

The Predictive Value of Fragmented QRS Complex in Diagnosis of Myocardial Ischemia

Ahmed M. Bendary, Islam S. Abdelmaged, Ahmed A. Mohamed, Mahmoud Sh. Abdelmoneim

Department of cardiovascular medicine, Benha faculty of medicine, Benha University, Egypt.

Correspondence to: Islam S. Abdelmaged, Department of cardiovascular medicine, Benha faculty of medicine, Benha University, Egypt.

Email:

dr.islam.mansour88@gmail.com

Received:

Accepted:

Abstract

Background: Fragmented QRS (fQRS) on the ECG is a straightforward, affordable, and widely accessible indicator of myocardial fibrosis and scarring. **Aim:** This study aimed to assess the predictive value of (fQRS) in diagnosing myocardial ischemia. It evaluated its incremental prognostic significance in patients having single-photon emission computed tomography (SPECT) for exercise-induced myocardial ischemia. **Methods:** This observational case-control research was executed on 206 patients who underwent exercise myocardial perfusion SPECT for suspected stable chronic CAD. All patients were subjected to demographic, clinical, and laboratory data, electrocardiography, echocardiography, and SPECT myocardial perfusion imaging. The existence of fQRS was determined based on electrocardiographic criteria. Multivariate logistic regression analysis was applied to predict myocardial ischemia, and the incremental prognostic value of fQRS was determined utilizing hierarchical regression analysis. **Results:** The patients had a mean age of 53 ± 10 years, and more than one-quarter (28.2%) had fQRS. Patients with myocardial ischemia (Group I) had a greater prevalence of fQRS than the control group fQRS (42.3% vs. 23.4%, $P = 0.009$). In multivariate analysis, fQRS significantly predicted myocardial ischemia (OR = 2.298, 95%

CI = 1.102 – 4.792, $P = 0.026$). Furthermore, compared to traditional risk factors and a combination of conventional risk factors and STT alterations, the fQRS demonstrated an added predictive value (Global $X^2 = 34.612$). **Conclusions:** Fragmented QRS complex is a promising ECG marker significantly associated with myocardial ischemia. Its inclusion in risk assessment models enhances predictive accuracy, aiding early CAD diagnosis and risk stratification in patients with stable chronic coronary artery disease

Keywords: Myocardial Ischemia; Fragmented QRS Complex; Coronary Artery Disease; Predictive Value; SPECT Imaging.

Introduction

Coronary artery disease (CAD) is a substantial reason for morbidity and mortality. Enhanced electrocardiographic (ECG) parameters are necessary for quick and accurate CAD detection since CAD must be diagnosed and identified as early as possible ⁽¹⁾. The ventricular myocardium's inhomogeneous activation is represented by a fragmented QRS (fQRS) complex found on a 12-lead ECG ⁽²⁾.

According to an earlier study, a terminal conduction delay or fQRS may result from cardiac scar tissue altering the form of the QRS ^(3, 4).

Previous research has established the effectiveness of fQRS as a diagnostic tool for the identification of myocardial infarction (MI) and its prognostic importance as a cardiac event determinant, such as the onset of heart failure (HF) and mortality following acute coronary syndrome (ACS). Furthermore, myocardial perfusion single-photon emission computed tomography (SPECT) investigations have demonstrated that fQRS indicates cardiac scar tissue formation ^(5, 6).

Non-invasive imaging methods, including exercise myocardial perfusion SPECT, have been crucial in recent years for the assessment of CAD ⁽⁷⁾. These imaging techniques contribute to the diagnosis and risk classification of CAD patients by providing vital details regarding myocardial perfusion and function. However, it is yet unknown if fQRS has the diagnostic capacity to foretell myocardial ischemia in patients who may have CAD and lack cardiac scar formation. The objective of this research was to determine the predictive value of

fragmented QRS complex (fQRS) in the diagnosis of myocardial ischemia and evaluate its incremental prognostic significance in a cohort of patients underwent exercise myocardial perfusion SPECT.

Material and methods

Study design

This was observational case-control research among patients who underwent exercise myocardial perfusion SPECT for testing suspected CAD at Benha University Hospital and Aldoah Hospital (Cairo, Egypt) from December 2021 to May 2023. Our main goal was to research the accuracy of the fQRS complex in the diagnosis of myocardial ischemia by contrasting consecutive patients who demonstrated myocardial ischemia on myocardial perfusion SPECT, (ischemia group), with those patients whose SPECT myocardial scan was normal (control group).

Sample size

The estimated total sample size was 206 patients. Adjustments were made to power and alpha at 0.05 and 0.8, respectively collected ⁽⁸⁾.

Key inclusion criteria for this study encompassed the enrolment of all individuals who had undergone exercise myocardial perfusion SPECT as part of their clinical assessment for suspected CAD.

Key exclusion criteria were patients who underwent a myocardial SPECT and showing cardiac scarring; Patients with an echocardiographic ally detected left ventricular ejection fraction (LVEF) of <

50%; Patients with history of percutaneous coronary intervention (PCI).

Demographics, clinical characteristics [Age, Sex, body mass index, smoking, and family history], and cardiovascular risk factors [Hypertension, diabetes mellitus, hyperlipidaemia, and prior cerebrovascular diseases] were collected from the patients.

Ethical approval: The study was approved by the Ethical committee of Benha Faculty of Medicine, Benha University {M.D.11.8.2021}.

Electrocardiography

12-lead ECGs were collected on the closest day before and after exercise myocardial perfusion SPECT and were examined by two different cardiologists.

fQRS is characterized as variations in the QRS morphology (120 ms) with various RSR' patterns, such as extra R (R') waves, notching, S waves, or >1 R' wave in two adjacent leads (5). In ECGs displaying a bundle branch block pattern with QRS duration >120ms, fQRS was characterized as a variety of RSR' patterns, such as >2 R waves (R'), >2 notches in R waves, or S waves in two adjacent leads (9).

A pathological Q wave is deeper than one-fourth size the voltage of the following R wave or lasts longer than 0.04 seconds (5).

Echocardiography

The HP Sonos 5500 set with a 2.5 MHz transducer was used for the transthoracic echocardiographic evaluation. The patients were lying on their left side or supine when the images were obtained. Echocardiography was done to assess (1) Left ventricular end-diastolic volume (LVEDV); (2) Left ventricular end-systolic volume (LVESV); (3) Left ventricular end-diastolic dimension (LVEDD); (4) Left ventricular end-

systolic dimension (LVESD); and (5) Ejection fraction (EF), which was determined with modified biplane method of Simpson utilizing this equation: $LVEF = (LVEDV - LVESV) / LVEDV$.

SPECT Myocardial Perfusion Imaging

Patients were instructed to quit utilizing beta blockers, CCB, or long-acting nitrates 48 hours before the stress test. Using a common 2-day stress-rest procedure, myocardial perfusion SPECT pictures were obtained Technetium-99m (Tc-99m) sestamibi was administered intravenously. SPECT images were captured 40–60 min after Tc-99m sestamibi injection using specialized software called Auto QUANT 6.0 from Philips Medical Systems in Cleveland, Ohio. The at-rest pictures were captured in 2nd day using the same protocol. The pictures and ECG data for the patients were examined visually and semi-quantitatively by two separate doctors. A 17-segment model and perfusion scoring system were used to interpret myocardial perfusion (0 being normal perfusion, 1 being ambiguous hypoperfusion, 2 being mild hypoperfusion, 3 being severe hypoperfusion, and 4 being missing perfusion). Calculations were made for the summed stress scores (SSS), summed rest scores (SRS), and summed difference scores (SDS). An SDS of 2 or more under the results of at-rest imaging and an SSS of 4 or less signify a reversible problem (ischemia). It was determined that scans with perfusion deficiencies during stress and at rest showed a fixed defect (scar). Perfusion faults with and without reversibility were thought to show that ischemia and scarring were present simultaneously (8).

Coronary Angiography

After the perfusion scan, angiography was performed on the patients with myocardial ischemia on myocardial perfusion SPECT. All angiographies were recorded at Al-Doaa hospital, using German Siemens Axiom Artis angiography apparatus analyzed by experienced cardiologists (two for each angiogram)

Statistical analysis:

SPSS version 28 was utilized for data administration and statistical analysis (IBM, Armonk, New York, United States). Kolmogorov-Smirnov test and direct data visualization techniques were utilized to determine whether quantitative data is normal. Quantitative data were summarised utilizing medians and ranges or means and standard deviations following normality. Percentages and numbers were used as a summary of categorical data. Quantitative data were contrasted between research groups and according to fQRS status utilizing either the independent t-test for normally distributed quantitative variables or the Mann-Whitney U test for non-normally distributed quantitative variables. Chi-square or Fisher's exact test was utilized to compare categorical data. Myocardial ischemia was predicted utilizing multivariate logistic regression analysis. According to the presence of f-wQRS and significant angiographic stenosis, patients were divided into true positive (TP), true negative (TN), false positive (FP), and false negative (FN). Sensitivity, specificity and accuracy were calculated as follows: Sensitivity = $TP / (TP + FN)$, Specificity = $TN / (TN + FP)$, and Accuracy = $(TN + TP) / (TN + TP + FN + FP)$. Calculations were performed to identify odds ratios (OR) and their 95% confidence intervals (CI). Global X^2 value and hierarchical

regression analysis were utilized to determine the incremental prognostic value of fQRS. All statistical tests have two sides. A threshold of 0.05 was utilized to identify significant P values.

Results

There were 224 patients who underwent exercise myocardial perfusion SPECT for evaluation of myocardial ischemia, 18 patients were excluded from our study due to the presence of scar tissue. 206 patients were finally included (52 ischemic and 154 non-ischemic).

General, clinical, and laboratory characteristics

The mean age of the studied patients was 53 ± 10 years. There was a male predominance (65.5%). The mean BMI was 29.6 ± 4 . Hypertension and diabetes were reported in 45.6% and 29.6%, respectively. Dyslipidemia was reported in 41.7%. Only 7.8% had previous CVD. One-third (33.5%) were current smokers. The mean hemoglobin was 13.76 ± 1.08 g/dl. The mean creatinine was 0.96 ± 0.22 mg/dl. The median LDL-C was 121.7mg/dl, ranging from 56 to 207. The mean LVEF was $65.8 \pm 4.7\%$. Only 3.9%, 2.9%, and 12.1% had pathological Qs, AF, and ST-T changes, respectively. The most frequent SPECT defect location was anterior (55.8%). The mean SSS was 13.6 ± 3.3 . The mean SRS was 0.94 ± 1.35 . The mean SDS was 12.56 ± 277 . Single vessel disease incidence was (48.1%). Two vessel disease was (25%), Three vessel disease was (26.9%). More than one-quarter (28.2%) had fQRS (*Table 1*).

Group I demonstrated significantly higher age (56 ± 9 vs. 52 ± 11 , $P = 0.045$), male gender (80.8% vs. 60.4%, $P = 0.008$), hypertension (59.6% vs. 40.9%, $P = 0.019$), diabetes (48.1% vs. 23.4%, $P < 0.001$),

smoking (46.2% vs. 29.2%, P = 0.025), lower LVEF (64.4 ±6 vs. 66.3 ±4, P = 0.042) and fQRS (42.3% vs. 23.4%, P = 0.009). (Table 1).

No significant variations were observed concerning BMI (P = 0.303), previous CVD (P = 0.565), haemoglobin level

(p=0.359), serum creatinine (p=0.056), LDL-C (P = 0.162), pathological Qs (P = 0.987), AF (P = 1.0), ST-T changes (P = 0.187) (Table 1).

Table 1: General, clinical, and laboratory characteristics of the studied groups

		Total (n = 206)	Group I (n = 52)	Group II (n = 154)	P- value
Age (years)	Mean ±SD	53 ±10	56 ±9	52 ±11	0.045*
Gender					
Males	n (%)	135 (65.5)	42 (80.8)	93 (60.4)	0.008*
Females	n (%)	71 (34.5)	10 (19.2)	61 (39.6)	
BMI (Kg/m²)	Mean ±SD	29.6 ±4	30.1 ±3.7	29.4 ±4.1	0.303
Hypertension	n (%)	94 (45.6)	31 (59.6)	63 (40.9)	0.019*
Diabetes	n (%)	61 (29.6)	25 (48.1)	36 (23.4)	<0.001 *
Dyslipidemia	n (%)	86 (41.7)	31 (59.6)	55 (35.7)	0.003*
Previous CVD	n (%)	16 (7.8)	5 (9.6)	11 (7.1)	0.565
Current smoking	n (%)	69 (33.5)	24 (46.2)	45 (29.2)	0.025*
Hemoglobin (gm/dl)	Mean ±SD	13.76 ±1.08	13.88 ±1.1	13.72 ±1.08	0.359
Creatinine (mg/dl)	Mean ±SD	0.96 ±0.22	1.01 ±0.22	0.94 ±0.22	0.056
LDL-C (mg/dl)	Median (range)	121.7 (56 - 207)	135.5 (56 - 207)	120.5 (58.4 - 178.4)	0.162
LVEF (%)	Mean ±SD	65.8 ±4.7	64.4 ±6	66.3 ±4	0.042*
Pathological Qs	n (%)	8 (3.9)	2 (3.8)	6 (3.9)	0.987
AF	n (%)	6 (2.9)	1 (1.9)	5 (3.2)	1
ST-T changes	n (%)	25 (12.1)	9 (17.3)	16 (10.4)	0.187
SPECT defect location					
Anterior	n (%)	29 (55.8)	29 (55.8)	-	-
Inferior	n (%)	14 (26.9)	14 (26.9)	-	-
Lateral	n (%)	9 (17.3)	9 (17.3)	-	-
SSS (%)	Mean ±SD	13.6 ±3.3	13.6 ±3.3	-	-
SRS (%)	Mean ±SD	0.94±1.35	0.94±1.35	-	-
SDS (%)	Mean ±SD	12.56±2.77	12.56±2.77	-	-
Coronary angiography					
Single vessel disease		25(48.1)	25(48.1)	-	
Two vessel disease		13(25.0)	13(25.0)	-	
Three vessel disease		14(26.9)	14(26.9)	-	
fQRS	n (%)	58 (28.2)	22 (42.3)	36 (23.4)	0.009*

*Significant P-value; BMI: Body mass index; CVD: Cardiovascular disease; LVEF: Left ventricular ejection fraction; AF: Atrial fibrillation; SPECT: single-photon emission computed tomography; SSS, sum stress score; SDS, sum difference score; SRS, sum rest score; fQRS: Fragmented QRS

f-QRS

SPECT defect location significantly differed according to the presence of fQRS ($P = 0.024$), with the inferior and lateral locations being higher in patients with f-QRS (45.5% and 18.2%, respectively) than in those without f-QRS (13.3% and 16.7%, respectively). In contrast, the anterior location was lower in those with f-QRS (26.4%) than in those without f-QRS (70%). The number of vessels affected significantly differed according to the presence of fQRS with incidence of three vessel disease being higher in patients with f-QRS (40.9%) than in those without f-QRS (16.7%) ($P = 0.023$). (**Table 2**).

No substantial variations were noted concerning all other parameters, including age ($P = 0.456$), gender ($P = 0.104$), BMI ($P = 0.294$), hypertension ($P = 0.633$), diabetes ($P = 0.536$), dyslipidemia ($P = 0.947$), previous CVD ($P = 0.774$), smoking ($P = 0.639$), hemoglobin ($P = 0.349$), creatinine ($P = 0.626$), LDL-C ($P = 0.981$), LVEF ($P = 0.726$), pathological Qs ($P = 0.315$), AF ($P = 0.675$), ST-T changes ($P = 0.352$), and SSS% ($P = 0.439$), SRS% ($P = 0.885$) and SDS% ($P = 0.364$) single vessel disease ($P = 0.376$), two vessel disease ($P = 0.331$) (**Table 2**).

Table 2: General, clinical, and laboratory characteristics of the studied groups according to f-QRS status

		Total	fQRS		P-value
			Yes (n = 58)	No (n = 148)	
Age (years)	Mean \pm SD	53 \pm 10	54 \pm 11	53 \pm 10	0.456
Gender					
Males	n (%)	135 (65.5)	43 (74.1)	92 (62.2)	0.104
Females	n (%)	71 (34.5)	15 (25.9)	56 (37.6)	
BMI (Kg/m ²)	Mean \pm SD	29.6 \pm 4	30 \pm 3.7	29.4 \pm 4.1	0.294
Hypertension	n (%)	94 (45.6)	28 (48.3)	66 (44.6)	0.633
Diabetes	n (%)	61 (29.6)	19 (32.8)	42 (28.4)	0.536
Dyslipidemia	n (%)	86 (41.7)	24 (41.4)	62 (41.2)	0.947
Previous CVD	n (%)	16 (7.8)	5 (8.6)	11 (07.1)	0.774
Current smoking	n (%)	69 (33.5)	18 (31)	51 (34.1)	0.639
Hemoglobin (gm/dl)	Mean \pm SD	13.76 \pm 1.1	13.87 \pm 1.05	13.72 \pm 1.1	0.349
Creatinine (mg/dl)	Mean \pm SD	0.96 \pm 0.22	0.97 \pm 0.21	0.95 \pm 0.23	0.626
LDL-C (mg/dl)	Median (range)	121.7 (56 - 207)	119.8 (56 - 207)	123 (58.4 - 178.4)	0.981
LVEF (%)	Mean \pm SD	65.8 \pm 4.7	66 \pm 5.3	65.8 \pm 4.4	0.726
Pathological Qs	n (%)	8 (3.9)	1 (1.7)	7 (4.7)	0.315
AF	n (%)	6 (2.9)	2 (3.4)	4 (2.7)	0.675
ST-T changes	n (%)	25 (12.1)	9 (15.5)	16 (10.8)	0.352
SPECT defect location†					
Anterior	n (%)	29 (55.8)	8 (36.4)	21 (70)	0.024*
Inferior	n (%)	14 (26.9)	10 (45.5)	4 (13.3)	
Lateral	n (%)	9 (17.3)	4 (18.2)	5 (16.7)	
SSS (%)	Mean \pm SD	13.6 \pm 3.3	13.2 \pm 3.4	13.9 \pm 3.2	0.439
SRS (%)	Mean \pm SD	0.95 \pm 1.35	0.91 \pm 1.27	0.97 \pm 1.43	0.885
SDS (%)	Mean \pm SD	12.56 \pm 2.77	12.27 \pm 2.93	12.93 \pm 2.66	0.346
Coronary angiography					
Single vessel disease					
Two vessel disease	Mean \pm SD	25 (48.1)	9 (40.9)	16 (53.3)	0.376
Three vessel disease	Mean \pm SD	13 (25)	4 (18.2)	9 (30)	0.331
	Mean \pm SD	14 (26.9)	9 (40.9)	5 (16.7)	0.023*

*Significant P-value; †reported for patients with ischemia only; BMI: Body mass index; CVD: Cardiovascular disease; LVEF: Left ventricular ejection fraction; AF: Atrial fibrillation; SPECT: single-photon emission computed tomography; fQRS: Fragmented QRS.

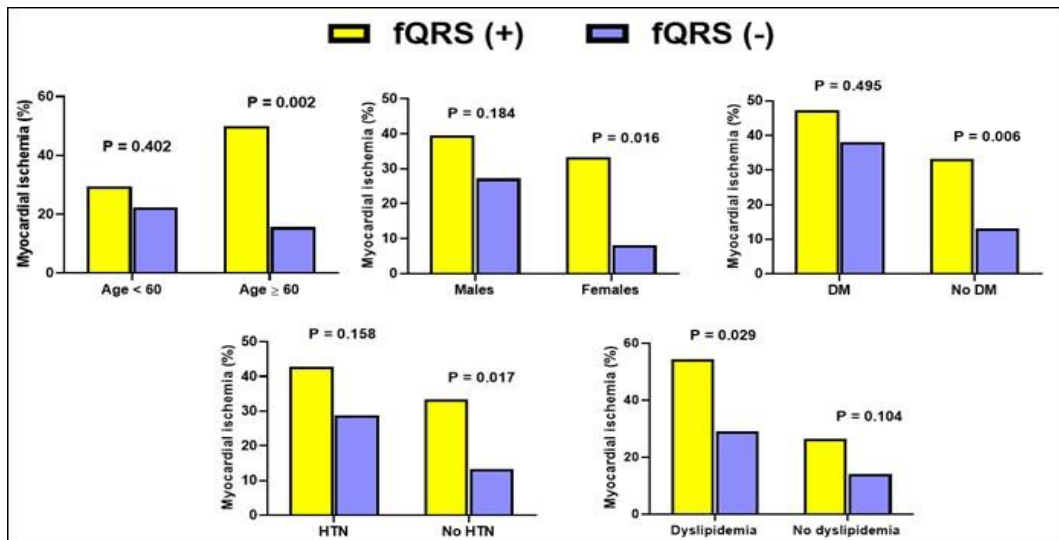


Fig. 1 Myocardial ischemia according to fQRS status in different subgroups

Myocardial ischemia according to fQRS status in different subgroups:

Myocardial ischemia was compared according to fQRS status in various subgroups, including age groups (<60 years and ≥ 60 years), gender (males and females), diabetes (patients with and without diabetes), hypertension (patients with and without hypertension), and dyslipidemia (patients with and without dyslipidemia).

Results revealed that in those with age ≥ 60, myocardial ischemia was substantially greater in those with positive fQRS than in those with negative fQRS ($P = 0.002$), with no significant variation in the age group of < 60. In females, myocardial ischemia was substantially greater in those

with positive fQRS than in those with negative fQRS ($P = 0.016$), with no significant variation in males. In patients without diabetes, myocardial ischemia was substantially greater in those with positive fQRS than those with negative fQRS ($P = 0.006$), with no significant variation in the diabetic group. In patients without hypertension, myocardial ischemia was significantly greater in those with positive fQRS than those with negative fQRS ($P = 0.017$), with no significant variation in the hypertensive group. In patients with dyslipidemia, myocardial ischemia was substantially greater in those with positive fQRS than in those with negative fQRS ($P = 0.029$), with no significant difference in the non-dyslipidemic group (**Fig. 1**).

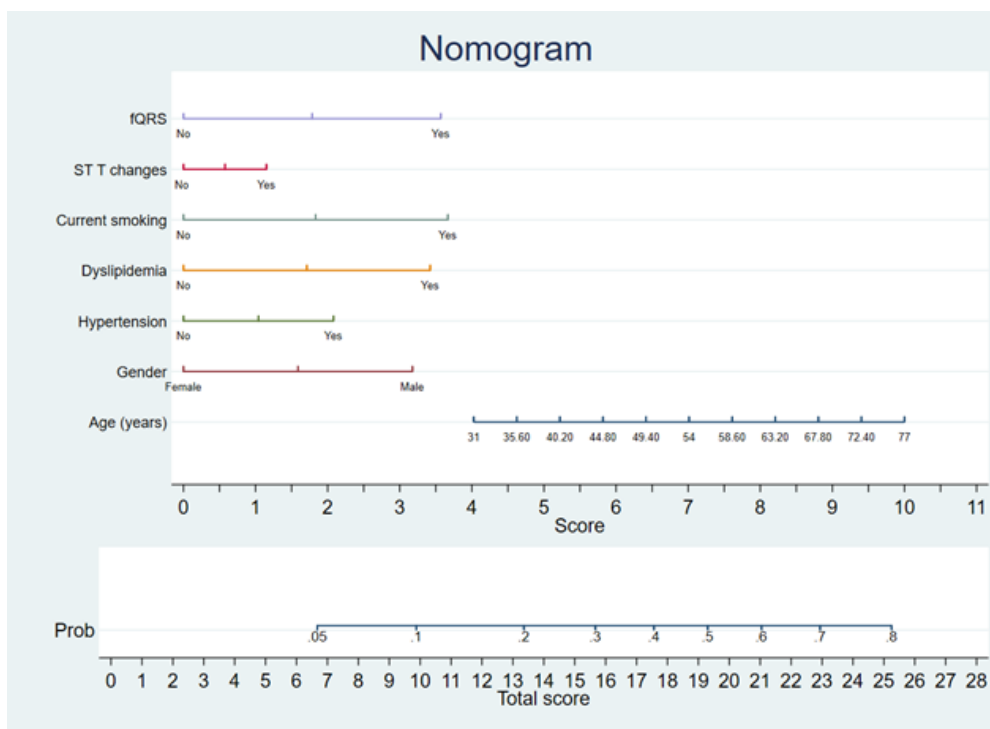


Fig. 2 Nomogram for prediction of myocardial ischemia

Prediction of myocardial ischemia:

Multivariate logistic regression analysis was carried out to predict myocardial ischemia. Variables were selected clinically. The model indicated that fQRS, dyslipidemia, and smoking were significant predictors of myocardial ischemia. fQRS was correlated with two times elevated risk of myocardial ischemia

(OR = 2.298, 95% CI = 1.102 – 4.792, P = 0.026). Dyslipidemia was associated with twice the risk of myocardial ischemia (OR = 2.22, 95% CI = 1.068 – 4.617, P = 0.033). Smoking was correlated with two times elevated risk of myocardial ischemia (OR = 2.351, 95% CI = 1.105 – 5.003, P = 0.027) (**Table 3, Fig. 2**).

Table 3: Multivariate logistic regression analysis to predict myocardial ischemia

	OR (95% CI)	P-value
Age (years)	1.031 (0.993 - 1.07)	0.110
Female gender	0.477 (0.201 - 1.133)	0.094
ST-T changes	1.308 (0.443 - 3.863)	0.627
fQRS	2.298 (1.102 - 4.792)	0.026*
Hypertension	1.624 (0.782 - 3.372)	0.193
Dyslipidemia	2.22 (1.068 - 4.617)	0.033*
Current smoking	2.351 (1.105 - 5.003)	0.027*

*Significant P-value; OR: Odds ratio; 95% CI: 95% Confidence interval; fQRS: Fragmented QR

Validity of fQRS in prediction of myocardial ischemia:

When considering stress myocardial perfusion SPECT as a gold standard test, sensitivity of using fQRS alone in prediction of myocardial ischemia was 42.31%, and specificity was 76.62%. Positive and negative predictive values were 37.93% and 79.73%, respectively, accuracy was 67.96%

Incremental prognostic value of fQRS:

The incremental prognostic value of fQRS for predicting myocardial ischemia was assessed using global X^2 via hierarchical regression analysis. When including diabetes, hypertension, dyslipidemia, and smoking, the global X^2 was 27.844. It increased to 28.151 after the inclusion of ST-T changes. After adding fQRS, the global X^2 increased to 34.612 (**Table 4**, **Fig. 3**).

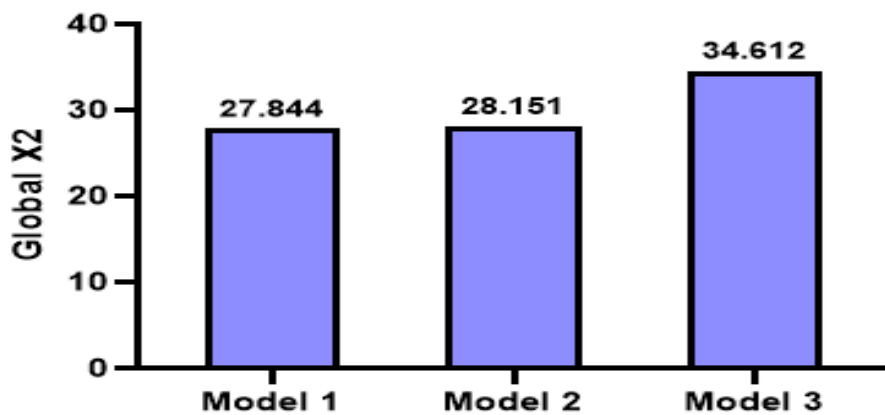


Fig. 3 Incremental prognostic value of fQRS for prediction of myocardial ischemia

Table 4: Incremental prognostic value of fQRS for prediction of myocardial ischemia

	Global X^2
Model 1 (DM + HTN + Dyslipidemia + smoking)	27.844
Model 2 (DM + HTN + Dyslipidemia + smoking + ST-T changes)	28.151
Model 3 (DM + HTN + Dyslipidemia + ST-T changes + fQRS)	34.612

DM: Diabetes Mellitus, HTN: Hypertension.

Discussion

Fragmented QRS on the ECG is a straightforward, affordable, and widely accessible indicator of myocardial fibrosis and scarring^(10, 11). Fragmented QRS is linked to HF and is a risk factor for death and arrhythmic events in some conditions^(12, 13). The current work assessed the predictive value of (fQRS) in diagnosing myocardial ischemia and evaluated its incremental prognostic significance in

patients having SPECT for exercise-induced myocardial perfusion.

The mean age of the studied patients was 53 ± 10 years. There was a male predominance (65.5%). The most frequent SPECT defect location was anterior (55.8%). The mean defect percentage was 13.6 ± 3.3 . More than one-quarter (28.2%) had fQRS. Group I demonstrated significantly higher age, male gender,

hypertension, diabetes, smoking and fQRS (42.3% vs. 23.4%, $P = 0.009$).

Investigated nuclear exercise stress tests and coronary angiography results to establish the presence of myocardial ischemia in 150 patients (60.5 ± 8.5 years, 102 men) with electrocardiograms (ECGs) showing this condition. Additionally, they looked at ECGs taken from 601 patients; 315 were males, aged 58.5 ± 10.0 , and failed a nuclear exercise stress test (control group). They reported that patients with myocardial ischemia showed higher rates of fQRS (32.0% vs. 22.1%, $p = 0.011$) and other risk factors, for instance, age, hypertension, dyslipidemia, diabetes, and smoking⁽²⁾. The results of another study to determine if the existence of fQRS on 12-lead ECG would enhance PPV of ETT in patients with an intermediate risk of CAD showed that the mean age of patients was 51.3 ± 11.3 years, with 74 of them being male (77.9%). Also, age, DM, and hypertension were considerably greater in the significant CAD group than in the nonsignificant CAD group. Forty-seven individuals (49.5%) had fQRS. In contrast to the nonsignificant CAD group, the significant CAD group had a greater prevalence of fQRS. (85.1% vs 14.9%, $P < 0.001$)⁽¹⁴⁾.

In addition, noted that the frequency of fQRS on ECG was substantially greater in the ischemic group than in non-ischemic patients⁽¹⁵⁾. Also, they observed that patients with ischemia experienced considerably more fQRS episodes than patients with adequate perfusion (54.8% vs. 23.8%, respectively; $P < 0.001$)⁽⁸⁾.

According to our results, SPECT defect location significantly differed according to the presence of fQRS ($P = 0.024$), with the inferior and lateral locations being higher

in patients with f-QRS (45.5% and 18.2%, respectively) than in those without f-QRS (13.3% and 16.7%, respectively). In contrast, the anterior location was lower in those with f-QRS (26.4%) than in those without f-QRS (70%).

In addition, we have found the high prevalence of three vessel disease demonstrated on coronary angiography in patients with f-QRS (27.3%) when compared to those without f-QRS (16.7%) $P=0.023$. So, the presence of f-QRS complexes was not only associated with the Presence of coronary artery disease but also with more extent of obstructive coronary stenosis.

In the current study, myocardial ischemia was stratified by fQRS status in subgroups, displaying significant differences. Those aged ≥ 60 and females with positive fQRS had significantly higher myocardial ischemia. Patients without diabetes or hypertension also exhibited significantly elevated myocardial ischemia with positive fQRS ($P = 0.006$ and $P = 0.017$, respectively). Dyslipidemic patients showed significantly higher myocardial ischemia when presenting positive fQRS.

Another study found that 181 patients (24.1%) had an ECG that showed fQRS⁽²⁾. Men were more likely to have the fQRS. Individuals with fQRS were more likely to experience myocardial ischemia ($n = 48$, 26.5%) than those without fQRS ($n = 102$, 17.9%). An examination of subgroups revealed that fQRS was a determinant of myocardial ischemia in patients ≥ 60 years old and those who were current smokers, had hypertension, diabetes, and a normal lipid profile. They also discovered that men with myocardial ischemia had a greater prevalence of fQRS identification.

The present work used multivariate logistic regression analysis to predict myocardial ischemia. The model indicated that fQRS, dyslipidemia, and smoking were substantial determinants of myocardial ischemia. Dyslipidemia, smoking, and fQRS were linked with a two times elevated risk of myocardial ischemia.

After controlling for age, sex, current smoking, ST-T changes on the ECG, and histories of hypertension, diabetes, and hyperlipidemia, multivariate logistic regression analysis conducted in the study revealed that fQRS was an independent determinant of myocardial ischemia as seen on SPECT (OR 1.580, 95% CI 1.020–2.446, $P = 0.040$). They discovered fQRS as a determinant of myocardial ischemia in addition to current smoking, hypertension, diabetes, hyperlipidemia, and ST-T alterations on the ECG ⁽²⁾.

Additionally, The incidence of substantial CAD is greater when fQRS is evident on ECG than when it is absent in individuals with chest pain who are believed to have an intermediate pretest risk of major CAD and who would be recommended for a diagnostic CAG if a stress test result was positive (OR = 2.839, $P < 0.001$) ⁽¹⁴⁾.

According to meta-analysis, patients with STEMI and non-STEMI had higher mortality rates, severe adverse cardiac events, worsening LV function, and multivessel disorder when fQRS was present in an admission ECG ⁽¹⁶⁾.

Additionally, according to, fQRS is a reliable indicator of death in ACS patients ⁽¹⁷⁾. Prior research on myocardial scars as CAD determinants primarily focused on their identification. Our research, however, demonstrated that the appearance of fQRS on the ECG is related to myocardial ischemia, even in the absence of scar

tissue. Using multivariate analysis, displayed that fQRS was a reliable indicator of myocardial ischemia in people with intermediate coronary stenosis. (OR=7.202, CI 95%, 4.195-12.367; $p<0.001$) ⁽¹⁵⁾. However, a functional examination like myocardial SPECT did not show the lack of myocardial scar; they also recommend the existence of fQRS on the ECG is related to myocardial ischemia when the fractional flow reserve is low and the coronary stenosis is moderate ⁽¹⁵⁾.

Patients with intermediate stenosis, as determined by CAG, underwent MPI, according to, According to the authors' findings from multivariate analysis, the existence of fQRS on the ECG was a reliable indicator of myocardial ischemia (OR=11.181; CI=3.900-32.057; $p<0.001$) ⁽⁸⁾. Additionally, numerous investigations revealed that fQRS indicated the existence of ischemia and myocardial scarring ⁽¹⁸⁻²⁰⁾. These outcomes support the conclusions of our investigation, indicating that fQRS can be utilized to recognize ischemia myocardium.

Our research stands out from other studies because it shows how valuable fQRS is as a diagnostic tool for identifying myocardial ischemia, supported by anatomical and functional modalities/imaging.

Our results showed that the sensitivity of fQRS alone in detecting myocardial ischemia CAD was 42.3%, specificity was 76.6%, positive predictive value was 37.9 %, negative predictive value was 79,9 %, and overall accuracy was 67.96 %.

Of note, the incremental prognostic value of fQRS for predicting myocardial ischemia was assessed using global X^2 via hierarchical regression analysis. When

including diabetes, hypertension, dyslipidemia, and smoking, the global X^2 was 27.844. It increased to 28.151 after the inclusion of ST-T alterations. After adding fQRS, the global X^2 increased to 34.612. Confirming our findings, discovered that fQRS has improved predictive value over traditional risk variables ($\chi^2 = 5, P = 0.032$) and across an assortment of traditional risk variables and STT changes ($\chi^2 = 9, P = 0.014$)⁽²⁾.

Finally, this study had some limitations, as it was observational. Consequently, it is impossible to rule out the possibility that factors that cannot be evaluated or are unknown had an impact on the results of the study. The study primarily focuses on fQRS and its association with myocardial ischemia. Other potential confounding variables or risk factors for myocardial ischemia, such as genetic factors or lifestyle habits (e.g., diet, physical activity), were not considered. Yet, further multi-center studies are needed to validate our findings.

Conclusions

Fragmented QRS complex shows promise as a valuable ECG marker with a significant association with myocardial ischemia. Its inclusion in risk assessment models improves the predictive accuracy in myocardial ischemia. Therefore, it may help in early diagnosis and risk stratification of CAD patients.

References:

1. Cassar, A., Holmes Jr, D. R., Rihal, C. S., and Gersh, B. J. Chronic coronary artery disease: diagnosis and management. In *Mayo Clinic Proceedings 2009* (Vol. 84, No. 12, pp. 1130-1146). Elsevier.
2. Cho, H. J., Yoon, J. Y., Kim, N., Jang, S. Y., Bae, M. H., Lee, J. H., et al. Predictive value of a fragmented QRS

- complex in diagnosing patients with myocardial ischemia. *Clinical Cardiology* 2019, 42(3), 379-384.
3. El-Sherif, N. The rsR' pattern in left surface leads in ventricular aneurysm. *Heart* 1970, 32(4), 440-448.
 4. Rad, M. A., Baboli, N. T., Barzigar, A., Keirkhah, J., Soltanipour, S., Bonakdar, H. R., et al. The role of the fragmented QRS complexes on a routine 12-lead ECG in predicting non-responsiveness to cardiac resynchronization therapy. *The Anatolian Journal of Cardiology* 2015, 15(3), 204.
 5. Das, M. K., Khan, B., Jacob, S., Kumar, A., and Mahenthiran, J. "Significance of a fragmented QRS complex versus a Q wave in patients with coronary artery disease." *Circulation* 113, 21 (2006): 2495-2501.
 6. Das, M. K., Suradi, H., Maskoun, W., Michael, M. A., Shen, C., Peng, J., et al. "Fragmented wide QRS on a 12-lead ECG: a sign of myocardial scar and poor prognosis." *Circulation: Arrhythmia and Electrophysiology* 1, 4 (2008): 258-268.
 7. Amini, M., Pursamimi, M., Hajianfar, G., Salimi, Y., Saberi, A., Mehri-Kakavand, G., et al. Machine learning-based diagnosis and risk classification of coronary artery disease using myocardial perfusion imaging SPECT: A radiomics study. *Sci Rep.* 2023;13:14920.
 8. Caliskan B, Korkmaz AN, and Erdem F. Contribution of fragmented QRS on myocardial perfusion imaging in the assessment of functionally significant coronary artery stenoses. *Eur Rev Med Pharmacol Sci.* 2016;20:1575-81.
 9. Costa Filho, F. F., Chaves, Á. J., Ligabó, L. T., Santos, E. M. D., Silva, D. T. D., Puzzi, M. A., G. et al. Efficacy of Patient Selection for Diagnostic Coronary Angiography in Suspected Coronary Artery Disease. *Arq Bras Cardiol.* 2015;105:466-71.
 10. Basaran, Y., Tigen, K., Karaahmet, T., Isiklar, I., Cevik, C., Gurel, E., et al. Fragmented QRS complexes are associated with cardiac fibrosis and significant intraventricular systolic dyssynchrony in nonischemic dilated

- cardiomyopathy patients with a narrow QRS interval. *Echocardiography*. 2011;28:62-8.
11. **Take Y, and Morita H.** Fragmented QRS: What Is The Meaning? *Indian Pacing Electrophysiol J*. 2012;12:213-25.
 12. **Oner, E., Erturk, M., Birant, A., Kalkan, A. K., Uzun, F., Avci, Y., et al.** Fragmented QRS complexes are associated with left ventricular systolic and diastolic dysfunctions in patients with metabolic syndrome. *Cardiol J*. 2015;22:691-8.
 13. **Toukola, T., Junttila, M. J., Holmström, L. T., Haukilahti, M. A., Tikkanen, J. T., Terho, H., .et al.** Fragmented QRS complex as a predictor of exercise-related sudden cardiac death. *J Cardiovasc Electrophysiol*. 2018;29:55-60.
 14. **Tusun, E., Ilter, A., Besli, F., Erkus, E., Altiparmak, I. H., and Bozbay, M.** Fragmented QRS Is Associated with Improved Predictive Value of Exercise Treadmill Testing in Patients with Intermediate Pretest Likelihood of Significant Coronary Artery Disease. *Ann Noninvasive Electrocardiol*. 2016;21:196-201.
 15. **Korkmaz, A., Yildiz, A., Demir, M., Ozyazgan, B., Sahan, E., Acar, B., et al.** The relationship between fragmented QRS and functional significance of coronary lesions. *J Electrocardiol*. 2017;50:282-6.
 16. **Güngör, B., Özcan, K. S., Karataş, M. B., Şahin, İ., Öztürk, R., and Bolca, O.,** Prognostic Value of QRS Fragmentation in Patients with Acute Myocardial Infarction: A Meta-Analysis. *Ann Noninvasive Electrocardiol*. 2016;21:604-12.
 17. **Das, M. K., Michael, M. A., 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.
 18. **Mahenthiran, J., Khan, B. R., Sawada, S. G., and Das, M. K.** Fragmented QRS complexes not typical of a bundle branch block: a marker of greater myocardial perfusion tomography abnormalities in coronary artery disease. *J Nucl Cardiol*. 2007;14:347-53.
 19. **Chatterjee S, and Changawala N.** Fragmented QRS complex: a novel marker of cardiovascular disease. *Clin Cardiol*. 2010;33:68-71.
 20. **Ozdemir, S., Tan, Y. Z., Colkesen, Y., Temiz, A., Turker, F., and Akgoz, S.** Comparison of fragmented QRS and myocardial perfusion-gated SPECT findings. *Nucl Med Commun*. 2013;34:1107-15.

To cite this article: Ahmed M. Bendary, Islam S. Abdelmaged, Ahmed A. Mohamed, Mahmoud Sh. Abdelmoneim. The Predictive Value of Fragmented QRS Complex in Diagnosis of Myocardial Ischemia. *BMFJ* XXX, DOI: 10.21608/bmfj.2023.252371.1967