ORIGINAL ARTICLE

Prognostic value of positive T wave in lead aVR in patients with non-ST segment myocardial infarction

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Background: Lead aVR provides prognostic information in various settings in patients with ischemia. We aim to investigate the role of a positive T wave in lead aVR in non-ST segment myocardial infarction (NSTEMI).

Methods: In a prospective cohort study, we included 400 patients with NSTEMI. Presentation electrocardiogram (ECG) was investigated for presence of a positive T wave as well as ST segment elevation (STE) in aVR and study variables were compared. Predictors of primary outcome defined as hospital major adverse cardiovascular events (MACE) and secondary outcome, defined as three-vessel coronary disease and/or left main coronary artery stenosis (3VD/LMCA) stenosis in angiography, were determined in multivariate logistic regression analysis.

Results: Patients with a positive T wave in aVR were significantly older and were more likely to be female. Left ventricular ejection fraction was significantly lower in patients of positive T group. Positive T group was more likely to have 3VD/LMCA stenosis (58.3% vs. 19.8%, $p < .001$). The prevalence of a positive T wave in aVR was significantly higher in MACE group (54.9 % vs. 24.8%, $p < .001$). However, in multivariate analysis, it was not an independent predictor of MACE (OR: 1.083 95% CI: [0.496–2.365], p : .841). Though, it was independently associated with presence of 3VD/LMCA stenosis (OR: 3.747 95% CI: [2.058–6.822], $p < .001$).

Conclusion: Though positive T wave in lead aVR was more common in patients with MACE; it was not an independent predictor. Additionally, a positive T wave in aVR was an independent predictor of 3VD/LMCA stenosis in NSTEMI.

KEYWORDS

coronary angiography, lead aVR, myocardial infarction, prognosis

1 | INTRODUCTION

Non-ST elevation myocardial infarction (NSTEMI) is responsible for about two-third of all myocardial infarctions (MI) (Roger et al., 2010). Although, there is still much debate over the optimal therapeutic approaches and the use of early invasive revascularization procedures in patients with NSTEMI (Amsterdam et al., 2014;

Bangalore & Faxon, 2010; Shishehbor et al., 2006), development of prognostic scores has helped physicians to choose the most appropriate approach for each patient (Amsterdam et al., 2014; Antman et al., 2000; Granger et al., 2003). In contrast to established electrocardiographic (ECG) signs of ST segment elevation myocardial infarction (STEMI), NSTEMI may present with nonspecific ST segment and T-wave changes or even a normal ECG (Amsterdam et al.,

2014). While the ECG findings have been used in risk stratification models of NSTEMI patients, the lead aVR is not investigated for this purpose in these studies (Antman et al., 2000; Granger et al., 2003).

Lead aVR as an augmented and unipolar limb lead, once believed to provide no further information except reciprocal information from the lateral limb and precordial leads, is now increasingly being investigated for the changes in different circumstances (Gorgels, Engelen, & Wellens, 2001; Tamura, 2014). While, some recent studies have revealed the value of ST segment changes in lead aVR in NSTEMI patients (Barrabes, Figueras, Moure, Cortadellas, & Soler-Soler, 2003; Misumida et al., 2016; Taglieri et al., 2011; Yan et al., 2007), the prognostic role of a positive T wave in lead aVR is not known in this patient population. Having a positive T wave in lead aVR was associated with increased risk of cardiovascular mortality in general population (Anttila et al., 2011; Tan, Engel, Myers, Sandri, & Froelicher, 2008). In addition, having a positive T wave in lead aVR in patients with prior MI was proved to have a prognostic value for mortality and rehospitalization for heart failure (HF) (Torigoe et al., 2012). On the other hand, in patients with NSTEMI, ST segment elevation (STE) in lead aVR is suggested as an indicator of increased hospital mortality in some (Barrabes et al., 2003; Taglieri et al., 2011) but not all studies (Yan et al., 2007). Besides, STE in aVR on presentation ECG was suggested as an indicator for severe coronary artery disease in NSTEMI (Barrabes et al., 2003; Misumida et al., 2016; Yan et al., 2007). However, the role of a positive T wave for determining the extent of coronary stenosis is not well known. Identifying patients with higher risk for severe coronary artery stenosis may lead to change of therapeutic approach in this patient population.

Regarding these facts, we designed this prospective cohort study to investigate the admission ECG of patients with NSTEMI for presence of a positive T wave in lead aVR and determine its' association with major adverse cardiovascular events (MACE) in our cardiac center. We also examined the relationship of a positive T wave in lead aVR with having left main coronary artery (LMCA) stenosis and/or three-vessel coronary artery disease (3VD) in patients who underwent coronary angiography (CAG) during hospitalization.

2 | MATERIAL AND METHODS

This is a prospective cohort study including 400 consecutive patients with a final diagnosis of NSTEMI, admitted to our tertiary cardiac care center from March 2015, through March 2016. Patients with left bundle branch block, implanted pace maker, severe valvular diseases as well as patients without acute symptoms on presentation or without interpretable admission ECG were not included in this study. Ethics and research committee of affiliated university reviewed the study protocol and approved the study design. Informed was obtained from participants. All patient information remained confidential during entire study stages.

2.1 | Study design and variables

Demographic information, comorbidities and cardiac risk factors, admission vital signs and New York Heart Association (NYHA) functional class, two-dimensional echocardiographic findings, laboratory data as well as the primary treatment for NSTEMI were documented in prepared questionnaires. In patients who had undergone CAG, the angiographic findings were also recorded. In-hospital complications including evidence of heart failure, cardiogenic shock, reinfarction, and stroke as well as in-hospital mortality were logged for each patient.

First admission ECGs were reviewed by a certified cardiologist, blinded to the patient information and outcomes. Presence of a positive T wave and the amplitude of positive T wave when present were determined in each ECG and matched to the related patient's information. ST segment elevation in lead aVR, presence of an abnormal Q wave in other leads and ECG signs of left ventricular hypertrophy and left axis deviation were also recorded. Patients were categorized into two groups according to the presence or absence of a positive T wave in lead aVR and compared regarding study endpoints.

2.2 | Definitions and study endpoints

NSTEMI was diagnosed in patients with suggestive symptoms of acute coronary syndrome with an elevated cardiac troponin-I (cTnI) concentration exceeding the 99th percentile of normal reference value without ST segment elevation for fulfilling the criteria for STEMI based on third universal definition of myocardial infarction (Thygesen et al., 2012).

Positive T wave in lead aVR was defined as T wave >0 mV. Having a flat T wave or a T inversion >0 mV in lead aVR was considered a Negative T wave. The positive T wave group was also categorized into three subgroups according to T wave amplitude as follows: T wave >0.1 mV, $0.05 \leq$ T wave ≤ 0.1 mV, and $0 <$ T wave <0.05 mV. ST segment elevation in aVR was considered as positive if elevation of ST segment was more than 0.05 mV.

Standard 12-leads ECG was recorded on admission using a paper speed of 25 mm/s and standardization of 1 mV/10 mm. Left ventricular ejection fraction was determined by two-dimensional echocardiography, using biplane Simpson's method, within 24 hr of admission for all patients. Coronary artery stenosis in CAG was defined as stenosis of 70% or greater of coronary artery lumen. Stenosis in LMCA was defined as stenosis of 50% or greater of LMCA lumen. MACE, defined as occurrence of heart failure, cardiogenic shock, reinfarction, stroke or in-hospital mortality was our primary endpoint. Secondary endpoint of study was having 3VD/LMCA stenosis in patients who underwent CAG during hospitalization.

2.3 | Statistical analysis

Continuous variables were presented as mean $\pm$ standard deviation (SD) or median with 25%–75% interquartile range as appropriate. Categorical variables were reported as count and percentage. For

comparing continuous variables, independent *t* test or equivalent nonparametric Mann–Whitney *U* test was used. For comparing categorical variables, Chi-square test or Fischer test was performed as appropriate. Among variables which were readily present on admission, the ones with a *p* value of <.05 were entered into multivariate analysis. Multivariate logistic regression analysis was performed to determine independent predictors of MACE. In a separate model, independent predictors of LMCA stenosis and/or having 3VD were determined. For each endpoint, we used two different models. In the first model, we entered the variable “positive T wave in aVR” to other nonelectrocardiographic variables. In the second model, we entered the variable “STE in aVR” to other nonelectrocardiographic variables. The software program used to analyze the data was IBM SPSS Statistics for Windows (Version 22.0.; IBM Corp, Armonk, NY, USA). A *p* value <.05 was considered statistically significant.

3 | RESULTS

The mean age of our study population was 63.93 ± 13.05 years old. Among 400 patients, 285 (71.3%) were male and 115 (28.8%) were female. In-hospital mortality occurred in 19 patients (4.8%) and MACE occurred in 82 patients (20.5%) during the hospitalization period. The mean length of hospitalization after excluding deceased patients was 6.16 ± 3.51 days. CAG was performed in 311 patients (77.7%). Among these patients, 94 (30.2%) had 3VD/LMCA stenosis.

3.1 | Electrocardiographic findings

Positive T wave in lead aVR was present in 124 patients (31.0%). Negative T wave and flat T wave were present in 252 patients (63.0%) and 24 patients (6.0%), respectively. Among 124 patients with positive T wave, 42 (33.9%) had a T-wave amplitude of <0.05 mV, 49 (39.5%) had an amplitude between 0.05 to 0.1 mV and 33 (26.6%) had amplitude of more than 0.1 mV. Regarding the ST segment changes in lead aVR, 122 patients (30.5%) had STE ≥ 0.05 mV, 276 patients (69.0%) had a flat ST segment and only two patients (0.5%) had ST depression ≥ 0.05 mV. The simultaneous presence of STE and positive T wave was seen in 86 patients (21.5%).

The mean age of patients with positive T wave in aVR was significantly higher than patients without positive T wave in aVR (68.34 ± 11.43 vs. 61.93 ± 13.27 years, $p < .001$). Patients with positive T wave in aVR were less likely to be male (58.9% vs. 76.8%, $p < .001$). The prevalence of hypertension, diabetes mellitus, hyperlipidemia, and prior MI were all significantly higher in patients with positive T wave in lead aVR (Table 1). However, the prevalence of smoking, positive family history of cardiovascular diseases, prior angioplasty and prior coronary artery bypass grafting (CABG) were similar in two groups (Table 1). The NYHA functional class 3–4 upon presentation was significantly more common in patients with positive T wave in aVR (11.3% vs. 2.9%, $p < .001$). The mean heart rate was also significantly higher in the group with positive T-wave aVR; however, systolic and diastolic blood pressures were similar in

TABLE 1 Comparison of patients with and those without a positive T wave in lead aVR regarding demographic, clinical, laboratory, and electrocardiographic findings

	T-wave positive N = 124	T-wave flat or negative N = 276	p value
Age (years)	68.34 ± 11.43	61.93 ± 13.27	<.001
Gender (male)	73 (58.9%)	212 (76.8%)	<.001
Hypertension	83 (66.9%)	141 (51.1%)	.003
Diabetes mellitus	50 (40.3%)	66 (23.9%)	.001
Hyperlipidemia	26 (21.0%)	35 (12.7%)	.048
Smoking	39 (31.5%)	94 (34.1%)	.691
Family history	7 (5.6%)	12 (4.3%)	.757
Prior angioplasty	7 (5.6%)	18 (6.5%)	.826
Prior CABG	6 (4.8%)	8 (2.9%)	.380
Prior MI	23 (18.5%)	26 (9.4%)	.016
NYHA functional class 3–4	14 (11.3%)	8 (2.9%)	<.001
Systolic blood pressure (mmHg)	131.90 ± 25.28	130.15 ± 19.19	.449
Diastolic blood pressure (mmHg)	78.57 ± 13.86	79.53 ± 12.09	.487
Heart rate (bpm)	81.84 ± 12.00	76.64 ± 13.15	<.001
Creatinine (mg/dl)	1.1 [0.9–1.4]	1.1 [1.0–1.7]	.001
Peak cTNI (ng/ml)	3.6 [2.0–12.6]	3.0 [2.0–5.4]	.065
Left ventricular ejection fraction (%)	30.0 [21.2–35.0]	45.0 [35.0–55.0]	<.001
ST elevation in lead aVR	86 (69.4%)	36 (13.0%)	<.001
Left ventricular hypertrophy	17 (13.7%)	15 (5.4%)	.008
Left axis deviation	12 (9.7%)	25 (9.1%)	.853
Abnormal Q wave	20 (16.1%)	31 (11.2%)	.232

patients with and those without positive T wave in aVR. Patients with positive T wave had significantly higher range of creatinine levels than the other group, but peak cTNI level was similar in two groups (Table 1). Left ventricular ejection fraction (LVEF) was significantly lower in patients with a positive T wave in aVR (Median, [25%–75%] interquartile: 30.0%, [21.2–35.0] vs. 45.0% [35.0–55.0], $p < .001$).

Table 2 shows the coronary angiographic findings, therapeutic methods and outcomes in patients with and without positive T wave in lead aVR. Patients with positive T wave in aVR were less likely to undergo CAG (67.7% vs. 82.2%, $p = .002$). Most patients in both groups had positive angiographic findings with no significant difference (95.2% vs. 92.1%, $p = .339$). However, patients with positive T wave in aVR were significantly more likely to have 3VD/LMCA stenosis (58.3% vs. 19.8%, $p < .001$). Among revascularized patients,

	T-wave positive N = 124	T-wave flat or negative N = 276	p value
Coronary angiography	84 (67.7%)	227 (82.2%)	.002
CAG results			
Normal	4 (4.8%)	18 (7.9%)	
One vessel disease	15 (17.9%)	76 (33.5%)	
Two vessel disease	16 (19.0%)	88 (38.8%)	
Three-vessel disease	41 (48.8%)	42 (18.5%)	
Left main coronary artery stenosis	8 (9.5%)	3 (1.3%)	<.001
Three-vessel disease/left main disease	49 (58.3%)	45 (19.8%)	<.001
Positive CAG findings	80 (95.2%)	209 (92.1%)	.339
In revascularized patients			
Angioplasty	27 (39.7%)	146 (79.8%)	
CABG	41 (60.3%)	37 (20.2%)	<.001
Outcomes			
Hospital stay length (days)	7.37 ± 4.89	5.56 ± 2.80	<.001
Heart failure	35 (28.2%)	33 (12.0%)	<.001
Hospital mortality	13 (10.5%)	6 (2.2%)	.001
Major adverse cardiovascular events	45 (36.3%)	37 (13.4%)	<.001

CABG, coronary artery bypass grafting; CAG, coronary angiography.

those in positive T-wave group were significantly more likely than the other group to undergo CABG (60.3% vs. 20.2%, $p < .001$).

3.2 | Study endpoints

Patients with and those without MACE are compared in Table 3. Patients in MACE group were significantly older and had a higher prevalence of diabetes mellitus and prior MI. Systolic and diastolic blood pressures were lower in MACE group. Heart rate, peak cTNI, and serum creatinine levels were all significantly higher in MACE group. The prevalence of a positive T wave in aVR was significantly higher in MACE group (54.9% vs. 24.8%, $p < .001$). Similarly, STE in lead aVR was significantly more common in MACE group (52.4% vs. 24.8%, $p < .001$). The simultaneous presence of STE and positive T wave in lead aVR was significantly more common in the MACE group (46.3% vs. 15.1%, $p < .001$). Those in MACE group were more likely to undergo CAG and in revascularized patients, CABG was more common than angioplasty in MACE group (Table 3).

In multivariate analysis for prediction of MACE, a positive T wave was not an independent predictor of MACE (OR: 1.083 95% CI: [0.496–2.365], $p = .841$). STE in aVR was not also an independent predictor of MACE in multivariate analysis (OR: 1.267 95% CI: [0.598–2.685], $p = .537$; Table 4).

Patients who underwent CAG were compared regarding the presence of 3VD/LMCA stenosis in Table 3. Patients in 3VD/LMCA stenosis group were significantly older and were more likely to be female. They also had higher prevalence of hypertension, diabetes, and prior

TABLE 2 Comparison of patients with and those without a positive T wave in lead aVR regarding coronary angiography results and outcomes

history of CABG. The NYHA functional class of 3–4 on presentation was more common in 3VD/LMCA stenosis group. The prevalence of a positive T wave in lead aVR was significantly higher in patients with 3VD/LMCA stenosis (52.1% vs. 16.1%, $p < .001$). The prevalence of a STE in lead aVR was significantly higher in patients with 3VD/LMCA stenosis (51.1% vs. 14.7%, $p < .001$). The prevalence of simultaneous positive T wave and STE in lead aVR was also significantly higher in patients with 3VD/LMCA stenosis (26.2% vs. 16.1%, $p < .001$).

In multivariate analysis, a positive T wave in lead aVR was independently associated with presence of 3VD/LMCA stenosis in CAG (OR: 3.747 95% CI: [2.058–6.822], $p < .001$). Similarly, ST elevation in aVR was independently associated with 3VD/LMCA stenosis in CAG (OR: 3.916 95% CI: [2.137–7.175], $p < .001$; Table 4).

4 | DISCUSSION

According to the findings of this study, the presence of a positive T wave in lead aVR in patients with NSTEMI is not independently associated with higher incidence of MACE in hospitalized patients. However, a positive T wave in lead aVR is an independent predictor of three-vessel disease and/or left main coronary artery stenosis in NSTEMI patients. Similarly, ST segment elevation in lead aVR is independently associated with three-vessel disease and/or left main coronary artery stenosis but not MACE in NSTEMI.

T wave, which represents the repolarization of ventricles, can be inverted due to disruption of normal physiologic repolarization of

TABLE 3 Comparison of study variables regarding occurrence of major adverse cardiovascular events (presented in left panel) and presence of three-vessel coronary disease or left main coronary artery stenosis in patients who underwent coronary angiography (presented in right panel)

	Major adverse cardiovascular events			3VD/LMCA stenosis		
	Yes N = 82	No N = 318	p value	Yes N = 94	No N = 217	p value
Age	69.46 ± 11.28	62.50 ± 13.11	<.001	64.15 ± 10.11	59.12 ± 11.99	<.001
Gender (male)	55 (67.1%)	230 (72.3%)	.349	62 (66.0%)	172 (79.3%)	.015
Hypertension	51 (62.2%)	173 (54.4%)	.205	60 (63.8%)	96 (44.2%)	.002
Diabetes mellitus	34 (41.5%)	82 (25.8%)	.005	37 (39.4%)	45 (20.7%)	.001
Hyperlipidemia	18 (22.0%)	43 (13.5%)	.058	12 (12.8%)	25 (11.5%)	.849
Smoking	24 (29.3%)	109 (34.3%)	.391	32 (34.0%)	88 (40.6%)	.311
Family history	1 (1.2%)	18 (5.7%)	.163	5 (5.3%)	13 (6.0%)	.816
Prior MI	16 (19.5%)	33 (10.4%)	.039	24 (11.1%)	12 (12.8%)	.701
Prior angioplasty	4 (4.9%)	21 (6.6%)	.749	10 (10.6%)	14 (6.5%)	.204
Prior CABG	5 (6.1%)	9 (2.8%)	.272	8 (8.5%)	3 (1.4%)	.004
NYHA FC 3–4	16 (19.5%)	6 (1.9%)	<.001	8 (8.5%)	4 (1.8%)	.009
Systolic BP (mmHg)	124.72 ± 21.22	132.23 ± 21.02	.004	133.20 ± 25.04	130.70 ± 19.20	.338
Diastolic BP (mmHg)	75.43 ± 12.56	80.21 ± 12.51	.002	80.38 ± 14.66	80.67 ± 11.79	.854
Heart rate (bpm)	85.97 ± 14.61	76.25 ± 11.7	<.001	77.36 ± 10.88	76.21 ± 10.88	.440
LVEF (%)	32.0 [25.0–40.0]	50.0 [45.0–55.0]	<.001	45.0 [35.0–50.0]	50.0 [45.0–55.0]	<.001
Peak cTNI ng/ml	3.0 [2.0–8.9]	2.8 [1.8–4.9]	.021	2.75 [1.72–4.95]	2.8 [1.7–5.2]	.903
Creatinine mg/dl	1.3 [1.1–1.8]	1.1 [0.9–1.2]	<.001	1.1 [[0.96–1.20]	1.1 [0.9–1.2]	.820
T-wave status in lead aVR						
Flat TW	5 (6.1%)	19 (6.0%)		5 (5.3%)	11 (5.1%)	
Negative TW	32 (39.0%)	220 (69.2%)		40 (42.6%)	171 (78.8%)	
Positive TW	45 (54.9%)	79 (24.8%)	<.001	49 (52.1%)	35 (16.1%)	<.001
T-wave amplitude in positive T-wave group in lead aVR						
<0.05 mV	11 (24.4%)	31 (39.2%)		15 (30.6%)	18 (51.4%)	
0.05–0.1 mV	13 (28.9%)	36 (45.6%)		21 (42.9%)	12 (34.3%)	
>0.1 mV	21 (46.7%)	12 (15.2%)	.001	13 (26.6%)	5 (14.3%)	.131
P-TW in aVR	45 (54.9%)	79 (24.8%)	<.001	49 (52.1%)	35 (16.1%)	<.001
STE in aVR	43 (52.4%)	79 (24.8%)	<.001	48 (51.1%)	32 (14.7%)	<.001
P-TW+STE in aVR	38 (46.3%)	48 (15.1%)	<.001	34 (26.2%)	17 (7.8%)	<.001
LVH	4 (4.9%)	28 (8.8%)	.360	6 (6.4%)	19 (8.8%)	.650
Left axis deviation	8 (9.8%)	29 (9.1%)	.832	10 (10.6%)	18 (8.3%)	.522
Abnormal Q wave	14 (17.1%)	37 (11.6%)	.196	13 (13.8%)	23 (10.6%)	.442
Undergoing CAG	45 (54.9%)	266 (83.6%)	<.001			
CAG results						
Normal coronary	2 (4.4%)	20 (7.5%)				
1 vessel disease	5 (11.1%)	86 (32.3%)				
2 vessel disease	12 (26.7%)	92 (34.6%)				
3 vessel disease	21 (46.7%)	62 (23.3%)				
Left main CA stenosis	5 (11.2%)	6 (2.3%)	<.001			
Normal angiography	2 (4.4%)	22 (8.3%)	.594			
3 VD/LMCA stenosis	26 (57.8%)	68 (25.6%)	<.001			
Medical follow-up	8 (18.6%)	46 (17.6%)	.831	12 (13.0%)	42 (19.7%)	.192
In revascularized patients						
Angioplasty	13 (37.1%)	160 (74.1%)		22 (27.5%)	151 (88.3%)	
CABG	22 (62.9%)	56 (25.9%)	<.001	58 (72.5%)	20 (11.7%)	<.001

3 VD/LMCA Stenosis, three-vessel disease or left main coronary artery stenosis; BP, blood pressure; CA, coronary artery; CABG, coronary artery by-pass grafting; CAG, coronary angiography; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NYHA FC, New York Heart Association functional classification; P-TW, positive T wave; STE, ST segment elevation; TW, T wave.

	Multivariate odds ratio [95% confidence interval]	p value
Multivariate logistic regression analysis for prediction of three-vessel disease or left main coronary artery stenosis		
Age	1.016 [0.990–1.044]	.231
Gender (male)	0.682 [0.362–1.285]	.237
NYHA functional class 3–4	1.169 [0.280–4.889]	.830
Hypertension	1.533 [0.838–2.804]	.166
Diabetes	1.853 [0.983–3.495]	.057
Prior CABG	5.914 [1.353–25.846]	.018
Left ventricular ejection fraction	0.959 [0.927–0.992]	.015
Positive T wave in aVR	3.747 [2.058–6.822]	<.001
ST elevation in aVR ^a	3.916 [2.137–7.175]	<.001
Multivariate logistic regression analysis for prediction of major adverse cardiovascular events		
Age	1.020 [0.989–1.053]	.208
Diabetes mellitus	0.610 [0.261–1.429]	.255
Prior myocardial infarction	0.316 [0.108–0.921]	.035
Systolic blood pressure	0.996 [0.797–1.014]	.694
Heart rate	1.037 [1.006–1.069]	.020
NYHA functional class 3–4	2.361 [0.556–10.035]	.244
Creatinine	1.055 [0.970–1.142]	.211
Peak cTNI	1.015 [0.970–1.147]	.580
Left ventricular ejection fraction	0.822 [0.781–0.865]	<.001
Positive T wave in aVR	1.083 [0.496–2.365]	.841
ST elevation in aVR ^a	1.267 [0.598–2.685]	.537

CABG, coronary artery bypass grafting; NYHA functional class, New York Heart Association Functional Classification.

^aEach of the variables ST elevation in aVR and positive T wave in aVR was entered into the model separately.

TABLE 4 Multivariate regression analysis for prediction of major adverse cardiovascular events as well as prediction of three-vessel disease or left main coronary artery stenosis based on available data on patient presentation

cardiac myocytes. Inversion of T wave in lead aVR manifests as a positive T wave (Dilaveris, Antoniou, Gatzoulis, & Tousoulis, 2017; de Luna et al., 2014). ST segment elevation in lead aVR may occur as a result of global subendomyocardial ischemia, which can be caused by 3VD/LMCA stenosis (Tamura, 2014).

Despite the fact that the presence of a positive T wave in lead aVR was associated with higher rate of MACE in our study, it cannot be used as an independent prognostic factor. Since the established prognostication factors are widely used, this ECG finding does not provide further information beyond what is known in terms of risk stratification (Antman et al., 2000; Chase et al., 2006; Fox et al., 2006). There are few studies in which prognostic value of a positive T wave in lead aVR is investigated. Anttila et al. surveyed 6,354 subjects with an age more than 30 years who participated in the field health examination including an at-rest ECG recording. They found the prevalence of T wave in aVR, defined as having a positive or isoelectric T wave in lead aVR, to be 2.2%. The presence of this finding was independently associated with long-term cardiovascular mortality in general population. It should be noted that this study lacked echocardiographic data (Anttila et al., 2011). In another study

by Tan et al. in which 24,270 consecutive male veterans with ECGs obtained for clinical reasons were followed up, T-wave amplitude in lead aVR was proved to be a powerful prognostic marker for estimating risk of cardiovascular mortality after adjustment for age and heart rate. The result was the same in a subset of 2,250 patients with clinical data in whom adjustment for potential clinical confounding factors was performed (Tan et al., 2008). Badheka et al. followed up 7,928 participants enrolled in the National Health and Nutrition Examination Survey (NHANES) III and showed that the amplitude of T wave in lead aVR was an independent predictor of cardiovascular mortality. In addition, adding this factor could improve Framingham risk score model discrimination and calibration with better reclassification of intermediate-risk subjects (Badheka et al., 2013). Shinozaki, Tamura, & Kadota (2011), examined 122 patients with anterior wall old MI and found that a positive T wave (≥ 1 mm) in lead aVR was significantly associated with reduced cardiac function. Okuda et al. (2011), investigated 331 patients with narrow QRS complexes admitted for worsening heart failure and found a more positive T wave in lead aVR as an independent prognostic factor for risk stratification in heart failure patients.

Although there are no studies regarding the prognostic role of T wave in lead aVR in NSTEMI patients, there are few studies in which T wave in lead aVR has been investigated in patients with coronary artery diseases. Torigoe et al. retrospectively studied 167 patients with prior MI and found an upright T wave (amplitude >0 mV) in lead aVR as an independent predictor of cardiac death or hospitalization for heart failure in their study population (Torigoe et al., 2012). In another study, Ayhan et al. included 169 patients with anterior wall STEMI undergoing primary PCI. They found that patients with positive T wave in lead aVR were older with higher prevalence of multivessel disease. In-hospital mortality was also higher in positive T-wave group after adjustment in multivariate analysis. In this study, a positive T wave was defined as a T wave ≥ 0.1 mV (Ayhan et al., 2013). In a study by Kobayashi et al. the independent role of a positive T wave in aVR, defined as a T wave >0 mV, for 1 year MACE was proved in 190 studied patients with first anterior wall STEMI. However, in-hospital MACE was not statistically significant in patients with and those without positive T wave in lead aVR (Kobayashi, Misumida, Aoi, & Kanei, 2017).

According to the results of our study, presence of a positive T wave in lead aVR on presentation is independently associated with 3VD/LMCA stenosis in NSTEMI patients who undergo CAG during hospitalization. In a recent study, Icen et al. investigated the value of lead aVR in 306 patients with NSTEMI. They determined the amplitude of T wave and ST segment deviation in lead aVR and calculated a ratio by dividing the variable with larger absolute value by other variable with a smaller absolute value in lead aVR. They showed that this ratio was strongly and independently associated with coronary artery severity in coronary angiography determined by Syntax Score (Icen & Koc, 2017).

We also explored the association of STE in lead aVR with hospital outcomes in NSTEMI patients and found no independent association of STE in aVR with MACE. However, STE in aVR independently predicted 3VD/LMCA stenosis in CAG. Similar to this finding, in one study Misumida et al. (2016), evaluated 379 patients with NSTEMI and found an independent association of STE in lead aVR and 3VD/LMCA stenosis. Similarly, Kosuge et al. studied 310 NSTEMI patients to identify the predictors of 3VD/LMCA stenosis. In their study, STE in lead aVR was reported to be an independent predictor of 3VD/LMCA stenosis (Kosuge et al., 2005). Regarding the role of STE in aVR as an independent predictor of adverse outcomes, our results were in contrast to a study by Barrabes et al. in which they investigated 775 patients with NSTEMI and found STE in lead aVR as an independent predictor of in-hospital mortality. The prevalence of LMCA stenosis and 3VD were significantly higher in patients with STE in aVR (Barrabes et al., 2003). In another study by Taglieri et al. (2011), ST depression plus STE in lead aVR was associated with high-risk coronary lesions and predicted in-hospital and 1-year cardiovascular mortality in patients with NSTEMI/unstable angina. In a substudy of global registry of acute coronary events (GRACE), Yan et al. investigated the prognostic significance of STE in aVR and its association with significant 3VD/LMCA stenosis, among 5,064 patients with NSTEMI/UA. Similar to our results, STE in aVR was not an independent predictor of in-hospital mortality as well as 6-month

mortality after adjusting for other prognosticators in the GRACE risk model. In addition, having an STE more than 0.1 mV in lead aVR was revealed to be independently associated with 3VD/LMCA stenosis (Yan et al., 2007).

In conclusion, a positive T wave in lead aVR in NSTEMI patients indicates a higher risk presentation profile with increased risk of having 3VD/LMCA stenosis later in CAG. However, presence of a positive T wave in aVR on presentation ECG does not have an independent role in predicting hospital MACE in NSTEMI. The same findings apply to the presence of STE in aVR on presentation ECG in NSTEMI patients.

4.1 | Limitations

This is a single center study in which a snap shot ECG on presentation was analyzed. The potential dynamic changes in ST segment and T wave were not investigated in this study. Moreover, we studied the extent of coronary artery stenosis only in patients who underwent CAG during hospitalization. As the rate of CAG was different with regard to T-wave group, our findings regarding the 3VD/LMCA stenosis may not be applicable to all patients with NSTEMI.

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