The Usefulness of Fragmented QRS in Predicting the Successful Reperfusion by using non Invasive Criteria of Reperfusion in STEMI after Thrombolytic Therapy

Zuber Suleman Kothi[1], Abdul Mateen Athar[2], Ashok P. Yenkanchi[3], Ayesha Siddiqua begum.G[4], Syed Musheer Hussaini[5]

ABSTRACT

Introduction: QRS fragmentation (fQRS) on electrocardiogram was determined as one of the indicator of mortality and morbidity in ST elevated myocardial infarction. However in this group of patients there are only few studies done so far to evaluate thrombolytic response in presence of fQRS on admission. Hence, the aim of study was to investigate the clinical characteristics of patients with the fragmented QRS and to determine whether fQRS can be used as a predictor of thrombolytic therapy response using non invasive markers for reperfusion in patients admitting for the first time with STEMI.

Material and Methods: Taking into account all the inclusion and exclusion criteria's 50 patients were divided into two groups as fQRS positive and fQRS negative in this observational study. Demographic, laboratory and electrocardiographic data on admission were recorded. Based on reperfusion criteria patients were divided into two groups: 1) SCR + VE: Successful coronary reperfusion 2) SCR – VE: Failed coronary reperfusion.

Results: In this study fQRS was detected in 16 patients out of 50. In the fragmented QRS group the thrombolytic failure was higher compared to fQRS negative group ($p<0.001$). In addition patients with fQRS had higher CK-MB levels on admission, low left ventricular ejection fraction compared to fQRS negative group.

Conclusion: The occurrence of fQRS is beneficial in identifying the patients with thrombolytic failure. Hence in patients with STEMI fQRS helps in risk stratification and can be used as an indicator for early revascularization.

Keywords: STEMI, fragmented QRS, reperfusion

INTRODUCTION

Myocardial infarction is becoming an increasingly important problem in developing countries. In the industrialized world despite impressive advances in diagnosis and management, acute myocardial infarction continues to be a major public health problem. Of particular concern from a global perspective are the burden of disease in developing country become similar to those now afflicting developed countries.[1] In acute MI the immediate therapeutic objective is to obtain coronary artery reperfusion, which can only be confirmed definitely by coronary angiography. However to look for reperfusion angiographically it becomes difficult because only a few medical centres can provide this facility particularly in developing countries and this invasive technique carries an inherent risk too. Although 60 to 70% of treated patient can be successfully reperfused.[2,3] Thrombolytic treatment fails in a substantial proportion. These "non responsive" patients have a significantly high mortality rate[3,4] and may therefore be candidate for emergency angioplasty or coronary artery bypass surgery. For this reason, there is a need to identify some simple bedside non invasive markers at admission which can predict the reperfusion success in patients with STEMI who undergo thrombolytic therapy. So that these patients can be directed to early PCI.

Acute myocardial infarction may affect the QRS complex as well as the ST segment. For this reason, several QRS complex changes on admission ECG such as fragmented QRS can help us to provide important prognostic information on the success of reperfusion. Several studies have shown that QRS fragmentations on surface ECG have been associated with larger infarcted area as well as with increased mortality, morbidity, sudden cardiac death and recurrent adverse cardiovascular events.[5-8] According to Chatterjee S and Changawala N cardiac fibrosis was the main causative mechanism for fQRS.[9] Additionally, fQRS may represent altered ventricular depolarization, which can be derived from mechanisms such as non-homogeneous activation of ischemic ventricles in the setting of STEMI.

Kocamen et al found that patients without fQRS achieved increased ST resolution, higher reduction in QRS duration and better myocardial reperfusion in comparison to patients with fQRS after PCI.[10] But there are only few studies done so far which has used fragmented QRS to predict the reperfusion success using only non invasive criteria of successful thrombolysis in patients with STEMI.

The aim of this study was to investigate the clinical characteristics of patients with the fragmented QRS and to determine whether fQRS can be used as a predictor of thrombolytic therapy response using non invasive markers for reperfusion in patients admitting for the first time with STEMI.

MATERIAL AND METHODS

All the patients with acute STEMI who satisfied the inclusion and exclusion criteria were included in the study. Total of 60

[1]Assistant Professor, [3]Professor, Department of Medicine, Al-Ameen Medical College and Hospital, Athani Road, Vijayapur, [2]Assistant Professor, Department of Medicine, ST John's Medical College, Kormangala, Bangalore, Karnataka, [4]Junior Resident, Medlife Clinic, Bangalore, [5]Senior Resident, Department of Community Medicine, Prathima Institute of Medical College, Dist-Karimnagar, Telangana, India

Corresponding author: Dr. Zuber Suleman Kothi, Assistant Professor, Department of Medicine, Al-Ameen Medical College and Hospital, Athani Road, Vijayapur-586108, Karnataka, India.

How to cite this article: Zuber Suleman Kothi, Abdul Mateen Athar, Ashok P. Yenkanchi, Ayesha Siddiqua begum.G, Syed Musheer Hussaini. The usefulness of fragmented QRS in predicting the successful reperfusion by using non invasive criteria of reperfusion in STEMI after thrombolytic therapy. International Journal of Contemporary Medical Research 2016;3(10):2965-2968.

patients were admitted to CCU with STEMI during a period of 12months.10 patients were excluded from study as they had contraindication for thrombolysis.

The study protocol was approved by the institutional review boards of Al-ameen medical college and written informed consent was obtained from all patients and their families after full discussion of the study process.

Inclusion Criteria

1. Following diagnostic criteria of acute STEMI on ECG
   a. >2mm ST segment elevation at the J point in at least two chest leads or
   b. >1mm ST segment elevation in at least two limb leads or
   c. Reciprocal ST segment depression (V2-V3) due to posterior wall damage.
2. Elevated cardiac biomarkers
3. Patient with typical ischemic symptoms

Exclusion Criteria

1. Patients with pericardial and myocardial diseases.
2. Patients on digoxin, amiodarone which make ST-T changes difficult to interpret.
3. Patients with valvular heart disorders, infiltrative disorders and thyroid disorders.
4. Patients having bundle branch block on ECG (LBBB or RBBB),
5. Patients with fQRS in old ECGs.
6. Patient with contraindication for thrombolytic therapy.
7. Patients not giving informed consent.

Patients were treated and ECGs were taken as per the standard treatment protocol of acute STEMI.

Fragmented QRS complex on ECG was defined by the presence of various RSR' patterns and included[11]

1. Notching of the down stroke or upstroke of the S wave, or
2. The presence of >1 R', or
3. An additional R wave (R') or
4. Notching of the R wave.

These should be present in two contiguous leads, corresponding to a major coronary artery territory on the resting 12-lead ECG. A Ophuis et al reported presence of 3 or more non-invasive markers of reperfusion predict TIMI 3 flow accurately in 80% cases. He also reported use of more than one indices for reperfusion can predict TIMI 3 flow with 78% sensitivity and specificity.[12] Rivas HA et al. used 50% or more ST segment elevation resolution and maximum peak of CPK and CPK-MB fraction within first 12 hrs of treatment as major criteria for reperfusion and chest pain reduction and development of reperfusion arrhythmias in first 2 hours of treatment as minor criteria. Successful thrombolysis was determined in those patients who had two major criteria and one minor criteria. By using these criteria he showed that successful reperfusion occurs in more than 50% of patients.[13] Previous study indicates that the combined analysis of noninvasive reperfusion markers enhances the predictability of coronary artery patency to a clinically useful degree[14]

So based on above observation the success rate of thrombolysis was evaluated taking non invasive markers of reperfusion. Reperfusion criteria: 1) ≥ 50% reduction in ST elevation within 120 min of thrombolytic therapy. 2) ≥ 2 times rise in CK-MB level within 120 min of thrombolytic therapy. 3) Development of reperfusion arrhythmias within 120 min of thrombolytic therapy. 4) Significant reduction of chest pain. Based on above 4 criteria patients were divided into two groups: 1) SCR + VE: Successful coronary reperfusion group when two or more criteria are present. 2) SCR – VE: Failed coronary reperfusion when less than two criteria are present.

Aim of study is to investigate the clinical characteristics of patients with the fragmented QRS and to determine whether fQRS can be useful in predicting thrombolytic therapy response using non invasive markers in patients admitting for first time with STEMI.

STATISTICAL ANALYSIS

SPSS 16.0 version was used for performing statistical analysis. Continuous variables were given as mean ± standard deviation where as categorical variables were expressed as frequencies and percentage. Continuous variables were compared by student t-test and the chi-square test was used for the categorical variables between two groups. Statistical significance was defined as $p < 0.05$.

RESULTS

The baseline characteristic of the study groups are shown in table 1. Accordingly out of 50 STEMI patients 16 had fragmented QRS 34 had no fragmented QRS. Hence based on QRS positivity the study population was divided into two groups. fQRS positive (presence of fragmented QRS) and fQRS negative (absence of fragmented QRS) groups. The mean age of fragmented QRS was 58.47±11.33. Whereas the mean age of non fragmented QRS group was 56.68±10.03. No statistically significance was noted with regards to hypertension, diabetes, smoking, family history of CAD and BMI. However there was significant increase in the CK-MB level in patients with fragmented QRS at the time of admission which was statistically significant. ($p < 0.001$).

There was significant difference detected in the incidence of MACE (major adverse cardiac events) in the fragmented QRS group ($p < 0.001$). Of the obtained events in fQRS goup, 4 had heart failure and arrhythmias, 6 had hypotension and 3 died in hospital. Left ventricular ejection (LVEF) was impaired in fQRS group compared to non fQRS group which was statistically significant. ($p<0.001$). Table-2 shows association of different reperfusion criteria with fragmented QRS.

In terms of success rate of thrombolytic therapy as shown in table-3 the rate of failed thrombolysis was higher in fragmented QRS group compared to non fragmented QRS group which was significant. ($p<0.001$)

DISCUSSION

Whether the presence of fQRS on admission ECG can significantly predicted failed thrombolysis in patients with STEMI who underwent thrombolytic therapy which was the aim of our study. Although there have been a larger number of studies indicating that the presence of fQRS is associated with insufficient angiographic reperfusion in patients treated with primary PCI.[15] But there are limited number of studies investigating the relationship between fQRS and myocardial reperfusion using non invasive markers of reperfusion in acute STEMI patients receiving thromblytic therapy. To the best of

Characteristics	fQRS +ve (n=16)	fQRS -ve (n=34)	P value
Age (years)	58.47±11.33	56.68±10.03	0.342
Sex			
Male (36)	12	24	0.988
Female (14)	4	10	0.988
BMI	25.61±5.39	23.47±3.13	0.330
Family history of CAD	4	10	0.998
Smoking history	5	15	0.751
Diabetes	4	12	0.112
Hypertension	6	19	0.282
Dyslipideamia	5	21	0.752
Systolic blood pressure (mmHg)	130±24	128±20	0.828
Diastolic blood (mmHg)	74±12	70±11	0.952
CK-MB (at admission)	110±20	64±11	<0.001
Pain to prick time (hrs)	4±2	3±2	0.298
Plasma blood glucose (mg/dl)	150±14	140±15	0.928
EF (%)	34±12	41±11	<0.001

Table-1: Baseline clinical characteristics of study groups

Criterias	fQRS +ve (n=16)	fQRS -ve (n=34)	P value
Resolution of Chest pain	11	14	0.291
>2 times increase in CK-MB level at 2 hour	4	25	<0.001
ST segment resolution >50% after 2 hours in infarct leads	7	21	< 0.001
Reperfusion arrhythmias	5	24	< 0.001

Table-2: Association of reperfusion criteria's with fQRS

	fQRS +ve (n=16)	fQRS -ve (n=34)	P value
SCR +ve (%)	6	28	< 0.001
SCR -ve (%)	10	6	< 0.001

Table-3: Incidence of fQRS and its relation with successful thrombolysis

our knowledge, this is the first study that has examined the fQRS and its association with multiple bedside reperfusion markers in predicting the thrombolytic response.

STR is the most important electrocardiographic parameter for assessing the efficacy of reperfusion therapy and an inadequate (< 50%) STR is a marker for failed thrombolysis.[16] As STR is a parameter that is assessed after the administration of fibrinolytic therapy, waiting for this therapy can result in treatment failure loss of valuable time, and increased myocardial necrosis. The presence of a noninvasive parameter that can predict treatment failure before undergoing TT may indicate primary PCI as the first treatment option in these patients, which may reduce adverse outcomes. A parameter to be used for this purpose must be quick, inexpensive, noninvasive, and easy to apply.

In present study we found that CK-MB levels were more in patient with fQRS group compare to –ve fQRS on admission (p<0.001). In studies conducted by Cetin et al. it was found that fragmented QRS was associated with higher cardiac CPK-MB levels on admission in patients with STEMI.[10,17] The increase in level of CK MB levels in fQRS group might be because of larger ischemic area of myocardium which is seen in patients with fQRS.

Previous studies showed the negative correlation between the presence of fQRS and left ventricular function by echocardiography.[18,19] In our study, we found that patients with fQRS had lower LVEF compared with patients without fQRS by echocardiography (p<0.001).

There is strong correlation between fQRS and malignant cardiac arrhythmia as observed by_Erdogan et al.[20], frequency of MACE (major adverse cardiac event) among the patients with fragmented QRS was significantly higher (29.4% vs 5.9%; p <0.01) in study conducted by Ari et al.[21]

In our study there was significant difference detected in the incidence of MACE (major adverse cardiac events) in the fragmented QRS group ($p < 0.001$) compared to non fragmented fQRS group on presentation. Of the obtained events in fQRS goup, 4 had heart failure and arrhythmias, 6 had hypotension and 3 died in hospital. In hospital mortality rate were found to be significantly higher in the fragmented QRS group which was similar to other studies.

In a study done by Tanriverdi Z et al showed that patients with STEMI who had fQRS on ECG had higher rate of thrombolysis failure.[22]

Another study by Kocaman et al. found that patients without fQRS achieved increased STR and better myocardia reperfusion in comparison with patients with fQRS[10]

In our study out of 16 fQRS +ve patients 10 had failed thrombolysis (p<0.001) and out of 34 fQRS –ve patients only 6 had failed thrombolysis which was statistically significant. (p<0.001) which is similar to above studies.

In summary in our study patients with STEMI who had fQRS on ECG on admission had higher rate of MACE (major adverse cardiac events), mortality, low ejection fraction on echocardiography and failure of thrombolysis. Hence it may be better to first choose an invasive therapy rather than thromblytic therapy in patients with fQRS, and therefore, these patients should be referred for primary PCI without delay.

CONCLUSION

fQRS has emerged as a practical and easily identifiable

diagnostic tool for predicting in hospital cardiac events in patients with STEMI. The occurrence of fQRS is beneficial in identifying the patients with increased rate of major cardiac events, death risk, and thrombolytic failure. Hence in patients with STEMI fQRS helps in risk stratification and can be used as an indicator for early revascularization.

Study limitations

Our study has several limitations. First, this study is limited by its small patient population analyzed. Second, the effect of fQRS on long-term clinical outcomes of patients is also absent in this study. Although significant results were obtained in our current study, these results should be supported by further multicenter, prospective, and large scale studies in the future.

REFERENCES

1. Yusuf S, Vaz M, Pais P. Tackling the challenge of cardiovascular disease burden in developing countries. Am Heart J. 2004;148:1.
2. Mardar VJ, Sherry S. Thrombolytic therapy; Current status. N Engl J Med. 1988;318:1512-1520.
3. Kennedy JW, Ritchie JL, Davis KB, Fritz JK. The western Washington randomized trial of intracoronary streptokinase in acute myocardial infarction, A 12 month follow up report. N Eng J Med. 1985;312:1073-1078.
4. Topol EJ, Califf RM, Kereiakes DJ, George BS. Thrombolysis and angioplasty in myocardial infarction. J Am Coll Cardiol. 1987;10:65B-74B.
5. Das MK, Michael MA, Suradi H, Peng J, Sinha A, Shen C, et al. Usefulness of fragmented QRS on a 12-lead electrocardiogram in acute coronary syndrome for predicting mortality. Am J Cardiol. 2009;104:1631-7.
6. Korhonen P, Husa T, Konttila T, Tierala I, Mäkijärvi M, Väänänen H, et al. Fragmented QRS in prediction of cardiac deaths and heart failure hospitalizations after myocardial infarction. Ann Noninvasive Electrocardiol. 2010;15:130-7.
7. Das MK, Saha C, El Masry H, Peng J, Dandamudi G, Mahenthiran J, et al. Fragmented QRS on a 12-lead ECG: a predictor of mortality and cardiac events in patients with coronary artery disease. Heart Rhythm. 2007;4:1385-92.
8. Pietrasik G, Goldenberg I, Zdzienicka J, Moss AJ, Zareba W. Prognostic significance of fragmented QRS complex for predicting the risk of recurrent cardiac events in patients with Q-wave myocardial infarction. Am J Cardiol. 2007;100:583-6.
9. Chatterjee S, Changawala N. Fragmented QRS complex: a novel marker of cardiovascular disease. Clin Cardiol. 2010;33:68-71.
10. Kocaman SA, Cetin M, Kiris T, Erdogan T, Canga A, Emre D, et al. The importance of fragmented QRS in prediction of myocardial infarction and reperfusion parameters in patients undergoing primary percutaneous coronary intervention. Korean Circ J. 2012;42:674-83.
11. Das MK, Khan B, Jacob S, Kumar A, Mahenthiran J. Significance of a fragmented QRS complex versus a Q wave in patients with coronary artery disease. Circulation. 2006;113:2495-2501.
12. A ophuis, F Bar, F Vermeer, W Janseen, P Deoevendas, R Haest et al. Angiographic assessment of prospectively determined non invasive reperfusion indices in acute myocardial infarction. Heart Augest. 2000:84:164-70.
13. Rivas HA, Villalobos VR. Evaluation of successful thrombolysis in acute myocardial infarction by noninvasive criteria of reperfusion. Rev. Mex. Cardiol. 1997;8:85-92.
14. Stefan H. Hohnloser, Markus Zabel, Wolfgang Kasper, Thomas Meinertz, Hanjorg Just, Assessment of Coronary Artery Patency After Thrombolytic Therapy: Accurate Prediction Utilizing the Combined Analysis of Three Noninvasive Markers. JACC. 1991;18:44-9.
15. Dursun H, Zulkif Tanriverdi, Sefa Gul, Tugce Colluoglu and Dayimi Kaya The usefulness of fQRS and QRS distortion for predicting reperfusion success and infarct-related artery patency in patients who underwent thrombolytic therapy. Coronary Artery Disease. 2015;26:692–698
16. de Lemos JA, Braunwald E. ST segment resolution as a tool for assessing the efficacy of reperfusion therapy. J Am Coll Cardiol. 2001;38:1283–1294.
17. Çetin M, Kocaman SA, Erdoğan T, Canga A, Durakoğlugil ME, Şatıroğlu Ö, et al. The independent relationship of systemic inflammation with fragmented QRS complexes in patients with acute coronary syndromes. Korean Circ J. 2012;42:449–457.
18. Xu Y, Qiu Z, Xu Y, Bao H, Gao S, Cheng X. The role of fQRS in coronary artery disease. A meta-analysis of observational studies. Herz. 2015;40 (Suppl 1):8–15.
19. Lee CW, Hong MK, Yang HS, Choi SW, Kim JJ, Park SW, Park SJ. Determinants and prognostic implications of terminal QRS complex distortion in patients treated with primary angioplasty for acute myocardial infarction. Am J Cardiol. 2001;88:210–213.
20. Erdogan T, Kocaman SA, Çetin M et al. Relationship of fragmented QRS complexes with inadequate coronary collaterals in patients with chronic total occlusion. J. Cardiovasc. Med., 2012;13:499-504.
21. Ari H, Cetinkaya S, Ari S, Koca V, Bozat T. The prognostic significance of a fragmented QRS complex after primary percutaneous coronary intervention. Heart Vessels. 2012; 27:20-8.
22. Tanriverdi Z, Dursun H, Simsek MA, Unal B, Kozan O, Kaya D. The predictive value of fragmented QRS and QRS distortion for high-risk patients with STEMI and for the reperfusion success. Ann Noninvasive Electrocardiol. 2015.;20:578-85.

Source of Support: Nil; **Conflict of Interest:** None

Submitted: 04-09-2016; **Published online**: 15-10-2016