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A Cross-Sectional Study of Correlation of Fragmented QRS Complex and the Clinical Outcomes in a Patient with Non-ST Elevation Myocardial Infarction

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ABSTRACT

A relatively recent ECG marker that has attracted growing attention in recent years is the fragmented QRS complex (fQRS). Present study was aimed to study correlation of fragmented QRS complex and the clinical outcomes in a patient with non-ST elevation myocardial infarction. Present study was single-center, Cross Sectional Observational Study, conducted in patients of Age >18 years, having confirmed NSTEMI. During this study, all NSTEMI patients were divided into 2 groups. Group A was of patients who were diagnosed as NSTEMI and have fQRS complex in ECG and Group B was of patients who were diagnosed as NSTEMI but have no fQRS complex in ECG. Findings suggest that older age, smoking, diabetes, and specific coronary artery involvement are associated with a higher likelihood of fQRS. In contrast, gender, hypertension and single or double-vessel coronary disease do not show significant associations with fQRS in this study. Anterior ECG leads in detecting LAD lesion. -In lead V1-V2, the sensitivity is 64.58%, with a specificity of 100%. The PPV and NPV are 100% and 48.48% respectively. The LR (-) of 0.35 suggests a moderate decrease in the likelihood of LAD lesion. In lead V3-V4, the sensitivity rises to 97.92%, indicating these leads correctly identify nearly all LAD lesions, with 100% specificity. The PPV and NPV are also 100% and 94.12% respectively. The LR- of 0.02 further suggests a minimal decrease in the likelihood of LAD lesion. The diagnostic accuracy of ECG leads using fQRS complexes was significantly higher for detecting coronary lesions in patients with NSTEMI.

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Key Words
Fragmented QRS complex, non-ST elevation myocardial infarction, ECG findings, coronary lesions

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INTRODUCTION

A common manifestation of acute coronary syndrome (ACS), non-ST-elevation myocardial infarction (NSTEMI) is a significant global cause of morbidity and mortality. Approximately 1.5 million hospital admissions in the United States alone are attributable to ACS, making it a major factor in hospital admissions[1]. It has a high rate of morbidity and mortality and makes up about half of all cases of acute coronary syndrome (ACS). Therefore, for effective management and better outcomes, early and accurate diagnosis of NSTEMI is essential[2,3].

Chest pain, elevated cardiac biomarkers and dynamic Electrocardiography (ECG) changes, such as ST-segment depression or T-wave inversion, are all characteristics of this common clinical syndrome. The evaluation of patients with suspected ACS requires the use of electrocardiography (ECG), which offers crucial information on the presence and severity of myocardial ischemia and infarction[4]. Several ECG variables, such as ST-segment deviation, T-wave inversion and QT interval prolongation, have been researched to help with the diagnosis of NSTEMI. These parameters, however, are not unique to NSTEMI and can be affected by a number of non-cardiac factors[5,6].

A relatively recent ECG marker that has attracted growing attention in recent years is the fragmented QRS complex (fQRS). It is a recently discovered ECG parameter that indicates myocardial fibrosis and has been linked to poor cardiac outcomes in a number of populations, including those with ACS[7,8]. Present study was aimed to study correlation of fragmented QRS complex and the clinical outcomes in a patient with non-ST elevation myocardial infarction.

MATERIALS AND METHODS

Present study was single-center, Cross Sectional Observational Study, conducted in department of general medicine, at Bharati Vidyapeeth Deemed to be University Medical College, Dhankawadi, Pune, India. Study was conducted during the period of June 2022 to January 2024. Study was approved by institutional ethical committee.

Inclusion Criteria:

- Patients of Age >18 years, having confirmed NSTEMI, willing to participate in present study.

Exclusion Criteria:

- Patients with ST Elevation myocardial infarction.
- Patients with previously implanted implantable cardioverter-defibrillator (ICD) or has a clinical indication for an ICD at the time of enrolment.
- Patients with cardiomyopathy, myocarditis or any congenital heart disease.
- Patients with permanent atrial fibrillation.
- Patients having Right bundle branch block and incomplete right bundle branch block.

Study was explained to participants in local language and written informed consent was taken. Diagnosis of NSTEMI was made by looking for signs and symptoms of myocardial ischemia such as crushing pain or tightness in the chest that may spread to the shoulder or other parts of the upper body, chest pain that occurs when one at rest, shortness of breath, sweating and anxiety and for T wave inversion or ST segment depression in any of the ECG leads plus the positive troponin levels.

All patients were subjected to a detailed history and clinical examination. NYHA Grading, Electrocardiogram, Serum Troponin T or Serum Troponin I levels, 2D Echocardiography was done in all subjects and coronary angiography was done wherever possible. During this study, all NSTEMI patients were divided into 2 groups. Group A was of patients who were diagnosed as NSTEMI and have fQRS complex in ECG and Group B was of patients who were diagnosed as NSTEMI but have no fQRS complex in ECG. Then the NYHA Grading, ECG findings of both groups were correlated with 2D Echocardiography findings and coronary angiography findings. Findings of both groups were compared and in this study, we assessed correlation of fQRS with the clinical outcomes of NSTEMI. Clinical parameters like age, diabetes, hypertension and duration of NSTEMI were taken into consideration.

The collected data was coded and entered in Microsoft Excel sheet. The data was analysed using SPSS (Statistical Package for social sciences) version 25.0 software. The results were presented in tabular and graphical format. For Qualitative data various rates, ratios and percentages (%) were calculated. Chi-square test/Fisher's exact test was used to find the association between 2 or more attributes for qualitative data variables. In this study, the results were analysed using Chi square test and ROC curve. $P<0.05$ considered as statistically significant.

RESULTS AND DISCUSSIONS

Out of a total of 114 cases, the fQRS group comprises 64 cases (56.14 %), while Normal QRS group includes 50 cases (43.86 %). In present study, observed age distribution difference, NYHA classifications, hospitalisation durations and smoking status between the fQRS and Normal QRS groups was statistically significant. While observed difference in gender distribution, diabetes mellites and hypertension

between the fQRS and Normal QRS groups was not statistically significant.

Table 1: General Characteristics

	fQRS (n=64)	Normal QRS (n=50)	p-value
Age (years)			
>55	47(73.44%)	27(54%)	0.03
≤55	17(26.56%)	23(46%)	
Gender			
Male	40(63.5%)	26(52%)	0.26
Female	24(37.5%)	24(48%)	
NYHA on admission			<0.001
1	0	5 (10%)	
2	12(18.75%)	24 (48%)	
3	42(65.63%)	20 (40%)	
4	10(15.63%)	1 (2%)	
Duration of Hospitalisation in Days			
1	3 (4.68%)	13 (26%)	<0.001
2	4 (6.25%)	11 (22%)	
3	28 (43.62%)	20 (40%)	
4	26 (40.62%)	6 (12%)	
5	3 (4.68%)	0	
Comorbidities			
Diabetes Mellitus	50	26	0.003
Hypertension	50	36	0.45
Smoking	30 (46.9%)	13 (26%)	0.022

In present study, inferior wall hypokinesia and anterior wall hypokinesia was significantly more common in the fQRS group compared to the normal QRS group, difference was statistically significant (P-value of 0.001). However, lateral wall hypokinesia and septal wall hypokinesia did not show significant differences between the two groups, with P-values of 0.43 and 0.087, respectively.

Table 2: Distribution of Patients According to 2D ECHO Findings.

2D ECHO findings	fQRS (n=64)	Normal QRS (n=50)	p-value
Inferior wall Hypokinesia	37	14	0.001
Lateral wall Hypokinesia	25	16	0.43
Anterior wall Hypokinesia	42	17	0.001
Septal wall Hypokinesia	32	17	0.087

Among the 64 individuals with fQRS, majority had EF between 41-45% (45.31%) while among the 50 individuals with Normal QRS, majority had EF between 46-50% (40%). The P value of less than 0.001 indicates that the differences in EF distribution between the fQRS and Normal QRS groups are statistically significant.

Among the 64 individuals with fQRS, 20 had single-vessel disease, 22 had double-vessel disease, and 19 had triple-vessel disease. In contrast, among the 50 individuals with Normal QRS, 11 had single-vessel disease, 21 had double-vessel disease, and 6 had triple-vessel disease.

Findings suggest that fQRS is more commonly associated with LAD and RCA involvement in this patient population, potentially reflecting more extensive coronary artery disease in those with fQRS. The analysis of left circumflex artery (LCX) occlusion percentages between the fQRS group (n=64) and the non-fQRS group (n=50) shows no statistically significant differences, with a p-value of 0.74. The comparison of right coronary artery (RCA) occlusion percentages between the fQRS group (n=64) and the non-fQRS group (n=50) reveals a statistically significant difference, with a p-value of 0.013.

Table 3: Coronary Artery Characteristics.

Characteristics	fQRS (n=64)	Normal QRS (n=50)	p-value
Ejection fraction			
< 30%	1 (1.56%)	0	<0.001
30-35%	5 (7.81%)	2 (4%)	
36 -40%	4 (6.25%)	0	
41-45%	29 (45.31%)	9 (18%)	
46-50%	21 (32.81%)	20 (40%)	
>50%	4 (6.25%)	19 (38%)	
Single-vessel disease	20	11	0.27
Double-vessel disease	22	21	0.41
Triple-vessel disease	19	6	0.03
Coronary vessel involvement			
Left Anterior Descending Artery	42	19	0.003
Left Circumflex Artery	23	13	0.08
Right Coronary Artery	38	16	0.003
Percentage of occlusion LAD			
90% < D <100%	7	2	0.1
70% < D =90%	28	9	
50% = D =70%	7	8	
Percentage of occlusion LCX			
90% < D <100%	6	2	0.74
70% < D =90%	10	6	
50% = D =70%	7	5	
Percentage of occlusion RCA			
90% < D <100%	13	1	0.013
70% < D =90%	19	7	
50% = D =70%	6	8	

The analysis indicates significant associations between fragmented QRS (fQRS) and age (P=0.03, OR=2.36, 95% CI: 1.07-5.17), smoking (P=0.02, OR=2.51, 95% CI: 1.13-5.59), diabetes mellitus (P=0.004, OR=3.30, 95% CI: 1.46-7.42) and coronary artery lesions in the Left Anterior Descending artery (P=0.003, OR=3.11, 95% CI: 1.44-6.72) and Right Coronary artery (P=0.01, OR=2.85, 95% CI: 1.28-6.33). These findings suggest that older age, smoking, diabetes and specific coronary artery involvement are associated with a higher likelihood of fQRS. In contrast, gender, hypertension and single or double-vessel coronary disease do not show significant associations with fQRS in this study.

Table 4: Logistic Regression Analysis.

Parameters	p-value	OR	95% CI
Age	0.03	2.36	1.07-5.17
Gender	0.26	0.65	0.30-1.38
Smoking	0.02	2.51	1.13-5.59
Diabetes Mellitus	0.004	3.30	1.46-7.42
Hypertension	0.45	1.39	0.59-3.27
Left Circumflex Artery	0.09	2.21	0.88-5.60
Right Coronary Artery	0.01	2.85	1.28-6.33
Left Anterior Descending Artery	0.003	3.11	1.44-6.72
Single-vessel disease	0.27	1.61	0.69-3.78
Double-vessel disease	0.45	0.72	0.34-1.55
Triple-vessel disease	0.03	3.10	1.13-8.48

Anterior ECG leads in detecting LAD lesion. -In lead V1-V2, the sensitivity is 64.58%, with a specificity of

100%. The PPV and NPV are 100% and 48.48% respectively. The LR (-) of 0.35 suggests a moderate decrease in the likelihood of LAD lesion. In lead V3-V4, the sensitivity rises to 97.92%, indicating these leads correctly identify nearly all LAD lesions, with 100% specificity. The PPV and NPV are also 100% and 94.12% respectively. The LR- of 0.02 further suggests a minimal decrease in the likelihood of LAD lesion.

Inferior ECG leads (II, III, aVF) using Fqrs in detecting RCA lesion. -These leads show a sensitivity of 92.68, with a specificity of 95.65%. The positive predictive value (PPV) is high at 97.44%. The negative predictive value (NPV) is 88%. The positive likelihood ratio (LR+) of 21.32, while the negative likelihood ratio (LR-) of 0.08. Overall, leads II, III and aVF demonstrate strong diagnostic accuracy for detecting RCA lesion, with high sensitivity and specificity, making them reliable indicators in clinical settings.

Lateral ECG leads in detecting LCX lesion-In lead V5-V6, the sensitivity is 73.33%, with a specificity of 94.12%. The positive predictive value (PPV) is high at 91.67%. However, the negative predictive value (NPV) is notably low at 0.28%. The positive likelihood ratio (LR+) of 12.47, while the negative likelihood ratio (LR-) of 0.28. In contrast, lead I and AVL show a lower sensitivity of 40% but a specificity of 88.24%. The PPV is 75%, while the NPV is 62.50%. The LR+of 3.4, whereas the LR-of 0.68.

Table 5: Distribution of Diagnostic Efficacy Measures of ECG Leads

	Sensitivity	Specificity	PPV	NPV	LR (+)	LR (-)
Anterior ECG leads						
fQRS Lead v1, v2	64.58%	100%	100%	48.48%	-	0.35
fQRS Lead v3, v4	97.92%	100%	100%	94.12%	-	0.02
Inferior ECG leads						
fQRS Lead II, III, aVF	92.68%	95.65%	97.44%	88%	21.32%	0.08%
Lateral ECG leads						
fQRS Lead V5, V6	73.33%	94.12%	91.67%	0.28 %	12.47	0.28
fQRS Lead I avL	40.%	88.24%	75%	62.50 %	3.4	0.68

In two adjacent leads of a typical 12-lead ECG, the presence of an additional R wave, a notching in the S wave's nadir, or the downstroke of the R wave is referred to as fQRS. Although the exact cause of fQRS is unknown, conduction delays and/or heterogeneous myocardial scar formation are believed to be its causes[7]. In patients with NSTEMI, fQRS has been linked to a higher risk of adverse cardiovascular events, such as ventricular tachycardia (VT), ventricular fibrillation (VF) and sudden cardiac death (SCD)[9,10]. The identification of fQRS on ECG as an additional prognostic marker offers a non-invasive, readily available and cost-effective method for enhancing risk stratification in NSTEMI patients. The clinical implications of fQRS in the diagnosis and management of NSTEMI are still uncertain due to the inconsistent results. Consequently, we hypothesize that fQRS is a valuable indicator of NSTEMI and may possess superior diagnostic precision in comparison to other ECG parameters.

In this study out of a total of 114 patients, the fQRS group comprises 64 (56.14%) patients. In contrast, the Normal QRS group includes 50 (43.86%) patients. In our study, individuals with fQRS were more likely to be older than 55 years, indicating a potential association between fQRS and advanced age. This finding is statistically significant with a P value of 0.03. Similar findings were noted by Guo[11] Luo[12] and Das[13].

The analysis of New York Heart Association (NYHA) functional classification on admission between individuals with fragmented QRS (fQRS) and those with Normal QRS reveals substantial differences in functional status. The P value of <0.001 indicates that these differences in NYHA classifications between the fQRS and Normal QRS groups are statistically significant. The significant differences in NYHA classifications between the fQRS and Normal QRS groups highlight the clinical relevance of fQRS as an indicator of worse functional status[13].

In our study significant differences were observed in the duration of hospitalization between fQRS and Normal QRS groups (P<0.001), indicating potential implications for patient management. This indicates that patients with fQRS may require longer hospital stays, possibly due to more severe cardiac conditions or complications. This aligns with findings from Luo G *et. al.* on the predictive value of fragmented QRS for cardiovascular events in acute myocardial infarction that link fQRS with worse cardiac outcomes and longer hospitalization periods[12].

In our study there was a notable prevalence of smoking among individuals with fQRS compared to those with Normal QRS, with a statistically significant P value of 0.022. The study performed by Bayramoglu[14] on association between fragmented QRS complexes and left ventricular dysfunction in healthy smokers stated that there is significant relationship between smoking and individuals with fQRS and normal QRS. Study by Das[13] on significance of a fragmented QRS complex versus a q wave in patients with coronary artery disease reported that no difference in smoking among individuals with fQRS compared to those with Normal QRS (P=0.77).

In this study, we observed significant differences in the prevalence of regional wall hypokinesia between individuals with fragmented QRS (fQRS) and those with a normal QRS complex on a 2D echocardiogram. These findings are consistent with previous studies that have demonstrated an association between fQRS and myocardial scar or ischemia, often resulting in regional wall motion abnormalities.

For instance, Das[13] found that fQRS is a marker of myocardial scar and is associated with a higher incidence of wall motion abnormalities, particularly in the anterior and septal walls. Similarly, Pietrasik and Zareba[15] reported that patients with fQRS on their

ECG had more pronounced regional wall hypokinesia, particularly in the anterior and septal regions, compared to those with a normal QRS complex.

The comparison of ejection fraction (EF) distribution between individuals with fragmented QRS (fQRS) and those with normal QRS in this study reveals a statistically significant difference, with a $p<0.001$. This significant difference in EF distribution underscores the clinical importance of recognizing fQRS on ECG as a potential indicator of more severe myocardial involvement, which may necessitate more aggressive therapeutic interventions and closer monitoring.

The higher prevalence of triple-vessel disease in the fQRS group observed in our study supports the hypothesis that fQRS is a marker of more severe and widespread coronary artery disease. This reinforces the clinical significance of identifying fQRS on an electrocardiogram, as it may indicate the need for more aggressive diagnostic and therapeutic strategies to manage the underlying CAD and prevent adverse outcomes. The relatively higher occurrence of single-vessel disease in individuals with normal QRS suggests that these patients may have less extensive coronary involvement, which could translate into a better prognosis compared to those with fQRS.

The LAD artery, often referred to as the widow-maker due to its crucial role in supplying a significant portion of the left ventricle, was more frequently involved in individuals with fQRS. This is consistent with previous studies that have highlighted the association between fQRS and more extensive coronary artery involvement, especially in critical arteries like the LAD. For instance, Das[13] and Pietrasik and Zareba[15] both found that fQRS is often associated with significant lesions in major coronary arteries, including the LAD and is linked to worse clinical outcomes. The higher prevalence of RCA involvement in the fQRS group also aligns with studies indicating that fQRS may be a marker of more widespread ischemic disease, involving multiple major coronary arteries. This supports the hypothesis that fQRS on an electrocardiogram is indicative of more severe and extensive coronary artery disease, requiring more aggressive management to mitigate the risk of adverse cardiovascular events.

In contrast, the lower incidence of LAD and RCA lesions in the normal QRS group suggests that these individuals may have less extensive coronary artery involvement. This further underscore the importance of recognizing fQRS as a potential marker of more severe coronary pathology. Additionally, we found considerable variation in the distribution of coronary lesions, especially with regard to particular arteries like the LAD and RCA, indicating a possible link between these lesions and the existence of fQRS.

In previous study by Guo[11] the sensitivity, specificity and positive and negative predictive values of fQRS in ECG leads II, III and aVF were 92.3%, 65.5%, 85.6 and 79.2%, respectively., the sensitivity, specificity and positive and negative predictive values of fQRS in ECG leads I, aVL and V6 were 89.4%, 71.7%, 83.5 and 80.9%, respectively. Study reported that specificity of fQRS complexes in identifying lesions in the left circumflex and right coronary arteries was lower for the inferior and lateral leads than that for the limb leads (65.5% versus 71.7%)., however, the former had higher sensitivity (92.3% versus 89.4%). The frequencies of fQRS complexes recorded in each ECG lead could identify the culprit vessel and this was particularly useful when the LAD was the culprit vessel. In addition, the diagnostic accuracy of fQRS complexes was significantly higher than that of ischemic T-waves for the diagnosis of NSTEMI.

Overall, the results from this study suggest that while V5-V6 are highly effective in detecting LCX lesions, leads I and aVL have more limited sensitivity and diagnostic performance. This highlights the importance of using a combination of ECG leads to enhance the accuracy of diagnosing LCX lesions and underscores the utility of V5-V6 as a key component in the diagnostic evaluation of lateral wall myocardial involvement. This study highlights the significance of taking age, smoking status, comorbidities and specific coronary artery involvement into account when assessing risk factors associated with fragmented QRS complex (fQRS). Overall, it offers insightful information about the relationship between fragmented QRS complex and clinical outcomes in patients with non-ST elevation myocardial infarction.

Overall, the findings from this study suggest that while leads V1-V2 are useful for detecting fQRS, leads V3-V4 are superior in both sensitivity and reliability. This reinforces the importance of a comprehensive ECG evaluation, particularly focusing on anterior leads, for the accurate detection of fQRS and its associated risk factors. The consistency of these results with existing literature further validates the clinical relevance of anterior ECG leads in the assessment of myocardial pathology.

Further studies on the predictive value of fragmented QRS (fQRS) complexes in patients with non-ST-elevation myocardial infarction (NSTEMI) could focus on expanding the understanding of the pathophysiological mechanisms underlying fQRS formation and its specific relationship with myocardial scarring and fibrosis. Prospective studies with larger, more diverse patient populations could help validate fQRS as a robust marker for adverse outcomes, such as arrhythmias, heart failure and mortality.

Limitations of present study were single-Center Design, small sample size (which could reduce statistical power and the reliability of the results), selection Bias (study included a specific subset of NSTEMI patients) and

short follow-up period (may not capture the full spectrum of outcomes associated with NSTEMI and fQRS, limiting understanding of the long-term predictive value of fQRS).

CONCLUSION

The frequency of fQRS complexes was higher in elderly and diabetic patients with NSTEMI. The diagnostic accuracy of ECG leads using fQRS complexes was significantly higher for detecting coronary lesions in patients with NSTEMI. The frequency of fQRS complexes recorded in each of the ECG leads can be used to identify culprit vessels in patients with NSTEMI.

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