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Original Article

Left Ventricular Diastolic Function in Systemic Hypertension: A Cross-sectional Study

Mohammed Suhel Siddiqui[1], Deepshikha Evane[2], Michel Swett[2], Pavan Diwan[2]

[1]Associate Professor and Head, Department of Cardiology, Superspeciality Hospital, Netaji Subhashchandra Bose Medical College, Jabalpur, Madhya Pradesh, India, [2]Senior Resident, Department of Cardiology, Superspeciality Hospital, Netaji Subhashchandra Bose Medical College, Jabalpur, Madhya Pradesh, India

Abstract

Introduction: Hypertensive patients have impaired left ventricular (LV) relaxation with characteristic changes in LV filling dynamics. About half of the patients with congestive heart failure have preserved LV ejection fraction (LVEF) and isolated diastolic dysfunction, i.e., isolated diastolic heart failure.

Materials and Methods: A cross-sectional study consisting of 100 hypertensive patients attending the cardiology outpatient department and admitted to Cardiology wards of N.S.C.B. Medical College and Hospital, Jabalpur, was undertaken to assess diastolic dysfunction with preserved systolic function using 2D-transthoracic echocardiogram (TTE).

Results: The diastolic dysfunction was seen in almost half of the study cases. There was a slight preponderance of female sex, in this abnormal diastolic function group. Dyspnea on exertion appeared to be the most common presenting symptom and was present in 63% patient of abnormal diastolic function. No correlation was found between the duration of disease and the presence of diastolic dysfunction. There is a positive correlation between the stage of hypertension and prevalence of diastolic dysfunction. Diastolic blood pressure was significantly associated with diastolic dysfunction. LVEF was found to be preserved in all patients in this study. Diastolic dysfunction can easily be detected by non-invasive echocardiography. Abnormality of diastolic function appears early in the course of disease.

Conclusion: Diastolic dysfunction can be a primary cause for cardiac failure and it may also present in asymptomatic and or newly diagnosed hypertensive patients. In view of its early diagnosis by noninvasive 2D-TTE, we can intervene at early course of disease.

Key words: CCF, Diastolic dysfunction, Diastolic heart failure, Hypertension, Transthoracic echocardiogram

INTRODUCTION

Hypertension is one of the most common diseases afflicting humans throughout the world. Because of the associated morbidity and mortality and the cost to society, hypertension is an important public health challenge. Hypertension is the most important modifiable risk factor for coronary heart disease, stroke, congestive heart failure, end-stage renal disease, and peripheral vascular disease. Several clinical studies have reported that 30–50% of patients with congestive heart failure have preserved left ventricular (LV) systolic function and isolated diastolic dysfunction, i.e., isolated diastolic heart failure.[1-3] Preliminary data from the Framingham study indicate that hypertension is the most common underlying cardiovascular disease in patients with isolated diastolic heart failure. Hypertension is postulated to impair diastolic function via multiple mechanisms even without impairment of systolic function.[4,5]

Hypertensive patients have impaired LV relaxation even in the absence of systolic dysfunction and many previous clinical studies have reported characteristic changes in LV filling dynamics[6,7] as decreased peak mitral early diastolic filling wave (E) velocity, increased peak mitral atrial contraction wave (A) velocity, and a decreased ratio of peak mitral E to A velocities (E/A). This altered flow velocity curve is associated with the presence of impaired LV

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Corresponding Author: Mohammed Suhel Siddiqui, Department of Cardiology, Superspeciality Hospital, Nataji Subhashchandra Bose Medical College, Jabalpur, Madhya Pradesh, India.

relaxation[8-11] and the decreased E/A is called an "abnormal relaxation" pattern and has been used as an indicator of diastolic dysfunction in patients with hypertension. This pattern has been described in 30–50% of patients with hypertension with or without preserved systolic function.[12]

Paradoxically, although diastolic function should be more impaired in the presence of more severe and long-standing hypertension associated with marked LV hypertrophy, its traditional index of "abnormal relaxation" does not appear worse, and most studies have not demonstrated a good correlation of this pattern with LV hypertrophy. Thus, the transmitral flow velocity curve may change from the abnormal relaxation pattern into a normal appearing pattern despite the presence of more severe diastolic dysfunction. Such normalization is called "pseudo normalization."

The purpose of this study is to look for the prevalence of LV diastolic dysfunction (LVDD) in hypertensive individuals attending the Cardiology outpatient department (OPD), super specialty hospital NSCB Medical College, Jabalpur to establish the correlation of LV diastolic function with stage of hypertension (according to JNC 7) duration of hypertension and physical findings of patients and to find out prevalence of silent diastolic dysfunction in hypertensive patient. The disease processes that result in diastolic dysfunction affect various components that determine LV filling, Myocardial ischemia delays the energy-dependent deactivation of contractile elements leading to slowed and incomplete ventricular relaxation.[13,14]

MATERIALS AND METHODS

This study was a cross-sectional study and was carried out in the Department of Cardiology, super specialty Hospital, N.S.C.B. Medical College and Hospital, Jabalpur (M.P.), after considering inclusion and exclusion criteria, hypertensive patients were randomly taken from cardiology OPD or ward of Department of Cardiology, N.S.C.B. Medical College and Hospital. A detailed history was taken, clinical examination and investigations were performed as per study protocol in all cases. In this study, a total of 100 hypertensive patients were taken who met selection criteria and provided verbal consent. The duration of the study was from September 2022 to October 2023. All patients with primary hypertension (systolic and/or diastolic) with or without heart failure enrolled in this study. Patients with a history of Type 2 diabetes mellitus and secondary hypertension are excluded from this study.

A detailed clinical history of subjects was taken as per study protocol, each subject underwent a detailed physical examination and systemic examination. A standard 12 lead electrocardiogram was recorded in all subjects to look for any abnormalities. Routine hematological and biochemical investigations including, hemoglobin concentration, blood sugars, blood urea, and serum creatinine were done, 2D echocardiography was done to evaluate LV chamber size and E/A ratio by Pulse wave Doppler study. A history of hypertension given by the patients or relatives which was verified with previous records-OPD tickets, or discharge cards. A history of treatment for hypertension was also included. Newly detected hypertensives were diagnosed on the basis of office blood pressure (BP) recorded in the arms with a Mercury Sphygmomanometer.

Measurement of BP will follow all standard protocols, especially for the patients older than 65 years, receiving antihypertensive therapy, check for postural changes by taking readings after 5 min of supine, then immediately 3 min after standing and for routine follow-up, a patient should sit quietly for 5 min with arm bared and supported at the level of the heart and the back resting against a chair. The patient should have no coffee and should not have smoked within 30 min preceding the readings. The patient should have ingested no exogenous adrenergic stimulants (e.g. phenylephrine in nasal decongestants). Readings were obtained in a quiet, warm setting. Before recording BP apparatus should be checked properly like the bladder cuff should encircle at least 80% of the circumference and cover 2/3rd of the length of the arm, While recording BP number of readings, on each occasion, take at least 2 readings, separated by as much time as is practical, if readings vary by >5 mm of Hg, take additional readings until two readings are close. For diagnosis obtain 3 sets of readings, each at least 1 week apart. Initially, take pressure in both arms, if the pressures differ use the arm with higher pressure. If the arm pressure is elevated, then take the pressure in one leg, particularly in patients younger than 30 years.

Careful BP recording is done by keeping the bell of the stethoscope over the brachial artery (confirm the bell setting by lightly tapping it) and rapidly inflating the cuff to 20–30 mmHg above the systolic BP determined by palpatory method to detect an auscultatory gap. Deflate the cuff at a rate of 2 mmHg/s, listening for phase 1 and phase V (phase IV for children) Korotkoff sound. Phase 1 is the first appearance of any sound and phase V at the disappearance of the sound which is the diastolic BP (DBP) in adults. Listen for 10–20 mm of Hg below phase V for any further sound, then deflate the cuff rapidly and completely and allow the subject to rest for at least 30 s. If Korotkoff sounds are weak, then ask the patient to raise the arm and open and close the hand 5–10 times, then inflate the bladder quickly.

Essential hypertension is the name given to a group of persons whose arterial pressures are raised and in whom no specific disease can be found to account for the raised pressure. It is thus diagnosed by exclusion its clinical manifestations represent the consequences of raised arterial pressure on the cardiovascular system.

In renal artery stenosis, we found considerable elevation of BP developing quickly and is diagnosed by renal artery Doppler study and renal angiography. In chronic pyelonephritis, there is history of recurrent urinary tract infection, and quantitative estimation of white cells and bacteria in urine is noticed. Most importantly, essential hypertension usually represents a more or less gradual rise of pressure with age. Therefore, young adults with gross hypertension nearly always have secondary hypertension. A strong family history of hypertension along with the intermittent finding of elevated pressure in the past favors the diagnosis of essential hypertension. And usually exclude the cause of secondary hypertension.

A qualified cardiologist has performed the trans thoracic echocardiography examination on all subjects, with the subjects in the left lateral position. Two-dimensional and M-mode echocardiography was performed by GE E 90 echocardiography machine. Two-dimensional guided M-mode echocardiography was performed at the parasternal long axis view and apex; left ventricular internal diameter at end-systole and end-diastole as well as IV septum and Posterior wall thickness were assessed in accordance with the recommendations of the American Society of Echocardiography by "leading edge to lead edge" method with patient lying in the left lateral decubitus and slight rotation. LV end-systolic dimension and LV end-diastolic dimension measured in 2D echo at the level of mitral leaflet tips as largest and smallest LV dimensions, respectively. The thickness of the interventricular septum was assessed from parasternal long axis view in 2D echocardiography.

Diastolic dysfunction in hypertension is characterized by impaired early diastolic relaxation, Prolonged isovolumic relaxation time, Reduced E velocity, Reduced E/A ratio, and prolonged deceleration slope. Results of continuous data were presented as mean ± standard deviation. Chi-square analysis was performed on dichotomous categorized data to analyze the association to compare continuous data between two groups of Student's (unpaired) "t" test applied and the Fisher's exact test was used for comparison of categorical data.

RESULTS

A total of 100 hypertensive patients were included in the study. The number of males was 51% and that of females was 49% in this study. The patient's age ranged from 36 to 70 years. Most cases were between 40 and 69 years (92 out of 100) with mean being 54.68 years with a standard deviation of 8.54 years. Males constituted 51% and females 49% of the study. Males constituted 51% and females 49% of the study group.

Out of 49 patients with LVDD, 51% were female and 48.98% were male Out of 51 males 24 (47.06%) were found to have LVDD. In females, 24 (51.02%) out of a total of 49 were found to have LVDD. The prevalence of LVDD was slightly higher (51.02% as compared to 47.06%) in females. The mean systolic BP and DBP in cases were 144.02 ± 7.3 and 89.14 ± 5.82 mmHg, respectively.

Mean systolic and DBP both was found to be higher in patients with diastolic dysfunction. However, diastolic dysfunction was found to be significantly associated with high DBP ($P < 0.0001$) but not with high systolic BP. The duration of hypertension ranges from 3 months to 7 years. With 54 patients were newly detected hypertensives. Most of the patients with LVDD were new patients (30 out of 49, i.e., 61.22%). Percentage prevalence of diastolic dysfunction increased with stages of hypertension with maximum prevalence in patients with stage II hypertension (81.25%) t = 2.6583, $P = 0.0092$. The thickness of the interventricular septum was significantly increased in patients with diastolic dysfunction, X2 = 30.44, $P < 0.0001$.

The presence of the left ventricular hypertrophy (LVH) was significantly associated with diastolic dysfunction. A significant difference of the internal diameter of the left ventricle was observed among asymptomatic patients with and without diastolic dysfunction. All internal diameters of the left ventricle were found to be significantly lower in asymptomatic patient with diastolic dysfunction. E/A ratio were also found to be significantly lower in asymptomatic patient with diastolic dysfunction.

DISCUSSION

Hypertension is one of the most common diseases afflicting humans throughout the world. After considering inclusion and exclusion criteria we have taken 100 hypertensive patients in this study. After detailed history and clinical examination, all patients were subjected to a complete 2D echocardiography evaluation. Diastolic function was assessed by transmitral flow velocity curves and E/A ratio. There were 100 hypertensive patients in our study with 51% male and 49% female patients. This male preponderance is comparable with previous studies. Patients' age ranges from 36 to 70 years with most of the patients 92% belongs to 40–69 years of age group. The mean age of our study group

was 54.68 ± 8.54 years. This was comparable to the mean age of cases in studies Mottram *et al.*[15,16] (58.18 years), Yamamato *et al.*[17] (69.16 years),[18] (54.48 years), and Adewole *et al.*[18] (59 ± 10.4 years).

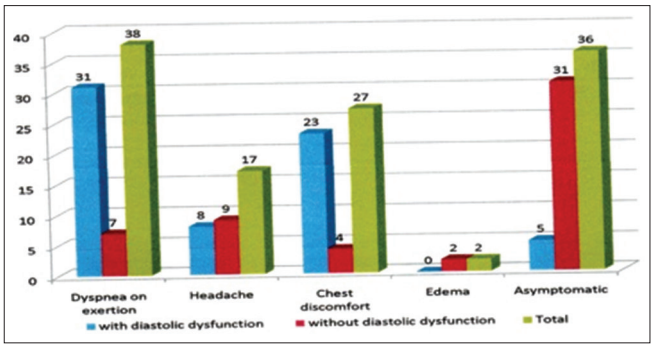
All previous studies have a mean age more than 50 years and our observation is consistent with above mentioned studies. The overall prevalence of diastolic dysfunction in our study was 49% (49 out of 100). Mottram *et al.*[15] had found prevalence of 52.87% (37 out of 70), while Rusconi *et al.*[19] had found the prevalence of 51% in their study. In another study carried out by Mohamed *et al.*[20] the prevalence of diastolic dysfunction was found to be 44% (22 out of 50).

Mottram *et al.*[15] had found that female sex was an independent predictor of diastolic dysfunction. In their study, they found female predominance, although insignificant, in the diastolic dysfunction group (22 females, i.e., 59.46% out of 37 patients of diastolic dysfunction). In our study, there was a slight preponderance of female with diastolic dysfunction (female 51.02% vs. male 48.98%).

Our observation was comparable with above-mentioned study. In our study, there was 54% newly diagnosed hypertension patient. Among previously diagnosed patients duration of hypertension ranged from 1 month to 7 years. Diastolic dysfunction was present in 61.22% newly diagnosed (30 out of 54) and 41.3% (19 out of 46) previously diagnosed patients. However, the inference was not statistically significant as there were a substantial number of patient who was newly diagnosed. Giuseppe Schillaci *et al.*[21] also did not find any significant correlation between the duration of hypertension and reduced E/A ratio in individuals in their study. In their prospective follow-up study on 1839 hypertensive patients with average follow-up period of 4.4 + 2 years (range: 1.0–10.8 years), they had found a significant correlation between reduced E/A ratio and increased cardiovascular events but there was no significant difference of duration of hypertension between normal and reduced E/A ratio group. In another study conducted by Masliza *et al.*[22] in 2005 found 18.6% prevalence of diastolic dysfunction in newly diagnosed hypertension patients. This marked difference of the prevalence of diastolic dysfunction in newly diagnosed patients may be due to younger population group (mean age 43.115.7 years) in their study.

Dyspnea on exertion (NYHA I) and chest discomfort in the form of chest tightness, non radiating/radiating chest pain were appear to be the most common symptoms in patients with diastolic dysfunction.

The underlying path physiological abnormality in diastolic dysfunction is impaired relaxation of the left ventricle

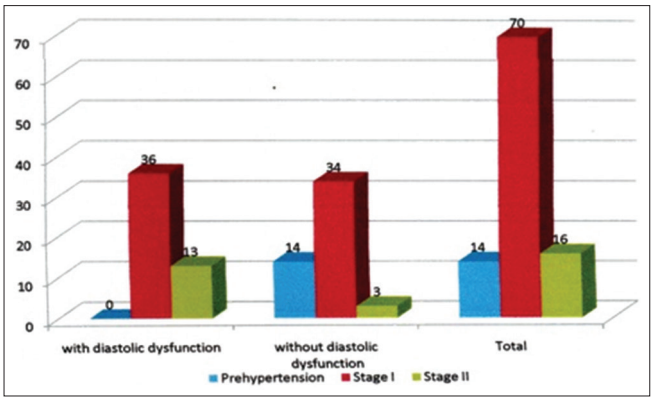


resulting in reduced LV compliance. This reduced compliance causes inadequate filling of the left ventricle at normal diastolic pressures. Therefore, to maintain LV filling and cardiac output, left atrial pressure must increase to a level that creates a pressure gradient great enough to provide adequate ventricular filling. Not uncommonly, this elevation of the left atrial pressure will be transmitted into the pulmonary vascular system leading to pulmonary congestion and shortness of breath.[23,24]

Out of 49 patients with diastolic dysfunction, 31 (61.22%) presented with dyspnea and 23 (46.94%) patients with chest discomfort. Most of the patient with diastolic dysfunction has more than 1 symptom on presentation. This is comparable with various previous studies in which dyspnea appeared as the most common presenting symptom (ranging from 35% to 50%). In our study, 36 (36%) patients were asymptomatic out of these 36 patients, 5 (13.9%) patients had diastolic dysfunction. In Cleveland clinical study by Halley *et al.*, 2011, (11.2%) of patients had an abnormal diastolic function. In mayo clinical survey by Redfiled *et al.*[25] in 2003, the prevalence of abnormal diastolic function was 29%. Our observations were consistent with these studies.

Both systolic and DBP was higher in patient with abnormal diastolic function. However, only a high level of DBP was found to be significantly associated with abnormal diastolic function. Mottram *et al.* had also found DBP to be significantly associated with diastolic dysfunction a finding similar to our study. Our study did not find any association between abnormal E/A ratio and duration of hypertension and systolic BP. No other study except Masliza *et al.*'s[22] study had found an association between systolic BP, duration of hypertension, and diastolic dysfunction. The percentage prevalence of diastolic dysfunction increased with stages of hypertension with maximum prevalence in patients with stage II hypertension.

Diastolic dysfunction as defined by E/A ratio was found to be abnormal in 49% of patients in our study. E/A ratio observed in our study was significantly lower in patients



with abnormal diastolic function. (Abnormal E/A ratio; 1.49 ± 0.27 vs. 1.33 ± 0.33) were significantly lower in patients with abnormal diastolic function. Masliza *et al.*[22] found abnormal E/A ratio in only 18.6% of their cases. This could be due to lesser duration of hypertension in their cases. In Masliza's 103 study, all subjects were newly diagnosed hypertensives (duration <6 months), whereas in our study 54% of patients were newly diagnosed.

Internal diameters of the left ventricle during systole and diastole are reflective of both systolic and diastolic function. LVEDD and LVESD in patients with normal diastolic function and with abnormal diastolic function was 4.38 ± 0.52, 4.42 ± 0.44, and 3.23 ± 0.51, 3.26 ± 0.45, respectively, in this study. Although both dimensions were lower in patient with abnormal diastolic function, their association with diastolic dysfunction had found to be not significant in our study.

Echo parameter	Diastolic dysfunction		*P*-value
	Present (mean±SD)	Absent (mean±SD)	
LVEDD (cm)	4.38±0.52	4.42±0.44	0.678
LVESD (cm)	3.23±0.51	3.26±0.45	0.755
LA (cm)	2.53±0.33	2.41±0.31	0.064
IVS (cm)	1.37±0.23	1.19±0.12	0.0001*
EF (%)	59.76±5.90	60.41±5.68	0.576

IVS: Interventricular septum, LVEF: LV ejection fraction

However, both these dimensions were significantly reduced in asymptomatic patients with diastolic dysfunction in our study. This reduced dimension in asymptomatic patients may reflect the role of impaired relaxation and restrictive filling during diastole in respective patients. Increased thickness of interventricular septum s/o LVH was 1.37 ± 0.23 and 1.19 ± 0.12 in patients of abnormal and normal diastolic function respectively, found to be significantly higher in patient with diastolic dysfunction. In their study Mottram *et al.* also found LVH to be positively associated with diastolic dysfunction. A similar correlation was found in study by Giuseppe Schillaci *et al.*[21]

Increased thickness of interventricular septum (IVS) was found as a major pathophysiologic abnormality for diastolic dysfunction in newly diagnosed hypertension patients in our study. This association may be due to long subclinical course of disease in hypertensive patient. Patient with diastolic heart failure has preserved ejection fraction, in our study, all patients had LV ejection fraction (LVEF), calculated from LVEDD and LVESD, within normal limits and there was no significant difference in ejection fraction between patient with normal and abnormal diastolic function.

CONCLUSION

In this study, total of 51% were male and 49% were females and the mean age of subjects was 54.68 ± 8.54 years. The diastolic dysfunction was seen in almost half (49%) of cases. There was a slight preponderance of female sex (51.02% as compared to 48.98%) in this abnormal diastolic function group. Thirty out of 54 (55.55%) newly diagnosed hypertensive had diastolic dysfunction. Dyspnea on exertion was appeared to be the most common presenting symptom, and was present in 63% patient of abnormal diastolic function, no correlation was found between duration of disease and presence of diastolic dysfunction. There is a positive correlation with stage of hypertension and percentage prevalence of diastolic dysfunction. DBP was significantly associated high with diastolic dysfunction.

LVEF was found to be preserved in all patients in this study. All LV internal diameters were less in patient with diastolic dysfunction. Increased thickness of IVS (suggestive of LVH) was significantly associated with diastolic dysfunction. Diastolic dysfunction can be a primary cause for cardiac failure but it may also precede an impairment of LV systolic function. In view of its early diagnosis by noninvasive 2D-echocardiography and the availability of effective treatment with ARB's and Beta-blockers, diastolic function assessment should be a routine in hypertensive patients so that we can intervene at more early and appropriate time in the course of disease.

Diastolic dysfunction can easily be detected by noninvasive echocardiography. Abnormality of diastolic function appears early in the course of the disease, even can be present in asymptomatic patient. The use of E/A ratio for the measurement of diastolic function has some limitations. Ideally, measurements of pulmonary venous flow or tissue-Doppler imaging should be performed to identify patients with pseudonormalisation pattern. The study included patients who were on medications, diastolic function may be affected by medications as has been shown in several previous studies and this may affect the prevalence of diastolic dysfunction in the hypertension.

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