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Fragmented QRS Complex as a Predictor of High Risk in Acute Coronary Syndrome

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Abstract: Background: To detect the potential in hospital prognostic value of fQRS complex in patients with acute coronary syndrome (ACS) & investigate whether FQRS complex can be used to distinguish patients with early NSTEMI from those with unstable angina. Methods: It included 150 patients with acute NSTEMI and unstable angina. All patients were subjected to Grace score calculation, ECG to detect ischemic changes and detect presence or absent of fQRS, transthoracic echo to detect LV ejection fraction and recording in-hospital outcome. Results: Patients with fQRS have significant higher Killip class>2, higher troponin &CKMB levels, higher grace score, increased LVEDD & LVESD and significantly lower LVEF%. LVEF is significantly lower among patients with fQRS than patients with not fQRS in NSTEMI patients while there is no significant difference of LVEF % between both groups in unstable angina patients. There is significant association between fQRS and higher prevalence of NSTEMI and higher incidence of heart failure, arrhythmia and bad outcome. By multivariate analysis, NSTEMI (p =0.003) and high HR (p =0.004) and fragmented QRS (p =0.00) were the only significant predictors for bad outcome. FQRS have the ability to diagnose NSTEMI in 47.9% of cases, fQRs can truly exclude NSTEMI in 72.7% of case. Conclusion: Among patients with ACS, the presence of fQRS was associated with an increase incidence of complication, worse outcome, larger LV dimensions, and lower LVEF. The presence of fQRS in acute coronary syndrome patients could predict the presence of NSTEMI with fair diagnostic value.

Keywords: ACS (NSTEMI, Unstable Angina), Fragmented QRS Complex, Hospital Outcome

1. Background

ACS refers to a spectrum of clinical presentations ranging from those for ST-segment elevation myocardial infarction (STEMI) to presentations found in non–ST-segment elevation myocardial infarction (NSTEMI) or in unstable angina. NSTEMI usually determined by increased level of circulating cardiac enzymes in the absence of ST elevation, whereas unstable angina (UA) does not involve any significant elevation in circulating cardiac biomarkers. [1] Fragmented of QRS complexes (fQRS) is seen commonly on the standard 12 leads surface electrocardiograms (ECG) with a narrow or wide QRS complex and it was defined as presence of an additional R wave (R') or notching in the nadir of the S wave, or the presence of more than one R' in two contiguous leads, corresponding to a major coronary artery territory on resting 12-lead ECG with filter range 0.16-100 Hz, AC filter 60 Hz, paper speed 25 mm/s, and 10 mm/mV.5. [2, 3] The presence of fQRS on 12 leads ECG is associated with myocardial scarring, ischemia and fibrosis and originates from the deterioration the process of signal transduction and ventricular depolarization. [4] Das et al 2008 The presence of fQRS in coronary artery disease (CAD) patients is significantly associated with major adverse cardiac events (MACE) and left ventricular dysfunction. [5, 6]

As the standard method of differentiation between

NSTEMI and UA is measuring of cardiac biomarkers as high-sensitivity cardiac troponin (hscTn). However, there is a lag time hscTn between the beginnings of symptoms of NSTEMI to the rise of hscTn to a level that could diagnose NSTEMI ranges from one hour to three or four hours. [7, 8] Another problem in using hscTn is the different cut-off values used in different assays. In addition some demographic criteria of patients like age may have an effect on the cut-off values to be used. [9] Further problem about the use of hsTn is its availability especially in the developing countries with limited health resources like Egypt. As the fQRS complex can be detected as early as several hours after AMI. [10] So, it might be useful to use another easy and widely available method using fQRS complex to detect high risk patients with acute NSTEMI among patients with acute coronary syndrome.

2. Patients and Methods

2.1. Patients

This a cross-sectional observational study was carried out in cardiology department, Zagazig University hospital from December 2018 to June 2019. It included 150 patients with acute coronary syndrome include unstable angina and non-ST elevation myocardial infarction (NSTEMI). NSTEMI was defined as elevation in cardiac markers without ST segment elevation in patients presenting withischemic chest pain (rest pain or may be triggered with minimal exertion and can be new onset or increased in severity and frequency or precipitated with less effort than prior angina). [11]. Patients with acute STEMI, complete or incomplete bundle branch block, pre-excitation syndrome, pacemaker implantation and patients with fQRS in old ECGs were excluded from the study. Informed consent obtained from every patient for participation in the study.

2.2. Methods

All patients were subjected to the following: Complete history taking with special emphasis to CAD risk factors likes hypertension, diabetes mellitus, dyslipidemia, smoking and family history, history of stroke, transient ischemic attacks, history of peripheral vascular diseases, history of old percutaneous coronary interventions (PCI), or history of coronary artery bypass grafting (CABG). Thorough physical examination included KILLIP class. Grace score was detected for each patient (Figure 1). Recording in-hospital mortality and complications such asarrythmia (ventricular tachycardia and/or ventricular fibrillation). heart failure, cardiogenic shock and stroke. Resting 12-lead ECG: ECG was done on admission at a paper speed of 25 mm/second and amplification of 10 mm/mv; to detect ST segment depression or T wave inversion and detect presence or absent of fQRS. Electrocardiographic examinations will be performed with the naked eye by two independent physicians. The fQRS was defined by the presence of various RSR‘ patterns (QRS duration < 120 ms), which included an additional R wave (R‘ prime) or notching of the R wave or S wave, or the presence of more than one R prime (fragmentation) without typical bundle branch block in two contiguous leads corresponding to a major lead set for major coronary artery territory. [12]. Laboratory investigations: with special emphasis to cardiac markers [troponin I (cTnI), and creatine kinase-MB (CK-MB)], creatinine & complete blood count (CBC), hemoglobin level (Hb), total leukocytic count (WBCs), lymphocyte-neutrophil ratio, red blood cell distribution width (RDW), platelet count, and RDW/platelets ratio, random blood sugar and lipid profile. Transthoracic echocardiography (TTE): All patients underwent TTE during hospitalization in first 72 hours using Siemens machine using probe S5. We measured LV volumes and ejection fraction (EF) using 2D biplane Simpson's method. Both left ventricle end diastolic (LVED) and end systolic (LVES) volumes in apical four chamber (A4C) and apical two chamber (A2C) views were measured. End-systole was defined as the frame with the smallest cavity area and end diastole as the frame with the largest LV cavity area, the EF was then calculated. [13] The mean of the two readings of biplane ejection fraction was then taken. Our patients were divided according to presence or absent of fragmented QRS complex on ECG upon admission into 2 groups: fragmented QRS (FQRS) group: 56 patients and non-fragmented QRS (FQRS) group: 94 patients.

2.3. Statistical Analysis

Data collected throughout history, basic clinical examination, laboratory investigations and outcome measures coded, entered and analyzed using Microsoft Excel software. Data were then imported into Statistical Package for the Social Sciences (SPSS version 20.0) (Statistical Package for the Social Sciences) software for analysis. According to the type of data qualitative represent as number and percentage, quantitative continues group represent by mean ± SD, the following tests were used to test differences for significance;. difference and association of qualitative variable by Chi square test (X^2). Differences between quantitative independent groups by t test or Mann Whitney, Multivariate analysis investigated parameters were entered into a logistic regression model to determine which of these factors is considered as a significant risk factor and identify its risk estimate (Odds ratio & 95% CI).. Receiver operating characteristic (ROC) was used to assess the cut off value of troponin. P value was set at <0.05 for significant results & <0.001 for high significant result. sensitivity, specificity, PVV and NPV were calculated Sensitivity = (true +ve / all +ve) × 100, Specificity= (true -ve / all -ve) × 100, PVP = (True +ve / all +ve by fQRS) × 100 and PVN= (true -ve / all -ve) × 100.

3. Results

Our patients were divided according to presence or absent of fragmented QRS complex on ECG upon admission into 2 groups: fragmented QRS (fQRS) group: 56 patients and non-

fragmented QRS (fQRS) group: 94 patients

Patients with fQRS have significant higher Killip class>2 compared with patients with non fQRS (p <0.05) with no significant difference between both groups regards regarding age, sex or BMI and the prevalence of risk factors (p> 0.05). Table 1.

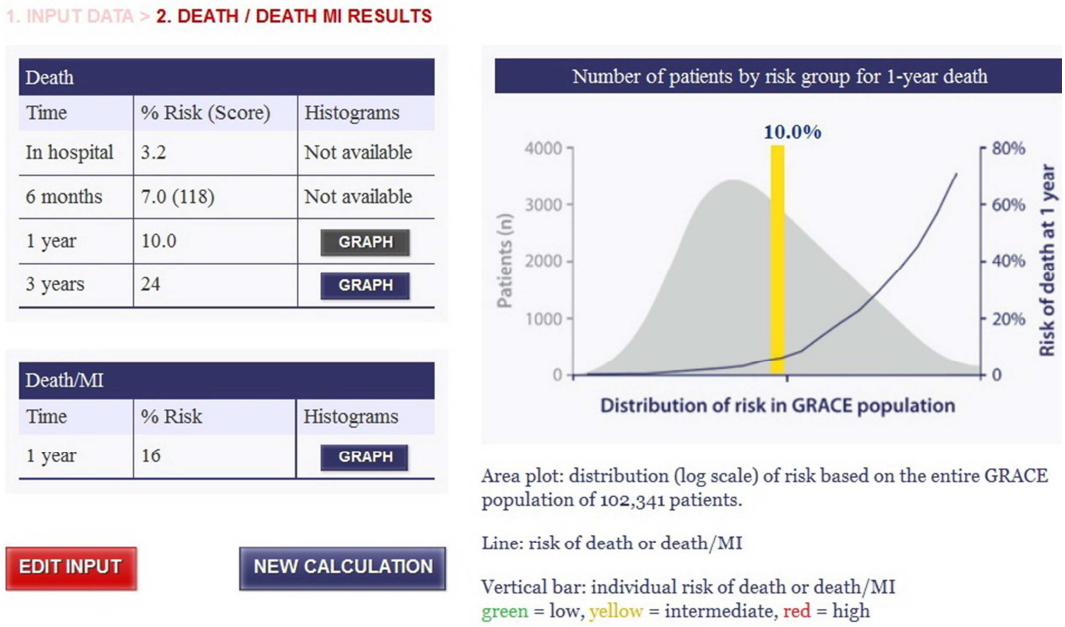

Figure 1. *Online calculation of grace score, assessment the risk of one year, 3 year mortality, and one year death or MI. (http://gracescore.org).*

Table 1. *Demographic &clinical characteristic of the studied population.*

			No Fragmented QRS (N=94)	Fragmented QRS (N=56)	t/X^2	P
Age (years)			60.44±9.02	59.82±11.27	0.373	0.709
Weight (Kg)			84.08±13.9	84.58±20.7	-0.178	0.859
Height (cm)			165.6±11.5	161.0±19.42	1.821	0.071
BMI (Kg/m)			31.4±5.09	29.8±4.64	1.923	0.056
SEX	Male Femal	N&%	60 (63.8% 34 (46.2%)	30 (53.6%) 26 (46.4%	0.98	0.32
DM		N &%	48 (51.1%)	31 (55.4%)	0.25	0.61
HTN			58 (61.7%)	40 (71.4%)	1.46	0.22
Smoker			29 (30.9%)	24 (42.9%)	2.21	0.13
Dyslipidemia			43 (45.7%)	30 (53.6%)	0.86	0.35
History IHD			42 (44.7%)	26 (46.4%)	0.043	0.83
CVA			3 (3.2%)	1 (1.8%)	0.26	0.6
COPD			9 (9.6%)	1 (1.8%)	3.42	0.064
Family history			14 (14.9%)	4 (7.1%)	1.99	0.15
Pain at rest			46 (48.9%)	23 (41.1%)	0.87	0.35
Killip class	1.00 2.00 3.00 4.00		80 (85.1%) 4 (4.3%) 9 (9.6%) 1 (1.1%)	30 (53.5%) 7 (12.5%) 14 (25%) 5 (8.9%)	18.87	0.0002**

DM: Diabetes mellitus, HTN; hypertension, IHD; ischemic heart disease, COPD; chronic obstructive pulmonary disease, CVA; cerebrovascular attak. t; student t test, X^2: Chi-square test, P> 0.05 is not significant,
** p< 0.05 is significant

Patients with fQRS have significant higher troponin &CKMB levels, higher grace score, increased LVEDD & LVESD and significantly lower LVEF% compared with patients with no fQRS (p < 0.05), with non- significant difference between both groups regards other laboratory blood tests, chest pain duration, vital signs or medication (SBP, DBP and HR). (p > 0.05). Table 2.

Table 2. *Lab, echo, medication and clinical characters of the studied groups.*

Lab	Fragmented QRS =56	No Fragmented QRS (N=94)	t/ Mann Whitney	P
HB (g/dl)	12.92±2.18	12.58±2.16	0.916	0.361
WBC (10^3/ul)	9.57±3.43	9.31±3.93	0.420	0.675
RDW/Plate (%)	0.07±0.38	0.066±0.28	1.361	0.176

Lab	Fragmented QRS =56	No Fragmented QRS (N=94)	t/ Mann Whitney	P
RDW (%)	16.14±4.8	16.37±5.8	-0.208	0.835
Neutrophylic/Lymphocytic (%)	3.88±1.4	4.64±1.4	-0.781	0.436
Platelet (10^3/ul)	239.37±72.1	259.56±87.6	-1.455	0.148
Creatinine (mg/dl)	1.13±0.44	1.3±0.42	-.764	0.446
CK-MB (ng/ml)	54 (0.9-300)	34 (0.7-220)	3.839	0.00**
troponin (pg/ml)	890 (20-5819)	583 (3.3-5040)	4.134	0.00**
Chest pain duration (min)	121.49 ±191.45	155.74 ±210.72	1336.0	0.113
Wide QRS	0.09±0.02	0.1±0.02	-0.757	0.450
EF %	49.32±12.07	56.87±11.3	2.228	0.031*
LVEDD (mm)	55.04±9.16	42.08±6.7	-5.229	0.00**
LVESD (mm)	35.99±6.5	29.86 ± 6.93	5.45	0.00**
SBP (mmHg)	136.73±27.36	136.8±28.9	-0.016	0.987
DBP (mmHg)	81.96±15.5	83.67±14.7	-0.673	0.502
Heart Rate (beates /min)	79.62±18.56	81.44±16.58	-0.622	0.535
Grace score	195.16±32.1	97.12±28.7	-8.352	0.00**
Probability death	9.16±3.1	6.11±0.31	3.887	0.00**
B blocker (N&%)	44 (78.6%)	76 (80.9%)	0.11	0.73
ACE	41 (73.2%)	73 (77.7%)	0.38	0.53
Diuretic	11 (19.6%)	20 (21.3%)	0.057	0.81
Ca channel blocker	6 (10.7%)	14 (14.9%)	0.53	0.46

EF%; ejection fraction, LVEDD; Left Ventricular End Diastolic Diameter, left ventricular end-systolic diameter (LVESD), SBP; systolic blood pressure, DBP; diastolic blood pressure.
tests: student t- test/ Mann-Whitney test

LVEF is significantly lower among patients with fQRS than patients with not fQRS in NSTEMI patients while there is no significant difference of LVEF % between both groups in unstable angina patients. Table 3.

Table 3. *Comparison of ejection fraction (EF) among the studied groups in patients with NSTEMI and unstable angina.*

		FQRS (N=35)	No F QRS (N=38)	t test	P
LVEF%	NSTEMI	46.36 ± 11.25	57.54 ±12.5	4.214	0.00**
		FQRS (N=21)	No FQRS (N =56)		
LVEF%	unstable angina	51.17±15.32	54.28 ± 14.2	1.214	0.138

EF: ejection fraction, tests: student t- test

There is significant association between fQRS and higher prevalence of NSTEMI and higher incidence of heart failure, arrhythmia and bad outcome compared to patients wih no fQRS. Table 4 and figure 2.

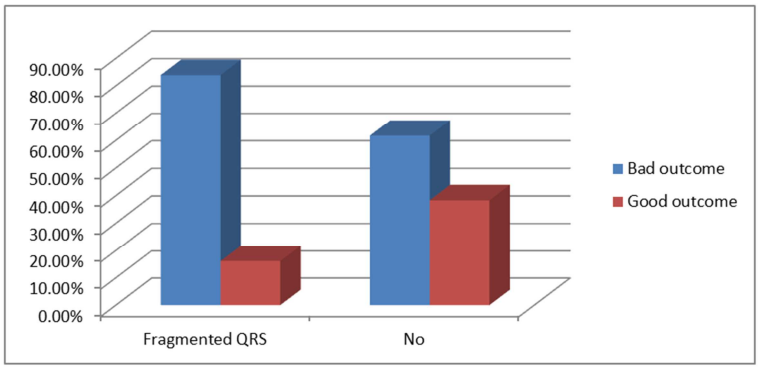

Figure 2. *Outcome among fragmented QRS and not fragmented.*

Table 4. *Outcome and complication distribution between studied groups.*

	ECG Fragmented		X^2	P
	No (N=94)	Yes (N=56)		
Diagnosis (N&%) NSTEMI	38 (40.4%)	35 (62.5%)	5.13	0.02*
Unstable angina	56 (59.6%)	21 (37.5%)	15.96	0.00**
Complication: Arrhythmia	1 (1.1%)	7 (12.5%)	6.9	0.008*
Heart failure	7 (7.5%)	18 (32.2%)	15.4	0.00**
Chest pain	28 (29.8%)	20 (35.7%)	0.56	0.45
Mortality	1 (1.1%)	1 (1.8%)	0.13	0.7
Cardiogenic shock	2 (2.1%)	2 (3.6%)	0.28	0.59

		ECG Fragmented		X^2	P
		No (N=94)	Yes (N=56)		
Stroke		1 (1.1%)	0	0.6	0.43
Outcome	Good	36 (38.3%)	9 (16.1%)	8.25	0.004*
	Bad	58 (61.7%)	47 (83.9%)		

$X^{2:}$ Chi-square test, P> 0.05 is not significant,** p< 0.05 is significant

By univariate analysis, we found that bad out come significantly associated with HTN (p=0.043), dyslipidemia (p= 0.017), Ca channel blocker use (p= 0.002), Fragmented QRS (p = 0.004), NSTEMI diagnosis (p=0.00) and higher KILLIP class >2 (p =0.001), higher cardiac enzymes, higher blood pressure& heart rate, high grace score, higher RDW, LVEDD, LVESD and lower LVEF% & Hb level.(p < 0.05). Table 5.

Table 5. *Univariate analysis for predictors of bad outcome.*

			Outcome		X^2	P
			GOOD (N=45)	BAD (N= 105)		
SEX	MALE	N&%	31 (68.9%)	59 (56.2%)	2.11	0.14
	FEMALE		14 (31.1%)	46 (43.8%)		
DM			20 (44.4%)	59 (56.2%)	1.74	0.18
HTN			24 (53.3%)	74 (70.5%)	4.08	0.043*
Smoker			13 (28.8%)	40 (38.1%)	1.16	0.22
Dyslipidemia			8 (17.8%)	65 (61.9%)	5.9	0.017*
History IHD			19 (42.2%)	49 (46.7%)	0.25	0.61
CVD			2 (4.4%)	2 (1.9%)	0.78	0.37
COPD			3 (6.7%)	7 (6.7%)	0.0	1.0
Family history			5 (11.1%)	13 (12.4%)	0.048	0.82
Pain at rest			24 (53.3%)	45 (42.9%)	1.39	0.23
FQRS			9 (20%)	47 (44.8%)	8.25	0.004*
B _blocker			32 (71.1%)	88 (83.8%)	3.17	0.075
ACE			37 (82.2%)	77 (73.3%)	1.36	0.24
Diuretic			13 (28.9%)	18 (17.1%)	2.65	0.104
CA channel blocker			0	20 (19%)	9.89	0.002*
NTG			23 (51.1%)	61 (58.1%)	0.62	0.43
NSTEMI			10 (22.2%)	63 (60%)	17.6	0.00**
Killip class	1.00		42 ((93.3%)	68 (64.7%)		
	2.00		1 (2.2%)	10 (9.5%)		
	3.00		1 (2.2%)	22 (20.9%)	15.7	0.001**
	4.00		0	6 (5.7%)		

	Good outcome (N=45)	Bad outcome N=105	t/ Mann Whitney	P
Age (years)	61.22±8.79	59.78±10.33	-0.817	0.415
Weight (Kg)	82.8±13.8	84.86±17.89	0.662	0.509
Height (cm)	165.75±6.12	163.08±17.56	-0.992	0.323
BMI	30.2±5.27	31.06±4.84	0.977	0.330
Chest pain duration (min)	120.74 ±180.23	150.69 ±220.56	0.809	0.419
Wide QRS	0.099±0.021	0.0998±0.02	-0.035	0.972
ECHO_EF%	59.33±10.46	42.91±12.1	-4.202	0.00**
LVEDD (mm)	43.82±8.9	51.72 ±7.16	6.41	0.00*
LVESD (mm)	29.86±6.9	35.86 ±6.63	5.45	0.00*
HB (g/dl0	13.54±1.81	12.35±2.22	-3.159	0.002
WBC (10^3/ul)	10.25±3.1	9.04±3.21	-1.829	0.069
RDW/Plate (%)	0.068±0.28	0.073±2.14	1.553	0.122
RDW (%)	13.9±1.54	17.31±5.8	2.951	0.004*
Neutrophylic/Lymphocytic (%)	5.2±1.2	4.81±1.3	-1.794	0.075
Platelet (10^3/ul)	249.04±79.9	253.3±83.9	0.289	0.773
Creatinine (mg/dl)	1.01±0.37	1.33±0.35	1.359	0.176
CK_MB (ng/ml)	19 (0.7-255)	58 (3.0-300)	4.591	0.00**
Troponin (pg/ml)	626 (3-5030)	1181 (3.3-5819)	2.607	0.010*
SBP (mmHg)	127.04±27.75	140.9±27.5	2.826	0.005*
DBP (mmHg)	78.44±14.99	85.0±14.6	2.499	0.014*
Heart Rate (b/m)	76.08±13.3	82.77±18.4	2.194	0.030*
Grace score	94.4±30.8	192.96±33.4	3.965	0.00**
Probability death	5.14±1.5	10.53±2.3	-1.396	0.165

$X^{2:}$ Chi-square test tests: student t- test/ Mann- Whitney test
P> 0.05 is not significant. ** p< 0.05 is significant

By multivariate analysis, we found that NSTEM (p =0.003) and high HR (p =0.004) and fragmented QRS (p =0.00) were the only significant predictors for bad outcome. Table 6

Table 6. *Multivariate Logistic Regression for predictors of bad outcome.*

	Wald	P	OR	95% C. I.	
				Lower	Upper
HTN	0.458	0.498	1.611	405	6.414
Dyslipidemia	2.401	0.121	0.391	119	1.282
Ca channel blocker	0.051	0.998	0.197	0.001	0.231
NSTEMI	8.949	0.003*	0.138	0.038	0.506
LAB_HB	1.549	0.213	0.813	0.587	1.126
RDW	2.924	0.087	1.342	0.958	1.881
Fragmented qrs	12.541	0.00**	5.254	1.258	14.325
CK_MB	3.150	0.076	0.987	0.974	1.001
Troponin	624	0.429	1.000	1.000	1.001
SBP	1.472	0.225	971	0.927	1.018
DBP	1.834	0.176	1.061	0.974	1.156
Heart Rate	8.153	0.004*	1.869	1.021	1.919

P> 0.05 is not significant
** p< 0.05 is significant

Table 7 shows that sensitivity of fQRs in diagnosis of NSTEMI is 47.9% means that FQRS have the ability to diagnose NSTEMI in 47.9% of cases, fQRs can truly exclude NSTEMI in 72.7% of case.

Table 7. *Validity of Fragmented QRS in diagnosis of NSTEMI among the studied cases.*

Fragmented QRS	Diagnosis of NSTEMI		Total
	Positive	negative	
positive	35 (23.3%) true +ve	21 (14.0%) False +ve	56 (37.3%)
Negative	38 (25.3%) false-ve	56 (37.3%) true-ve	94 (62.7%)
Total	73 (48.6%)	77 (51.3%)	150 (100%)
Sensitivity	Specificity	PPV	NPV
47.9%	72.7%	62.5%	59.9%

PPV= positive predictive value, NPV= negative predictive value.

Figure 3 shows that area under ROC curve = 0.9 & 95% CI (0.84-0.95) sensitivity of troponin above cutoff level 115.8 pg/ml in diagnosis of NSTEMI is 94.5% and Specificity=72.7% with high statistical significance (p=0.000)

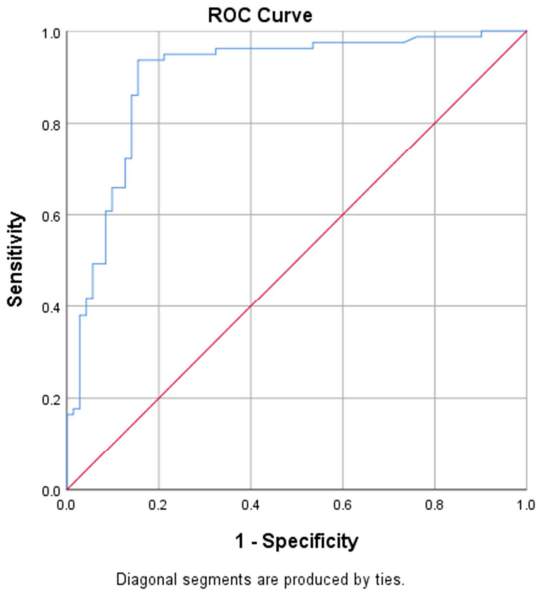

Figure 3. *Validity of troponin in diagnosis of NSTEMI among the studied cases with ROC curve.*

4. Discussion

The current study was conducted on patients with acute coronary syndrome to investigate the value of fragmented QRS complexes in detecting patients with NSTEMI and its prognostic impact. In our results, we found that in patients with fQRS there was a significantly higher incidence of patients with NSTEMI, Killip's class III and IV, and more incidence of complications and bad outcome. In patients with fQRS, mean CK-MB and troponin level were significantly higher, mean LV dimensions were significantly higher, mean LVEF was significantly lower, and mean Grace Score was significantly higher. After performing multivariate logistic regression analysis, the only significant predictors of bad outcome were fQRS, NSTEMI and heart rate. Sensitivity and specificity of fQRS in predicting NSTEMI were 47.9% and 72.7% respectively.

It has been long known that fQRS complexes originate from abnormal forms of ventricular depolarization. These forms occur as a result of non-homogeneous electrical activation of either ischemic injured ventricular myocardium or myocardial scar. [14] Many investigators had reported the significant association between the presence of fQRS and the short-term and long outcome and mortality in STEMI patients [15-17] However, our study was conducted on non ST-segment elevation acute coronary syndrome patients. In

patients with various presentations of IHD, the presence of fQRS was associated with myocardial scarring. In a study performed by (Chatterjee and Changawala, [2] the sensitivity of fQRS for diagnosing myocardial the presence of scar was 72.7% for anterior scar, 62.9% for posterior or lateral scar, and was 82.7% for inferior scar. These values were even higher than those of pathological Q waves that reported a sensitivity of 22.2%, 17.1%, and 50% for anterior, posterolateral, and inferior scars, respectively. Even in the presence of left bundle branch block (LBBB), seeking for fQRS was found to be helpful for non-invasive prediction of significant coronary artery stenosis in patients with suspected coronary artery disease [18] Also fQRS was found to be helpful in detecting myocardial scar and as an independent predictor in patients with LBBB [4] In our study, patients with fQRS had a significantly higher mean CK-MB and troponin level which denotes a larger area of myocardial necrosis. In concordance with our results, (Lorgis et al., [19] have found that STEMI patients with fQRS had significantly larger infarct size, impaired LV systolic function, increased LV volumes and more incidence of LV remodeling. They concluded that fQRS is a reliable marker of infarct size and acute LV remodeling. However, on the other side, (Carey et al., [20] have found that was not a useful in prediction of infarct size in patients with ischemic cardiomyopathy. In our study, patients with fQRS had significantly LV dimensions and lower EF than those with non fQRS. This difference was apparent in the whole study group, in unstable angina group, as well as in NSTEMI group. Our results were concordant to those of [19]. Also Chew et al., [21] have found that fQRS after myocardial infarction was associated with increased LV size and impaired LV function and was a valuable maker of unfavorable LV remodeling. In our study, patients with fQRS had significantly higher Killip class of heart failure and significantly higher Grace Score. Similar to our results, Li et al., [22] have found a strong association between fQRS and Killip class in patients with NSTEMI. They also found that the presence of fQRS was associated with more extensive coronary artery disease and significantly higher number of stenosed coronary arteries. However, the results of Umapathy et al., [23] were discordant to ours. Umapathy and his colleagues found that in patients with acute STEMI, there was no significant association between fQRS and major adverse cardiac events, LV dysfunction, or Killip class on short term 30 days follow-up. However, they found that the presence of fQRS in STEMI patients was an independent predictor of impaired microvascular myocardial reperfusion. In our study, we have found a strong association between fQRS and outcome. Incidence of arrhythmia, heart failure, and bad outcome were significantly higher in patients with fQRS. Various studies had shown that the presence of fQRS was found to be predictor for bad outcome. In a study by (Lu et al., [24] they studied the prognostic effect of fQRS in patients with hypertrophic cardiomyopathy (HCM). They have found that the presence of fQRS in this group of patients was associated with an adverse outcome. The presence of fQRS in HCM patients could predict a higher risk of all-cause mortality, a higher risk of cardiovascular disease mortality, and a higher risk of heart failure-related deaths. In a study performed by (Igarashi et al., [25], they found that fQRS was an independent risk factor for developing ventricular arrhythmias and sudden cardiac death in patients with non-ischemic cardiomyopathy treated with cardiac resynchronization. In a recently published study by (Attachaipanich and Krittayaphong, [26], they studied the value of fQRS in predicting in-hospital life-threatening arrhythmic complications in after STEMI. They have concluded that fQRS was found to be an independent predictor of in-hospital life-threatening arrhythmic events in these patients. In recently published meta-analysis by (Kanitsoraphan et al., [27], they studied the effect of fQRS on all-cause mortality in patients with heart failure and reduced ejection fraction (HFrEF). In their meta-analysis, Kanitsoraphan and his colleagues found that fQRS in baseline electrocardiogram was associated with increased all-cause mortality up to 1.63-fold in this group of patients. They concluded that fQRS could be a valuable predictor of clinical outcome in patients with HFrEF. [27] In our study, we have found that there were more patients diagnosed as NSTEMI among patients with fQRS than among patients without. In a recently published study by (Puelacher et al., [28], assessed the relative incidence and compared the characteristics and outcome of unstable angina (UA) and NSTEMI. Despite their similar clinical presentations and treatment strategies, Puelacher and his colleagues have found that all-cause mortality was significantly higher in patients with NSTEMI compared with UA patients despite of similar incidence of future non-fatal myocardial infarction was comparable between the two groups. [17] So, it seems that early detection of NSTEMI among patients with acute coronary syndrome might be useful. The standard method of differentiation between NSTEMI and UA is measuring of cardiac biomarkers and the most important and widely used in practice is the high-sensitivity cardiac troponin (hscTn)[7, 8] However, there is a lag time hscTn between the beginnings of symptoms of NSTEMI to the rise of hscTn to a level that could diagnose NSTEMI. This time lag differs according to the method of assay used and the cut-off value but it generally ranges from one hour [8] to three or four hours [7]. Another problem in using hscTn is the different cut-off values used in different assays. Also some clinical and demographic criteria of patients may have an effect on the cut-off values to be used. In a study that was conducted by (Riedlinger et al., [9] they evaluated the impact of age on the diagnostic performance of high-sensitivity troponin T (hsTnT) under routine conditions. They found that there were significant differences in hsTnT levels between age-groups in all patients. They also found that more than 70% of patients aged 75 years or more without NSTEMI had hsTnT concentrations above the 99th percentile of a healthy reference population. They concluded that patients' age might be useful to be considered at least as an influencing factor on hsTnT concentrations at admission and should be included in the clinical interpretation of hsTnT concentrations. They

recommended that implementation of age-specific cut-off values could be considered at least for single troponin testing at admission. Further problem about the use of hsTn is its availability. This problem seems to be more evident in developing countries with limited health resources like Egypt. So, it might be useful to use another method to detect patients with high mortality and morbidity risk, patients with NSTEMI among patients with acute coronary syndrome. Our results suggest that fQRS which is a easy, cheap and widely available method, seems to be useful in diagnosing NSTEMI as well as in predicting in-hospital complications and outcome among patients with acute coronary syndrome.

5. Conclusion

Among patients with acute coronary syndrome, the presence of fQRS was associated with an increase incidence of complication, worse outcome, larger LV dimensions, and lower LVEF. The presence of fQRS in acute coronary syndrome patients could predict the presence of NSTEMI with fair diagnostic value. FQRS diagnosis of NSTEMI and increase heart rate, are the only independent predictors for bad outcome among in acute coronary syndrome patients.

Study Limitations

In addition to relatively small number of patients and being a single center study, the main limitation of our study is that we diagnosed fQRS in the surface 12-lead ECG visually. Also absence of long term follow up.

Abbreviations

NSTEMI	Non ST elevation myocardial infarction
STEMI	ST elevation myocardial infarction
UA	unstable angina
fQRS	Fragmented QRS complexes
hscTn	high-sensitivity cardiac troponin
CAD	coronary artery disease
MACE	major adverse cardiac events
CKMB	creatine kinase myocardial band
TnI	troponin
PCI	percutaneous coronary interventions
CABG	coronary artery bypass grafting
CBC	complete blood count
Hb	hemoglobin level
WBCs	total leukocytic count
RDW	red blood cell distribution width
TTE	Transthoracic echocardiography
EF	ejection fraction
LVESD	left ventricle end systolic diamention
LVEDD	left ventricle end diastolic diamention
SBP	systolic blood pressure
DBP	diastolic blood pressure
HR	heart rate
HTN	hypertension

Declarations

Ethics approval and consent to participate: Informed written consent was obtained to be eligible for enrollment into the study. The study was done according to the rules of the Local Ethics Committee of Faculty of Medicine, Zagazig University, Egypt.

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