ASSESSMENT OF DIASTOLIC FUNCTION BY COMBINED TRNSMITRAL AND PULMONARY VENOUS FLOW VELOCITY CURVES

Nagabhushana S¹, Ranganatha M², Amith Kumar³, Virupakshappa⁴

HOW TO CITE THIS ARTICLE:

Nagabhushana S, Ranganatha M, Amith Kumar, Virupakshappa. "Assessment of Diastolic Function by Combined Transmitral and Pulmonary Venous Flow Velocity Curves." Journal of Evolution of Medical and Dental Sciences 2014; Vol. 3, Issue 14, April 07; Page: 3815-3830, DOI: 10.14260/jemds/2014/2363

ABSTRACT: BACKGROUND: Several clinical studies have reported that 30% to 50% of patients with congestive heart failure have preserved left ventricular systolic function and isolated diastolic dysfunction. Detection of diastolic dysfunction is important factor in cardiac evaluation of hypertensives. **MATERIAL AND METHODS:** retrospective study carried out in Medicine department, SIMS, Shimoga for one year from Jan 2013 to Jan 2014. 50 patients who are hypertensive without any abnormality were studied general and systemic examination done, 2d echocardiography done in which transmitral flow velocity (E/A) and pulmonary venous A duration- mitral A duration (Δd) is measured. **RESULT:** 32% of subjects were newly diagnosed hypertensives in our study. 56% of cases had normal diastolic function as defined by E/A ratio (>1), 18% of cases in our study with normal E/A ratio were found to have pseudonormal pattern of diastolic function. LVDD of 62% is found in this study. CONCLUSION: The abnormal diastolic function as assessed by abnormal E/A ratio was seen in 44% of cases. Abnormal Δd was found in 18% of cases out of 56% who had normal E/A ratio. These cases are said to have 'pseudonormal' pattern of diastolic function. The current study demonstrated that the presence of LV diastolic dysfunction in hypertensive patients is actually greater than previously reported by studies that analyzed transmitral flow velocity curves alone. To avoid overlooking patients with diastolic dysfunction, the combined analysis of transmitral and pulmonary venous flow velocity curves is recommended.

KEYWORDS: Diastolic function, pseudonormal pattern, E/A ratio, echocardiography.

INTRODUCTION: Hypertension i.e. high blood pressure has been an enigma that has attracted scientific mind from time immemorial. Over the past decade, progress in understanding of hypertension has proceeded at an unprecedented rate, with developments in a wide spectrum of scientific fields ranging from epidemiology to molecular biology, providing new insights into its mechanisms and management. Yet, many issues remain unresolved, and in particular, diastolic dysfunction of the heart still remains "a riddle inside an enigma"

Several clinical studies have reported that 30% to 50% of patients with congestive heart failure have preserved left ventricular systolic function and isolated diastolic dysfunction, i.e. isolated diastolic heart failure.¹⁻³ Preliminary data from 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}

Left ventricular filling dynamics can be accurately assessed invasively in the cardiac catheterization laboratory using manometer-tipped catheters placed in the left ventricle with direct measurement of filling pressures. However, due to the invasive nature, high cost, and limited availability of laboratories, invasive approach to assess diastolic dysfunction remains impractical for

widespread use. Therefore currently only noninvasive methods are being used to assess LV filling dynamics, with pulsed doppler echocardiography, and by the pulsed doppler transmitral flow velocity curve which has a biphasic pattern, with early diastolic wave (mitral E wave) and atrial contraction wave (mitral A wave).

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 as^{6,7} 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 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 % to 50 % of patients with hypertension with or without preserved systolic function.^{12, 13} Paradoxically, although diastolic function should be more impaired in the presence of more severe and long standing hypertension associated with marked L V 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. A reasonable explanation for this paradox has evolved with use of doppler echocardiographic assessment of diastolic function. More advanced hypertensive heart disease is likely to be associated with reduced LV compliance as well as impaired relaxation, resulting in an elevation of LV filling pressure and an increase in E\A.

Thus, the transmitral flow velocity curve may change from the abnormal relaxation pattern into a normal-appearing pattern in spite of the presence of more severe diastolic dysfunction. Such normalization is called "pseudonormalization". If diastolic function of LV is assessed with transmitral flow velocity curve alone, both patients with truly normal pattern and those with pseudonormal pattern are recognized to have normal diastolic function, and the presence of diastolic dysfunction among many patients will remain unrecognized.

The current study was designed to assess prospectively diastolic dysfunction in hypertensive patients with preserved left ventricular function by combined transmitral flow velocity curve and pulmonary venous Doppler analysis, particularly focusing on the limitation of the transmitral flow velocity curve alone to detect diastolic dysfunction.

TREATMENT: The treatment of patients with diastolic dysfunction remains problematic. Therapy should focus on the management of the underlying disease process (hypertension). However, control of symptoms and relief of precipitating factors are also very important. Treatment of underlying systemic hypertension is important in regression of left ventricular hypertrophy and improvement in diastolic dysfunction. However, studies showing that this improvement leads to improved symptoms and prognosis in these patients are lacking.

The mainstay of pharmacologic therapy for patients with diastolic heart failure includes diuretics, nitrates, calcium channel blockers (CCBs), beta-blockers (BBs) and angiotensin-converting enzyme inhibitors (ACEI). Diuretics are useful in relieving symptoms of pulmonary congestion. However, as these patients rely on higher filling pressures to maintain cardiac output, overdiuresis can reduce stroke volume and cardiac output, leading to fatigue, postural hypotension, and renal failure. Nitrates may be useful in enhancing relaxation by reducing right ventricular pressure and

volume, leading to reduced pericardial restraint and improved LV filling.¹⁴ As well, animal models have shown an improvement in LV relaxation with endogenous nitric oxide.¹⁵ The negative inotropic and chronotropic properties of the CCBs make them likely to be effective in treating diastolic dysfunction. Studies have yielded conflicting results with many showing improved relaxation, ^{16, 17} but others showing no change in the rate of relaxation.¹⁸

BBs have no direct effects on myocardial relaxation; however, they may be effective by slowing heart rate and reducing myocardial demand and ischemia. ACEI have not been as well studied, but may hold some promise¹⁹, they may be particularly effective in the settings of hypertension with left ventricular hypertrophy and in the situation of concomitant systolic dysfunction.²⁰

Other general therapy includes simple dietary measures such as salt and fluid restriction and heart rate control in situations of tachycardia. The maintenance of sinus rhythm and atrioventricular synchrony is very important, atrial fibrillation being poorly tolerated in these patients and a common precipitating cause of diastolic heart failure. Most of these therapeutic recommendations for treating diastolic heart failure are empirical and based on the results of small clinical studies with surrogate endpoints. There are, as yet, no randomized, controlled clinical trials evaluating the effects of these treatments on patient outcomes and prognosis.

Normal Range.^{21, 22}

LVIDd	:	3.6 to 5.4 cms.
LVIDs	:	2.4 to 4.2 cms.
EF (ejection fraction)	:	\geq 50%
DT	:	<220 msec
E/A	:	>1

AIMS AND OBJECTIVES: To assess diastolic dysfunction in hypertensive patients with preserved left ventricular systolic function by combined transmitral flow velocity curve and pulmonary venous Doppler analysis, particularly focusing on the limitation of the transmitral flow velocity curve alone to detect diastolic dysfunction.

MATERIALS AND METHODS:

STUDY DESIGN: This was a retrospective study where hypertensive patients attending the outpatient department of mc gann hospital attached to Shimoga Institute of Medical Science, were selected randomly for enrollment into the study, after consideration of inclusion and exclusion criteria. A detailed history was taken, clinical examination and investigations performed in all cases.

STUDY SUBJECTS: A total of 50 patients diagnosed to have hypertension with preserved systolic function (EF > 50%) were studied from January 2013 to January 2014.

Informed consent was taken from all the study subjects.

In cases investigations were done in the clinical biochemistry laboratory of mc gann hospital. Echocardiographic studies were performed by anon interventional cardiologist.

INCLUSION CRITERIA: Ambulatory asymptomatic patients diagnosed to have hypertension (BP> 140/90 mmHg, average of two recordings taken at two separate occasions).

EXCLUSION CRITERIA:

Patients with ischemic heart disease with or without symptoms. Patients with stroke within previous 6 months. Patients with congestive heart failure. Patients with atrial fibrillation. Patients with severe hypertension BP> 200/140. Patients with valvular heart disease. Patients with Diabetes mellitus. Patients with serum creatinine>1.5 mg/dl.

METHODOLOGY: A detailed clinical history of subjects was each subject underwent a detailed physical examination& systemic examination.

A standard 12 lead ECG 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.

Echocardiography: A qualified cardiologist performed the transthoracic echocardiographic examination on all subjects, with the subjects in the left lateral position. Two-dimensional and M-mode Echocardiography was performed on Hewlett Packard SIM 7000 using 3.5 MHz transducer. Blood pressure and heart rate were measured at the time of echocardiography. Ejection fraction was calculated by measuring the internal diameter of left ventricle (LV) at the end diastole (LVIDd) & at the end systole (LVIDs) using the Penn convention method.

Two-dimensional and two-dimensional guided M-mode echocardiograms and pulsed Doppler transmitral and pulmonary venous flow velocity curves were obtained. The transmitral flow velocity curves were recorded with the sample volume at the mitral tips, and the pulmonary venous flow velocity curves were recorded with the sample volume 1 to 2 cm into the right superior pulmonary vein using the guidance of color flow doppler imaging with the transducer placed at the cardiac apex. The averaged values of all echocardiographic parameters of at least 3 consecutive beats were used for the analysis. Doppler velocity curves were recorded at a horizontal sweep speed of 100mm/s.

Left ventricular diastolic dysfunction was assessed by decreased E/A ratio (transmitral flow velocity curve). Normal E/A ratio was defined as E/A ratio \geq 1. Abnormal E/A ratio was defined as E/A ratio <1.

Further echocardiographic evaluation was done to look for "pseudonormalization" defined as E/A ratio ≥ 1 and pulmonary venous A duration- mitral A duration (Δd) ≥ 0 .

In simple terms pseudonormalization was considered to be present when E/A ratio was normal but Δd was abnormal. Pulmonary venous A wave was determined by pulmonary venous flow velocity curves.

E deceleration time [E (dt)] and Pulmonary venous A wave amplitude (Pva) were the other values calculated.

STATISTICAL METHODS: Chi-square and Fisher Exact test were used to find the significance of proportions of diastolic dysfunction with various study parameters. Odds ratio was used to find the strength of relationship between the study parameters and diastolic dysfunction. The Student 't' test has been used to find significance of mean pattern of study parameters between cases and controls. Analysis of variance has been used to find the significance of Echo parameters between the categories of diastolic dysfunction.^{23, 24}

- 1. Chi-Square Test.^{23,24}
- 2. Fisher Exact Test.^{23,24}
- 3. Odds ratio= ad/bc
- 4. Student t test.^{23,24}
- 5. Analysis of Variance: F test for K Population means.^{23, 24}

Statistical Software: The Statistical software namely SPSS 11.0 and Systat 8.0 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc.

ANALYSIS OF RESULTS:

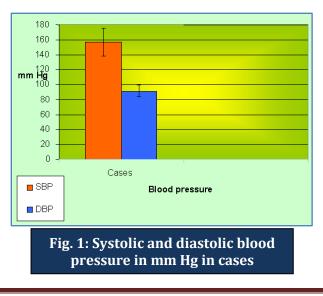
DEMOGRAPHICS: A prospective cross sectional study consisting of 50 hypertensive cases attending the outpatient departments of mc gann hospital was undertaken to assess diastolic dysfunction with preserved systolic function using echocardiography.

A total of 50 hypertensive patients were included in the study. The number of males was 29 (58%) and that of females was 21 (42%). The patient's age ranged from 23 to 64 years (Table 1). Fifty age and sex matched healthy controls were also evaluated to obtain the normal E/A ratio values in different age groups.

Blood pressure Cases (n=50) Mean \pm SI		
SBP in mm Hg	152.86±16.56	
DBP in mm Hg 90.34±8.67		
Table 1: Mean blood pressure in cases		

SBP: Systolic blood pressure.

DBP: Diastolic blood pressure.



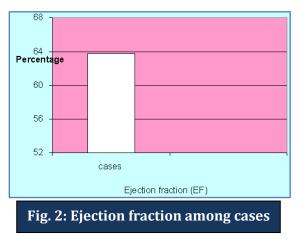
The mean systolic blood pressure and diastolic blood pressure in cases was 152.86±16.56 and 90.34±8.67 mmHg respectively (Table 1).

Echo parameters	Cases (n=50) Mean \pm SD	
EF %	62.56±3.67	
LVIDS (cms)	2.67±0.47	
LVIDD (cms) 4.57±0.65		
Table 2: Echo parameters of cases		

EF: ejection fraction

LVIDS: left ventricular internal diameter systolic.

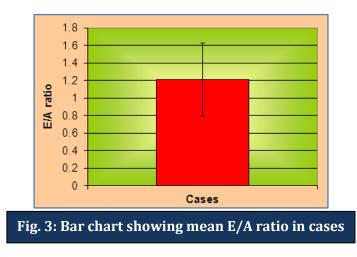
LVIDD: left ventricular internal diameter diastolic.



Ejection fraction was normal (>50%) in cases (Table 2).

E/A ratio	Cases (n=50)	
Range	0.58-2.74	
Mean ± SD 1.32±0.57		

Table 3: Comparison of E/A ratio of cases



The E/A ratio ranged from 0.5 to 2.74 in cases with a mean of 1.32 ± 0.57 . In E/A ratio was significantly lesser in cases, when compared to normal (>1) (p=0.001) (Table 3).

Diastolic function defined by E/A ratio	Number (n=50)	%	E/A Mean± SD
Normal E/A ratio	28	56.0	$1.66{\pm}0.66$
Abnormal diastolic function (E/A abnormal)	22	44.0	0.78± 0.17
Table 4: Diastolic dysfunction defined by E/A ratio in cases			

E/A ratio normal- E/A ratio \geq age and sex adjusted mean value -2SD.

E/A ratio abnormal- E/A ratio < age and sex adjusted mean value -2SD.

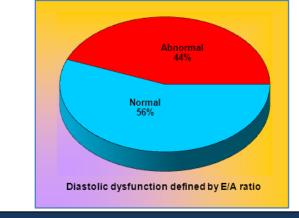


Fig. 4: Pie chart showing diastolic dysfunction defined only by E/A ratio

Fifty six percent of cases had normal diastolic function as defined by E/A ratio, as compared to 44% who had abnormal diastolic function. E/A ratio was significantly lower in cases who had abnormal diastolic function as compared to cases who had normal diastolic function (P<0.001) (Table 4).

Diastolic dysfunction defined by Δd ratio	Δd	
	Mean± SD	
Normal diastolic function(19)	-36.10 ± 23.59	
(E/A- normal, ∆d- normal)	-30.10 ± 23.39	
Pseudo normal (9)	51.78 ± 17.67	
(E/A –Normal, ∆d- abnormal)	51.70 ± 17.07	
Abnormal diastolic function(22)	-36.09 ± 22.57	
(E/A abnormal, ∆d- normal)	-30.09 ± 22.57	
Table 5: Diastolic dysfunction defined by Δd		

Cases who had normal diastolic function as defined by normal E/A ratio values were further analyzed with regard to Δd (pulmonary venous A wave duration- mitral A wave duration), whose value if more than or equal to '0' indicated diastolic dysfunction. Out of 56% of cases with normal diastolic function (defined by E/A ratio), Δd was found to be abnormal in 18% (9 cases). These

J of Evolution of Med and Dent Sci/eISSN-2278-4802, pISSN-2278-4748/Vol. 3/Issue 14/Apr 07, 2014 Page 3821

patients would have been characterized as having normal diastolic function if E/A ratio was used alone. Thus estimation of Δd resulted in detection of 9 more cases of diastolic dysfunction. This group of cases with normal E/A ratio but abnormal Δd was considered to be having "pseudo normal pattern" of diastolic dysfunction. The mean E/A ratio of pseudo normal group was 1.55 ± 0.16, was comparable with the group which had normal diastolic function (1.51 ± 0.23), but was significantly higher than the group which had abnormal diastolic function (0.80 ± 0.22) (p< 0.001).

Diastolic dysfunction defined by E/A	Number	%	E/A Mean± SD	
Normal diastolic function (E/A- normal, ∆d- normal)	19	38	1.51 ± 0.23	
Pseudo normal (E/A –Normal, ∆d=abnormal)	9	18	1.55 ± 0.16	
Abnormal diastolic function (E/A abnormal, Δd- normal)	22	44	0.78 ± 0.17	
Total 50 100 1.21±0.42				
Table 6: E/A ratio in cases with normal, pseudo normal				
and abnormal diastolic function				

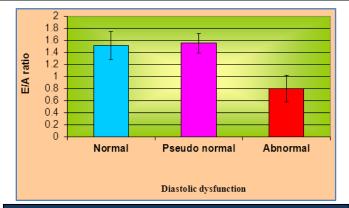
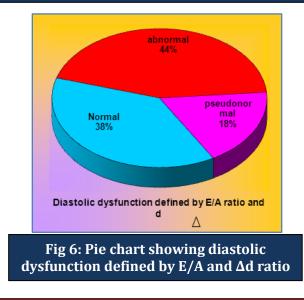


Fig 5: Bar chart showing E/A ratio values in normal, pseudonormal and abnormal groups



Sixty two percent of cases had diastolic dysfunction as defined by abnormal E/A ratio and Δd (Table 14).

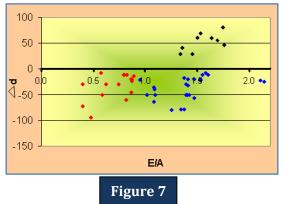


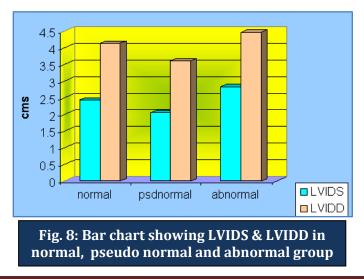
Figure 7: Relation between E/A ratio and Δd in cases with normal diastolic function (blue), cases with pseudo normal pattern (black) and cases with abnormal diastolic function (red).

Among all the cases E/A ratio was normal in 19 cases. Twenty two cases had E/A ratio less than age adjusted normal range indicating abnormal diastolic function. Nine cases had pseudo normal pattern (E/A normal, Δd abnormal).

Echo parameters	Normal	Diastolic dys	function	
Mean \pm SD	diastolic function	Pseudo normal	Abnormal	p value
(Min-Max)	(n=19)	(n=9)	(n=22)	
Ejection Fraction %	63.26±4.47 (56-72)	61.33±1.58 (59-64)	65.09±4.63 (58-74)	0.075
LVIDS	$2.44{\pm}0.30$	2.05 ± 0.51	$2.84{\pm}0.47$	0.000
	(2.00-3.00)	(1.30-2.70)	(2.10-3.50)	0.000
ממועד	4.13±0.38	3.61±0.74	4.47 ± 0.47	0.000
LVIDD	(3.50-4.90)	(2.60-4.60)	(3.40-5.10)	0.000
Table 6: Echo parameters in cases with diastolic dysfunction				

LVIDS: left ventricular internal diameter systolic.

LVIDD= left ventricular internal diameter diastolic.



Ejection fraction was normal among all groups of cases. Both LVIDS and LVIDD were maximum in the group with abnormal diastolic function and minimum in the group with pseudo normal pattern. Both values were statistically significant (p=0.000 for each). This was indicative of restrictive filling pattern of LV due to decreased compliance (Table 6).

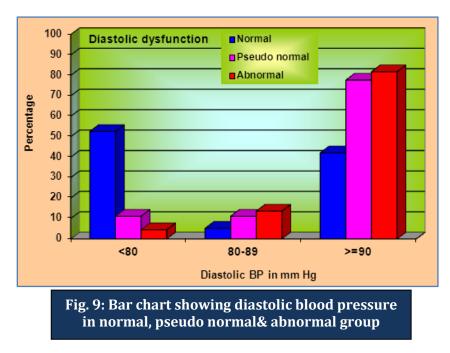
	Normal Diastolic dysfu		function
Duration of hypertension	diastolic function	Pseudo normal	Abnormal
	(n=19)	(n=9)	(n=22)
\leq 6 months	6 (31.5%)	3 (33.3%)	7 (31.8%)
6-12 months	5(26.3%)	2(22.2%)	3 (13.6%)
>12 months	8(42.1%)	4(44.4%)	12 (54.5%)
Table 7: Correlation of Diastolic dysfunction with duration of hypertension			

Cases with diastolic dysfunction are more likely to have hypertension more than 12 months (odds ratio-1.46). In cases with pseudo normal pattern, duration of hypertension was more likely to be more than 6 months (64% of cases) (Table 7).

Systolic BP	Normal	Diastolic dysfunction		odds ratio
in mm Hg	diastolic function	Pseudo normal	Abnormal	ouusiatio
III IIIII IIg	(n=19)	(n=9)	(n=22)	
≤ 140	7(36.8%)	1 (11.1%)	4 (18.1%)	0.32
140-159	6(31.6%)	3 (33.3%)	7 (31.8%)	1.03
160-179	5(26.3%)	2 (22.2%)	8 (36.3%)	1.33
≥180	1(5.3%)	3(33.3%)	3 (13.6%)	4.32
Table 8: Systolic blood pressure in cases with diastolic dysfunction				

With progressive rise in systolic blood pressure there was an increased tendency to develop diastolic dysfunction [odds ratio- $0.32(SBP \le 140)$ to 4.32 (SBP ≥ 180)].

Diastolic BP	Normal	Diastolic dys	p value	
in mm Hg	diastolic function	Pseudo normal	Abnormal	p value
8	(n=19)	(n=9)	(n=22)	
<80	10(52.6%)	1(11.1%)	1 (4.5%)	0.001
80-89	1 (5.2%)	1(11.1%)	3 (13.6%)	0.637
≥90	8(42.1%)	7 (77.7%)	18 (81.8%)	0.005
Table 9: Diastolic blood pressure in hypertensive patients with diastolic dysfunction				



Both diastolic blood pressures <80 &≥90 mm Hg were significantly associated with diastolic dysfunction (Table 9).

Diastolic dysfunction	No. of patients with LVH		
Normal (19)	3 (16%)		
(E/A- normal, ∆d- normal)	5 (10%)		
Pseudo normal (9)	2 (220%)		
(E/A –Normal, ∆d=abnormal)	2 (22%)		
Abnormal (22)	E (2204)		
(E/A abnormal, ∆d- normal)	5 (23%)		
Table 10: Diastolic dysfunction in relation to left ventricular hypertrophy (LVH)			

There was no association between LVH and diastolic dysfunction.

DISCUSSION: The aim of our study was to assess the diastolic function in hypertensive patients with preserved left ventricular function by combined transmitral flow velocity curve and pulmonary venous Doppler analysis, particularly focusing on the limitation of the transmitral flow velocity curves alone to detect diastolic dysfunction.

This retrospective cross-sectional study was done on a relatively homogeneous and ambulatory hypertensive population.

Subjects in our study underwent echocardiographic examination where diastolic function was assessed by transmitral flow velocity curves and E/A ratio [ratio of mitral early diastolic filling wave (E) velocity to mitral atrial contraction wave (A) velocity].

In our study, an E/A ratio value of 1.0 was arbitrarily chosen as the lower limit to detect impaired relaxation like in other study²⁵. the values for the E/A ratio observed in our impaired relaxation group (abnormal E/A ratio; 0.78 ± 0.17) were significantly lower than the normal value.

Majority of cases in our study were males (58%). A similar male preponderance was noted in several earlier studies.²⁶⁻²⁹

Diastolic dysfunction as defined by E/A ratio was found to be abnormal in 44% of cases in our study. Mottram et al²⁶had found abnormal E/A ratio in 40% of their patients which is comparable to our finding. Other investigators have found a lower proportion of cases with abnormal E/A ratio in their study group.

Yamamato et al²⁷ found abnormal E/A ratio in 31% of their cases, which may be due to lower mean DBP in their cases as compared to our study (74 v/s 91 mm Hg). Masliza et al³⁰ Found abnormal E/A ratio in only 18.6% of their cases. In Masliza's³⁰study all subjects were newly diagnosed hypertensives (duration less than 6 months), whereas only 32% of subjects were newly diagnosed hypertensives in our study.

PSEUDONORMAL GROUP: Cases with normal E/A ratio were further evaluated for pseudonormal pattern of diastolic function defined by Δd , an indicator of LV filling and diastolic function. Eighteen percent of cases in our study with normal E/A ratio were found to have pseudonormal pattern of diastolic function i.e. normal E/A ratio but abnormal Δd . Other studies which have looked for diastolic function by Δd have found results similar to ours. Pseudo normal pattern was found 23% in Yamamato's²⁷study and 13% inMottram's²⁶study.

Internal diameters of left ventricle during systole and diastole are reflective of both systolic and diastolic function. Both LVIDD and LVIDS were significantly higher in abnormal diastolic function group and significantly lesser in patients with pseudo normal pattern of diastolic function. Although both group of cases had diastolic dysfunction of varying degree, increased LVIDD and LVIDS signify dilatation of LV and decreased LVIDD and LVIDS signify reduced compliance of LV. Earlier studies have not evaluated LVIDS and LVIDD in three groups of diastolic function.

Diastolic BP level \geq 90 mmHg was significantly associated with diastolic dysfunction. Mottram et al²⁶ have also found, elevation in diastolic blood pressure to be significantly associated with diastolic dysfunction. Indeed the study considered the diastolic BP to be an independent risk factor for diastolic dysfunction. Diastolic blood pressure is dependent on peripheral resistance and increases afterload of the heart. Increased afterload may promote myocyte hypertrophy and may also directly slow LV relaxation and contribute to diastolic dysfunction. Our study also found correlation between DBP< 80 mmHg and normal diastolic function (p=0.001). This has not been shown by previous studies.

Although earlier studies had found correlation between left ventricular hypertrophy and diastolic dysfunction, ³¹ recent studies including our study have not confirmed the association. Masliza et al³⁰ also did not find correlation between LVH and diastolic dysfunction and have suggested that a compensatory physiological mechanism in response to pressure load during early hypertension even before onset of demonstrable LVH may be the cause for diastolic dysfunction.^{32,33,34}

The major finding of this study was that LV diastolic dysfunction is much more prevalent than previously suggested (62% of the hypertensive population studied), in subjects with hypertension

who were free of clinically detectable heart disease. In addition to revealing a prevalence of LVDD of 62%, this study also unmasked a significant number of subjects (18%) with a pseudo normal pattern of diastolic filling by use of Δd for evaluation of diastolic dysfunction similar to previous studies.Mottram²⁶andYamamato²⁷have found abnormal diastolic function to be present in 53% and 55% of cases respectively comparable to our study.

Indeed, if we had classified subjects with a pseudo normal pattern as subjects with a normal pattern of left ventricle filling, the prevalence in the present study for LVDD would have decreased by 18%. The recognition of the pseudo normal pattern is all the more important because it is considered an intermediary stage between impaired relaxation and restrictive filling.

Clinical Implications: The current findings have potential relevance in clinical practice for evaluation of hypertensive patients as diastolic dysfunction may be an early manifestation of cardiac involvement in hypertension.² Most echocardiographic laboratories perform limited analysis of diastolic function. Indeed, many perform only the mitral inflow analysis and report diastolic function as normal in the presence of a normal appearing mitral inflow signal. The referring clinician must be aware that a normal transmitral flow velocity curve does not necessarily indicate normal diastolic function. Therefore the use of Δd to detect pseudonormal pattern of diastolic dysfunction is important. Whether the presence of diastolic dysfunction should alter the approach to therapy in the hypertensive patients is yet to be examined clinically, studies have shown that anti-hypertensive such as ACE inhibitors may be more useful in this condition.

The presence of diastolic dysfunction also provides an additional evidence of end-organ damage.³⁵ The frequency of isolated diastolic heart failure in elderly hypertensive patients suggests that asymptomatic hypertensive patients with diastolic dysfunction may be at risk of progression to diastolic heart failure. More longitudinal studies of hypertensive patients with evidence of diastolic dysfunction are needed to determine the predictive value of these noninvasive indicators of diastolic dysfunction.

Study limitations: Our study group consisted of small homogeneous group of hypertensives. As echocardiographic examination could be performed in lesser number of patients than was desirable. Hence, the prevalence of LV diastolic dysfunction obtained in the current study may not be identical when applied to a larger or different population of hypertensives, and a future study with larger population may be required.

The study included patients who were on medications. Diastolic function may be affected by medications as has been shown in several previous studies. This may affect the prevalence of diastolic dysfunction in the current study subjects. The medications were continued by the patients in our study for ethical reasons.

CONCLUSIONS: Diastolic function assessment was done on asymptomatic ambulatory hypertensive patients. Majority were males (58%). The abnormal diastolic function as assessed by abnormal E/A ratio was seen in 44% of cases. There was a preponderance of female sex in this abnormal diastolic function group. Diastolic blood pressure was significantly associated with diastolic dysfunction.

Abnormal Δd was found in 18% of cases out of 56% who had normal E/A ratio. These cases are said to have 'pseudo normal' pattern of diastolic function.

LVIDS and LVIDD were decreased in pseudo normal group and increased in abnormal group indicating reduced compliance and dilatation of LV respectively. Both decreased and increased diastolic blood pressure was negatively and positively associated with diastolic dysfunction. The diastolic dysfunction was seen in patients with LVH, however this is statistically not significant indicating LVH is not the only cause for diastolic dysfunction in hypertensives.

The current study demonstrated that the presence of LV diastolic dysfunction in hypertensive patients is actually greater than previously reported by studies that analyzed transmitral flow velocity curves alone. To avoid overlooking patients with diastolic dysfunction, the combined analysis of transmitral and pulmonary venous flow velocity curves is recommended.

SUMMARY: Ambulatory hypertensives cases had abnormality in diastolic function as assessed by transmitral doppler signals (E/A ratio). The comparison of transmitral flow and pulmonary vein flow patterns indicates that more number of cases with normal transmitral flow pattern (56%) had abnormal pulmonary venous doppler analysis (Δ d) (18%). The current study demonstrated that the presence of LV diastolic dysfunction in hypertensive patients is actually greater than previously reported by studies that analyzed transmitral flow velocity curves alone. To avoid overlooking patients with diastolic dysfunction, the combined analysis of transmitral and pulmonary venous flow velocity curves is recommended.

BIBLIOGRAPHY:

- 1. Senni M, Tribouilloy CM, Rodeheffer RJ et al. Congestive heart failure in the community: a study of all incident cases in Olmsted County, Minnesota, in 1991. Circulation. 1998; 98:2282–2289.
- 2. Vasan RS, Larson MG, Benjamin EJ, Evans JC, Reiss CK, Levy D. 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. 1993; 33:1948-1955.
- 3. Soufer R, Wohlgelernter D, Vita NA et al. intact systolic left ventricular function in clinical congestive heart failure. Am J Cardiol. 1985; 55:1032–1036.
- 4. Hirota Y. A clinical study of left ventricular relaxation. Circulation. 1980; 62:756-763.
- 5. Bonow RO, Udelson JE. Left ventricular diastolic dysfunction as a cause of congestive heart failure: mechanisms and management. Ann Intern Med. 1992; 117:502-510.
- 6. Kitabatake A, Tanouchi J, Masuyama T et al. Limited atrial compensation to reduced early diastolic filling in hypertensive patients with advanced left ventricular hypertrophy: a Doppler Echocardiographic study. Heart vessels. 1989; 5:33-40.
- 7. Phillips RA, Coplan NL, Krakoff LR et al. Doppler Echocardiographic analysis of left ventricular filling in treated hypertensive patients. J Am Coll Cardiol. 1987; 9:317-322.
- 8. Yamamoto K, Redfield MM, Nishimura RA. Analysis of left ventricular diastolic function. Heart. 1996; 75(suppl 2):27-35.
- 9. Nishimura RA, Abel MD, Hatle LK, Tajik AJ. Assessment of diastolic function of the heart: background and current applications of Doppler echocardiography, part II: clinical studies. Mayo Clin Proc. 1989; 64:181-204.
- 10. Appleton CP, Hatle LK. The natural history of left ventricular filling abnormalities: assessment by two-dimensional and Doppler echocardiography. Echocardiography. 1992; 9:437-457.

- 11. Thomas JD, Choong CY, Flachskampf FA, Weyman AE. Analysis of the early transmitral Doppler velocity curves: effect of primary physiological changes and compensatory preload adjustment. J Am Coll Cardiol. 1990; 16:644-655.
- 12. Verdecchia P, Schillaci G, Guerrieri M et al. Prevalence and determinants of left ventricular diastolic filling abnormalities in an unselected hypertensive population. Eur Heart J. 1990; 11:679-691.
- 13. Fouad FM. Cardiac function and dysfunction in hypertension. Cleve Clin J Med. 1994; 61:351-355.
- 14. Smith ER, Smiseth OA, Knigma I et al. Mechanism of action of nitrates: role of changes in venous capacitance and in the left ventricular diastolic pressure-volume relation. Am J Med 1984; 76A:14-21.
- 15. Groot-Mason R, Anning P, Evans H, Lewis MJ, Shah AM. Modulation of left ventricular relaxation in isolated ejecting heart by endogenous nitric oxide. Am J Physiol 1994; 267(Heart Circ Physiol 36):H1804-H1813.
- 16. Bonow RO, Dilsizian V, Rosing DR et al. Verapamil-induced improvement in left ventricular diastolic filling and increased exercise tolerance in patients with hypertrophic cardiomyopathy: short-term and long-term effects. Circulation 1985;72(4):853-864.
- 17. Lorell BH, Paulus WJ, Grossman W, Wynne J, Cohn PF. Modification of abnormal left ventricular diastolic properties by nifedipine in patients with hypertrophic cardiomyopathy. Circulation 1982;65(3):499-507.
- 18. Nishimura RA, Schwartz RS, Holmes DR, Tajik AJ. Failure of calcium channel blockers to improve ventricular relaxation in humans. J Am Coll Cardiol 1993;21:182-188.
- 19. Haber HL, Powers ER, Gimple LW et al. Intracoronary angiotensin converting enzyme inhibition improves diastolic function in patients with hypertensive left ventricular hypertrophy. Circulation 1994;89:2616-2625.
- 20. Hayashida W, Van Eyll C, Rousseau MF, Pouleur H. Regional remodeling and non-uniform changes in diastolic function in patients with left ventricular dysfunction: modification by long-term enalapril treatment. J Am Coll Cardiol 1993;22:1403-1410.
- 21. Rakowski H, Appleton C, Chan KL et al. Canadian consensus recommendations for the measurement and reporting of diastolic dysfunction by echocardiography: from the investigators of Consensus on Diastolic Dysfunction by Echocardiography (review). J Am Soc Echocardiogr 1996;9:736–760.
- 22. Normal values of Doppler echocardiographic measurements in adults(Table A-7), Appendices in Harrison's Principles of Internal Medicine, 15th ed Braunwald et al. McGraw Hill and Company 2001; Vol. 2: A-5.
- 23. Bernard Rosner (2000), Fundamentals of Biostatistics, 5th Edition, Duxbury.
- 24. M. Venkataswamy Reddy (2002), Statistics for Mental Health Care Research, NIMHANS publication, INDIA.
- 25. Rakowski H, Appleton CP, Chan KL, Dumesnil JG, Honos G, Jue J et al. Canadian Consensus Recommendations for the Measurement and Reporting of Diastolic Dysfunction by Echocardiography. J Am Soc Echocardiogr 1996;9:736-760.
- 26. P M Mottram, B A Haluska, R Leano, S Carlier, C Case, T H Marwick. Relation of arterial stiffness to diastolic dysfunction in hypertensive heart disease. Heart 2005;91:1551–1556.

- 27. Kazuhiro Yamamato, Daniel J, Wilson, Vincent J, Canzanello, Margaret M et al. left ventricular diastolic dysfunction in patients with hypertension and preserved systolic function. Mayo Clin Proc. 2000;75:148-155.
- 28. B Mitra, SD Singh, S Basu, D Kumar, S Mondal, Ka Sema et al. A Profile of Clinical, Electrocardiographic and Echocardiographic Studies of Left Ventricular Hypertrophy in Hypertension Patients. Indian Heart J 2005; 57: 529–531.
- 29. Adewole A. Adebiyi, Akinyemi Aje, Okechukwu S. Ogah, Dike B et al. Left Ventricular Diastolic Function Parameters in Hypertensives. Journal of the National Medical Association, January 2005:97, no. 1; 41-45.
- M Masliza, S Mohd Daud, Y Khalid, 2005 Young Investigator's Award Winner: Assessment of Diastolic Function in Newly Diagnosed Hypertensives. Ann Acad Med Singapore 2005;34:684-688.
- 31. Hoit BD, Walsh RA. Diastolic function in hypertensive heart disease. In: Gaasch WH, LeWinter M, editors. Left Ventricular Diastolic Dysfunction and Heart Failure. Philadelphia: Lea and Febiger, 1994:354 –372.
- 32. Lorell BH. Diastolic dysfunction in pressure overload hypertrophy and its modification by angiotensin II; current concepts. Basic Res Cardiol. 1992;87(suppl 2):163-172.
- Kass DA, Wolff MR, Ting CT. et al. Diastolic compliance of hypertrophied ventricle is not acutely altered by pharmacological agents influencing active processes. Ann Intern Med. 1993;119:466-473.
- 34. Sobue T, Yokota M, Iwase M, Ishihara H. Influence of left ventricular hypertrophy on left ventricular function during dynamic exercise in the presence or absence of coronary artery disease. J Am Coll Cardiol. 1995;25:91-98.
- 35. Bella JN, Palmieri V, Roman MJ, Liu JE, Welty TK, Lee ET, Fabsitz RR, Howard BV, Devereux RB. Prognostic significance of abnormal peak early to late diastolic filling ratio in middle-aged to elderly adult American Indians: the Strong Heart Study (Abstract). J Am Coll Cardiol 2000;35 (Suppl. A):293A.

AUTHORS:

- 1. Nagabhushana S.
- 2. Ranganatha M.
- 3. Amith Kumar
- 4. Virupakshappa

PARTICULARS OF CONTRIBUTORS:

- 1. Assistant Professor, Department of General Medicine, Shimoga Institute of Medical Sciences (SIMS), Shimoga.
- 2. Assistant Professor, Department of General Medicine, Shimoga Institute of Medical Sciences (SIMS), Shimoga.
- 3. Assistant Professor, Department of General Medicine, Shimoga Institute of Medical Sciences (SIMS), Shimoga.

4. Professor, Cardiologist and HOD, Department of General Medicine, Shimoga Institute of Medical Sciences (SIMS), Shimoga.

NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Nagabhushana S, Near GK School, Jenukalleshwari Krupa, Aashok Nagar, 2nd Cross, Shimoga – 577201. E-mail: sn_bhushan@yahoo.co.in

> Date of Submission: 08/03/2014. Date of Peer Review: 10/03/2014. Date of Acceptance: 19/03/2014. Date of Publishing: 07/04/2014.