The Relationship Between fragmented QRS Complexes (fQRS) and the Severity of Coronary Artery Lesion in Coronary Artery Disease: A Cross-sectional Study

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ABSTRACT

Background: *The severity of coronary artery lesion is commonly used as a predictor of mortality, major adverse cardiovascular event (MACE), and revascularization in coronary artery disease (CAD). Fragmented QRS complex (fQRS) is used as a marker of myocardial ischemia in patients with CAD. The relationship between the two should be studied further. The objective of this study was to determine the relationship between fQRS and the severity of coronary lesion in patients with CAD.* ***Methods****: A cross-sectional study was conducted at Cipto Mangunkusumo Hospital Jakarta. Secondary data were taken from 172 patients with CAD who underwent percutaneous coronary intervention (PCI) from January to June 2018 with total sampling. Patients were divided into two groups based on the existence of fQRS. Demographic, clinical, and corangiography characteristics (Gensini score, total vascular lesion, and vascular lesion significance) were studied. Data were analyzed using agreement test and chi-square.* ***Results****: fQRS was present in 94 subjects (54.6%). Bivariate analysis showed a significant difference between fQRS with mild-moderate Gensini score as well as mild-severe Gensini score (kappa = 0.721 and 0.820; p<0.001), fQRS with significant CAD (kappa = 0.670; p<0.001), and fQRS with multivessel CAD (kappa = 0.787; p<0.001).* ***Conclusion****: There is a significant relationship between fQRS and the degree of severity of coronary lesion in CAD patients.*

Keywords*: coronary artery disease, fragmented QRS, Gensini score.*

INTRODUCTION

Coronary artery disease (CAD) is one of the biggest health problems worldwide. CAD increasing morbidity, mortality and causing significant socioeconomic burden. An estimated 7.4 million (12.9%) deaths are caused by CAD, and it is one of the leading causes of health care cost.[1]

The severity and complexity of coronary artery lesion in CAD patients is commonly used as a predictor of mortality, major adverse cardiovascular events (MACE), and the need for revascularization.[2] Coronary angiography remains a standard diagnostic tool to evaluate coronary lesions. Gensini score is considered the most commonly used and major scoring system

to determine the severity and complexity of coronary lesions.[2-4] Although both the Gensini scoring system and coronary angiography have a lot of advantages, coronary angiography is an invasive procedure available only in certain centers and can be expensive.

Fragmented QRS (fQRS) complexes are novel electrocardiographic signals, which form because of non-homogenous conduction to the area of myocardial ischemic or scar. This causes *zigzag* conduction around the ischemic or scarred myocardium, resulting in the "fragmentation" of QRS complexes.[5,6] fQRS is used as a marker of myocardial ischemia in patients with CAD and can be used to detect coronary lesions.[7] Q waves can disappear over time, and as there is no Q wave formation, fragmented QRS complexes are the only sign of scarring or impaired perfusion in the myocardium.[8] Electrocardiogram (ECG), which detects fQRS, is a tool that is easily accessible, non-invasive, and cost-effective.

In this study, we evaluated the relationship between fQRS and the degree of severity of coronary lesions in CAD patients with different approaches. Instead of using a numerical form like previous studies, the Gensini score has more clinical meaning in categorical form. The division of complexity degree in categorical form can determine the further risk of MACE, prognosis, as well as planning therapy[8,9]. This study will also use a different methodological approach from previous studies, namely not only looking at the magnitude of the effect (significance) but also the strength of the relationship between the two variables with the suitability test. In addition, this study includes both narrow and wide fQRS criteria that have not been carried out in other studies. Moreover, research on this matter has not been carried out on the Indonesian population. The prevalence of CAD events varies by ethnicity and population in Indonesia, including Southeast Asian ethnicities, where the prevalence of CAD is quite high and there are no similar studies in these ethnic groups.[8,9] This has led to a lack of attention regarding the benefits of screening and stratification of the complexity of coronary lesions with fragmented QRS complexes in Indonesia. This study was made to assess the relationship of fQRS on the ECG in identifying the degree of complexity of coronary lesions in CHD patients in Indonesia.

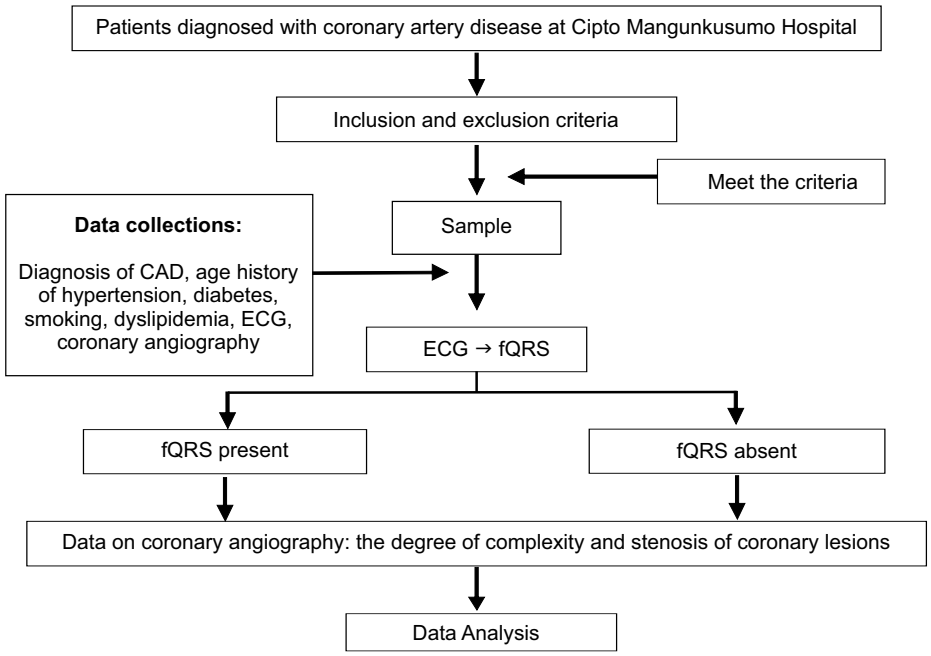

Figure 1. Protocol of the study.

METHODS

Study Design and Population

This study was a cross-sectional study conducted at the Cipto Mangunkusumo Hospital in Indonesia. The subjects of this study were obtained from the medical records of patients with CAD who underwent percutaneous coronary intervention (PCI) at Cipto Mangunkusumo Hospital from January to June 2018 with total sampling. Sample size calculation used two proportions comparison and obtained a minimum sample size of 165 subjects.

The inclusion criteria were patients aged ≥ 18 years diagnosed with CAD via corangiography. The exclusion criteria of this study were incomplete ECG and corangiography data, patients with incomplete right bundle branch block (RBBB) or pathological Q wave, patients with congenital heart disease, ventricular aneurysm, dilated cardiomyopathy, arrhythmogenic right ventricular dysplasia, or Brugada syndrome, and patients with normal coronary artery with fQRS in coronary territories. The study protocol was approved by the ethics committee of Faculty of Medicine Universitas Indonesia (Reference no. 0442/UN2.F1/ETIK/2018).

Electrocardiography

In the ECG data used, ECG was performed within seven days before the coronary angiography. The ECG examination used the Bionet/Cardiotouch 3000® ECG machine with low pass filter cut off (150 Hz), AC 60 Hz, 25 mm/s, 10 mm/mV settings. The fQRS was defined as the presence of various RSR' patterns, which included an additional R wave (R') or notching of the R or S wave in the presence of fragmentation (more than one R') in two contiguous leads corresponding to a major coronary artery territory.[5] The fQRS in wide QRS complex (≥ 120 ms) was included and defined as the QRS complex with >2 R' waves or notches in the R or S wave in a wide QRS complex of bundle branch block, or paced QRS, or premature ventricular complexes (PVC) in 2 contiguous leads.[9] Incomplete RBBB were excluded in this study.

The presence of fQRS was detected with the naked eye and analyzed by three independent observers blinded to angiography and clinical data. The inter-observer variability between observer 1 and observer 2 was 94.1% (k = 0.859) and between observer 1 and observer 3 was 91.2% (k = 0.810).

Coronary Angiography

Angiographic data of the patients were obtained from the catheter laboratory in the Cipto Mangunkusumo records and evaluated using this data. Complexity of coronary lesion was assessed by the degree of stenosis, by the number of vessels involved, and by a severity score, using Gensini score. Significant stenosis was defined as the diameter of stenosis calculated as ≥ 50% with quantitative angiography. If more than one vessel was involved, it was defined as multivessel stenosis.[10]

Gensini score were used to define the angiographic complexity of the coronary atherosclerotic lesion. The Gensini score is the sum of all segment scores. The severity numbers reflecting the specific percentage luminal diameter stenosis of the epicardial coronary arteries are 1 for 1–25% stenosis, 2 for 26–50% stenosis, 4 for 51–75% stenosis, 8 for 76–90% stenosis, 16 for 91–99% stenosis, and 32 for 100% stenosis. These numbers are multiplied by a constant number determined according to the territory of the coronary arteries. The Gensini scoring system is divided into three degree categories, i.e., mild for score <25, moderate for score 25–53, and severe for score > 53.[3]

Statistical Analysis

Statistical analysis in this study were carried out with SPSS for Windows (version 24.0, SPSS, Chicago, Illinois, USA). All quantitative variables were evaluated with the Kolgomorov-Smirnov test for normality. Quantitative variables were expressed as mean value with standard deviation (normal distribution data) or as median with interquartile range (non-normal distribution). Qualitative variables were expressed as percentages. Bivariate analysis was performed using an agreement test (kappa test) and a chi-square test or Fisher's exact test. A r value of more than 0.6 was considered good relationship, and a p value < 0.05 was considered statistically significant.

RESULTS

Of the 232 patients who underwent coronary angiography from the catheter laboratorium registry at Cipto Mangunkusumo from January to June 2018, 60 subject were excluded from our analysis because of pathological Q wave (n = 40), normal angiography in fQRS lead (n = 10), incomplete bundle branch block (n = 4), lack of ECG data (n = 2), and bad quality of ECG (n = 4). The data for final study of 172 subjects were enrolled in this study. Examples of various morphologies of fQRS on the ECG are shown in **Figure 2**.

The study showed the presence of fQRS in 94 (56%) patients. Fragmented QRS complexes was higher in male patients, elderly patients (age ≥ 60 years), diabetics, patients with hypertension, dyslipidemics, and smokers. In the study groups, the fQRS group was associated with the location of coronary lesion with higher incidence than the non-fQRS group. A baselines characteristic of the two groups (fQRS present versus absent) are shown in **Table 1**.

The group with fQRS demonstrated higher frequency of significant stenosis, multivessel disease, and high Gensini score compared to the non-fQRS group (**Table 2**). Bivariate analysis showed that fQRS was significantly positively associated with significant stenosis (kappa = 0.670), multivessel disease (kappa = 0.787), and high Gensini score (kappa = 0.820) (**Table 3**).

DISCUSSION

The study found that there was a higher frequency of fQRS among elderly, males, diabetics, hypertensions, dyslipidemics, and smokers with CAD. This finding was in agreement with Das et al. (2006), Sen et al. (2014), Bekler et al. (2015), and Rahman et al. (2016).[5, 11-13] All these are traditional risk factors for coronary atherosclerosis. These risk factors can trigger and aggravate the process of atherosclerosis, which causes the formation of lipid plaques resulting in coronary lesions. The process of progression of atherosclerosis in vascular causes perfusion changes, causing ischemic and myocardial infarction, which can be characterized by fQRS formation in ECG.[14-16]

In our study, fQRS had a significantly higher frequency among patient with severe degree of complexity coronary lesion. Patients with fQRS had significantly higher Gensini score, both consistent between numeric score and category group, in patients with CAD. Bivariate analysis

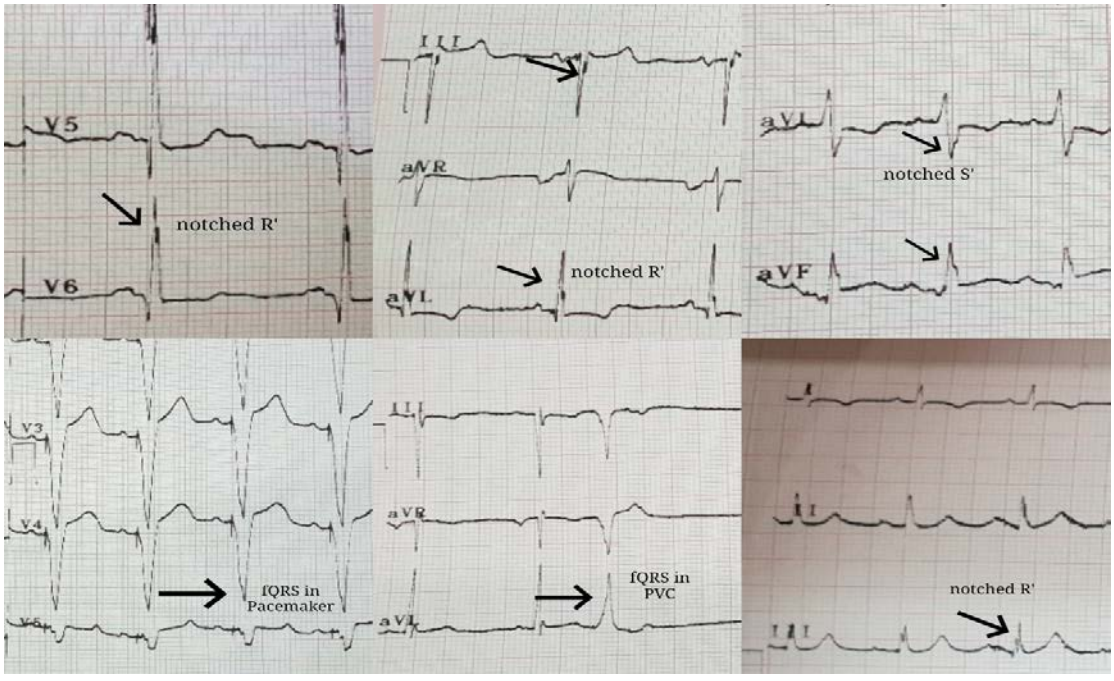

Figure 2. The various types of fragmented QRS complexes (fQRS) used for the study.

Table 1. Baseline characteristics of the study population.

Characteristics	Total N = 172	fQRS group (n%) n = 94 (54.6%)	Non-fQRS group (n%) n = 78 (45.3%)
Gender, n (%)			
Male	124	75 (60.5)	49 (39.5)
Female	48	19 (39.6)	29 (60.4)
Age (years)			
Mean, (SD)		59 (9.9)	58 (9.7)
Age category, n (%)			
< 60 years	94	48 (51.1)	46 (48.9)
≥ 60 years	78	46 (59.0)	32 (41.0)
Risk Factor			
Diabetic, n (%)			
Yes	79	49 (62.0)	30 (38.0)
No	93	48 (48.4)	57 (51.6)
Hypertension, n (%)			
Yes	120	63 (52.5)	57 (47.5)
No	52	31 (59.6)	21 (40.4)
Dyslipidemia, n (%)			
Yes	93	63 (67.7)	30 (32.3)
No	79	31 (39.2)	48 (60.8)
Smoker, n (%)			
Yes	94	66 (70.2)	28 (29.8)
No	78	28 (35.9)	50 (64.1)
Coronary Lesion			
LAD, n (%)	126	77 (61.1)	49 (38.9)
LCx, n (%)	92	48 (52.2)	44 (47.8)
RCA, n (%)	94	84 (89.4)	10 (10.6)

fQRS = fragmented QRS complexes; SD = Standard deviation; DM = Diabetes Mellitus; LAD = Left Anterior Ascending artery; LCx = Left Circumflex artery; RCA = Right Coronary Artery

Table 2. Comparison of coronary lesion complexity between fQRS and non-fQRS

	fQRS group (n%) n = 94 (546%)	Non-fQRS group (n%) n = 78 (45.3%)	P
Gensini Score			
Median, IQR*	85 (55.3)	8 (29.8)	< 0.001
*Non normal distribution			
Degree of complexity (Gensini)			
Mild, n (%)	4 (6.7)	56 (93.3)	< 0.001
Moderate, n (%)	13 (50.0)	13 (50.0)	
Severe, n (%)	77 (89.5)	9 (10.5)	
Degree of stenosis			
Non-significant (< 50%)	2 (7.1)	26 (92.9)	< 0.001
Significant (≥ 50%)	92 (63.9)	52 (36.1)	
Number of involved vessels			
Single	8 (21.1)	30 (78.9)	< 0.001
Multi	84 (80.8)	22 (19.2)	

IQR = Interquartile range; fQRS = fragmented QRS complexes

in this study showed that fQRS was significantly positively associated with complexity and severity of coronary lesion. Thus, the presence fQRS could predict and identify the complexity of coronary lesions.

This result may not only be due to an increase in the scar tissue but also jeopardized ischemic myocardium, which may in turn also contribute to non-homogenous conduction in the myocardium.[17] Das et al.[5] showed that the presence of an fQRS could detect the presence of a regional myocardial scar. Myocardial ischemia

can also alter the conduction causing the presence of fQRS, which showed the phenomenon formation of fQRS due to "electrical death" compared to "cells death". The concepts of myocardial stunning and hibernation may explain this phenomenon. At the cellular level, depletion of energy due to ischemia can cause critical stenosis. This process causes a conduction disturbance in the electrical homogeneity that can be expressed by fQRS formation on the ECG.[17]

The increase of infarct and ischemic area may be due to an increase in critical stenosis in more complex or severe coronary lesion. El-Dosouky et al. showed that fQRS could detect coronary stenosis in accordance with vascular territories.[7]

Study Limitations

There are several limitations in our study. This was a single-center study. It was nonrandomized, but we were careful to include subjects according to our inclusion and exclusion criteria. A second limitation is the relatively small sample size, but the sample size met the minimum requirement.

CONCLUSION

This study found a significant relationship between fQRS and the degree of severity of coronary lesion in CAD patients. The presence of fQRS, both narrow and wide, was associated with a higher degree of complexity of coronary lesions. We suggest that fQRS can be used as a predictive tool in identifying the complexity of coronary lesions and stratifying high risk CAD patients.

ACKNOWLEDGMENTS

We thank to Cipto Mangunkusumo Hospital and Faculty of Medicine Universitas Indonesia.

CONFLICT OF INTEREST

There is no conflict of interest.

FUNDING

This study was not supported financially by any grants.

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