Original article

Fragmented QRS (fQRS) as a Prognostic Factor in Patients with Anterior ST Segment Elevation Myocardial Infarction and Undergoing Thrombolytic Therapy

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ABSTRACT

Background: Many predictors were investigated to identify higher risk anterior STEMI patients who need more aggressive treatment and closer follow up. In this study, we aimed to investigate the prognostic significance of the fragmentation of the QRS complex on the admission ECG of patients with anterior ST segment elevation myocardial infarction and undergoing thrombolytic therapy during hospital course and one month after discharge. **Patients and methods:** This prospective study was performed on a total of 86 patients who were presenting with anterior ST segment elevation myocardial infarction undergoing thrombolytic therapy. They were divided into non-fQRS group of 43 patients and fQRS group of 43 patients. Both groups were followed up during hospital stay and one month after discharge. **Results:** Our study results revealed that Reperfusion was significantly less frequent in fQRS group than in non-fQRS group. Recurrent angina was significantly more frequent in fQRS group than in non-fQRS group at month-1 and overall. Additionally, Coronary intervention was significantly more frequent in fQRS group than in non-fQRS group at hospital and overall. As regarding MACE, it was significantly more frequent in fQRS group. After one month follow up, significantly less left ventricular recovery was evident as well as more left ventricular dysfunction in fQRS group. **Conclusion:** The occurrence of fQRS in ECGs of anterior STEMI patients suggests less frequent successful fibrinolysis, more myocardial injury and hospital events as well as inadequate left ventricular recovery after 1-month follow-up period and could have predictive value of high risk patients.

Keywords: Fragmented QRS; Anterior ST Segment; Thrombolytic Therapy.

Introduction

The ST-segment elevation myocardial infarction (STEMI) is a serious condition with various acute and chronic complications. It is associated with in-hospital adverse cardiovascular events in the form of mortality and morbidities, most commonly heart failure [1]. The best treatment option for (STEMI) patients is primary coronary intervention. However, Fibrinolysis treatment is recommended in some situations when coronary intervention is not available within 90

minutes, onset of symptoms less than 12 hours and with absent contraindications.

Fragmentation in the QRS complex (notching) has been suggested to be due to a dysfunction in intraventricular conduction, [2]. QRS fragmentation has been linked to more adverse cardiovascular events and it implies decreased myocardial reperfusion and more incidence of LV dysfunction [3 and 4].

Therefore, the objective of the current study was to investigate the prognostic significance of the fragmentation of the QRS complex of patients with anterior ST segment elevation myocardial infarction and undergoing thrombolytic therapy during hospital stay and one month follow up after discharge.

AIM OF THE WORK

The aim of this study is to investigate the prognostic significance of the fragmentation of the QRS complex found on the admission ECG of patients with anterior ST segment elevation myocardial infarction and undergoing thrombolytic therapy during hospital course and one month after discharge.

PATIENTS AND METHODS

After ethical committee approval and informed consent from the patients, this prospective study was conducted at tertiary care hospital at National Heart Institute from January 2021 till July 2022 and performed on a total of 86 patients who were presenting with anterior ST segment elevation myocardial infarction undergoing thrombolytic therapy. The research was accepted by the Benha Faculty of Medicine's Ethics Committee {M.s.20.8.2020}.

Study population:

Patients presented with anterior ST segment elevation myocardial infarction (as defined in *(5)* and underwent streptokinase thrombolytic therapy divided into two groups:

Study group (fQRS group): included patients who presented with anterior ST segment elevation myocardial infarction undergoing thrombolytic therapy and their ECG at time of presentation was showing evidence of fragmented QRS.

Control group (non-fQRS group): included patients with matched risk factors and age with the study group and presented with anterior ST segment elevation myocardial infarction undergoing thrombolytic therapy using streptokinase and their ECG was showing no evidence of fragmented QRS at time of presentation. To get this group we reviewed more than 400 cases admitted with anterior wall myocardial infarction at national heart institute emergency department.

Inclusion criteria:

Patients between 18-65 years old of age, patients with anterior ST segment elevation myocardial infarction undergoing thrombolytic therapy.

Exclusion criteria:

Patients who have previous documented myocardial infarction or other structural heart disease, patients with bundle branch blocks (QRS duration more than 120 ms), patients who has contraindication to fibrinolytic treatment, patients with heart failure symptoms prior to hospitalization or previously diagnosed with heart failure, major co-morbidity such as severe renal

impairment, liver failure and severe chest infection.

Study procedure:

Review of medical history:

The time onset of symptoms, presence or absence of previous infarction or angina and previous revascularization, presence or absence of risk factors for ischemic heart disease, diabetes, smoking, hypertension, dyslipidemia and positive family history of ischemic heart disease (IHD) especially those with first degree relation.

All patients were eligible for thrombolytic treatment and received (streptokinase 1500,000 IU over 30 min) as primary intervention was not accessible within 90 min. Absolute and relative Contraindications for Thrombolytic Treatment were considered as mentioned in [6].

Successful reperfusion was considered to be ≥50% resolution of baseline ST segment elevation 90–120 minutes after the onset of thrombolytic therapy. Patients who had failed fibrinolysis were treated with rescue coronary intervention within 60 minutes. Also patients with successful reperfusion and had hemodynamic instability, recurrent chest pain or re-infarction underwent coronary angiography and intervention.

Full clinical examination

General examination, pulse and blood pressure measurement of the patients, as well as chest auscultation to assess pulmonary congestion, auscultation of the heart for the presence of additional heart sounds or murmurs.

Laboratory work:

Random blood sugar, complete blood count, kidney function, and serum troponin, were done.

Electrocardiography:

The resting 12-lead ECG (filter range, 0.15–100 Hz, 25 mm/s, 10 mm/mV) was analyzed. We considered [7] definition of fragmented QRS as additional wave on R (RSR') or (rsr') or (rsR') as shown in column 1, 2 and 3 of the figure below, notch on R or S waves nadir as shown on column 4 and 5 of the figure or more than one R' on 2 successive leads with a duration of less than 120 mins as shown in column 6 below. **Fig 1**
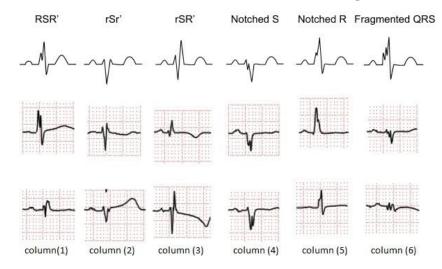

Fig.1: Forms of FQRS

Echocardiography:

All patients were examined by echocardiography both during hospital admission and during one month follow up. We assessed regional wall abnormalities using wall motion score index and left ventricular systolic function by estimating LV Ejection fraction (EF) using modified Simpson methods [8]

Follow up during hospital stay:

During hospital stay, patients were followed up for incidence of successful reperfusion, recurrent chest pain, intervention during hospital stay, major arrhythmia, LV dysfunction, hemodynamic instability, re-infarction, major bleeding complication, mortality and MACE.

Follow up during one month after discharge:

Patients were followed up for one month after hospital discharge through subsequent clinic visits and phone calls to assess: vital signs, recurrent chest pain, need for intervention, palpitations or arrhythmia, LV dysfunction, hemodynamic instability, mortality and MACE.

Medical treatment during hospital stay and after discharge:

Both groups were treated with maximum tolerated full anti-ischemic and anti-failure treatment according to latest Esc guidelines.

Statistical analysis:

IBM SPSS-22 program (Inc, Chicago, IL, USA) has been used to preform statistical analysis. Data have been examined for normal distribution via the Shapiro Walk testing. Qualitative data have been presented as frequency and relative percentage. Chi square testing ($\chi2$) has been utilized to determine change among 2 or more groups of qualitative variables. Quantitative data have been presented as mean ± SD (Standard deviation). Nondependent sample t-testing has been utilized in comparing among 2 nondependent groups of normal distribution variables (parametric data) &Mann-Whitney testing. Data were collected and submitted to statistical analysis. The following statistical tests and parameters were used. The level of significance was taken at P value < 0.050 is significant, otherwise is non-significant.

Results

Of the 43 patients of fragmented QRS group enrolled during the study period, the mean age was 54.4±6.2 years, 30 (69.8%) patients were male, 13 (30.2%) were females, 12 (27.9%) had diabetes mellitus, 24 (55.8%) patients were hypertensive, 16 patients (37.2%) had dyslipidemia, 28 patients (65.1%) were smokers and 4 patients (9.3%) had positive family history of CAD.

Of the 43 patients of non-fragmented QRS group enrolled during the study period, the mean age was 55.7±6.5 years, 32 (74.4%) patients were male and 11 (25.6%) were females. 10 patients (23.3%) had diabetes mellitus, 27 patients (62.8%) were hypertensive, 15 patients (34.9%) had dyslipidemia, 27 patients (62.8%) were smokers and 5 patients (11.6%) with positive IHD family history **(Table 1).**

No statistically significant differences between the studied groups regarding baseline demographic characteristics and comorbidities among the studied groups**.**

Successful reperfusion was less frequent in fQRS group (27 (62.8%) of 43 patients) than in non-fQRS group (38 (88.4%) of 43 patients) the difference statistically was significant (#0.006*).

The need to do intervention at hospital and at overall was significantly more frequent in fragmented group, While was insignificantly more frequent at 1-month follow up. Total of 20 patients in fragmented QRS group underwent coronary intervention (46.5 %). 18 cases (41.9 %) had the intervention during same hospital stay (16 cases with failed pharmacological reperfusion and two other cases with recurrent chest pain after successful fibrinolysis).

Additionally, there were two cases who had coronary intervention during one month post discharge as they presented with acute coronary syndrome (5.3 %). On the other hand, a total of 7 patients in non-fragmented QRS group underwent coronary intervention (16.3 %). 6 cases (14%) had the intervention during same hospital stay (5 cases with failed pharmacological reperfusion and another case with cardiogenic shock after successful fibrinolysis). Additionally, there was a single case who had coronary intervention during one month post discharge who presented with acute coronary syndrome (2.4 %).

Accordingly, mortality was statistically non-significantly more frequent in fQRS group than in non-fQRS group.

Hemodynamically significant arrhythmia was more frequent in fragmented QRS group (7 patients during hospital stay (16.3%), 2 patients in one month follow up (5%) and 7 patients overall (16.3%)) than non-fragmented group which were 3 patients during hospital admission (7%), 1 patients in one month follow up (2.4%) and 3 patients overall (7%), the difference statistically was non-significant at overall.

Hemodynamic instability occurred in fragmented QRS group side in 12 patients during hospital stay (27.9%), 4 patients during one month follow up (10%) and 13 patients overall (30.2%) while occurred in the non-fragmented QRS side in 7 patients during hospital stay (16.3%), 2 patients in one month follow up (4.8%) and 8 patients overall (18.6%). The difference statistically was non-significant **(Table 2).**

Ejection fraction during both hospital stay and after one month follow up was significantly lower in fQRS group than in non-fQRS group. Left ventricular end systolic dimensions during hospital admission and after one month follow up were significantly more in fQRS patients than in non-fQRS patients. Left ventricular end diastolic dimensions during hospital admission and after one month follow up were higher in fQRS patients than in non-fQRS patients. The differences were significant only during hospital stay.

Left ventricular dysfunctions were more frequent in fQRS group than in non-fQRS group. The differences were non-significant except for Left ventricular dysfunction in month-1 which was significant.

Wall motion score index done during hospital stay and after one month follow up was significantly more in fQRS group than in non-fQRS group with mean value of 1.99 and 1.66, respectively during hospital stay and 1.76 and 1.44, respectively during one month follow up.

Left ventricular recovery was considered in our study to be the improvement of LV

systolic function by 5% or more. LV Recovery was significantly more frequent in non-fQRS group, 19 patients (45.2 %) than in fQRS group, 9 patients (23.7 %) **(Table 3).**

Table 1: Baseline demographic characteristics:

Variables		fQRS (n=43)	Non-fQRS (n=43)	p-value
Age (years)	Mean±SD	54.4±6.2	55.7±6.5	^0.362
	Range	41.0–65.0	36.0–64.0	
Sex	Male	30 (69.8%)	32 (74.4%)	#0.631
(n, %)	Female	13 (30.2%)	11 (25.6%)	
Smoking, (n, %)		28 (65.1%)	27 (62.8%)	#0.822
Hypertension		24 (55.8%)	27 (62.8%)	#0.510
Diabetes mellitus		12 (27.9%)	10 (23.3%)	#0.621
Dyslipidemia		16 (37.2%)	15 (34.9%)	#0.822
Family history of IHD		4 (9.3%)	5 (11.6%)	§0.999
Previous IHD		14 (32.6%)	16 (37.2%)	#0.651
Time of onset of pain	Mean±SD	6.8±1.7	6.3±2.2	^0.274
(hours)	Range	3.0–12.0	2.0–11.0	

IHD: (Ischemic heart disease). ^ (Independent t-test). # (Chi square test). § (Fisher's Exact test)

Table 2: clinical findings

Findings	fQRS (n=43)	Non-fQRS (n=43)	p-value
Reperfusion incidence			
Success	27 (62.8%)	38 (88.4%)	#0.006*
Failure	16 (37.2%)	5 (11.6%)	
Need to do intervention:			
In-hospital	18 (41.9%)	6 (14.0%)	#0.004*
Month-1 (n=38, 42)	2 (5.3%)	1 (2.4%)	§0.602
Overall	20 (46.5%)	7 (16.3%)	#0.003*
Mortality in both groups:			
In-hospital	3 (6.9%)	1 (2.3%)	§0.616
Month-1	2 (4.7%)	0 (0.0%)	§0.494
Overall	5 (11.6%)	1 (2.3%)	§0.202
Recurrent angina:			
In-hospital	10 (23.3%)	6 (14.0%)	#0.268
Month-1 (n=39, 42)	20 (51.3%)	11 (26.2%)	#0.020*
Overall	25 (58.1%)	15 (34.9%)	#0.031*
MACE in both groups			
In-hospital	21 (48.8%)	8 (18.6%)	#0.003*
Month-1 (n=38, 42)	5 (12.5%)	2 (4.8%)	§0.259
Overall	21 (48.8%)	9 (20.9%)	#0.007*
Major arrhythmias:			
In-hospital	7 (16.3%)	3 (7.0%)	#0.178
Month-1 (n=38, 42)	2 (5.0%)	1 (2.4%)	§0.611
Overall	7 (16.3%)	3 (7.0%)	#0.178
hemodynamic instability:			
In-hospital	12 (27.9%)	7 (16.3%)	#0.194
Month-1 (n=38, 42)	4 (10.0%)	2 (4.8%)	§0.427
Overall	13 (30.2%)	8 (18.6%)	#0.209

*#Chi square test. *Significant   Some cases had event at both times. §Fisher's Exact test. *Significant*

Table 3: Echocardiography findings:

	Time	fQRS (n=43)	Non-fQRS (n=43)	p-value	
		Ejection fraction (%)			
In-hospital	Mean±SD	39.1±9.3	45.3±7.3	^<0.001*	
	Range	24.0–60.0	31.0–64.0		
Month-1 (n=38, 42)	Mean±SD	43.8±9.1	49.8±7.4	^0.002*	
	Range	27.0–61.0	34.0–65.0		
		Left ventricular end systolic dimension (cm)			
In-hospital	Mean±SD	3.7±0.5	3.4±0.3	^0.001*	
	Range	2.8–4.9	2.6–4.1		
Month-1 (n=38, 42)	Mean±SD	3.5±0.5	3.3±0.4	^0.017*	
	Range	2.7–4.4	2.5–4.5		
		Left ventricular end diastolic dimension (cm)			
In-hospital	Mean±SD	4.9±0.3	4.8±0.2	^0.016*	
	Range	4.6–6.1	4.2–5.5		
Month-1 (n=38, 42)	Mean±SD	5.0±0.4	4.9±0.4	^0.257	
	Range	4.1–5.8	4.3–6.0		
		Left ventricular dysfunction (EF less than 55%)			
In-hospital		40 (93.0%)	35 (81.4%)	#0.106	
Month-1 (n=38, 42)		32 (84.2%)	25 (59.5%)	#0.015*	
Overall		40 (93.0%)	35 (81.4%)	#0.106	
		WMSI			
In-hospital	Mean±SD	**1.99±0.38**	**1.66±0.31**	**<0.001***	
	Range	**1.30–2.70**	**1.00–2.20**		
Month-1 (n=38,42)	Mean±SD	**1.76±0.36**	**1.44±0.31**	**<0.001***	
	Range	**1.10–2.50**	**1.00–2.10**		
		Left ventricular recovery during one month			
Recovery	9 (23.7%)	19 (45.2%)		**#0.044***	
No recovery	29 (76.3%)	23 (54.8%)			

NA: Not applicable. . ^ (Independent t-test). # (Chi square test). § (Fisher's Exact test)

Discussion

Left ventricular dysfunction in patients after an acute myocardial infarction (MI) is considered important predictor of morbidity and mortality. Besides myocardial stunning, which usually improves within weeks after revascularization, scar formation is another major cause or irreversible left ventricular systolic dysfunction. Methods used to diagnose scaring of the myocardium include MRI, histopathological examination, and scintigraphy [9]. However, those are considered expensive and less available compared with surface ECG, especially in acute situation.

Potential ECG fragmentation mechanism was examined by autopsy findings in patients with myocardial infarction and left ventricular aneurysm. Significant myocardial necrosis, with islands of viable myocardial tissue interspersed in fibrous tissue [10]. Accordingly, determining the prognostic significance of fQRS in EF recovery in acute anterior STEMI patients who treated with thrombolytic treatment is our main point of interest.

This study was conducted and aimed to investigate the prognostic value of the fragmentation of the QRS complex in

admission surface ECG of patients with anterior ST segment elevation myocardial infarction and undergoing thrombolytic therapy during hospital course and one month after discharge.

This prospective study was held in tertiary care hospital at National Heart Institute from January 2021 till July 2022 and performed on a total of 86 patients who were presenting with anterior ST segment elevation myocardial infarction undergoing thrombolytic therapy.

During this study, of more than 400 patients with anterior wall myocardial infarction examined in National heart institute during the study period, 86 matched patients were included in the study (43 in each group).

Study group (fQRS group): included patients who presented with anterior ST segment elevation myocardial infarction undergoing fibrinolytic therapy and their ECG was showing evidence of fragmented QRS.

Control group (non-fQRS group): included patients who matched risk factors and age with the study group and presented with anterior ST segment elevation myocardial infarction receiving fibrinolytic therapy and their ECG was showing no evidence of fragmented QRS.

Our study results revealed that successful reperfusion was significantly less frequent in fQRS group (62.8%) than in non-fQRS group (88.4%) *(p value=0.006)*. *Patients with failed fibrinolysis were treated with coronary intervention within 60 minutes which were 16 patients in* fQRS group and 5 patients in non-fQRS group. Accordingly, the need for coronary intervention was significantly more frequent in fQRS group (46.5%) than in

non-fQRS group (16.3%) *(p value=0.003*).*

Our results showed that Left ventricular dysfunction (month-1) was significantly more frequent in fQRS group than in non-fQRS group *(p value=0.015),* which indicates better left ventricular recovery in non-fQRS group. Wall motion score index was significantly more in fQRS group than in non-fQRS group *(p <0.001*)* during hospital stay and after one month follow up.

Similarly, [1] conducted a prospective study for patients who presented with acute anterior STEMI and received thrombolytic therapy. He found that the presence of fQRS was associated with poor improvement of LVEF after a 12-months follow-up. Additionally, [4] reported that fQRS may be a marker of more functional deterioration of left ventricle. Other retrospective studies involving STEMI patients proved that fragmented QRS is significantly related to higher NT-proBNP and lower LVEF, and is a prognostic marker of impaired local ventricular systolic function [11].

On the other hand, our follow-up period of patients was relatively short as the previous studies tracked the follow-up for 12 months after treatment such as [12 and 13] who examined the significance of fQRS and its association with left ventricular dysfunction. They reported that EF was significantly lower in the fQRS group compared to the non-fQRS group at a 12 months follow-up.

Recurrent angina was significantly more frequent in fQRS group than in non-fQRS group at month-1 and overall *(p value=0.020, 0.031),* respectively. This was in agreement with [13] study which revealed fQRS group had higher

thrombolysis failure rates than the non-fQRS group. Also, [14] revealed that the appearance of fragmented QRS was associated with more vascular reperfusion failure.

Our study results also reported that major arrhythmias and hemodynamic instability (in-hospital, month-1 and overall) were more frequent in fQRS group than in non-fQRS group, the difference statistically was non-significant. This was in concordance with [15] who showed that there were no significant differences in major arrhythmias in patients with fQRS compared with patients without fQRS at their discharge time. Also, [16] concluded that in patients with ACS who underwent successful revascularization (TIMI = 3), the presence of f-QRS was not associated with a higher incidence of arrhythmias compared to patients without f-QRS in the short-time follow-up.

In discordance to our results, [17] found a significant fQRS association with ventricular tachycardia events. Additionally, [18] have shown that fQRS patients had significantly higher risk of arrhythmia and sudden death.

Mortality in our results was noted more in fQRS group than in non-fQRS group at month-1 and overall (*p value=0.49, 0.20*) respectively*,* which was statistically non-significant. This was in agreement with [5] who suggested that cardiovascular mortality is frequently more with fQRS which may be due to ventricular arrhythmia, sudden cardiac death or cardiogenic shock. On the other hand, some studies have shown that f-QRS in the superficial ECG is not a reliable predictor mortality [19]*.*

Our work showed that there is significant correlation between MACE and fQRS side both in hospital and overall (***P=0.003 and 0.007,*** respectively). Similarly, [20] reported that significantly more cardiac events in patients with coronary artery disease was associated with the presence of QRS fragmentation. Also, this was consistent with [21] who found a significant correlation between QRS fragmentation with in-hospital MACE in acute myocardial infarction.

Conclusion

The main result of the present study is that the occurrence of fQRS in ECGs of anterior STEMI patients and undergoing fibrinolytic therapy suggests more serious myocardial ischemic injury, more hospital events and inadequate left ventricular recovery during one month follow up. Additionally, adverse effects in the form of failed pharmacological reperfusion, left ventricular dysfunction, major arrhythmias, hemodynamic instability, recurrent chest pain and the need for coronary intervention were more frequent in the fQRS presenters.

Assessment of fQRS on surface ECG is a non-expensive, non-invasive, and easy method for suspecting high-risk acute anterior STEMI patients who have lower chance of successful thrombolytic therapy as well as lower left ventricular EF recovery. Accordingly, these patients should be treated more aggressively, preferably with primary coronary intervention if available, and should be followed up more closely.

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