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Comparative Analysis of Risk Factors for Heart Failure with Preserved Vs Reduced Ejection Fraction in Patients with Heart Failure

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ABSTRACT

Aims: The prevalence of heart failure with preserved ejection fraction (HFpEF) has increased in the past two decades. Although it has been demonstrated that left ventricular (LV) diastolic and vascular functional abnormalities are generally observed in HFpEF, it remains to be clinically elucidated how an asymptomatic stage progresses to symptomatic HFpEF .We aimed to identify risk factors associated with incident HFpEF and to compare it with systolic heart failure (SHF). **Methods and Results:** The study included 100 patients of heart failure, 50 patients were having ejection fraction≤50% and 50 of them were having ejection fraction ≥50%. We included patients of heart failure who were admitted in coronary care unit of services hospital Lahore or they had more than one visit to the outpatient clinic of services hospital Lahore and had an echocardiographic report recorded. Patients with serum creatinine ≥2.0 mg/dL and patients with significant valvular heart diseases were excluded from the study. Mean age of patients was 53±9Y.Mean hemoglobin of patients was 11±2g/dl.62% patients were smokers and 38% were nonsmoker.57% patients were female and 43% were male.63% of all patients were suffering from coronary artery disease and 37% patients were not.66% patients were obese and 34% patients were not obese.65% patients were suffering from Diabetes mellitus and 35% patients were not.54% patients were hypertensive and 46% patients were not suffering from hypertension.43% patients had restrictive dysfunction on echocardiography and 43% patients had non restrictive pattern on echocardiography. Among those with EF≥50 80% patients were smokers and 20% were non smokers (P=>0.00).75% patients of EF≥50 were female and 25% patients were male(P=0.001).35% patients were diabetics and 65% patients were non diabetics.(P=.9)65% patients were hypertensive and 35% patients were not.(p=0.028).36% patients were suffering from coronary artery disease and 65% patients were not suffering from coronary artery disease(P=0.00).46% of these patients were having restrictive echocardiographic abnormalities on mitral valve inflow interrogation (p=0.00).26% of these patients were obese(P=0.00).Multiple logistic regression analysis revealed that obesity, female gender, age, smoking, and impaired LV compliance and history of hypertension were independently associated with the prevalence of HFpEF whereas anemia and diabetes mellitus was not. **Conclusions:** Female gender, history of hypertension, age, smoking and obesity was independently associated with the prevalence of HFpEF whereas anemia diabetes mellitus was not.

INTRODUCTION

Heart failure (HF) with preserved left-ventricular systolic function is becoming recognized as an important clinical syndrome.Heart failure is a major public health burden and the lifetime risk of developing heart failure in a 40 year old is around 20%[1,2]. About 50% of patients presenting with heart failure have normal ejection fraction (HFNEF)[3,4]. The prognosis of CHF patients with preserved systolic function is similar to those with systolic dysfunction. The widespread use of echocardiography in the diagnosis of CHF has resulted in the emergence of the new entity of

diastolic heart failure. There have been several studies from different parts of the world reporting on the epidemiology of CHF, the relative frequencies of systolic and diastolic heart failure, as well as the profile of risk factors contributing to the emergence of this epidemic in various regions of the world.[5-9] Recent research revealed that mortality of hospitalized patients with HFNEF is comparable to patients with systolic heart failure (SHF). Diabetes is a growing epidemiological burden and a major contributor to cardiovascular disease. In male patients with diabetes, the risk to develop heart failure is doubled in comparison to non-diabetic patients, but it is five times the risk of non-diabetic patients in women[10]. Moreover, diabetes is an independent predictor of poor outcome once SHF or HFNEF have developed[11,12]. We here conducted a study to look for the relative frequency of systolic versus diastolic heart failure in our population.The aim of the present study was to compare risk factors for heart failure in patients with SHF and HFNEF.

MATERIALS AND METHODS

It was a single center, open label, cross sectional study conducted in services hospital Lahore from January 2011 to July 2011. The study was conducted in Medical Unit 2 of Services Institute of Medical Sciences/Services Hospital, Lahore. The study included fifty patients of heart failure with ejection fraction ≥50% and 50 patients with EF≤50%.Patients with serum creatinine ≥2.0 mg/dl, valvular heart disease, cardiomyopathies and pericardial diseases were excluded from the study. The records of the patients were scrutinized for simple demographic data, e.g. age, gender, etc. All patients routinely had a detailed history, a thorough clinical examination, an ECG and a chest X-ray. Echocardiographic study of left ventricular function was performed after making the diagnosis of heart failure. All the patients underwent two dimensional, M mode, Doppler and color Doppler echocardiography by SSA-580 nemio XGEcho machine in the left lateral decubitus position, using 3.5 MHz transducer by a consultant physician experienced in echocardiography, in services hospital Lahore.

Mitral inflow interrogation allowed measurement of early diastolic filling (E wave), atrial contribution to LV filling (A wave), and the rapidity of pressure equalization between left ventricle and left atrium during early filling (deceleration time). The diastolic mitral flow pattern was classified into normal, abnormal relaxation pattern, pseudo-normalization, and restrictive pattern. In terms of processing our results, patients were analyzed according to one of two mitral flow patterns: (1) a restrictive pattern when E/A was, 1 and deceleration time was ≤140 ms, and (2) A non-restrictive pattern when E/A was ≥1 and deceleration time was ≥140 ms. The diagnosis of CHF was made according to the Framingham criteria[13]. Major criteria were paroxysmal nocturnal dyspnoea, orthopnoea, raised jugular venous pulse, lung crepitations, cardiomegaly and gallop sounds. Minor criteria were ankle edema, night cough, and dyspnoea on exertion, hepatomegaly, pleural effusion and tachycardia.

The diagnosis of predominantly systolic heart failure required a minimum of two major criteria or one major plus two minor criteria and LVEF≤50%. The diagnosis of predominantly diastolic heart failure required the following three conditions to be present simultaneously, *i.e.* (1) the a fore mentioned clinical criteria; (2) a LVEF equal to or more than 50%; (3) evidence of abnormal LV diastolic function as depicted by mitral inflow Doppler examination. Risk factors for heart failure were sought. Hypertension was defined as the presence of systolic BP≥ 140 mmHg and/or diastolic BP≥ 90 mmHg on at least two occasions, or if the patient was receiving antihypertensive drug treatment. The diagnosis of diabetes mellitus was made if the patient was receiving insulin or an oral hypoglycemic agent. Obesity was defined as BMI ≥30Kg/m^2.

CAD was considered to be present and a cause for heart failure if there was evidence of a definite myocardial infarction from history, ECG or echocardiogram, or there was a long history of stable angina pectoris, or there was significant disease on coronary angiography. Valvular heart disease was considered to be a primary cause of heart failure if there was echocardiographic evidence of valvular disease of more than moderate severity. Other risk factors for heart failure like

obesity, anemia, smoking diabetes and hypertension was recorded. Multiple logistic regression analysis was applied to look for association of heart failure with normal ejection fraction and patients having systolic heart failure and risk factors. Chi square test was applied to compare the patients of systolic vs. diastolic heart failure. All data analyses were performed with a commercially available statistical analysis software package (SPSS 16 for Windows).

RESULTS

Mean age of patients was 53±9% Y. Mean hemoglobin of patients was 11±2g/dl. 62% patients were smokers and 38% were nonsmoker, 57% patients were female and 43% were male. 63% of all patients were suffering from coronary artery disease and 37% patients were not suffering from coronary artery disease. 66% patients were obese and 34% patients were non obese.65% patients were suffering from Diabetes mellitus and 35% patients were not. 54% patients were hypertensive and 46% patients were not suffering from hypertension. 46% patients had restrictive dysfunction on echocardiography and 43% patients had non restrictive pattern on echocardiography. Among those with EF ≥50 (Table 1), 46% of patients were having restrictive echocardiographic abnormalities on mitral valve inflow interrogation (p=0.00), Figure 1. 26%patients were obese (P=.00), Figure 2. Eighty percent of these patients were smokers and 20% were non smokers (P=>.00), Figure 3. In diastolic heart failure group 45% patients were more than 60 Y old (p=0.00), Figure 4. Seventy five percent patients of EF ≥50 were female and 25% patients were male (P=.001), Figure 5. Thirty five percent of these patients were diabetics and 65%patients were not suffering from diabetes mellitus (P=.9), Figure 6. Sixty five percent patients were hypertensive and 35% patients were not (p=.028), Figure 7. Thirty six percent patients were suffering from coronary artery disease and 65% patients were not suffering from coronary artery disease (P=.001). Multiple logistic regression analysis revealed that age, obesity, female gender, impaired LV compliance and history of hypertension were independently associated with the prevalence of HFpEF whereas diabetes mellitus and anemia was not (Table 2).

Table 1: Clinical characteristics of CHF patients

Variable	Diastolic CHF (n=50)	Systolic CHF (n=50)	*P* value
Age (>60years)	45	27	0.00
Female	38	19	.001
Coronary artery disease	15	48	0.000
Hypertension	33	21	.044
Diabetes mellitus	32	33	.558
Smoking	41	21	0.00
Obesity	26	8	0.00
Echo restrictive pattern	46	2	0.00

Table 2: Adjusted odd ratios (or) for CHF with preserved systolic function.

Independent risk factor	Adjusted OR	95.0% C.I.for EXP(B) Lower	Upper	P value
Gender (women)	.265	1.377	17.048	.014
Hypertension	.300	.091	.987	.066
Age	.269	.071	.996	.049
Diabetes	.859	.290	2.547	.784
dysfunction	.344	.150	.790	.012
Smoking	7.418	2.261	24.339	.001
Obesity	.284	.083	.974	.045
Hemoglobin	1.364	.992	1.876	.0.056

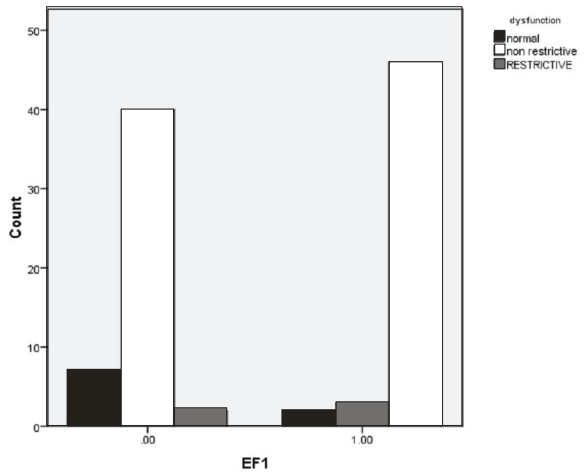

Fig. 1: Patterns of echocardiographic dysfunction in patients. (For Figures 1-7. EF1, Diastolic heart failure; EF0, systolic heart failure).

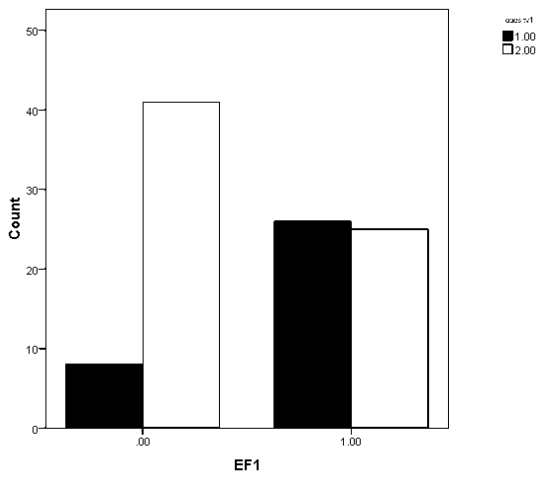

Fig. 2: Relation of obesity and EF in patients (1, Obese; 2, Non obese).

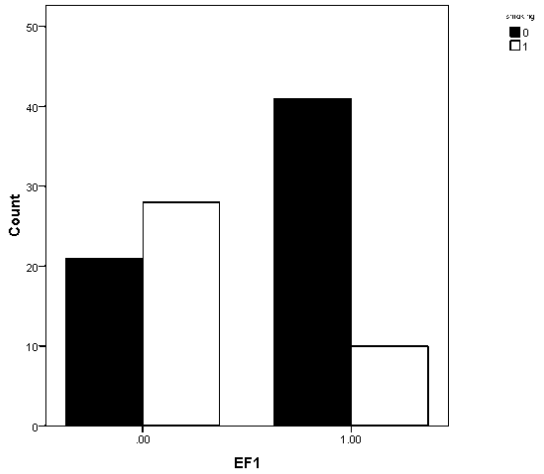

Fig. 3: Relation of smoking and EF in patients. (0, Smokers; 1, Non smokers).

DISCUSSION

In a large proportion of patients with heart failure, systolic ventricular function is preserved. Despite the clinical differences between patients with preserved and impaired systolic ventricular function, the medium-term prognosis was similar in both groups.[9] Among hospitalized patients, mortality rates are comparable between patients with systolic dysfunction and those with preserved systolic function. However, patients with heart failure with systolic dysfunction may have higher readmission rates.[10]

It is increasingly recognized that the syndrome of congestive heart failure may occur in the absence of any abnormality of left ventricular systolic function.

In this situation, the clinical picture of heart failure, particularly the presence of symptoms and/ or signs of pulmonary congestion, is usually considered a consequence of an abnormal diastolic function of the left ventricle (diastolic heart failure). However, in the individual patient, several other

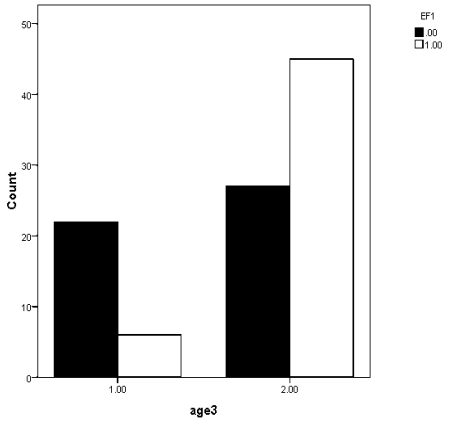

Fig. 4: Relation of age and EF in patients. (0 ≤50, 1≥50)

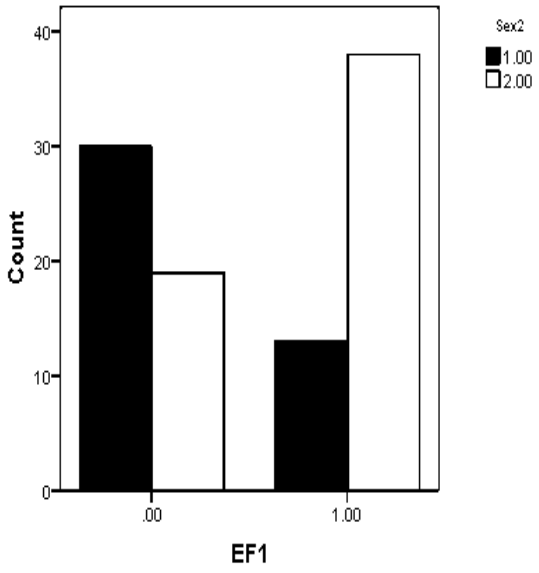

Fig. 5: Relationship of sex and Ejection fraction (1, Male; 2, female).

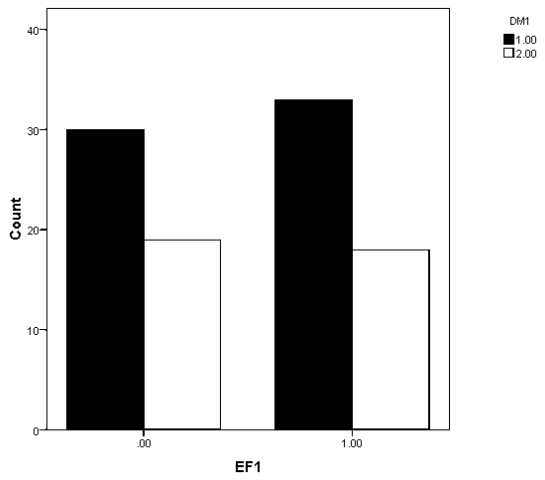

Fig. 6: Relation of diabetes mellitus and EF in patients. (1, Diabetics; 2, Non diabetics).

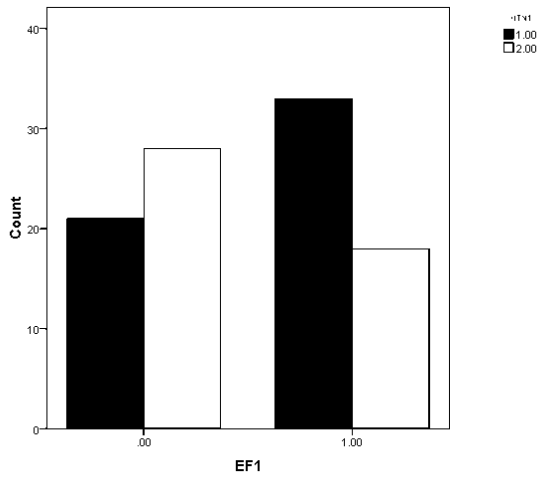

Fig. 7: Relation of Hypertension and EF in patients. (1. Hypertensive; 2, Non hypertensive).

potential causes should be taken into account before attributing to an isolated diastolic dysfunction of the left ventricle the pathogenetic role of clinical presentation. In fact, diagnosis of diastolic heart failure, represents an exclusion diagnosis in the clinical setting. Prevalence of heart failure with preserved left ventricular systolic function is widely variable among the different studies, from 13% to over 70%, with most reports showing a prevalence of 30-40%. According to an analysis of the studies published, heart failure with preserved left ventricular systolic function seems to be more common in the female sex and in elderly patients, and it is associated with hypertension and electrocardiographic or echocardiographic evidence of left ventricular hypertrophy. Atrial fibrillation, either paroxysmal or chronic, is common and may represent a precipitating factor of clinical deterioration. According to most studies, patients with preserved left ventricular systolic function show, compared to patients with reduced left ventricular systolic function, a better prognosis, as indicated by a lower mortality and hospital readmission rates. Regarding the therapy of these patients, it is known that there are virtually no well-controlled studies of the effect of pharmacological treatment on outcome[11]. In a previous study done evidence of CAD or previous myocardial infarction was present in 72% of patients with systolic CHF and the rest of this group was treated as heart failure of no ischemic origin. In our study the diastolic CHF group evidence of coronary disease was present in only 25% of the patients (P-0.01).

Systemic hypertension was present in 60% of the systolic CHF patients, while almost all patients (94%) with diastolic CHF had hypertension (P-0.01).

Diabetes mellitus was present with equal frequency in both groups (35%) Diastolic parameters on echocardiography showed that 89% patients with normal LVEF had either abnormal relaxation pattern or normal pseudo-normalization pattern (non-restrictive). In contrast, the restrictive pattern was more common in the systolic LV failure group (45% vs. 11%; P-0.01)[15]. The same observation is recorded in our study. Regarding risk factors for heart failure, the majority of patients (72%) with systolic CHF had evidence of CAD, while in diastolic CHF the picture is dominated by hypertension[16]. More than one-third in both groups of heart failure has diabetes mellitus. A notable feature in our CHF patients is the aggregation of risk factors, leaving only 10% of the study group with neither CAD, hypertension nor diabetes. Out of the three risk factors, hypertension stands out as the most common predisposing risk factor for CHF[17]. These results are in agreement with the Framingham study[18]. Patients with predominantly systolic heart failure had a statistically higher hospitalization rate than those suffering from diastolic CHF[18].

Mortality rate was higher in patients with reduced LV systolic function but this was not of statistical significance. Studies diverge regarding the natural history of CHF with preserved systolic function, while many report a better prognosis compared to systolic CHF[14, 18]. Others report a similar mortality rate[19,20]. At least two publications of patients in their sixties reach a similar conclusion[21,22].

Although age- and sex-specific HF incidence is not increasing, overall HF survival has improved, and the number of people aged ≥65 years is increasing rapidly[23]. Thus, the absolute number of patients with HF will continue to increase. Half of the patients with HF have a preserved ejection fraction (HFpEF), and the remainder display reduced ejection fraction (HFrEF)[24-26]. The proportion of patients with normal ejection fraction (EF) is increasing steadily because of increased incidence and/or increasing physician recognition of the syndrome.[24, 27-30] Studies have reported that the subset of patients with preserved systolic function comprises at least 40% of all cases of heart failure and that it is more common in older people[27, 37]. The literature also suggests that the prevalence of CHF with preserved systolic function is higher in women than in men.[27,31-34]

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