Original Article

Evaluation of Left Atrial Volume and its Correlation to Left Ventricular Ejection Fraction in Hypertensive Patients

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ABSTRACT

Objective: Increase in left atrial size in patients with hypertension increases the risk of stroke, heart failure, morbidity and mortality. Aim of this study was to correlate the LAV to left ventricular function and effective antihypertensive therapy (ARB and thiazide diuretics) in hypertensive patients.

Study Design: Cross- sectional study

Place and Duration of Study: This study was conducted at the Cardiology OPD, Medicare Cardiac & General Hospital. Karachi, Pakistan from February 2021 to February 2022.

Materials and Methods: Five hundred hypertensive patients, with uncontrolled blood pressure ≤140/90mm Hg and controls with blood pressure ≥120/80mm Hg on antihypertensive therapy were included in the study. Echocardiography was performed (using GE-vivid S60), Measurements of LAV (normal range: 20-34mm/ ml^2), left ventricular function and ejection fraction were also recorded.

Results: On echocardiography assessment, four hundred (80%) of these were on antihypertensive therapy with angiotensin receptor blockers (ARB) with or without hydrochlorothiazide and had satisfactory blood pressure control. One hundred (20%) were with uncontrolled hypertension. Fifty five (11%) of uncontrolled hypertensive patients had increased LAV (≥34 mm/ml^2) and left ventricular dysfunction (systolic/diastolic) with reduced left ventricular ejection fraction (25-40).

Conclusion: This study concludes that echocardiography is a most convenient and non-invasive procedure to measure LAV, left ventricular dysfunction and ejection fraction in hypertensive patients. 2-Dimension and doppler echocardiography and can guide clinician for management of hypertension and prevention of cardiovascular complications.

Key Words: Resistant Hypertension, LAV (Left Atrial Volume), Left ventricular ejection fraction (LVEF), Angiotensin converting enzyme inhibitors (ARB), Left ventricular functions (LVF).

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INTRODUCTION

Uncontrolled hypertension is the most common cause of left atrial enlargement due to increased pre-load leading to left ventricular dysfunction.[1,3] Hypertension is amongst the highest threats to global health as it can cause serious coronary artery as well as renal diseases, which is a major burden on the health sector of developing countries.

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Although echocardiography is a second line investigation for evaluating hypertensive patient, it is a useful tool to determine the outcome of hypertensive patient's left atrial volume, left ventricular dysfunction, left ventricular ejection fraction and selection of appropriate choice of antihypertensive therapy.[3,4] Echocardiography is mostly recommended under the likely hood of left atrial (LA) dilation or left ventricular (LV) dysfunction, associated coronary or valvular heart diseases.[3] In early stages of hypertension, the left ventricular function is preserved. Left atrial volume (LAV) assessment is important but normally not done as a first-line investigation to determine the effectivity of antihypertensive therapy, but is recommended in later stages or uncontrolled hypertension and on suspected signs or symptoms of left ventricular dysfunction and when findings may show increased left atrial size, decreased LV systolic/ diastolic function and reduced ejection fraction.[3] With conventional echocardiography left arterial volume (LAV), left ventricular functions and ejection fraction can be measured by two-dimensional volumetric echocardiography.[4] Tissue Doppler imaging, the three-dimensional echocardiography, are newer

echocardiographic modalities in the evaluation of hypertensive patients. Newer echocardiographic parameters are important in the diagnosis and management of uncontrolled hypertension.[3,4]

Normal left atrial volume (LAV) and function is required for the maintenance of normal cardiac function.[1,2] LA enlargement and LV dysfunctional abnormalities may cause cardiovascular diseases and arrhythmias such as atrial fibrillation, left atrial enlargement is an important predictor of cardiovascular events such as atrial fibrillation, stroke, heart failure and mortality. Studies have shown that LA structural remodeling and/or functional impairment might be the main cause of the pathogenesis and development of ventricular disorders, such as heart failure with or without reduction in ejection fraction.[4,5] However, LAV, especially LV functions, are insufficiently studied because of measurement difficulties. Standard echocardiography only routinely measures the LA diameter. Tissue Doppler imaging has limited accuracy of measurement and hence of limited use in clinical and even research settings. Hypertensive patients with LA enlargement had shown impaired left atrial functions when compared to normotensive patients.[4,5] Thus echocardiography in studies has been suggested as being a useful tool in diagnosis of cardiovascular risks in hypertensive patients.[3-12]

The appropriate management of hypertension is most effective in reducing life threatening conditions which may cause morbidity and mortality. The various classes of antihypertensive agents including ARBs, ACE inhibitors diuretics, beta-blockers, calcium channel blockers, diuretics, alpha blockers and vasodilators are used as monotherapy or combination therapy to manage hypertension. ARB have been found to be highly effective as monotherapy or in combination with diuretics and calcium channel blockers.[13-16]

Uncontrolled hypertension is a cause of serious cardiovascular diseases and life- long disabilities such as cerebrovascular diseases, ischemic heart diseases, heart failure, peripheral vascular diseases and end stage kidney diseases etc. In addition to antihypertensive therapy, life style modification, salt restriction, weight reduction in over weight and obese patients are useful in control of blood pressure. Antihypertensive drug therapy has a significant role in prevention of severe outcomes of uncontrolled hypertension. ARB / ACE inhibitors, calcium channel blockers, beta blockers, alpha-blockers and diuretics are antihypertensive agents very useful as mono or combination therapy to control hypertension.[14-16] Tele medicine is a useful and cost-effective methodology to keep in touch with large number of patients. It is also convenient to provide reminder, keep record of blood pressure control and follow-up even from remote distances. Resistant hypertension is high blood pressure requiring combination therapy of three or more antihypertensive drugs.[15-19]

Appropriate blood pressure control should be used to prevent or slowdown left ventricular dysfunction. Studies on hypertensive patients have shown that angiotensin-converting enzyme inhibitors were the most effective antihypertensive drugs in reducing left ventricular mass.[13-19] This analysis showed that angiotensin-converting enzyme inhibitors, beta blockers, and calcium channel blockers reduced left ventricular mass by reducing wall thickness, whereas diuretics reduced left ventricular mass by reducing left ventricular volume.[16-18]

The aim of this study is to determine the left atrial volume by echocardiography and function of hypertensive patients visiting cardiac OPD. Also, to determine effectively of prescribed antihypertensive therapy, ARB (angiotensin receptor blockers) and ACEI (angiotensin converting enzyme inhibitors) as monotherapy or in combination with calcium channel blockers or thiazide diuretics to prevent cardiac morbidities due to uncontrolled hypertension.

MATERIALS AND METHODS

The cross-sectional study was conducted on five hundred hypertensive patients visiting cardiac OPD of Medicare Cardiac & General Hospital, Karachi from February 2021 to February 2022.

Five hundred hypertensive patients visiting cardiac OPD , were referred for echocardiography to Department of Sonology at Medicare Cardiac and General Hospital, Karachi were included in the study. All participants were asked to give informed consent. Ethical approval was obtained from the Ethical Review Committee (ERC) of Sohail University, Karachi. Protocol #:0O085/21

Performa and consent form were filled in by participants. Echocardiography performed by (GE-vivid S60) was done for measurement of left atrial volume by using Simpson's biplane method. All of these patients were on antihypertensive therapy. Four hundred hypertensive patients had controlled hypertension, whereas one hundred patients had uncontrolled hypertension. In these hypertensive patients, echocardiography was performed to determine LAV (normal range: 20-34 ml), left ventricular function and ejection fraction were also recorded. All those patients with any other comorbidity were excluded from this study. 2-Dimension echocardiographic Doppler was performed. Anteroposterior diameter was taken in parasternal long-axis view, longitudinal and transverse diameters in 4-chamber view.

Left Atrial Volume and Left Atrial Function

Left atrial volume was determined by area-length method using apical four chamber (A1) and apical two chamber (A2): $0.785 \times \frac{A1 \times A2}{L}$

Where A1 (area 4 chamber), A2 (area 2 chamber) and L (maximum length).

Doppler Echocardiography: Left ventricular diastolic function. Peak E wave and Peak A wave. E/A left ventricular diastolic function.

Figure No.1: Two- dimensional calculation for LAV by modified Simpson's method: A1 (Area 4 chambers), A2 (area 2 chambers) and L (maximum length)

Inclusion Criteria: Hypertensive patients without any cardiovascular or renal complications or pregnancy were included in the study.

Exclusion Criteria: Hypertensive patients with cardiovascular complications, renal diseases or pregnancy were excluded from the study.

Statistical Analysis: All the data was entered in IBM SPSS Statistics 25. All values were given as mean ± SD and percentages. The bar graph plotted for antihypertensive therapy and left ventricular function. Scatterplot was drawn to find correlation between LAV and left ventricular ejection fraction.

RESULTS

For five hundred hypertensive patients, echocardiography was performed as diagnostic tool for measurement of LAV (Left atrial volume). In univariate analysis, LA volume was increased in 11% (n=55) of hypertensive patients and increase in left atrial volume was correlated to left ventricular ejection fraction. Clinical characteristics of hypertensive patients included (Table 1) age range 20-90 years (mean 55 years), gender ratio – male (n=272) 54% to female (n=228) 46%, LAV normal range (28-34 mm/ml^2) in 400 hypertensive patients, LAV (36-90mm/ml^2) in one hundred hypertensive patients.

The variables recorded were blood pressure in uncontrolled hypertensive patients above 140/90mm Hg and in controlled hypertensive patients 130/80 mm Hg or less. LAV in controlled hypertensive (mean = 32, range 27- 34), LAV in uncontrolled hypertensive patients (mean 45, range 36- 49). Ejection fraction (EF) in four hundred and forty eight patients (55- 60 %), in fifty five uncontrolled hypertensive patients EF (range 30-50%). Normal ventricular function was recorded in four hundred and forty- two patients. Fifty five of uncontrolled hypertensive patients were found with mild (n =20) or moderate (n =30) or severe dysfunction (n =5) respectively (Table 2). Graph 1 shows bar graph for antihypertensive therapy and LV functions. Graph 2: shows distribution of participants on different antihypertensive therapy. Graph 3: is the scatterplot showing the correlation between left atrial volume (LAV) and left ventricular ejection fraction (LVEF).

Table No.1: Clinical Characteristics of hypertensive patients, participated in the study

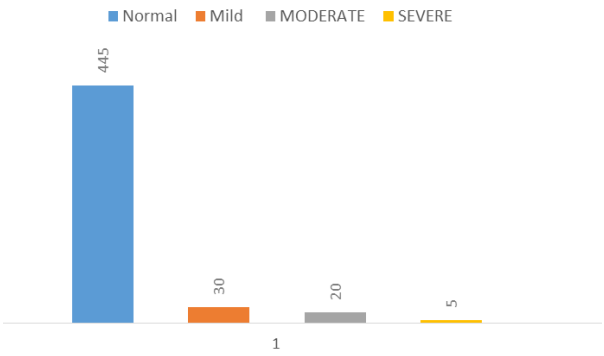
Variables	Hypertensive N=500	Uncontrolled BP (≥140/90mmhg) n= 100	Controlled BP (≤130/80 mmHg) n= 400
BP (mm Hg)	Normal: ≤130/80	100	400
	Elevated: ≥140/90		
Age - Years	Mean: 55 SD 7.2	55 ±7	53 ±7
	Range: 20-90		
Gender	Male: 272 (54%)	55(55%)	217(54%)
	Female: 228 (46%)	45(45%)	183(46%)
Echocardiography:			
LA Volume(N)	Mean = 27 (20- 29)	45	400
LA Volume (E)	Mean = 45 (36-49)	55	
LVEF % (N)	55- 60 %	45	400
LVEF % (Reduced)	25-50%	55	
LV Function:			
Normal Function	445	45	400
Mild Dysfunction	30	30	
Moderate dysfunction	20	20	
Severe Dysfunction	05	05	

BP=Blood Pressure, LA=Lower Atrial, N= Normal, E=Elevated, LVEF= Left Ventricular Ejection Fraction, LV=Left Ventricular

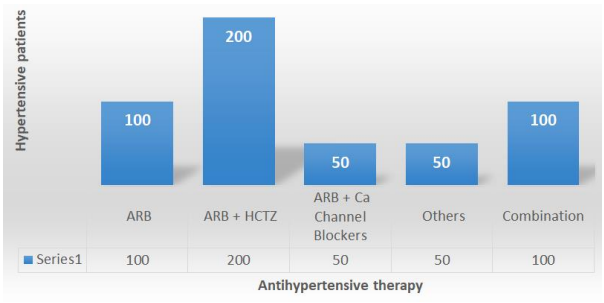
Table No. 2: Variables of hypertensive patients

Variables N=500	Uncontrolled n=100	Controlled n=400
BP (mm Hg)	≥140/90	≥ 120/80
LAV (mm/ml^2)	36+ 15	28 + 7
LVF	Mild, Moderate, Severe Dysfunction.	Normal
LVEF (%)	25-40	55- 60
Antihypertensive therapy:		
• **ARB**	Combination≤3 100	100
• **ARB+ Hydrochlorothiazide**		200
• **ARB+ Ca Channel Blockers**		50
• **Others**		50

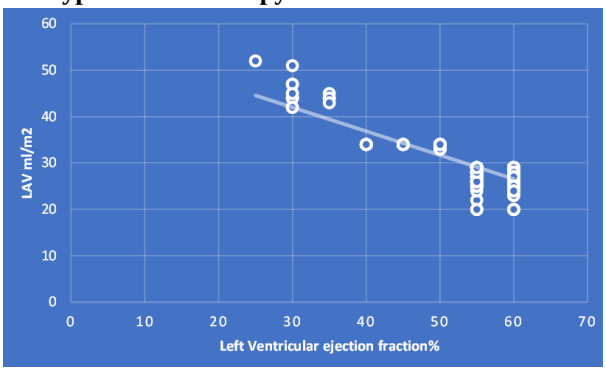
BP=Blood Pressure, LAV= Left Atrial Volume, LVF=Left Ventricular Function, EF= Ejection Fraction %



Graph No.1: Showing normal LVF and mild, moderate and severe left ventricular dysfunctions on echocardiograph of hypertensive patients



Graph No.2: Hypertensive patients on antihypertensive therapy



Graph 3: Scatterplot showing correlation of Left atrial volume (LAV) and left ventricular ejection fraction (LVEF)

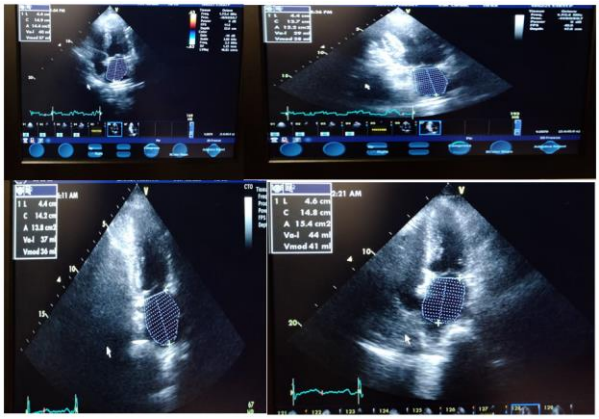


Figure No. 2: Echocardiography showing increased Left Atrial Volume (LAV) in uncontrolled hypertension patients

DISCUSSION

Hypertension is the most common cause of coronary artery diseases, stroke, atrial fibrillation, cardiac failure, morbidity and mortality caused by uncontrolled hypertension. This study has shown that high incidence of hypertension and uncontrolled hypertension being cause of systolic and diastolic dysfunction and reduced ejection fraction. 2-Dimensional and Doppler echocardiography was done. Out of a total of five hundred hypertensive patients on antihypertensive therapy (ARB, ACEI, Calcium Channel blockers, diuretics, beta blockers). Four hundred of these patients were on Angiotensin receptor blockers (alone ± diuretic) and had controlled blood pressure. Although one hundred patients in the study sample were found to have uncontrolled hypertension ≥ 140/90 mmHg despite on regular antihypertensive therapy. On performing 2-dimensional and doppler echocardiography, 39(8%) of these hypertensive patients had have increase in LAV, LA-index, left ventricular dysfunction and reduced left ventricular ejection fraction.

Studies have shown hypertension and obesity are risk factors for left atrial enlargement, that is a risk factor

for cardiovascular morbidity and mortality.[1-5] Studies also have demonstrated that echocardiography is a useful tool not only in determining LAV and index, left ventricular function (systolic and diastolic dysfunction), reduced ejection fraction as ultrasound is sensitive to asymptomatic organ damage.[5-14] Thus, being useful in investigation for appropriate lifestyle modification and antihypertensive therapy in these patients. Appropriate management is essential to prevent development of complications of coronary artery diseases, stroke, cardiac failure, renal failure morbidities and mortality. ARB have been useful therapy in control of hypertension in controlled hypertensives patients.[15-20] Ineffective control of hypertension is a cause of serious cardiovascular diseases and lifelong disabilities such as cerebrovascular diseases, ischemic heart diseases, heart failure, peripheral vascular diseases and end stage kidney diseases, etc. In addition to life style modification, salt restriction, weight reduction in over weight and obese patients is also called for. Antihypertensive drug therapy has a significant role in prevention of severe outcomes of uncontrolled hypertension. ARB / ACE inhibitors, calcium channel blockers, beta blockers, alpha-blockers and diuretics are antihypertensive agents very useful as mono or combination therapy to control hypertension. Tele medicine is useful intervention and is effective in keeping in touch with large number of patients, is convenient and a cost-effective method. Also, it is convenient for providing reminders, record of blood pressure control and follow-up even from remote distance. Resistant hypertension is defined as uncontrolled blood pressure despite the use of different combination of antihypertensive drugs, including a diuretic, usually thiazide-like, a long-acting calcium channel blocker, and a blocker of the renin- angiotensin system, either an ACE (angiotensin-converting enzyme) inhibitor or an ARB (angiotensin receptor blocker).[13,14] ARBs should also be the first choice in hypertensive patients without organ damage, and at the initial stages of atherosclerotic disease. Moreover, ACE-inhibitors might be used in patients who have already developed organ damage or cardiac comorbidities, but who tolerate this drug well

Resistant hypertension is uncontrolled hypertension (BP ≥140/90mmHg) with monotherapy, such patients require ≥ 3 antihypertensive drugs (ARB, ACE inhibitors, thiazide diuretics, calcium channel blockers) in order to control the high blood pressure which can cause cardiovascular diseases, renal failure and organ damage due to uncontrolled hypertension.[20-23] Study by Shah et al[24] shown high prevalence of hypertension in urban , male population of Pakistan, and suggestions of preventive measures . Thus, prolong uncontrolled hypertension in patients should be managed appropriately, as it may lead to increased left atrial volume (LAV), left ventricular dysfunction (diastolic and systolic) and reduction in ejection fraction.

CONCLUSION

This study concludes that echocardiography is a most convenient and non-invasive procedure to measure LAV, left ventricular dysfunction and ejection fraction in hypertensive patients. Left atrial enlargement, left ventricular systolic and diastolic dysfunction and reduced ejection fraction determined by 2-Dimension and doppler echocardiography and can guide clinician for management and early prevention of cardiovascular complications.

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Author's Contribution:

Concept & Design of Study:	Samia Perwaiz Khan
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Revisiting Critically:	Samia Perwaiz Khan
Final Approval of version:	Samia Perwaiz Khan

Conflict of Interest: The study has no conflict of interest to declare by any author.

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