ORIGINAL RESEARCH ARTICLE

Biventricular imaging markers to predict outcomes in non-compaction cardiomyopathy: a machine learning study

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Abstract

Aims   Left ventricular non-compaction cardiomyopathy (LVNC) is a genetic heart disease, with heart failure, arrhythmias, and embolic events as main clinical manifestations. The goal of this study was to analyse a large set of echocardiographic (echo) and cardiac magnetic resonance imaging (CMRI) parameters using machine learning (ML) techniques to find imaging predictors of clinical outcomes in a long-term follow-up of LVNC patients.
Methods and results   Patients with echo and/or CMRI criteria of LVNC, followed from January 2011 to December 2017 in the heart failure section of a tertiary referral cardiologic hospital, were enrolled in a retrospective study. Two-dimensional colour Doppler echocardiography and subsequent CMRI were carried out. Twenty-four hour Holter monitoring was also performed in all patients. Death, cardiac transplantation, heart failure hospitalization, aborted sudden cardiac death, complex ventricular arrhythmias (sustained and non-sustained ventricular tachycardia), and embolisms (i.e. stroke, pulmonary thromboembolism and/or peripheral arterial embolism) were registered and were referred to as major adverse cardiovascular events (MACEs) in this study. Recruited for the study were 108 LVNC patients, aged 38.3 ± 15.5 years, 48.1% men, diagnosed by echo and CMRI criteria. They were followed for 5.8 ± 3.9 years, and MACEs were registered. CMRI and echo parameters were analysed via a supervised ML methodology. Forty-seven (43.5%) patients had at least one MACE. The best performance of imaging variables was achieved by combining four parameters: left ventricular (LV) ejection fraction (by CMRI), right ventricular (RV) end-systolic volume (by CMRI), RV systolic dysfunction (by echo), and RV lower diameter (by CMRI) with accuracy, sensitivity, and specificity rates of 75.5%, 77%, 75%, respectively.
Conclusions   Our findings show the importance of biventricular assessment to detect the severity of this cardiomyopathy and to plan for early clinical intervention. In addition, this study shows that even patients with normal LV function and negative late gadolinium enhancement had MACE. ML is a promising tool for analysing a large set of parameters to stratify and predict prognosis in LVNC patients.

Introduction

Left ventricular (LV) non-compaction cardiomyopathy (LVNC) is considered a genetic heart disease,[1] related to intrauterine arrest of the process of myocardial compaction, leading to prominent ventricular trabeculations and deep intertrabecular recesses,[2–4] with a two-layer myocardial structure: non-compacted (NC) and a compacted (C) layer. This disease can lead to heterogeneous clinical manifestations ranging from completely asymptomatic to end-stage heart failure, malignant arrhythmias, thromboembolic

events, and death. Currently, the increase in awareness of this disease is due to the increased number of diagnoses owing to improvements in cardiovascular imaging techniques and familial screening.[5–7] Notwithstanding, there is a concern about overdiagnosis of this disease.

Many studies have demonstrated clinical and imaging prognostic indices in a long-term follow-up of LVNC patients to identify a subgroup with more severe cardiac impartment.[8–10]

However, neither the prognostic value of the combination of echocardiographic and cardiac magnetic resonance imaging (CMRI) parameters nor parameters from both ventricles have clearly predicted major adverse cardiovascular events (MACEs). A recent meta-analysis involving 2501 patients showed that those who had LV systolic dysfunction [LV ejection fraction (LVEF) less than 45%] had a poor prognosis. On the other hand, the burden of LV trabeculation is not a fefeature related to MACE. Noteworthy, right ventricular (RV) evaluation was not included in the meta-analysis paper.[11]

The interest in diagnostic methods in cardiology with higher accuracy is growing, and machine learning (ML) is an emerging tool in this context. Previous studies showed its ability to identify interaction patterns among many variables,[12,13] with interesting findings in different subsets, mainly focusing on heart failure.[14–18] Thus, the objective of this study was to evaluate the predictive value of parameters from echo, CMRI, and both combined methods on outcomes in a long-term follow-up of a large subset of LVNC patients by using the ML algorithm.

Methods

Study population

Included in this retrospective study were 108 patients with echo and/or CMRI criteria of LVNC, who were followed from January 2011 to December 2017 in a heart failure outpatient clinic at a university cardiology centre. Baseline clinical data were obtained from electronic medical records of our institution—clinical and complementary cardiological exam records.

Only patients with a high pre-test probability were included.[19] Two-dimensional colour Doppler echocardiography was carried out, and all patients met Chin *et al.*,[5] Jenni *et al.*,[6] and Stöllberger *et al.*[7] echo criteria, whereas subsequent CMRI findings fulfilled Petersen *et al.*[20] criteria. Twenty-four hour Holter monitoring was also performed for all the patients, who were treated according to current heart failure guidelines.[21] Events such as death, cardiac transplantation, heart failure hospitalization, aborted sudden cardiac death, complex ventricular arrhythmias (sustained and non-sustained ventricular tachycardia that were included in the 24 h Holter Monitoring Protocol), and embolisms (i.e. stroke, pulmonary thromboembolism, and/or peripheral

arterial embolism) were registered and are jointly referred to as MACEs in this study. Patients with other cardiac or systemic diseases were excluded.

Heart failure was diagnosed based on clinical findings (signs and symptoms),[21] and it was supported by echo and CRMI exams (LVEF was less than 40%). In this study, LV diastolic dysfunction was characterized by echo criteria in moderate and significant patterns, according to the guidelines.[22] These patients were treated in accordance with the heart failure guidelines,[21] with drugs like angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, diuretics, spironolactone, and beta-blockers. Hospitalization for heart failure was considered in those patients who had symptomatic heart failure (New York Heart Association III or IV), at any time during this follow-up study, even with optimized therapy, also in accordance with the current heart failure guidelines.[21] The Ethics Committee approved the protocol, and all patients gave written informed consent.

Echocardiographic imaging protocol

Comprehensive echo studies were performed with a Sequoia 512 ultrasound machine (Acuson, Mountain View, CA, USA) with a 2.5 MHz harmonic imaging transducer. The following echo parameters were evaluated: aortic root and left atrium dimension (cm); left atrium enlargement; RV dimension (cm); LVEF (%) by Simpson biplane modified method and LV systolic dysfunction; LV fractional shortening (%); diastolic septum wall thickness (cm); diastolic posterior wall thickness (cm); LV end-diastolic dimension (cm); LV end-systolic dimension (cm); bidimensional LV end-diastolic and end-systolic volumes (mL); LV mass index by American Society of Echocardiography (ASE) (g/m^2); relative wall thickness; RV systolic dysfunction; pulmonary hypertension (>35 mmHg); and LV diastolic dysfunction classified as normal, grades I to III. All these indices were acquired and calculated according to guidelines of chamber quantification[23] and diastolic dysfunction.[22] In this study, pulmonary hypertension was considered when pulmonary systolic artery pressure was higher than 35 mmHg,[24] and LV systolic dysfunction was classified as mild (40% to 50%), moderate (30% to 39%), or severe (<30%).

Cardiac magnetic resonance imaging imaging protocol

Cardiac magnetic resonance imaging studies were performed with two different scanners: 1.5 T CMR scanner (Philips Achieva, Best, The Netherlands) or 1.5 T GE CV/i CMR System (Wakeusha, Wisconsin, USA). A similar CMRI protocol was adopted in all studies according to the following parameters: slice thickness 10 mm, ACQ matrix 152 × 150, flip angle 40°,

and inversion time increment 150 ms for the Philips Achieva scanner and slice thickness 8 mm, ACQ matrix 256 × 128/ 256 × 192, flip angle 45°/20°, and inversion time none/150 to 250 ms for the GE CV/i scanner. Ventricular function, volumes, and mass were obtained from at least 10 short-axis ventricular slices, imaged with a steady-state free precession pulse sequence, covering the entire LV. Late gadolinium enhancement (LGE) images were acquired 10–20 min after an intravenous bolus of 0.2 mmol/kg of gadolinium-based contrast, with an inversion-prepared gradient echo sequence.

All CMRI images were analysed using cvi42 software (Circle Cardiovascular Imaging Inc. Calgary, Canada) by a trained reader. End-systolic and end-diastolic LV volumes, LV mass, and LVEF were measured by standard methods.[25] The pattern of LGE was classified as subendocardial, midwall, subepicardial, or transmural.

The following CMRI parameters were studied: NC/C myocardial ratio; LGE; left atrium dimension (cm); left atrium enlargement; right atrium enlargement; septum thickness (cm); lateral wall thickness (cm); LV end-diastolic dimension (cm); LV end-systolic dimension (cm); LV end-diastolic volume (mL); indexed LV end-diastolic volume (mL/m^2); LV end-systolic volume (mL); indexed LV end-systolic volume (mL/m^2); LV mass (g); LVEF by the Simpson method; LV systolic dysfunction; RV major axis (cm); RV minor axis (cm); RV end-diastolic volume (mL); indexed RV end-diastolic volume (mL/m^2); RV end-systolic volume (mL); indexed RV end-systolic volume (mL/m^2); RV ejection fraction (%); RV systolic dysfunction; aortic root dimension (cm); ascending aorta dimension (cm); descending aorta dimension (cm); and pulmonary artery trunk dimension (cm).

Twenty-four hour Holter monitoring protocol

Holter monitoring (Cardios®, Cardio Systems, São Paulo, Brazil) with three-channel recording was used for 24 h electrocardiography monitoring of each patient. Each beat was automatically classified and labelled by the Cardios software using the template-matching technique. Then, a single senior cardiologist performed a blinded evaluation over all exams and classified ventricular beats, non-ventricular beats, and artefacts. Non-sustained ventricular tachycardia and sustained ventricular tachycardia were reported.

Machine learning

The ML algorithm has two main phases: (i) a phase in which missing parameters are estimated and (ii) a phase in which predictive parameters are selected. The overall structure of the ML framework is illustrated in *Figure 1*.

Missing parameter estimation

Because not all CMRI and echo parameters were available for all the subjects studied, the ML framework included a 'data imputation' step during which the missing parameters (2% of the CMRI and 15% of the echo data) were estimated through a learning method called 'SVDimpute'.[26,27]

Figure 1 Overall structure of the proposed machine learning framework. The 'SVDimpute' method was first used to estimate the missing CMRI and echocardiographic parameters of the subjects (empty fields in the upper left panel). The complete data (the bottom left panel), with green fields representing the estimated missing parameters, were then fed into a parameter selection algorithm comprising sequential forward selection to explore the space of the parameters and DWKNN as a classifier to evaluate the predictive powers of the parameters. The outcome of the feature selection phase was a small subset of the parameters that enabled categorization of the control and patient groups with high accuracy. DWKNN, distance-weighted k-nearest neighbour.
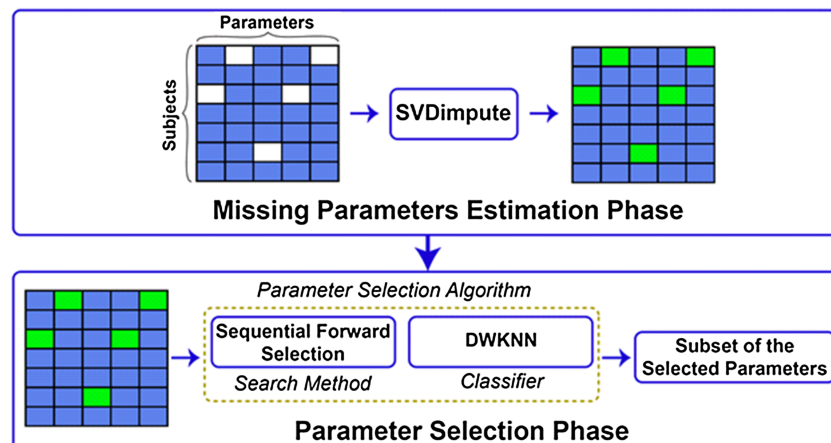
Parameter selection

As the CMRI and echo measurements resulted in a fairly large set of parameters (i.e. 47 parameters in this study), whereas not all of these parameters have added prognostic power, a parameter selection (also called feature selection) approach was used whereby a subset of the parameters was found to best predict MACE.[27] Hereto, we used a 'wrapper parameter selection' method[28] that was composed of a 'sequential forward selection' as a search method to explore the space of the parameters and of the 'distance-weighted k-nearest neighbor'[29] as a classifier to assess the predictive power of the parameters.

Performance evaluation

As is common in ML, the subjects were randomly split into a 'training set' for building the feature selection algorithm and a 'testing set' for evaluating the predictive power of different combinations of the selected parameters. The training set consisted of 74 subjects, where the same number of subjects was randomly selected from the patients with and without MACE during follow-up, and the testing set contained the remaining 34 subjects. This process was repeated 50 times (i.e. cross-validation), and a subset of the parameters that resulted in the best average classification performance was chosen. Using this process, we made sure that all subjects were used in the training and testing sets and that the selected parameters were not biased towards a subset of the subjects. All data analysis was performed in MATLAB 2015 (The MathWorks, Inc., Natick, Massachusetts, USA).[30]

Statistical analysis

Initially, all variables were analysed in a descriptive form. For the quantitative variables, the analysis was done by observing the minimum and maximum values and calculating the means and standard deviations after assessment of normal data distribution. Absolute and relative frequencies were calculated for the qualitative variables. For the comparison of means between groups, a Student's *t*-test was used. To evaluate the homogeneity between proportions, the χ^2 test or Fisher's exact test was applied.[23] The software used for the calculations was SPSS v 17.0 (SPSS Inc, Chicago, IL). The level of significance used for the tests was 5%.

Results

Study population

A total of 108 patients from 1 to 69 years of age, 38.3 ± 15.5 years, 52 men (48.1%) were included in the study, as shown in *Table 1*. The mean time of follow-up was 5.8 ± 3.9 years during which 47 patients (43.5%) had at least one MACE (*Table 2*).

Echocardiography results

Echo findings for patients with and without MACE during follow-up are reported in *Table 3*. Patients who experienced at least one event had significantly larger left atrial dimension; RV dimension; decreased LVEF and LV fractional shortening; increased LV end-diastolic and end-systolic

Table 1 Baseline clinic parameters of both groups of patients

Baseline parameters	Group with events (47), mean ± SD	Group without events (61), mean ± SD	*P* value
Age	40.9 ± 15.0	34.0 ± 15.7	0.022[a]
Male gender	Male: 51%	Male: 46%	0.595[c]
Body surface (m^2)	1.7 ± 0.3	1.8± 0.2	0.169[a]
Follow-up (months)	69 ± 36.5	70 ± 50.9	0.752[b]
LVNC family history	15%	62%	0.001[c]
Syncope	23%	13%	0.164[c]
Arterial hypertension	40%	28%	0.170[c]
Diabetes mellitus	8%	8%	1.000[d]
Dyslipidaemia	27%	28%	0.981[c]
Coronary artery disease	0%	0%	-
Chronic renal disease	12%	2%	0.041[d]
Smoking	38%	18%	0.019[c]
Alcoholism	8%	3%	0.400[d]

LVNC, left ventricular non-compaction cardiomyopathy.
P < 0.05.
[a]Student's *t*-test.
[b]Wilcoxon test.
[c]χ^2 test.
[d]Fisher's exact test.

dimension; volumes and indexed LV mass; RV systolic dysfunction; and impaired LV diastolic dysfunction ($P < 0.05$).

Cardiac magnetic resonance imaging results

Cardiac magnetic resonance imaging data set was available in 107 patients (*Table 4*). In one patient, a pacemaker was implanted due to total atrioventricular block, and CMRI was not performed. Patients with events during follow-up had increased left atrium dimension, LV end-systolic and end-diastolic dimension, volumes and mass, and decreased biventricular ejection fraction. The NC/C ratio did not show statistically significant differences between both groups. The presence of LGE was related to MACE (*Table 4*). In spite of 34% of patients in the MACE group having LGE, this represented only ~5.4% of all analysed segments (43 out of 799 segments), considering a 17-segment model.[31]

Table 2 Major adverse cardiovascular events frequency in non-compaction cardiomyopathy patients

Events	Number of patients (total: 47)	Frequency (%)
Death	6	12.8
Cardiac transplantation	2	4.2
Heart failure hospitalization	26	55.3
Aborted sudden cardiac death	2	4.3
Complex ventricular arrhythmias	29	61.7
Total embolic events	8	17.0
Stroke	7	14.9
Arterial embolism	1	2.1
Pulmonary thromboembolism	0	0

Echo and cardiac magnetic resonance imaging machine learning analysis

The algorithm selected the following combination of indices to best predict MACE by both methods: for echo parameters, (i) LVEF, (ii) RV systolic dysfunction, (iii) LV end-diastolic volume, and (iv) LV mass index and for CMRI parameters, (i) LVEF, (ii) RV end-systolic volume, (iii) LGE, and (iv) RV lower axis. Finally, when the algorithm analysed both methods, the best parameters were as follows: (i) LVEF (CMRI), (ii) RV end-systolic volume (CMRI), (iii) RV systolic dysfunction (echo), and (iv) RV lower axis (CMRI), with accuracy, sensitivity, and specificity rates of 75.5%, 77%, and 75%, respectively (*Figures 2* and *3*).

Discussion

This is the first study to evaluate the combination of two imaging methods, echo and CMRI, in the prognostic stratification in a long-term follow-up evaluation of a large number of patients with LVNC using ML tool stratification. Thus, clinical, echo, and CMRI data were analysed in a combined manner, where the data in both imaging methods were evaluated for the diagnosis and prognostication of this disease. Surprisingly, we noticed the importance of biventricular assessment when applying both methods in prognostic stratification; we also found it significant that the RV dysfunction by echocardiogram showed additive value to the CMRI parameters in the severity of disease (*Figure 2*). LVEF was the most important parameter in this and in previous studies for detection of MACE.[2,9] Although adding RV dysfunction to LVEF did not substantially improve the results, the use of the combination

Table 3 Echocardiographic parameters in non-compaction cardiomyopathy patients with/without major adverse cardiovascular events

Echocardiographic parameters	Group with events (47), mean ± SD	Group without events (61), mean ± SD	*P* value
Left atrium dimension (mm)	43.2 ± 8.0	37.8 ± 8.1	<0.001
Aortic root dimension (mm)	28.9 ± 5.1	28.7 ± 4.0	0.775
RV dimension (mm)	27.0 ± 7.1	24.3 ± 4.3	0.025
LV ejection fraction (%)	37.1 ± 13.9	51.7 ± 15.2	<0.001
LV fractional shortening (%)	19.2 ± 7.5	27.4 ± 8.8	<0.001
Septum thickness (mm)	9.2 ± 1.9	8.9 ± 1.4	0.320
Posterior wall thickness (mm)	9.1 ± 1.4	8.5 ± 1.4	0.048
LV end-diastolic dimension (mm)	60.4 ± 10.9	53.9 ± 9.9	0.002
LV end-systolic dimension (mm)	49.3 ± 12.5	39.2 ± 12.6	<0.001
LV end-diastolic volume (mL)	186.7 ± 80.3	142.6 ± 66.3	0.002
LV end-systolic volume (mL)	126.2 ± 72.3	79.3 ± 62.3	<0.001
Indexed LV mass (g/m^2)	140.2 ± 59.5	102.3 ± 38.8	<0.001
Relative wall thickness	0.3 ± 0.1	0.3 ± 0.1	0.092
Left atrium enlargement	63.0%	27.9%	0.0019
LV systolic dysfunction	76.6%	44.3%	0.0005
RV systolic dysfunction	29.8%	8.2%	0.0206
LV diastolic dysfunction	61.7%	31.1%	0.0208
Pulmonary hypertension	25.5%	11.5%	0.0572

LV, left ventricle/ventricular; RV, right ventricle/ventricular.
Student's *t*-test. $P < 0.05$.

Table 4 Cardiac magnetic resonance imaging parameters in non-compaction cardiomyopathy patients with/without major adverse cardiovascular events

CMRI parameters	Group with events (47), mean ± SD	Group without events (n = 61), mean ± SD	P value
NC/C ratio	3.3 ± 1.1	3.0 ± 0.8	0.213
Left atrium dimension (cm)	3.6 ± 0.8	3.2 ± 0.8	0.006
Septum thickness (cm)	0.8 ± 0.2	0.8 ± 0.2	0.608
Lateral wall thickness (cm)	0.7 ± 0.2	0.7 ± 0.2	0.892
LV end-diastolic dimension (cm)	6.3 ± 1.2	5.7 ± 0.9	0.001
LV end-systolic dimension (cm)	5.3 ± 1.3	4.1 ± 1.2	<0.001
LV end-diastolic volume (mL)	218.9 ± 108.7	165.8 ± 59.7	0.004
Indexed LV end-diastolic volume (mL/m^2)	127.0 ± 58.6	91.2 ± 29.1	<0.001
LV end-systolic volume (mL)	142.5 ± 99.2	85.1 ± 56.1	<0.001
Indexed LV end-systolic volume (mL/m^2)	89.4 ± 67.3	46.9 ± 29.2	<0.001
LV Mass (g)	137.5 ± 55.8	114.4 ± 41.1	0.019
LV ejection fraction (%)	35.7 ± 15.6	52.4 ± 15.4	<0.001
RV major axis (cm)	7.4 ± 1.4	7.7 ± 1.3	0.256
RV minor axis (cm)	4.0 ± 0.8	4.1 ± 0.6	0.677
RV end-diastolic volume (mL)	138.5 ± 58.2	139.4 ± 40.8	0.929
Indexed RV end-diastolic volume (mL/m^2)	80.8 ± 29.9	76.6 ± 18.1	0.389
RV end-systolic volume (mL)	78.1 ± 54.3	64.7 ± 27.6	0.129
Indexed RV end-systolic volume (mL/m^2)	45.5 ± 29.5	36.6 ± 13.6	0.0591
RV ejection fraction (%)	46.1 ± 15.6	52.0 ± 11.5	0.031
Aortic root dimension (cm)	2.7 ± 0.5	2.8 ± 0.5	0.877
Ascending aorta dimension (cm)	2.8 ± 0.6	2.6 ± 0.5	0.074
Descending aorta dimension (cm)	2.1 ± 0.5	2.02 ± 0.3	0.229
Pulmonary artery trunk dimension (cm)	2.4 ± 0.5	2.3 ± 0.5	0.247
Left atrium enlargement	57.4%	35%	0.0593
Right atrium enlargement	23.4%	16.7%	0.3827
LV dysfunction	83.0%	41.7%	<0.0001
RV dysfunction	31.9%	15%	0.1122
Presence of late gadolinium enhancement	34.0%	8.3%	0.0009
Late gadolinium enhancement prevalence in total cardiac segments	5.4%	0.7%	0.0009

LV, left ventricle/ventricular; NC/C, non-compacted/compacted ratio; RV, right ventricle/ventricular.

of only 4 out of 46 parameters allowed a significant increase in accuracy, sensitivity, and specificity rates. Furthermore, the replacement of LGE (CMRI) by RV dysfunction (echo) also improved the performance. This form of assessment allows us to score the greatest impact markers in the prognosis of these patients, thus serving as a guide to determine which patient should have a more emphatic and early approach. More recent tools such as the use of myocardial deformation indices would also provide earlier and more robust data on the unfavourable evolution of patients with LVNC, and more studies are needed to clarify the role of RV involvement in LVNC as a primary impairment or secondary compromising to LV dysfunction.

The diagnosis of LVNC remains controversial because there is no gold standard method, as demonstrated when the three echocardiographic diagnostic criteria (Chin, Jeni, and Stöllberguer) were used in a single population, and only 29.8% of the patients fulfilled the three proposed criteria.[31,32] We used the three echocardiographic criteria as the first imaging method for LVNC diagnosis to improve the diagnostic specificity, and these patients all underwent CMRI to confirm the diagnosis; family screening was also performed.

Our results are in line with recent prospective studies[2,9] with 2.3 and 2.9 years of follow-up and a meta-analysis with 28 studies,[11] which demonstrated that functional class III/IV,

reduction in LVEF, ventricular remodelling, pulmonary arterial hypertension, and the presence of LGE were markers of poor prognosis. Another odd fact is that the NC/C ratio did not have prognostic implications as described in previous publications,[11] which increases scepticism about the primary and single aetiology of LVNC. The NC/C ratio is important for the diagnosis, but not for LVNC prognosis.

In our study, 17.0% of patients with MACE had normal LVEF and 66.0% of this group did not have LGE. Among patients with LGE, this represented only 5.4% of the total analysed segments, showing that even patients with normal function and no LGE are at risk of MACE. Moreover, LGE was present in almost 28% of the patients with MACE and in only 9.7% of all patients. Similar findings are also shown by Andreini *et al.*, who demonstrated that LGE has a prognostic impact.[10] Recently, the importance of extracellular volume quantification as a CMRI parameter in predicting ventricular arrhythmias in patients with LVNC has been demonstrated, showing the interstitial fibrosis as a predisposing factor in ventricular arrhythmias, even in patients with low LGE.[33]

Another piece of interesting data in our sample is that almost 30% of patients with MACE had normal diastolic function patterns on echo. Thus, 14.8% of the LVNC patients had normal systolic and diastolic LV functions, no LGE, and still had adverse outcomes, which showed the severity of

Figure 2 The results of receiver operating characteristic analyses on the classification outcomes obtained when using only echo or CMRI markers and a combination of both markers. For the latter case, the selected echo and CMRI markers are written in blue and red, respectively. The classification results at different steps of the parameter selection process were statistically compared. AUC, area under the curve; Echo, echocardiogram; CMRI, cardiac magnetic resonance imaging; NS, not significant; LGE, late gadolinium enhancement; LV, left vetricular; LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; RV, right ventricular; Dysfun.grd, dysfunction grade; RVESV, right ventricular end-systolic volume.
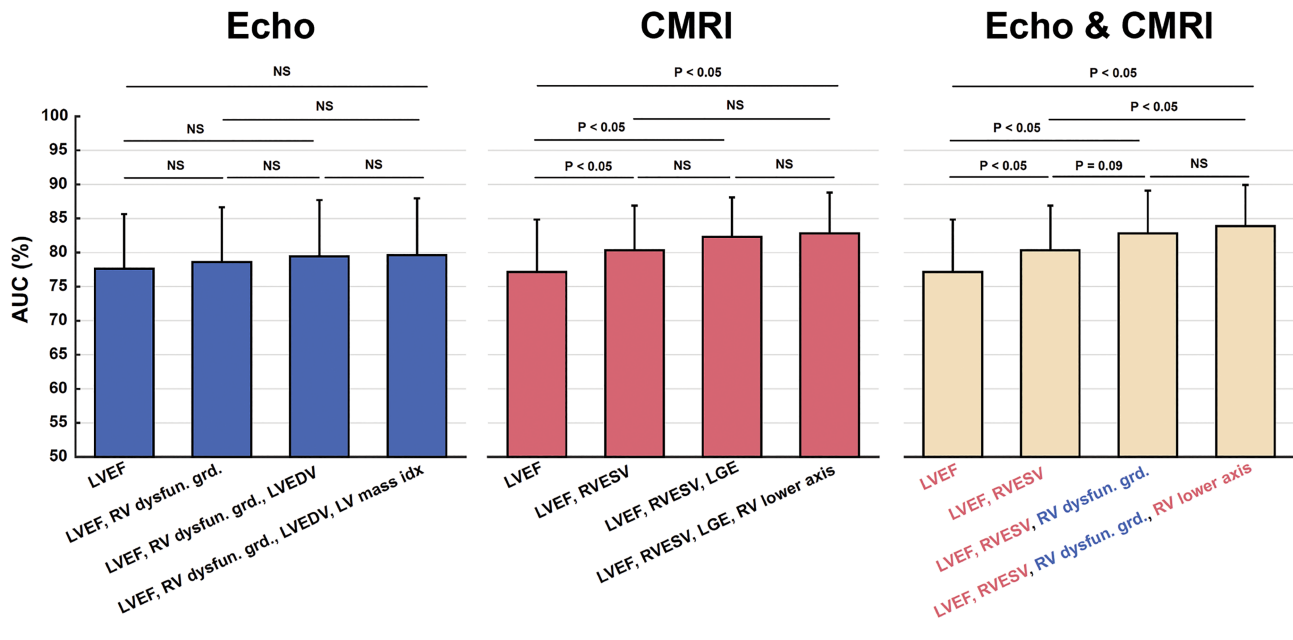
Figure 3 Accuracy, sensitivity, and specificity rates (%) (mean ± SD) obtained with the optimal cut-off values of the receiver operating characteristic analyses presented in *Figure 2*. CMRI, cardiac magnetic resonance imaging.
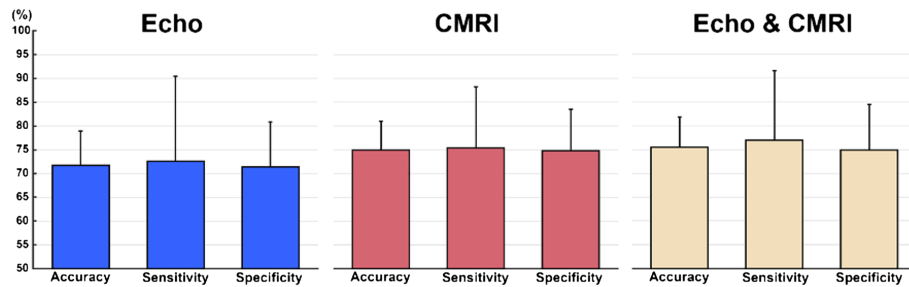
LVNC even in patients in the early disease. It is important that this health condition be considered by the physician when required to give permission for physical activity, professional or recreational. More prospective studies with a larger number of patients are needed to verify these findings.

This diagnostic and prognostic phenotypic heterogeneity results from a lack of knowledge about genetic mutations and their phenotypic expression. Van Waning *et al.* demonstrated the incremental value of the presence of genetic mutations in the risk stratification of LVNC patients.[34] The patients who had these mutations, in addition to ventricular remodelling and systolic dysfunction, had a worse prognosis than those without them.

Study limitations

Many different criteria have been suggested for LVNC diagnosis, and the use of quantification of LV non-compacted myocardial mass is another acceptable criterion.[35] In this study, we used the Petersen[20] criteria associated with three current echocardiographic criteria[5–7] to judge the ML algorithm.

We only included image parameters in the ML model, ruling out clinical data. The main goal of this study was to focus on determining findings from echo and CMRI that could be related in our established clinical outcome. Moreover, we did not compare it with other types of

cardiomyopathy, which certainly would enrich our findings. This is an ongoing study.

In this study, deformation indices for ventricular analysis were not included given that they were not a routine tool in our department in the beginning of the follow-up.

patients with normal ventricular function and without LGE had cardiac events. ML is a promising tool for analysing a large set of parameters in order to stratify patients with LVNC and to predict prognosis.

Conclusion

Our findings show the importance of biventricular assessment to detect high-risk patient profiles to plan a more aggressive therapeutic approach. The combination of the following parameters is the best method to predict MACE: LVEF (CMRI), RVESV (CMRI), RV systolic dysfunction (echo), and RV lower axis (CMRI) with high accuracy, sensitivity, and specificity. In addition, this study shows that even

Conflict of interest

None declared.

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