Occurrence and Morphology of Ventricular Arrhythmias in Apparently Normal Hearts in Relation to Late Gadolinium Enhancement on Cardiovascular Magnetic Resonance

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Abstract

Introduction: Cardiac magnetic resonance (CMR) is the gold standard for evaluating myocardial fibrosis. Few studies have explored the association between ventricular arrhythmias (VAs) and fibrosis in apparently normal hearts. We aimed to investigate the association between the occurrence and morphology of VAs and left ventricular late gadolinium enhancement (LV-LGE) in patients without known structural heart diseases. Methods: This study enrolled 78 patients with apparently normal hearts who underwent simultaneous 24-h ambulatory Holter electrocardiogram (ECG) and CMR examinations. The presence and extent of LGE was determined using CMR imaging and compared based on occurrence and morphology of VAs. The clinical characteristics were also recorded and calculated. Results: LV-LGE was observed in 19 (37.3%) and 4 (14.8%) patients with and without VAs, respectively (P=0.039). It was more frequently observed in patients with polymorphic VAs (P=0.024) and ST-segment depression (P=0.001), and its extent was greater in polymorphic VAs than monomorphic VAs, with a difference that approached significance (P=0.055). In multivariate analyses adjusted for other clinical variables, the presence of ST-segment depression (HR: 8.83; 95% CI: 2.23-35.50; P=0.002), drinking (HR: 6.84; 95% CI: 1.63-28.56; P=0.008), and polymorphic VAs (HR: 25.24; 95% CI: 3.88-164.06; P=0.001) were associated with greater prevalence of LV-LGE. Conclusion: In this cohort of patients without structural heart diseases, myocardial fibrosis was associated with multiple VA morphologies and ST-segment depression on Holter ambulatory ECG measurements.

Introduction

Ventricular arrhythmias (VAs) are commonly recorded electrocardiographic abnormalities, including premature ventricular complexes (PVCs), non-sustained ventricular tachycardia (NSVT), accelerated idioventricular rhythm, sustained ventricular tachycardia (SVT), and ventricular fibrillation (VF).[1] These arrhythmias, especially PVCs, can be observed in individuals without structural heart diseases.[2-7] In these conditions, they are usually believed to be benign.[3,6,8] However, frequent and polymorphic VAs, as well as malignant ventricular arrhythmias, could contribute to worse prognoses, such as cardiomyopathies, high heart failure risks, and even sudden cardiac death (SCD).[3, 4, 6, 9-11]

Myocardial fibrosis/scars provide potential substrates for the initiation and perpetuation of ventricular arrhythmias,[11-13] which propagate around localized scar regions and along slow conduction zones.[12]Previous studies have reported that myocardial fibrosis plays an important role in risk stratifications of nonischemic cardiomyopathy.[12-14] Cardiac magnetic resonance (CMR) imaging with late gadolinium enhancement (LGE)

is a noninvasive tool that can accurately identify and quantify ventricular myocardial fibrosis.[12,15] Conversely, the presence of VAs can result in myocardial fibrosis. A previous study reported that multiple PVC morphologies could increase the prevalence of left ventricular fibrosis in patients undergoing ablation.[11] It is unclear whether VAs in apparently normal hearts could induce fibrosis. To date, few studies have explored the association between VAs occurrence and morphologies and left-ventricular late gadolinium enhancement (LV-LGE) characteristics in apparently normal hearts.

Therefore, the purpose of our study was to investigate the relationship between VA occurrence and morphologies and LV-LGE characteristics in patients without known structural heart diseases.

Methods

Study population

From May 2018 to July 2019, 281 patients with history of VAs were evaluated with both contrast-enhanced CMR imaging and 24-hour ambulatory Holter electrocardiogram (ECG) simultaneously within the timeframe of one month in our institution. Of the 281 patients, 15 were excluded because the interval between CMR and Holter ECG examinations was greater than one month, 176 were excluded due to the presence of structural heart diseases, defined by clinical histories and echocardiographic results (early coronary artery diseases, previous myocardial infarction, valvular heart diseases, and a family history of inheritable conditions, including channelopathies, hypertrophic cardiomyopathy, or arrhythmogenic right ventricular cardiomyopathy). Twelve were excluded based on severe LGE image artifacts that affected measurements (**Figure 1**). The final study population included 78 patients without structural heart disease. The study protocol was approved by the institutional review board at our institution, and all participants provided written informed consent.

CMR protocol

All CMR examinations were performed on a 3T MR scanner (MAGNETOM Skyra, Siemens Healthcare, Erlangen, Germany) with a 18-channel phased-array body coil at the anterior combined with the spine coil at the posterior. All images were acquired under the electrocardiogram (ECG)-gated breath-hold condition. All patients were scanned with the same protocol. The protocol consisted of stacks of balanced steady-state free-precession (b-SSFP) cine images acquired in the three long-axis (two-, three-, and four-chamber) views and consecutive short-axis views covering the left ventricle from base to apex (TR/TE 3.4 ms /1.3 ms, flip angle 50°, FOV 300 × 340 mm^2, matrix size 256 × 144, slice thickness 8 mm with a 2-mm gap, average temporal resolution 44.8 ms, scan time 14-22 heart beats per slice). LGE images were acquired using a segmented T1-weighted phase-sensitive inversion recovery (PSIR) SSFP sequence 10 to 15 min after bolus contrast injection (gadolinium-DTPA, 0.2 mmol/kg, Magnevist, Schering, Berlin, Germany) in the same planes as the short-axis cine images. Consecutive body-axial LGE images, covering the whole heart from the pulmonary bifurcation to just below the diaphragm, were also obtained.

Ambulatory Holter ECGs

Ambulatory Holter ECG recordings were obtained in a standard fashion with a portable tape recorder, and simulated V1 to V5 leads. Holter ECG recordings were analyzed on a DelMar Reynolds AccuPlus (model 403) MARS Holter Analysis Workstation (GE Medical Systems Information Technologies, Inc., Milwaukee, USA). Arrhythmia frequency recordings were normalized to 24 h and did not include a complete 24-h period of uninterrupted and interpretable rhythms, owing to noise or a loss of signal. In patients with more than one Holter ECG recording, the study closest in time to the CMR was analyzed. Ventricular tachycardia (VT) is defined as a cardiac arrhythmia with three or more consecutive complexes emanating from the ventricles with a heart rate of greater than 100 bpm. NSVT is defined as VT with three or more beats, that spontaneously ends in less than 30 seconds. SVT is defined as VT lasting more than 30 seconds and/or requiring termination due to hemodynamic compromise in less than 30 seconds.[16] Patients with VAs were divided into monomorphic (VAs with a single QRS morphology) and polymorphic groups (VAs with multiple QRS morphologies).[16, 17] A downsloping shift of 0.1 mV or more from the isoelectric baseline of the ST-

segment, that occurred at least 0.08 s after the junction (J)-point, was defined as ST-segment depression. VAs burden was defined as the number of VAs divided by the total beats.

Image analyses

All MRI examinations were transferred to an offline workstation with the commercial postprocessing software, CVI42 (Circle Cardiovascular Imaging Inc., Calgary, Canada). Endocardial and epicardial contours rendered by automated analyses on short-axis cine images at end-diastolic and end-systolic phases were manually reviewed and corrected as necessary. The trabeculae and papillary muscles were included in the ventricular blood pool. The most basal short-axis slice measurement was defined as having an LV circumference of at least 270° surrounded by myocardium. The most apical short-axis slice measurement was defined as the last slice where the LV cavity was visible. LV morphologic and functional parameters, including the ejection fraction (EF), end-diastolic volume (EDV), end-systolic volume (ESV), stroke volume (SV), and myocardial mass, were obtained. All parameters were indexed to body surface area (BSA).

LGE was considered present if seen in both axial planes and extended beyond localized ventricular insertion areas. The patterns were classified as linear, patchy, or a combination of the two. The locations were classified as ventricular septal, LV free wall, or as occurring at both locations. The distribution was classified as midmyocardium and non-midmyocardium. The mean signal intensity and standard deviation (SD) were derived, and a threshold of $\geq$5SD above the mean was used to define as the LGE areas. Adding the LGE areas of all short-axis slices yielded the total volume (g), which was also expressed as a proportion of the total LV myocardium (% LGE).

All CMR analyses were performed by two independent radiologists (with 15 and 5 years of experience in cardiovascular radiology, respectively), and a third radiologist provided adjudication, if necessary. All CMR analyses were performed by observers blinded to the clinical and 24-h ECG data.

Statistical analyses

The normality of data distributions was analyzed using the Kolmogorov–Smirnov test. All numeric data with normal distributions were reported as mean ± SD, and an independent sample t test was adopted. Otherwise medians (25th-75$^{\text{th}}$ percentile) were reported, and the Mann-Whitney U test was used. Clinical characteristics and CMR parameters between the subgroups were compared using an independent sample t test/Mann-Whitney U test for continuous variables. The chi-square test was used for noncontinuous variables and was expressed as proportions (or the Fisher exact test for subgroups containing $\leq$5 observations). Predictors of LV-LGE were assessed using logistic regression analyses. The multivariable regression model included all clinical characteristics and VA characteristics, selected based on univariate predictors of LV-LGE with a P <0.10. All statistical analyses were performed using SPSS (version 23.0, Chicago, IL). A two-sided P-value <0.05 was considered statistically significant.

Results

Patients and clinical characteristics

Detailed patients' demographic information and clinical characteristics are presented in **Table 1** . The average age was 40.7 ± 17.3 years (range 11 to 73 years). Of the 78 study patients, 48 (61.5%) were male. None were taking any antiarrhythmic medications, including amiodarone.

Regarding the 24-h ambulatory Holter ECG, 51 (65.4%) of the 78 study patients had ventricular arrhythmias (VAs), including 51 (65.4%) with PVCs (range 1 to 39,860, median 54), 18 (23.1%) with couplets (range 1 to 4,438, median 39), and 13 (16.7%) with runs of NSVT. The number of NSVT runs in 24 h was from 1 to 3859 (median 2), with 3 to 39 beats in the longest burst (median 8), and with ventricular rates of 148.2 ± 48.6 beats/min. SVT runs were present in one patient. When patients were divided into different groups according to VA morphologies, 43 had monomorphic VAs, and 8 had polymorphic VAs (4 also had polymorphic VT). ST-segment depression was observed in 16 patients (20.5%).

Patients with VAs were older than those without VAs (P=0.023). However, no gender distribution differences were identified between the VAs and non-VAs groups (P=0.763). Moreover, patients with VAs were more likely to have hypertension (P=0.025). There were no significant differences regarding patients age, gender distribution, or other clinical characteristics between the monomorphic and polymorphic VAs group.

CMR findings

LV-LGE was evident in 23 (29.5%) of the 78 patients, occupying 8.1% ± 8.6% (range: 0.3% to 34.2%) of the LV myocardium. Among patients with LV-LGE, twelve patients (52.2%) showed only one fibrotic area, while 11 (47.8 %) showed multiple fibrotic lesions. LGE areas were linear in 12 (52.2%) patients, patchy in 6 (26.1%), and a combination of the two (n=5, 21.7%) in 23. LGE areas were localized to the ventricular septum (n=18, 78.3%), LV free wall (n=1, 4.3%), or both locations (n=4, 17.4%). LGE distributions were midmyocardial in 20 (87.0%) and non-midmyocardial in 3 (13.0%). An example of a patient without VAs but with LGE is shown in **Figure 2** . Another example of a patient with polymorphic VAs and multiple LGE was present in **Figure 3** .

Conventional cardiac functional parameters were not associated with VAs occurrence and morphologies (**Table 2**).

The relationship of arrhythmias with LGE

The presence of LV-LGE was significantly more common in patients with VAs than in those without VAs (37.3 % vs. 14.8 %, P=0.039). LV-LGE was also more common in patients with polymorphic VAs than those with monomorphic VAs (75.0% vs. 30.2%, P=0.024), as shown in **Figure 4** . In patients with VAs, LV-LGE was not associated with the number of VAs, single PVCs, coupled PVCs, PVC burdens, or the presence of NSVTs found on the Holter ECG results over a 24 h period. **Table 3**shows detailed information regarding the association between VAs frequencies and morphologies, and the presence of LGE in patients with VAs. As shown in **Figure 4** , the presence of LV-LGE was significantly more common in patients with ST-segment depression than in those without ST-segment depression (62.5% vs. 21.0%, P=0.001). As to the extent of LV-LGE, patients with polymorphic VAs tended to have greater LV-LGE volume compared with those with monomorphic VAs (14.2 ± 14.6% vs 5.6 ± 3.8%, P=0.055). The extent of LV-LGE uptake was not significantly different between patients with and without VAs and between patients with or without ST-segment depression. LV-LGE in the midmyocardium was more common in patients with polymorphic VAs than in those with monomorphic VAs (50.0% vs 0.0 %, P=0.015). Polymorphic VAs (P=0.408) and ST depression (P=0.855) were not associated with multiple fibrotic substrates.

Predicting the presence of LV-LGE

Patients with LV-LGE were older than patients without LV-LGE (48.0 ± 15.0 years vs. 37.7±17.5 years; P=0.019). The area under the receiver operating characteristic curve, generated to assess the capability of age to discriminate patients with and without LV-LGE (cut off 37.7 years old), was 0.677. In patients older than 37 years had a 3.66-fold higher risk of LV-LGE than patients younger than 37 years. Patients with BMI >21.6 kg/m^2 had a 10.70-fold higher risk of having LV-LGE than patients with BMI [?] 21.6kg/m^2. Moreover, patients with LV-LGE were more likely to have a history of hypertension and drinking alcohol, and to have VA polymorphisms and ST-segment depression. In the multivariable analyses adjusted for other clinical variables, only the presence of ST-segment depression [hazard ratio (HR) 8.83, 95% CI 2.23-35.50, P=0.002], drinking alcohol (HR 6.84, 95% CI 1.63-28.56, P=0.008), and VA polymorphisms (HR 25.24, 95% CI 3.88-164.06, P=0.001) were independent predictors of LV-LGE. The results of the univariable and multivariable logistic regression analyses regarding 24-hour ambulatory Holter ECG predictors of LV-LGE are summarized and presented in **Table 4** .

Discussion

This study evaluated the correlation between the occurrence and morphology of VAs and LGE in patients with apparently normal hearts. The results demonstrated that LGE is more common in patients with VAs than those without VAs, especially in those with polymorphic VAs and ST-segment depression. Moreover,

polymorphic VAs and ST-segment depression were associated with a 25.24-fold increase and an 8.83-fold increase in the occurrence of LV-LGE, respectively. The frequency and burden of VAs have no impact on the presence of LV-LGE. LV-LGE extent tended to increase in patients with polymorphic VAs.

Our study demonstrated that patients with VAs were more prone to show LGE which was similar to results seen in a previous study. Ghannam et al.[18] reported that one-quarter of the patients with frequent PVCs were found to have myocardial scars. The presence of myocardial fibrosis represents an increased risk of death.[1, 19] Moreover, a previous study reported that patients with PVCs had an odds ratio (OR) of 1.72 for the combined end-points of all-cause mortality, cardiovascular mortality, and sudden cardiac death compared with those without PVCs.[20] This could be one reason why LGE was more common in patients with VAs. The present analysis showed that VAs frequencies and burdens have no impact on the presence of LGE. However, Adabag et al.[14] reported that myocardial fibrosis, detected on CMR imaging in patients with hypertrophic cardiomyopathy, was associated with an increased frequency of ventricular tachyarrhythmias.[14] That study showed that patients with LGE had a 7-fold higher risk of NSVT than patients without LGE. In our study, the constituent ratio of NSVT was 26.3% (5/19) versus 25.0% (8/32) in patients with and without LGE, respectively. A similar constituent ratio between the two groups could have been due to selection bias because of the small number of enrolled patients. Further studies with larger sample sizes are needed to clarify the association between LGE and NVST. Moreover, the lower VAs burdens of our study could also have contributed to the deviating results. Regarding VAs morphology and LGE occurrence, the results of this study showed that patients with polymorphisms and ST-segment depression were more likely to have LGE. A previous study[21] reported that polymorphic PVCs (OR=4.25) were significantly associated with the presence of LGE, consistent with this study. Moreover, Niemann et al.[22] reported LGE was eliminated when ST-segment alterations were absent. Our study also showed that patients with ST-segment depression had an 8.83-fold higher risk of having LV-LGE. In terms of the extent of LGE between subgroups, inconsistent results have been presented in previous studies.[14, 18, 23]Adabag et al.[14] demonstrated that LGE was similar in patients with hypertrophic cardiomyopathy with and without PVCs, while Ghannam et al.[18] reported that patients with inducible VT had larger fibrotic volumes compared with non-inducible patients. Similarly, our study showed no association between the extent of LV-LGE and the presence or burdens of VAs. Nevertheless, patients with polymorphic VAs tended to have increased LV-LGE extent. Most LV-LGE (20/23, 87.0%) were distributed in the midmyocardium, in this study. A previous study[1] showed that LGE was also present in the midmyocardium and were associated with increased risks for sudden cardiac death, indicating that these patients should be followed up closely. In the multivariable analysis, polymorphisms and ST-segment depression were associated with an increased incidence of LV-LGE. Muser et al.[21] reported that having multiple VAs morphologies is a risk factor for the presence of concealed myocardial structural abnormalities. Since they used CMR imaging and looked at LGE, the conclusions of that study support the results of our study. Some limitations should be acknowledged in this study. First, only a few cases had LGE (23/78) that could lead to biased results. In future studies, we plan to enroll a greater number of patients to strengthen the results. Second, due to the particularity of CMR, the study only focused on the influence of VAs on LV-LGE regardless of the influence on right ventricular LGE. Third, in morphologic terms, the study only analyzed the origins and ST-segments. Additional studies evaluating more ECG details, such as QRS complexes, amplitudes, and durations, are needed. Finally, the present study lacked follow-up regarding the effects of having LGE on patient prognosis. Our team will perform follow-up studies to further understand the influence of fibrosis in patients without known structural heart disease.

Conclusions

In conclusion, VAs polymorphism and ST-segment depression indicate a higher probability of having LV-LGE on CMR imaging. Since LGE plays a vital role in risk stratification, therapies should be administered early to prevent myocardial fibrosis in patients with the above-mentioned ECG characteristics and without known structural heart diseases.

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References

1. Marthe A J Becker, Jan H Cornel , Peter M van de Ven, Albert C van Rossum, Cornelis P Allaart, Tjeerd Germans. The prognostic value of late gadolinium-enhanced cardiac magnetic resonance imaging in nonischemic dilated cardiomyopathy: a review and meta-Analysis. JACC Cardiovasc Imaging 2018;11:1274-1284.

2. Brienesse SC, Sverdlov AL. Premature ventricular complexes: benign, pathogenic or just a marker of myocardial disease? Heart Lung Circ 2019;28:351-353.

3. Luebbert J, Auberson D, Marchlinski F. Premature ventricular complexes in apparently normal hearts. Card Electrophysiol Clin 2016;8:503-514.

4. Saurav A, Smer A, Abuzaid A, Bansal O, Abuissa H. Premature ventricular contraction-induced cardiomyopathy. Clin Cardiol 2015;38:251-258.

5. Frigy A, Csiki E, Carasca C, Szabo IA, Moga VD. Autonomic influences related to frequent ventricular premature beats in patients without structural heart disease. Medicine (Baltimore) 2018;97:e11489.

6. Baman TS, Lange DC, Ilg KJ, Gupta SK, Liu TY, Alguire C, et al. Relationship between burden of premature ventricular complexes and left ventricular function. Heart Rhythm 2010;7:865-869.

7. Yoshinori Kobayashi. Idiopathic ventricular premature contraction and ventricular tachycardia distribution of the origin, diagnostic agorithm, and catheter ablation.J Nippon Med Sch 2018;85:87-94

8. Ip JE, Lerman BB. Idiopathic malignant premature ventricular contractions. Trends Cardiovasc Med 2018;28:295-302.

9. Mirco von Rotz, Stefanie Aeschbacher, Matthias Bossard, Tobias Schoen, Steffen Blum, Susanna Schneider, et al. Risk factors for premature ventricular contractions in young and healthy adults. Heart 2017;103:702-707.

10. Latchamsetty R, Bogun F. Premature ventricular complex ablation in structural heart disease. Card Electrophysiol Clin 2017;9:133-140.

11. Oebel S, Dinov B, Arya A, Hilbert S, Sommer P, Bollmann A, et al. ECG morphology of premature ventricular contractions predicts the presence of myocardial fibrotic substrate on cardiac magnetic resonance imaging in patients undergoing ablation. J Cardiovasc Electrophysiol 2017;28:1316-1323.

12. Shin DG, Lee HJ, Park J, Uhm JS, Pak HN, Lee MH, et al. Pattern of late gadolinium enhancement predicts arrhythmic events in patients with non-ischemic cardiomyopathy. Int J Cardiol 2016;222:9-15.

13. Di Marco A, Anguera I, Schmitt M, Klem I, Neilan TG, White JA, et al. Late gadolinium enhancement and the risk for ventricular arrhythmias or sudden death in dilated cardiomyopathy: systematic review and meta-analysis. JACC Heart Fail 2017;5:28-38.

14. Adabag AS, Maron BJ, Appelbaum E, Harrigan CJ, Buros JL, Gibson CM, et al. Occurrence and frequency of arrhythmias in hypertrophic cardiomyopathy in relation to delayed enhancement on cardiovascular magnetic resonance. J Am Coll Cardiol 2008;51:1369-1374.

15. Gala Caixal, Francisco Alarcon, Till F Althoff, Marta Nunez-Garcia, Eva Maria Benito, Roger Borras. Accuracy of left atrial fibrosis detection with cardiac magnetic resonance: correlation of late gadolinium enhancement with endocardial voltage and conduction velocity. Europace 2020. doi: 10.1093/europace/euaa313. Online ahead of print.

16. Al-Khatib SM, Stevenson WG, Ackerman MJ, Bryant WJ, Callans DJ, Curtis AB, et al. 2017 AHA/ACC/HRS guideline for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: a report of the American College of Cardiology/American Heart Association Task Force on clinical practice guidelines and the Heart Rhythm Society. J Am Coll Cardiol 2018;72:e91-e220.

17. Edmond M Cronin, Frank M Bogun, Philippe Maury, Petr Peichl, Minglong Chen, Narayanan Namboodiri, et al. 2019 HRS/EHRA/APHRS/LAHRS expert consensus statement on catheter ablation of ventricular arrhythmias. J Interv Card Electrophysiol 2020;27:1-154.

18. Michael Ghannam, Konstantinos C Siontis, Myra Hyungjin Kim, Hubert Cochet, Pierre Jais, Mehdi Juhoor Eng, et al. Risk stratification in patients with frequent premature ventricular complexes in the absence of known heart disease. Heart Rhythm 2020;17:423-430.

19. Disertori M, Rigoni M, Pace N, Casolo G, Mase M, Gonzini L, et al. Myocardial fibrosis assessment by LGE Is a powerful predictor of ventricular tachyarrhythmias in ischemic and nonischemic LV dysfunction: a meta-analysis. JACC Cardiovasc Imaging 2016;9:1046-1055.

20. Victor Lee, Harry Hemingway, Rami Harb, Tom Crake, Pier Lambiase. The prognostic significance of premature ventricular complexes in adults without clinically apparent heart disease: a meta-analysis and systematic review. Heart 2012;98:1290-1298.

21. Daniele Muser, Pasquale Santangeli, Joseph B Selvanayagam, Gaetano Nucifora. Role of Cardiac Magnetic Resonance Imaging in Patients with Idiopathic Ventricular Arrhythmias. Curr Cardiol Rev 2019;15:12-23.

22. Niemann M, Hartmann T, Namdar M, Breunig F, Beer M, Machann W, et al. Cross-sectional baseline analysis of electrocardiography in a large cohort of patients with untreated Fabry disease. J Inherit Metab Dis 2013;36:873-879.

23. Halliday BP, Baksi AJ, Gulati A, Ali A, Newsome S, Izgi C, et al. Outcome in dilated cardiomyopathy related to the extent, location, and pattern of late gadolinium enhancement. JACC Cardiovasc Imaging 2019;12:1645-1655.

Table 1. Baseline patient characteristics

Parameters	All patients (n=78)	VAs occurrence VAs(-) (n=27)	VAs occurrence VAs(+) (n=51)	P value	VAs morphology mono (n=43)	VAs morphology poly (n=8)	P value
Age (years old)	40.7±17.3	34.8±16.9	43.86±16.9	0.023	43.0±15.7	48.4±23.0	0.088
Gender(male)	48(61.5%)	16(59.3%)	32(62.8%)	0.763	28(65.1%)	4(50.0%)	0.333
Hypertension	17(21.8%)	2(7.4%)	15(29.4%)	0.025	13(30.2%)	2(25.0%)	0.565
Diabetes	2(2.6%)	0(0%)	2(3.9%)	0.297	2(4.7%)	0(0%)	0.708
Smoking	17(21.8%)	6(22.2%)	11(21.6%)	0.947	11(25.6%)	0(0%)	0.121
Drinking	14(18.0%)	2(7.4%)	12(23.5%)	0.078	12(27.9%)	0(0%)	0.097
BMI (kg/m^2)	23.7±3.6	23.3±3.7	23.8±3.6	0.540	24.0±3.7	22.8±3.0	0.354
Total beats	103645.5±22018	109389.8±28147	100604.3±17532	0.133	99589.3±17836.4	106060.4±15696	0.705

Note: All numeric data were reported as mean ± standard deviation. For non-numeric data, the numbers in parentheses are in percentages. VAs = ventricular arrhythmias; mono represents monomorphic VAs; poly represents polymorphic VAs.

Table 2. Cardiac functional parameters associated with the occurrence and morphology of VAs

Parameters	VAs occurrence VAs(-) (n=27)	VAs occurrence VAs(+) (n=51)	P value	VAs morphology mono (n=43)	VAs morphology poly (n=8)	P value
EDVI (ml/m2)	81.8±15.3	84.5±21.4	0.152	84.8±22.0	82.6±19.3	0.516
ESVI (ml/m2)	37.8±15.5	41.6±19.3	0.625	41.1±19.5	44.6±19.1	0.533
SVI (ml/m2)	42.0±14.3	43.6±12.8	0.761	45.5±11.1	32.9±16.6	0.156
CI (l/min/m2)	4.2±6.9	2.9±0.8	0.532	3.0±0.8	2.5±0.8	0.831
LVEF (%)	54.6±13.6	53.5±13.4	0.838	54.7±12.9	47.1±15.5	0.146
LVMI (g/m2)	0.8±0.2	0.9±0.5	0.242	0.9±0.5	0.9±0.3	0.869

Note: All numeric data were reported as mean ± standard deviation. VAs = ventricular arrhythmias; mono represents monomorphic VAs; poly represents polymorphic VAs; EDVI = end-diastolic volume index; ESVI = end-systolic volume index; SVI = stroke volume index; CI = cardiac output index; LVEF = left ventricular ejection fraction; LVMI = left ventricular mass index.

Table 3. The presence of left ventricular late gadolinium enhancement (LV-LGE) and its association with the frequency and morphology of ventricular arrythmias (VAs)

	LV-LGE (-) (n=32)	LV-LGE (+) (n=19)	P value
Frequency			
VAs beats	32 (2-1648)	104 (4-3285)	0.447
VAs burden (%)	0.33 (0.02-14.4)	0.95 (0.04-39.4)	0.391
couplet	0 (0-1)	0 (0-60)	0.189
Single	29 (2-1604)	89(4-3201)	0.612
NSVT (n, %)	8 (25.0%)	5 (26.3%)	0.917
Runs of NSVT	0(0-0)	0 (0 -1)	0.909
Morphology			
Polymorphisms (n, %)	2 (6.3%)	6 (31.6%)	0.024
ST-segment depression (n, %)	4(12.5%)	8(42.1%)	0.020

Note: All numeric data were reported as median (25th-75th) for abnormal distribution data. For non-numeric data, the numbers in parentheses are the percentages. NSVT = non-sustained ventricular tachycardia.

Table 4. Clinical and 24-hour ambulatory Holter electrocardiographic (ECG) predictors of left ventricular late gadolinium enhancement (LV-LGE) in univariable and multivariable Cox regression analyses

Parameters	LV-LGE status LV-LGE (-) (n=55)	LV-LGE status LV-LGE (+) (n=23)	HR (95% CI)	P value	overall percentage correct

Univariate Analysis	**Clinical characteristic**					
	Age>37 ys	24 (43.6%)	17 (73.9%)	3.66 (1.25-10.69)	0.018	70.5%
	Hypertension	7(12.7%)	10(43.5%)	5.28 (1.68-16.56)	0.004	74.4%
	Drinking	6(10.9%)	8(34.8%)	4.36 (1.30-14.55)	0.017	73.1%
	BMI>21.6kg/m^2	36 (65.5%)	22 (95.7%)	10.70 (1.34-85.81)	0.026	70.5%
	Occurrence					
	VAs	32 (58.2%)	19 (82.6%)	3.41(1.02-11.38)	0.046	70.5%
	Morphology					
	Polymorphism	2 (3.6%)	6 (26.1%)	9.35 (1.72-50.74)	0.010	75.6%
	ST-segment depression	4 (7.3%)	8 (34.8%)	6.28 (1.93-20.50)	0.002	75.6%
Multivariate analysis	ST-segment depression	Model 1	Model 1	6.28 (1.93-20.50)	0.002	75.6%
	ST-segment depression	Model 2	Model 2	8.97 (2.52-31.87)	0.001	79.5%
	Polymorphism			15.22 (2.56-90.53)	0.003	
	ST-segment depression	Model 3	Model 3	8.83 (2.23-35.50)	0.002	82.1%
	Drinking			6.84 (1.63-28.56)	0.008	
	Polymorphism			25.24 (3.88-164.06)	0.001	

Note: Parameters with univariate predictors of LV-LGE with a P <0.10 were listed. The multivariable regression model included all clinical characteristics (age, hypertension, drinking, and body mass index [BMI]) and VA characteristics (VA occurrence, polymorphisms, and ST-segment depression), selected based on the univariate predictors of LV-LGE with P <0.10.

Figure legends

Figure 1. A Flowchart showing the patients selection process based on inclusion and exclusion criteria. CMR = cardiac MRI.

Figure 2. A late gadolinium enhancement (LGE) image of short-axis view (A), and an electrocardiogram (ECG) tracing (B) in a 20-year-old woman. No obvious LGE uptake was observed on LGE images. The ECG tracing indicated a normal rhythm.

Figure 3. A late gadolinium enhancement (LGE) image of short-axis view (A), and an electrocardiogram (ECG) tracing (B) in a 31-year-old man. The LGE images showed multiple, patchy, high signal intensity areas in the midmyocardium (white arrow). The ECG tracing indicated premature ventricular complexes with multiple origins.

Figure 4. The relationship of late gadolinium enhancement (LGE) and ventricular arrhythmias (VAs) regarding the occurrence and morphology of VAs and ST-segment depression. Higher LGE ratios were

demonstrated in patients with VAs, polymorphic VAs (poly), and ST-segment depression compared with patients without VAs, with monomorphic VAs (mono), and without ST-segment depression. Note: "+" represents positive; "-" represents negative.