ORIGINAL ARTICLE

ST-Segment Elevation of Right Precordial Lead (V_4R) Is Associated with Multivessel Disease and Increased In-Hospital Mortality in Acute Anterior Myocardial Infarction Patients

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Background: ST segment elevation of chest lead V_4R is associated with worse prognosis in acute inferior ST-elevation myocardial infarction (STEMI). This study tried to determine the relationship between ST elevation in the right precordial lead V_4R and acute anterior STEMI.

Methods: Prospective study of 144 consecutive anterior STEMI patients: all had 15-lead ECG recordings (12 conventional leads and V_3R-V_5R) obtained. Patients were classified into two groups on the basis of presence (Group I, 50 patients) or absence (Group II, 94 patients) of ST-segment elevation ≥0.5 mm in lead V_4R.

Results: Multivessel involvement was significantly higher in Group I compared with Group II (54% and 23% respectively, $P < 0.001$). Major adverse cardiac events and in-hospital mortality was also significantly higher for those in Group I ($P < 0.02$ for both). A significant correlation was found between in-hospital mortality and those in Group I ($P = 0.03$, OR: 6.27, CI: 1.22–32.3). There was an independent relationship between in-hospital mortality and V_4R-ST elevation ($P = 0.03$, OR: 11.64, CI: 1.3–27.4).

Conclusion: ST segment elevation in chest lead V_4R is associated with multivessel disease and increased in-hospital mortality in patients with anterior STEMI that had undergone primary percutaneous coronary intervention to the left anterior descending artery.

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V_4R; anterior myocardial infarction; in-hospital mortality; major adverse cardiac events; left anterior descending artery

Coronary artery disease is the leading cause of death worldwide.[1] The electrocardiogram (ECG) is a reliable diagnostic tool for diagnosis of ST-elevation myocardial infarction (STEMI). For accurate diagnosis and prediction of coronary artery lesions, different derivatives of the ECG are being proposed and used over time. The right precordial lead V_4R is used for identification of right ventricular involvement following an acute inferior STEMI.[2] Over time, it has been found that,

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the involvement of right ventricular infarction predicts worse prognosis in acute inferior STEMI.[3,4] This right ventricular involvement may result in arrhythmias, mostly conduction abnormalities, and also ventricular fibrillation (VF)/tachycardia.[5,6] Thus, elevation at V_4R, is being used as a prognostic tool in inferior STEMI patients. Additionally, the presence of V_4R elevation could predict the site of coronary lesions, detect the culprit artery, and enhance the usage of fibrinolytic treatment in acute inferior wall STEMI.[7,8]

Although, the prognosis of acute inferior STEMI is better than acute anterior STEMI, the presence of V_4R elevation indicating right ventricular involvement, is related with worse prognosis in acute inferior STEMI.[3,4] In contrast to inferior STEMI, lead V_4R elevation has not being evaluated well in acute anterior wall STEMI, neither for diagnosis or prognosis. Limited data suggest a V_4R ST elevation could be related with worse prognosis in acute anterior wall STEMI.[9] This study is designed to determine the probable relationship between ST-segment elevation of lead V_4R and acute anterior STEMI in patients treated with primary percutaneous coronary intervention (PCI).

METHODS

Patients

A total of 144 consecutive patients (123 men) admitted to the emergency department with acute anterior STEMI undergoing primary PCI within 12 hours of onset of symptoms were recruited to this prospective study. The mean age ± SD was 57.3 ± 12.3 years. The study was conducted between October 2012 and October 2013. All patients underwent primary PCI to the left anterior descending (LAD) coronary artery. Patients presenting to hospital after 12 hours of symptom onset were excluded. The study protocol was approved by the local research ethics committee.

Analysis of Data

Baseline and follow-up demographic data, and laboratory and clinical data were collected. These included, age, gender, past history of smoking, hypertension (HT), diabetes mellitus (DM), hyperlipidemia, coronary artery bypass grafting (CABG), door-to-balloon time, PCI procedure details, Killip class on admission, post-PCI thrombolysis in myocardial infarction (TIMI) 3 flow, and presence of multivessel disease. Left ventricular ejection fraction (LVEF) was measured by echocardiography using the modified Simpson's method with a System V echo machine (Vingmed, GE, Horten, Norway) prior to hospital discharge.[10]

A 15-lead resting ECG (12 conventional leads and 3 right chest leads: V_3R-V_5R) was obtained on admission to hospital, at 60 minutes and 24 hours after hospitalization. The ST-segment elevation was measured manually. Patients were classified into two groups on the basis of presence (Group I) or absence (Group II) of ST-segment elevation (defined as ≥1 mm) in lead V_4R. Patients with bundle branch (left and right) block and that have a marked LV hypertrophy were excluded.

Coronary Angiography, Primary Angioplasty, and Stenting

Just after diagnosis of acute anterior STEMI, coronary angiography was performed via a percutaneous femoral approach by an interventional cardiologist. All patients were given aspirin 300 mg (unless contraindicated) and clopidogrel 300–600 mg prior to coronary angiography. Patients' angiographic data and TIMI flow classification of the infarct-related artery were used.[11] Primary coronary intervention was performed to just the infarct-related artery using balloon angioplasty and/or stent implantation according to lesion anatomy. For each procedure, interventional success was assumed if the stenosis of the infarct-related artery was reduced by >50% with TIMI III flow after primary PCI. The drugs administered during and after the PCI procedure were in accordance with current European Society of Cardiology PCI Guidelines.[12]

Definition

The time from onset of symptoms to the first balloon inflation was the pain to balloon time. The door-to-balloon time was the time from first contact at the emergency room to the first balloon inflation. Patients clinical status at the emergency department was evaluated according to the Killip clinical examination.[13] Glomerular filtration rate was measured at bedside by using the Cockcroft–Gault (C–G) formula.[14] Multivessel disease was assumed if >50% stenosis in >2

coronary arteries was present. The Syntax score was measured by using the syntax score website (www.syntaxscore.com) by an interventional cardiologist blinded to the study. Reinfarction was described as chest pain recurrence accompanied by ST segment reelevation. Contrast-induced nephropathy was defined as a rise in serum creatinine >0.5 umol/L or ≥25% increase of the basal creatinine level within 48 hours of contrast agent administration.[14,15] Persistent (>30 minutes) and marked hypotension (systolic arterial pressure <80 mmHg) with signs of hypoperfusion was defined as cardiogenic shock. Major adverse cardiac events (MACE) were composed of target vessel revascularization (PCI or surgical), reinfarction and in-hospital cardiovascular mortality.

Statistical Analysis

Quantitative variables were expressed as mean ± standard deviation, and qualitative variables were expressed as percentage (%). Comparison of parametric values between two groups was performed using the 2-tailed Student *t* test. Categorical variables were compared by the likelihood ratio chi-square w^2 test or Fisher's exact test. Multivariate logistic regression analysis was performed to identify independent predictors of in-hospital cardiovascular mortality. A 2-sided $P < 0.05$ was considered as significant. All statistical analyses were performed by using SPSS version 15.0 for Windows (SPSS, Inc., Chicago, IL, USA).

RESULTS

A total of 144 patients were recruited (123 men and 21 women). Baseline patient demographics and laboratory findings are presented in Tables 1 and 2. There were 50 patients (mean age 61 ± 12.3 years) in Group I and 94 patients (mean age 55 ± 12.6 years) in Group II. There were no statistically significant differences between the two groups in relation to age, sex, smoking, history of HT, DM, previous myocardial infarction, door-to-balloon time, prodromal angina, systolic blood pressure, heart rate, and laboratory findings such as creatinine, glomerular filtration rate, cholesterol level, hemoglobin concentration, CK-MB, and troponin levels. Group I patients were older compared with Group II patients (61 ± 12.3 vs 55.4 ± 12.6, P = 0.01).

Table 1. Baseline Characteristics and Clinical Outcomes of Study Population

Variable	V_4R ST ≥0.5 mm N = 50	V_4R ST < 0.5 mm N = 94	P Value
Age (year)	61 ± 12.3	55.4 ± 12.6	0.01
Sex (women)	9 (6.25%)	12 (8.33%)	0.4
Smoking	31 (21.52%)	76 (52.77%)	0.09
Diabetes mellitus	12 (8.33%)	16 (11.11%)	0.23
Hypertension	23 (15.97%)	34 (23.61%)	0.21
Metabolic syndrome	24 (16.66%)	38 (26.38%)	0.33
Prodromal angina	23 (15.97%)	52 (36.11%)	0.46
PBT (minutes)	212.3 ± 177.9	172 ± 92.8	0.08
DBT (minutes)	27.6 ± 11.6	26.6 ± 9.2	0.56
SBP (mm/Hg)	130 ± 29.4	126 ± 25.6	0.42
Killip class >1	9 (6.25%)	17 (11.80%)	0.99
Heart rate	89 ± 21.7	84.6 ± 18.1	0.15
Previous MI	4 (2.77%)	11 (7.63%)	0.51
Hyper-lipidemia	19 (13.19%)	44 (30.55%)	0.28

PBT = pain to balloon time; DBT = door-to-balloon time; SBP = systolic blood pressure; MI = myocardial infarction.

The angiographic data of both groups are shown at Table 3. The angiographic results were comparable including pre- and postangiographic TIMI grade, proximal LAD involvement, and measured syntax score. However, presence of multivessel disease was significantly higher in Group I patients ($P < 0.001$). In-hospital adverse events are shown in Table 4. MACE, mostly driven by increased in-hospital mortality was significantly higher in Group I patients compared with Group 2 (8 vs 4 and 6 vs 2, P = 0.01 for both).

Univariate and multivariate logistic regression analysis results are shown in Table 5. Multivariate analysis revealed an independent relationship between in-hospital mortality and V_4R-ST segment elevation and KILLIP class > I (P = 0.03, OR: 11.64, CI: 1.3–27.4 and P = 0.03, OR: 44.76, CI: 3.6–101.4, respectively).

DISCUSSION

This study has shown that, as in acute inferior STEMI, ST elevation in chest lead V_4R is associated with increased in-hospital major adverse clinical events in acute anterior STEMI. A recent study, similarly designed with this study, had

Table 2. Laboratory Findings of the Study Population

	V_4R ST > 0.5 mm N = 50	V_4R ST < 0.5 mm n = 94	P Value
Admission creatinine, umol/L	0.75 ± 0.42	0.9 ± 0.22	0.35
GFR, mL/min/1.73 m^2	100.5 ± 36.3	108.3 ± 36	0.28
Admission glucose, mg/dL	156.8 ± 64.3	158.7 ± 60.8	0.86
Total cholesterol, mg/dL	187.4 ± 33.4	193.7 ± 57.3	0.5
LDL, mg/dL	121.7 ± 31.5	127.2 ± 52.6	0.52
HDL, mg/dL	42.6 ± 10.3	40.3 ± 10.3	0.22
Triglycerides, mg/dL	130.4 ± 61.1	131.2 ± 92.7	0.96
Hemoglobin, g/dL	13.4 ± 1.7	14.1 ± 1.8	0.04
Platelet, 103/mL	230.4 ± 56	217.7 ± 60.8	0.23
WBC, 103/mL	11.5 ± 3.6	12.4 ± 3.7	0.21
Peak CK-MB, IU/mL	177.1 ± 112.9	217.1 ± 168	0.14
Peak troponin, ng/mL	42 ± 14.1	43.9 ± 19.7	0.55

GFR = glomerular filtration rate; LDL = low-density lipoprotein; HDL = high-density lipoprotein; WBC = white blood cell; CK-MB = creatin kinase-myocardial band.

Table 3. Angiographic Findings of Study Population

	V_4R ST ≥ 0.5 mm n: 50	V_4R ST < 0.5 mm n: 94	P Value
Pre-TIMI 0-1	46 (92%)	81 (86.2%)	0.56
Pre-TIMI 2	3 (6%)	11 (11.7%)	0.56
Pre-TIMI 3	1 (2%)	2 (2.1%)	0.56
Post-TIMI 0-1	5 (10%)	4 (4.2%)	0.56
Post-TIMI 2	7 (14%)	16 (17%)	0.56
Post-TIMI 3	38 (76%)	74 (78.8%)	0.56
LAD proximal	28 (19.44%)	61 (42.36%)	0.26
Tirofiban	22 (15.27%)	42 (29.16%)	0.94
Syntax score	20.4 ± 6.8	19.7 ± 6.4	0.62
Stent length	20.6 ± 8.4	21.8 ± 5.8	0.37
Stent diameter	2.99 ± 0.57	3.2 ± 0.34	0.02
Multivessel disease	27 (54%)	22 (23%)	<0.001

TIMI = thrombolysis in myocardial infarction; LAD = left anterior descending artery.

shown a relationship between V_4R-ST elevation and combined end point of death, acute heart failure, and primary VF in patients with acute anterior STEMI.[9] They proposed that, infarction or ischemia of a specific segment of myocardium could be more related to acute heart failure risk and VF initiation rather than infarct size and elevation of cardiac enzymes.[9] They found an independent relationship between the involvement of middle anteroseptal wall motion impairment and VF.[9] Different studies have proposed the importance of the interventricular septum at initiating arrhythmias following myocardial infarction or acute ischemia.[16,17] Another study has shown the importance of the interventricular septum at the initiation of the torsade de pointes in canine wedge preparations.[18] Previously it has been shown that the presence of a larger conal branch of right coronary artery results in absence of ST segment elevation in lead V_1.[19,20] This is strongly associated with V_3R elevation. It has been shown that a larger conal branch protect the interventricular septum.[20] In this study, the global LVEF and cardiac enzyme elevation were similar in both groups as was VF incidence, in contrast to the study by Barsheshet et al.[9] The presence of proximal LAD lesion was similar in both groups in our study, similar to Barsheshet et al.[9] In this study, the middle anteroseptal wall motion was not evaluated. In the study by Barsheshet et al. the incidence of primary VF and acute heart failure was higher in the V_4R elevated group.[9] Also in-hospital mortality was significantly higher in the V_4R-ST elevation group. Both in this study and the Barsheshet et al. study, the presence of a large conal branch of right coronary artery was not recorded.

Table 4. In-Hospital Adverse Events of Study Population

	V_4R ST ≥ 0.5 mm n: 50	V_4R ST < 0.5 mm n: 94	P Value
In-hospital mortality	6 (4.16%)	2 (1.38%)	0.01
TVR	2 (1.38%)	2 (1.38%)	0.52
Reinfarction	3 (2.08%)	1 (0.69%)	0.09
MACE	8 (5.55%)	4 (2.77%)	0.01
Dialysis	2 (1.38%)	2 (1.38%)	0.52
CIN	19 (13.19%)	27 (18.75%)	0.27
Shock	6 (4.16%)	6 (4.16%)	0.25
AF	14 (9.72%)	12 (8.33%)	0.08
IABP	5 (3.47%)	4 (2.77%)	0.18
CHF	12 (8.33%)	19 (13.19%)	0.6
VT/VF	9 (6.25%)	12 (8.33%)	0.4
Acute thrombus	3 (2.08%)	1 (0.69%)	0.08
Transfusion (n)	2 (1.38%)	2 (1.38%)	0.52
Ejection fraction (%)	34.7 ± 9.9	34.6 ± 9.3	0.97
Hospitalization (day)	5.7 ± 3.9	5.4 ± 3.1	0.61

TVR = target vessel revascularization; CIN = contrast-induced nephropathy; AF = atrial fibrillation; MACE = major adverse cardiac events; IABP = intra-aortic balloon pump; CHF = congestive heart failure; VT = ventricular tachycardia; VF = ventricular fibrillation.

Table 5. Univariate and Multivariate Analysis of Possible Predictors of In-Hospital Major Adverse Cardiac Events

	Univariate			Multivariate		
	OR	CI	P	OR	CI	P
Age	1.12	1.04–1.196	0.002			
$V_4R \geq 0.5$	6.27	1.22–32.3	0.03	11.64	1.3–27.4	0.03
Killip class >1	43.1	5.02–370.3	0.03	44.76	3.6–101.4	0.03
Post-TIMI < 3	6.73	1.5–29.9	0.01			

TIMI = thrombolysis in myocardial infarction.

Different incidence of VF between studies could be resulted from the different presence of a large conal branch.

In our study, V_4R-ST elevation patients had significantly higher multivessel involvement. Michaelides et al. demonstrated that, in patients with Q wave, extended anterior MI, addition of right-sided chest leads (V_3-V_5), to standard exercise testing significantly increased the low sensitivity of the standard exercise test to detect multivessel involvement.[21] Previous studies have clearly defined that, the presence of multivessel disease is associated with increased in-hospital and late mortality.[22,23] Even though the procedural success rate, postprocedural TIMI flow, and myocardial blushing rate were similar in single- and multivessel disease, early and 1-year mortality, re-infarction rate, and MACE were higher in the multivessel disease-treated group.[24] It was found that multivessel disease was a powerful independent predictor of mortality.[24] Similarly in this study the procedural success rate and postprocedural TIMI flow rate were similar, multivessel disease was more frequent in the V_4R-ST elevation group. In line with previous studies, we believe that V_4R-ST elevation is associated with multivessel disease and results in increased in-hospital MACE. This could be a probable explanation of the increased in-hospital MACE in the V_4R-ST elevation group.

Our study has some limitations. It is a single center study. Global LVEF was evaluated, rather than regional wall motion impairment. That is why the relation between specific wall region could not be assessed. Also right ventricular function was not assessed. The combined end points were relatively small and the study should be repeated in larger cohort. In this study the conal branch of right coronary artery was not recorded and

evaluated. Also the LAD branches that supply the right ventricular wall was not recorded.

In conclusion, ST segment elevation of V_4R is associated with multivessel disease in acute anterior STEMI and could predict increased in-hospital MACE mostly derived by mortality. V_4R segment elevation could be used for risk stratification of acute anterior wall STEMI prior to the emergent coronary angiography.

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