

HFpEF: A HARBINGER OF MASQUERADING CORONARY ARTERY DISEASE IN PATIENTS WITH STABLE ESSENTIAL HYPERTENSION

J Nambirajan¹, P. Balaji Pandian², D Chakkravarthi³, Abhishek Kumar Tiwari⁴

Received : 12/01/2023
Received in revised form : 22/02/2023
Accepted : 07/03/2023

Keywords:

Coronary artery disease, hypertension, heart failure with preserved ejection fraction, diastolic dysfunction.

Corresponding Author:

Dr. Abhishek Kumar Tiwari,
Email: keystoneabhishek@gmail.com

DOI: 10.47009/jamp.2023.5.2.241

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2023; 5 (2); 1140-1143



¹Associate Professor & HOD, Cardiology, Government Coimbatore Medical College and Hospital, Coimbatore, Tamil Nadu, India

²Associate Professor in Cardiology, Government Kilpauk Medical College and Hospital, Chennai, Tamil Nadu, India.

³Assistant Professor in Cardiology, Government Coimbatore Medical College and Hospital, Coimbatore, Tamil Nadu, India

⁴Post Graduate in Cardiology, Government Coimbatore Medical College and Hospital, Coimbatore, Tamil Nadu, India

Abstract

Background: Derangement of LV diastolic properties in hypertensive subjects has been linked to adverse cardiovascular outcomes including the amplified risk of heart failure with preserved ejection fraction and atrial fibrillation. We aim to find whether the early recognition of LV diastolic performance alteration may signal the presence of CAD, indicating the need for a more aggressive approach in terms of pharmacological treatment and invasive evaluation. **Materials and Methods:** Prospectively observational cohort study. 200 Hypertensive patients >18 years, with or without Heart failure with preserved Ejection fraction(Hfpef), were evaluated for LV structure and diastolic and systolic function, and were followed-up at least once a year for incidence of CAD. **Result:** 165 patients, mean follow up of 365± 82 days. Sample mean age 48± 10.5 years, 115 patients (69.63%) were males. Baseline blood pressure 146.8± 16/82.5±11 mm Hg). Out of the patients having HFpEF in the background of hypertension, 19(24.05%) developed CAD, of these 11 patients had developed ACS and the rest were found to be having CAD on stress testing using treadmill test. Non included in this the patients without HFpEF 11(12%) developed CAD (P<0.05). This indicated the significant relationship between HFpEF and CAD irrespective of the fact that hypertension itself is a risk factor for CAD. **Conclusion:** Our study concluded that the development of HFpEF was an independent risk factor for the development of CAD in hypertensive patients.

INTRODUCTION

Left ventricular (LV) HFpEF represents a universal pathophysiologic consequence of arterial hypertension that can be detected in the early stages of the disease, even sooner than the appearance of LV hypertrophy in the scene.^[1] In addition to hypertension, myocardial ischemia is very often observed with LV HFpEF, for the most part the delayed relaxation pattern.^[2]

Derangement of LV diastolic properties in hypertensive subjects has been linked to adverse cardiovascular outcomes including the amplified risk of heart failure with preserved ejection fraction and atrial fibrillation.^[3-5] Furthermore, some authors have called for more belligerent treatment of hypertensives with impaired LV diastolic function in terms of improved prognosis.^[6]

The inference of LV diastolic properties in daily clinical practice is performed with the use of established echocardiographic indices that are for the most part derived from mitral inflow Doppler studies. However, for the reason that these are dependent on LV loading conditions, other techniques such as tissue Doppler imaging have garnered interest due to their more insightful detection of LV HFpEF in hypertensive patients.^[7,8] The non-invasive recognition of coronary artery disease (CAD) remains an imperative goal in the management of hypertensive subjects. The aim of the present study shall be to investigate the credible additional role of echocardiographic LV diastolic dysfunction, indices in the determination of hypertensive with CAD.

MATERIALS AND METHODS

The study was planned as a prospectively observational cohort study conducted at a tertiary care centre, in the state of Tamil Nadu, India, with inflow of patients from 18 different spoke hospitals. The study was conducted in proper accordance with the Code of Ethics of the World Medical Association for experiments involving humans. The study pledged to abide by the declaration of Helsinki. The study started after getting the proper approval from the ethical committee of our institution. The study included following category of patients (1) The patients having essential hypertension who are 18 years or above, (2) Echocardiography including doppler study of standard quality to enable performing the calculation of LV diastolic & systolic function, (3) follow-up of upto one year is possible. Patients with a known history of coronary artery disease as well as those with congenital heart disease, clinically significant valvular disease, cardiomyopathy, chronic obstructive pulmonary disease, renal insufficiency, AV conduction disturbances, atrial fibrillation and diabetes mellitus were excluded from the study. The patient who had a previous diagnosis of heart failure with reduced ejection fraction were not included in the study population. Presence of any form of arrhythmia and conduction defect also mandated the exclusion of the patient from the study.

For the appropriate diagnosis of hypertension the 2021 European Society of Hypertension/European Society of Cardiology Guidelines for the office and out of office blood pressure measurements were used. The office blood pressure measurement guidelines were used; Office blood pressure measurements were done using digital sphygmomanometer. Three readings in sitting posture were averaged to calculate the final reading. The ECHO was performed using GE machine using 2.5-5 MHz probe based on the patient characteristics. The wall motion abnormalities and the ejection fraction were evaluated. The Doppler ECHO was done for the diagnosis of diastolic dysfunction. The diastolic dysfunction was diagnosed using 'The American Society of Echocardiography recommendations for the

evaluation of left ventricular diastolic function by echocardiography'. The presence of diastolic dysfunction in patients with a normal LVEF was diagnosed if two of the following four variables were present:

* Septal $e' < 10$ cm/sec

* Average $E/e' > 14$

* LA volume index > 34 mL/m²

* Peak TR velocity > 2.8 m/sec

Statistical Analysis

Continuous variables were reported as means of the values with their standard deviations (SD) for the normally distributed variables and as median for variable which were non-normally distributed, additionally the discrete variables were denoted as absolute values and percentages. For the values which were normally distributed, the analysis used the unpaired ANOVA (one-way). The proportional difference was studied using the Chi-square test. A P value of < 0.05 was considered as significant.

RESULTS

200 hypertensive patients who fulfilled the inclusion criteria were enrolled in the study but, 35 patients were lost in follow-up. The patients were divided into 2 equal groups of 100 patients each, by the presence and absence of the presence of HFpEF. The patient characteristic is given in [Table 1]. The patients were studied for the follow-up of 365 ± 82 days. Sample had a mean age 48 ± 10.5 years, of which 115 patients (69.63%) were males. Baseline blood pressure $146.8 \pm 16/82.5 \pm 11$ mm Hg. The ASCVD risk of the sample was calculated and it was found to be $10.5 \pm 9.1\%$. 65 (39.9%) were found to be having a borderline CV risk, 35 patients (21%) of patients had a low CV risk, 49 (29.6%) were of moderate CV risk and 16 patients (9.6%) had a high CV risk burden. 1/10 of the patients were diabetics; but around quarter of those (26.32%) had dyslipidemia, 18 patients admitted to being a smoker. The blood pressure monitored at the time of enrolling the patient was $146.8 \pm 11/83.8 \pm 6$ mm Hg and heart rate was 68.8 ± 10.4 /min. The frequency of patients who could not achieve the guideline directed blood pressure at follow up was 56 (33.9%) ($p < 0.005$).

Table 1: The Characteristic of the patients in the two groups.

	WITH HFpEF N=79	Without HFpEF N=86	p
Age (years)	52.6 ± 9.5	56.6 ± 8.2	0.312
Male sex (%)	65%	61%	0.005*
Smoking status (%)	(52.4%)	(33.5%)	0.402
Dyslipidemia (%)	(45.8%)	(43%)	0.681
BMI (kg m ⁻²)	26.9 ± 4.1	25.4 ± 3.9	0.5121
SBP (mm Hg)	145 ± 13	139 ± 6	0.1229
DBP (mm Hg)	84 ± 8	81 ± 8	0.2259
Pulse pressure (mm Hg)	63 ± 12	57 ± 8	0.4719

The mean E/e' ratio was calculated at the beginning of the study and at follow up, this demonstrated a value of 13.2 ± 3.5 . E/e' ratio > 14 was found in 38%

(64 patients). Also, e' septal velocity < 7 cm/sec or an e' lateral velocity < 10 cm/sec was found in 30% of the patient. Pearson correlation coefficient

between systolic blood pressure during follow-up and mean tissue Doppler septal e' wave was -0.3065 ($p < 0.005$), mean E/e' ratio 0.41658 ($p < 0.005$), mean tissue Doppler septal s' wave -0.413 ($p < 0.005$). Out of the patients having HFpEF in the background of hypertension 19(24.05%) developed CAD, of these 11 patients had developed ACS and the rest were found to be having CAD on stress testing using treadmill test. Non included in this the patients without HFpEF 11(12%) developed CAD ($P < 0.05$). This indicated the significant relationship between HFpEF and CAD irrespective of the fact that hypertension itself is a risk factor for CAD.

DISCUSSION

Arterial hypertension is one of the chief risk factors allied with the development of CAD, acting for the most part by promoting atherosclerosis. Additionally, it is an indispensable determinant of LV HFpEF, and it can be present even ahead of the manifestation of LV hypertrophy. Notably, hypertension-induced myocardial ischemia may have a influential role in the development of LV HFpEF even in the case of hemodynamically non-significant coronary stenosis. In hypertensive subjects, several studies^[9,10] have shown a momentous diminution of the coronary flow reserve even in the presence of intact coronary blood flow at rest. In addition, coronary blood flow is positively allied to IVRT, and intact SERCA function, which facilitates the efflux of calcium ions from the cytoplasm for the duration of diastole, is energy-dependent on ATP. Thus, myocardial ischemia may lead to LV relaxation impairment.

Despite the imperative contribution of invasive hemodynamic studies in the estimation of LV relaxation, echocardiographic examination prevails in daily clinical practice. Several methods are available, including conventional pulsed Doppler of mitral inflow and pulmonary venous flow, which are highly dependent on LV loading conditions. Consequently, the inference of LV diastolic performance based solely on these is more or less inadequate and most likely unconvincing. Novel echocardiographic techniques, such as mitral flow propagation velocity and tissue Doppler imaging, are primarily independent of LV preload changes and are considered superior to conventional pulsed Doppler mitral inflow measurements for the comprehensive evaluation of LV diastolic function.

In a study that examined the amendment of LV diastolic function during angioplasty-induced ischemia, an analysis of the flow propagation velocity showed that early filling is highly dependent on the LV relaxation rate, particularly through the phenomenon of asynchrony. However, there is a relative lack of such studies in the setting of essential hypertension. As hypertension represents a major risk factor for CAD, it is crucial to thoroughly investigate hypertensive patients for

the possible presence of myocardial ischemia, as ischemic symptoms in hypertensives may be atypical in nature. Moreover, the standard treadmill exercise test may be inconclusive, particularly in hypertensives with LV hypertrophy, and for this reason, alternative methods such as the echocardiographic stress test are proposed for the detection of ischemia.

In our study of 165 patients, the blood pressure monitored at the time of enrolling the patient was $146.8 \pm 11/83.8 \pm 6$ mm Hg and heart rate was 68.8 ± 10.4 /min. The frequency of patients who could not achieve the guideline directed blood pressure at follow up was 56(33.9%) ($p < 0.005$). This reiterated the unmet need of hypertension.

The mean E/e' ratio was calculated at the beginning was 13.2 ± 3.5 . E/e' ratio >14 was found in 38% (64 patients). Also, e' septal velocity < 7 cm/sec or an e' lateral velocity < 10 cm/sec was found in 30% of the patient. Pearson correlation coefficient between systolic blood pressure during follow-up and mean tissue Doppler septal e' wave was -0.3065 ($p < 0.005$), mean E/e' ratio 0.41658 ($p < 0.005$), mean tissue Doppler septal s' wave -0.413 ($p < 0.005$). Out of the patients having HFpEF in the background of hypertension 19(24.05%) developed CAD, of these 11 patients had developed ACS and the rest were found to be having CAD on stress testing using treadmill test. Not included in this, the patients without HFpEF 11(12%) developed CAD ($P < 0.05$). This indicated the significant relationship between HFpEF and CAD irrespective of the fact that hypertension itself is a risk factor for CAD

Although this was statistically significant but 21 patients who developed CAD had a predefined increased ASCVD risk. Although there has been found to be a positive correlation between the presence of HFpEF, but whether this is independent of ASCVD risk remains to be determined.

Limitations

The study was a single centre study hence lacked the diversity of patient being enrolled. Although fairly reliable 2D echocardiography was used to obtain the diastolic function, but the global longitudinal strain by speckle tracking wasn't used. The patients who developed CAD and reported were recorded, but compulsory stress testing for all the patients wasn't done to uncover any hidden CAD in the remaining patients.

CONCLUSION

Hypertension has always been considered an uncanny ally of coronary artery disease. The development of impaired LV relaxation and HFpEF in hypertensive patients have been herewith proven time and again, but whether the patients with hypertension and HFpEF have any direct correlation wasn't studied in Indian population. Our study concluded that the development of HFpEF was an

independent risk factor for the development of CAD in hypertensive patients.

REFERENCES

1. Aeschbacher BC, Hutter D, Fuhrer J, Weidmann P, Delacrétaiz E, Allemann Y . HFpEF precedes myocardial hypertrophy in the development of hypertension. *Am J Hypertens* 2001; 14: 106–113.
2. Sasaki O, Hamada M, Hiwada K . Effects of coronary blood flow on left ventricular function in essential hypertensive patients. *Hypertens Res* 2000; 23: 239–245.
3. Tsang TS, Barnes ME, Gersh BJ, Bailey KR, Seward JB . Risks for atrial fibrillation and congestive heart failure in patients ≥ 65 years of age with abnormal left ventricular diastolic relaxation. *Am J Cardiol* 2004; 93: 54–58.
4. Aurigemma GP, Gottdiener JS, Shemanski L, Gardin J, Kitzman D . Predictive value of systolic and diastolic function for incident heart failure in the elderly: the Cardiovascular Health Study. *J Am Coll Cardiol* 2001; 37: 1042–1048.
5. Redfield MM, Jacobsen SJ, Burnett JC Jr, Mahoney DW, Bailey KR, Rodeheffer RJ . Burden of systolic and diastolic ventricular dysfunction in the community: appreciating the scope of the heart failure epidemic. *JAMA* 2003; 289: 194–202.
6. Mancia G, De Backer G, Dominiczak A, Cifkova R, Fagard R, Germano G, et al. 2007 Guidelines for the management of arterial hypertension: The Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *Eur Heart J* 2007; 28: 1462.
7. Farias CA, Rodriguez L, Garcia MJ, Sun JP, Klein AL, Thomas JD . Assessment of diastolic function by tissue Doppler echocardiography: comparison with standard transmitral and pulmonary venous flow. *J Am Soc Echocardiogr* 1999; 12: 609–617.
8. De Boeck WL, Cramer MJ, Oh JK . Spectral pulsed tissue Doppler imaging in diastole: a tool to increase our insight in and assessment of diastolic relaxation of the left ventricle. *Am Heart J* 2003; 146: 411–419.
9. Hamouda MS, Kassem HK, Salama M, El Masry M, Shaaban N, Sadek E, Khandheria BK, Seward JB, Elhendy A . Evaluation of coronary flow reserve in hypertensive patients by dipyridamole transesophageal Doppler echocardiography. *Am J Cardiol* 2000; 86: 305–308.
10. Palombo C, Kozakova M, Magagna A, Bigalli G, Morizzo C, Ghiadoni L, Virdis A, Emdin M, Taddei S, L'Abbate A, Salvetti A . Early impairment of coronary flow reserve and increase in minimum coronary resistance in borderline hypertension. *J Hypertens* 2000; 18: 453–459.