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Correlation between brain-type natriuretic peptide (BNP) levels & left ventricular ejection fraction (LVEF) in heart failure

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Abstract

Background: A significant proportion of patients diagnosed as heart failure have preserved ejection fraction. However, the differentiation between heart failure with reduced & preserved ejection fraction is difficult.

Method: The medical records of young patients (20–40 years) admitted during the two years 2014 & 2015 and diagnosed with Heart Failure were scrutinized in an attempt to determine the proportion of patients with preserved vs reduced ejection fraction and to assess the relationship between their Brain-type Natriuretic Peptide (BNP) levels & Left Ventricular Ejection Fraction (LVEF) in both the groups.

Results: After Statistical analysis, it was found that around 36% of heart failure patients had preserved ejection fraction. There was a negative correlation between BNP levels & LVEF in both heart failure with reduced ejection fraction (HFrEF) as well as that with preserved ejection fraction (HFpEF). Majority of patients in HFpEF group were females. Mean BNP level in HFpEF group was significantly lower than that in the HFrEF group.

Conclusion: Around one third of patients had Heart Failure with preserved systolic function, of which majority are females. There is a strong negative correlation between BNP levels and LVEF% in both the groups. Thus. BNP levels can be used in the differentiation of HFpEF and HFrEF.

Keywords: Heart Failure, BNP levels, LVEF, Preserved & reduced ejection fraction

Introduction

Heart failure is one of the global epidemics accounting for significant morbidity and mortality. It is a condition characterized by inability of the heart to pump enough blood to meet the body's oxygen and nutrient requirements[1]. Commonly known as Congestive Cardiac failure (CCF) or Congestive Heart Failure (CHF), it may be due to poor pumping capacity (systolic dysfunction) or increased stiffness of the walls (diastolic dysfunction). CHF can affect both the young & the old. The common morbidities which affect the elderly population including Diabetes mellitus, Hypertension, Ischemic heart disease, musculoskeletal disorders, hypothyroidism etc[2]. Often present with a common symptom of breathlessness which reflects left ventricular dysfunction, the causes in the young being, Congenital anomalies, different types of Cardiomyopathy, Myocarditis & certain drugs[3,9]. CHF poses a lot of diagnostic challenges as the clinical features often overlap. Moreover, a significant proportion of heart failure patients have preserved ejection fraction (diastolic dysfunction with normal LVEF)[4], which complicates the situation further. The inter-related sequence of events which plays a role in pathophysiology in such patients makes diagnosis & treatment monitoring more challenging. This diagnostic uncertainty leads to prolonged and recurrent hospitalization, unnecessary diagnostic and therapeutic interventions & thus increases health care costs. There emerges a need for an adjunctive biomarker which can aid in the diagnosis of CHF patients with preserved ejection fraction.

Brain-type natriuretic peptide, also called B- type natriuretic peptide (BNP) is a 32-amino acid neurohormone, secreted by the ventricles, due to excessive stretching of cardiomyocytes as a result of increased intracardiac volume or pressure[5]. It is a simple, non-invasive blood test which reflect LV dysfunction & thus, can be an important biomarker useful in the diagnosis and prognostication of CCF and also in monitoring the response to treatment. It reflects the diastolic filling abnormalities in patients with normal systolic function. LVEF is an indicator of the proper functioning of the heart. It is a measure of the capacity of the left ventricle to pump adequate amount of blood to all parts of the body.

Aim of the study

To determine the proportion of young heart failure patients with preserved and reduced ejection fraction and to assess the correlation between BNP levels & LVEF in both the groups.

Site of study

Sri Ramachandra Medical College Hospital, Porur, Chennai-600116.

Methods

The study was approved by the Institutional Ethics Committee of Sri Ramachandra Medical College Hospital. A total of 75 medical records of CCF patients admitted over the past two years (2014 & 2015) were

scrutinized for their BNP levels & LVEF. Patients younger than 20 years & older than 40 years were excluded. Patients with history of diabetes, hypertension, respiratory disease & renal failure were also excluded.

The Echocardiograms of the participants were analysed and reported by competent cardiologists and LVEF (%) was estimated. Serum BNP levels in this study were measured using chemiluminescent microparticle immunoassay on Abbott Architect I 1000 system. A LVEF of > 50% and serum BNP level of < 100ng/ml were considered to be normal.

Statistical analysis and Results

Mean age of the patients was 35.4±2.8 years. 62% (46) were males & 38% (29) were females. Of the 75 CHF patients who underwent Echocardiogram, around 36% (27) had normal ejection fraction (HFpEF) & 64% (48) had reduced ejection fraction (HFrEF). A significant proportion of the former group were females (70%), in contrast to a majority of males (75%) in the latter.

All statistical analyses were performed with the Statistical Package for the Social Sciences statistical software package for Windows, version 16.0 (SPSS Inc., Chicago, IL, USA), and a two-tailed p value of <0.05 was considered statistically significant. Correlation between BNP levels and LVEF was assessed. A strong negative correlation was noted between BNP levels and LVEF % in both the groups (p value 0.002 vs 0.007 in HFrEF and HFpEF groups respectively - Table 1 & 2). Mean LVEF % of the two groups were 34.43% and 55.92% respectively. Median BNP levels were 291.1 ng/ml & 2091.1 ng/ml respectively. Thus, BNP levels in the former group were significantly lower than that in the latter group (Fig. 3 & 4).

Table 1: Correlation between BNP levels and LVEF in HFrEF group

		BNP	LVEF %
BNP	Pearson Correlation	1	-.445**
	Sig. (2-tailed)		.002
	N	48	48
LVEF %	Pearson Correlation	-.445**	1
	Sig. (2-tailed)	.002	
	N	48	48
**Correlation is significant at the 0.01 level (2-tailed).			

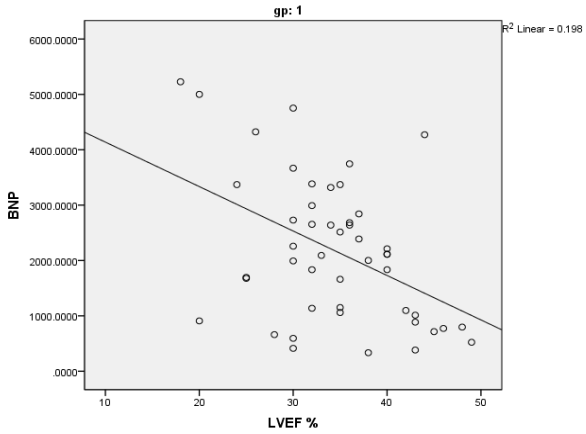

Fig. 1: Scatter plot for correlation of BNP levels and LVEF: HFrEF group

Table 2: Correlation between BNP levels and LVEF in HFpEF group

		BNP	LVEF %
BNP	Pearson Correlation	1	-.505**
	Sig. (2-tailed)		.007
	N	27	27
LVEF %	Pearson Correlation	-.505**	1
	Sig. (2-tailed)	.007	
	N	27	27
**. Correlation is significant at the 0.01 level (2-tailed).			

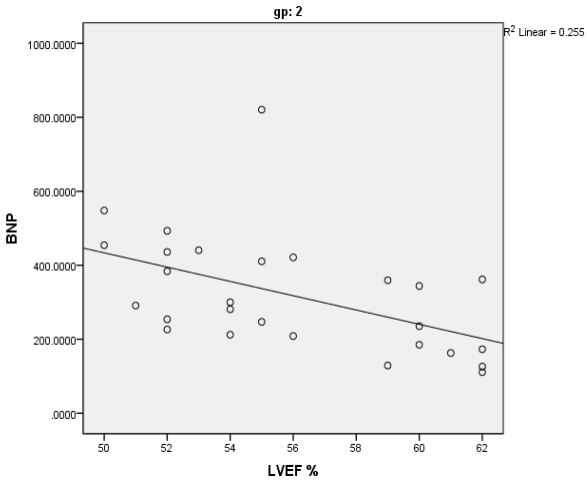

Fig. 2: Scatter plot for correlation of BNP levels and LVEF: HFpEF group

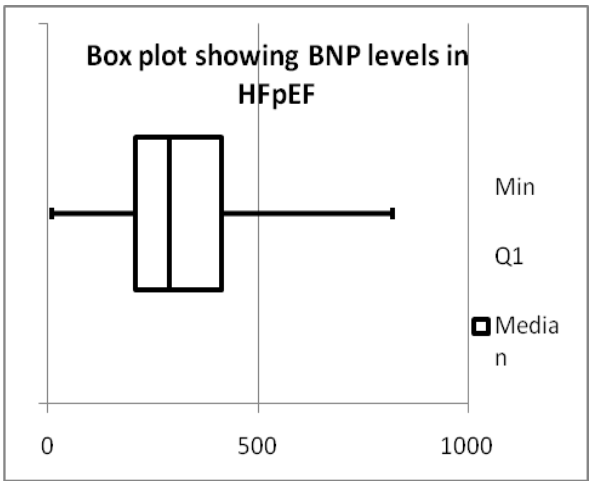

Fig. 3

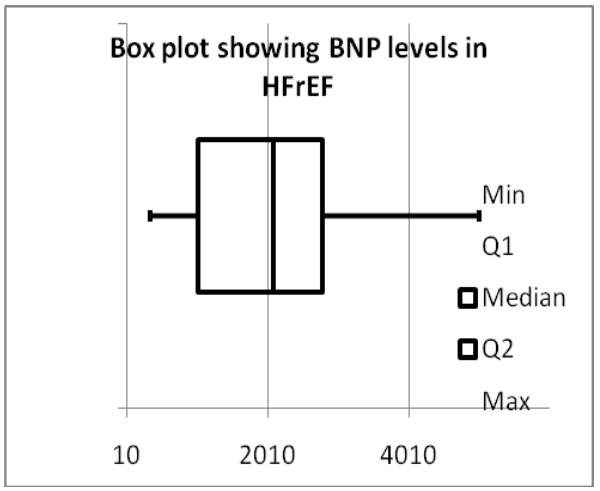

Fig. 4

Discussion

Heart failure is considered to be a disease of the elderly population[6]. The reason could be appropriate management of acute conditions leading to improved longevity of patients who progress to Heart Failure, increased exposure to risk factors and age-related changes. As age advances, both the number and function of cardiac myocytes are found to decrease, irrespective of the presence or absence of cardiovascular disease[6]. This could be explained by increased necrosis or apoptosis and decreased regenerative capacity of the ageing cardiac myocytes leading to impairment in the repair of myocyte loss, ultimately ending up in hypertrophy of remaining cells.

Altered Calcium metabolism and age-related changes in contractile proteins may also play a role. Moreover, the ageing myocardium may be affected by abnormal extracellular matrix metabolism leading to increased to increased collagen content and development of fibrosis. Myocardial fibrosis is contributed by upregulation of various mechanism like Renin - Angiotensin system, inflammation and oxidative injury. All these factors put together lead to increased prevalence of left ventricular hypertrophy and impaired relaxation ultimately resulting in causation of Heart Failure with preserved ejection fraction (HFpEF). Thus, a significant proportion of elderly Heart Failure patients have preserved systolic function[7], whereas, majority of young patients present with Heart Failure with reduced systolic function (HFrEF)[8].

Several lines of evidence exist which demonstrate the proportion of heart failure patients with non-systolic dysfunction. Most studies on Heart failure had been on older patients and there is very little evidence regarding the pathophysiology and progression of the disease in the young[9]. Thus, this study was chosen to be done on patients between ages 20 and 40 years, though there is no well defined strategy to categorise patients as young or old. The results of this study show that around 36% of patients studied had preserved ejection fraction according to echocardiogram findings. There are significant differences in the underlying pathology and the risk factors involved in the causation of HFpEF and HFrEF. The major criteria for diagnosing HFpEF include signs and symptoms of Heart Failure, normal left ventricular systolic function, evidence of LV filling abnormalities or diastolic stiffness[10], history of atrial fibrillation and preponderance of female sex whereas, HFrEF patients show evidence of LV pumping abnormalities and history of previous myocardial infarction or bundle branch block[11]. The symptoms of Heart failure include lower limb edema, elevated Jugular Venous Pressure (JVP), lung crackles, wheeze, cardiac murmur etc and the signs include Radiological evidence of cardiomegaly, pleural effusion, pulmonary edema etc.[2], In this study, patients categorised under the HFpEF groups belong to Class I / II NYHA functional classification, whereas, those in HFrEF group belong to Class III / IV[12]. Diagnosis of appropriate type of heart failure is important because the treatment modalities differ for different types of heart failure and it is essential to reduce the morbidity & mortality caused by misdiagnosis. With this background, we aimed at differentiating the heart failure with systolic dysfunction from that with non-systolic dysfunction based on LVEF % and BNP levels.

Brain-type Natriuretic peptide is a biologically active 32-amino acid neurohormone. It is produced after cleavage of a 108- amino acid prohormone, as a result of stretching of cardiomyoytes following pressure or volume overload. The BNP levels are indicative of left ventricular dysfunction and increase with increasing severity of Heart Failure. BNP can thus be used as a clinical indicator of Heart Failure in patients with unexplained dyspnoea, as a prognostic marker, as a guide to drug titration and as a predictor of future cardiovascular events[3]. It reflects abnormal diastolic filling properties in patients with preserved ejection fraction[13,14].

Ejection Fraction is a measure of the capacity of the heart to pump blood out of the left ventricle, which

implies that it is an indicator of the left ventricular function. People with normal ejection fraction pump enough blood to other parts of the body, but those with reduced EF do not. In this study, CHF patients were categorised into two groups: those with LVEF > 50% were grouped as HFpEF and those with LVEF <50% were grouped as HFrEF.

After statistical analysis, a significant negative correlation was found to exist between BNP levels & LVEF in both HFrEF and HFpEF groups (p value <0.002 vs <0.007) which implies that BNP levels increase with increasing severity of heart failure which is reflected by a falling trend of LVEF% (HFrEF). However, the BNP levels in HFpEF group were significantly lower than that in the HFrEF group indicating a diastolic function (poor filling capacity) in these patients. Majority were females (70%) in HFpEF group. This is similar results obtained by authors of some other studies[15]. However, several studies have noticed certain limitations of BNP in the diagnosis of HFpEF. Several other biomarkers like ST2, Galectin-3 etc are emerging which also require further studies to become established markers of HFpEF[16,17].

Conclusion

Around one-third of the patients had Heart Failure with preserved ejection fraction. Females are found to have stable ventricular function than males. A strong negative correlation between BNP levels and LVEF in both Heart Failure with preserved as well as reduced ejection fraction has been noted though less significant in the HFpEF group. Hence, despite certain limitations of BNP, in clinical laboratories which cannot afford expensive tests like ST2, preponderance of female sex, a normal ejection fraction, mild to moderate elevation in BNP levels, a relevant past history along with the signs and symptoms of Heart Failure can go in favour of Heart failure with preserved ejection fraction and aid in the diagnosis of the same.

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