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Left Ventricular Diastolic Function in Patients with Heart Failure with Preserved Ejection Fraction

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ABSTRACT

Background: Left ventricular heart failure in sitting of preserved left ventricular ejection fraction constitutes up to 50% of heart failure. It increases with age and is correlated with the presence of systemic hypertension and left ventricular hypertrophy. It has significant morbidity, approaching that of systolic heart failure. Heart failure preserved ejection fraction (HFpEF) is a clinical syndrome resulting from increased resistance in the filling of the left ventricle (LV) leading to symptoms of congestion although the exact cause continues to be unknown and the identification of markers that predict HFpEF risk have not been proven.

Aim of the Work: Assessment of left ventricular diastolic function in patients with heart failure and preserved ejection fraction.

Patients and Methods: This study included 90 patients with ages ranging from 30 to 70 years old referred to Al Hussein University Hospital, Bab Al Shearia University Hospital, Cardiology Outpatient Clinic suffering from low functional capacity, exertional dyspnea and even exertional chest discomfort. Over a period from November 2015 to May 2018. The study population was divided into two groups according to incidence of positive stress ECG. Group A (patient group): Patients with positive stress ECG. Group B (control group): Patients with negative stress ECG.

Results: This study included (90) patients with their ages ranging from 30 to 70 years referred to (Al Hussein University Hospital), (Bab Al Shearia– University Hospital) cardiology outpatient clinic from November 2015 to September 2017, with low functional capacity, exertional dyspnea and even exertional chest discomfort and are evaluated to rule out coronary artery disease (CAD). Those patients were evaluated by stress ECG and Transthoracic Echodoppler and Tissue Doppler imaging. The study population was divided into two groups according incidence of positive stress ECG into: Groups according incidence of positive stress ECG. Group I patients group: Included 60 patients presented by chest pain with dyspnea NYHA class 1 (12 patients), class II (37 patients), or class III (11 patients) with mean age 54.05±7.9 years, this group included 19 females (31.7%) and 41 males (68.3%), Group II control group: Included 30 patients with mean age 52.7±5.11 years. Female number was 13(43%) and males were 17(60%).

Conclusion: The assessment of diastolic function is now essential on routine testing for HF. The noninvasive nature of echocardiography has allowed an increase in diagnosis and awareness of diastolic dysfunction.

Keywords: Left Ventricular Diastolic Function, Heart Failure, Preserved Ejection Fraction

INTRODUCTION

Left ventricular heart failure in sitting of preserved left ventricular ejection fraction constitutes up to 50% of heart failure that increases with age and is correlated with the presence of systemic hypertension and left ventricular hypertrophy. In addition, it has significant morbidity, approaching that of systolic heart failure [(1)].

Heart failure preserved ejection fraction (HFpEF) is a clinical syndrome resulting from increased resistance in the filling of the left ventricle (LV) leading to symptoms of congestion [(2)] although the exact cause continues to be unknown and the identification of markers that predict HFpEF risk have not been proven [(3)].

Data from the National Health and Nutrition Examination Survey (NHANES) suggest an estimated 5.7 million Americans have HF and HFpEF accounting for at least 50 % of all HF hospital admissions and forecasts a 46 % increase in HFpEF prevalence by 2030 [(4)].

However, biomarkers that enable prevention, diagnostic and treatment guidelines and population-specific characteristics are not evident in the literature. The pathophysiologic understanding of HF has changed notably over the last 25 years [(5)].

Terminology has evolved to include HF syndromes with ejection fraction (EF) < 50 % described as diastolic heart failure (DHF), and as the pathophysiological mechanisms of HF became clearer, the terms were changed to HFpEF and heart failure reduced ejection fraction (HFrEF) which are currently used [(6)].

Although the understanding of HFpEF pathophysiology has progressed, definitive research on population specific pathophysiology, consistent use of biomarkers and guidelines for diagnosis and treatment are not yet established [(5)].

Heart failure is a clinical syndrome resulting from impairment of ventricular filling or ejection of blood, consequently limiting cardiac output (CO) to the body at rest or with exertion, or

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requiring increases in cardiac filling pressure to maintain CO [2].

The cardinal symptomatic manifestations of HF are dyspnea, fatigue, and exercise intolerance, regardless of EF. Despite similar symptoms, HFpEF patients differ from HFrEF in that they tend to be somewhat older and more likely to be female, obese, hypertensive, and in atrial fibrillation [7].

AIM OF THE WORK

Assessment of left ventricular diastolic function in patients with heart failure and preserved ejection fraction.

PATIENTS AND METHODS

This study included 90 patients with ages ranging from 30 to 70 years old referred to Al Hussein University Hospital and Bab Al Shearia University Hospital, Cardiology Outpatient Clinic suffering from low functional capacity, exertional dyspnea and even exertional chest discomfort. Over a period from November 2015 to May 2018. **The study was approved by the Ethics Board of Al-Azhar University.**

The study population was divided into two groups according to incidence of positive stress ECG.

- Group A (patient group): Patients with positive stress ECG.

- Group B (control group): Patients with negative stress ECG.

Exclusion criteria: We excluded from the study patients with: 1- Mitral stenosis. 2- Sever mitral regurgitation. 3- Atrial fibrillation. 4- Conduction distubances. 5- Prosthetic mitral valve. 6- Patients with ejection fraction <50%

All patients were subjected to:

1- Complete history taking: Including name, age, sex, special habits, history of drug intake or previous hospital admission with special consideration to history of risk factors of ischemic heart disease, and comorbid condition.

2- Thorough clinical examination: All patients were subjected to thorough clinical general and cardiac examination.

3- Electrocardiographic examination: Standard 12-lead surface ECG was done for every patient with special consideration to ECG signs of myocardial ischemia; ST segment elevation or depression and\or T wave invertion.

4- Transthoracic echocardiographic examination: All patients were examined in the left lateral decubitus position with a commercially available ultrasound transducer and equipment (X5-1 adult probe, A Philips IE 33 phased array system).

5- Transmitral Doppler assessment of LV diastolic function.

6- Tissue Doppler Imaging (TDI)

Statistical Analysis: Data were collected, revised, coded and entered to the Statistical Package for Social Science (IBM SPSS) version 20. Student T test was used to analyze quantitative data while Chi square test was used to analyze qualitative data, which were presented as number and percentages while quantitative parametric data were presented as mean and standard deviations.

RESULTS

Table (1): Comparison between control group and patients group regarding demographic data of the studied patients

		Control group	Patients group	Chi-square test	
		No.= 30	No.= 60	X2	P-value
Sex	Female Male	13 (43.3%) 17 (56.7%)	19 (31.7%) 41 (68.3%)	1.188	0.276
Age	Mean±SD Range	52.70 ± 5.11 43 – 66	54.05 ± 7.90 32 – 70	-0.850*	0.398

*: Independent t-test; P > 0.05: Non significant; P < 0.05: Significant; P < 0.01: Highly significant.

There was no statistically significant difference found between control group and patients group regarding sex and age of the studied patients.

Table (2): Comparison between control group and patients group regarding incidence of risk factors.

Risk Factors		Control group		Patients group		Chi-square test	
		No.	%	No.	%	X^2	P-value
HTN	No Yes	20 10	66.7% 33.3%	31 29	51.7% 48.3%	4.566	0.032
DM	No Yes	23 7	76.7% 23.3%	36 24	60.0% 40.0%	4.807	0.028
Smoking	No Yes	25 5	83.3% 16.7%	45 15	75.0% 25.0%	0.804	0.369
F.H	No Yes	28 2	96.7% 3.3%	49 11	81.7% 18.3%	3.894	0.048
Dyslipidemia	No Yes	19 11	63.3% 36.7%	36 24	60.0% 40.0%	0.094	0.759

There was no statistically significant difference found between control group and patients group regarding smoking and dyslipidemia of the studied patients while there was statistically significant difference found regarding HTN, DM, F.H.

Table (3): Comparison between control group and patients group regarding site of ischemia by ECG.

Site of Ischemia by ECG	Control group		Patient group		Chi-square test	
	No.	%	No.	%	X2	P-value
Anterior	3	10.0%	18	30.0%	4.472	0.034
Anterior, inferior	0	0.0%	3	5.0%	1.552	0.212
Anterolateral	0	0.0%	1	1.7%	0.506	0.476
Anteroseptal	0	0.0%	2	3.3%	1.023	0.311
Inferior	3	10.0%	6	10.0%	0.000	1.000
INFEROLATERAL	0	0.0%	1	1.7%	0.506	0.476
Interior	1	3.3%	1	1.7%	0.256	0.612
Interofaeral	0	0.0%	2	3.3%	1.023	0.311
Lateral	4	13.3%	3	5.0%	1.936	0.164
No	0	0.0%	13	21.7%	7.597	0.006
Normal	19	63.3%	10	16.7%	19.943	0.000

There was no statistically significant difference found between control group and patients group regarding Anterior, inferior, Anterolateral, Anteroseptal, Inferior, INFEROLATERAL, Interior, Interofaeral, Lateral of the studied patients while there was statistically significant difference found between control group and patients group regarding Anterior, No, Normal.

Table (4): Comparison between control group and patients group regarding pulmonary venous flow.

Pulmonary Venous Flow		Control group	Patients group	Independent t-test	
		No.= 30	No.= 60	t	P-value
Sv	Mean±SD Range	29.67 ± 7.80 17 – 42	34.43 ± 13.32 15 – 76	1.805	0.075
Dv	Mean±SD Range	37.63 ± 6.43 24 – 49	43.73 ± 16.45 11 – 80	1.952	0.054
Av	Mean±SD Range	27.63 ± 5.30 18 – 36	31.13 ± 9.51 11 – 66	1.869	0.065
Aa	Mean±SD Range	61.67 ± 24.37 20 – 100	65.07 ± 19.98 20 – 100	-0.706	0.482
Ad	Mean±SD Range	73.13 ± 21.33 39 – 110	79.40 ± 22.93 25 – 130	-1.250	0.214
Adur	Mean±SD Range	126.67 ± 16.88 100 – 150	123.83 ± 30.52 40 – 230	0.473	0.638

There was no statistically significant difference found between control group and patients group regarding Aa, Ad, Adur of the studied patients while there was statistically significant difference found between control group and patients group regarding Sv, Dv, Av.

DISCUSSION

In our study, our goal was evaluation of left ventricular diastolic function in patients with heart failure and preserved left ventricular ejection fraction. We selected 90 patients, careful history was taken, clinical examination was done and risk factors were identified.

In all patients, full echocardiography examination was done, left atrial diameter and volume were calculated, transmitral flow Doppler & pulmonary view flow Dopplar were done and tissue Doppler on mitral annulus was done.

We found that left atrial diameter (LAD) and left atrial volume (LAV) were the most important and powerful indicators of diastolic dysfunction with superiority to left atrial diameter (LAD).

Left atrial (LA) enlargement has been proposed as a parameter of diastolic burden and a predictor of common cardiovascular outcomes, such as atrial fibrillation, stroke, congestive HF, and cardiovascular death [8]. Therefore, assessment of LA size may be useful to judge mitral flow velocity parameters. In addition, the LA may become less spherical as it remodels. LA volume is proposed as a better index of LA remodeling. LA volume displays a somewhat stronger association with the presence of CV disease in the general population [9].

Tsang et al. [10] reported that, left atrial volume is an indicator to diastolic dysfunction while the ejection fraction is indicator to systolic dysfunction. They found that indexed LA volume (mL/m^2) was strongly associated with the grade of diastolic dysfunction. They reported that LA volume was more predictive of future atrial fibrillation and other CV events than LA dimension in variable clinical populations. It was different from our results, which showed that LAD was more important.

In agreement with our results, ***Yoshida et al.*** [11] determined LAV and LAD indices in addition to the ratio of peak early diastolic mitral flow velocity (E) to E' (E/E' ratio) in 91 patients with all three of the followings: HF, LVEF of greater than 55%, and normal mitral E/A ratio between 0.8 and 1.5. They concluded that LAV and LAD indices were more useful in detecting HF and normal EF patients than E' related parameters.

Gottdiener et al. [12] showed that the left atrium might enlarge more in the anteroposterior direction than in the superoinferior direction in the condition of HF. This observation may at least partially support afore mentioned idea that the LAD might be more affected by some clinical and echocardiographic measurements than the LAV index.

Doppler echocardiographic assessment of transmitral flow provided a noninvasive means of identifying patients with elevated left atrial pressures.

Nishimura and Tajik [13] reported that mild diastolic dysfunction was characterized by impaired relaxation of the LV without elevation of LV filling pressures. This means that the ventricle took a longer time to fill (lengthening the DT), with an increased reliance on the atrial component of diastolic filling (reducing the E/A ratio). Worsening diastolic function is associated with rising left atrial pressures. This results in a higher early diastolic gradient across the mitral valve, with rapid equalization of the pressures in the left atrium and ventricle. Initially, this normalizes the DT and mitral E/A ratio (pseudonormalization), but ultimately the mitral E wave becomes markedly predominant and the DT becomes much abbreviated [14].

Kasner et al. [15] concluded that of all echocardiographic parameters investigated, the LV filling index E/E' was identified as the best index to detect diastolic dysfunction in HFNEF in which the diagnosis of diastolic dysfunction was confirmed by conductance catheter analysis. They recommend its use as an essential tool for noninvasive diagnostics of diastolic function in patients with HFNEF.

Pulsed-wave TDI performed in the apical view is a useful technique to evaluate LV diastolic function and to measure mitral annular velocities. The primary measurements included systolic, early diastolic E', and late diastolic A' annular velocities. The E' velocity was determined by LV relaxation, preload, systolic function, and LV pressure. A value >10 cm/s was consistent with normal function. The main hemodynamic determinants of the A' velocity are LA systolic function and LVEDP. The E' velocity could be used to correct for the effect of LV relaxation on mitral flow E velocity in patients with cardiac disease. The annular E'/A' ratio and the mitral E velocity to tissue Doppler E' velocity (E/E') ratio could predict LV filling pressures [16].

As a rule of thumb, pulmonary vein flow D velocity and its DT always parallel the MV flow E wave and its DT. Therefore, with abnormal relaxation, pulmonary vein D velocity and its DT were reduced while pulmonary vein S velocity was relatively increased. The atrial reversal wave (Ar or AC) in the PV is reflective of end-diastolic pressure. If it is I prominent (Ar usually equal to or greater than 0.4 m/s, and Ar duration is 30 ms greater than the duration of the mitral A wave), end-diastolic pressure is probably elevated [14].

CONCLUSION

The assessment of diastolic function is now essential on routine testing for HF. The noninvasive nature of echocardiography had allowed an increase in diagnosis and awareness of diastolic dysfunction. Of all echocardiographic parameters investigated, the left atrial diameter (LAD) was identified as the best index to detect diastolic dysfunction in HFNEF. We recommend its use as an essential tool for noninvasive diagnosis of diastolic function in patients with heart failure with normal ejection fraction.

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