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ORIGINAL ARTICLE
Heart Failure

Simple Electrocardiographic Score Can Predict Left Ventricular Reverse Remodeling in Patients With Non-Ischemic Cardiomyopathy

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Background: Left ventricular reverse remodeling (LVRR) is a favorable response in non-ischemic, non-valvular cardiomyopathy (NICM) patients. Recently, 18-lead body surface electrocardiography (ECG), the standard 12-lead ECG with synthesized right-sided/posterior chest leads, has been developed, but its predictive value for LVRR has not been evaluated.

Methods and Results: Of 216 consecutive hospitalized NICM patients with LV ejection fraction (LVEF) ≤35%, we studied 125 who received optimization of their heart failure treatment and had 18-lead ECG and echocardiography data available for evaluating LVRR, defined as an absolute increase in LVEF ≥10% concomitant with LVEF ≥35% after 1-year optimized treatment. Most 18-lead ECG parameters in the NICM patients differed from those in 312 age- and body mass index-matched subjects with normal echocardiography. LVRR occurred in 59 NICM patients and they had a larger QRS amplitude in the limb leads (I, II, aVR, and aVF), precordial leads (V3–V6), and synthesized leads (syn-V4R–5R), decreased QRS axis and duration, and lower prevalence of fragmented QRS than those without LVRR. The ECG score using 3 selected parameters (QRS amplitude in aVR ≥675 μV; QRS duration <106 ms without fragmentation; and QRS axis <67°) was associated with the incidence of LVRR even after adjusting for optimized treatment.

Conclusions: The standard 12-lead ECG parameters are sufficiently predictive of LVRR in NICM patients.

Key Words: Cardiomyopathy; Electrocardiography; Reverse remodeling

Left ventricular reverse remodeling (LVRR) occurs in response to optimized treatment that reduces neurohormonal or hemodynamic factors in patients with cardiomyopathy and a reduced left ventricular ejection fraction (LVEF).[1] Identifying the possibility of LVRR when planning a treatment strategy for cardiomyopathy can provide a clinical advantage because LVRR is correlated with better prognosis.[2,3] LVRR occurs more often in patients with non-ischemic and non-valvular cardiomyopathy (NICM) compared with those with ischemic cardiomyopathy,[4,5] and wide QRS or left bundle branch block on the body surface electrocardiography (ECG) is a known indicator of a lower chance of LVRR occurring in NICM patients.[3,6] This, however, is not an adequate assessment of the potential for LVRR because of its low accuracy. ECG is a routine examination, therefore, ECG parameters with better predictive value for LVRR will be helpful in the clinical setting.

Recently, the synthesized 18-lead ECG, the standard 12-lead ECG with 6 additional synthesized leads (posterior, V7, V8, V9; right ventricular [RV] areas, V3R, V4R, V5R), has been developed. Additional information obtained from the synthesized 18-lead ECG can help to identify myocardial damage in coronary artery disease,[7] but its significance in NICM has not been examined. We hypothesized that the synthesized 18-lead ECG would provide good information reflecting the myocardial viability. Therefore, we examined the ability of various parameters from the synthesized 18-lead ECG to predict LVRR in NICM patients with reduced LVEF.

Methods

Subjects

We screened the medical records of 216 consecutive NICM patients aged ≥18 years old with LVEF ≤35% who were admitted to Osaka University Hospital from January 2011 to March 2016, and who received any optimization of their heart failure (HF) therapy, such as an uptitration of cardioprotective medications. Acute myocarditis was not

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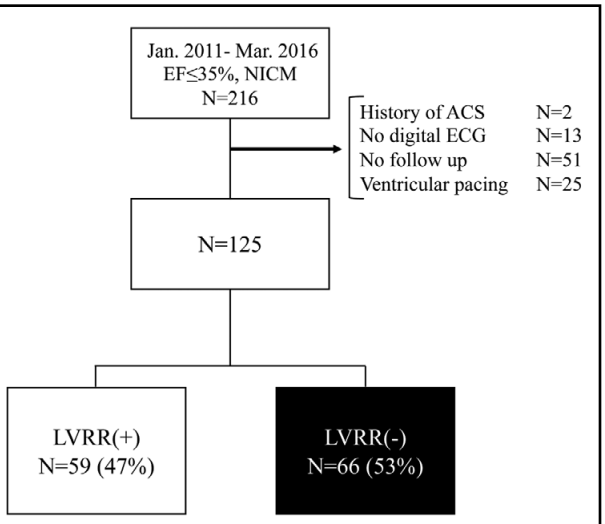

Figure 1. Flowchart of subject selection. Left ventricular reverse remodeling (LVRR) was noted in 59 patients (47%) at 1 year after optimized heart failure therapy. ACS, acute coronary syndrome; ECG, electrocardiography; EF, ejection fraction; NICM, non-ischemic and non-valvular cardiomyopathy; VAD, ventricular assist device.

included in NICM. The patients were excluded if they had (1) a history of acute coronary syndrome (n=2); (2) no digital ECG (n=13); (3) no follow-up (n=51); or (4) ventricular pacing (n=25). The patient characteristics and synthesized 18-lead ECG parameters before the optimization of the HF therapy and after around 1 year (median, 12 months; range, 10–15 months) were obtained as baseline and after 1 year of follow-up, respectively. Disease duration was defined as the period from the appearance of the HF symptoms, documentation of LVEF <50%, or diagnosis of cardiomyopathy. Control subjects (controls, n=312), who were matched by age and body mass index (BMI) to the NICM patients, were selected from the subjects who underwent echocardiography as screening for cardiovascular disease at Osaka University Hospital during the same period, and whose echocardiographic parameters (LVEF, LV end-diastolic dimension [LVDd], interventricular septum and posterior thickness, left atrial dimension, RV dimension, and degree of valvar regurgitation or stenosis) were in the normal range.[8] This study was approved by the Osaka University School of Medicine Review Board with a waiver of informed consent.

Definition of LVRR

LVRR was defined as an absolute increase in LVEF ≥10%[9] concomitant with LVEF ≥35%[10] after a 1-year optimized HF therapy (introduction or uptitration of β-blockers, renin-angiotensin system [RAS] blockers, or non-pharmacological therapy, including cardiac resynchronization therapy and a surgical repair of mitral regurgitation). The study patients were divided according to the presence or absence of LVRR at 1 year of follow-up into 2 groups: an LVRR (+) group and LVRR (−) group. The patients who underwent implantation of an LV assist device (LVAD) or died due to cardiac causes during the follow-up period were included in the LVRR (−) group.

Synthesized 18-Lead ECG

Resting standard surface 12-lead ECG was recorded on an ECG-1550 (Nihon Kohden, Tokyo, Japan; filter range, 0.05–150 Hz; AC filter, 60 Hz, 25 mm/s, 10 mm/mV). Six synthesized leads, namely, the right-sided/posterior chest leads (syn-V3R, V4R, V5R, and syn-V7, V8, and V9) were reconstructed from the digitally recorded standard 12-lead signals using an algorithm[11] and were also analyzed. When the dominant morphology of 10 s of recorded QRS waves was a paced QRS, the rhythm was defined as ventricular pacing. The heart rate (HR), PR time, QRS duration, amplitude, and axis, QT time, and T-wave axis were automatically measured based on the dominant morphology. The QRS amplitude was defined as the sum of the maximum positive and negative deflections. We defined the presence of a fragmented QRS (f-QRS) on 12-ECG according to a previous study.[12,13] Briefly, f-QRS was defined as the presence of various RSR' patterns (QRS duration <120 ms) with or without Q waves, which included an additional R wave (R') or notching of the R wave, notching of the S wave, or the presence of >2 R' (fragmentation) in 2 contiguous leads corresponding to a major lead set (anterior, inferoposterior, and lateral; **Supplementary Figure 1**). The ECG was analyzed without using any magnification, and a fragmentation was considered to be present if a visually identifiable signal was seen in more than half of the complexes of a particular lead. Strain pattern was defined as the presence of a downsloping convex ST segment with an inverted asymmetrical T wave opposite the QRS axis in leads V5 and/or V6.[14]

Endomyocardial Biopsy (EMB)

The EMB data obtained during clinical practice (n=106) were analyzed. At least 3 tissue samples from the RV septum were collected for histology and were fixed in 10% neutral buffered formalin, and then paraffin embedded. Specimens were stained with hematoxylin-eosin and Masson's trichrome, and the degree of myocardial fibrosis and hypertrophy was assessed using a semiquantitative scoring system by an experienced physician blinded to the clinical data as previously described.[15,16]

Statistical Analysis

Continuous variables are expressed as mean±SD. Differences in the clinical variables between the 2 groups were evaluated using Student's t-test or non-parametric Mann-Whitney U-test, as appropriate. In analyzing the ECG score with the clinical variables, the chi-squared trend test, Cochrane-Armitage trend test, and Jonckheere-Terpstra trend test were used for categorical and non-categorical data analyses. Steel test or Bonferroni correction was used for multiple comparisons. On receiver operating characteristic (ROC) curve analysis, the optimal cut-off point and area under the ROC curve (AUC) were determined automatically based on Youden's index. P<0.05 was considered to be statistically significant. Statistical analysis was performed using JMP Pro 14.0.0 (SAS Institute, Cary, NC, USA) and R version 3.4.1 ([2017-06-30]; "Single Candle"© 2017 The R Foundation for Statistical Computing).

Results

Clinical Characteristics

Of 125 NICM patients, 59 (47%) were classified into the LVRR (+) group. Three patients died of cardiac causes

Table 1. Baseline NICM Patient Characteristics vs. LVRR Status

	LVRR (+) (n=59)	LVRR (−) (n=66)	P-value
Age (years)	51±15	51±15	0.96
Male	44 (75)	42 (64)	0.19
BMI (kg/m^2)	22.8±4.5	21.8±3.9	0.28
SBP (mmHg)	114±22	97±13	<0.001
DBP (mmHg)	69±16	58±9	<0.001
LVDd (mm)	63±8	70±11	<0.001
LVDs (mm)	56±9	64±12	<0.001
LVEF (%)	24±6	23±8	1.00
MR ≥ moderate	9 (15)	25 (38)	<0.01
NYHA functional class I/II/III/IV (%)	7/58/25/10	3/36/36/24	0.03
β-blocker use	10 (17)	46 (70)	<0.001
RAS blocker use	9 (15)	39 (59)	<0.001
CRT implantation	0 (0)	2 (3)	0.18
AAD class III	2 (3)	17 (26)	<0.001
Hb (g/dL)	14.6±2.7	13.4±1.8	<0.01
Cr (mg/dL)	1.32±2.06	1.07±0.62	0.10
LogBNP	2.45±0.53	2.7±0.45	<0.01
Etiology			<0.001
DCM	36 (29)	52 (42)	
dHCM	1 (2)	9 (14)	
Secondary cardiomyopathy	22 (18)	5 (4)	
Disease duration (months)	23±43	94±112	<0.001
Hypertension	27 (46)	6 (9)	<0.001
Diabetes	19 (32)	15 (34)	0.23
Dyslipidemia	21 (36)	21 (32)	0.66
Smoking	38 (64)	35 (53)	0.20

Data given as mean±SD or n (%). AAD, anti-arrhythmic drug; BMI, body mass index; BNP, B-type natriuretic peptide; Cr, creatinine; CRT, cardiac resynchronisation therapy; DBP, diastolic blood pressure; DCM, dilated cardiomyopathy; dHCM, dilated hypertrophic cardiomyopathy; Hb, hemoglobin; LVDd, left ventricular end-diastolic dimension; LVDs, left ventricular end-systolic dimension; LVEF, left ventricular ejection fraction; LVRR, left ventricular reverse remodeling; MR, mitral regurgitation; NICM, non-ischemic and non-valvular cardiomyopathy; NYHA, New York Heart Association; RAS, renin-angiotensin system; SBP, systolic blood pressure.

and 20 had LVAD implantation during the follow-up period, and were classified into the LVRR (−) group (**Figure 1**). The baseline clinical characteristics are listed in **Table 1**. Between the LVRR (+) and LVRR (−) group, systolic blood pressure (SBP), LVDd, New York Heart Association (NYHA) functional class, use of β-blockers and RAS blockers, logB-type natriuretic peptide (BNP), etiology, and disease duration differed, whereas age, gender, BMI, and LVEF did not. Optimized HF therapy during the follow-up period was as follows: introduction or uptitration of β-blockers (73%) or RAS blockers (51%), CRT implantation (21%), cardioversion and/or catheter ablation of arrhythmia (10%), valvular surgery (7%), and skeletal myoblast sheet transplantation (2%). During follow-up, LVDd and LVEF in the LVRR (+) group improved (53±6 mm, 53±10%, respectively).

Synthesized 18-Lead ECG Parameters

First, we checked the gender differences in the synthesized 18-lead ECG parameters in the controls (**Supplementary Figure 2**). The QRS amplitude in the limb leads, synthesized right-sided leads, and posterior leads did not differ between the genders, whereas the PR time and QRS duration were prolonged, and the T axis and QRS amplitude in V2, V3, V4, and V5 were larger in male than female control subjects. Next, we assessed the differences in the ECG parameters between the control and NICM patients given the gender difference in the controls. Many parameters without a gender difference, such as the synthesized right-sided and posterior leads, significantly differed between the 2 groups (**Figure 2**). When we compared the NICM patients, stratified according to the presence of LVRR, with the controls, the LVRR (+) NICM patients had a preserved QRS amplitude in leads II, aVR, and aVF, smaller QRS axis, and larger QRS amplitude in leads I, III, and syn-V7 than the controls, whereas the LVRR (−) patients did not. In contrast, of the parameters with a gender difference, PR time, QRS duration, T axis, and QRS amplitude in leads V2 and V3 in both the male and female NICM patients differed from those in the controls (**Figure 3**). When we compared the NICM patients according to the presence of LVRR with the controls, the male and female LVRR (+) NICM patients had an increased amplitude in leads V2 and V3, whereas the LVRR (−) patients did not. Next, we assessed the differences in the ECG parameters between the 3 groups: controls; NICM LVRR (+); and LVRR (−) (**Table 2**). In the NICM patients, an increased QRS amplitude in some limb leads (I, II, aVR, aVF), the precordial leads (V3–V6), and synthesized right-sided leads (syn-V4R, V5R), a smaller QRS axis, shorter QRS duration, and the

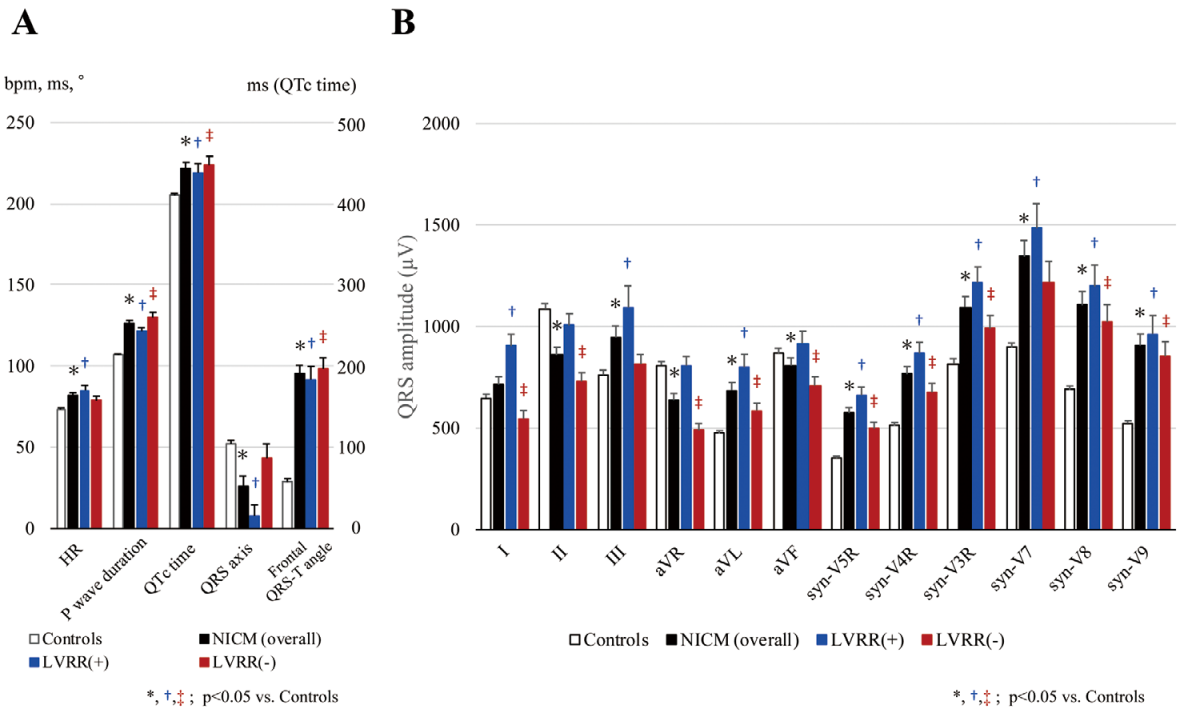

Figure 2. Synthesized 18-lead electrocardiogram (ECG) parameters with no gender difference in non-ischemic and non-valvular cardiomyopathy (NICM) patients according to left ventricular reverse remodeling (LVRR) status. (**A**) P-wave duration, corrected QT (QTc) time, and frontal QRS-T angle in the NICM patients differed from those in the controls. (**B**) The QRS amplitude in leads I, III, aVL, and syn-V7 was larger in the LVRR (+) group, whereas the QRS amplitude in leads II and aVR was smaller in the LVRR (–) group, than in the controls. Error bars, SEM. bpm, beats/min; HR, heart rate.

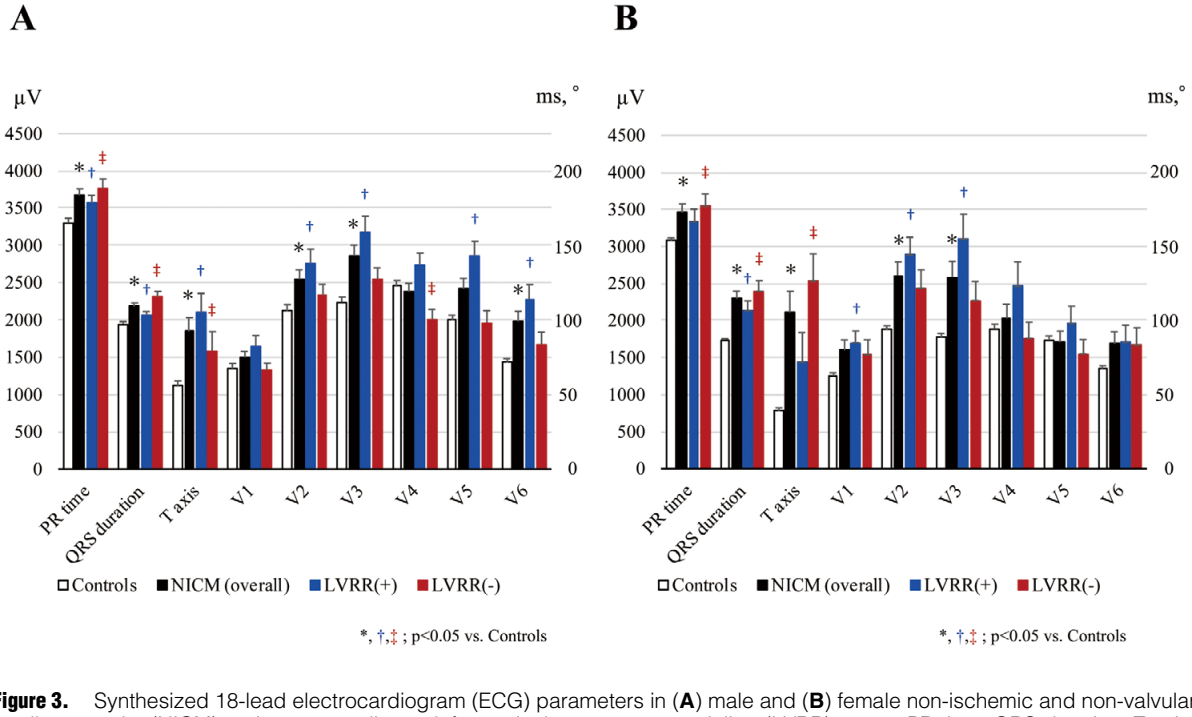

Figure 3. Synthesized 18-lead electrocardiogram (ECG) parameters in (**A**) male and (**B**) female non-ischemic and non-valvular cardiomyopathy (NICM) patients according to left ventricular reverse remodeling (LVRR) status. PR time, QRS duration, T axis, and QRS amplitude in leads V2 and V3 in both the (**A**) male and (**B**) female NICM patients differed from those in the controls. Error bars, SEM.

Table 2. ECG Parameters vs. LVRR Status

	Controls	LVRR(+)	LVRR(–)	P-value			AUC for detecting LVRR
				LVRR(+) vs. controls	LVRR(–) vs. controls	LVRR(+) vs. LVRR(–)	
AT/AF		14 (24)	11 (17)			0.32	
HR (beats/min)	73±1	85±3	79±3	<0.001	0.40	0.25	
P-wave duration (ms)	107±1	121±2	130±3	<0.001	<0.001	0.22	
PR time (ms)	158±2	174±4	184±5	0.02†	<0.001†	0.44†	
QRS duration (ms)	91±1	104±2	117±3	<0.001†	<0.001†	0.01†	0.64
Narrow QRS‡		47 (80)	41 (62)			0.03	
Fragmented QRS (–)§		36 (61)	16 (24)			<0.01	
Corrected QT time (ms)	411±1	438±4	448±6	<0.001	<0.001	0.41	
QRS axis (°)	52±2	8±7	43±9	<0.001	0.44	<0.01	0.66
T-wave axis (°)	45±2	96±11	96±11	<0.001†	<0.001†	1.00†	
Frontal QRS-T angle (°)	29±2	92±8	98±7	<0.001	<0.001	1.00	
Strain T pattern		16 (27)	17 (26)			0.86	
QRS amplitude (I) (μV)	650±18	905±58	547±40	<0.001	<0.001	<0.001	0.75
QRS amplitude (II) (μV)	1,088±25	1,006±59	731±43	0.45	<0.001	<0.001	0.71
QRS amplitude (III) (μV)	762±25	1,095±106	815±48	<0.001	0.44	0.06	
QRS amplitude (aVR) (μV)	811±16	807±46	489±34	1.00	<0.001	<0.001	0.76
QRS amplitude (aVL) (μV)	472±16	799±66	588±36	<0.001	<0.001	0.051	
QRS amplitude (aVF) (μV)	869±25	918±59	709±44	0.65	<0.001	<0.01	0.66
QRS amplitude (syn-V5R) (μV)	352±11	661±42	496±33	<0.001	<0.001	0.01	0.65
QRS amplitude (syn-V4R) (μV)	511±16	869±53	676±45	<0.001	<0.001	0.03	0.63
QRS amplitude (syn-V3R) (μV)	818±24	1,217±76	990±66	<0.001	0.04	0.11	
QRS amplitude (V1) (μV)	1,286±36	1,667±108	1,405±95	<0.01	0.85	0.27	
QRS amplitude (V2) (μV)	1,963±47	2,786±160	2,370±130	<0.001†	<0.01†	0.11†	
QRS amplitude (V3) (μV)	1,940±45	3,154±183	2,443±136	<0.001†	<0.01†	<0.01†	0.65
QRS amplitude (V4) (μV)	2,094±49	2,670±142	1,914±118	<0.001†	<0.01†	<0.001†	0.71
QRS amplitude (V5) (μV)	1,829±43	2,678±166	1,814±125	<0.001†	1.00†	<0.001†	0.69
QRS amplitude (V6) (μV)	1,376±32	2,133±163	1,668±138	<0.001	1.00	0.01	0.65
QRS amplitude (syn-V7) (μV)	898±22	1,485±121	1,220±102	<0.001	0.11	0.08	
QRS amplitude (syn-V8) (μV)	689±18	1,199±104	1,022±86	<0.001	<0.001	0.26	
QRS amplitude (syn-V9) (μV)	522±14	966±90	855±72	<0.001	<0.001	1.00	

Data given as mean±SE or n (%). †Adjusted for gender; ‡QRS duration <120 ms; §Assessed when QRS duration <120 ms. AT/AF, atrial tachycardia/atrial fibrillation; AUC, area under curve; ECG, electrocardiogram; HR, heart rate; LVRR, left ventricular reverse remodeling.

absence of f-QRS were associated with the incidence of LVRR. Considering these results and the gender differences in the ECG parameters, we selected 3 parameters: QRS amplitude in aVR (highest AUC for the QRS amplitudes; cut-off for the presence of LVRR, 675 μV; OR, 1.38 per 100-μV increase; 95% CI: 1.19–1.60, P<0.001), QRS duration without f-QRS (cut-off, 106 ms; OR, 4.0; 95% CI: 1.56–10.2, P<0.001), and QRS axis (cut-off, 67°; OR, 1.01 per 1° decrease; 95% CI: 1.00–1.02, P<0.01). Then, we created a simple ECG score, which was calculated by assigning 1 point for the presence of each of these 3 parameters. The AUC (0.82) of the ECG score using those 3 factors indicated a good prediction of LVRR, but the addition of the QRS amplitude in syn-V5R did not increase the predictive value (AUC, 0.81). The ECG score had a positive correlation with the incidence of LVRR at 1 year (**Figure 4**; P for trend <0.001). The ECG score also had a negative correlation with disease duration (P<0.001), logBNP (P<0.001), and presence of NYHA III/IV (P=0.04), and had a positive correlation with SBP (P<0.001). The correlation between the ECG score and incidence of LVRR still remained significant even after adjusting for the parameters that differed between the LVRR (+) and

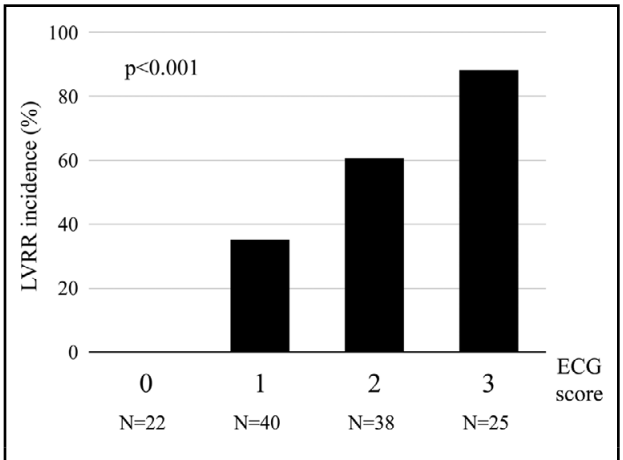

Figure 4. Left ventricular reverse remodeling (LVRR) incidence according to electrocardiography (ECG) score in patients with non-ischemic and non-valvular cardiomyopathy. The ECG score consisted of 3 independent parameters: QRS amplitude in aVR ≥675 μV; QRS duration <106 ms without fragmentation; and QRS axis <67° (P<0.001).

LVRR (−) NICM patients (**Table 3**).

ECG Score, Cardiac Magnetic Resonance and EMB

The ECG score was negatively correlated with the presence of late gadolinium enhancement (P<0.001) and LV end-diastolic volume (P<0.01), but not with LV mass on cardiac magnetic resonance (CMR, n=49; **Figure 5**). The degree of fibrosis and hypertrophy on EMB was associated with ECG score (**Figure 5**).

Changes in ECG Parameters After LVRR

Of 59 LVRR (+) NICM patients, the ECG parameters during follow-up were available for 46 patients. Compared with baseline, the QRS duration decreased during follow-up (102±6 vs. 98±6 ms, P=0.04). In contrast, prevalence of f-QRS (50% vs. 57%, P=0.53) and QRS axis (15±22° vs. 24±22°, P=0.20) did not change (**Supplementary Figure 3**). There was no difference in the QRS amplitude in lead aVR between that at baseline and that during follow-up (843±111 μV vs. 806±111 μV; P=0.26).

Table 3. Correlation Between ECG Score and Incidence of LVRR

ECG score	OR (95% CI)	P-value
Unadjusted	4.6 (2.7–8.0)	<0.001
Model 1	4.2 (1.8–9.7)	<0.001
Model 2	4.7 (2.2–8.8)	<0.001
Model 3	4.4 (2.2–9.1)	<0.001

Model 1, adjusted for age, etiology (DCM, dHCM, or secondary cardiomyopathy), dose of additional β-blockers (carvedilol equivalent), and logBNP. Model 2, adjusted for age, SBP, BMI, and ejection fraction. Model 3, adjusted for age, disease duration, MR ≥ moderate, and NYHA functional class III/IV. Abbreviations as in Tables 1,2.

Discussion

This study was an initial report evaluating the predictive value of the synthesized 18-lead ECG (standard 12-lead and synthesized 6-lead) parameters for LVRR in NICM patients with reduced LVEF. There were 3 major findings in the present study. First, most of the synthesized 18-lead ECG parameters in the NICM patients with reduced LVEF differed from the control subjects who had normal echocardiographic data. Second, the NICM patients who achieved LVRR with 1-year optimized HF therapy had a larger QRS amplitude in the limb leads (I, II, aVR, aVF), precordial leads (V3–V6), and synthesized chest leads (syn-V4R, V5R), smaller QRS axis, shorter QRS duration, and lower prevalence of f-QRS than those without LVRR. On ROC analysis the most predictive lead for LVRR among the QRS amplitude was aVR, not synthesized right-sided or posterior chest leads. Third, we created a simple ECG score consisting of 3 independent parameters: QRS amplitude in aVR; QRS duration without fragmentation; and QRS axis, which was a good predictor of LVRR. In the model with disease duration and baseline or titrated β-blocker dose, the ECG score was still associated with the

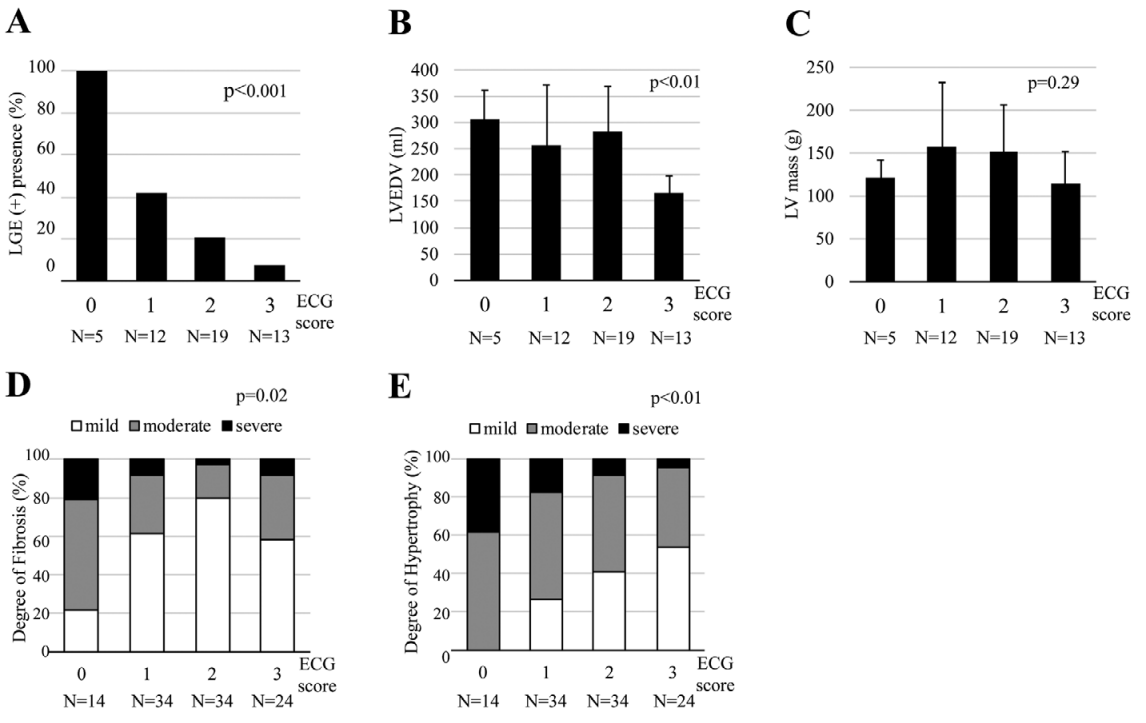

Figure 5. (**A**–**C**) Cardiac magnetic resonance and (**D**,**E**) endomyocardial biopsy findings according to electrocardiography (ECG) score in non-ischemic and non-valvular cardiomyopathy (NICM) patients. ECG score consisted of 3 independent parameters: QRS amplitude in aVR ≥675 μV; QRS duration <106 ms without fragmentation; and QRS axis <67°. Error bars, standard deviation. LGE, late gadolinium enhancement; LVEDV, left ventricular end-diastolic volume.

incidence of LVRR. The ECG score was associated with the severity of the HF and presence of myocardial hypertrophy and fibrosis. This indicates that the ECG score may be a comprehensive index related to the myocardial damage. In subgroup analysis with the patients who had right heart catheter data (n=83) or tricuspid annular plane systolic excursion (TAPSE; n=42), uptitrated dose of β-blocker was associated with the ECG score, whereas stroke volume, systemic vascular resistance, systolic pulmonary artery pressure and TAPSE were not (data not shown). This simple ECG score may be a useful marker for identifying NICM patients who will achieve LVRR with optimal treatment.

QRS Components and LVRR in NICM Patients

Although a decreased sum of the QRS amplitudes has been reported to be associated with adverse outcomes in NICM patients,[17] its predictive ability for LVRR is unknown. In NICM patients with severely reduced LVEF, low QRS amplitude may reflect decreased electrical activity of the entire heart. In the present NICM patients, decreased QRS amplitude in the precordial leads and synthesized right-sided chest leads was associated with the absence of LVRR, but compared with the control subjects, the QRS amplitude in the NICM patients was significantly increased, even in the NICM patients without LVRR, who were considered to have poor myocardial viability. Interestingly, the increased QRS amplitude normalized after the patients achieved an improved LV function with decreased heart size. This indicates that the QRS amplitude in the precordial and right-sided chest leads in NICM patients may reflect both myocardial viability and heart size. In contrast, a preserved QRS amplitude in lead aVR was also associated with the presence of LVRR. Although the reason why aVR was the best out of the 18 leads for predicting LVRR was unclear, it may be because aVR is a representative lead of the electric activity of the entire heart, because the average QRS axis in the NICM patients was 27±65°. In this study, prolonged QRS duration and presence of f-QRS were also associated with the absence of LVRR. This is consistent with previous reports.[4,6] A prolonged QRS duration may be related to severe LV dysfunction and structural changes in the conduction system.[6] The presence of f-QRS was considered to represent a heterogeneous activation of the ventricles due to myocardial scar and/or ischemia. Basaran et al argued that f-QRS complexes in NICM patients with narrow QRS is associated with intraventricular systolic dyssynchrony and subendomyocardial fibrosis on CMR.[18] In the present study, in 36 patients with narrow QRS who had CMR data, there was no association between f-QRS (34%) and late gadolinium enhancement (25%; P=0.49). One explanation may be the difficulty in detecting diffuse cardiac fibrosis in advanced NICM patients on late gadolinium enhancement on CMR.[19]

ECG Score

There have been several reports on ECG score with the standard 12-lead ECG. The Selvester QRS Scoring System (54 criteria, 32 points) is a well-known ECG score for predicting poor outcome in ischemic heart disease.[20] Recently, Hiraiwa et al reported on its usefulness as a predictor of cardiac events in non-ischemic dilated cardiomyopathy patients,[21] but its predictive value for myocardial reversibility is still unknown and the score is not simple for screening assessments. In this study, we created an ECG score with 3 independent parameters in order to simplify it as much as possible while maintaining predictive value. Additional information from the right-sided leads of the synthesized 18-lead ECG indicate that the condition of the RV may be associated with LVRR in NICM patients. The QRS amplitude in the synthesized right-sided leads, however, was correlated with that in lead aVR (P<0.001), and it lost significance for predicting LVRR in the model with lead aVR. Therefore, additional information in the synthesized right-sided leads failed to improve the predictive value of the ECG score on 12-lead ECG. An assessment using lead aVR may reflect the information of the whole heart, including the RV.

Study Limitations

There were several limitations to the present study. First, this was a retrospective, single-center study. The sample size of the NICM patients was relatively small. The present hospital is one of the core institutes for heart transplantation in Japan, but is not a community hospital, therefore there might have been a referral filter bias. Second, CMR, an assessment method for cardiomyopathy, was performed in less than half of the patients. Third, the amount of β-blockers and the disease duration at baseline varied. We analyzed the data by adjusting them with these parameters, but an unadjusted bias may have remained. Fourth, in this study, we classified the patients who died or were still on LVAD support at 1-year follow-up into the non-LVRR group because they did not achieve, at least, an obvious cardiac recovery. They might, however, have had reversible myocardium, and correct classification for them may be possible once accurate evaluation of LV recovery on LVAD support is established. Fifth, anti-arrhythmic drugs might have had some influence on the QRS morphology. Finally, although the synthesized and actual waveforms are almost identical,[22] the data directly recorded on the right-sided lead were not assessed in this study. Even with these limitations, we concluded that surface ECG was a universal, non-invasive, and very informative examination for predicting the potential for LVRR in NICM patients.

Conclusions

In planning a treatment strategy for NICM patients, assessing the ECG parameters can be helpful for evaluating whether there is a potential for LVRR.

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Disclosures

The authors declare no conflicts of interest.

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Supplementary Files

Please find supplementary file(s);
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