ISSN No:-2456-2165

The Relationship between Fragmented QRS and Coronary Arterial Lesion Severity in Patients with Acute Coronary Syndrome Inhaji Adam Malik General Hospital, Medan, Indonesia

Mega Almira[1], Refli Hasan[1], Yuke Sarastri[1], Harris Hasan[1],
Anggia Chairuddin Lubis[1], Teuku Bob Haykal[1].
[1]Department of Cardiologyand Vascular Medicine,
Faculty of Medicine, University of Sumatra Utara,
Medan, Indonesia

Abstract:-

Background: Fragmented QRS (fQRS) complexes are electrocardiogram (ECG) findings which reflect impaired ventricular depolarization due to heterogeneous electrical activation of ischemic and or injured myocardium. The usefulness of fQRS for detecting myocardial scar and for identifying high-risk patients has been expanded to various cardiac diseases, include coronary artery disease.

Objective: The purpose of this study was to determine the relationship between fQRS and the severity of coronary artery lesions as assessed by the SYNTAX score in patients with acute coronary syndromes (ACS).

Methods: The study involved acute coronary syndrome patients who underwent coronary angiography at Haji Adam Malik General Hospital in Medan in the period of September 2020 to June 2021. All subjects underwent ECG examination and SYNTAX score assessment. The fQRS included various morphologies of the QRS (<120 ms), which included an additional R wave (R′) or notching in the nadir of the S wave, or >1 R′ (fragmentation) in 2 contigu

ous leads, corresponding to a major coronary artery territory.SYNTAX score > 22 were defined as high lesion severity. Statistical analysis was performed to assess relationship of fragmented QRS with the severity of coronary artery lesions.

Results: A total of 54 consecutive subjects were included in this study. In fQRS group, 25 subjects (46,3%) had high SYNTAX score and 2 subjects (3.7%) had low SYNTAX score.While, 22 non-fQRS subjects (40,7%) had low SYNTAX score and only 5 subjects (9.3%) had high SYNTAX score. The troponin I (p<0,001), fQRS (p<0,001), and multivessel disease (p<0,008) were significantly higher in high SYNTAX group.From multivariate analysis, Patients with fQRS compared with non-fQRS patients had 35x risk of experiencing high lesion severity. fQRS had strong positive correlation with the SYNTAX score (r=0.648; p<0.001).

Conclusion: There is a relationship between fQRS and the severity of coronary artery lesions as assessed by the SYNTAX score in patients with acute coronary syndrome.

Keywords:- *fragmented QRS, SYNTAX score, acute coronary syndrome*

I. INTRODUCTION

Coronary artery disease (CAD) is caused by plaque builds up in the wall of coronary arteries that supply blood to the heart muscle. This disease is one of the most common cardiovascular diseases.

Risk stratification by identify the severity of coronary artery lesions is useful for establish an appropriate management strategy in acute coronary syndrome. A large number of scoring systems and laboratory parameters have been used in clinical practice to assess the severity and complexity of coronary artery lesions. The most commonly used is the SYNTAX score.[1] SYNTAX score system is formulated comprehensively to describe the complexity of coronary artery lesions based on the results of angiography and predict the final outcome of percutaneous coronary interventions (PCI) or coronary artery bypass grafting (CABG).[2,3]

Although this scoring system has many benefits, it requires an invasive method by performing coronary angiography. Therefore, an accessible, cost-effective, and non-invasive method is still needed to perform risk stratification by determining the level and severity of coronary artery lesions in patients with acute coronary syndromes.

Electrocardiogram (ECG) is the most useful, readily available, and commonly used first diagnostic tool in the diagnosis of ACS. fQRS on the ECG arise from defects in signal transduction processes and ventricular depolarization, which is associated with the presence of myocardial scar or ischaemia.[5,6] Partial damage to the conduction system in the ventricles causes notching of the QRS segment on the ECG.[6]

In this study, the authors investigated whether there was a relationship between fragmented QRS and the severity of coronary artery lesions as assessed by the SYNTAX score

ISSN No:-2456-2165

inpatients withacute coronary syndrome in Haji Adam Malik General Hospital Medan.

II. METHOD

A. Research population

The data of this study were taken from acute coronary syndrome patients who underwent coronary angiography at Haji Adam Malik General Hospital Medan in the period of September 2020 to June 2021 with the consecutive sampling method . The study involved 54 patients with acute coronary syndrome in Haji Adam Malik General Hospital. Patients with arrhythmia, QRS complex duration ≥120 ms, history of CABG, history of PCI, unstable angina pectoris were excluded from the study.

B. Electrocardiogram and Coronary Angiography

ECG on admission was performed to assess fQRS. The fQRS included various morphologies of the QRS (<120 ms), which included an additional R wave (R′) or notching in the nadir of the S wave, or >1 R′ (fragmentation) in 2 contiguous leads, corresponding to a major coronary artery territory.

Coronary angiography data of the patients were obtained from catheter laboratory records. The presence and extent of CAD were identified. More than 50% stenosis in any epicardial artery or any side branch more than 1.5 mm in diameter was considered as significant CAD. Coronary lesions that do not meet these criteria were categorized as nonsignificantCAD.The severity of CAD was estimated using SYNTAX score. SYNTAX score > 22 were defined as high SYNTAX or high lesion severity.

C. Statistical analysis

All statistical studies were carried out with the program SPPS. Quantitative variables were expressed as the mean value ± standard deviation or median (minimum–maximum), and qualitative variables were expressed as percentages (%). All measurements were evaluated with the Kolmogorov-Smirnov test. A comparison of parametric values between the two groups was performed using the Mann-Whitney U-test or student t test. Categorical variables were compared by the chi square test or Fisher's exact test. For determination of high SYNTAX scores, univariate and multivariate analysis were performed using Enter and Backward-Conditional logistic regres- sion analysis, respectively. A p value < 0.05 was considered statistically significant.

D. Research results

A total of 54 patients were enrolled in this study (81,5% Male and 18,5% Female). The risk factors that we found were 81% smoking, 53% hypertension and 46% Diabetes. 35 patients (64,8%) were STEMI and 19 patients (35,2%) were NSTEMI. The distribution of the characteristics of the research subjects is presented in Table 1.

Characteristics	Total (n = 54)
Age (years)	53.83±9.125
Gender, n(%)	
Male	44 (81.5%)
Female	10 (18.5%)
Hypertension, Yes	29 (53%)
Diabetes, Yes	25 (46%)
Smoking, Yes	44 (81%)
Heart Rate	75.5 (54-115)
Systolic Pressure	133±19.4
Diastolic Pressure	70 (60-110)
Laboratory	
Hemoglobin (g/dl)	14.5 (11.7-16.2)
Leukocytes(/µL)	11,420 (5,740-23,990)
Platelets(/µL)	246,000 (155,200-407,000)
urea (mg/dl)	24 (13-73)
Creatinine (mg/dl)	1.02 (0.5-2.8)
Sodium (mEq/L)	136.46±3.28
Potassium(mEq/L)	3.94±0.50
Chloride(mEq/L)	104 (92-121)
Admission BG (mg/dl)	178 (69-555)
Fasting BG (mg/dl)	119 (75-257)
HbA1C (%)	6.35 (5.20-14.0)
Total Cholesterol (mg/dl)	176.95±29.63
Triglycerides (mg/dl)	147.5 (76-416)
HDL (mg/dl)	34.5(19-66)
LDL (mg/dl)	123 (49-182)
CKMB (U/L)	80 (21-925)
Troponin I (ng/mL)	2.35 (0.05-27)
ACS, n(%)	
STEMI	35 (64.8%)
NSTEMI	19 (35.2%)
Lesions, n(%)	
1VD	23 (42.6%)
MVD	31 (57.4%)
EF (%)	47.5±9.6
SYNTAX Score	22.45±9.14

BG : Blood Glucose

Table 1: Characteristics of Research Subjects

From 54 research subjects, the mean age of subjects with high SYNTAX score was 53.43±9.21 years and the mean age of subjects with low SYNTAX score was 54, 33±9.18 years. There were no statistically significant differences in age, gender, risk factors, vital sign examination, laboratory values and echocardiography between these two groups. In the analysis of the study groups, the troponin I (p<0,001), fQRS (p<0,001), and multivessel disease (p<0,008) were significantly higher in high SYNTAX group (Table 2) . The characteristics of the research subjects based on the SYNTAX score are presented in Table 2.

ISSN No:-2456-2165

Characteristics	SYNTAX Score		p value
	High (>22) n=30	Low (≤ 22) n=24	
Age (years)	53.43±9.21	54.33±9.18	0.722
Gender, n(%)			
Male	25 (56.8)	19 (43.2)	0.736
Female	5 (50.0)	5 (500)	
Hypertension, Yes	16 (55.2)	13 (44.8)	0.951
Diabetes, Yes	15 (60.0)	10 (40.0)	0.542
Smoking, Yes	23 (52,3)	21 (47.7)	0.309
Heart Rate	74 (60-115)	80 (54-98)	0.638
Systolic Pressure	131±20.4	135±18,13	0.282
Diastolic Pressure	70 (65-110)	70 (60-100)	0.556
Laboratory			
Hemoglobin (g/dl)	14.17±1.23	14.63±0.98	0.145
Leukocytes (/µL)	10,795 (5,900-23,990)	12,845 (5,740-17,020)	0.459
Platelets (/µL)	243,000 (155,200-407,000)	254,500 (197.00-354,000)	0.607
urea (mg/dl)	24 (13-66)	24 (17-73)	0.793
Creatinine (mg/dl)	1.07 (0.60-2.80)	0.90 (0.50-1.56)	0.261
Sodium (mEq/L)	136.03±3.87	137.00±2.32	0.262
Potassium (mEq/L)	3.90±0.50	4.00±0.50	0.505
Chloride (mEq/L)	102 (92-121)	105 (92-121)	0.552
Admission BG (mg/dl)	161 (79-296)	186.5(69-555)	0.497
Fasting BG (mg/dl)	140.50 (75-257)	115 (82-257)	0.233
HbA1C (%)	6.2 (5.20-12.80)	6.5 (5.4-14.0)	0.701
Total Cholesterol (mg/dl)	171.13±32.06	184.22±24.97	0.107
Triglycerides (mg/dl)	133 (80-416)	186 (76-288)	0.192
HDL (mg/dl)	34.5 (19-52)	34.5 (26-66)	0.787
LDL (mg/dl)	119.10±31.39	133.66±25.27	0.071
CKMB (U/L)	77.5 (30.0-925.0)	85.5 (0.21-450.0)	0.389
Troponin I (ng/mL)	5 (0.05-27.00)	1.2 (0.05-8.0)	<0.001
ACS, n(%)			
STEMI	18 (51.4)	17 (48.6)	0.407
NSTEMI	12 (63.2)	7 (36.8)	
Lesions, n(%)			
1VD	8 (34.8)	15 (65.2)	0.028
MVD	22 (71.0)	9 (29.0)	0.008
EF (%)	45.96±9.90	49.41±9.05	0.192

BG : Blood Glucose

Table 2: Characteristics of research subjects based on the SYNTAX . score

25 fQRS subjects (46,3%) had high SYNTAX score and 2 fQRS subjects (3,7%) had low SYNTAX score. In non-fQRS group, 5 subjects (9,3%) had high SYNTAX score and 22 subjects (40.7%) had low SYNTAX score. Based on the analysis, there was statistically significant relationship between the fragmented QRS and the severity of coronary artery lesions in patients with acute coronary syndromes (p<0.001).

	Severity of coronary artery lesion n(%)		Total	p value
	high SYNTAX score (>22)	Low SYNTAX score(≤22)		
fQRS	25 (46.3)	2 (3,7)	27 (50.0)	<0.001
non-fQRS	5 (9.3)	22 (40.7)	27 (50.0)	
Total	30 (55.6)	29 (44.4)	54 (100.0)	

Table 3: Relationship between fragmented QRS and severity of coronary artery lesions as assessed by the SYNTAX score in patients with acute coronary syndromes

Multivariate analysis were made for high SYNTAX score . The variables included in the multivariate analysis werehemoglobin, KGDN. Total cholesterol, triglycerides, LDL, MVD, Troponin I, EF, fQRS.Compared with non-fQRS patient, fQRS patient had a 35x risk for experiencing high lesions severity [β 3,573; OR 35,622 (95% CI 5,89-215,16) p<0.001]. Elevated troponin I levels had a 1.3x risk of coronary artery lesion severity but not statistically significant with [β 0.302; OR 1,352 (CI 95% 0.973-1.879) p value = 0.072].

Variable	p value	OR	ß (95% CI)
fQRS	0.000	36.622	3.573 (5.898-215.162)
Troponin_I	0.072	1.352	0.302 (0.973-1.879)

Table 4: Multivariate analysis of high SYNTAX

The results of this study indicate that the sensitivity value of fQRS is 83.3%, the specificity of fQRS is 91.7%, the positive predictive value (NPP) is 92.6% and the negative predictive value (NPN) is 81.5% (table 5).

Variable	p	n
Sensitivity	0.833	30
Specificity	0.917	24
NPP	0.926	27
NPN	0.815	27

Table 5: Value of sensitivity, specificity, positive predictive value (NPP), and negative predictive value (NPN) of fragmented QRS with SYNTAX score

The relationship between number of fragmented QRS locations and the SYNTAX score in patients with acute coronary syndrome is presented in Figure 1. A total of 27 subjects found fQRS had strong correlation with the SYNTAX score and the direction of the correlation was positive and statistically significant. [r=0.648; p<0.001].

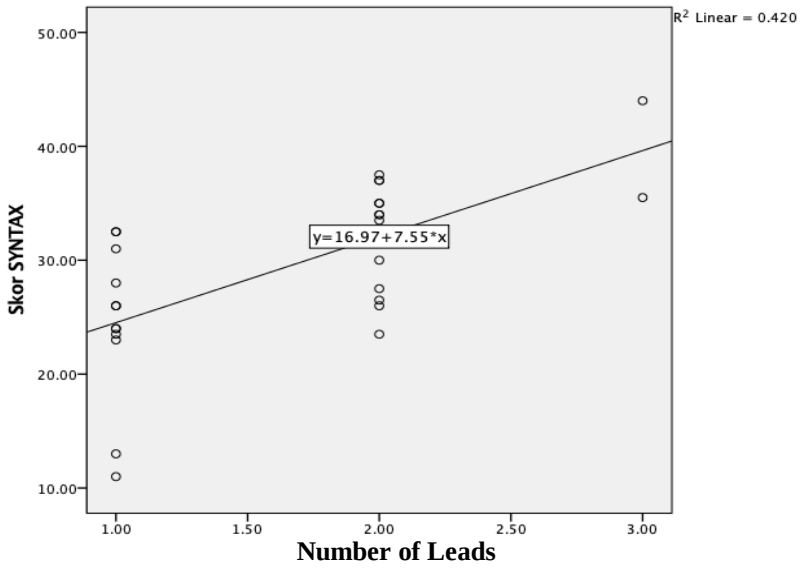

Fig. 1: The relationship between the number of fQRSleads and theSYNTAX score

III. DISCUSSION

In this study, it was found that fragmented QRS in patients with acute coronary syndromes was associated with the severity of coronary artery lesions as assessed by the SYNTAX score. A total of 54 consecutive subjects were included in this study. In fQRS group, 25 subjects (46,3%) had high SYNTAX score and 2 subjects (3.7%) had low SYNTAX score While, 22 non-fQRS subjects (40,7) had low SYNTAX score and only 5 subjects (9.3%) had high SYNTAX score. There was statistically significant relationship between fQRS and the severity of coronary artery lesions in patients with acute coronary syndromes ($p < 0.001$). The troponin I ($p<0,001$), fQRS ($p<0,001$), and multivessel disease ($p<0,008$) were significantly higher in high SYNTAX group Patients with fQRS compared with non-fQRS patients had 35x risk of experiencing high lesion severity. fQRS had strong positive correlation with the SYNTAX score ($r=0.648$; $p<0.001$).

The basic characteristics of research subjects showed that the mean age of the research subjects was 54 years, the , the mean age of subjects with fQRS n was 52 years and the mean age of subjects with non-fQRS was 55 years. The majority of the subjects were 44 male (81.5%) and 10female (18.5%). These results are similar to the findings of Bekler et al.in Turkey who reported that patients with fQRS in patients with acute coronary syndrome had a mean age of 65 years and 63 years in non-fragmented QRS.[1]Yuksel et al. (2015) also reported that the frequency of male subjects was more than female with a ratio of 1.6:1 with a mean age of 60.4 years.[14]The current findings are also supported by the

ISSN No:-2456-2165

theory that male gender and age are risk factors for the occurrence of acute coronary syndromes.

Rahman et al. in Egypt found a correlation of QRS fragmentation and severity of coronary artery lesions in patients with NSTEMI. Fragmented QRS is more common in the elderly, men, smokers, diabetes and dyslipidemia. A higher frequency of QRS fragmentation was also found in patients with multivessel disease, high troponin levels and high syntax scores.[7]

Bekler et al. demonstrated that the number of fQRS leads on a 12-lead ECG at admission was associated with severity in patients with ACS.[1] The SYNTAX score can evaluate the severity of coronary heart disease, and it has been demonstrated that they are associated with both short-term and long-term cardiovascular risk and revascularization.[8] This scoring systems reflect coronary anatomy, arterial morphology, and severity of stenosis in atherosclerotic lesions.[9]

Fragmented QRS results from fibrosis or scar and regional myocardial ischemia, leading to heterogeneous electrical activation of the myocardium. Fragmented QRS has been shown to be associated with myocardial fibrosis in patients with ischemic or non-ischemic left ventricular dysfunction.[10]

Pietrasik and Zaręba demonstrated the sensitivity of fQRS in detecting myocardial lesions, and confirmed that the presence of fQRS can be used to predict cardiac events. These results indicate that the fQRS is a non-invasive ECG parameter that is easily evaluated and is associated with cardiac fibrosis.[5] These data also explain why the number of fQRS leads was significantly higher in ACS patients with high SYNTAX scores in our study.

Study of Ma X et al, in 227 STEMI patients showed fragmented QRS as an independent predictor of incomplete ST segment resolution after primary PCI.[15] The presence of fQRS on the admission ECG can significantly predict failed thrombolysis in patients undergoing thrombolytic therapy.[16] Another study by Chew, et al. in 693 myocardial infarction (MI) patients revealed that fQRS was associated with a lack of favorable left ventricular remodeling.[17] The number of fQRS on ECG leads was also independently associated with hospitalization in heart failure patients with a history of myocardial infarction.[18] The studies showed that the presence of fQRS on the ECG was useful for identifying high-risk patients and poor prognosis patients in ACS.

fQRS is a simple, widely available and inexpensive marker for ACS patients. In an era of universal health coverage with limited financial support, cost-effective diagnostic tools and prognostic markers will be urgently needed. Further research on fQRS will make it more recognized and used especially if it has been established as a pathognomonic ECG finding. Further studies will be needed to confirm the use of fQRS in patients with ACS.[13]

IV. CONCLUSION

There is a relationship between fragmented QRS and the severity of coronary artery lesions in patients with acute coronary syndrome in Haji Adam Malik General Hospital. We suggest that fragmented QRS on admission ECG can be used as a tool for prediction of higher risk patients with acute coronary syndrome.

REFERENCES

[1.] Bekler, A., Barutcu, A., Tenekecioglu, E., et al. 2015. The Realtionship between fragmented QRS complexes and SYNTAX and Gensini scores in patients with acute coronary syndrome. KardiologiPolska. 73(4): 246-254.

[2.] Sianos, G., Morel, M.A., Kappetein, A.P., et al. 2005. The SYNTAX score: an angiographic tool grading the complexity of coronary artery disease. EuroIntervention. 1: 219-27.

[3.] Serruys, P.W., Onuma, Y., Garg, S., et al. 2009. Assessment of the SYNTAX score in the SYNTAX study. Eurointervention. 5(1): 50-6.

[4.] Simson, M.B., Utereker, W.J., Spielman, S.R., et al. 1983. Relation between late potentials on the body surface and directly recorded fragmented electrocardiograms in patients with ventricular tachycardia. Am J Cardiol. 51:105-12.

[5.] Pietrasik, G., Zareba, W. 2012. QRS Fragmentation: Diagnostic and prognostic significance. Cardiol J 19(2):114-21.

[6.] De Luna, B. 1998. Electrographic patterns of ischemia, injury and necrosis. In: Clinical electrocardiography, 2nd ed. Bayes de Luna. A textbook. Futura Publishing Company, Inc., Armonk, NY, pp. 141–42.

[7.] Rahman, H. A., Ghany, M. A. and Youssef, A. A. A. 2016. Correlation of fragmented QRS complexes with the severity of CAD (using SYNTAX score) in patients with non-ST elevation acute coronary syndromes. Egyptian Heart Journal. 68(2), pp. 125–129. doi: 10.1016/j.ehj.2016.01.005.

[8.] Niccoli, G. et al. 2013. Severity of coronary atherosclerosis in patients with a first acute coronary event: a diabetes paradox. European Heart Journal. 34(10), pp. 729–741. doi: 10.1093/eurheartj/ehs393.

[9.] Sinning, C. et al. 2013. Angiographic score assessment improves cardiovascular risk prediction: the clinical value of SYNTAX and Gensini application. Clinical Research in Cardiology. 102(7), pp. 495–503. doi: 10.1007/s00392-013-0555-4.

[10.] Basaran, Y., Tigen, K., Karaahmet, T. 2011. Fragmented QRS Complexes Are Associated With Cardiac Fibrosis And Significant Intraventricular Systolic Dyssynchrony In Nonischemic Dilated Cardiomyopathy Patients With A Narrow QRS Interval. Echocardiography 28: 62-8.

[11.] Ozcan, S. et al. 2013. The Prognostic Significance of Narrow Fragmented QRS on Admission Electrocardiogram in Patients Hospitalized for Decompensated Systolic Heart Failure. Clinical Cardiology. 36(9), pp. 560–564. doi:

10.1002/clc.22158.
[12.] Peters, S., Trümmel, M,.Koehler, B. 2008. QRS Fragmentation in Standard ECG as a Diagnostic Marker of Arrhythmogenic Right Ventricular Dysplasia Cardiomyopathy. Heart Rhythm. 5(10):1417-1421.
[13.] Ranitya, R. 2019. Fragmented QRS (fQRS) in Acute Coronary Syndrome: Is It a More Potential Marker Than Predicted?. Acta medicaIndonesiana. 51(1), pp. 1–2.
[14.] Yuksel M, Yildiz A, Oylumlu M. The association between platelet/ lymphocyte ratio and coronary artery disease severity. *Anatol J Cardiol*. 2015; 15: p. 640-7
[15.] Ma X. Duan W. Poudel P. Ma J. Sharma D. Xu Y. Fragmented QRS complexes have predictive value of imperfect ST-segment resolution in patients with STEMI after primary percutaneous coronary intervention. Am J Emerg Med. 2016; 34(3): p. 398 - 402.
[16.] Kothi ZS, Athar AM, Yenkanchi AP, Begum AS, Hussaini SM. The usefulness of fragmented QRS in predicting the successful reperfusion by using non invasive criteria of reperfusion in STEMI after thrombolytic therapy. Int J Contemp Med Res. 2016; 3(10): p. 2965-2968.
[17.] Chew D, Sas R, Vaid H, Kavanagh K, Tan-Mesiatowsky CLE, Southern D, Howarth A, et al. The presence of fragmented QRS complexes early after acute myocardial infarction is associated with subsequent lack of favorable left ventricular remodeling. J Am Coll Cardiol. 2017; 69(11): p. 226.
[18.] Torigoe K, Tamura A, Kawano Y, Shinozaki K, Kotoku M, Kadota J. The number of leads with fragmented QRS is independently associated with cardiac death or hospitalization for heart failure in patients with prior myocardial infarction. J Cardiol. 2012; 59: P. 36-41.