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ORIGINAL ARTICLE

The Relationship Between ST-Segment Depression in Lead aVR and Coronary Microvascular Function in Acute Inferior Myocardial Infarction

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Received: 2 September 2021, Accepted: 21 December 2021, Published online: 10 March 2022

ABSTRACT

Objective: The aim of this study was to investigate the relationship between ST-segment depression in the aVR lead and coronary microvascular function in acute inferior myocardial infarction undergoing primary percutaneous intervention.

Methods: 287 patients with inferior myocardial infarction confirmed by coronary angiography were divided into two groups with and without ST-segment depression in lead aVR ≥ 0.1 mV on the 12 lead ECG. Electrocardiographic recordings were made for the evaluation of ST-segment resolution before and after primary PCI. Angiographic assessment in the infarct-related artery was performed by using the myocardial blush grade and thrombolysis in myocardial infarction flow.

Results: Overall, 51 of 287 patients had ST-segment depression in lead aVR. The number of patients with RCA-induced infarction was higher in the group with ST-segment depression in lead aVR. RCA involvement was present in 44 patients. Peak troponin was higher in the group with ST-segment depression in lead aVR compare to the other group (P <0.001). The MBG was more impaired, and the STR was less regressed in patients with ST depression in lead aVR (p<0,001). The ejection fraction of patients with ST-segment depression in lead aVR was lower.

Conclusion: We found that ST-segment depression in lead aVR was associated with impaired myocardial perfusion in patients with inferior myocardial infarction.

Keywords: Lead aVR, microvascular function, inferior myocardial infarction, myocardial blush grade

INTRODUCTION

Inferior myocardial infarction (MI) can be seen by the formation of transmural myocardial ischemia as a result of complete occlusion of the right coronary artery (RCA) or left circumflex artery (CX). The first electrocardiogram provides prognostic and clinic information and guides the treatment and follow-up process in case of an emergency.

The importance of lead aVR in determining infarct-related artery (IRA) in patients with inferior MI is uncertain. The lead aVR is often overlooked in traditional clinical practice because it is not adjacent to other electrocardiographic leads. Infarction of this critical area often leads to ST-segment elevation in lead aVR [1,2]. In a recent study, ST-segment depression in lead aVR has been associated with circumflex artery stenosis [3]. The previous studies demonstrated that ST-segment depression (STD) in lead AVR was related to impaired myocardial perfusion [4,5]. Thrombolysis in the flow of myocardial infarction (TIMI) 3 is known as effective recanalization of the epicardial vessel and is a key goal of therapeutic procedures. However, TIMI 3

flow does not always reflect the perfect myocardial reperfusion. Microvascular reperfusion is extremely associated with cardiovascular outcomes. The ST-segment resolution (STR) and myocardial blush grade (MBG) are electrocardiographic and angiographic markers of myocardial perfusion. During coronary angiography, the MBG assesses the degree of washing myocardial blush. A relation has been found between microvascular reperfusion and heart failure, left ventricular dilation, and mortality in several studies [6-8]. Furthermore, MBG during reperfusion has been shown to be a useful parameter in determining the prognosis of patients with acute MI [9,10].

All leads on the ECG, except lead aVR, are used to diagnose the occurrence, severity, and location of acute MI. The lead aVR is often ignored, although it provides useful information. Many studies have shown that even following successful re-canalization of the IRA, some cases do not experience complete cardiac reperfusion [10,11]. Therefore, early and simple tests should be used quickly to determine the high-risk patients. As a result, the goal of this study is to investigate the relationship between STD in lead aVR and coronary microvascular function in patients with inferior MI who had undergone primary percutaneous coronary intervention (PCI).

MATERIALS AND METHODS

Patients

Between January 2018 and December 2019, 298 patients were admitted to the coronary care unit with acute inferior or inferior plus lateral/apical MI who had undergone primary PCI. Patients were divided into two groups: those with STD in lead aVR and those without depression in lead aVR. STR and MBG were used for the evaluation of microvascular perfusion. The groups were classified as impaired reperfusion (STR <70% and MBG: 0-1) and normal reperfusion (STR >70% and MBG: 2-3).

Patients with the following conditions were excluded from the study: 1) a history of non-ST elevation MI, coronary artery bypass surgery, or PCI; 2) chronic kidney failure; 3) evidence of bundle branch block in the ECG; 4) patients with a heart valve prosthesis; 5) patients with insufficient coronary angiographic images for MBG evaluation. A total of 52 patients were excluded from the analysis; thirty-nine patients due to insufficient coronary angiographic images for MBG evaluation, four patients due to a history of coronary artery disease, three patients due to a history of coronary artery bypass surgery, two patients due to a history of heart valve prosthesis, two patients due to chronic kidney failure, and two patients due to left bundle branch block. After exclusions, 287 patients were enrolled.

Clinical, demographic, laboratory parameters, and echocardiography results were recorded for each patient on the first day of admission. Blood samples were collected from all patients on admission and then daily until the patients were discharged. Infarct-related artery, culprit lesion, lesion length, and other angiographic findings were recorded for each patient. The local ethics committee of our institution approved the study.

Electrocardiographic analysis

The ECG was examined for each patient, and the ST-segment was measured 80 ms after the J point at admission and 90 minutes after primary PCI. The diagnosis of inferior MI is based on ischaemic symptoms with a new 1 mm ST-segment elevation in two or more inferior leads (II, III, and aVF).

The STR is defined as the return of the elevated ST segment to the baseline over time. An ECG was obtained for the evaluation of the lead aVR on hospital admission, and STR was evaluated within 90 minutes after the procedure by two independent observers who were blinded to all patients' data. Intra- and inter-observer variability were both low (1% and 2%, respectively). Patients with an STD of at least 1.0 mm in lead aVR were included in the STD group, and an STD ≥2 mm was considered clinically significant. For ST segment resolution, the greatest ST segment elevation in the baseline ECG was used as a reference for the subsequent assessments of ST segment elevation. Microvascular function was considered normal in patients with ST segment resolution> 70%.

Coronary Angiography

The coronary angiography recordings were reviewed by two researchers who were not informed of the ECG findings. Coronary artery stenting (drug-eluting stent) was performed after initial balloon angioplasty. All patients received

300 mg aspirin and a 180 mg loading dose of ticagrelor, as well as intravenous heparin at 60-70 IU/kg i.v. before the procedure and 70-100 IU/kg i.v. during PCI. Using the glycoprotein IIb/IIIa inhibitor (tirofiban) was based on the decision of the operatör. During angiography, MBG was utilized to evaluate the washout of the myocardial blush. (11). The MBG was visually assessed in a catheterization laboratory using a sine film at a rate of 25 frames per second. In this study, coronary angiographic records were sufficient to monitor the contrast filling in the venous phase, and the coronary angiographic records were evaluated using the same images as the IRA. In the evaluation of MBG, a single vision was chosen from multiple orthogonal visions to minimize overlapping of non-infarcted regions. For the circumflex coronary artery, the lateral or right anterior oblique (RAO) pose was used, while the RAO pose was used for the right coronary artery. The TIMI flow grade was evaluated as described [12].

Echocardiography

Within 48 hours after primary PCI, an echocardiographic evaluation was performed according to the American Society of Echocardiography guidelines by two cardiologists who were blind to the study [13].

Statistical Analysis

SPSS version 24.0 was used for the analysis. The Shapiro-Wilks test was utilized to verify the distribution of data. The Mann-Whitney U test or Student's t-test was used to compare continuous variables between the groups. Chi-squared test or Fisher's exact test was used for categorical variables. Intra and interobserver variability for ECG parameters was analyzed in 30 randomly selected patients using the Bland-Altman method. Data are expressed as percentages for categorical variables and as mean ± SD for parametric variables. Statistical significance was considered when a p-value <0.05.

RESULTS

The ST-segment depression in lead aVR on the admission ECG was used to divide patients into two groups. The mean age of all patients was 62,1±12,4 and 77 (26%) patients were female. STD in lead aVR was detected in 51 patients. Patients with STD in lead aVR (group 1) were more likely to be male, and thirty-eight patients (74%) showed significant STD in lead aVR. One hundred and sixty-four (57%) patients had hypertension, 88 (30%) had diabetes mellitus, 187 (65%) were smokers, 8 (2%) had a family history, and 48 (16%) had hyperlipidemia. The most common coronary artery disease risk factor was smoking (65%), followed by hypertension (57%), diabetes mellitus (30%), hyperlipidemia (16%), and family history (2%).

Demographic and laboratory parameters of the patients are shown in Table 1. HT was higher in group 1. Group 1 had a lower and statistically significant left ventricular ejection fraction than the other group. Glucose, LDL, and mean platelet volume were higher in group 1. Peak cTNI was higher in group 1 compared to the other group ($p<0.001$).

The comparison of angiographic and electrographic parameters between groups is shown in Table 2. The IRA was RCA in 260 patients. In group 1, RCA was the majority of IRAs (44/86%) and CX was the IRA for seven patients. The three vessel disease rate was higher in group 1. Group 1 had lower MBG and TIMI flow than the other group. Group 1 had a larger RCA diameter and a longer lesion length than the other group.

STR was not observed in 45% of patients in group 1, and it was observed at a higher rate than in the other group. Furthermore, 76% (n:39) of patients in group 1 had STD in V1-2 leads. The rate of using tirofiban was higher in group 1. The transient complete atrioventricular block was observed in 11.6% of group 1 patients and was statistically significant.

The Student's t-test was used to compare continuous variables between the groups. Categorical variables were compared using a chi-squared test.

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DISCUSSION

To our knowledge, this is the first angiographic study to evaluate the relationship between STD in lead aVR and microvascular function in patients with inferior MI who underwent successful primary

Table 1. Demographic features and laboratory parameters of the patients.

	aVR lead depression (+) n:51	aVR lead depression (-) n:236	p
Age	63.1±12.5	62±12.4	0.56
Sex (F/M)	13/38	64/172	0.86
DM (n,%)	24 (47)	64 (27)	0.07
HT (n,%)	40 (78)	124 (52)	0.001
Smoking (n,%)	35 (68)	152 (64)	0.62
Family history (n,%)	4 (7)	4(1)	0.03
Glucose, mg/dL	183±87	157±83	0.04
LDL, mg/dL	120±33	113±21	0.04
White blood count, 10'9 /L	13.5±11.3	11.3±3.4	<0.001
Hematocrit, g/dL	44.6±7.1	42.5±5	0.006
Platelet count, 10'9 /L	255±62	256±61	0.91
Mean platelet volume, fL	10.9±1.2	9.7±1.1	<0.001
Peak Tn- I (ng/ml)	23.4±4.5	14.1±7.8	<0.001
Creatinine (mg/dL)	1.1±0.2	0.9 ±0.4	0.51
GFR	75.7±16	79±14	0.07
EF(%)	46.6±5.1	53.4±5	<0.001

Abbreviations: Tn-I: troponin, F: female, M: male, LDL: Low-density lipoprotein, MI: myocardial infarction, HT: hypertension, DM: diabetes mellitus, EF: ejection fraction, GFR: glomerular filtration rate.

Table 2. The comparison of angiographic and electrographic parameters between groups.

	aVR lead depression (+) n:51	aVR lead depression (-) n:236	p
Pain to balon time, hours	3.67±0.91	2.61±1.4	<0.001
Multivessel disease, n (%)			
1 vessel	12 (23.5)	88 (37.2)	0.12
2 vessels	26 (50.9)	108 (45.7)	0.11
3 vessels	13 (25.4)	40 (16.9)	0.04
Infarct-related artery, n (%)			
RCA	44 (86.2)	216 (91.5)	<0.001
CX	7 (13.7)	20 (8.5)	
Glycoprotein IIb/IIIa antagonist, n (%)	43 (84.3)	56 (23.7)	<0.001
ST-segment depression ≥ 0.1mv in V1-V2	39 (76.4)	108 (45.7)	<0.001
Complete heart block	6 (11.7)	-	<0.001
STR < 70%	28 (54.9)	-	<0.001
STR > 70%	23 (45)	236	
TIMI Flow	2.58±0.6	2.98±0.1	<0.001
Myocardial blush grade	2.03±0.5	2.91±1.3	<0.001
Stent diameter (mm)	3.6±3	3.02±0.4	0.008
Stent length (mm)	28.6±13.5	23.9±9.8	0.006

Abbreviations: Tn-I: troponin, F: female, M: male, LDL: Low-density lipoprotein, MI: myocardial infarction, HT: hypertension, DM: diabetes mellitus, EF: ejection fraction, GFR: glomerular filtration rate.

PCI. In the present study, MBG and TIMI flow, which are indicators of microvascular function, were lower in patients with STD in lead aVR.

Acute MI is the leading cause of heart failure, arrhythmia, and mortality in patients with cardiovascular disease. Impaired microvascular perfusion is a significant prognostic factor in patients treated with primary PCI following an acute MI. Inflammation and mediators secreted by platelets and leukocytes cause vascular damage and lead to impairment in microvascular function

[14,15]. In our study, mean platelet volume and white blood count were higher in patients with STD in lead aVR compared to other group.

In patients with acute MI, Karahan et al. discovered that a longer QRS duration after primary PCI tended to reflect the presence of decreased microvascular perfusion [16]. A previous study demonstrated that good myocardial perfusion after primary PCI was associated with increased survival [17,18]. Our study demonstrated that STD in lead aVR was related to poor myocardial perfusion in patients with inferior MI. In other words, compared with patients without STD in lead aVR, patients with STD in lead aVR showed less ST-segment resolution and worse myocardial blush. Although Nair et al. found that STD in lead aVR was more frequent in CX-related inferior MI than RCA-related inferior MI [4]. In our study, STD in lead aVR was higher in RCA-related inferior MI patients. Menown et al. reported that STD in lead aVR may be a reciprocal alteration due to ST-segment elevation in the apical and inferolateral walls. The blood flow to these myocardial segments is provided by the large posterolateral branch of LCX or the AV branch of RCA [3]. Yumiko et al. also observed that STD in lead aVR predicted Cx or RCA infarction with a large posterolateral branch [19]. In our study, the higher frequency of STD in lead aVR in RCA-related inferior MI could be explained by the greater diameter and length.

Iwakura et al. showed that large myocardial ischemia and infarction before re-canalization were both associated with the occurrence of the no-reflow phenomenon [20]. Manohara et al. suggest that STD in lead aVR may indicate a large IRA for acute MI [21]. In addition, Kosuge et al. reported that the presence of STD in lead aVR after primary PCI in the inferior MI was associated with impaired perfusion [22]. The large diameter of the vessel and the longer lesion associated with MI may increase the thrombus load, which may cause more impact on the myocardium and lead to STD in lead aVR. In our study, we found higher troponin values and lower ejection fractions in patients with STD in lead aVR compared to those without. In addition, in patients with STD in lead aVR, RCA diameter was larger and lesion length was longer than in the other group. These findings may demonstrate that patients with this ECG change have larger infarct sizes and are prone to more myocardial damage.

This study had a few limitations. The sample size was relatively small, and the follow-up time for cardiac complications was short. MBG assessment is a visual assessment method that is not quantitative. In addition, there was no evaluation of right-sided precordial leads (V4R), which help identify the culprit artery in the inferior MI. We did not use a thrombus aspiration device.

CONCLUSION

In our study, STD in lead aVR was associated with impaired myocardial perfusion in patients with inferior MI. Patients with inferior MI and STD in lead aVR are prone to worse angiographic outcomes and more myocardial damage. Therefore, effective treatment and follow-up should be provided to these patients.

Author contribution

Study conception and design: BA and MZK; data collection: BA; analysis and interpretation of results: MZK; draft manuscript preparation: BA. All authors reviewed the results and approved the final version of the manuscript.

Ethical approval

The study was approved by the ethics committee of our hospital (Protocol no: 684 Date: 12/02/2021).

Funding

The authors declare that the study received no funding.

Conflict of interest

The authors declare that there is no conflict of interest.

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