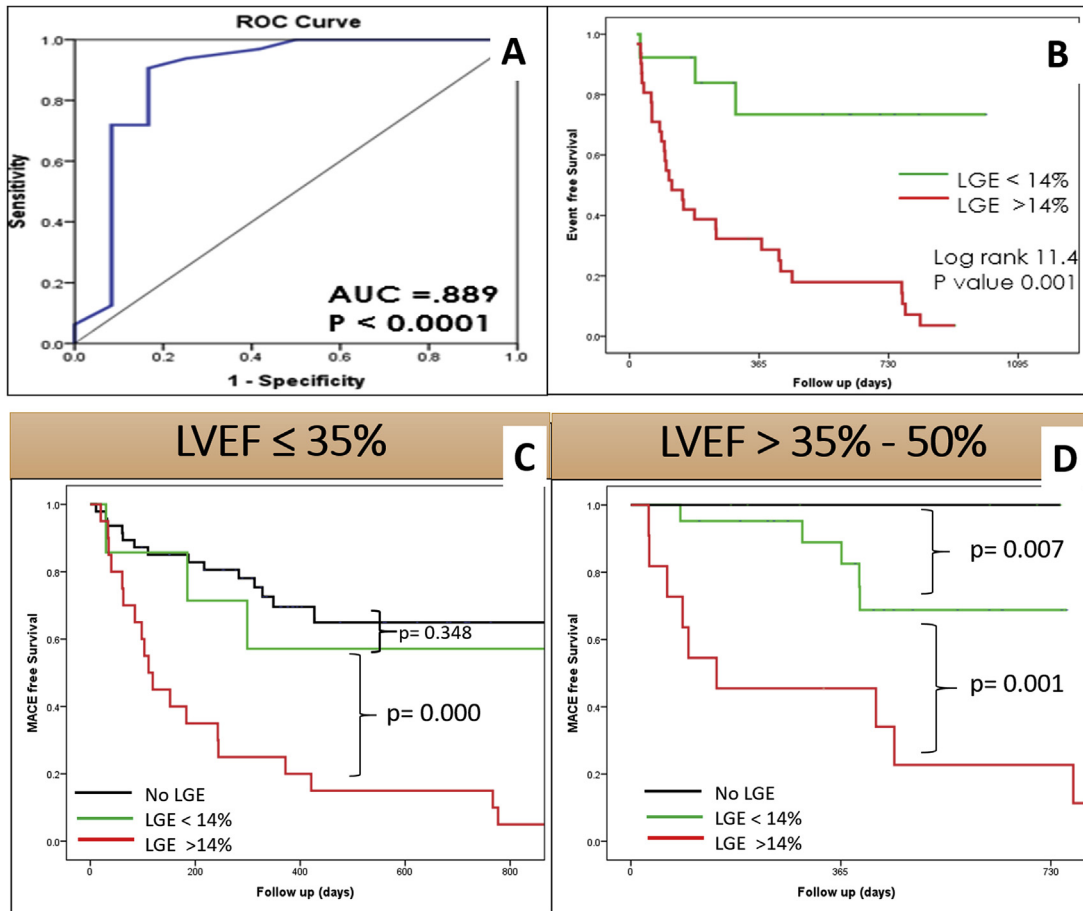
## 4. Discussion

This study is perhaps the first study from Indian subcontinent about CMR in NIDCM. Prevalence of LGE in NIDCM patients in our study is 39% which is comparable to the existing data.<sup>5–7</sup> To know the prognostic significance of LGE, we divided the patients based on presence or absence of LGE. NT pro BNP levels were high in LGE + ve group signifying they were sicker. Antiarrhythmic therapy was more prescribed in LGE + ve group indicating more incidences of arrhythmias than LGE –ve group.

Baseline CMR volumetric data showed no significant difference in LV dimensions and LVEF between the 2 groups. The existing literature also had differential views regarding this. Many studies showed increased LV dimensions and decreased LVEF in LGE + ve group, arguing for more fibrosis leading to more remodelled LV.<sup>8,9</sup> But, some other studies did not show any significant difference in LV dimensions and function between LGE + ve and LGE –ve group.<sup>10–12</sup> This depends upon the type and extent of fibrosis. In DCM patients, the previous histopathology studies showed fibrosis is of 2 types – either diffuse (interstitial) or segmental



**Fig. 2.** (A) Kaplan–Meier survival curve comparing event free survival (MACE) between LGE + ve and LGE –ve group, which shows significantly worse outcome in LGE + ve group (log rank 15.64,  $p < 0.0001$ ). Kaplan–Meier survival curve showing event free survival for cardiac mortality (B), heart failure hospitalization (C), SCD (D) and VT (E). All these showed significantly worse event free survival in LGE + ve group compared to LGE –ve group.



**Fig. 3.** (A) ROC curve plotted for determining of LGE volume for occurrence of MACE. Area under curve (AUC) = 0.889 with  $p < 0.001$  (B) Kaplan–Meier survival curve showing significant difference in event free survival rate between 2 groups (log rank 11.4,  $p < 0.001$ ). Kaplan–Meier survival curve of patients with LVEF  $\leq 35\%$  (C) and LVEF  $> 35\%–50\%$  (D) based on no LGE, LGE  $< 14\%$  of LV volume and LGE  $> 14\%$  of LV volume.

(replacement) fibrosis. LGE CMR can pick up the replacement fibrosis with good resolution but, it's poor in detecting the interstitial fibrosis. This may be the reason why these studies showed the lack of relationship between the presence of LGE or LGE volume, and LV volume and function.

On follow up, LGE + ve group showed significantly more adverse outcomes compared to LGE –ve group. The primary end point (MACE) and secondary endpoints (cardiac mortality, sustained VT, HF hospitalization) were significantly more in LGE + ve group. All patients who received CRT-D were LGE + ve. This

signifies that they had more incidences of ventricular arrhythmias than the LGE –ve group.

In Univariate analysis, presence of LGE is one of the major determinant of MACE (HR 2.96;  $p < 0.00001$ ) while LGE volume  $> 14\%$  of LV volume was the strongest predictor of MACE (HR 6.176,  $p = 0.003$ ). In Multivariate analysis, after adjusting age, LV function and other confounders, LGE extent  $> 14\%$  of LV volume and LGE positivity were the only two discriminators for MACE. This

**Table 3**  
Univariate Cox regression analysis for event free survival.

	HR	95% CI	p value
Univariate Cox regression			
Age (year)	0.986	0.970–0.986	0.079
Sex, Male	1.316	0.750–2.3.9	0.497
Diabetes Mellitus	0.900	0.461–1.759	0.758
NT pro BNP $> 1000$ pg/ml	2.82	0.933–8.54	0.050
Chest Xray, cardiomegaly	2.493	1.249–4.977	0.010
Antiarrhythmic drug therapy	2.002	1.047–3.828	0.036
LVEF (%)	0.962	0.933–0.993	0.015
RV SVI (ml/m <sup>2</sup> )	1.001	0.958–0.998	0.035
LGE, Presence	2.961	1.685–5.201	0.0001
LGE Volume $> 14\%$ OF LV	6.176	1.873–20.371	0.003
Multivariate Cox regression			
LGE, Presence	2.301	1.346–3.974	0.008
LGE Volume $> 14\%$ OF LV	8.894	2.618–28.856	0.0001

**Table 4**  
Individual hazard ratio of various LGE location, pattern and distribution for occurrence of MACE in comparison with that of LGE –ve patients.

	Number	HR	95% CI	p value
LGE Location				
Inter ventricular septum	38	3.046	1.726–5.376	0.0001
Anterior wall	21	2.957	1.530–5.715	0.001
Inferior wall	23	2.905	1.509–5.590	0.001
Lateral wall	16	2.389	1.144–4.988	0.020
Base of LV	27	2.731	1.474–5.058	0.001
Mid of LV	36	2.831	1.605–4.994	0.0001
Apex of LV	17	2.330	1.148–4.730	0.019
LGE Pattern				
Sub-endocardial	6	2.885	1.045–7.963	0.041
Mid myocardial	33	2.877	1.524–5.431	0.001
Sub epicardial	2	3.428	1.145–10.268	0.002
Transmural	3	2.212	1.112–6.567	0.048
LGE Distribution				
Global/Diffuse	8	2.975	1.174–7.539	0.022
Regional/patchy	33	2.911	1.593–5.317	0.001
Circumferential	3	2.823	1.124–6.453	0.046

clearly showed that quantification of LGE adds to the prognostic value of CMR in NIDCM patients.

In earlier studies the prognostic values of LGE in NIDCM has been documented.<sup>13–16</sup> One recent meta-analysis<sup>17</sup> has shown that LGE + ve NIDCM patients had higher risk of all-cause mortality, HF hospitalization, and sudden cardiac death. This meta-analysis put forward the concept of taking LGE as an independent entity for risk stratification of NIDCM.

Shimuzu et al<sup>18</sup> were one of the earlier investigators to visually quantify LGE volume in NIDCM patient. They showed that MACE was significantly higher in patients with LGE extent of >10% of LV volume compared to the patients with <10% of LV volume (36% vs 2%, Log rank,  $p = 0.0001$ ). Similarly Poyhonen et al,<sup>19</sup> also visually quantified LGE in NIDCM patients and showed that LGE volume >17% of LV volume was the best parameter to predict bad prognosis. We found LGE volume > of 14% of LV volume as the best predictor poor prognosis.

Studies till date either used visual analysis or the threshold based methods to quantify LGE. But, no significant disparity was observed between these two methods.<sup>20</sup> So, it is the need of the hour that the methodology of quantifying LGE should be standardized before considering it as a decision making tool.<sup>21</sup>

LGE was significantly associated with MACE irrespective of any location or distribution or pattern, though the septal LGE has the highest hazard ratio. This is in contrast to a recent study where septal LGE offers highest risk of cardiac mortality in comparison to free wall LGE.<sup>22</sup>

LGE denotes focal fibrosis, which may promote re-entry mechanism leading to ventricular tachycardia. Areas of fibrosis in NIDCM, detected by CMR as LGE were found as substrates for inducible VT.<sup>23</sup> This concept is also supported by the data from ICD patients showing more appropriate shock in LGE positive patients.<sup>10</sup> In addition, more fibrosis also can change the mechanical property of myocardium causing loss of ventricular compliance leading to increased incidence of heart failure.<sup>24</sup>

Based on our study we can say that LGE presence and its quantification helps in additional risk stratification in NIDCM patients. Currently ICD as a primary prophylaxis in NIDCM is indicated only based on LVEF criteria, ie LVEF <35%.<sup>25</sup> ICD implantation as per LVEF criteria had not shown any significant benefit in DEFINITE study.<sup>26</sup> LVEF, which is usually taken as a measure of LV function has been accepted as best predictor of mortality in NIDCM.<sup>27</sup> But LVEF was not found to be a predictor of ICD discharge.<sup>28</sup> Our study also showed that lower LVEF, though predicted MACE in univariate model, was not an independent predictor of MACE in multivariate model.

Currently there is no guideline for primary prophylactic ICD implantation in NIDCM patients with milder LV dysfunction (LVEF 35%–50%). In subgroup analysis we have shown that in patients with milder LV dysfunction (LVEF 35%–50%), any amount of LGE is associated with poor MACE. Lakdawala et al showed that LGE in CMR can be taken as an emerging indication for ICD in familial DCM patients.<sup>29</sup> randomized control study is required to know whether LGE guided ICD/CRT-D implantation will be beneficial in NIDCM patients or not.

## 5. Limitations

This is an observational follow up study design and a single centre study. LGE may miss diffuse interstitial fibrosis.<sup>30</sup> LGE quantification was performed by visual scoring method,<sup>4</sup> which though standardised, may lack precision. We regret unavailability of updated tools to quantify exact LV scar in grams in our setup.

## 6. Conclusion

LGE positive patients in CMR showed significantly higher combined major cardiac events including all-cause mortality, VT, SCD,

and heart failure hospitalisations. LGE extent, i.e., LGE >14% of LV volume gives an additional prognostic information beyond LVEF. Even in patients with mild to moderate LV dysfunction (LVEF 35%–50%) presence of LGE heralds poor cardiac outcome. Any location, pattern or distribution of LGE is significant for occurrence of adverse cardiac outcome. Further research, particularly randomized control trials are needed to determine whether CMR guided therapeutic intervention like ICD/CRT implantation or anti heart failure medicines can lower morbidity and mortality of NIDCM patients.

## Author contribution

Dibya Ranjan Behera: The principal investigator and corresponding author. Data collected and analysed by this author. This author also takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

Ajit Kumar V K: The idea of the present study was given by this author. This author also takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

Narayanan Nambodiri: This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

Sivasankaran S: This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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All authors have none to declare.

## Appendix A. Supplementary data

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.ihj.2020.06.011>.

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