

PREVALENCE OF RISK FACTORS IN PATIENTS WITH HEART FAILURE WITH NORMAL EJECTION FRACTION (HFNEF)

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Contribution

All the authors contributed significantly to the research that resulted in the submitted manuscript.

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ABSTRACT

Objective: To determine prevalence of risk factors in patients with heart failure with normal ejection fraction (HFNEF).

Methodology: This was a cross sectional descriptive study conducted at the Department of Cardiology, Lady Reading Hospital, Peshawar. Patients referred from Out Patient and Emergency Departments to the Echocardiography department meeting the criteria for HFNEF were included. All the patients were carefully scrutinized for common risk factors. They were subjected to detailed history and clinical examination. Their clinical record was checked, BMI calculated, ECG and Transthoracic echocardiography was performed. Data was analyzed on SPSS version 15.

Results: The total number of patients studied was 139. Males were 45.3% and females were 54.7%. Mean age \pm SD was 56.64 ± 10 years. Patients were divided into three groups on the basis of age. There were 42.4% patients in age group 40-54 years, 44.6% in age group 55-69 and 12.9% in age group 70 and above. Majority (51.8%) of the patients were in NYHA class II. Hypertension (59.7%) was the most common risk factor for HFNEF, followed by Coronary artery disease in 34.5%, Diabetes mellitus (DM) 33.1% and Obesity in 15.1%. A significant number of patients 21.6% had no obvious risk factor. Sixty one (43.88%) patients had more than one risk factor contributing to diastolic dysfunction.

Conclusion: Arterial hypertension, Coronary artery disease, diabetes mellitus and obesity are the major factors in patients with diastolic dysfunction and HFNEF. A significant proportion of patients have multiple risk factors for HFNEF.

Key Words: Heart Failure With Normal Ejection Fraction (HFNEF), Risk Factors, Diastolic Dysfunction, Transthoracic Echocardiography, Tissue Doppler Imaging (TDI)

INTRODUCTION

Heart failure affects approximately 4.8 million persons in the United States, with about 500,000 new cases diagnosed each year.^{1,2} Patients with an ejection fraction of 50 percent or higher were classified as having heart failure with normal ejection fraction (HFNEF), whereas those with an ejection fraction of less than 50 percent were classified as having heart failure with reduced ejection fraction (HFREF).³ Early studies suggested that as many as one third of patients presenting with overt heart failure have isolated diastolic heart failure^{4,5} but recent studies have shown a prevalence of diastolic heart failure of 50% in patients greater than 70 years of age.^{6,7}

The symptoms of heart failure may be identical whether failure is secondary to systolic or diastolic dysfunction, however, there are differences in the prognosis, characteristics of the patients, pathophysiology and treatment between the two conditions.⁸ Compared to patients with a low ejection fraction, those with preserved ejection fraction are older, more often women and are more likely to have a hypertensive aetiology.⁹ Hypertension is the most common cause of diastolic dysfunction and diastolic heart failure that is about 60%.¹⁰ Recent data suggested that coronary artery disease is a cause of diastolic dysfunction in approximately 1/3rd of patients.¹⁰ Obesity alone is the cause of 11% cases of cardiac failure in men and 14% of cases in women in United States.¹⁰ Many reports have shown a prevalence of about 30-60% of diastolic dysfunction even in well controlled diabetics.¹⁰ Studies have shown that with increasing glucose level the prevalence of dd increases in diabetics.¹¹ A history of coronary artery disease was associated with the greatest risk of heart failure (29.1% vs. 11.86%, OR 3.05, 95% CI) followed by diabetes (18.5% vs. 7.89%, OR 2.65, 95% CI), obesity (24.5% vs. 9.28%, OR 2.00, 95% CI) and hypertension (61.2% vs. 57.62%, OR 1.44, 95% CI) with the p-value of less than 0.001 for each.¹²

The most useful clinical tools for the assessment of left ventricular diastolic function is Conventional Doppler Echocardiography, not only utilized for diagnostic purposes but also for establishing prognosis and evaluating the effect of treatment.¹³ Tissue Doppler imaging (TDI), including the transmitral flow velocity to annular velocity ratio (E/E' index), which measures myocardial velocities during the cardiac cycle, is considered more reliable for diagnosing diastolic dysfunction.¹⁴

Heart failure with preserved ejection fraction becomes the most common form of heart failure, representing slightly more than half of all cases of heart failure.¹⁵ Its frequency increases dramatically with age underscoring the importance of this growing public health problem.¹⁵ One study indicates that the prognosis of patients with HFNEF is

poor, and just as severe as in patients with reduced ejection fraction.¹⁵ Thus, both conditions have a severe prognosis with 5 years mortality rates of almost 60%.¹⁵

The best strategy for avoidance of morbidity and mortality from HFNEF is prevention and control of risk factors. As the prevalence of HFNEF is high so the associated mortality is high and comparable to systolic heart failure. The rationale of my study is to determine the association between HFNEF and risk factors in our local population. This study has important public health implication, and will help the physicians in suggesting that targeting specific and most commonly found risk factor on the basis of odds ratio and control of those risk factors may have the greatest impact on reducing the number of heart failure with normal ejection fraction cases in our population.

The aim of our study was to determine the common and important risk factors leading to HFNEF.

METHODOLOGY

This was a cross sectional descriptive study conducted at the Department of Cardiology, Post Graduate Medical Institute, Lady Reading Hospital Peshawar from March 2011 to Nov 2011. The study was conducted after approval from hospital ethical and research committee.

Patients referred from Out Patient and Emergency Departments to the Echocardiography department of cardiology unit meeting the inclusion criteria were included in the study. The purpose and benefits of the study was explained to patients and a written informed consent was obtained.

Our study included all patients of both gender and age 40 years and above with Heart Failure with normal ejection fraction (HFNEF). HFNEF was diagnosed on the basis of all of the following features:

1. History of shortness of breath on exertion
2. Left ventricular ejection fraction of > 50% on Transthoracic Echocardiography
3. E to A ratio of < 1 on Transthoracic Echocardiography
4. E/E' > 15 on Transthoracic Echocardiography

Patients with congenital heart disease, valvular heart disease, rheumatic heart disease and technically difficult cases were excluded from the study.

All the patients were subjected to detailed history and clinical examination. Their clinical record was checked, BMI calculated and fresh ECG, Transthoracic echocardiography and lab investigation for blood sugars was done. All the patients were carefully scrutinized for the detection of common risk factors including obesity (BMI 30 or more),

hypertension (Patients taking antihypertensive medications or having blood pressure ≥ 140 mmHg systolic or ≥ 90 mmHg diastolic), diabetes (Random blood sugar >200 mg/dl or subject is on anti diabetic medications) and coronary artery disease (history of CAD or evidence of CAD on ECG/ echocardiography).

All the above mentioned information including name, age, gender and address were recorded in a pre designed Performa. Similarly care was taken during extraction of information to avoid responder bias. Confounders and other bias were controlled by strictly following exclusion criteria.

The statistical analysis performed using the statistical package for social sciences (SPSS Ver. 15.0). Numerical variables like age were presented as mean \pm SD. Categorical variables like gender and common risk factors (Coronary artery disease, hypertension, Diabetes mellitus and obesity) were presented as frequencies and percentages. Also chi square test was used to compare the age and sex in both the groups to see the effect modification. Data was presented as tables and graphs where appropriate.

RESULTS

The total number of patients studied was 139. Males were 45.3% (n=63) and females were 54.7% (n=76) (Table 1). Mean age \pm SD was 56.64 ± 10 years. Patients were divided into three groups on the basis of age. There were 42.4% (n=59) patients in age group 40-54 years, 44.6% (n=62) in age group 55-69 and 12.9% (n=18) in age group 70 and above. Majority of the patients were in NYHA class II at presentation (51.8%) (Table 1).

In the current study, Diabetes mellitus (DM) was noted as a risk factor of HFNEF in 33.1% (n=46) of the cases and was more common in males (39.7% vs. 27.6% p=0.15) (Table

Table 1: Baseline Characteristics of Study Population

Variable	Number of patients	Percentage
Male	63	45.3
Female	76	54.7
NYHA CLASS		
I	25	18.0
II	72	51.8
III	37	26.6
IV	05	03.6
AGE GROUP (YEARS)		
40-54	59	42.4
55-69	62	46.6
≥ 70	18	12.9
MEAN AGE \pm SD (Years)	56.64 ± 10	

Table 2: Distribution of Patients According to Risk Factors (N=139)

Risk Factors	Frequency	Percentage
Hypertension	83	59.7
Ischemic Heart Disease	48	34.5
Diabetes Mellitus	46	33.1
Obesity	21	15.1
Without obvious risk factors	30	21.6

2). Obesity was found as a risk factor of HFNEF in 15.1% (n=21) of the cases and it was equally common in males and females (14.3% vs. 15.8% p=1.0). Hypertension was noted as a risk factor of HFNEF in 59.7% (n=83) of the cases. Hypertension was more common in females vs males (63.2% vs. 55.6% p=0.389) Coronary artery disease (CAD) was noted as a risk factor of HFNEF in 34.5% (n=48) of the cases (Table 2). CAD as a risk factor was more common in males (38.1% vs. 31.6% p=0.47). A significant number of patients 21.6% (n=30) had no obvious risk factor.

Sixty one (43.88%) patients had more than one risk factor contributing to diastolic dysfunction. 13 (9.35%) had hypertension, 8 (5.76%) had CAD DM, 10 (7.19%) had DM and hypertension, 2 (1.44%) had hypertension and obesity, 2 (1.44%) had DM and obesity, 10 (7.19%) had hypertension plus CAD plus DM, 8 (5.76%) had HTN plus obesity plus DM, 4 (2.88%) had HTN plus CAD plus obesity, 2 (1.44%) had DM plus CAD plus obesity and in the last 2 (1.44%) had CAD, hypertension, DM and obesity (Table 3).

DISCUSSION

Heart failure with normal ejection fraction (HFNEF) or diastolic heart failure (DHF) is defined as failure of left ventricle to produce an adequate cardiac output at normal left ventricular filling pressure despite the presence of a normal left ventricular ejection fraction.¹⁶ Results of early studies suggested that as many as 40% of patients with heart failure have isolated HFNEF.¹⁷ However more recent data shows that the prevalence of diastolic dysfunction and diastolic heart failure is dependent on age, sex, study setting (e.g Hospital vs. Community), methods used to make the diagnosis (Echocardiography vs. Invasive techniques), LVEF cut off (40% vs. 50%) and the underlying disease that contribute to diastolic dysfunction.¹⁸ One study indicates that the prognosis of patients with HFNEF is poor, and just as severe as in patients with reduced ejection fraction.

In this study we found that majority of our patients were female (52.5%) and of less than 70 years old. This study indicates that coronary disease, hypertension, diabetes and

Table 3: Patients With More Than One Risk Factor (N=139)

Risk Factors	Frequency	Percentage
HTN+DM	10	7.19
HTN+IHD	13	9.35
DM+IHD	8	5.76
HTN+OBESITY	2	1.44
DM+OBESITY	2	1.44
HTN+IHD+DM	10	7.19
HTN+OBESITY+DM	8	5.76
HTN+CAD+OBESITY	4	2.88
DM+IHD+OBESITY	2	1.44
HTN+IHD+DM+OBESITY	2	1.44

obesity are common risk factors in patients with heart failure with normal ejection fraction in both men and women. The risk of heart failure is greatest for coronary disease and diabetes, while coronary disease and hypertension are responsible for the largest proportion of new diastolic heart failure cases in the population. Sex differences in the etiology of diastolic heart failure may exist with hypertension playing the greatest role in women and coronary disease in men and similar findings were noted by Dunlay et al.¹²

Hypertension as the risk factor of HFNEF was the largest group observed in the current study i-e 59.7% and was most common in women (63.2%). Similar finding were reported by Jonathan et al, who reported that hypertension is the most common risk factor for the DHF.¹⁹ The Framingham study showed that 75% of patients with DHF have hypertension.²⁰ All the previous studies showed that hypertension is the most common cause of diastolic dysfunction / DHF and DHF is the most common cause of morbidity and mortality in hypertensive patients especially African American even more than IHD (62% vs. 44%).

In this study, coronary artery disease as a risk factor for HFNEF is the second most common risk factor i-e (34.5%). Limited data is available on the prevalence of cardiac failure with preserved systolic function in patients with coronary artery disease. Some studies suggested that the prevalence of cardiac failure with preserved systolic function after myocardial infarction was as high as 45 %.²¹ These studies however are mostly case series so their estimates of prevalence may be subject to selection bias. The exact prevalence of patients with cardiac failure and preserved systolic function with CAD in the community is not known. Hellermann et al, reported that 30% of patients after myocardial infarction with heart failure have preserved left

ventricular systolic function which is consistent with our study results.²² Other studies showed this prevalence rate between 27-45% for patients with heart failure and preserved systolic function (EF>50 %) and coronary artery disease as the underlying condition and these results are also consistent with the current study results.²¹ Koren et al, also reported that CAD is a contributing factor of diastolic dysfunction in heart failure patients in approximately one third of patients which coincide with our results.²³

Obesity as a risk factor for HFNEF was noted in 15.1% in the cases (men=14.3, women=15.8). In one Study it was reported that obesity alone is the cause of 11% cases of HFNEF in men and 14 % of cases in women.²⁴

In the current study, 33.1% of the cases diabetes mellitus was noted as a risk factor of HFNEF. The prevalence of diabetes in men were 29.7% and in women were 27.6%. The presence of isolated diastolic dysfunction in diabetic patients in the absence of hypertension and IHD was first described by Rubler et al.²⁴. Braga et al, reported that diastolic dysfunction precedes the systolic changes in the diabetic heart even in the absence of CAD.²⁵ Many reports have shown prevalence of diastolic dysfunction from 30 - 60 % in diabetic persons and these results coincide with the current study. O,Connor et al, found that about 30 % patients with diastolic dysfunction / DHF also were suffering from diabetes mellitus in the absence of obstructive CAD and hypertension.²⁶ In our study 21.6% patients had no obvious risk factor fo HFNEF. This figure is similar to the what has been reported in another study.¹⁶

LIMITATIONS

There were certain study limitations. This was a small single centre study and more studies are recommended to validate these findings in our population. Majority of our study population was younger while risk factors for HFNEF increases with increasing age.

CONCLUSION

Isolated diastolic dysfunction and heart failure with normal ejection fraction in our population is not an uncommon entity. Coronary artery disease, arterial hypertension, obesity and diabetes mellitus are the major risk factors in patients with diastolic dysfunction and heart failure with normal ejection fraction.

REFERENCES

1. Ho KK, Pinsky JL, Kannel WB, Levy D. The epidemiology of heart failure: the Framingham study. *J Am Coll Cardiol* 1993;22:6-13.
2. Berry C, Murdoch DR, McMurray JJ. The economics of chronic heart failure. *Eur J Heart Fail* 2001;3:283-91.

3. Owan TE, Hodge DO, Herges RM, Jacobsen SJ, Roger VL, Redfield MM. Trend in prevalence and outcome of heart failure with preserved ejection fraction. *N Eng J Med* 2006;355:251-9.
4. Zile MR, Brutsaert DI. New concepts in diastolic dysfunction and diastolic heart failure: part I diagnosis, prognosis, and measurements of diastolic function. *Circulation* 2002;105:1387-93.
5. Gaasch WH, Schick EC, Zile MR. Management of left ventricular diastolic dysfunction. In: Smith TW, editor. *Cardiovascular therapeutics: a companion to Braunwald's heart disease*. Philadelphia: WB Saunders; 1996. p. 237-42.
6. Senni M, Tribouillois CM, Rodeheffer RJ. Congestive heart failure in the community: a study of all incident cases in Olmsted County, Minnesota, in 1991. *Circulation* 1998;98:2282-9.
7. Vasan R, Laeson MG, Benjamin EJ. Congestive heart failure in subjects with normal versus reduced left ventricular ejection fraction: prevalence and mortality in a population based cohort. *J Am Coll Cardiol* 1999;33:1948-55.
8. Haney S, Sur D, Xu Z. Diastolic heart failure: a review and primary care perspective. *J Am Board Fam Pract* 2005;18:189-98.
9. McMurray JJV, Carson PE, Komajda M, McKelvie R, Zile MR, Ptaszynska A, et al. Heart failure with preserved ejection fraction: clinical characteristics of 4133 patients enrolled in the I-PRESERVE trial. *Eur J Heart Failure* 2008;10:149-56.
10. Ali A, Abid AR, Azhar M. Risk factors of diastolic heart failure. *Professional Med J* 2006;13:410-6.
11. Stahrenberg R, Edelmann F, Mende M, Kockskämper A, Dungen HD, Scherer M, et al. Association of glucose metabolism with diastolic function along the diabetic continuum. *Diabetologia* 2010;53:1331-40.
12. Dunlay SM, Weston SA, Jacobsen SJ, Roger VL. Risk factors for heart failure: a population based case control study. *Am J Med* 2009;122:1023-8.
13. Hameedullah, Faheem M, Khan SB, Hafizulla M. Prevalence of asymptomatic left ventricular diastolic dysfunction in normotensive type 2 Diabetic patients. *J Postgrad Med Inst* 2010;24:188-92.
14. Kasner M, Westermann D, Steendijk P, Gaub R, Wilkenshoff U, Weitmann K, et al. Utility of Doppler echocardiography and tissue Doppler imaging in the estimation of diastolic function in heart failure with normal ejection fraction: a comparative Doppler-conductance catheterization study. *Circulation* 2007;116:637-47.
15. Tribouillois C, Rusinaru D, Mahjoub H, Souliere V, Levy F, Peltier M, et al. Prognosis of heart failure with preserved ejection fraction: a 5 year prospective population based study. *Eur Heart J* 2008;29:339-47.
16. Grossman W. Defining diastolic dysfunction. *Circulation* 2000;101:2020-1.
17. Vasan RS, Benjamin EJ, Levy D. Prevalence, clinical features and prognosis of diastolic heart failure: an epidemiologic perspective. *J Am Coll Cardiol* 1995;26:1565-74.
18. Smith GL, Masoudi FA, Vaccarino V. Outcomes in heart failure patients with preserved ejection fraction: mortality, readmission, and functional decline. *J Am Coll Cardiol* 2003;41:1510-8.
19. Jonathan PP, Klein L, Gheorghide M, Bonow RO. New insights into diastolic heart failure: role of diabetes mellitus. *Am J Med* 2004;116:64-75.
20. Kannel WB, Castelli WP, McNamara PM, McKee PA, Feinleib M. Role of blood pressure in the development of congestive heart failure. The Framingham study. *N Eng J Med* 1972;287:781-7.
21. Sweitzer NK, Stevenson LW. Diastolic heart failure: miles to go before we sleep. *Am J Med* 2000;109:683-5.
22. Hellermann JP, Jacobsen SJ, Reeder GS, Lopez-Jimenez, Weston SA, Roger VL. Heart failure after myocardial infarction: prevalence of preserved left ventricular systolic function in the community. *Am Heart J* 2003;145:742-8.
23. Koren MJ. Diastolic congestive heart failure. Jacksonville, Florida: Medical Director, Non-Invasive Cardiology, Memorial Hospital; 2002.
24. Rubler S, Dugash J, Yuçeoğlu YZ, Kumral T, Branwood AW, Grishman A. New type of cardiomyopathy association with diabetic glomeruloseclerosis. *Am J Cardiol* 1972;30:595-602.
25. Braga JC, Guimarães Filho FV, Padovani CR, Matsubara BB. Diastolic dysfunction in diabetic normotensive patients, regardless of the presence of microangiopathy. *Arq Bras Cardiol* 2005;84:461-6.
26. O'Connor CM, Gattis WA, Shaw L, Cuffe MS, Califf RM. Clinical characteristics and long term outcomes of patients with heart failure and preserved systolic function. *Am J Cardiol* 2000;86:863-7.