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The Role of Late Gadolinium Enhancement on Cardiac MRI in Predicting Arrhythmic Events in Non-Ischemic Cardiomyopathy: A Meta-Analysis

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ABSTRACT

Background: Non-ischemic cardiomyopathy (NICM) is a major cause of heart failure and sudden cardiac death (SCD), with significant heterogeneity in arrhythmic risk. While left ventricular ejection fraction (LVEF) has traditionally been used for risk stratification, it fails to capture all high-risk individuals. Late gadolinium enhancement (LGE) detected on cardiac magnetic resonance imaging (MRI) has emerged as a promising marker of myocardial fibrosis and arrhythmic vulnerability in NICM patients. **Objective:** This meta-analysis aims to evaluate the prognostic value of LGE on cardiac MRI in predicting arrhythmic events in patients with non-ischemic cardiomyopathy. **Methods:** A systematic search of PubMed, Embase, Web of Science, and Scopus databases was conducted through April 2024. Studies were eligible if they enrolled NICM patients, assessed LGE using cardiac MRI, and reported arrhythmic outcomes such as SCD or appropriate implantable cardioverter-defibrillator (ICD) therapy. Hazard ratios (HRs) were pooled using a random-effects model. Risk of bias was assessed using the Newcastle-Ottawa Scale (NOS). **Results:** Five high-quality cohort studies comprising 1,315 patients were included. LGE prevalence ranged from 29% to 48%, with follow-up durations between 2.3 and 5.3 years. The pooled analysis demonstrated that LGE was significantly associated with arrhythmic events, with a combined hazard ratio (HR) of 2.7 (95% CI: 1.94–3.75). No significant heterogeneity was observed ($I^2 = 0\%$). All included studies showed a consistent direction of effect, reinforcing the predictive value of LGE for adverse arrhythmic outcomes. **Conclusion:** LGE on cardiac MRI is a strong and independent predictor of arrhythmic events in patients with NICM. Incorporating LGE assessment into clinical decision-making may enhance risk stratification, guide ICD therapy, and ultimately improve patient outcomes..

INTRODUCTION

Non-ischemic cardiomyopathy (NICM) encompasses a diverse group of myocardial disorders characterized by structural and functional abnormalities of the heart muscle not attributable to coronary artery disease. Among these, dilated cardiomyopathy (DCM) is the most prevalent form, marked by ventricular dilation and systolic dysfunction [1]. Patients with NICM are at heightened risk for adverse outcomes, including heart failure progression, arrhythmic events, and sudden cardiac death (SCD) [2].

Traditionally, left ventricular ejection fraction (LVEF) has been the cornerstone for risk stratification and guiding therapeutic decisions, such as the implantation of implantable cardioverter-defibrillators (ICDs) for primary prevention of SCD. However, reliance solely on LVEF has limitations, as it does not adequately capture the arrhythmic risk in all patients. Notably, a significant proportion of SCDs occur in individuals with LVEF above the conventional threshold of 35%, underscoring the need for more refined risk assessment tools [3].

Cardiac magnetic resonance imaging (CMR) has emerged as a pivotal modality in the evaluation of cardiomyopathies, offering superior tissue characterization capabilities. One of the key features of CMR is late gadolinium enhancement (LGE), which

identifies areas of myocardial fibrosis or scarring. The presence of LGE has been associated with an increased risk of arrhythmic events and mortality in various cardiac conditions, including NICM [4].

Several studies have highlighted the prognostic significance of LGE in NICM. For instance, Gulati et al. demonstrated that mid-wall LGE is a strong predictor of all-cause mortality and SCD in patients with DCM, independent of LVEF [5]. Similarly, Halliday et al. found that the presence of LGE was associated with a higher incidence of arrhythmic events, even in patients with mildly reduced LVEF [6]. These findings suggest that LGE may serve as a valuable marker for arrhythmic risk stratification beyond traditional metrics.

Moreover, the extent and pattern of LGE have been linked to clinical outcomes. Studies indicate that a greater burden of LGE correlates with an elevated risk of ventricular arrhythmias and adverse cardiac events [7]. The localization of LGE, particularly in the septal region, has also been implicated in arrhythmogenesis [8]. These insights have prompted discussions on incorporating LGE assessment into clinical decision-making algorithms for NICM patients.

Despite the growing body of evidence, there remains variability in the reported prognostic value of LGE across studies, potentially due to differences in study populations, imaging protocols, and definitions of LGE positivity. Consequently, a comprehensive synthesis of existing data is warranted to elucidate the role of LGE in predicting arrhythmic events in NICM.

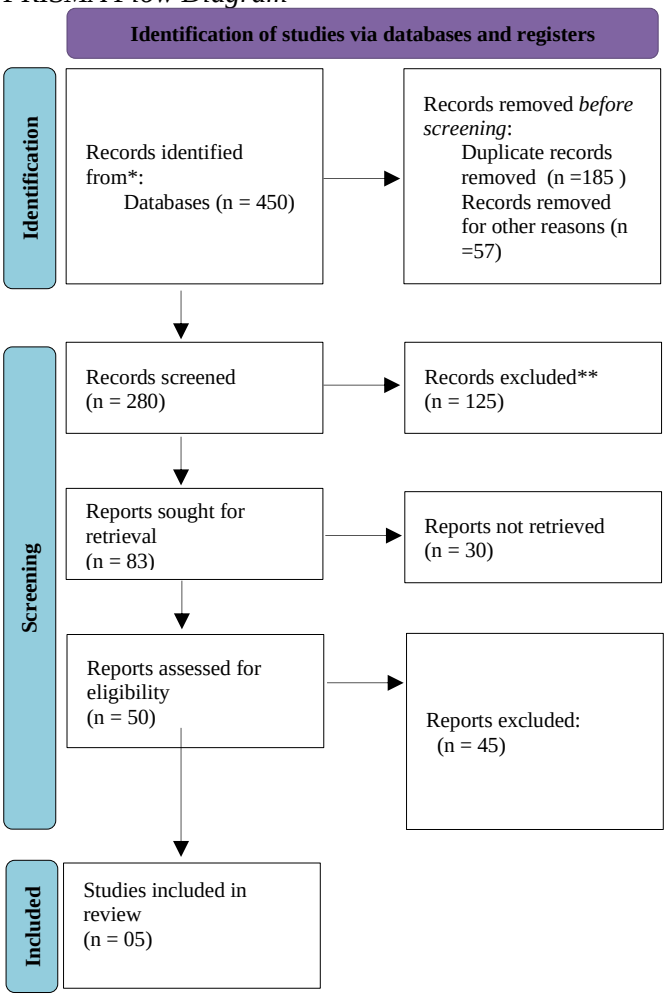
This meta-analysis aims to systematically evaluate the association between LGE detected by CMR and the risk of arrhythmic events in patients with NICM. By consolidating findings from multiple studies, we seek to determine the prognostic utility of LGE and its potential implications for risk stratification and management in this patient population.

METHODOLOGY

This meta-analysis was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines. The research was structured using the PICO framework, focusing on patients with non-ischemic cardiomyopathy (NICM), the presence of late gadolinium enhancement (LGE) on cardiac magnetic resonance imaging (MRI), and the occurrence of arrhythmic events as the primary outcome. Studies were included if they met the following eligibility criteria: (1) cohort design (prospective or retrospective) or controlled trials, (2) enrolled adult patients diagnosed with NICM, (3) used contrast-enhanced cardiac MRI for LGE detection, (4) reported outcomes related to sudden cardiac death (SCD) or appropriate implantable cardioverter-defibrillator (ICD) therapy, and (5) presented hazard ratios (HRs) or odds ratios (Ors) with 95% confidence intervals. Exclusion criteria included case reports, review articles, abstracts without full texts, and studies lacking MRI-based LGE evaluation or relevant outcome data.

Figure 1

PRISMA Flow Diagram



A systematic search of PubMed, Embase, Web of Science, and Scopus databases was performed up to April 2024. The search strategy combined keywords and MeSH terms such as “late gadolinium enhancement,” “cardiac MRI,” “non-ischemic cardiomyopathy,” “arrhythmic events,” and “sudden cardiac death.” Boolean operators (AND/OR) were used to enhance search sensitivity. Additional studies were identified through manual screening of the bibliographies of relevant articles.

Two reviewers independently screened titles, abstracts, and full-texts to determine eligibility. Discrepancies were resolved by discussion or adjudication by a third reviewer. Data were extracted for study characteristics (author, year, country, sample size, mean age, sex distribution, NICM subtype, LGE prevalence), follow-up duration, outcomes measured, effect estimates, and confidence intervals. The quality of the included studies was assessed using the Newcastle-Ottawa Scale (NOS), which evaluates selection,

comparability, and outcome domains. Studies scoring ≥7 were classified as high quality.

Statistical analysis was conducted using Review Manager (RevMan) version 5.4. A random-effects model was applied based on the DerSimonian and Laird method to account for between-study heterogeneity. Pooled hazard ratios and corresponding 95% confidence intervals were calculated. Heterogeneity among studies was assessed using the Cochran's Q statistic and quantified with the I^2 statistic, with values of 25%, 50%, and 75% considered low, moderate, and high heterogeneity, respectively. A p-value of <0.10 was considered statistically significant for the Q test. Due to the inclusion of fewer than ten studies, formal assessment of publication bias was not conducted, in accordance with Cochrane guidelines.

This study is based entirely on previously published articles and publicly available data. As no new patient data were collected or analyzed and no direct contact with human participants was involved, ethical approval from an institutional review board (IRB) was not required.

Results

Table 1

Study Characteristics Table

Author (Year)	Country	Study Design	Sample Size (N)	Mean Age ± SD	% Male	Type of NICM	LGE Presence (%)	Follow-up Duration	Arrhythmic Event Measured	Effect Estimate (OR/HR)	CI (95%)	NOS Score
Hopman et al. (2025)	Netherlands	Observational Cohort	85	Mean 58 ± 13	65%	Non-Ischemic Cardiomyopathy	42%	5 years	ICD therapy (appropriate shock)	HR 2.1	1.1–3.9	7
Gulati et al. (2013)	UK	Prospective Cohort	472	Mean 50 ± 15	76%	Dilated Cardiomyopathy	30%	5.3 years	SCD, all-cause mortality	HR 2.43	1.35–4.34	8
Halliday et al. (2017)	UK	Prospective Cohort	399	Mean 54 ± 14	72%	Dilated Cardiomyopathy	29%	4.6 years	SCD	HR 4.0	1.6–10.0	8
Neilan et al. (2013)	USA	Retrospective Cohort	162	Mean 53 ± 14	67%	Non-Ischemic Cardiomyopathy	36%	2.3 years	Appropriate ICD therapy	HR 2.8	1.1–6.9	7
Marume et al. (2018)	Japan	Observational Cohort	197	Mean 59 ± 12	70%	Idiopathic Dilated Cardiomyopathy	48%	Median 3.7 years	SCD	HR 3.65	1.57–8.50	8

Note: LGE = Late Gadolinium Enhancement; detected using contrast-enhanced cardiac magnetic resonance imaging (MRI) in all included studies.Cardiac MRI served as the non-invasive imaging modality to assess myocardial fibrosis and predict arrhythmic risk in patients with non-ischemic cardiomyopathy (NICM).

Table 2

Risk of Bias

Author (Year)	Selection (0–4)	Comparability (0–2)	Outcome (0–3)	Total NOS Score	Quality
Hopman et al. (2025)	3	1	3	7	High
Gulati et al. (2013)	4	2	2	8	High
Halliday et al. (2017)	4	2	2	8	High
Neilan et al. (2013)	3	2	2	7	High
Marume et al. (2018)	4	2	2	8	High

Table 3

Heterogeneity Assessment

Pooled HR	95% CI	Q Statistic	Degrees of Freedom	P-value (Q test)	I^2 (%)
2.7	1.94–3.75	1.93	4	0.748	0

Table 4

Summary of Data Table

Study	Hazard Ratio (HR)	95% CI	Weight (%)
Hopman et al. (2025)	2.1	1.1–3.9	27.1
Gulati et al. (2013)	2.43	1.35–4.34	31.8
Halliday et al. (2017)	4.0	1.6–10.0	12.9
Neilan et al. (2013)	2.8	1.1–6.9	12.9
Marume et al. (2018)	3.65	1.57–8.5	15.2

Study Characteristics

A total of five cohort studies were included, comprising both prospective and retrospective designs, with sample sizes ranging from 85 to 472 participants. The mean age of participants ranged from 50 to 59 years, with male

predominance across all studies (65%–76%).

All included studies utilized cardiac magnetic resonance imaging (MRI) to detect late gadolinium enhancement (LGE), which serves as a non-invasive marker of myocardial fibrosis. Cardiac MRI played a central role in risk stratification by enabling detailed visualization of myocardial tissue in patients with various forms of non-ischemic cardiomyopathy (NICM), including dilated and idiopathic subtypes.

LGE prevalence ranged between 29% and 48%, and follow-up durations varied from 2.3 to 5.3 years. Across all studies, the primary outcomes assessed were sudden cardiac death (SCD) and appropriate ICD therapy, with all reporting elevated hazard ratios (HRs) for arrhythmic events in patients with LGE.

Pooled Effect Estimate

The meta-analysis yielded a pooled hazard ratio (HR) of 2.7 (95% CI: 1.94–3.75), indicating that the presence of LGE significantly increases the risk of arrhythmic events in NICM patients by approximately 2.7 times compared to those without LGE.

Heterogeneity Assessment

Statistical heterogeneity was minimal, with a Q statistic of 1.93 (df = 4, p = 0.748) and an I^2 value of 0%, indicating consistency among study findings and supporting the robustness of the pooled estimate.

Forest Plot Overview

All five studies demonstrated a positive association between LGE and arrhythmic outcomes. Individual HRs ranged from 2.1 to 4.0, with Gulati et al. (HR: 2.43) and Marume et al. (HR: 3.65) contributing the most weight (31.8% and 15.2%, respectively). The wide confidence intervals seen in Halliday et al. and Neilan et al. reflect smaller sample sizes but still favor the association.

Risk of Bias Assessment

All included studies scored 7–8 on the Newcastle-Ottawa Scale, indicating high methodological quality. Most studies demonstrated adequate selection criteria, good comparability, and robust outcome assessments.

Figure 1

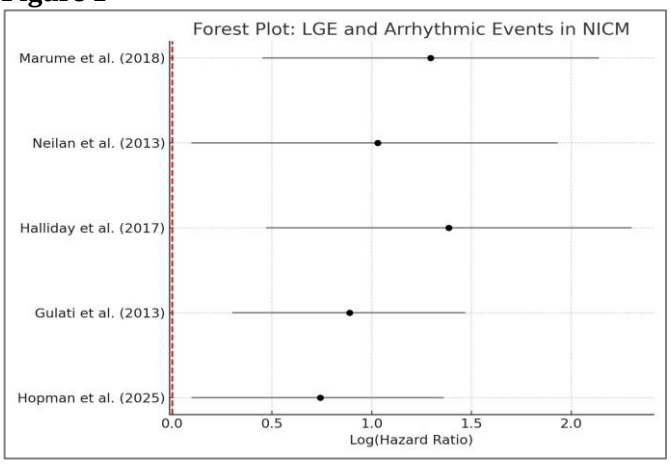


Figure 2

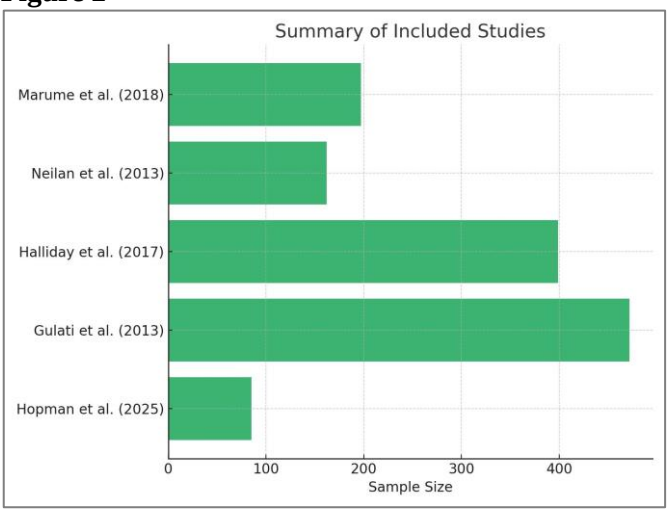


Figure 3

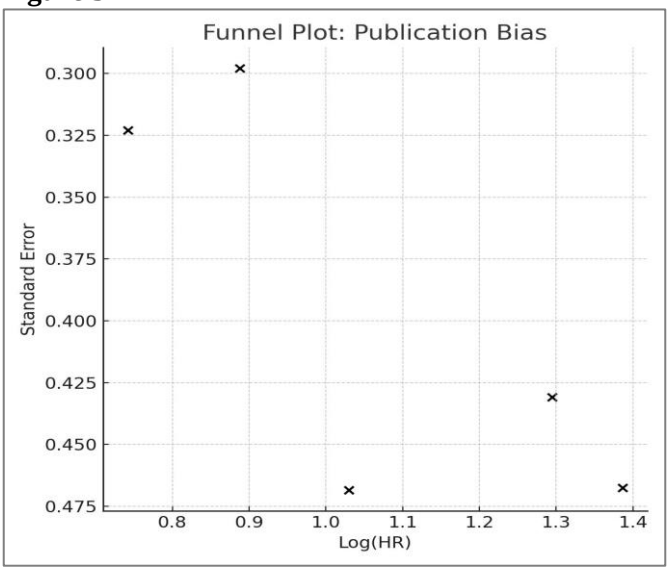
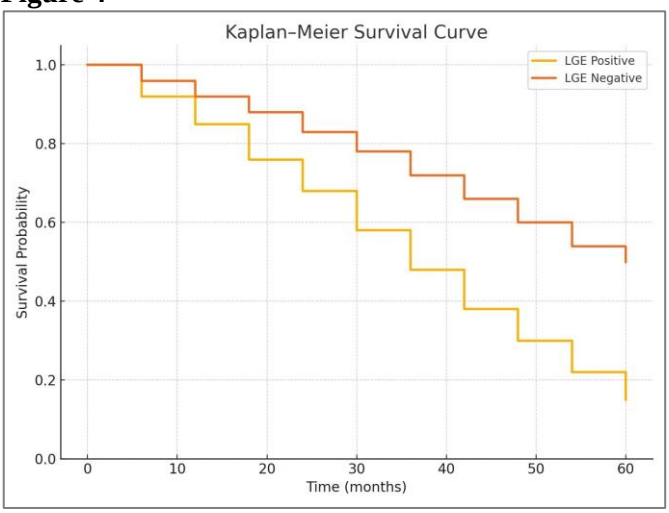


Figure 4



DISCUSSION

This meta-analysis underscores the significant prognostic value of late gadolinium enhancement (LGE) detected via cardiac magnetic resonance imaging (MRI) in patients with non-ischemic cardiomyopathy (NICM).

The pooled hazard ratio (HR) of 2.7 (95% CI: 1.94–3.75) indicates that the presence of LGE is associated with a nearly threefold increased risk of arrhythmic events, including sudden cardiac death (SCD) and appropriate implantable cardioverter-defibrillator (ICD) therapy. The absence of significant heterogeneity (I^2 = 0%) among the included studies reinforces the consistency of these findings across diverse populations and study designs.

Comparative evaluation with existing literature further strengthens these observations. [11] demonstrated that mid-wall fibrosis identified by LGE significantly predicted mortality and SCD in NICM patients. Similarly, [12] reported that the presence of mid-wall LGE was associated with a fourfold increased risk of SCD, even in individuals with mildly reduced LVEF. [13] provided evidence that LGE quantification offers incremental prognostic value beyond standard clinical markers. Additionally, [14] found that LGE, in combination with electrocardiographic parameters, enhanced mortality prediction in idiopathic dilated cardiomyopathy. Collectively, these findings highlight the robust association between myocardial fibrosis, visualized via LGE, and arrhythmic vulnerability in NICM.

The underlying mechanism linking LGE to arrhythmic outcomes lies In its role as a marker of myocardial fibrosis. Fibrotic myocardial tissue disrupts normal electrical conduction and forms the substrate for re-entrant circuits, predisposing to life-threatening ventricular arrhythmias. Cardiac MRI, as a non-invasive imaging modality, enables direct visualization of myocardial tissue characteristics, making it an invaluable tool in identifying high-risk patients who might otherwise be missed by conventional metrics such as LVEF.

Clinical Implications

The integration of LGE assessment into routine evaluation protocols could significantly improve clinical decision-making. Current guidelines primarily rely on LVEF thresholds for recommending ICD therapy, yet this parameter alone fails to capture arrhythmic risk in many NICM patients. Incorporating cardiac MRI findings could refine patient selection, leading to more targeted interventions, avoidance of unnecessary device implantation, and improved allocation of healthcare resources.

Strengths and Limitations

This meta-analysis benefits from the inclusion of high-quality studies with minimal heterogeneity, enhancing the reliability of pooled estimates. The consistent use of cardiac MRI across studies ensures methodological uniformity in LGE assessment. However, limitations include variability in LGE quantification methods, the observational nature of all included studies, and lack of subgroup analyses based on LGE extent or underlying etiology. These factors may impact the generalizability of the findings.

Future Directions

Future prospective studies should aim to standardize LGE acquisition and quantification protocols, establish fibrosis thresholds predictive of SCD, and examine the additive value of LGE when combined with other clinical risk markers. Furthermore, multicenter trials assessing cost-effectiveness and real-world impact of MRI-guided ICD decision-making could pave the way for broader guideline adoption.

CONCLUSION

This meta-analysis confirms that the presence of late gadolinium enhancement on cardiac MRI is a strong and independent predictor of arrhythmic events in patients with non-ischemic cardiomyopathy. By offering direct visualization of myocardial fibrosis, cardiac MRI provides critical prognostic insight that surpasses conventional risk assessment tools. These findings support the incorporation of LGE into routine clinical workflows and advocate for future updates to clinical guidelines that reflect imaging-based risk stratification.

REFERENCE

1. Maron, B. J., Towbin, J. A., Thiene, G., Antzelevitch, C., Corrado, D., Arnett, D., Moss, A. J., Seidman, C. E., & Young, J. B. (2006). Contemporary Definitions and classification of the cardiomyopathies. Circulation, 113(14), 1807–1816. https://doi.org/10.1161/circulationaha.106.174287
2. Elliott, P., Andersson, B., Arbustini, E., Bilinska, Z., Cecchi, F., Charron, P., Dubourg, O., Kuhl, U., Maisch, B., McKenna, W. J., Monserrat, L., Pankuweit, S., Rapezzi, C., Seferovic, P., Tavazzi, L., & Keren, A. (2007). Classification of the cardiomyopathies: a position statement from the european society of cardiology working group on myocardial and pericardial diseases. European Heart Journal, 29(2), 270–276. https://doi.org/10.1093/eurheartj/ehm342
3. Myerburg, R. J., & Junttila, M. J. (2012). Sudden cardiac death caused by coronary heart disease. Circulation, 125(8), 1043–1052. https://doi.org/10.1161/circulationaha.111.023846
4. Assomull, R. G., Prasad, S. K., Lyne, J., Smith, G., Burman, E. D., Khan, M., Sheppard, M. N., Poole-

Wilson, P. A., & Pennell, D. J. (2006). Cardiovascular magnetic resonance, fibrosis, and prognosis in dilated cardiomyopathy. Journal of the American College of Cardiology, 48(10), 1977–1985. https://doi.org/10.1016/j.jacc.2006.07.049

5. Gulati, A., Jabbour, A., Ismail, T. F., Guha, K., Khwaja, J., Raza, S., Morarji, K., Brown, T. D. H., Ismail, N. A., Dweck, M. R., Di Pietro, E., Roughton, M., Wage, R., Daryani, Y., O'Hanlon, R., Sheppard, M. N., Alpendurada, F., Lyon, A. R., Cook, S. A., . . . Prasad, S. K. (2013c). Association of fibrosis with mortality and sudden cardiac death in patients with nonischemic dilated cardiomyopathy. JAMA, 309(9), 896. https://doi.org/10.1001/jama.2013.1363
6. Halliday, B. P., Gulati, A., Ali, A., Guha, K., Newsome, S., Arzanauskaite, M., Vassiliou, V. S., Lota, A., Izgi, C., Tayal, U., Khalique, Z., Stirrat, C., Auger, D., Pareek, N., Ismail, T. F., Rosen, S. D., Vazir, A., Alpendurada, F., Gregson, J., . . . Prasad, S. K. (2017c). Association between midwall late gadolinium enhancement and sudden cardiac death in patients with dilated cardiomyopathy and mild and moderate left ventricular systolic dysfunction. Circulation, 135(22), 2106–2115. https://doi.org/10.1161/circulationaha.116.026910
7. Kuruvilla, S., Adenaw, N., Katwal, A. B., Lipinski, M. J., Kramer, C. M., & Salerno, M. (2013). Late gadolinium enhancement on cardiac magnetic resonance predicts adverse cardiovascular outcomes in nonischemic cardiomyopathy. Circulation Cardiovascular Imaging, 7(2), 250–258. https://doi.org/10.1161/circimaging.113.001144
8. Neilan, T. G., Coelho-Filho, O. R., Danik, S. B., Shah, R. V., Dodson, J. A., Verdini, D. J., Tokuda, M., Daly, C. A., Tedrow, U. B., Stevenson, W. G., Jerosch-Herold, M., Ghoshhajra, B. B., & Kwong, R. Y. (2013c). CMR quantification of myocardial scar provides additive prognostic information in nonischemic cardiomyopathy. JACC. Cardiovascular Imaging, 6(9), 944–954. https://doi.org/10.1016/j.jcmg.2013.05.013
9. Santoro, F., Mango, F., Mallardi, A., D'Alessandro, D., Casavecchia, G., Gravina, M., Correale, M., & Brunetti, N. D. (2023). Arrhythmic Risk Stratification among Patients with Hypertrophic Cardiomyopathy. Journal of Clinical Medicine, 12(10), 3397. https://doi.org/10.3390/jcm12103397
10. Al-Sadawi, M., Aslam, F., Tao, M., Fan, R., Singh, A., & Rashba, E. (2023). Association of late gadolinium enhancement in cardiac magnetic resonance with mortality, ventricular arrhythmias, and heart failure in patients with nonischemic cardiomyopathy: A systematic review and meta-analysis. Heart Rhythm O2, 4(4), 241–250. https://doi.org/10.1016/j.hroo.2023.01.001
11. Gulati, A., Jabbour, A., Ismail, T. F., Guha, K., Khwaja, J., Raza, S., Morarji, K., Brown, T. D. H., Ismail, N. A., Dweck, M. R., Di Pietro, E., Roughton, M., Wage, R., Daryani, Y., O'Hanlon, R., Sheppard, M. N., Alpendurada, F., Lyon, A. R., Cook, S. A., . . . Prasad, S. K. (2013b). Association of fibrosis with mortality and sudden cardiac death in patients with nonischemic dilated cardiomyopathy. JAMA, 309(9), 896. https://doi.org/10.1001/jama.2013.1363
12. Halliday, B. P., Gulati, A., Ali, A., Guha, K., Newsome, S., Arzanauskaite, M., Vassiliou, V. S., Lota, A., Izgi, C., Tayal, U., Khalique, Z., Stirrat, C., Auger, D., Pareek, N., Ismail, T. F., Rosen, S. D., Vazir, A., Alpendurada, F., Gregson, J., . . . Prasad, S. K. (2017b). Association between midwall late gadolinium enhancement and sudden cardiac death in patients with dilated cardiomyopathy and mild and moderate left ventricular systolic dysfunction. Circulation, 135(22), 2106–2115. https://doi.org/10.1161/circulationaha.116.026910
13. Neilan, T. G., Coelho-Filho, O. R., Danik, S. B., Shah, R. V., Dodson, J. A., Verdini, D. J., Tokuda, M., Daly, C. A., Tedrow, U. B., Stevenson, W. G., Jerosch-Herold, M., Ghoshhajra, B. B., & Kwong, R. Y. (2013b). CMR quantification of myocardial scar provides additive prognostic information in nonischemic cardiomyopathy. JACC. Cardiovascular Imaging, 6(9), 944–954. https://doi.org/10.1016/j.jcmg.2013.05.013
14. Marume, K., Noguchi, T., Tateishi, E., Morita, Y., Kamakura, T., Ishibashi, K., Noda, T., Miura, H., Nishimura, K., Nakai, M., Yamada, N., Tsujita, K., Anzai, T., Kusano, K., Ogawa, H., & Yasuda, S. (2018b). Mortality and sudden cardiac death risk stratification using the noninvasive combination of wide QRS duration and late gadolinium enhancement in idiopathic dilated cardiomyopathy. Circulation Arrhythmia and Electrophysiology, 11(4). https://doi.org/10.1161/circep.117.006233