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The role of Fragmented QRS in Patients with Heart Failure with Preserved Ejection Fraction

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ABSTRACT

Fragment FQRS has also been reported in a variety of cardiac conditions such as ischemic and dilated cardiomyopathy, sarcoidosis, myocarditis, arrhythmogenic ventricular dysplasia and Brugada syndrome. FQRS was associated with increased risk of arrhythmic events and was noticed to be associated with lower ejection fraction. The aim of our study was role of Fragmented QRS in 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 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 good parameter to discriminate congestive heart failure patients with and without FQRS with sensitivity 81.5%, specificity 69.6% and accuracy 72.9%.

Conclusion: FQRS was found to be an independent risk factor for increased cardiac events. FQRS is considered to be an indicator of myocardial fibrosis or scar tissue.

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

INTRODUCTION

It has been show 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 m s), 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)].

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The aim of our study was investigate the relationship FQRS exercise tolerant patients with heart failure with preserved ejection fraction

SUBJECTS 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

Written informed consent was obtained from all children' parents or their relatives and the study were approved by the research ethical committee of Faculty of Medicine, Zagazig University (International review board IRB#:5852-l-3-2019). The work has been carried out in accordance with 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:

1. Typical symptoms of heart failure; representative signs of heart failure;
2. The LVEF ≥50% (by echocardiography);
3. Evidence of diastolic dysfunction on echocardiography (mitral inflow E/A ratio, e′ measured at the mitral annulus, and E/e′ ratio).

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 candidacy for revascularization, left atrial enlargement, valvular heart disease.

All patients will be subjected in 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 beeen 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. In order to compare parametric quantitative variables between two groups, Student t test was performed. Qualitative variables were compared using 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.

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RESULTS

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

Table1:Showed that. 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). where 57 patients of them were non smokers (59.4%), 39 patients of them were smokers (40.6%)

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)	

Table2: defined that, mean PWD (cm) was 1.06±0.2cm range 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 (3): frequency distribution of FQRS among studied heart failure with preserved ejection fraction patients

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

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Table3: defined that, 28.1% of heart failure with preserved ejection fraction FQRS

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

	FQRS		t	p
	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 4:showed 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 (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
		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

Tabe5: shows ROC curve of 6 minute Waking test to discriminate of congestive heart failure patients with and without FQRS with an (AUC) 0.84 . So, 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 (6): validity data of FQRS to discriminate heart failure' patients ability to do 6minute Waking test (n=96).

Parameter	Six minute walk test		**sensitivity**	**specificity**	**PPV**	**NPV**	**accuracy**	**AUC**	**p**
	unable	Able							

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FQRS present absent	 11 1	 16 68	 91.7%	 80.9%	 40.7%	 98.6%	 82.3%	 0.86	 0.0001

Table 6; shows ROC curve of FQRS to discriminate ; heart failure patients ability to do 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 six minute walking test with sensitivity=91.7%,specificity 80.9% and accuracy =82.3%.

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)]

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)]

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. [(6)]

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 attending to cardiology department of Zagazig university during the period of the study and their status fulfil the inclusion and exclusion criteria. The aim of our study was investigate the relationship FQRS exercise tolerant patients with heart failure with preserved ejection fraction

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—70). 57 patients were non-smokers (59.4%) while 39 patients were smokers (40.6%).

Sandesara and colleagues[(7)] did a study that cleared that smoking is an important risk factor in the development of HFpEF and is considered as 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 range from 0 to 1.4. Mean IVS (cm) was 1.09±0.17 with range from 0.6 to 1.3. Mean of LVEDD was 44.4±2.9 with range from 40 to 52. In addition, mean LVEDS was 40.5±2.2 with range from 37 to 45. Mean EF was 63.9±7.5 with range from 50 to 75. E/A ratio mean was 1.2±0.34 with range from 0.6 to

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1.7. Mean LAD was 3.7±0.32.5 with range from 3.1 to 4.3 while E/e-mean was 14.8±2.6 with range from 11 to 20.

Obokata and colleagues [8] 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 statistically significant relation between FQRS among the studied heart failure with preserved ejection fraction patients with age and smoking. It is obvious that old age patients, who are smoker are more likely to be exposed to FQRS disorder.

In agreement to our results, **Alattar and colleagues** [9] examined the relationship of 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 statistically significant difference between 6 minutes' walk test of heart failure with preserved ejection fraction patients with and without FQRS where p value equal 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 congestive heart failure patients with and without FQRS with sensitivity 81.5%, specificity 69.6% and accuracy 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 sensitivity 91.7%, specificity 80.9% and accuracy 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 20 W 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 limaiting exercise capacity and more detailed understanding of pulmonary vascular physiology. [10]

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 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 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 E/A ratio with IVS (cm) of heart failure patients.

Conclusion : FQRS was found to be an independent risk factor for increased cardiac events. FQRS is considered to be an indicator of myocardial fibrosis or scar tissue.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request

Conflicting Interest (If present, give more details): No Conflict of Interest

No financial disclosure

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Not applicable

Declarations

-Ethics approval and consent to participate

Written informed consent was obtained from all patients and the study was approved by the research ethical committee of Faculty of Medicine, Zagazig University (International review board IRB#:5852-l-3-2019). The study was done according to The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

-Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

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