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ORIGINAL PAPER

Cardiac magnetic resonance and galectin-3 level as predictors of prognostic outcomes for non-ischemic cardiomyopathy patients

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Abstract This study was aimed at determining whether late gadolinium enhancement (LGE) in conjunction with Galectin-3 (Gal-3) level offered more precise prognosis of non-ischemic cardiomyopathy (NICM) in comparison to LGE alone. Results of LGE and Gal-3 expression in 192 patients with NICM, including 85 subjects with dilated cardiomyopathy (DCM) and 107 with hypertrophic cardiomyopathy (HCM), were examined. As suggested by the characteristics of LGE and Gal-3 levels, patients were divided into four groups: LGE positive + low Gal-3 (n = 10 for DCM, n = 15 for HCM), LGE positive + high Gal-3 (n = 25 for DCM, n = 51 for HCM), LGE negative + low Gal-3 (n = 32 for DCM, n = 29 for HCM), LGE negative + high Gal-3 (n = 18 for DCM, n = 12 for HCM). Primary endpoints over the follow-up period included major adverse cardiac events (MACEs). Kaplan–Meier survival analysis and univariate Cox proportional hazard models were used to analyze the survival status of patients with NICM. The optimal cut-off value of Gal-3 level for two types of NICM was determined by receiver operating characteristic analysis (13.38 U/L for DCM and 14.40 U/L for HCM). The combination of LGE and Gal-3 levels offered a more significant prognostic value than using LGE alone for both DCM and HCM (DCM $P = 0.001 < 0.012$; HCM $P = 0.037 < 0.040$). Moreover, the Cox proportional hazard model suggested that both LGE status [Hazard ratio (HR) = 2.62, $P = 0.017$] and Gal-3 level (HR = 1.16, $P = 0.013$) were significant predictors of MACEs in DCM, while they did not appear to have significant prognostic values for HCM ($P = 0.06$ and 0.64). Furthermore, the multivariate analysis only confirmed LGE as an independent element in predicting prognosis of DCM (HR = 12.19, $P = 0.026$). In conclusion, LGE status was an independent indicator of DCM prognosis, yet the insignificant role of LGE in HCM prognosis could be limited by sample size.

Keywords Late gadolinium enhancement · Cardiovascular magnetic resonance · Galectin-3 · Non-ischemic cardiomyopathy · Dilated cardiomyopathy · Hypertrophic cardiomyopathy · Prognosis · Major adverse cardiac events

Introduction

Non-ischemic cardiomyopathy (NICM) includes two subtypes of dilated cardiomyopathy (DCM) and hypertrophic cardiomyopathy (HCM), which affects approximately 0.05 and 0.2 % of the world population, respectively [1, 2]. DCM is a universal cardiovascular disease that results in almost 33 % of heart failure (HF) cases. Although various therapeutic strategies have been developed for DCM, conspicuous morbidity and mortality of DCM are still considered as major issues to be solved for the purpose of minimizing social and economic costs resulted from DCM [3]. On the other hand, HCM is a genetic cardiomyopathy which is characterized by substantial increase in both interstitial and replacement fibrosis which may become patchy or diffuse [4]. Cardiac fibrosis which is triggered by both neurohormonal activation and myocardial vulnerability is a key mechanism to the progression of myocardial remodeling which is responsible for arrhythmias, sudden cardiac death (SCD) and adverse

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remodeling of left ventricular (LV) [5–7]. Therefore, it is worthwhile to precisely identify myocardial fibrosis (MF) which is a key signal for both DCM and HCM.

To date, several clinicopathologic correlation studies have indicated that MF may proffer a substratum for adverse cardiovascular events including malignant ventricular arrhythmias and SCD [8, 9]. Endomyocardial biopsy has been considered as a conventional approach for clinical assessment of MF, but it has several inherent limitations including invasiveness, small myocardial sample size and possible complications [10]. More recently, cardiovascular magnetic resonance (CMR) imaging technique has been rapidly developed as a preferred imaging tool for characterization and diagnosis of DCM and HCM. CMR provides clinicians with superior clinical assessment of cardiac morphology and function [6, 11]. Apart from that, delayed enhancement of CMR (DE-CMR) is known to be compatible with myocardial scarring and the enhancement degree of CMR is associated with the severity of cardiac functional abnormalities particularly contributed by NICM [12].

CMR with late gadolinium enhancement (LGE) has emerged as a powerful and noninvasive tool that is able to accurately identify and quantify ventricular MF [13]. This imaging modality not only offers incremental characterization of tissues but also identifies the presence of NICM in about two-thirds of HCM patients and at least one-third of DCM patients [14]. As suggested by previous studies on CMR, ventricular LGE was able to forecast several adverse events of DCM patients including failure-related hospitalization and death [15–18]. Since LGE depends on different signal intensity between focal MF and normal myocardium, LGE exhibited limited ability to identify diffuse interstitial fibrosis which is very common in patients with DCM [19]. Thus, patients with high risk of NICM are likely to be misdiagnosed by LGE and the feasibility of LGE combined with other techniques should be clarified.

Galectin-3 (Gal-3) is a β-galactoside-binding lectin secreted by activated macrophages. In addition, Gal-3 has been suggested to be associated with several mechanism pathways of MF observed in patients with HF and it is correlated with extracellular matrix update [20, 21]. Gal-3 also has been hypothesized as a risk marker and mediator for both fibrosis and inflammation that are critical to LV remodeling process [22, 23]. As suggested by several studies, up-regulated Gal-3 was observed in cardiomyopathy, myocarditis and hypertensive heart disease models which were constructed on rats whereas suppressed LV systolic function and disclosed aortic stenosis were identified in hypertrophied human ventricular myocardium [20, 24, 25]. Other studies also provided evidence that Gal-3 exhibited a prognostic role in both predicting LV remodeling status and forecasting mortality of chronic HF patients [26–28].

Nevertheless, significant relationship between LGE and clinical assessment of DCM/HCM has not been clarified. Furthermore, researches have not been carried out for determining the feasibility of LGE-CMR combined with Gal-3 in evaluating patients with NICM. As a result, we conducted this study to assess the prognostic value of CMR combined with Gal-3 level for patients with NICM (HCM and DCM).

Materials and methods

Ethics statement

All study procedures were agreed by the Institutional Ethics Committee of the First Hospital of Chenzhou. Informed consent was obtained from patients prior to study commencement.

Patient samples

The prospective observational study recruited a total of 192 NICM patients with 85 DCM cases and 107 HCM cases who received both LGE-CMR and cardiac catheterization imaging at the First Hospital of Chenzhou.

As suggested by the criteria of the American Heart Association, DCM patients were diagnosed with the follow conditions: patients received optimal medical therapy with left ventricular ejection fraction (LVEF) <45 %, LV diastolic dimension >55-mm, traditional signs or symptoms of HF, absence of obvious coronary artery disease revealed by perfusion imaging or other approaches [3]. As suggested by HCM guidelines released by European Society of Cardiology in 2014, any radiographical results that suggested ventricular wall thickness of one or more LV myocardial segments to be ≥15 mm among adult patients could serve as the evidence of HCM development [29]. Subjects with ischemic cardiomyopathy, myocarditis, hypertensive heart disease, valvular heart disease and secondary cardiomyopathy were excluded. In addition, patients with chronic or acute inflammatory diseases, severe chronic kidney disease and hematological malignancies which may have potential influence on Gal-3 level were excluded.

CMR protocol

CMR examinations were carried out using a 1.5-T scanner (Symphony Maestro Upgrade, Germany) in conjunction with a steady-state acquisition imaging (TrueFisp) system including ECG-triggered breath-hold gradient-echo. Patients were placed with supine position and morphologic images were examined in cardiac short axis and two/three/four chamber long axis. LV outflow tract was viewed using fast-field echo cine images. Typical imaging parameters were set as:

6-mm slice thickness, 4-mm gap, 256 × 192 matrix, 1.5-ms TE, 40–45-ms TR and 50° flip angle. After gadolinium had been injected into peripheral bolus for 10 min (0.2 mmol/kg of body weight, Shering AG, Germany), MF and/or scar was evaluated on DE multislice long-axis, short-axis and four-chamber views. Typical imaging parameters were set as: 6-mm slice thickness, 4-mm gap, 256 × 192 matrix and the inversion time was optimized according to previously research methods [30].

LGE analysis

LGE analysis was performed by two blinded investigators and a third investigator was consulted in the case of disagreement. CAAS MRV 3.4 software (Pie Medical, Netherlands) was implemented for LGE analysis. Both epicardial and endocardial contours were created for assessing myocardial mass. MF was presented when myocardium signal in any region was increased due to other reasons rather than image artifact on two orthogonal or contiguous slices. MF patterns were categorized into the following conditions when they were identified: diffuse, sub-endocardial based, sub-epicardial based, RV insertion site, mid-wall striae and mid-wall patchy.

Quantification of the LV end-diastolic volume (LVEDV), LV end-systolic volume (LVESV), LVEF and LV mass were conducted using semi-automated contour tracing of epicardial and endocardial borders on imaging datasets of sequential short axis. Mass and volume measurements were indexed to body surface area (BSA). Technique of Signal Threshold versus Reference Myocardium (STRM) was used to quantify the extent of MF [14, 31]. Scar signal was assessed by three separate thresholds above the mean signal in the normal region which was the largest contiguous region of homogenously nulled myocardium. Total area of MF was calculated as: the accumulated area with enhancement signals multiplied by the slice thickness and then the total area of MF was presented as a percentage with respect to the total LV mass.

Blood samples and Gal-3 evaluation

Gal-3 was measured using serum samples which were immediately centrifuged and stored at −80 °C prior to the analysis. Serum Gal-3 levels were measured using an enzyme-linked immunosorbent assay (ELISA) which was carried out by a specific kit (Waltham, USA) and the detection threshold was set as 1.13 ng/ml.

Follow-up study and endpoints

Follow-up study was conducted through telephone interviews or outpatient record reviews and relevant data were obtained during the follow-up period (i.e. 7 years). All patients were advised to continue their medications in order to prevent HF. Regular follow-up interviews with/without standard 12-lead ECG were carried out in the outpatient clinic every 2–4 months. Besides that, patients were recommended to undergo 24-h ambulatory Holter monitoring and arrhythmia management if they had palpitations or unusual symptoms. Ventricular tachycardia was diagnosed if Holter or ECG suggested more than 100 beats of ventricular depolarization per minute for more than three consecutive times. Endpoints of the follow-up study included major adverse cardiac events (MACEs) including cardiac death, arrhythmic event (ventricular fibrillation and ventricular tachycardia) and aggravated HF. The aggravated HF was defined as that the functional class of HF increased by ≥1 degree based on evaluations that extra drugs were prescribed for HF, or that symptomatology was indicated to be worsened.

Statistical analysis

All statistical analyses results were obtained from SPSS 18.0 software (Chicago, Illinois, USA). Data were presented in the form of mean ± standard deviation (SD). The two-tailed student's t test, one-way analysis of variance (ANOVA) or non-parametric test was used to analyze between-group comparisons, whereas the Chi square test was used for assessing differences in categorical variables between two groups. Cut-off values of Gal-3 were determined based on results from Receiver Operating Characteristic (ROC) curve analysis. The Kaplan–Meier method was used to create survival curves and difference in survival times among groups was assessed by the log-rank test. Hazard ratio (HR) of adverse cardiac events and their 95 % CIs were calculated using the univariate Cox proportional hazards regression model. $P < 0.05$ provided sufficient evidence of statistical significance.

Results

Clinical characteristics

Baseline clinical characteristics of patients with DCM and those with HCM were shown in Table 1. There were no significant differences in age, BMI, NYHA class, indexed LVEDV, indexed LV mass and LVEF between the LGE positive and LGE negative group among DCM patients (all $P > 0.05$). Besides, patients with LGE positive had significantly higher indexed LVESV and higher Gal-3 level (all $P < 0.05$) compared to patients with LGE negative.

Similarly, no significant differences were found in age, BMI, NYHA class, indexed LVEDV, indexed LVESV, indexed LV mass, LVEF or Gal-3 level between the LGE

Table 1 Characteristics of the study patients

Group	DCM			HCM		
	With LGE (n = 35)	Without LGE (n = 50)	*P*	With LGE (n = 66)	Without LGE (n = 41)	*P*
Age (year)	56.5 ± 15.2	53.9 ± 14.9	0.43	52.4 ± 15.5	52.3 ± 14.7	0.98
Sex, male (n)	28	36		49	32	
BMI	25.1 ± 4.6	24.4 ± 4.3	0.47	24.1 ± 4.3	24.2 ± 3.5	0.9
NYHA class (n)			0.66			0.19
I	10	10		31	26	
II	15	24		24	12	
III/IV	10	16		11	3	
Gal-3 (U/L)	15.43 ± 6.32	13.17 ± 4.15	0.05	17.86 ± 6.27	16.12 ± 5.93	0.16
AF	9	15		5	1	
CMR data						
Indexed LVEDV (ml/m^2)	119.2 ± 35.7	122.0 ± 32.0	0.71	65.7 ± 14.4	66.2 ± 13.9	0.86
Indexed LVESV (ml/m^2)	95.4 ± 38.1	75.3 ± 18.6	<0.01	18.9 ± 3.2	18.2 ± 3.5	0.29
Indexed LV Mass (g/m^2)	88.2 ± 24.0	93.9 ± 24.7	0.29	105.9 ± 38.3	96.4 ± 31.2	0.18
LVEF (%)	42.0 ± 13.6	43.2 ± 13.5	0.69	71.8 ± 7.8	72.6 ± 7.7	0.61
Medications (n)						
β-blockers	30	43		28	17	
ACEi/ARBs	31	44		23	15	
Other medicines	19	25		14	8	

Values are mean ± SD

DCM dilated cardiomyopathy, *HCM* hypertrophic cardiomyopathy, *LGE* late gadolinium enhancement, *BMI* body mass index, *NYHA* New York Heart Association, *Gal*-3 galectin-3, *AF* atrial fibrillation, *CMR* cardiac magnetic resonance, *LV* left ventricular, *EDV* enddiastolic volume, *ESV* end-systolic volume, *EF* ejection fraction

positive and LGE negative group in HCM patients (all $P > 0.05$). In addition, patients with HCM exhibited remarkably higher levels of Gal-3, indexed LV mass and LVEF as well as lower levels of indexed LVEDV and indexed LVESV in comparison to DCM patients.

Cut-off value of Gal-3 for predicting cardiac events

As suggested by the results from follow-up study, 26 cardiac events were observed among 85 patients in the DCM group. ROC curve suggested that the optimal cut-off value of Gal-3 for predicting cardiac events was 13.28 U/L in the DCM group. This cut-off value was associated with a sensitivity of 0.769, specificity of 0.610 and area under the ROC curve (AUC) of 0.64 for predicting cardiac events (Fig. 1a). Then DCM patients were sub-grouped into four groups as follows: LGE positive + low Gal-3 (Gal-3 < 13.38 U/L, n = 10), LGE positive + high Gal-3 (Gal-3 > 13.38 U/L, n = 25), LGE negative + low Gal-3 (Gal-3 < 13.38 U/L, n = 32) and LGE negative + high Gal-3 (Gal-3 > 13.38 U/L, n = 18).

On the other hand, 22 cardiac events were observed among 107 HCM patients. As suggested by the ROC curve, the cut-off value of Gal-3 for predicting cardiac events was 14.40 U/L in the HCM group, with a sensitivity of 0.864, specificity of 0.482 and area under the ROC curve (AUC) of 0.63 (Fig. 1b). Then patients in the HCM group were also allocated into four groups: LGE positive + low Gal-3 (Gal-3 < 14.40 U/L, n = 15), LGE positive + high Gal-3 (Gal-3 > 14.40 U/L, n = 51), LGE negative + low Gal-3 (Gal-3 < 14.40 U/L, n = 29), LGE negative + high Gal-3 (Gal-3 > 14.40 U/L, n = 12).

There were 4 cardiac deaths, 16 arrhythmic events and 6 aggravated HFs in the DCM group whereas 3 cardiac deaths, 14 arrhythmic events and 5 aggravated HFs were observed in the HCM group (Tables 2, 3). For patients with DCM, the LGE positive + high Gal-3 group was more likely to have cardiac events compared to the other three groups ($P = 0.004$, Table 2). A similar trend with respect to the likelihood of cardiac events was observed in patients with HCM ($P = 0.004$, Table 3).

Prognostic value of CMR and Gal-3

Kaplan–Meier survival analysis by CMR or Gal-3 status was displayed in Fig. 2. The LGE positive group had significantly lower cardiac event-free survival rate compared with the LGE negative group in DCM patients ($P = 0.012$,

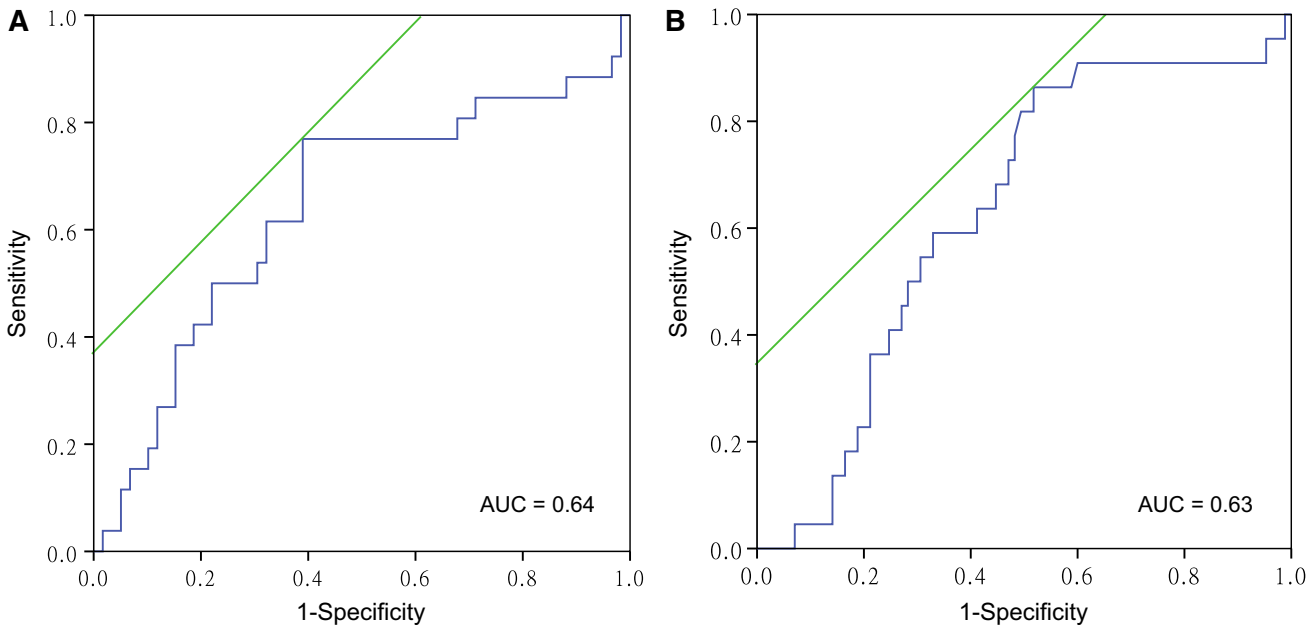

Fig. 1 Receiver operating characteristics (ROC) curve for predicting cardiac events by Gal-3 level. **a** ROC analysis in DCM patients. **b** ROC analysis in HCM patients. *Gal-3* galectin-3; *DCM* dilated cardiomyopathy; *HCM* hypertrophic cardiomyopathy

Table 2 Incidence of cardiac events during follow-up in DCM patients

DCM	All patient	LGE positive		LGE negative		*P*
		Low Gal-3	High Gal-3	Low Gal-3	High Gal-3	
All cardiac events	26\85	2\10	14\25	4\32	6\18	0.004
Cardiac death	4	0	3	1	1	
Arrhythmic event	16	2	8	3	3	
Aggravated heart failure	6	0	3	1	2	

Values are cardiac events\all patients in the group

Table 3 Incidence of cardiac events during follow-up in HCM patients

HCM	All patient	LGE positive		LGE negative		*P*
		Low Gal-3	High Gal-3	Low Gal-3	High Gal-3	
All cardiac events	22\107	1\15	18\51	2\29	1\12	0.004
Cardiac death	3	0	3	0	0	
Arrhythmic event	14	1	11	1	1	
Aggravated heart failure	5	0	4	1	0	

Values are cardiac events\all patients in the group

Fig. 2a), while the high Gal-3 group exhibited remarkably lower survival rate compared with the low Gal-3 group ($P < 0.001$, Fig. 2b). Meanwhile, similar trends were observed in HCM patients (all $P < 0.05$, Fig. 2c, d).

Kaplan–Meier survival analysis which combined CMR with Gal-3 was suggested in Fig. 3. The LGE negative + low Gal-3 group had significantly higher survival rate compared with other groups among DCM patients (all $P < 0.05$), the LGE positive + low Gal-3 group had insignificantly higher rate than the LGE positive + high Gal-3 group but lower rate than the LGE negative + higher Gal-3 group (all $P > 0.05$, Fig. 3a). For HCM patients, survival rate in the LGE positive + low Gal-3, LGE negative + low Gal-3 and LGE negative + high Gal-3 group were very similar (all $P > 0.05$), whereas the LGE positive + high Gal-3 group exhibited significantly lower survival rate than the LGE negative + low Gal-3 group($P = 0.04$, Fig. 3b).

As suggested by univariate Cox regression analysis, LGE presence, age, Gal-3 and indexed LVESV were all significant predictors of all cardiac events in DCM patients, while only age and BMI were associated with cardiac events in HCM patients (all $P < 0.05$ Table 4). Patients with presence of LGE, older age and higher levels of indexed LVESV and BMI were associated with higher risk of cardiac events (OR > 1). Nonetheless, after execution of multivariate analysis, it appeared that merely LGE presence and age were notably correlated with prognosis of DCM, yet no significance emerged when HCM was considered.

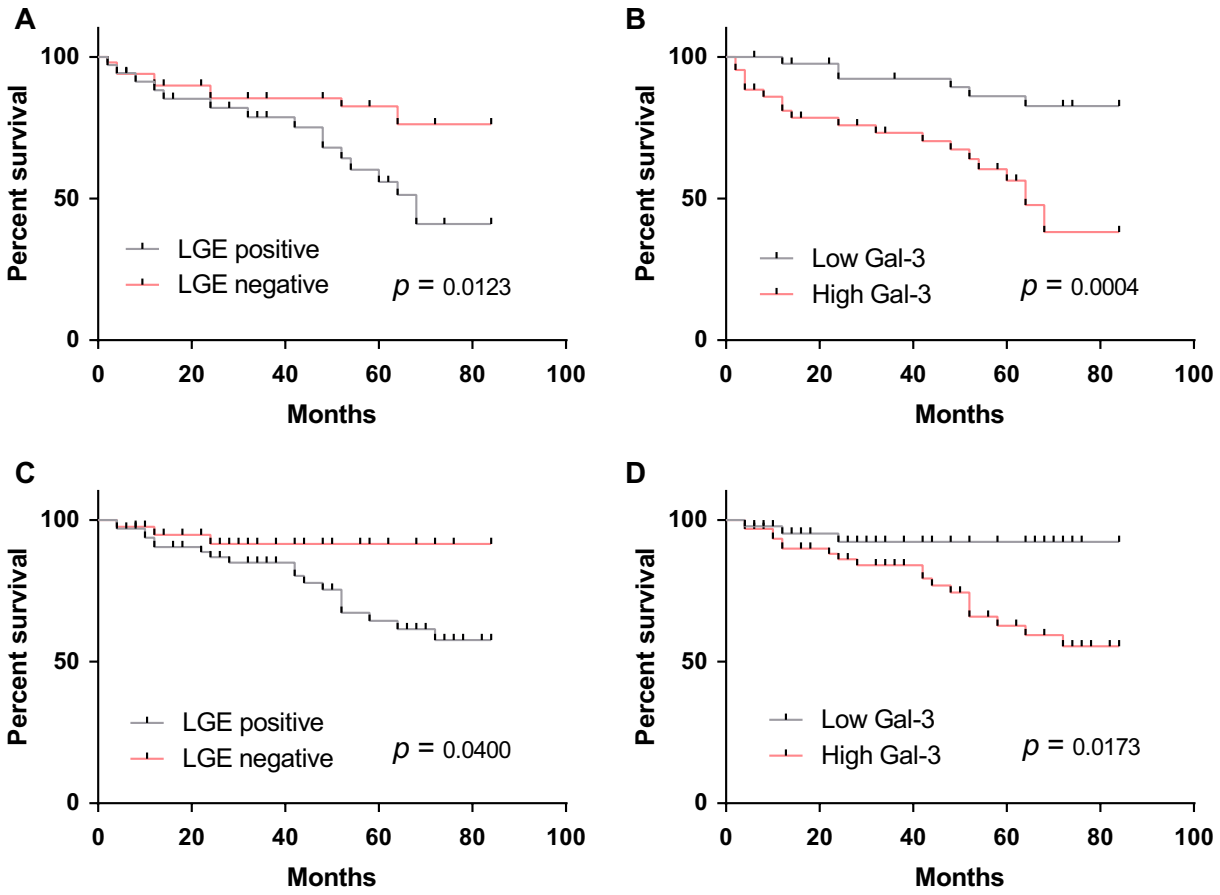

Fig. 2 Kaplan–Meier analyses of major adverse cardiac event-free survival status. **a** MACE-free survival status of DCM patients with and without LGE. **b** MACE-free survival status of DCM patients with low and high levels of Gal-3. **c** MACE-free survival status of HCM patients with and without LGE. **d** MACE-free survival status of HCM patients with low and high levels of Gal-3. *DCM* dilated cardiomyopathy, *MACE* major adverse cardiac event, *HCM* hypertension cardiomyopathy, *LGE* late gadolinium enhancement, *Gal-3* galectin-3

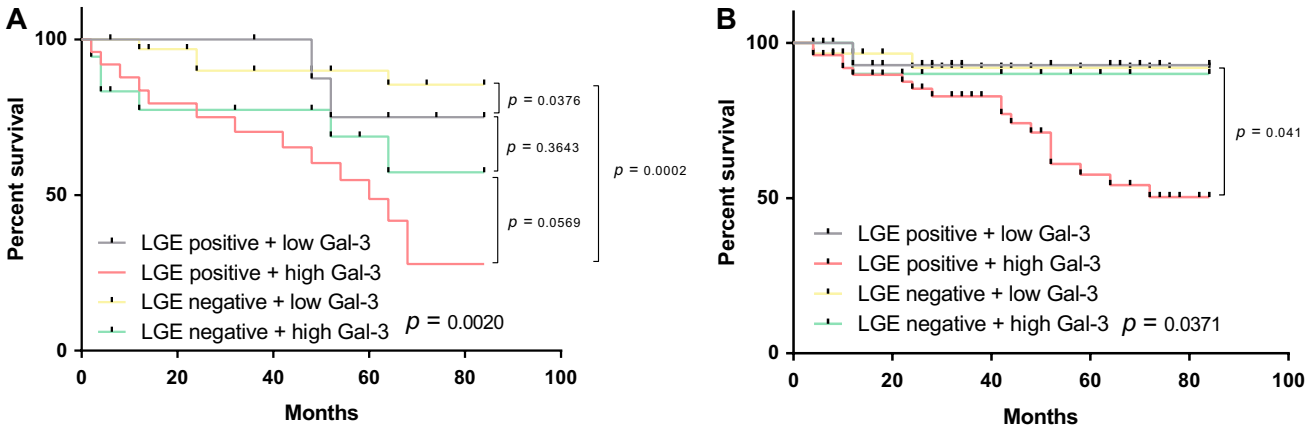

Fig. 3 Kaplan–Meier analyses of major adverse cardiac event-free survival status in DCM (**a**) and HCM (**b**) predicted by the combination of LGE status and Gal-3 level. *DCM* dilated cardiomyopathy, *HCM* hypertension cardiomyopathy, *LGE* late gadolinium enhancement, *Gal-3* galectin-3

Discussion

DCM and HCM were two types of myocardium dysfunctions that belonged to NICM [32], and CMR provided a noninvasive approach for detecting and characterizing both DCM and HCM [33]. Besides that, LGE was always used as an important indicator of CMR because it was able to precisely visualize infiltration areas and MF [34]. We analyzed

Table 4 Univariable and multivariate Cox regression analysis of risk factors for all cardiac events

Disorders	Dilated cardiomyopathy						Hypertension cardiomyopathy					
Factors	Univariate analysis			Multivariate analysis			Univariate analysis			Multivariate analysis		
	HR	95% CI	*P*	HR	95% CI	*P*	HR	95% CI	*P*	HR	95% CI	*P*
Presence of LGE	2.62	1.19–5.79	0.017	12.19	1.35–110.00	0.026	3.31	0.98–11.21	0.055	$3.19\times e^{6}$	$0.02–5.32\times e^{14}$	0.121
Age	1.48	1.32–1.67	<0.001	1.49	1.23–1.81	<0.001	1.44	1.27–1.62	<0.001	10.27	0.82–128.43	0.071
BMI	0.99	0.71–1.38	0.969	3.65	0.65–20.54	0.142	1.43	1.03–1.97	0.031	130.45	$0.01–2.48\times e^{6}$	0.333
Gal-3	1.16	1.03–1.30	0.013	1.04	0.79–1.36	0.795	1.02	0.94–1.10	0.644	0.92	0.50–1.72	0.802
Indexed LVEDV	0.98	0.96–1.01	0.218	0.99	0.94–1.03	0.528	0.95	0.86–1.05	0.318	0.61	0.27–1.37	0.229
Indexed LVESV	1.02	1.01–1.03	0.005	0.98	0.94–1.03	0.450	1.40	0.96–2.04	0.079	2.82	0.37–21.29	0.316
Indexed LV Mass	0.98	0.94–1.02	0.297	1.01	0.96–1.07	0.684	0.98	0.96–1.01	0.140	0.98	0.84–1.15	0.823
LVEF	1.02	0.95–1.10	0.552	1.11	0.96–1.29	0.171	0.87	0.59–1.27	0.467	3.49	0.08–153.84	0.518

LGE late gadolinium enhancement, *BMI* body mass index, *Gal-3* galectin-3, *LVEDV* left ventricular end diastolic volume, *LVESV* left ventricular end systolic volume, *LVEF* left ventricular ejection fraction, *HR* hazards ratio, *CI* confidence interval

different clinical characteristics of NICM patients based on LGE status (positive or negative) and concluded that no significant differences in age, BMI, NYHA class, indexed LVEDV, indexed LV mass and LVEF between the two groups were observed in DCM or HCM patients. As suggested by a single-center cohort study in China conducted by Li et al., no significant difference in mortality was observed among DCM patients with different genders or ages [35]. However, DCM patients with LGE positive exhibited significantly higher level of indexed LVESV compared to patients with LGE negative and this trend was not observed in HCM patients. Additionally, HCM patients exhibited significantly lower indexed LVEDV and LVESV levels along with much higher indexed LV mass and LVEF in comparison to DCM patients. Similarly, Cheng et al. reported that lower LVEDV and LVESV levels were identified in DCM patients compared with healthy individuals whereas no significant difference in age or gender distributions was observed between these two groups of individuals [36].

On the other hand, whether LGE was an independent risk factor for NICM or whether LGE is associated with other established prognostic factors [37] still remained elusive [38]. A cohort study conducted revealed that difference in LGE and clinical results among DCM patients were not significant [39]. Another study conducted by Vergaro et al. suggested that LGE which was able to cardiac fibrosis has emerged as a powerful predictor of LV remodeling and LGE was useful for evaluating risk of DCM [40]. Apart from that, LGE was particularly associated with hospitalization and mortality resulted from HF in NICM patients [41]. Our study demonstrated that LGE positive group in both DCM and HCM patients exhibited significantly lower cardiac event-free survival rate. As suggested by the univariate Cox regression model, we discovered that LGE presence was a significant predictor of cardiac events in DCM patients whereas its prediction was not significantly reflected in HCM patients.

Galectin-3 was involved in multiple immune reactions including activation and migration of different cells as well as cell apoptosis [42]. Selecn et al. reported that Gal-3 level was correlated with the degree of LV hypertrophy [43]. As suggested by our experiments, the LGE positive group in both HCM and DCM patients had remarkably higher level of Gal-3 and this trend was consistent with the study conducted by Selecn et al. who concluded that Gal-3 level was increased in both NICM and HF patients [40, 43, 44].

Results from Kaplan–Meier survival analysis indicated that higher levels of Gal-3 were associated with lower survival rate and higher MACE rate in both DCM and HCM patients. The prognostic value of Galectin-3 for predicting events such as HF in the long-term was confirmed by Benjimin [45]. Though the number of research conducted on this topic has increased, it is still challenging to obtain

evidence on the intrinsic relationship between Gal-3 and MRI in patients with NICM [40]. We sub-divided DCM and HCM patients into four groups by LGE status and Gal-3 level in our study in order to examine how these two factors influenced the survival status of HCM and DCM patients. As suggested by the Kaplan–Meier survival analysis, the LGE positive + high Gal-3 group exhibited significantly lower survival rate in comparison to other groups and this provided evidence of their prognostic values for NICM patients. Other studies also suggested that the presence of cardiac fibrosis was associated with right ventricular dysfunction which may be triggered by higher prevalence of right ventricular dilation and systolic impairment in HF patients [46]. On top of that, Freed concluded that the presence of LGE was correlated with restricted right ventricular function assessed by MRI [47]. Our study supported the notion that LGE status together with Gal-3 level were capable of predicting clinical outcomes in NICM patients and this conclusion was consistent with the notion that Gal-3 was directly involved in cardiac remodeling and progression of heart failure syndromes.

Conclusions

This study enabled us to clarify the relationship between LGE and Gal-3 in predicting the survival status of NICM patients whereas a few limitations should be addressed with great caution. For instance, issues such as loss of follow-up may cause missing data and affect the completeness of data collection which may have significant impact on the statistical analysis. As a result of this, how Gal-3 and LGE are related to the pathophysiology and progression of NICM should be further studied in order to address these limitations.

Compliance with ethical standards

Conflict of interest All Authors have no conflicts of interest to disclose.

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