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Fragmented QRS and Exercise Tolerance in Patients with Heart Failure with Preserved Ejection Fraction

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ABSTRACT

Background: Fragment QRS (fQRS) complex is a myocardial conduction abnormality that indicates myocardial scar. The significance of fQRS lies in the fact that it just requires a surface ECG for its recording and the value of information about the condition of the heart it dispenses based on the clinical setting.

Objective: Our study aimed to investigate the relationship between FQRS exercise tolerant patients with heart failure with preserved ejection fraction.

Patients and methods: The study was an observational cross-sectional study. It was conducted at the Cardiology Department, Zagazig University Hospitals. The studied sample consisted of 95 patients with diastolic dysfunction. All patients were stratified into two groups according to the presence or absence of fragmented QRS complex in resting surface ECG. Electrocardiogram, conventional echocardiographic examination, tissue doppler imaging, and 6 minutes walk test were done.

Results: There was a statistically significant difference between 6 minutes walk test of heart failure with preserved ejection fraction patients with and without FQRS. In addition, we found that 6 minutes walk test is considered a good parameter to discriminate congestive heart failure patients with and without FQRS with a sensitivity of 81.5%, specificity of 69.6%, and accuracy of 72.9%.

Conclusion: The value of FQRS in cardiology is much higher than what is being understood currently. FQRS is considered to be an indicator of myocardial fibrosis or scar tissue and has already been observed to be closely associated with a greater probability of adverse cardiac consequences and reduced tolerance of exercise in patients with HFpEF.

Keywords: Fragmented QRS, Exercise Tolerance, Heart failure, Preserved Ejection Fraction.

INTRODUCTION

It was shown in some studies that a subtle abnormality within the QRS complex can represent conduction disturbance and myocardial scar. A notch in the QRS complex in patients with left ventricular hypertrophy has been suggested to be a result of an intraventricular conduction defect [(1)].

However, the diagnostic and prognostic values of these subtle abnormalities within the QRS complex were not clarified in prior studies. Fragmented QRS complex in patients with coronary artery disease (CAD) was associated with myocardial conduction block due to myocardial scar detected by myocardial single-photon emission tomography (SPECT) [(2)].

It is defined as additional notches in the QRS complex. Though initially fQRS was defined in the setting of normal QRS duration (<120 ms), later it has been expanded to include conditions with wide QRS complexes as in bundle branch block, ventricular ectopy, and paced rhythm, when more than 2 notches are present. It is an important, yet often overlooked marker of mortality and arrhythmic events in many cardiac diseases[(3)].

Our study aimed to investigate the relationship FQRS exercise tolerant patients with heart failure with a preserved ejection fraction.

PATIENTS AND METHODS

The observational cross-sectional study was conducted at the Cardiology Department, Zagazig University Hospitals, on 95 patients with diastolic dysfunction during the period from December 2019 to July 2020.

Ethical consent:

Written informed consent was obtained from all children's parents or their relatives and the study was approved by the research ethics committee of the Faculty of Medicine, Zagazig University. The work has been carried out following The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Inclusion criteria:

Patients with HFpEF and the inclusion criteria were based on the following: Typical symptoms of heart failure; representative signs of heart failure. The LVEF ≥50% (by echocardiography), and Evidence of diastolic dysfunction on echocardiography (mitral inflow E/A ratio, e′ measured at the mitral annulus, and E/e′ ratio).

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Exclusion criteria:

Subjects with impaired cognition, atrial fibrillation, chronic obstructive pulmonary disease (COPD), asthma, severe hepatic disease, severe renal impairment, hyperthyroidism, arthritis, ankle, knee or hip injuries, and muscle wasting. Patients with recent myocardial infarction, unstable angina, patients with pacemaker implantation, patients with enlarged LV dimension, patients with the candidacy for revascularization, left atrial enlargement, valvular heart disease.

All patients were subjected to the following:

Complete history taking, Complete general examination, 12 lead ECG, Echocardiography, Six-minute walk test.

Electrocardiogram: Standard 12-lead surface resting ECGs (filter range, 0.5–150 Hz, 25 mm/s, 10 mm/mV) were recorded for all the patients.

Conventional echocardiographic examination:

All transthoracic echocardiographic studies were been underwent using the GE Vivid 9 Vingmed System (Norway, Horten), which is equipped with 2.5–4 MHz transducers.

Tissue Doppler imaging: Doppler tissue echocardiography will be performed using transducer frequencies between 3.5 and 4.0 MHz.

Six-minute walking test: All 96 patients were stratified into two groups according to the presence or absence of fragmented QRS complex in resting surface electrocardiogram (ECG): group one, which included those with fQRS **(FQRS+)** and group two included those without fQRS **(FQRS-)**

Statistical analysis

Analysis of data was done using Statistical Program for Social Science version 20 (SPSS Inc., Chicago, IL, USA). Quantitative variables were described in the form of mean and standard deviation. Qualitative variables were described as number and percent. To compare parametric quantitative variables between two groups, the Student t-test was performed. Qualitative variables were compared using the Chi-square (X2) test or Fisher's exact test when frequencies were below five. Pearson correlation coefficients were used to assess the association between two normally distributed variables. When a variable was not normally distributed, A P-value < 0.05 is considered significant.

RESULTS

Table1: heart failure patients were 72 males (75.0%) and 24 females (25.0%), the mean age of all patients was 61.2±4.6 years and ranged from (51—70). Out of them, 57 patients were non-smokers (59.4%), while the other 39 patients were smokers (40.6%).

Table (1): Demographic characteristics of heart failure with preserved ejection fraction patients (n=96):

Variables		
Age per years Mean ±SD Range	61.2±4.6 51-70	
Sex	**n.**	**%**
Males Females	72 24	75.0 25.0
Smoking Non-smokers Smokers	57 39	59.4 40.6

Table 2: defined that, the mean PWD (cm) was 1.06±0.2cm ranging from 0 to 1.4cm. Mean IVS was 1.09±0.17cm range from 0.6 to 1.3cm, mean of LVEDD was 44.4±2.9 range from 40 to 52. In addition; mean LVEDS was 40.5±2.2range from 37 to 45, Mean EF was 63.9±7.5range from 50 to 75, E/A ratio mean was 1.2±0.34 range from 0.6 to 1.7, Mean LAD was 3.7±0.32.5mm range from 3.1 to 4.3mm E/e-mean was 14.8±2.6range from 11 to 20.

Table (2): Echo finding of studied heart failure with preserved ejection fraction patients (n=96):

Variables	**Mean ± SD**	**Range**
PWD (cm)	1.06±0.2	.00-1.4
IVS (cm)	1.09±0.17	0.6-1.3
LVEDD	44.4±2.9	40-52
LVEDS	40.5±2.2	37-45
EF	63.9±7.5	50-75
E/A ratio	1.2±0.34	0.6-1.7
LAD	3.7±0.32	3.1-4.3
E/e-	14.8±2.6	11-20
C_LVH(n.%) Present Absent	64(66.7) 32(33.3)	

Table 3: defined that, 28.1% of heart failure with preserved ejection fraction FQRS.

Table (3): Frequency distribution of FQRS among studied heart failure with preserved ejection fraction patients

	N.	**%**
FQRS Absent Present	 69 27	 71.9 28.1

Table 4: there is a statistically significant difference between Echo finding in heart failure with preserved ejection fraction patients and FQRS where p-value =0.029 of LVEDD, EFand E/e- p-value =0.0001, Evident heart failure patients with FQRS had high, E/e-, and lower LVEDD, EF value.

Table (4): Relation between FQRS among studied congestive heart failure patients and their Echo finding.

	FQRS		t	p-value
	No (n.69)	Yes (n.27)		
PWD (cm)	1.04±0.21	1.1±0.17	1.47	0.14
IVS (cm)	1.09±0.18	1.08±0.16	0.28	0.78
LVEDD	44.7±3.2	43.6±1.9	2.2	0.029*
LVEDS	40.4±2.4	40.7±1.7	0.67	0.49
EF	65.7±7.4	59.3±5.3	4.7	0.0001*
E/A ratio	1.22±0.23	1.13±0.36	1.2	0.24
LAD	3.7±0.33	3.76±0.28	0.45	0.65
E/e-	13.6±1.7	17.8±2	10.3	0.0001*

t-test of significant *significant p<0.05

Table 5: ROC curve of 6-minute Waking test to discriminate of congestive heart failure patients with and without FQRS with an (AUC) 0.84. So, the 6-minute Waking test good parameter to discriminate heart failure patients and FQRS with sensitivity=81.5%, specificity 69.6%, and accuracy =72.9%.

Table (5): Validity data of six-minute Waking test to discriminate FQRS among patients (n=96).

	Cut off	FQRS		Sensitivity	Specificity	PPV	NPV	Accuracy	AUC	p-value
		Affected	Unaffected							
Six minute Waking test	<300ms ≥300ms	22 5	21 48	81.5%	69.6%	51.2%	90.6%	72.9%	0.84	0.0001

Table 6: ROC curve of FQRS to discriminate; heart failure patients ability to do the six-minute Walking test, an (AUC) 0.86. So, FQRS good parameter to discriminate heart failure with preserved ejection fraction patients unable to do more than 300ms by the six-minute walking test with sensitivity=91.7%, specificity 80.9%, and accuracy =82.3%.

Table (6): validity data of FQRS to discriminate heart failure' patients ability to do the 6-minute Waking test (n=96).

Parameter	Six-minute walk test		sensitivity	specificity	PPV	NPV	accuracy	AUC	p-value
	Unable	Able							
FQRS Present Absent	 11 1	 16 68	91.7%	80.9%	40.7%	98.6%	82.3%	0.86	0.0001

DISCUSSION

Heart failure (HF) is a clinical syndrome of dyspnea, fatigue, and fluid retention secondary to impaired cardiac function. Cardiac function may be impaired structurally or functionally with resultant decreased ejection or filling capacity both of which can reduce cardiac output and/or increase intracardiac pressures at rest or during exercise. Systolic dysfunction leading to reduced left ventricular ejection fraction (LVEF) (LVEF < 40%) had long been believed to be the predominant cause of heart failure [4, 5].

However, HF remains to be a growing health problem in the community despite recent improvements in the management of HF with reduced ejection fraction (HFrEF). Another subset of heart failure which occurs in the setting of normal or near-normal left ventricular ejection fraction (LVEF > 50%) has been evolving for the last two decades. This distinct HF subtype has been called HF with preserved ejection fraction (HFpEF). Once included in HFpEF, the newly defined HF with midrange EF (HFmrEF) comprises the HF patients with EF between 40 and 50% [5, 6].

Nearly twenty-five years ago, fragmented QRS (FQRS) electrocardiograms were for the first time recorded in bipolar leads from canine hearts 15 days after experimentally induced acute ischemia. In that study, FQRS correlated with widely separated myofibrils with distorted orientation leading to slow and inhomogeneous activation. Recent studies have confirmed the association between FQRS and myocardial scar [7, 8].

In our study, regarding the demographic data of the studied patients, 72 were males (75.0%) and 24 were females (25.0%). The mean age of all patients was 61.2±4.6 years and ranged from (51 to 70). 57 patients were non-smokers (59.4%) while 39 patients were smokers (40.6%).

Sandesara and colleagues[9] did a study that cleared that smoking is an important risk factor in the development of HFpEF and is considered a significant predictor of death in this population. They analyzed the relationship between smoking and heart failure-specific outcomes in patients with HFpEF. Their study included 1,717 (mean age=71±10 years; 50% male; 78% white) patients in the Americas. There were 116 (7%), 871 (51%), and 729 (42%) patients whose smoking status was classified as current, former, or never, respectively.

In addition, we analyzed the Echo findings of the studied heart failure with preserved ejection fraction patients, mean PWD (cm) was 1.06±0.2 with a range from 0 to 1.4. Mean IVS (cm) was 1.09±0.17 with a range from 0.6 to 1.3. The mean of LVEDD was 44.4±2.9 with a range from 40 to 52. In addition, the mean LVEDS was 40.5±2.2 with a range from 37 to 45. Mean EF was 63.9±7.5 with a range from 50 to 75. E/A ratio mean was 1.2±0.34 with a range from 0.6 to 1.7. Mean LAD was 3.7±0.32.5 with a range from 3.1 to 4.3 while E/e-mean was 14.8±2.6 with a range from 11 to 20.

Obokata and colleagues [10] found that subjects with HFpEF displayed higher right and left heart filling pressures with higher pulmonary artery pressures by catheterization in comparison with non-cardiac dyspnea (NCD). Medial and lateral E/e′ data were obtainable in almost all subjects at rest (99% and 95%, respectively). As expected, LV diastolic function was impaired in subjects with HFpEF in comparison with NCD, with higher transmitral E velocity, shorter deceleration time, lower medial and lateral e′ velocities, higher E/e′ ratio, larger left atrial (LA) volume index, and higher TR velocity.

We studied the relation between FQRS among the studied heart failure with preserved ejection fraction patients and their socio-demographic characteristics. Our results showed a statistically significant relation between FQRS among the studied heart failure with preserved ejection fraction patients with age and smoking. Old age patients, who are smokers are more likely to be exposed to FQRS disorder.

In agreement with our results, **Alattar and colleagues** [11] examined the relationship between FQRS and EF. Their results demonstrated that the median age of the FQRS group was 71 years (56.3–81.8) and 51% of them were smokers.

Our study also showed that there was a statistically significant difference between 6 minutes walk test of heart failure with preserved ejection fraction patients with and without FQRS where the p-value equals 0.0001. Evident congestive heart failure patients with FQRS had lower 6 minutes walk test value.

Our results cleared that 6 minutes walk test good parameter to discriminate between congestive heart failure patients with and without FQRS with a sensitivity of 81.5%, specificity of 69.6%, and accuracy of 72.9%. We also found that FQRS is a good parameter to discriminate heart failure with preserved ejection fraction patients who are unable to do 6 minutes walk test with a sensitivity of 91.7%, specificity of 80.9%, and accuracy of 82.3%.

However, sensitivity was reduced with this approach, leading to a lower negative predictive value, and suggesting that a peak effort noninvasive exercise test might be optimal. In contrast, measuring PCWP at 20W alone discriminated HFpEF from NCD with very high sensitivity and perfect specificity. Although some might consider this finding as being sufficient to abandon maximal invasive exercise testing, it is important to consider that other valuable information can be obtained with peak testing, including insight on the roles of cardiac versus peripheral factors in limiting exercise capacity [12, 13, 14] and more detailed understanding of pulmonary vascular physiology [15, 16].

Our results demonstrated that there is a statistically positive correlation between 6 minutes walk test with EF of heart failure with preserved ejection fraction patients. While there is a statistically negative correlation between 6 minutes walk test with age and E/e- of heart failure with preserved ejection fraction patients. There is also a statistically positive correlation between EF with 6 minutes walk test of heart failure patients. While there is a statistically negative correlation between EF with age, LVEDS, and E/e- of congestive heart failure patients. We also found that there is a statistically negative correlation between the E/A ratio with IVS (cm) of heart failure patients.

CONCLUSION

The value of FQRS in cardiology is much higher than what is being understood currently. FQRS is considered to be an indicator of myocardial fibrosis or scar tissue and has already been observed to be closely associated with a greater probability of adverse cardiac consequences and reduced tolerance of exercise in patients with HFpEF.

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