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Relation between fragmented QRS complex and severity of coronary artery disease evaluated by SYNTAX score

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***Abstract*---**Background: CAD is a CVD that is the main reason for mortality worldwide. CAD is an inflammatory atherosclerotic disorder characterised by stable or unstable angina, sudden cardiac death or MI. Objective: Measuring the relationship between fQRS complex and CAD severity in CA cases. Patients and Methods: This research was conducted on 120 cases that performed coronary catheterization and with developed CAD. All cases underwent clinical examination, and 12-lead ECG. CA was performed using Philips machine under local anesthesia using seldinger technique. Results: Our findings revealed highly significant correlation between prevalence of fQRS and SYNTAX score. There was statistically significant increased Syntax score in patients Inf. Notched R when compared Syntax score of patients without spikes in Inf. Notched R, statistically significant increased Syntax score in cases with non-Inf. Notched R when compared Syntax score of patients without non-Inf. Notched R statistically significant increased Syntax score in patients with Inf. Notched S compared with patients without Inf. Notched S. There was highly significant difference between prevalence of fQRS on admission and after PCI. Conclusion: fQRS complex is a simply assessed, noninvasive ECG

parameter that predict the occurrence of significant CAD and validation of fQRS as Surveillance tool for CAD.

***Keywords*---**CAD, cardiovascular disease, SYNTAX score.

Introduction

Coronary artery disease (CAD) is a cardiovascular disorder (CVD) that is the primary reason for mortality in industrial and developing nations. CAD is an inflammatory atherosclerotic disorder characterised by stable and unstable angina, sudden cardiac death, and myocardial infarction (MI) [(1)]. Fragmented QRS (fQRS) complexes are new electrocardiographic signals that indicate diminished ventricular depolarization because of heterogeneous electrical activation of ischemic and/or damaged ventricular myocardium. fQRS is an effective diagnostic of myocardial scar based on a 12-lead electrocardiogram (ECG) recording; it is characterised by extra spikes inside the QRS complex. fQRS on a 12-lead resting ECG involve an additional R wave (), the formation of the R wave, the downstroke or upstroke of the S wave, or the presence of >1 in 2 contiguous leads corresponding to a significant coronary artery territory [(2)].

In theory, fQRS is typically the result of local myocardial fibrosis/scarring and ischemia, both of that result in heterogeneous myocardial electrical activation. In circumstances of ischemia or non-ischemic left ventricular (LV) dysfunction, fQRS is associated with myocardial fibrosis [(3)]. The SYNTAX score was developed as an anatomic method to assist cardiac surgeons in determining the difficulty of CAD. The SYNTAX score assisted the choice between percutaneous coronary intervention (PCI) and coronary artery bypass grafting as the preferred revascularization technique (CABG) [(4)]. A correlation among the SYNTAX score and non-invasive factors enables the benefits of the SYNTAX score to be obtained with no angiography. Preceding research demonstrated the correlation among non-invasive indicators as laboratory parameters and SYNTAX score, however ECG components and SYNTAX score were examined less frequently [(4)].

Aim of the work

To measure the relation between fQRS complex and severity of CAD in cases undergoing Coronary angiography (CA).

Patients and methods

The research was conducted on Cath lab Unit of cardiology department, Assiut Faculty of Medicine, Al-Azhar University.
Study design: A Cross sectional research

Patients

One hundred and twenty Egyptian cases that performed coronary catheterization and had proven CAD were involved in the research. This research took place in the period from June 2021 to December 2021.

Sample size calculation: It was determined by utilizing the subsequent formula: N = (Z / Δ) ² X P (100 – P). Z: a percentage of slandered regular distribution defined by 95% confidence level = 1.96. Δ: the width of the confidence interval = 12. P: the prevalence of disease = 46.4% according to previous studies. N = (1.96/12) ² X 46.4 (100 – 46.4). The result was 66 patients, we raised the samle to 120 case to get more informative results.
Inclusion criteria: Patients proved as having CAD.
Exclusion criteria: cases had AF, end-stage renal and liver disease, hemodynamically unstable cases, implanted implantable cardioverter-defibrillator (ICD), myocarditis, cardiomyopathies, ventricular paced rhythm and Wolff-Parkinson-White syndrome.

Methodology

All cases were subjected to the following

Consent form: Approving research: - The research was approved by Committee of Internal Medicine Department and Committee of Faculty of Medicine and then by the ethical committee at Al-Azhar University. Patient Consent: - Each participant in the recent investigation was informed of the nature and specifics of the research then provided written consent.
History and Clinical Examination: Complete history taking, which include age, sex, smoking, alcohol intake, history of other comorbid conditions such as hypertension, diabetes mellitus, Cerebrovascular stroke, medications, cardiac history, peripheral artery disease and family history. Full Clinical Examination: Full Clinical Examination include assessment of general condition, vital signs. Abdominal, chest and heart examination were assessed with focus on manifestations of cardiac disease. Blood pressure ≥140/90 mmHg defined as hypertension [5]. According to American Diabetes Association (ADA) recommendations, Diabetes was classified as fasting blood glucose 126 mg/dl and/or glycosylated haemoglobin >6.5% or using hypoglycemic medications or by self-reported history of diabetes.
Twelve-lead electrocardiogram (ECG): FUKUDA's standard 12-lead ECG will record at 25/mm/s paper speed and 10 mm/mV gain. Additional or crochetage wave, noting down the nadir of the S wave, or fragmentation of the RS or QS complexes characterised the fQRS pattern. [6].
Resting echocardiography: Transthoracic echocardiography was accomplished in all cases with a Medison transducer (model-Sonoace X6; Medison Co. Ltd), power 100–120/200–240 V, 0.8/5 A, 50/60 Hz, with 2.5–5 phased array. All echocardiographic measurements done following 20–30 minutes of rest with the case in the position of left lateral decubitus and calm respiration, utilizing a 2–4 MHz transducer and supported by recording resting electrocardiography for assessment of left ventricular functions and possible resting wall motion abnormalities, and exclude myopathy and myocarditis [7].
Coronary angiography: CA was performed using Philips machine (USA) under local anesthesia using seldinger technique. The procedure is sterile, and all potential access sites must be disinfected [8] and prepared according to A percutaneous transfemoral technic of Judkins [9].
Premedication: Sedation, anti-allergic, antiemetic

Contrast media: Xenetix 300mg/ml (Iobitridol). Maximum amount = 5(body weight)/Sr. Creatinine.
Catheters: Judkins (J) & William (W) JL 3.5 & JL 4, JR 3.5 & JR 4
Approaches: Percutaneous techniques usually from femoral artery was used.
Projections: Selective left and right coronary angiograms done in multiple angulated views: AP (anteroposterior) cranial & caudal. LAO (Left Anterior Oblique) cranial & caudal. RAO cranial & caudal. Lateral view.
The SYNTAX score is a rating method designed to assess the seriousness of CAD by CA, based on coronary anatomic risk factors. These factors are small vessel/diffuse disease, the number of lesions, bifurcation, trifurcation, tortuosity, calcification, total occlusion, thrombus, diffuse lesion and ostial stenosis, [10].

Data Analysis

Version 24 of SPSS was utilized to analyse the data. The numerical data were expressed as mean± standard deviation (for data with a normal distribution) and median (interquartile range) (for data with an irregular distribution). The qualitative information was expressed as a frequency and a percentage. A small standard deviation (SD) indicates that the values tend to cluster around the set's mean, whereas a big SD indicates that the values are distributed over a wider range. The median is the value separating the upper and lower halves of the data set. The primary benefit of median over mean is that the median is less affected by a tiny fraction of extremely big or small values.

Following tests were conducted: When comparing two means, a t-test for significance based on independent samples was used (for data with a normal distribution). The Mann–Whitney U test was employed to evaluate two means (abnormally dispersed information). When comparing multiple means, the Kruskal-Willis test is used (for abnormally distributed data). The Chi-square test was utilised to compare non-parametric data. P-values 0.05 were regarded as significant P-values 0.001 were deemed very significant P-values greater than 0.05 were deemed insignificant.

Results

Table (1): Description of demographic data in all studied cases

		Studied cases (N = 120)	
Age (years)	Mean ±SD	55.6 ± 7.8	
	Min - Max	38 – 71	
Sex	Male	72	60%
	Female	48	40%
BMI (kg/m²)	Mean ±SD	27.8 ± 3.3	
	Min - Max	20 – 33.6	
Smoking	Non-smoker	60	50%
	Smoker	60	50%

Table (2): Description of comorbid diseases in all studied patients

		Studied patients (N = 120)	
DM	No	36	30%
	Yes	84	70%
HTN	No	60	50%
	Yes	60	50%

Table (3): Description of f-QRS in ECG before PCI in all studied patients

		Studied patients (N = 120)	
Inf. Notched R	No	54	45%
	Yes	66	55%
Non Inf. Notched R	No	48	40%
	Yes	72	60%
Inf. Notched S	No	58	48.3%
	Yes	62	51.7%
Non Inf. Notched S	No	92	76.7%
	Yes	28	23.3%

Table (4): Comparisons of f-QRS before and after PCI

	Before PCI (n = 120)		After PCI (n = 120)		P-value
Inf. Notched R	66	55%	38	31.7%	0.009 S
Non Inf. Notched R	72	60%	32	26.7%	0.0002 HS
Inf. Notched S	62	51.7%	26	21.7%	0.0006 HS
Non Inf. Notched S	28	23.3%	10	83.3%	0.024 S

Table (5): Description of Syntax Score in all studied cases

		Studied cases (N = 120)
Syntax score	Mean ±SD	19.3 ± 14.9
	Min - Max	1 – 55

Table (6): Correlation between Syntax score and demographic data

(n = 120)		N		Syntax score	Test	P-value
Sex	Male	72	60%	18.6 ± 13.7	T = 0.44	0.659 NS
	Female	48	40%	20.4 ± 16.9		
Marital status	Married	78	65%	20.2 ± 15.6	KW = 0.4	0.818 NS
	Not married	38	31.7%	17.1 ± 13.6		
	Divorced	4	3.3%	22.5 ± 21.9		
Socioeconomic status	Low	48	40%	20.3 ± 18.4	T = 0.41	0.678 NS
	Moderate	72	60%	18.7 ± 12.4		

Smoking	Non-smoker	60	50%	20.5 ± 15.5	T = 0.59	0.557 NS
	Smoker	60	50%	18.2 ± 14.6		
Residence	Rural	70	58.3%	21.02 ± 15.7	T = 1.04	0.299 NS
	Urban	50	41.7%	16.9 ± 13.9		

Table (7): Correlation between Syntax score and comorbid diseases

(n = 120)		N		Syntax score	Test	P-value
DM	No	36	30%	14.7 ± 14.2	MW = 277	0.103 NS
	Yes	84	70%	21.3 ± 15.1		
HTN	No	60	50%	19.8 ± 15.6	MW = 438	0.859 NS
	Yes	60	50%	18.8 ± 14.6		

Table (8): Correlation between Syntax score and ECG

(n = 120)		N		Syntax score	Test	P-value
Inf. Notched R	No	54	45%	16.5 ± 15.1	MW = 288.5	0.033 S
	Yes	66	55%	22.7 ± 14.4		
Non Inf. Notched R	No	48	40%	13.8 ± 14.6	MW = 256.5	0.008 S
	Yes	72	60%	22.9 ± 14.3		
Inf. Notched S	No	58	48.3%	17.4 ± 16.4	MW = 295.5	0.041 S
	Yes	62	51.7%	21.04 ± 13.5		
Non Inf. Notched S	No	92	76.7%	17.9 ± 15.5	MW = 223.5	0.085 NS
	Yes	28	23.3%	23.9 ± 12.3		

Discussion

CAD is a CVD that is the main reason for mortality in both industrialized and developing nations. CAD is an inflammatory atherosclerotic disorder characterised by stable and unstable angina, MI, and sudden cardiac death [(1)]. FQRS complexes are unique electrocardiographic signals that suggest ventricular depolarization impairment because of heterogeneous electrical activation of ischemia and/or injured ventricular myocardium. According to 12-lead ECG recordings, fQRS is a reliable indicator of myocardial scar. fQRS is described as the addition of spikes to the QRS complex. fQRS complexes contain an extra R wave (R0), getting of the R wave and the downstroke or upstroke of the S wave, or the presence of >1 R0 in 2 adjacent leads corresponding to a substantial coronary artery region. [(2)].

Theoretically, it is generally accepted that fQRS is caused by local myocardial fibrosis/scar and ischemia, both of that resulting in heterogeneous myocardial electrical activation. fQRS has been associated to myocardial fibrosis in cases with ischemia or non-ischemic dysfunction of the left ventricle (LV). [(3)]. The SYNTAX score was developed as an anatomic method to assist cardiologists and cardiac surgeons in determining the difficulty of CAD. The SYNTAX score aided in deciding between PCI and CABG as the most appropriate method for revascularization [(4)].

A correlation among the SYNTAX score and non-invasive factors enables the benefits of the SYNTAX score to be obtained without angiography. Earlier research demonstrated the correlation between non-invasive indicators as laboratory parameter and SYNTAX score, however ECG components and SYNTAX score were examined less frequently [4]. The purpose of our research was to assess the relationship between fQRS complex and severity of CAD in cases undergoing CA. The average age of all studied cases was 55.6 ± 7.8 years, there were 72 males (60%) and 48 females (40%), the mean BMI in all studied patients was 27.8 ± 3.3 kg/m², 60 patients (50%) were smokers. 84 patients (70%) were diabetic, and 60 patients (50%) were hypertensive. The mean score in all studied patients was 19.3 ± 14.9.

Our findings demonstrated highly significant correlation between prevalence of fQRS and SYNTAX score. There was statistically significant (p-value = 0.033) increased Syntax score in patients with Inf. Notched R (22.7 ± 14.4) when compared Syntax score of patients without spikes in Inf. Notched R (16.5 ± 15.1), significant (p-value = 0.008), increased Syntax score in cases with Non-Inf. Notched R (22.9 ± 14.3) when compared Syntax score of patients without non-Inf. Notched R (13.8 ± 14.6) and Statistically significant (p-value = 0.041) increased Syntax score in patients with Inf. Notched S (21.04 ± 16.4) when compared with Syntax score of patients without Inf. Notched S (17.4 ± 16.4).

Results obtained in this study agreed with Al-Daydamony and Mustafa who conducted a study including 56 cases with signs indicating CAD and complete LBBB performed CA. Considerably more cases with obstructive CAD were associated with fQRS (p=0.000053). Cases with fwQRS had a significantly higher Gensini score than cases had no fwQRS (p<0.00001). The only significant independent predictor of obstructive CAD was f-wQRS. sensitivity wQRS's in predicting obstructive CAD was 80.1%, specificity was 73.3%, positive predictive value was 72.4%, negative predictive value was 81.54%, and overall accuracy was 76.8%, p= 0.0022. [11].

Das and his colleagues have evaluated the efficacy of several forms of f-wQRS to echocardiography and left ventriculography in diagnosing myocardial scar. They discovered that the sensitivity of fQRS in forecasting myocardial scar was 88.6 %, the specificity was 94.4 %, the positive predictive value was 95.9 %, and the negative predictive value was 85 %. The sensitivity of fQRS in detecting myocardial scar was 88.6%, specificity was 90.2%, positive predictive value was 95.1%, and negative predictive value was 78.7% [12].

Mahfouz et al. ECGs obtained from 172 subjects had chest pain and a moderate likelihood of CAD. CCTA was utilised to detect the existence and evaluate CAD. In this research, 74% (43%) of the studied population had CCTA-documented CAD. Cases with fQRS were significantly more likely to have CAD than cases without fQRS (p 0.001). In cases with CCTA evidence of CAD, the incidence of fQRS was greater than in those with no CCTA evidence of CAD. fQRS was a substantial independent indicator of CAD, as established by multivariate analysis. Patients with fQRS were shown to have greater levels of hs-CRP and LDL-cholesterol, despite similar cardiovascular risk factors in both groups. These results recommend that systemic inflammatory variations, in conjunction with high LDL-

cholesterol, have a substantial effect on the development of ischemic changes that initiate fibrosis, scarring, and consequently ventricular electrical aberration conduction abnormalities, resulting in fQRS [13].

In concordance with the current study, Abdelrahman et al. two-hundred and twenty patients with ACS were enrolled. 12-leads ECG showed fQRS in 74 cases and 146 cases with no fQRS. Group A showed more serious lesions than Group B. In-hospital the rate of MACE was considerably greater in group A based on ACS-related comorbidities. They found that the existence of fQRS on the surface ECG through ACS indicates myocardial scarring or fibrosis and indicates the seriousness of coronary lesions [2].

The findings of Take and Morita in 2012, support this result, the researchers discovered that fQRS in ACS occurred within 48 h (particularly within 24 h) of the beginning of symptoms and remained afterward. fQRS detected on 12-lead ECG in 55% of instances with STEMI and 50% of cases with NSTEMI, but in only 3.7% of cases with unstable angina pectoris. Even though the sensitivity of the fQRS for STEMI and NS-TEMI were 55% and 50%, respectively, the specificity of the fQRS for AMI was 96% [14].

In concordance with the current study, Abdel Rahman et al., conducted prospective research involved 104 cases with NSTE ACS that performed invasive CA for recognition of CAD. ECG was performed on every patient, which revealed f-QRS in 50 individuals and inverted T wave or depressed ST in 54 cases. Cases had multi-vessel disorder, severe coronary artery stenosis, a positive Troponin I level, and a high Syntax score were found to have a higher frequency of f-QRS. Patients with triple vascular disease were more likely to have f-QRS than those had 1 or 2 vessel CAD. Significantly more instances with severe coronary artery stenosis exhibited f-QRS than those with mild or moderate lesions. f-QRS was more prevalent in instances with a high Syntax score compared to those with a low or moderate score. [2].

In consistent with this the findings, Guo et al., investigated the importance of fQRS complexes in detecting culprit lesions in cases with NSTMI [15]. This was agreed with the outcomes of the Bekler et al. study, that examined the correlation among fQRS complexes, SYNTAX and Gensini scores in cases with ACS. They assessed 302 cases (223 males and 79 females) had ACS (133 STEMI, 107 NSTEMI, and 62 USAP). An fQRS was observed in 70 cases (fQRS group) but not present in 232 cases (non-fQRS group). They found that the fQRS group had significantly elevated SYNTAX score (p 0.001), Gensini score (p 0.001), NYHA class (p 0.001), QRS duration (p 0.001), number of disease vessels (p = 0.003), and extremely sensitive troponin T levels (p = 0.026). In multivariate analysis, the number of fQRS leads was an independent predictor of a high SYNTAX score and a high Gensini score (HR 5.79, 95% CI 2.78–12.06, p 0.001, HR 3.41, 95% CI 1.32–8.40, p = 0.016, respectively). [3].

ElDosouky and Abomandour assessed the presence of fQRS in 74 cases with ACS who were separated into two groups: Group I consist of (52) cases had fQRS, and Group II consist of (22) cases without fQRS. They found that the existence of fQRS for the diagnosis of CAD was more sensitive, more specific, had a larger positive

predictive value, and was more accurate than the presence of pathogenic Q waves and ischemic ST-segment depression [16]. In line with these observations, Eyuboglu et al. included 336 consecutive cases performing CA for possible CAD. The cases were classified into two groups based on the existence or lack of fQRS on admission. 79 (23.5%) cases with fQRS on entrance. There was a significantly different among cases had fQRS and non-fQRS as regard the existence of stenotic CAD (40.5% vs. 10.5%, p<0.001) and multi vessel disease (25,3% vs. 5.1%, p<0.001). Significantly more cases had SYNTAX score >22 experienced fQRS than those had SYNTAX score 22 ≤22 [17].

In the same line with our findings Khalil et al., 215 studied cases with initial STEMI enrolled for primary PCI. based on the admission ECG, they were divided into three groups: group I had QRS distortion or fQRS, group II had both QRS distortion and fQRS, and group III had neither QRS distortion nor fQRS. Using the SYNTAX risk score, the severity of coronary artery lesions was analysed. According to regression analysis, fQRS was an independent predictor of both CAD severity and in-hospital mortality. Diabetes was a marker independently of CAD severity (OR: 2.851, P = 0.012), whereas hospital mortality was predicted by a high SYNTAX score (OR: 6.113, P 0.001). The FQRS has a good predictive value for in-hospital adverse events and CAD severity as determined by the SYNTAX score in patients of STEMI. [18].

This was in accordance with the findings, Tanriverdi et al., discovered that QRS distortion and fQRS were independently related with a bad prognosis, while the combined usage of fQRS was associated with an even worse prognosis and for rapid risk evaluation of ACS cases (STEMI) treated with primary PCI, its distortion gives greater predictive value than the existence of fQRS or QRS distortion alone [19].

Ghoneim et al. conducted a study on 150 patients who had acute STEMI and treated with thrombolytic and/or primary PCI. The average age of the cases involved in this research was 57.6 ± 11.2 years, with 68% of them male. 10% of cases performed primary PCI, whereas 90% of cases had thrombolytic therapy and secondary PCI. Before reperfusion, fQRS was found in 99 (66%) cases, QRS distortion was found in 120 (80%) cases. While following reperfusion, fQRS was found in 42 (28%) of cases, QRS distortion was found in 24 (16%) cases. Both FQRS and QRS distortion were found in 84 cases (56%). There was highly significant difference among cases with fQRS on admission and those without regarding SYNTAX score, reperfusion result and EF (p value <0.001) [20].

Conclusion

fQRS complex is an simply assessed, noninvasive ECG measures that predict the presence of significant CAD. Validation of fQRS as Surveillance tool for CAD in cases with risk factors.

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