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Importance of lead aVR on predicting adverse cardiac events in patients with noncompaction cardiomyopathy

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Abstract

Background: Noncompaction cardiomyopathy (NCCM) is a relatively rare cardiac abnormality with high rates of mortality and morbidity. T-wave amplitudes during ventricular repolarization in lead aVR (TaVR) have been reported to be associated with the prognosis of various cardiovascular diseases. This study sought to investigate the prevalence and prognostic role of positive TaVR in patients with NCCM.

Methods: We evaluated consecutive 161 patients with NCCM (65.8% men, mean age 42.5 ± 15.2 years old). Presentation electrocardiogram was assessed regarding classical parameters as well as T-wave amplitudes in lead aVR. The primary endpoint was defined as composite lethal arrhythmic events, including sudden cardiac death, ventricular fibrillation, or sustained ventricular tachycardia or appropriate implantable cardioverter–defibrillator shock. Heart failure requiring hospitalization, cardiovascular death, and all-cause mortality were also investigated as secondary endpoints.

Results: Patients with positive TaVR showed higher rates for arrhythmic events, hospitalization for heart failure, and death compared with patients without it. In multivariate Cox model, after adjusting for other known clinical and electrocardiographic risk factors, the positive TaVR was found to be a strong independent predictor of primary endpoint (HR: 4.8, 95% CI: 1.2–19.3; p = .025) and all-cause death (HR: 3.5, 95% CI: 1.0–12.1; p = .045).

Conclusion: Our findings revealed that positive TaVR is significantly and independently associated with adverse outcomes in NCCM patients. This unique ECG criterion in the often ignored lead provides incremental information beyond what is available with other traditional risk factors.

KEYWORDS

electrocardiography, lead aVR, noncompaction cardiomyopathy, risk stratification, sudden cardiac death, T wave

1 | INTRODUCTION

Noncompaction cardiomyopathy (NCCM) is a relatively rare cardiac abnormality with characteristic morphology consisting of a two-layered myocardial structure with a thin epicardial layer and a noncompacted, thickened endocardial layer with multiple prominent ventricular trabeculations and deep intertrabecular recesses (Jenni, Oechslin, & van der Loo, 2007). The most commonly affected parts of the left ventricle by this process are inferior and lateral walls from the midcavity to the apex (Jenni, Oechslin, Schneider, Attenhofer Jost, & Kaufmann, 2001; Stollberger, Gerecke, Finsterer, & Engberding, 2013). The clinical course of these patients is highly heterogeneous, ranging from asymptomatic, coincidental discovery of the disease at one end of the spectrum to thromboembolic events, heart failure, and even sudden cardiac death (SCD) at the other end (Aras et al., 2006). Implantable cardioverter–defibrillators (ICDs) have been shown to be highly effective for the prevention of arrhythmic death (Kobza, Jenni, Erne, Oechslin, & Duru, 2008). Currently, knowledge about risk stratification, arrhythmogenesis, and prognosis is limited. Unfortunately, no reliable indicators of adverse outcomes have been established, and identifying high-risk patients most likely to benefit from an ICD is still a major clinical challenge.

The lead aVR is an often ignored lead in electrocardiographic (ECG) evaluation, but it may afford unique information as to some clinical settings such as ventricular tachyarrhythmias and left main coronary artery disease (Ducas et al., 2013; Kireyev, Arkhipov, Zador, Paris, & Boden, 2010; Vereckei, Duray, Szenasi, Altemose, & Miller, 2008). A positive T wave in lead aVR (TaVR), as a marker of repolarization abnormality, has been demonstrated to be predictive of the mortality and sudden cardiac death in the general population (Anttila et al., 2011; Badheka et al., 2013) as well as in certain cardiovascular disorders including ST-segment elevation myocardial infarction (STEMI), non-ST elevation myocardial infarction (NSTEMI), and heart failure (Ayhan et al., 2013; Icen & Koc, 2017; Kobayashi, Misumida, Aoi, & Kanei, 2017; Misumida et al., 2016; Okuda et al., 2011; Shinozaki, Tamura, & Kadota, 2011; Tan, Engel, Myers, Sandri, & Froelicher, 2008; Tanaka et al., 2017). However, no data are available as to T-wave alterations in lead aVR in patients with NCCM. Because the lead aVR sees the apical, lower lateral, and inferior regions of the left ventricle from the opposite side, we hypothesized that the presence of injured myocardium in these regions, as frequently seen in NCCM, would cause to an alteration in lead aVR. Therefore, the aim of this study was to analyze the prevalence of T-wave alterations in lead aVR and whether T-wave positivity in lead aVR predicts lethal arrhythmic events or a poor prognosis in patients with NCCM.

2 | MATERIAL AND METHODS

2.1 | Patient population

We retrospectively analyzed data on 161 consecutive patients (65.8% men, mean age 42.5 ± 15.2 years old) diagnosed with NCCM in our tertiary reference hospital from June 2001 to September 2017. Patients with left bundle branch block, ventricular pacing rhythm, a history of other known coinciding congenital, or acquired heart diseases and patients with significant missing data were not included. Demographic features, electrocardiographic, and echocardiographic parameters of all participants were attained from clinical presentation and examination recordings, clinical follow-up visits, medical charts of patients, and the electronic databases. This study was conducted according to the principles outlined in the Declaration of Helsinki, and the study protocol was approved by institutional ethics committee of our hospital.

2.2 | Echocardiography and NCCM definition

Patients were being assessed for NCCM with 2-dimensional and Doppler echocardiographic examinations by experienced echocardiographers. Left ventricular end-diastolic dimension (LVEDD), end-systolic dimension (LVESD), and left atrial (LA) diameter were measured. Left ventricular ejection fraction (LVEF) was calculated using the modified Simpson method. The noncompacted to compacted ratio was also assessed. In each patient, NCCM was diagnosed based on the presence of echocardiographic criteria previously described by Jenni et al. (2001). These criteria include (a) a characteristic thickened, two-layered myocardium with a compacted outer and a noncompacted inner layer, the ratio of noncompacted to compacted layer (NC/C) > 2 measured at end-systolic phase in parasternal short-axis view; (b) deep intertrabecular recesses filling with blood from the left ventricular cavity with color Doppler imaging; (c) typical distribution of the noncompacted walls are in the midlateral, midinferior, and apical left ventricle; and (d) absence of coinciding cardiac abnormalities for the isolated form of the disease.

2.3 | Evaluation of ECG findings

Standard 12-lead electrocardiograms (ECGs) were performed in a routine fashion in the supine position during quiet respiration and recorded at a paper speed of 25 mm/s and a standardization of 10 mm = 1 mV, in all patients. All ECGs were interpreted by two independent cardiologists who were blinded to all clinical and outcome data. Standard ECG parameters including heart rate, PR interval, QRS duration, QTc duration (Bazett's formula), right bundle branch block (RBBB), T-wave inversion, fragmented QRS (fQRS), J waves, and left ventricular hypertrophy (Sokolow & Lyon, 1947) were measured. In addition to these conventional ECG parameters, the polarity and amplitude of the T wave in lead aVR were evaluated. The amplitude of T wave in lead aVR was established as the first deflection after the QRS complex and/or maximum deviation from the PR isoelectric line. A positive (upright) T wave was defined as a wave with a dominant upward deflection (>0 mV) and a negative (nonupright) wave as one with dominant downward deflection (≤0 mV).

2.4 | Study endpoints

We described cardiac events as follows: an occurrence of appropriate implantable cardioverter–defibrillator discharge for fast ventricular

tachycardia/fibrillation (VT/VF); sustained VT or VF documented with ECG, telemetry monitoring, or Holter recording; SCD (witnessed, unexpected, and instantaneous collapse leading to death from a cardiac cause occurring <1 hr from symptom onset or within 24 hr of last having been observed in the usual state of health (if unwitnessed)); hospitalization for heart failure; cardiovascular death (SCD, death due to heart failure, and cardioembolic stroke-related death); and all-cause death. The follow-up duration was initiated with the date of his or her first evaluation and ended with the occurrence of death, arrhythmic event, or the date of his or her most recent evaluation.

The primary endpoint of the present study was a composite of lethal arrhythmic events that included SCD, documented VT, or VF or appropriate ICD therapy. Heart failure requiring hospitalization, cardiovascular death, and all-cause death were also assessed, respectively, as secondary endpoints. Follow-up for clinical endpoints was performed by review of medical records in our hospital. All interrogated ICD data were checked by cardiologists, who established whether ICD therapies were appropriate. We decided a cardiac event that occurred outside our hospital by direct interviews or phone calls with patients, their relatives, and/or their general practitioners. The cause of death was assessed by evaluating the hospital records, official hospital release forms, or death certificates obtained from National survival registry.

2.5 | Statistical analysis

Statistical analysis was performed using the SPSS statistical software version 23.0 (SPSS, Inc., IL, USA). Continuous variables were reported as mean ± *SD* and median with interquartile ranges as appropriate and categorical variables as frequency and percentage. To test the normality of distribution, Kolmogorov–Smirnov criterion was used. Comparisons of continuous variables between the 2 groups were analyzed with Student's *t* test for normally distributed variables and Mann–Whitney U test for variables without normal distribution. Chi-square or Fisher's exact test was utilized to compare categorical variables as appropriate. We first performed a univariate analysis to assess the relation of each variable with the occurrence of primary composite endpoint and all-cause death, respectively. Variables demonstrating a *p*-value < .05 in univariate analysis were entered in multivariate Cox proportional hazards model. Kaplan–Meier curve analysis was used for freedom from arrhythmic events, CV death, all-cause death, and heart failure requiring hospitalization in patients with or without positive TaVR. Differences between two patients groups were evaluated by use of the log-rank test. Receiver operating characteristic curve (ROC) analysis was utilized to find the optimum cutoff level for the amplitude of TaVR to predict the lethal arrhythmic events. The cutoff point was established using Youden's index. A *p*-value < .05 (using a two-sided test) was considered significant.

3 | RESULTS

From a total of 171 subjects with NCCM, 8 were excluded from this analysis because they had left bundle branch block and ventricular pacing rhythm (making the ECG uninterpretable) and 2 due to missing data in their files. The final study group consisted of 161 patients who fulfilled the inclusion criteria. Patients' baseline clinical, ECG, and echocardiographic characteristics are demonstrated in Table 1. A total of 10 patients (6.2%) had a family history of SCD, and 5 (3.1%) patients had unexplained syncope. Mean LV ejection fraction was 37.3 ± 13.3. One hundred and thirty-six (84.4%) patients were in sinus rhythm, whereas the remaining 25 (15.6%) were in atrial fibrillation. Cardiac magnetic resonance imaging (CMRI) was carried out in 34 patients, which further confirmed the diagnosis of NCCM. A total of 79 patients (49.1%) had ICD implantation.

We then compared patients with NCCM by the presence or absence of positive TaVR (Table 1). Positive TaVR was found in 66 (41.0%) of all study patients with no difference between both genders. In the positive TaVR group, the patients were older ($p = .042$) and had higher prevalence of atrial fibrillation ($p = .010$). With regard to echocardiographic parameters, patients with positive TaVR had higher LVEDD ($p < .001$), LVESD ($p = .007$), and lower EF ($p < .001$) in comparison to patients with negative TaVR. With regard to ECG parameters, patients with positive TaVR had increased width of QTc interval and QRS complex ($p = .004$ and $p = .019$, respectively) and higher prevalence of fragmented QRS ($p < .001$), as well as negative T waves ($p < .001$) in comparison to patients with negative TaVR.

During follow-up over a median (interquartile range [IQR]) of 36 (24–60) months, 6 (3.7%) patients died suddenly, 9 (5.6%) received an appropriate ICD therapy for VT/VF, and 7 (4.3%) resuscitated after cardiac arrest for a total of 22 (13.7%) patients with a combined primary endpoint. Table 2 shows the baseline characteristics, ECG, and echocardiographic parameters of the patients with and without the primary combined endpoint. As expected, patients in lethal arrhythmic event group had higher LVEDD ($p = .004$) and lower EF ($p = .002$) in comparison to patients with no event. With regard to ECG parameters, patients with arrhythmic event had increased width of QTc interval, higher prevalence of fragmented QRS, and T-wave inversion. Similarly, the prevalence of a positive T wave in lead aVR was significantly higher in lethal arrhythmic event group ($p < .001$).

Follow-up data and clinical outcomes were presented in Table 3. During follow-up period; cardiovascular death was observed as a secondary endpoint in 12 subjects (7.5%) (sudden death in 6 and death for progressive heart failure in 6), all-cause mortality was observed as a secondary endpoint in 17 subjects (10.6%), and heart failure requiring hospitalization was observed in 41 subjects (25.5%) among the study population. The presence of positive T wave in lead aVR was significantly associated with both primary and secondary study endpoints.

In Kaplan–Meier survival analysis, the cumulative incidence of lethal arrhythmic events occurred more frequently in patients with positive compared with negative TaVR (log-rank, $p < .001$, Figure 1). Also, patients with positive TaVR had a higher rate of hospitalization for heart failure, CV death, and all-cause death compared with patients without positive TaVR (log-rank, $p < .001$, $p < .001$ and $p = .003$, respectively. Figure 2).

TABLE 1 Baseline clinical, ECG, and echocardiographic characteristics of the study population according to the presence of positive T wave in lead aVR

	Total *n* = 161	aVR (+) *n* = 66	aVR (–) *n* = 95	*p* Value
Age	42.5 ± 15.2	45.4 ± 13.6	40.4 ± 10.6	**0.042**
Male gender, *n* (%)	106 (65.8%)	47 (71.2%)	59 (62.1%)	0.231
Hypertension, *n* (%)	27 (16.8%)	15 (22.7%)	2 (12.6%)	0.092
Diabetes, *n* (%)	11 (6.8%)	7 (10.6%)	4 (4.2%)	0.114
Smoking, *n* (%)	18 (11.2%)	7 (10.6%)	11 (11.6%)	0.847
BMI, (kg/m^2)	24 (21–27)	25 (20–28)	24 (21–27)	0.754
Coronary artery disease, *n* (%)	24 (14.9%)	13 (19.7%)	11 (11.6%)	0.155
Atrial fibrillation, *n* (%)	25 (15.6%)	16 (24.6%)	9 (9.5%)	**0.010**
Thromboembolic events, *n* (%)	9 (5.6%)	7 (10.6%)	2 (2.1%)	**0.021**
NYHA class III–IV	33 (20.5%)	18 (27.3%)	15 (15.8%)	0.076
Family history of SCD	10 (6.2%)	4 (6.1%)	6 (6.3%)	0.947
Syncope, *n* (%)	5 (3.1%)	2 (3.0%)	3 (3.2%)	0.963
Nonsustained VT, *n* (%)	31 (19.3%)	16 (24.2%)	15 (15.8%)	0.181
Medical treatment				
ACE inhibitor or ARB	83 (51.6%)	39 (59.1%)	44 (46.3%)	0.111
Beta-blockers	105 (65.2%)	48 (72.7%)	57 (60.0%)	0.095
Amiodarone	5 (3.1%)	2 (3.0%)	3 (3.2%)	0.963
Diuretics	51 (31.7%)	25 (26.3%)	26 (39.4%)	0.079
LVEDD (mm)	52.0 (46.0–60.0)	57.5 (49.0–6.24)	50.0 (46.0–54.0)	**<0.001**
LVESD	40.0 (34.0–49.0)	42.0 (38.0–50.0)	39.0 (26.0–48.0)	**0.007**
LVEF	37.3 ± 13.3	31.6 ± 10.4	41.3 ± 13.7	**<0.001**
LA diameter (mm)	41.0 (35.0–45.0)	42.0 (35.7–45.2)	39.0 (35.0–45.0)	0.141
Noncompact/compact ratio	3.0 (2.4–3.5)	3.1 (2.5–3.6)	3.0 (2.4–3.4)	0.062
Heart rate, beats/min	70 (65–74)	71.9 ± 12.4	69.7 ± 14.2	0.762
PR interval, ms	168 (136–198)	171.2 ± 37.9	177.9 ± 37.6	0.887
QRS duration, ms	108 (97–117)	112 (100–118)	101 (92–117)	**0.019**
QTc interval, ms	435 ± 43	447 ± 51	427 ± 34	**0.004**
Presence of J wave, *n* (%)	39 (24.2%)	11 (16.7%)	28 (29.5%)	0.062
Fragmented QRS, *n* (%)	85 (52.8%)	46 (69.7%)	39 (41.1)	**<0.001**
SV1 + RV5 leads, mV	30.9 ± 13.2	33.2 ± 14.2	29.3 ± 12.3	0.067
Left anterior fascicular block, *n* (%)	3 (1.9%)	0 (0.0%)	3 (2.2%)	0.145
Complete RBBB, *n* (%)	10 (6.2%)	2 (3.0%	8 (8.4%)	0.163
T-wave inversion (%)	58 (36.0%)	42 (63.5%)	16 (16.8%)	**<0.001**
aVR T-wave amplitude, mV	−0.2 ± 2.0	1.7 ± 1.2	−1.6 ± 1.0	**<0.001**

Note: Data are presented mean ± *SD*, median with interquartile ranges or *n* (%). Bolded values indicate statistical significance ($p < .05$).
Abbreviations: ACE: angiotensin-converting enzyme; ARB: angiotensin receptor blocker; BMI: body mass index; LA: Left atrium; LVEDD: left ventricular end-diastolic diameter; LVEF: left ventricular ejection fraction; NSVT: nonsustained ventricular tachycardia; RBBB: right bundle branch block; SCD: sudden cardiac death.

The receiver operating characteristic (ROC) analysis explored the discriminatory capability of T-wave amplitude in lead aVR for primary composite endpoint. Using a cutoff level of 0.1 mV for T-wave amplitude in lead aVR was determined to be an optimal point in discriminating lethal arrhythmic events (sensitivity 90.9%, specificity 66.9%, area under curve [AUC] = 0.791, CI 0.720–0.851; $p < .001$, Figure 3). In addition, the negative predictive value to predict primary endpoint was 97.8%.

Univariate Cox regression analyses showed that, LVEF, LVEDD, duration of QTc interval, T-wave inversion, and positive T waves in lead aVR were significantly associated with the primary endpoint (Table 4). However in the multivariate Cox model, positive TaVR (HR: 4.8, 95% CI: 1.2–19.3; $p = .025$) was the only independent predictor of the primary endpoint (Table 4). In addition, the presence of positive TaVR (hazard ratio 3.5, 95% CI 1.0–12.1, $p = .045$)

TABLE 2 Baseline characteristics of the study population according to the presence of lethal arrhythmic events

	Event (+) *n* = 22	Event (−) *n* = 139	*p* Value
Age	45.1 ± 15.1	42.0 ± 15.2	0.377
Male gender, *n* (%)	13 (59.1%)	93 (66.9%)	0.473
Hypertension, *n* (%)	4 (18.2%)	23 (16.5%)	0.849
Diabetes, *n* (%)	1 (4.5%)	10 (7.2%)	0.647
Smoking, *n* (%)	4 (18.2%)	14 (10.2%)	0.262
BMI, (kg/m^2)	23 (20–26)	24 (21–27)	0.221
Coronary artery disease, *n* (%)	5 (22.7%)	19 (13.7%)	0.268
Atrial fibrillation, *n* (%)	5 (23.8%)	20 (14.4%)	0.268
Thromboembolic events, *n* (%)	3 (13.6%)	6 (4.3%)	0.077
NYHA class III-IV	7 (31.8%)	26 (18.7%)	0.157
Family history of SCD	3 (13.6%)	7 (5.0%)	0.120
Syncope, *n* (%)	2 (9.1%)	3 (2.2%)	0.082
Nonsustained VT, *n* (%)	7 (31.8%)	24 (17.3%)	0.108
Medical treatment			
ACE inhibitor or ARB	10 (45.5%)	73 (52.5%)	0.538
Beta-blockers	17 (77.3%)	88 (63.3%)	0.201
Amiodarone	1 (4.5%)	4 (2.9%)	0.675
Diuretics	7 (31.8%)	44 (31,7%)	0.988
LVEDD (mm)	59.0 (50.0–69.0)	51.0(46.0–58.0)	**0.004**
LVESD (mm)	40.0 (37.2–57.2)	40.0(34.0–49.0)	0.227
LVEF (%)	29.1 ± 12.1	38.6 ± 13.1	**0.002**
LA diameter (mm)	41.0 (37.0–45.5)	41.0(35.0–45.0)	0.350
Noncompact/compact ratio	3.2 (2.8–3.5)	3.0(2.4–3.5)	0.128
Heart rate, beats/min	74 (65–80)	70 (65–73)	0.106
PR interval, ms	169 (131–198)	168 (136–198)	0.880
QRS duration, ms	118 (104–123)	110 (94–117)	0.257
QTc interval, ms	467 ± 47	430 ± 40	**<0.001**
Presence of J wave, *n* (%)	4 (18.2)	35 (25.2)	0.477
Fragmented QRS, *n* (%)	16 (72.7%)	69 (49.6%)	**0.044**
SV1 + RV5 leads, mV	32.5 ± 17.5	30.6 ± 12.5	0.541
Left anterior fascicular block, *n* (%)	0 (0.0%)	3 (2.2%)	0.487
Complete RBBB, *n* (%)	0 (0.0%)	10 (7.2%)	0.194
T-wave inversion (%)	13 (59.1%)	45 (32.4%)	**0.015**
Positive TaVR, *n* (%)	20 (90.9)	46 (33.1)	**<0.001**
aVR T-wave amplitude, mV	1.4 ± 1.0	−0.5 ± 2.0	**<0.001**

Note: Data are presented mean ± *SD*, median with interquartile ranges or *n* (%). Bolded values indicate statistical significance ($p < .05$).
Abbreviations: ACE: angiotensin-converting enzyme; ARB: angiotensin receptor blocker; BMI: body mass index; LA: Left atrium; LVEDD: left ventricular end-diastolic diameter; LVESD: left ventricular end-systolic diameter; LVEF: left ventricular ejection fraction; NSVT: nonsustained ventricular tachycardia; RBBB: right bundle branch block.

was also found as an independent predictor of all-cause mortality (Table 5).

In addition, there was a significant negative correlation between LVEF and T-wave amplitude in lead aVR ($p < .001$, Spearman's rho = −0.364) and significant positive correlation between LVEDD and T-wave amplitude in lead aVR ($p < .001$, Spearman's rho = 0.320).

4 | DISCUSSION

This study demonstrated that T-wave amplitude analysis in lead aVR provides prognostic information for NCCM patients beyond what is available from other well-known risk factors. The presence of positive TaVR remained a powerful and independent predictor of lethal arrhythmic events and mortality even after adjustment for

TABLE 3 Comparison of study endpoints according to the presence of positive T wave in lead aVR

Parameter	All *n* = 161	aVR (+), *n* = 66	aVR (−), *n* = 95	*p*
Lethal arrhythmic events	22 (13.7%)	20 (30.3%)	2 (2.1%)	**<0.001**
Sudden cardiac death	6 (3.7%)	5 (7.6%)	1 (1.1%)	**0.032**
Sustained VF/VT	7 (4.3%)	6 (9.1%)	1 (%1.1)	**0.014**
Appropriate ICD shock	9 (5.6%)	9 (13.6%)	0 (0.0%)	**<0.001**
Heart failure requiring hospitalization	41 (25.5%)	24 (36.4%)	17 (17.9%)	**0.008**
Cardiovascular death	12 (7.5%)	11 (16.7%)	1 (1.1%)	**<0.001**
All-cause death	17 (10.6%)	13 (19.7%)	4 (4.2%)	**0.002**

Note: Bolded values indicate statistical significance ($p < .05$).
Abbreviations: ICD: implantable cardioverter–defibrillator; VF: ventricular fibrillation; VT: ventricular tachycardia.

known risk factors such as LVEF, LV end-diastolic diameter, and other ECG risk markers. Furthermore, the presence of positive TaVR was significantly associated with all other secondary endpoints, hospitalization for heart failure, and cardiovascular death. To our knowledge, this study is the first of this kind to demonstrate that positive TaVR is a predictor of arrhythmic events and mortality in patients with NCCM.

NCCM has gained increasing attention in routine clinical practice in recent years due to its association with high rates of mortality and morbidity (Jenni et al., 2007). Importantly, these patients are liable to develop life-threatening ventricular tachyarrhythmias, which are still among their most frequent causes of death (Jenni et al., 2001). High-risk patients can be protected from arrhythmic death by ICD (Kobza et al., 2008). But, data as to risk stratification of cardiac events are limited owing to the scarcity of the disease. A number of clinical markers that influence prognosis have been described such as left ventricular dilatation, systolic dysfunction, and the extent of ventricular fibrosis (Andreini et al., 2016; Aras et al., 2006). However, not all patients at high risk can be identified with these risk factors. The lack of ability to predict prognosis precisely makes clinical decision-making challenging.

The lead aVR, a commonly neglected lead in rutin clinical practice, has been reported to have a unique diagnostic value in specific clinical settings including left main coronary artery lesions or diagnosis of cardiac arrhythmias (Ducas et al., 2013; Vereckei et al., 2008). In recent years, the presence of upright T wave in lead aVR, as a marker of repolarization abnormality, has been demonstrated to be an important predictor of adverse cardiac events in some clinical situations. Anttila et al. (Anttila et al., 2011) identified the prevalence of positive T wave in lead aVR to be 2.2% in the general population. They showed also the presence of this ECG finding was independently and strongly related with long-term cardiovascular mortality. In a study with 331 participants with narrow QRS complexes admitted for worsening heart failure, Okuda et al. (2011) demonstrated that a more positive T wave in lead aVR was an independent prognostic factor for risk stratification in heart failure patients.

In addition, previous reports have showed that positive TaVR is associated with sudden cardiac death which is possibly caused by ventricular arrhythmic events. A prior data from the Atherosclerosis Risk in Communities (ARIC) study (Rautaharju et al., 2013) reported a relation between the amplitude of the T wave

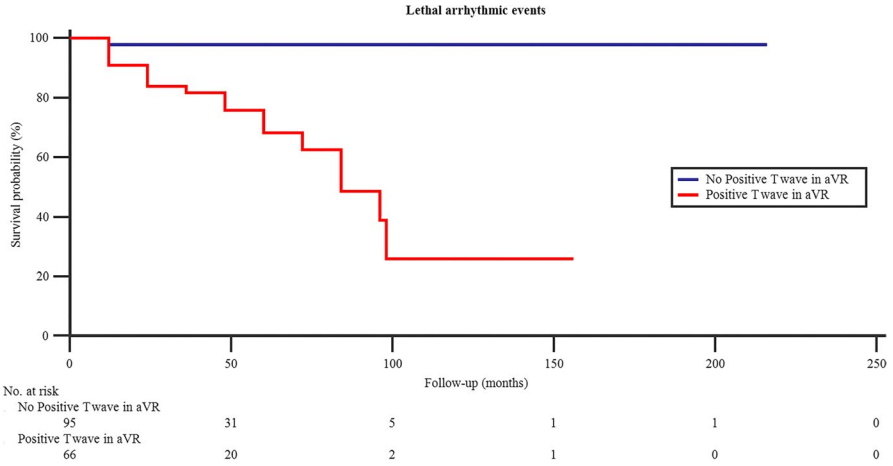

FIGURE 1 Kaplan–Meier curve analysis of the primary endpoint

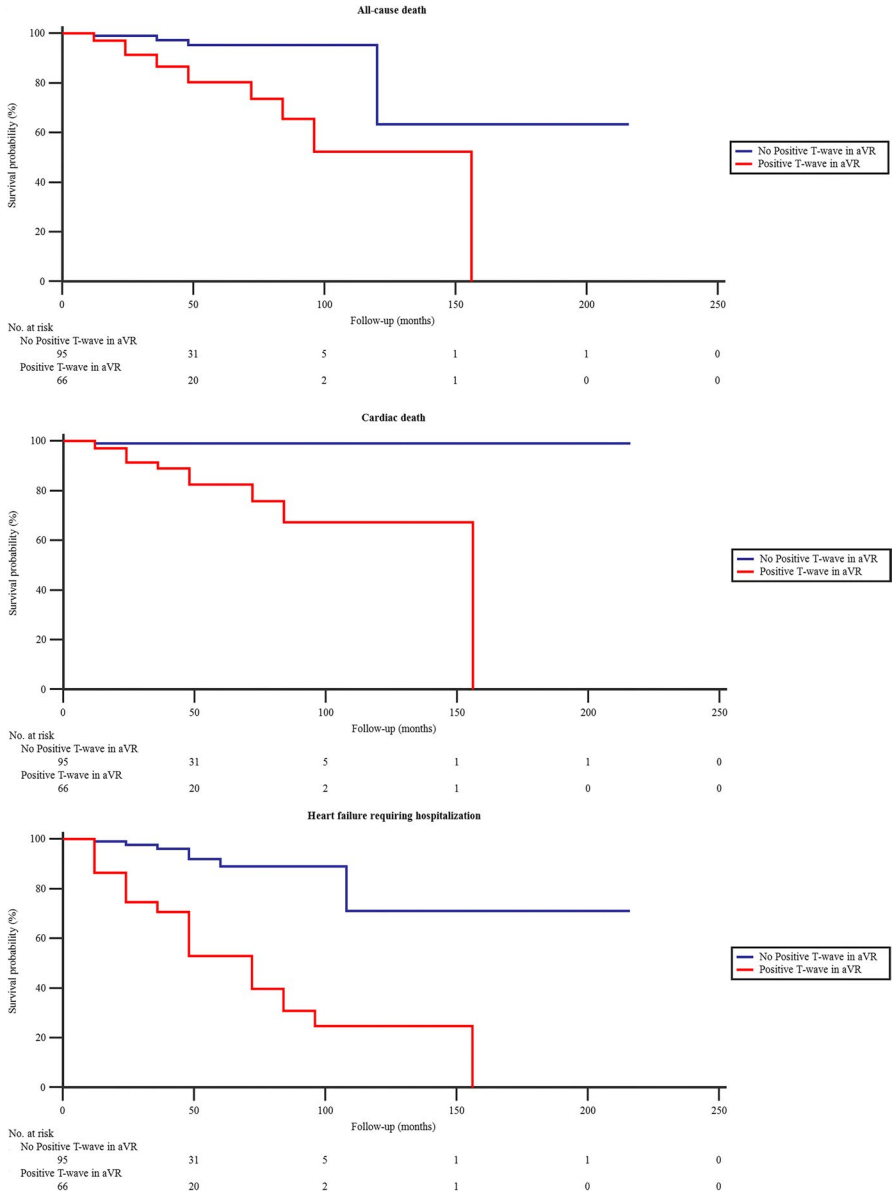

FIGURE 2 Kaplan–Meier curve analysis of the secondary endpoints

in lead aVR and cardiovascular mortality, including SCD. In another study, Al-Zaiti, Fallavollita, Canty, and Carey (2015) found that positive TaVR was significantly correlated with reduced EF and SCD presumably caused by major ventricular arrhythmic events. In a meta-analysis, T-wave amplitude in lead aVR was proved to be an important prognostic marker for arrhythmic events and SCD in ischemic heart failure patients (Al-Zaiti, Fallavollita, Wu, Tomita, & Carey, 2014). In a previous study from our group, we found that in patients with peripartum cardiomyopathy those with positive T waves in lead aVR had higher rates of left ventricular nonrecovery, arrhythmic events and mortality than those with negative T waves in lead aVR (Ekizler et al., 2019). In another study, Shinozaki et al. (2011) evaluated patients with old anterior wall MI who underwent cardiac catheterization and found patients with positive TaVR had lower LV ejection fractions, higher pulmonary arterial pressures, and greater LV end-diastolic and end-systolic volumes than those without it. In accordance with previous reports, in our study patients with a positive TaVR had lower LVEF, greater LVEDD and LVESD, and more severely reduced cardiac function. Thus, one may hypothesize that positive T-wave amplitude in lead aVR may be independently related with pathological LV remodeling.

The exact mechanism linking T wave positivity in lead aVR to the increased risk of cardiovascular mortality and SCD is speculative currently. Lead aVR is the only lead that opposes the direction of the main cardiac vector. All normally positive deflections on the surface ECG will be negative in this lead under normal circumstances (George, Arumugham, & Figueredo, 2010). The shape of the T wave is established by the spatial-temporal characteristics of ventricular repolarization, especially the asynchrony of phase 3 of the action potentials. When repolarization of injured myocardial cells is delayed comparing with that of normal cells, the direction of the T-wave vector alters toward the injured myocardial regions

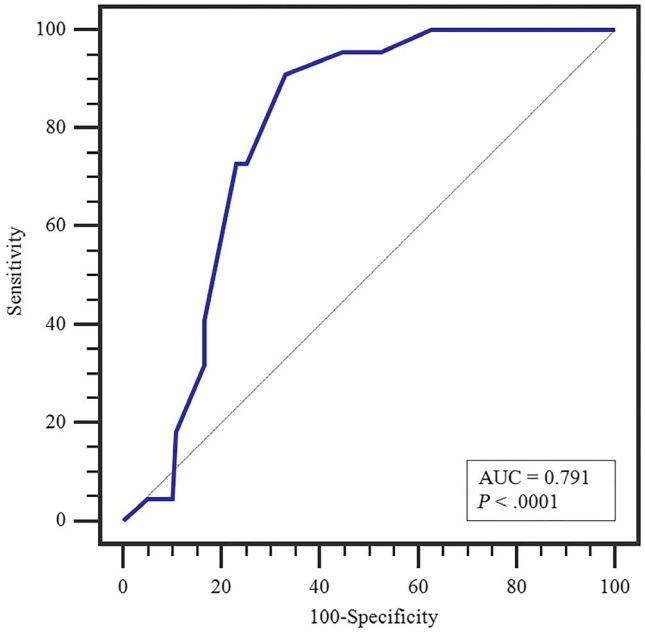

FIGURE 3 Receiver operating characteristic curve of T-wave amplitude in lead aVR for predicting primary endpoint

(George et al., 2010). The lead aVR sees the apical, lower lateral, and inferior regions of the left ventricle from the opposite side. Considering the position of the aVR lead, the presence of injured myocardium (ischemia and/or fibrosis) in the apical, lower lateral, and inferior regions of the left ventricle would make a normally negative T wave to be inverted and manifested as upright T wave in lead aVR (George et al., 2010). Because NCCM is a myocardial disease process most commonly affects the inferior and lateral walls from the midcavity to the apex of the left ventricle, it would be easily expected that it cause to inversion of T-wave vector to those injured regions due to the delayed repolarization, thus culminate in a positive T wave in lead aVR.

On the other hand, lead aVR has been neglected until recent years, primarily owing to the misconception that it gives only reciprocal information from the inferolateral and apical regions. It has been assumed that any myocardial injury that would cause T-wave inversions in the inferolateral leads would be accompanied by a reciprocally positive TaVR (Rautaharju et al., 2009). This assumption partly explains the high prevalence of T-wave inversion (63.5%) in our study population with positive TaVR. However, according to our study findings, only positive TaVR revealed a strong and independent relation with primary endpoint in terms of multivariate regression analysis. So, we postulated that positive T-wave amplitudes in lead aVR were not only mirror images of T-wave inversions in inferolateral leads, but also a more susceptible marker of myocardial injury and possibly widespread pathological remodeling in cases of NCCM.

The precise substrate for ventricular arrhythmic events in patients with NCCM is not delineated. Nevertheless, it is hypothesized that developmental blockage of conduction and the presence of intratrabecular recesses may create substrates for reentrant circuits (Derval, Jais, O'Neill, & Haissaguerre, 2009). Subendocardial ischemia and fibrosis have been demonstrated in NCCM patients anatomically and pathophysiologically. Jenni et al. (2001) revealed the histological findings of patients with NCCM showing ischemic lesions and interstitial fibrosis in the endocardium and prominent trabeculae. Previous studies utilizing cardiac MR imaging and scintigraphy with thallium-201 demonstrated that subendocardial perfusion defects correlate with regions of noncompacted myocardium in NCCM (Finsterer, Stollberger, & Feichtinger, 2002; Ichida et al., 1999). In addition, abnormal ion channel activity, cell-to-cell coupling, and microvascular dysfunction in the noncompacted myocardial segments were described in patients with NCCM (Steffel et al., 2009). Furthermore, it is assumed that increased trabeculation with deep intramyocardial recesses moving the Purkinje system deeper into the myocardium (Burke, Mont, Kutys, & Virmani, 2005). These alterations cause both delayed depolarization and inhomogeneous repolarization. This transmural heterogeneity may culminate in the development of lethal ventricular arrhythmias. The presence of positive TaVR on ECG has been accepted as a marker of repolarization abnormality. The mechanism of its occurence in NCCM has might be explained by this myocardial conduction delay and inhomogeneous repolarization of the ventricles because of myocardial scar and/or ischemia. Therefore, the percentage of positive TaVR (90%) found in this study in NCCM patients with lethal ventricular arrhythmic events could be significant. Interestingly, positive TaVR was also frequently (33%) observed in NCCM patients without ventricular arrhythmic events, possibly reflecting the high rates of repolarization abnormalities seen in NCCM patients.

While we attempt to differentiate between divergent etiologies of cardiac death (sudden vs. related to CHF), it is possible that there is some extent of misclassification. Therefore, we also reported all-cause death, because it is more objective and less biased than cardiac death. The presence of positive TaVR was also found as an independent predictor of all-cause death. Increased myocardial ischemia-/fibrosis-associated heart failure may be a probable mechanism for elevated mortality rates in patients with positive TaVR. Our findings support this hypothesis that patients with positive TaVR had significantly lower LVEF and higher left ventricular end-diastolic and end-systolic diameter than those without it. Importantly, the observed modest correlations of T-wave amplitudes with LV dysfunction and LV dilatation afford new insights in understanding the complex mechanisms involved in risk stratification using this simple risk marker.

We also studied other ECG findings, and also however, positive TaVR was superior to any other ECG findings in the establishment of patients most at risk for adverse cardiac events. This could be in part because lead aVR may afford sufficient information on a wide range of electrophysiological activities in the almost entirety of the regions which are affected by NCCM. This special feature of TaVR on a simple and widely available surface ECG may enable us to establish high-risk patients with NCCM.

TABLE 4 Univariate and multivariate Cox regression analyses for prediction of composite primary endpoint

	Univariate analysis			Multivariate analysis		
Variable	HR	95% CI	p Value	HR	95% CI	p Value
Age	1.007	0.979–1.036	0.639			
Gender	1.300	0.554–3.053	0.547			
Hypertension	1.071	0.361–3.173	0.902			
Diabetes	0.488	0.065–3.679	0.486			
Smoking	2.226	0.749–6.617	0.150			
BMI	0.916	0.817–1.027	0.135			
Coronary artery disease	1.422	0.520–3.888	0.493			
Atrial fibrillation	1.251	0.439–3.562	0.675			
Family history	1.769	0.513–6.104	0.367			
Syncope,	3.787	0.871–16.467	0.076			
Nonsustained VT	1.778	0.714–4.430	0.217			
NYHA class III–IV	1.914	0.778–4.706	0.157			
β-blocker	1.248	0.452–3.444	0.669			
ACE inhibitor or ARB	0.590	0.253–1.376	0.222			
Amiodarone	2.062	0.272–15.618	0.484			
LVEF	0.951	0.916–0.988	0.010	0.971	0.927–1.016	0.196
LVESD	1.016	0.972–1.062	0.486			
LVEDD (mm)	1.062	1.020–1.105	0.003	1.019	0.977–1.063	0.387
LA diameter (mm)	1.032	0.969–1.099	0.327			
Noncompact/compact ratio	1.787	0.810–3.945	0.151			
PR interval	0.997	0.983–1.011	0.668			
QRS duration	1.006	0.985–1.028	0.576			
QTc duration	1.010	1.001–1.019	0.026	1.005	0.995–1.014	0.348
Presence of J wave	0.840	0.283–2.498	0.754			
Fragmented QRS	2.140	0.832–5.503	0.114			
SV1 + RV5 leads, mV	1.015	0.986–1.045	0.315			
T-wave inversion	2.922	1.246–6.854	0.014	1.689	0.617–4.618	0.308
Positive T wave in lead Avr	9.215	2.724–31.170	<0.001	4.856	1.220–19.327	0.025
aVR T-wave amplitude	1.448	1.191–1.759	**<0.001**			

Abbreviations: ACE: angiotensin-converting enzyme; ARB: angiotensin receptor blocker; BMI: body mass index; CI: confidence interval; HR: hazard ratio; LA: left atrium; LV: left ventricle; LVEDD: left ventricular end-diastolic diameter; LVESD: left ventricular end-systolic diameter; LVEF: left ventricular ejection fraction; RBBB: right bundle branch block; SCD: sudden cardiac death

4.1 | LIMITATIONS

The present study should be interpreted with some limitations. First, the retrospective observational design may affect the strength of the study. Although one of the largest series of patients with NCCM was investigated, the study population was still limited in size due to the paucity of NCCM. Our study took place in a single tertiary referral center, which may decrease the generalizability of our results to the general NCCM population. We excluded patients with NCCM who had left bundle branch block or ventricular pacing rhythm, which could affect the results. Unfortunately, contrast-enhanced cardiovascular magnetic resonance which might have helped to improve the understanding of the underlying arrhythmia substrate was not performed at the initial evaluation in all NCCM patients, systematically. Another limitation is that we assessed only initial presenting electrocardiograms, and potential temporal alterations in T-wave amplitudes were not evaluated in this study. Rather than a causal association, we only showed a relation between positive T waves in lead aVR and adverse cardiac outcomes. Therefore, this study should be noted as hypothesis generating. Prospective and large-scale studies are necessary to confirm these findings and to clarify the underlying mechanism.

5 | CONCLUSION

This study provides evidence that positive TaVR is associated with increased arrhythmic events, more severe systolic dysfunction, CV

TABLE 5 Univariate and multivariate Cox regression analyses for prediction of all-cause death

	Univariate analysis			Multivariate analysis		
Variable	**HR**	**95% CI**	***p* Value**	**HR**	**95% CI**	***p* Value**
Age	1.015	0.982–1.050	0.374			
Gender	0.948	0.349–2.576	0.917			
Hypertension	1.655	0.566–4.839	0.358			
Diabetes	1.639	0.422–6.368	0.475			
BMI	0.938	0.822–1.070	0.341			
Coronary artery disease	1.741	0.590–5.139	0.315			
Atrial fibrillation	1.607	0.516–5.008	0.413			
Family history	1.435	0.113–9.104	0.342			
Syncope,	1.048	0.271–11.467	0.647			
Nonsustained VT	0.447	0.099–2.010	0.294			
NYHA class III–IV	1.918	0.654–5.622	0.235			
β-blocker	2.389	0.534–10.680	0.254			
ACE inhibitor or ARB	1.035	0.366–2.924	0.948			
Amiodarone	3.120	0.399–24.394	0.278			
LVEF	0.951	0.909–0.995	**0.031**	0.955	0.913–0.999	**0.047**
LVESD	1.017	0.966–1.072	0.521			
LVEDD (mm)	1.048	0.998–1.100	0.060			
LA diameter (mm)	1.101	1.023–1.184	**0.010**	1.071	0.973–1.180	0.162
Noncompact/compact ratio	1.405	0.597–3.303	0.436			
PR interval	1.021	1.002–1.040	0.059			
QRS duration	0.977	0.946–1.010	0.166			
QTc duration	1.013	1.003–1.024	**0.009**	1.002	0.991–1.013	0.758
Presence of J wave	0.271	0.035–2.071	0.208			
Fragmented QRS	0.853	0.316–2.303	0.754			
SV1 + RV5 leads, mV	0.947	0.906–0.989	**0.014**	0.949	0.909–0.991	**0.018**
T-wave inversion	1.815	0.694–4.744	0.224			
Positive T wave in lead aVR	3.440	1.209–9.788	**0.021**	3.530	1.026–12.145	**0.045**
aVR T-wave amplitude	1.364	1.095–1.699	**0.006**			

Abbreviations: ACE: angiotensin-converting enzyme; ARB: angiotensin receptor blocker; BMI: body mass index; CI: confidence interval; HR: hazard ratio; LA: left atrium; LV: left ventricle; LVEDD: left ventricular end-diastolic diameter; LVESD: left ventricular end-systolic diameter; LVEF: left ventricular ejection fraction; RBBB: right bundle branch block; SCD: sudden cardiac death

death, and all-cause death in NCCM patients. Beyond the insufficient understanding of the mechanisms, it is worthy of note that a simple subjective assessment of a positive T wave in lead aVR allows the recognition of patients at high risk of adverse CV outcomes. Therefore, we recommend that assessment of T-wave amplitude in lead aVR should be performed on a routine basis in patients with NCCM given its high sensitivity and negative predictive value for predicting adverse cardiac events. But further confirmatory studies are required before considering positive T wave in lead aVR as a prognostic marker to use in making management decisions in this challenging myocardial disorder.

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CONFLICT OF INTEREST

The authors report no financial relationships or conflicts of interest regarding the content herein.

DATA AVAILABILITY STATEMENT

The datasets supporting the conclusions of the study are included in the article. Any additional data will be available on request.

ETHICAL APPROVAL AND CONSENT TO PARTICIPATE

This study was submitted to and approved by the Ethics Commission of Turkiye Yuksek Ihtisas Training and Research Hospital. This is a retrospective study, so the content to participate is not applicable.

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REFERENCES

Al-Zaiti, S. S., Fallavollita, J. A., Canty, J. M., & Carey, M. G. (2015). The prognostic value of discordant T waves in lead aVR: A simple risk marker of sudden cardiac arrest in ischemic cardiomyopathy. *Journal of Electrocardiology*, *48*(5), 887–892. https://doi.org/10.1016/j.jelectrocard.2015.06.013

Al-Zaiti, S. S., Fallavollita, J. A., Wu, Y. W., Tomita, M. R., & Carey, M. G. (2014). Electrocardiogram-based predictors of clinical outcomes: A meta-analysis of the prognostic value of ventricular repolarization. *Heart and Lung*, *43*(6), 516–526. https://doi.org/10.1016/j.hrtlng.2014.05.004

Andreini, D., Pontone, G., Bogaert, J., Roghi, A., Barison, A., Schwitter, J., … Masci, P. G. (2016). Long-term prognostic value of cardiac magnetic resonance in left ventricle noncompaction: A prospective multicenter study. *Journal of the American College of Cardiology*, *68*(20), 2166–2181. https://doi.org/10.1016/j.jacc.2016.08.053

Anttila, I., Nikus, K., Nieminen, T., Jula, A., Salomaa, V., Reunanen, A., … Kähönen, M. (2011). Relation of positive T wave in lead aVR to risk of cardiovascular mortality. *The American Journal of Cardiology*, *108*(12), 1735–1740. https://doi.org/10.1016/j.amjcard.2011.07.042

Aras, D., Tufekcioglu, O., Ergun, K., Ozeke, O., Yildiz, A., Topaloglu, S., … Korkmaz, S. (2006). Clinical features of isolated ventricular noncompaction in adults long-term clinical course, echocardiographic properties, and predictors of left ventricular failure. *Journal of Cardiac Failure*, *12*(9), 726–733. https://doi.org/10.1016/j.cardfail.2006.08.002

Ayhan, E., Isik, T., Uyarel, H., Ergelen, M., Cicek, G., Ghannadian, B., & Eren, M. (2013). Prognostic significance of T-wave amplitude in lead aVR on the admission electrocardiography in patients with anterior wall ST-elevation myocardial infarction treated by primary percutaneous intervention. *Annals of Noninvasive Electrocardiology*, *18*(1), 51–57. https://doi.org/10.1111/j.1542-474X.2012.00530.x

Badheka, A. O., Patel, N. J., Grover, P. M., Shah, N., Singh, V., Deshmukh, A., … Cohen, M. G. (2013). ST-T wave abnormality in lead aVR and reclassification of cardiovascular risk (from the National Health and Nutrition Examination Survey-III). *American Journal of Cardiology*, *112*(6), 805–810. https://doi.org/10.1016/j.amjcard.2013.04.058

Burke, A., Mont, E., Kutys, R., & Virmani, R. (2005). Left ventricular noncompaction: A pathological study of 14 cases. *Human Pathology*, *36*(4), 403–411. https://doi.org/10.1016/j.humpath.2005.02.004

Derval, N., Jais, P., O'Neill, M. D., & Haissaguerre, M. (2009). Apparent idiopathic ventricular tachycardia associated with isolated ventricular noncompaction. *Heart Rhythm: The Official Journal of the Heart Rhythm Society*, *6*(3), 385–388. https://doi.org/10.1016/j.hrthm.2008.11.020

Ducas, R., Ariyarajah, V., Philipp, R., Ducas, J., Elliott, J., Jassal, D., … Hussain, F. (2013). The presence of ST-elevation in lead aVR predicts significant left main coronary artery stenosis in cardiogenic shock resulting from myocardial infarction: The Manitoba cardiogenic shock registry. *International Journal of Cardiology*, *166*(2), 465–468. https://doi.org/10.1016/j.ijcard.2011.11.003

Ekizler, F. A., Cay, S., Kafes, H., Ozeke, O., Ozcan, F., Topaloglu, S., … Aras, D. (2019). The prognostic value of positive T wave in lead aVR: A novel marker of adverse cardiac outcomes in peripartum cardiomyopathy. *Annals of Noninvasive Electrocardiology*, *24*(3), e12631. https://doi.org/10.1111/anec.12631

Finsterer, J., Stollberger, C., & Feichtinger, H. (2002). Histological appearance of left ventricular hypertrabeculation/noncompaction. *Cardiology*, *98*(3), 162–164. https://doi.org/10.1159/000066316

George, A., Arumugham, P. S., & Figueredo, V. M. (2010). aVR – the forgotten lead. *Experimental & Clinical Cardiology*, *15*(2), e36–44.

Icen, Y. K., & Koc, M. (2017). ST segment change and T wave amplitude ratio in lead aVR associated with coronary artery disease severity in patients with non-ST elevation myocardial infarction: A retrospective study. *Medicine (Baltimore)*, *96*(49), e9062. https://doi.org/10.1097/MD.0000000000009062

Ichida, F., Hamamichi, Y., Miyawaki, T., Ono, Y., Kamiya, T., Akagi, T., … Tomimatsu, H. (1999). Clinical features of isolated noncompaction of the ventricular myocardium: Long-term clinical course, hemodynamic properties, and genetic background. *Journal of the American College of Cardiology*, *34*(1), 233–240. https://doi.org/10.1016/S0735-1097(99)00170-9

Jenni, R., Oechslin, E., Schneider, J., Attenhofer Jost, C., & Kaufmann, P. A. (2001). Echocardiographic and pathoanatomical characteristics of isolated left ventricular non-compaction: A step towards classification as a distinct cardiomyopathy. *Heart*, *86*(6), 666–671. https://doi.org/10.1136/heart.86.6.666

Jenni, R., Oechslin, E. N., & van der Loo, B. (2007). Isolated ventricular non-compaction of the myocardium in adults. *Heart*, *93*(1), 11–15. https://doi.org/10.1136/hrt.2005.082271

Kireyev, D., Arkhipov, M. V., Zador, S. T., Paris, J. A., & Boden, W. E. (2010). Clinical utility of aVR-the neglected electrocardiographic lead. *Annals of Noninvasive Electrocardiology*, *15*(2), 175–180. https://doi.org/10.1111/j.1542-474X.2010.00359.x

Kobayashi, A., Misumida, N., Aoi, S., & Kanei, Y. (2017). Positive T wave in lead aVR as an independent predictor for 1-year major adverse cardiac events in patients with first anterior wall ST-segment elevation myocardial infarction. *Annals of Noninvasive Electrocardiology*, *22*(6), e12442. https://doi.org/10.1111/anec.12442

Kobza, R., Jenni, R., Erne, P., Oechslin, E., & Duru, F. (2008). Implantable cardioverter-defibrillators in patients with left ventricular noncompaction. *Pacing and Clinical Electrophysiology*, *31*(4), 461–467. https://doi.org/10.1111/j.1540-8159.2008.01015.x

Misumida, N., Kobayashi, A., Fox, J. T., Hanon, S., Schweitzer, P., & Kanei, Y. (2016). Predictive value of ST-segment elevation in lead aVR for left main and/or three-vessel disease in non-ST-segment elevation myocardial infarction. *Annals of Noninvasive Electrocardiology*, *21*(1), 91–97. https://doi.org/10.1111/anec.12272

Okuda, K., Watanabe, E., Sano, K., Arakawa, T., Yamamoto, M., Sobue, Y., … Ozaki, Y. (2011). Prognostic significance of T-wave amplitude in lead aVR in heart failure patients with narrow QRS complexes. *Annals of Noninvasive Electrocardiology*, *16*(3), 250–257. https://doi.org/10.1111/j.1542-474X.2011.00439.x

Rautaharju, P. M., Surawicz, B., Gettes, L. S., Bailey, J. J., Childers, R., Deal, B. J., … Heart Rhythm, S. (2009). AHA/ACCF/HRS recommendations for the standardization and interpretation of the electrocardiogram: Part IV: The ST segment, T and U waves, and the QT interval: A scientific statement from the American Heart Association Electrocardiography and Arrhythmias Committee, Council on Clinical Cardiology; the American College of Cardiology Foundation; and the Heart Rhythm Society: Endorsed by the International Society for Computerized Electrocardiology. *Circulation*, *119*(10), e241–250. https://doi.org/10.1161/CIRCULATIONAHA.108.191096

Rautaharju, P. M., Zhang, Z.-M., Warren, J., Gregg, R. E., Haisty, W. K., Kucharska-Newton, A. M., … Soliman, E. Z. (2013). Electrocardiographic predictors of coronary heart disease and sudden cardiac deaths in men and women free from cardiovascular disease in the Atherosclerosis Risk in Communities study. *Journal of the*

American Heart Association, *2*(3), e000061. https://doi.org/10.1161/JAHA.113.000061

Shinozaki, K., Tamura, A., & Kadota, J. (2011). Associations of positive T wave in lead aVR with hemodynamic, coronary, and left ventricular angiographic findings in anterior wall old myocardial infarction. *Journal of Cardiology*, *57*(2), 160–164. https://doi.org/10.1016/j.jjcc.2010.12.002

Sokolow, M., & Lyon, T. P. (1947). Criteria for the diagnosis of right ventricular hypertrophy using unipolar limb and precordial leads. *Am J Med*, *3*(1), 125. https://doi.org/10.1016/0002-9343(47)90136-8.

Steffel, J., Kobza, R., Namdar, M., Wolber, T., Brunckhorst, C., Luscher, T. F., … Duru, F. (2009). Electrophysiological findings in patients with isolated left ventricular non-compaction. *Europace*, *11*(9), 1193–1200. https://doi.org/10.1093/europace/eup187

Stollberger, C., Gerecke, B., Finsterer, J., & Engberding, R. (2013). Refinement of echocardiographic criteria for left ventricular non-compaction. *International Journal of Cardiology*, *165*(3), 463–467. https://doi.org/10.1016/j.ijcard.2011.08.845

Tan, S. Y., Engel, G., Myers, J., Sandri, M., & Froelicher, V. F. (2008). The prognostic value of T wave amplitude in lead aVR in males. *Annals of Noninvasive Electrocardiology*, *13*(2), 113–119. https://doi.org/10.1111/j.1542-474X.2008.00210.x

Tanaka, Y., Konno, T., Tamura, Y., Tsuda, T., Furusho, H., Takamura, M., … Hayashi, K. (2017). Impact of T wave amplitude in lead aVR on predicting cardiac events in ischemic and nonischemic cardiomyopathy patients with an implantable cardioverter defibrillator. *Annals of Noninvasive Electrocardiology*, *22*(6), https://doi.org/10.1111/anec.12452

Vereckei, A., Duray, G., Szenasi, G., Altemose, G. T., & Miller, J. M. (2008). New algorithm using only lead aVR for differential diagnosis of wide QRS complex tachycardia. *Heart Rhythm: The Official Journal of the Heart Rhythm Society*, *5*(1), 89–98. https://doi.org/10.1016/j.hrthm.2007.09.020

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