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The relationship between electrocardiographic findings and left ventricular apical thrombus

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Abstract. – OBJECTIVE: Persistent ST segment elevation, fragmented QRS (fQRS), and prominent R wave in lead aVR (Goldberger sign) are the parameters associated with ventricular aneurysm. The goal of this report was to examine the association with electrocardiographic findings (persistent ST elevation, QRS duration, LBBB, and Fragmented QRS [fQRS]) and LV apical thrombus in subjects following anterior MI.

PATIENTS AND METHODS: The study was a prospective and cross-sectional analysis that comprised of 220 consecutive subjects diagnosed after anterior MI. The echocardiographic features of patients were evaluated at least 6 weeks after anterior MI. A 12-point ECG was collected on all subjects admitted to the hospital. LBBB, persistent ST elevation, QRS duration and fQRS were evaluated in these patients.

RESULTS: The LV ejection fraction (LVEF) was lower in the thrombus group compared to the non-thrombus group (27.2 ± 7.1/33.2 ± 10.0, p=0.008). In patients with LV apical thrombus (LVAT); LBBB, persistent ST elevation, QRS duration and fQRS were higher compared to those without LVAT (p<0.05).

CONCLUSIONS: We demonstrated that the electrocardiographic findings (persistent ST elevation, QRS duration, LBBB, and fQRS) were closely associated with LVAT, and these findings were used as indicators of LV thrombi in anterior MI patients.

Key Words:
ECG, Left ventricular apical thrombus, Myocardial infarction, Fragmented QRS.

Introduction

Ventricular aneurysm is defined as outward left ventricular myocardium thickening with a reduction in contraction throughout the heart cycle. Left ventricular aneurysm usually develops in the apical region following anterior myocardial infarction (MI) and is caused by left anterior descendant (LAD) artery occlusion[1]. LV aneurysm is life-threatening causing heart failure or worsening of existing heart failure (HF). Systemic embolism occurs due to the frequent thrombus formation and can give rise to malignant ventricular arrhythmias[2]. Diagnostic methods, such as electrocardiogram (ECG), transthoracic ECG, and cardiac MRI have been used to diagnose LV apical thrombus (LVAT)[3].

Persistent ST segment elevation, fragmented QRS (fQRS), and R-wave in lead aVR (Goldberger sign) are the parameters associated with ventricular aneurysm[4]. ST segment elevation with acute STEMI usually regresses within two weeks of an acute event. LV persistent aneurysm should be considered when persistent ST elevation is detected on the ECG within 6 weeks after acute STEMI (usually anterior MI)[5]. The ECG variations associated with ischemic heart disease may be hidden due to altered ventricular pattern transmission in patients with left bundle branch block (LBBB)[6].

fQRS has been used to determine myocardial fibrosis following an ECG. The predictive fQRS relevance has been mostly demonstrated in patients with MI, (non)ischemia cardiomyopathy, arrhythmogenic RV dysplasia and hypertrophic cardiomyopathy[7-9]. Although myocardial fibrosis has been determined in LVAT, research on the relationship between fQRS and LVAT in Anterior MI subjects is lacking. A fQRS complex has been found in cardiac aneurysms[10]. Previous studies have shown that persistent ST elevation and fQRS are associated with apical aneurysms and no study on the relationship of LV apical thrombus to electrocardiographic findings (persistent ST elevation, QRS duration, LBBB, and fQRS) exists.

The goal of this report was to examine the association of ECG outcomes (persistent ST elevation, QRS duration, LBBB, and fQRS) and LV apical thrombus in subjects following anterior MI.

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Patients and Methods

The study was a prospective and cross-sectional analysis that was comprised of 220 consecutive patients diagnosed after anterior MI in our hospital between November 2020 and May 2021. The ECG features of patients were evaluated at least 6 weeks after anterior MI. We excluded subjects with a suspicion of subclinical myocardial association including a history of chronic inflammatory disease or acute infection, thrombotic hematological disorders, significant valvular heart disease, malignancy, end-stage renal or hepatic disease, premature atrial or ventricular beats, paced rhythms or any other secondary abnormality (LVH and Wolff-Parkinson-White pattern), and poor echogenicity.

Patient files were determine demographics (age and gender) and clinical characteristics including HT, Diabetes mellitus, hyperlipidemia, and smoking and drugs. Subjects were older than 18 years and provided written informed consent as an enrollment prerequisite. This study was performed according to the principles stated in the Declaration of Helsinki and was approved by the local ethics committee of the Van Training and Research Hospital.

Electrocardiographic Evaluation

A 12-lead ECG was done on all subjects. The ECGs were examined by seperate 2 clinicians blinded to the experimental design and clinical findings. If discrepancies occurred following analysis, a final diagnosis was determined together. The routine ECGs were recorded using Cardio Calipers version 3.3 on-screen digital caliper software. Lead V5 was designated for the ECG data to compare QRS duration.

The following criteria for fQRS were assessed: (R′) r-wave QRS complex duration of less than 120 milliseconds, notched R wave, notched S-wave, or presence of greater than 1R′ for at a minimum of two contiguous leads analogous to coronary artery regions lacking LBBB characteristics in accordance with past reports[11].

LBBB was classified based on the Minnesota Code. The LBBB diagnosis criteria were as follows: QRS greater than 120 milliseconds, QS or rS in lead V1, Monophasic R-wave with no Q wave in lead V6 and I3, ACC/AHA/HRS added notched R wave in lead I, aVL, V5, and V6, and occasional RS pattern in V5 and V6[12].

Echocardiographic Evaluation

A transthoracic ECG was performed and data was collected on the short and long parasternal axes of the apical 2-chamber that was evaluated in three cardiac cycles. The LVEF was measured using the Simpson's method (biplane). The LV endocardium was traced during end-diastole and -systole and the LV volumes of these intervals were calculated using M-mode in parasternal long axis view. LVEF was acquired using both volume measurements. An echodense mass in the LV was accepted as a thrombus based on the agreement of 2 independent cardiologists and a radiologist. Two independent cardiologists confirmed the analysis of echocardiographic findings, and the interobserver agreement was 96%.

Statistical Analysis

Statistical analyses were performed with SSPS v19.0 for Windows (Chicago, IL, USA). A Kolmogorov-Smirnov test was performed to determine data normality. Continuous and categorical data were expressed as mean±SD and percentages, respectively. A Chi-square test was done to determine variances between groups. A Student's *t*-test or a Mann Whitney U test was performed on single group comparisons. Univariate/multivariate logistic regression analyses were done to determine independent variables of presence of LVAT including age, gender, HT, DM, smoking, LVEF, sinus rhythm (SR), LBBB, aneurysmatic ST elevation, QRS duration and fQRS. Following univariate analyses, variables were subjected to multivariate logistic regression using a stepwise method. The results of the analyses were shown as odds ratio with a 95% confidence interval. For the ECG parameter (amount of ST elevation and QRS duration) ROC curves were determined and values with the greatest sensitivity/specificity for left ventricular apical thrombus prediction were chosen. A *p*-value of less than 0.05 was determined to be statistically significant.

Results

Subjects were analyzed following categorization into 2 groups: those with with LVAT (n=35) and those without LVAT (n=185). Demographics, as well as clinical findings, are shown in Table I. No significant changes were found between groups based on age, gender or BMI. Of the 35 subjects with thrombi, 27 were male (77%) and 136 of 185 non-thrombus patients were male (73%). The mean age of thrombus subjects was 59.1 ± 9.8, while subjects without thrombus had a mean age of 55.9 ± 14.0. No statistical significant difference

Table I. Clinical and demographic characteristics of patients with and without apical thrombus.

	Thrombi (+), n = 35	Thrombi (-), n = 185	p
Age, years	59.1 ± 9.8	55.9 ± 14.0	0.12
Male Gender, n (%)	27(77)	136(73)	0.65
BMI, kg/m^2	26.5 ± 3.1	25.9 ± 4.0	0.36
HT, n(%)	13(38)	60(37)	0.93
DM, n(%)	6(17)	44(26)	0.27
HL, n (%)	18(52)	71(46)	0.49
Smoking, n (%)	25(73)	84(52)	0.02
LVEF (%)	27.2 ± 7.1	33.2 ± 10.0	0.008
Systolic blood pressure (mmHg)	127.3 ± 14.4	129.4 ± 12.8	0.41
Diastolic blood pressure (mmHg)	68.2 ± 4.6	69.5 ± 5.1	0.24
Treatment			
Antiplatelet, n (%)	35(100)	185(100)	-
ACEI/ ARB, n (%)	30(88)	131(33)	0.48
Spironolactone, n (%)	21(60)	80(52)	0.40
Beta-Blocker, n (%)	31(91)	124(82)	0.21
Loop Diuretics, n (%)	12(35)	68(46)	0.22
Statin, n(%)	28(80)	132(71)	0.29

BMI: Body Mass Index, HT: Hypertension, DM: Diabetes mellitus, HL: Hyperlipidemia, LVEF: Left ventricular ejection fraction ACEI: Angiotensin-converting enzyme inhibitor, ARB: Angiotensin receptor blocker.

was observed for the groups based on HT, DM and HL, whereas smoking was significantly higher in thrombus group. Similarly, there was no statistical difference for the two cohorts at the time of admission, heart rate, systolic blood pressure and diastolic blood pressure. In addition, LVEF levels were reduced in the thrombus group when compared to the non-thrombus cohort. (27.2 ± 7.1/33.2 ± 10.0, $p = 0.008$). Patients' medications were similar between the two groups (Table I).

No statistical difference for sinus rhythm and heart rate was determined (sinus rhythm: 85% *vs.* 76%, $p = 0.23$; heart rate: 69.6 ± 5.2 bpm/71.0 ± 5.3 bpm, $p = 0.16$). LBBB, persistent ST elevation, QRS duration and fQRS were higher in patients 'with LVAT' as compared to 'without LVAT' (40% *vs.* 22%, $p = 0.03$; 34% *vs.* 14%, $p = 0.004$; 136.6 ± 19.6 mm/123.8 ± 25.9 mm; $p = 0.006$; 37% *vs.* 17%, $p = 0.008$, respectively) (Table II).

Regression analyses for LVAT in the study populations is shown in Table III. Male gender, DM, smoking status, LVEF, persistent ST elevation, QRS duration and fQRS were statistically significant. As shown in Table II, DM, smoking status, LVEF, persistent ST elevation, QRS duration and fQRS independently determined LVAT (DM: OR = 5.309, p: 0.016; Smoking: OR = 7.536, $p < 0.001$; LVEF: OR = 0.935, $p = 0.009$; persistent ST elevation: OR = 9.756, $p < 0.001$; QRS duration: OR = 1.030, $p = 0.005$; fQRS: OR = 10.717, $p = 0.002$).

According to the ROC analysis, sensitivity and specificity of ST elevation and QRS duration were statistically significant for LVAT. Figure 1 shows the ST elevation, and the AUC was measured by 0.74 [0.64-0.83] ($p < 0.001$). QRS duration (Figure 1) was also dtermined and the AUC was calculated using 0.66 [0.57-0.75] ($p = 0.002$). For the amount of ST elevation, ROC

Table II. Electrocardiographic properties of patients with and without apical thrombus.

	Thrombi (+), n =35	Thrombi (–), n =185	p
Sinus rhythm, n(%)	30(85)	142(76)	0.23
Heart rate (min)	69.6 ± 5.2	71.0 ± 5.3	0.16
Left bundle branch block, n(%)	14(40)	42(22)	0.03
Persistent ST elevation, n(%)	12(34)	26(14)	0.004
QRS duration (ms)	136.6 ± 19.6	123.8 ± 25.9	0.006
Fragmanted QRS, n(%)	13 (37)	32 (17)	0.008

Table III. Independent predictors of left ventricular apical thrombus in patients after anterior myocardial infarction.

Variable	Univariate			Multivariate		
	OR	95%CI	p	OR	95%CI	p
Age	1.017	0.967-1.069	0.521			
Male Gender	0.152	0.030-0.760	0.022	0.331	0.091-1.205	0.094
HT	1.390	0.427-4.526	0.585			
DM	0.181	0.037-0.881	0.034	5.309	1.363-20.677	0.016
Smoking	11.779	2.851-48.677	0.001	7.536	2.471-22.981	<0.001
LVEF	0.945	0.885-1.008	0.086	0.935	0.889-0.984	0.009
SR	1.055	0.222-5.019	0.946			
LBBB	1.689	0.481-5.932	0.414			
Persistent ST elevation	17.098	3.575-81.768	<0.001	9.756	3.138-30.336	<0.001
QRS duration	1.032	1.004-1.060	0.023	1.030	1.009-1.051	0.005
fQRS	30.702	4.672-201.769	<0.001	10.717	2.462-46.651	0.002

HT: Hypertension, DM: Diabetes mellitus, LVEF: Left ventricular ejection fraction, SR: Sinus rhythm, LBBB: Left bundle branch block.

analyses revealed a cut-off value of ≥ 2.5 as a predictor of LVAT with a sensitivity of 57% and a specificity of 85%. Similarly, QRS duration predicts LVAT development with a sensitivity of 68%, specificity of 68% and cutoff value of ≥132 msec (Figure 1).

Discussion

In the present report, the association of ECG findings and LVAT in subjects following anterior MI were determined. The principal findings of our study are:

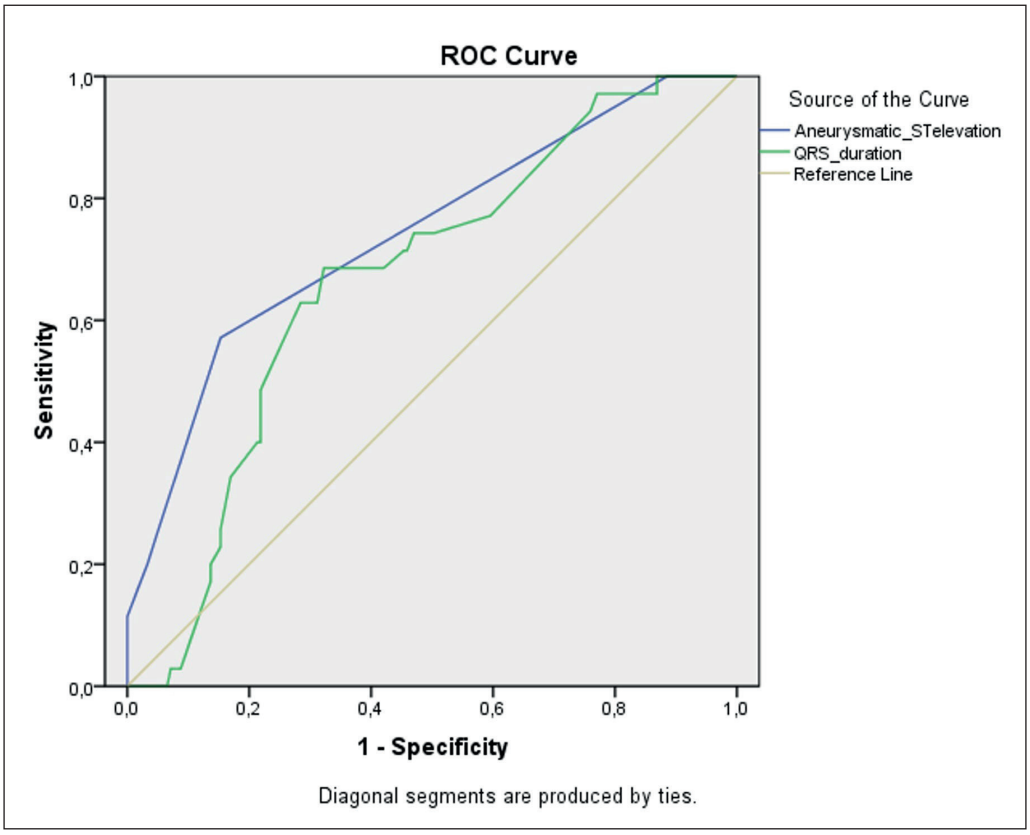

Figure 1. Sensitivity and specificity of amount ST elevation and QRS duration for left ventricular apical thrombus.

1. In patients with LVAT; LBBB, persistent ST elevation, QRS duration and fQRS were increased when compared to subjects without LVAT (40% *vs.* 22%, $p = 0.03$; 34% *vs.* 14%, $p = 0.004$; 136.60 ± 19.68 mm/123.83 ± 25.97 mm; $p = 0.006$; 37% *vs.* 17%, $p = 0.008$, respectively).
2. Multivariate analyses revealed that DM, smoking, LVEF, persistent ST elevation, QRS duration and fQRS are independent predictors of LVAT after ant-MI in patients with LV dysfunction.

LV aneurysms mostly occur as a complication of acute myocardial infarction. Thrombus is present in 2 out of 3 patients with LV aneurysm. The LV aneurysm, whose wall consists of a thin fibrotic tissue, usually has a dyskinetic movement. Thrombus development occurs in the LV due to Virchow's triad[13]. The LV thrombus formation is a potentially catastrophic impediment following MI, causing systemic embolism and increasing morbidity and mortality[14,15]. Multiple imaging modalities may be used to diagnose LVAT including transthoracic echocardiography (2D and 3D), transesophageal echocardiography, and cardiac MRI. Thrombus is determined in 50% of patients going to autopsy or surgery, despite the absence of thrombus on transthoracic echocardiography[16].

Electrocardiographic manifestations of left ventricle aneurysms are vary widely, and the persistent ST segment elevation is the most common finding after myocardial infarction[5,17,18]. Reddy et al[10] encountered fQRS in 55 of 110 patients with confirmed LV aneurysm with a sensitivity of about 50% and a specificity of 95%. Lamas et al[19] showed that anterior MI patients with a pathologic Q vawe in DI or in aVL show a greater than 50% chance of developing LV thrombus. The mechanism is thought to be related to insufficient reperfusion and transmural scar formation following an acute MI. In patients with LV aneurysm, Cohn et al[20] was detected persistent ST elevation at autopsy with different frequency, suggesting ECG as a screening tool to detect LV aneurysms. Persistent ST elevation showing LV aneurysm is also frequently found in patients with LVAT after anterior MI. Sagie et al[21] showed that precordial ECGs demonstrating three different types of ECG in 82 subjects after anterior MI. First, persistent ST elevation and positive T-wave are related to an increased risk for LVAT. Second, ST elevation and negative T wave is related to intermediate risk for LVAT. Third, isoelectric ST and negative T wave is associated with minimal risk for LVAT. Similarly, in this study, we presented that persistent ST elevation is augmented in subjects with thrombus in comparison to those without thrombus (34% *vs.* 14%, $p = 0.004$).

In acute coronary syndrome subjects, QRS complex may also change in addition to ischemic ST-segment changes. Açil et al[22] showed sustained QRS following admittance was associated with adverse cardiac events for subjects with LV systolic dysfunction following CA bypass graft isolation. QRS prolongation may show more severe ischemia and infarction development. Currently, no research has been published on the association between LV apical thrombus and QRS duration. We show in the present study that QRS duration was increased in subjects with thrombus compared to those without (136.6 ± 19.6 mm/123.8 ± 25.9 mm; $p = 0.006$). QRS duration with an AUC of 0.66 [0.57-0.75] was demonstrated (Figure 1) and ROC analysis that the QRS duration was a predictor of LVAT with a sensitivity of 68% and a specificity of 68%.

We assessed the electrical conduction by ECG in 56 subjects with LBBB and 45 subjects with fQRS were detected. Previous reports[6] have shown that subjects with LBBB are at higher risk for cardiovascular mortality, acute cardiac death, and heart failure. Acute MI with LBBB has a worse prognosis than acute MI with normal ventricular conduction. To our knowledge, no studies on the association between LVAT, fQRS and LBBB in patients after anterior MI have been done. LBBB was observed more frequently in the thrombus group in comparsion to those without thrombus (40% *vs.* 22%, $p = 0.03$). fQRS from an ECG correlated with myocardial fibrosis[23]. Attachaipanich et al[24] demonstrated that fQRS following admission was an independent predictor of acute arrhythmic events in STEMI patients. Although myocardial fibrosis is important in LVAT disease course, data concerning the relationship between fQRS and LVAT in anterior MI subjects is lacking. We showed that fQRS was more common thrombus subjects in comparison to those without thrombus (37% *vs.* 17%, $p = 0.008$).

Limitations

The major drawback was that thrombus diagnosis was not confirmed by MRI in our study. However, access to cardiac MRI is limited in our country and could not be done due to the shortage of this resource.

Conclusions

Previous studies have shown that persistent ST elevation and fQRS are associated with apical aneurysms, and there is no study on the relationship of LV apical thrombus to electrocardiographic findings. In this study, we demonstrated that the electrocardiographic findings (persistent ST elevation, QRS duration, LBBB and fQRS) were closely associated with LVAT. These findings were predictors of LV thrombus in anterior MI patients.

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Conflict of Interests

The authors report no conflicts of interest.

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