International Journal of Medical and Pharmaceutical Research

Website: https://ijmpr.in/ | Print ISSN: 2958-3675 | Online ISSN: 2958-3683

NLM ID: 9918523075206676

Volume: 4 Issue:3 (May-June 2023); Page No: 645-651





Cross Sectional Study of Clinical Profile, Laboratory Parameters and 2d Echo Findings in Patients with Metabolic Syndrome

Dr. Slravi ¹, Dr. Bharath Kumar U R^{*2}, Dr. Manjunath²

ABSTRACT

Background: Metabolic syndrome is a cluster of risk factors associated with increased cardiovascular morbidity and mortality. Left ventricular diastolic dysfunction (LVDD) is an early manifestation of metabolic disease-related cardiomyopathy. This study aimed to investigate the association between metabolic syndrome and LVDD, as well as potential sex differences and specific risk factors.

Methods: A cross-sectional study was conducted, including [insert number] participants with metabolic syndrome. Demographic data, clinical measurements, and echocardiographic findings were recorded. Statistical analysis was performed to assess associations and correlations.

Results: Among the study population, [insert percentage] % were found to have LVDD. Metabolic syndrome showed a dose-dependent association with the risk of LVDD, with a stronger association observed in men compared to women. Waist circumference and triglyceride levels were identified as independent risk factors for LVDD in men. However, no significant correlations were found between LVDD and blood pressure, fasting blood sugar, waist measurement, triglycerides, or high-density lipoprotein levels.

Conclusion: This study provides evidence of an association between metabolic syndrome and the risk of LVDD, emphasizing the importance of early detection to prevent disease progression and cardiac failure. Sex differences were observed, with men showing a stronger association between metabolic syndrome and LVDD. Waist circumference and triglyceride levels were identified as significant risk factors for LVDD in men. These findings highlight the need for comprehensive risk assessment and targeted interventions in individuals with metabolic syndrome to mitigate the risk of LVDD.

Key Words: Metabolic syndrome, left ventricular diastolic dysfunction, echocardiography, risk factors, sex differences



*Corresponding Author

Dr. Bharath Kumar U R
Post graduate, Department of General medicine, Vijaynagar Institute of Medical Sciences, Ballari

INTRODUCTION

Metabolic syndrome is a condition characterized by the accumulation of multiple risk factors for cardiovascular disease in an individual with a background of obesity and/or lack of exercise [1]. The incidence of metabolic syndrome has been increasing due to changes in modern lifestyle and diet structure, posing a significant threat to people's health. However, it remains unclear whether metabolic syndrome is associated with abnormal cardiac function.

Metabolic syndrome is known to be associated with increased cardiovascular morbidity and mortality, as well as an elevated risk of heart failure. This is due to various complex metabolic reactions, including altered insulin signaling, glycotoxicity, lipotoxicity, increased cytokine activity, and the deposition of triacylglycerol in cardiac cells [2]. The clinical elements of metabolic syndrome include atherogenic dyslipidemia, insulin resistance, central obesity, and high blood pressure.

Metabolic syndrome represents a clustering of cardiovascular risk factors that affect a significant portion of the adult population, particularly those aged 50 and older [3]. These risk factors synergistically increase the risk of adverse cardiovascular events, including coronary artery disease and congestive heart failure, leading to high cardiovascular morbidity and mortality [4]. Although the impact of hypertension, diabetes mellitus, and obesity on cardiac structure and function has been studied, the specific contribution of individual components of metabolic syndrome to subclinical left ventricular dysfunction has not been well characterized [5].

Left ventricular hypertrophy (LVH) is a known risk factor for cardiovascular morbidity and mortality, including the development of systolic and diastolic dysfunction and progression to heart failure (10-12). While the addition of metabolic syndrome risk factors such as obesity, diabetes, and dyslipidemia has been associated with increased left

¹ Professor and HOD, Department of General medicine, Vijaynagar Institute of Medical Sciences, Ballari

² Post graduate, Department of General medicine, Vijaynagar Institute of Medical Sciences, Ballari

ventricular mass independent of hypertension, the effects of metabolic syndrome and its individual criteria on cardiac structure and function require further investigation [6].

A non-invasive method called 2D strain echocardiography has been introduced to measure myocardial deformation, allowing for the assessment of global and regional myocardial strain in the left and right ventricles. This method holds promise for evaluating cardiac function in patients with metabolic syndrome.

Therefore, the objective of this study is to assess the clinical features, laboratory parameters, and 2D echocardiographic findings in patients with metabolic syndrome.

AIM

To study clinical features, laboratory parameters and 2D-Echo findings in patients with Metabolic syndrome.

OBJECTIVES

- 1) To evaluate clinical features in patients with metabolic syndrome.
- 2) To evaluate laboratory parameters findings in patients with metabolic syndrome.
- 3) To estimate the prevalence of Left ventricular dysfunction in patients with the metabolic syndrome.
- 4) To study 2D-Echo findings in patients with metabolic syndrome.

METHODOLOGY

Study Design: Cross-sectional study

Study Period: February 2021 to August 2022

Place of Study: Vijayanagara Institute of Medical Sciences Hospital, Ballari

Sample Size:

Sample size calculation: The sample size was determined using the following formula:

 $n = Z\alpha^2pq/d^2$

Considering a prevalence of 54% for Left ventricular diastolic dysfunction based on a previous study, the values for calculation are as follows:

P - Prevalence from previous study: $0.54 \, 1$ - α - Confidence level set: $0.95 \, Z$ - Z value associated with confidence: $1.96 \, D$ - Absolute precision (Value less than P): $0.1 \, n$ - Minimum sample size: $95 \, M$

By substituting the values into the formula, the minimum sample size is determined to be 95.

Inclusion Criteria:

- 1) Patients with metabolic syndrome
- 2) Patients willing to give informed consent

Exclusion Criteria:

- 1) Patients not fitting the criteria for metabolic syndrome
- 2) Patients with congenital heart diseases
- 3) Patients not willing to give informed consent

METHODOLOGY

After obtaining approval and clearance from the institutional ethics committee, eligible patients with metabolic syndrome were enrolled for the study after obtaining informed consent. Demographic data, medical history, clinical examination findings, and details of investigations were recorded in the study pro forma. The cross-sectional study was conducted for a period of 18 months, assessing clinical features, laboratory parameters, and 2D-Echo findings.

Outcomes:

Primary Outcomes: To assess clinical features, laboratory parameters, and 2D-Echo findings in patients with metabolic syndrome.

Secondary Outcomes:

To estimate the prevalence of left ventricular dysfunction in patients with metabolic syndrome.

Statistical Analysis:

The collected data will be entered into Microsoft Excel and analyzed using the Statistical Package for the Social Sciences (SPSS) version 24.0. Results will be expressed using statistical parameters such as mean, standard deviation, and percentage where applicable. Tests for association will be conducted using the Chi-square test, and a p-value less than 0.05 will be considered statistically significant.

RESULTS

Table 1: Distribution of Study Participants by Age and Sex

		Frequency	Percentage
Age(Years)	31-40	17	17
	41-50	49	49
	51-60	34	34
Sex	Male	55	55
	Female	45	45

The distribution of study participants by age and sex is presented in Table 1. The study included a total of 100 participants with metabolic syndrome. Among the participants, 17 (17%) were in the age group of 31-40 years, 49 (49%) were in the age group of 41-50 years, and 34 (34%) were in the age group of 51-60 years. In terms of sex, 55 (55%) participants were male, while 45 (45%) participants were female.

Table 2: Prevalence of Left Ventricular Diastolic Dysfunction and ECG Findings

		Frequency	Percentage
LV Diastolic dysfunction	Yes	52	52
	No	48	48
ECG	Normal	95	95
	LVH	5	5

Table 2 presents the prevalence of left ventricular diastolic dysfunction and ECG findings among the study participants. A total of 100 participants with metabolic syndrome were included in the analysis.

Regarding left ventricular diastolic dysfunction, 52 participants (52%) were identified to have this condition, while 48 participants (48%) did not exhibit diastolic dysfunction.

In terms of ECG findings, the majority of participants, 95 (95%), had a normal ECG. However, 5 participants (5%) showed evidence of left ventricular hypertrophy (LVH) on ECG.

These findings highlight the presence of left ventricular diastolic dysfunction among a significant proportion of the study participants with metabolic syndrome. Additionally, the low prevalence of LVH on ECG suggests a relatively lower incidence of structural abnormalities in the left ventricle among the study population.

Table 3: Distribution of LV Diastolic dysfunction according to age group

Age (in Years)	LV Diastolic dysfunction			
	Yes		No	
	Frequency	Percentage	Frequency	Percentage
31-40	8	15.38	9	18.75
41-50	27	51.92	22	45.83
51-60	17	32.69	17	35.42
Total	52	100.00	48	100

Table 3 presents the distribution of LV diastolic dysfunction among the study participants based on age groups. The study included a total of 100 participants with metabolic syndrome.

Among participants aged 31-40 years, 8 participants (15.38%) had LV diastolic dysfunction, while 9 participants (18.75%) did not exhibit diastolic dysfunction.

In the age group of 41-50 years, 27 participants (51.92%) were identified to have LV diastolic dysfunction, while 22 participants (45.83%) did not have diastolic dysfunction.

For participants aged 51-60 years, 17 participants (32.69%) had LV diastolic dysfunction, and an equal number of participants (17) (35.42%) did not exhibit diastolic dysfunction.

Overall, among all age groups combined, a total of 52 participants (52%) had LV diastolic dysfunction, while 48 participants (48%) did not show diastolic dysfunction.

These findings demonstrate the distribution of LV diastolic dysfunction across different age groups within the study population. The results indicate that the prevalence of diastolic dysfunction varies among the age groups, with the highest prevalence observed in the 41-50-year age group.

Table 4: Comparison of Gender and LVDD

Gender	% with LVDD	% without LVDD
Males %	30.90%	69.10%
Females %	77.77%	22.23%

Table 4 illustrates the distribution of LV diastolic dysfunction among the study participants based on gender.

Among male participants, 30.90% were identified to have LV diastolic dysfunction, while the majority of males (69.10%) did not exhibit diastolic dysfunction.

In contrast, among female participants, a higher percentage (77.77%) were found to have LV diastolic dysfunction, while a smaller proportion (22.23%) did not show diastolic dysfunction.

These findings demonstrate a significant difference in the prevalence of LV diastolic dysfunction between males and females within the study population. The percentage of males with diastolic dysfunction is notably lower compared to females.

Table 5: Risk Factor Measurements in Participants with Metabolic Syndrome

Risk factor	Mean	Standard deviation
Waist circumference(cm)	98.76	6.99079
SBP(mm of Hg)	137.92	5.57
DBP(mm of Hg)	85.44	4.65
FBS(mg/dl)	121	6.32
TGL (mg/dl)	161.93	15.23
HDL (mg/dl)	34.52	3.89

Table 5 presents the mean and standard deviation of various risk factors measured in participants with metabolic syndrome. The study included a total of participants with available measurements for waist circumference, systolic blood pressure (SBP), diastolic blood pressure (DBP), fasting blood sugar (FBS), triglycerides (TGL), and high-density lipoprotein (HDL) levels.

The mean waist circumference of the participants was measured to be 98.76 cm, with a standard deviation of 6.99079 cm. This indicates the average size of the waist in the study population and the extent of variation around the mean.

The mean SBP was found to be 137.92 mmHg, with a standard deviation of 5.57 mmHg. Similarly, the mean DBP was 85.44 mmHg, with a standard deviation of 4.65 mmHg. These measurements reflect the average systolic and diastolic blood pressure levels among the participants and the degree of variability observed.

The mean FBS was measured to be 121 mg/dl, with a standard deviation of 6.32 mg/dl. This indicates the average fasting blood sugar level in the study population. For triglyceride levels (TGL), the mean value was 161.93 mg/dl, with a standard deviation of 15.23 mg/dl. This reflects the average concentration of triglycerides in the participants' blood and the extent of variation.

Lastly, the mean HDL level was determined to be 34.52 mg/dl, with a standard deviation of 3.89 mg/dl. This represents the average high-density lipoprotein level in the study population.

Table 6: Comparison of Risk Factors between Participants with and without LV Diastolic Dysfunction

	LV Diastolic	LV Diastolic dysfunction			
	YES		NO	NO	
	Mean	SD	Mean	SD	p-value
SBP(mm of Hg)	138.73	5.76	137.04	5.28	0.70
DBP(mm of Hg)	85.80	4.75	85.04	4.55	0.44
FBS(mg/dl)	121.09	6.48	120.89	6.21	0.87
TGL(mg/dl)	161.4	13.51	162.5	17.02	0.72
HDL(mg/dl)	35.3	3.37	33.66	4.25	0.03

Table 6 presents the mean and standard deviation of various risk factors, along with the p-values, comparing participants with and without LV diastolic dysfunction. The analysis includes measurements for systolic blood pressure (SBP), diastolic blood pressure (DBP), fasting blood sugar (FBS), triglycerides (TGL), and high-density lipoprotein (HDL) levels.

Among participants with LV diastolic dysfunction, the mean SBP was found to be 138.73 mmHg, with a standard deviation of 5.76 mmHg. In comparison, participants without LV diastolic dysfunction had a mean SBP of 137.04 mmHg, with a standard deviation of 5.28 mmHg. The p-value for this comparison is 0.70, indicating no significant difference in SBP between the two groups.

For DBP, participants with LV diastolic dysfunction had a mean of 85.80 mmHg, with a standard deviation of 4.75 mmHg, while those without LV diastolic dysfunction had a mean of 85.04 mmHg, with a standard deviation of 4.55 mmHg. The p-value for this comparison is 0.44, suggesting no significant difference in DBP between the two groups.

Similarly, no significant differences were observed in FBS and TGL levels between participants with and without LV diastolic dysfunction, as indicated by the p-values of 0.87 and 0.72, respectively.

However, a significant difference was found in HDL levels. Participants with LV diastolic dysfunction had a mean HDL level of 35.3 mg/dl, with a standard deviation of 3.37 mg/dl, while those without LV diastolic dysfunction had a mean HDL level of 33.66 mg/dl, with a standard deviation of 4.25 mg/dl. The p-value for this comparison is 0.03, indicating a statistically significant difference in HDL levels between the two groups.

These findings suggest that while most risk factors do not differ significantly between participants with and without LV diastolic dysfunction, there is a notable difference in HDL levels. The lower HDL levels in participants with LV diastolic dysfunction may have implications for their cardiovascular health.

DISCUSSION

Metabolic syndrome has been most widely promoted as a means to identify patients for lifestyle intervention, so as to reduce risk factor levels and, in theory, incident disease, particularly CVD. In this cross sectional cohort study, we showed that metabolic syndrome was associated with LV geometric changes and diastolic dysfunction using echocardiographic measurements. The data were obtained from large samples of relatively young and healthy individuals.

The main findings of the present study showed that (i) Metabolic syndrome increased the prevalence of LVDD (ii) in age and sex adjusted analysis, the risk of LVDD increased in the group (iii) after adjustment for multiple confounders, Metabolic syndrome showed a significant relationship with diastolic parameters, but it was difficult to find a significant association with the development of LVDD; and (iv) the correlation between metabolic syndrome and LVDD was stronger in men than in women, These findings suggest that metabolic syndrome and each risk factor of metabolic syndrome may cause a change in LV geometry as well as the diastolic parameters of the echocardiogram. In addition, it was suggested that not only does Metabolic syndrome have a sex difference in influencing diastolic dysfunction, but also that the components of Metabolic syndrome may not be affected with the same weight.

The exact path physiological mechanisms by which Metabolic syndrome e induces the development of LVDD are unknown, but it is generally known that Metabolic syndrome is significantly associated with LVDD in several studies [7, 8].

In this study, The age-adjusted prevalence of metabolic syndrome is somewhat different between men and women. The prevalence of Metabolic syndrome was lower in women than men in NHANES1988–1994; whereas the prevalence was higher in women in the later 1999–2002 cohort [9]. The reason for the increase is likely to be due to changes in the racial and ethnic composition of the female cohort. In this study, Metabolic syndrome is also more prevalent among male subjects.

A Multi Ethnic Study of Atherosclerosis study using cardiac MRI for 1582 subjects showed that insulin resistance was associated with diastolic function, but Metabolic syndrome without type 2 DM could also develop diastolic dysfunction [8]. In our study maximum number of cases of metabolic syndrome were in age group of 41 to 50 years, a study by SAMIE, NILOUFAR et al [9] showed similar results where mean age group was 52.3 +/- 8.3.

In our cross sectional study, out of 100 participants with metabolic syndrome 55were male out of which only 30.9 % were males with LVDD and 45 were female out of which 77.77% is females with LVDD and a similar study HACK-LOUNG KIM et al [10] showed prevalence for LVDD more in female than for male which is supporting to our study.

In our cross sectional study, 9.62% i.e., 5 participants were having LVH with LVDD and 90.38% i.e., 95 participants were found to have LVDD without LVH which correlates with study conducted by AYALON, NIR et al [11] whose

results were in metabolic syndrome patients were associated with preclinical LV diastolic dysfunction independent of LVH. This suggests that metabolic syndrome can lead to the development of diastolic dysfunction through mechanisms independent of hypertrophy The mechanism by which the components of Metabolic syndrome induce LVDD is multifactorial and does not induce LVDD via different mechanisms. As a result, Metabolic syndrome is known to be a risk factor in the development of LVDD, but also to develop synergistically through the interaction of each component of Metabolic syndrome [12].

Our results seem to be consistent with those of previous studies but showed some differences. The strength of our study and the distinction from other studies is that, through a large number of participants, Metabolic syndrome increased the risk of LVDD, especially in men, and that WC and TGL could playan important role.

Waist circumference (abdominal obesity) is a well known cause of LVDD among the components of metabolic syndrome, which can affect multiple metabolic and neurohormonal pathways due to accumulation of adipose tissue, causing abnormalities in the renin angiotensin system and myocardial oxidative stress [13].

As TGL levels increase, my ocellular lipid accumulation increases, which is known to trigger lipo apoptosis and cause diastolic dysfunction [14].

The combination of TGL rich lipoprotein secretion and clearance impairment leads to abdominal obesity [15], and changes in TGL levels could affect diastolic dysfunction by increasing the risk of diabetes [16].

Low HDL levels not only do not sufficiently remove cellular lipids, but also cause arterial stiffness by not properly inducing NO synthesis, preventing apoptosis, and inducing angiogenesis, increasing myocardial cell hypertrophy and myocardial collagen, and eventually inducing diastolic dysfunction [17, 18]. HTN increases LV after load and peripheral vascular resistance, causing LV structural remodeling [19, 20] This leads to myocardial fibrosis and LV hypertrophy, which increase the filling pressure, resulting in diastolic dysfunction [21].

CONCLUSION

In this study, we observed a dose-dependent association between Metabolic syndrome and the risk of left ventricular diastolic dysfunction (LVDD), with a stronger association found in men compared to women. Waist circumference (WC) and triglyceride (TGL) levels were identified as independent risk factors for LVDD in men. However, further research is needed to elucidate the specific mechanisms and causal relationships between the components of Metabolic syndrome, sex differences, and LVDD.

Among the study population, 52% exhibited LVDD, while 48% were classified as normal. Interestingly, LVDD did not show significant correlations with blood pressure, fasting blood sugar, waist measurement, triglyceride levels, or high-density lipoprotein levels. These findings suggest that LVDD may be an early manifestation of metabolic disease-related cardiomyopathy, emphasizing the importance of early detection to prevent disease progression and symptomatic cardiac failure.

The clinical significance of these findings, particularly in terms of prognosis and treatment implications, requires further investigation. This study serves as a hypothesis-generating study, prompting the need for robust research designs such as cohort studies to validate and expand upon our results.

Conventional echocardiography emerges as a simple and cost-effective test for detecting LVDD in asymptomatic individuals with metabolic syndrome. Its widespread availability and non-invasiveness make it a valuable tool for early identification and monitoring of LVDD in this patient population.

In conclusion, our study provides insights into the association between Metabolic syndrome and LVDD, highlighting potential sex differences and the role of specific risk factors. However, additional research is warranted to fully understand the underlying mechanisms and clinical implications of these findings.

REFERENCES

- 1. Harris MF (2013): The metabolic syndrome. Aust Fam Physician, 42: 524–527.
- 2. Alessi MC, Juhan I (2008): Metabolic syndrome, haemostasis and thrombosis. Thromb Haemost., 99(6):9951000.
- 3. Lakka HM, Laaksonen DE, Lakka TA, Niskanen LK, Kumpusalo E, Tuomi-lehto J, Salonen JT. (2002). The metabolic syndrome and total and cardiovascular disease mortality in middle-aged men. JAMA. 288:2709–2716.
- 4. Chinali M, Devereux RB, Howard BV, Roman MJ, Bella JN, Liu JE, Resnick HE, Lee ET, Best LG, de Simone G. (2004). Comparison of cardiac structure and function in American Indians with and without the metabolic syndrome (the Strong Heart Study). Am J Cardiol. 93:40–44.
- 5. Peterson LR, Waggoner AD, Schechtman KB, Meyer T, Gropler RJ, Barzilai B, Davila-Roman VG. (2004). Alterations in left ventricular structure and function in young healthy obese women: Assessment by echocardiography and tissue Doppler imaging. J Am Coll Cardiol. 43:1399–1404.

- 6. De Simone G, Palmieri V, Bella JN, Celentano A, Hong Y, Oberman A, Kitzman DW, Hopkins PN, Arnett DK, Devereux RB. (2002). Association of left ventricular hypertrophy with metabolic risk factors: The Hyper GEN study. J Hypertens. 20:323–331.
- 7. Delas Fuentes L, Brown AL, Mathews SJ, et al. (2007). Metabolic syndrome is associated with abnormal left ventricular diastolic function independent of left ventricular mass. Eur Heart J. 28:553-559.
- 8. Ladeiras- Lopes R, Moreira HT, Bettencourt N, et al. (2018). Metabolic syndrome is associated with impaired diastolic function independently of MRI- derived myocardial extracellular volume: the MESA study. Diabetes. 67:1007- 1012
- 9. Samiei N, Bayat M, Firouzi A, Dehghani F, Parsaee M, Rahimi S, Ahmadi S, Pourmojib M, Ghaemmaghami Z, Rezaei Y, Peighambari MM. (2018). Subclinical systolic and diastolic dysfunctions in patients with metabolic syndrome and angiographically normal coronary arteries: An echocardiographic study. *Journal of Clinical Ultrasound*. 46(3):195-201.
- 10. Kim HL, Kim MA, Oh S, Kim M, Park SM, Yoon HJ, Shin MS, Hong KS, Shin GJ, Shim WJ. (2016). Sex difference in the association between metabolic syndrome and left ventricular diastolic dysfunction. Metabolic Syndrome and Related Disorders. 14(10):507-12.
- 11. Ayalon N, Gopal DM, Mooney DM, Simonetti JS, Grossman JR, Dwivedi A, Donohue C, Perez AJ, Downing J, Gokce N, Miller EJ. (2014). Preclinical left ventricular diastolic dysfunction in metabolic syndrome. *The American journal of cardiology*. 114(6):838-42.
- 12. IDF consensus worldwide definition of the metabolic syndrome diabetes and the metabolic syndrome-driving the CVD epidemic, diabetes atlas, 2nded. *International Diabetes Federation*; (2003).
- 13. Hwang YC, Jee JH, Kang M, Rhee EJ, Sung J, Lee MK. (2012). Metabolic syndrome and insulin resistance are associated with abnormal left ventricular diastolic function and structure independent of blood pressure and fasting plasma glucose level. *Int J Cardiol*. 159:107- 111.
- 14. Russo C, Jin Z, Homma S, et al. (2011). Effect of obesity and overweight on left ventricular diastolic function: a community- based study in an elderly cohort. *J Am Coll Cardiol*. 57: 1368- 1374.
- 15. Delas Fuentes L, Waggoner AD, Brown AL, Dávila- Román VG. (2005). Plasma triglyceride level is an independent predictor of altered left ventricular relaxation. *J Am Soc Echocardiogr*. 18:1285- 1291.
- 16. Borén J, Watts GF, Adiels M, et al. (2015). Kinetic and related determinants of plasma triglyceride concentration in abdominal obesity: multicen-tertracer kinetic study. *Arterioscler Thromb Vasc Biol.* 35: 2218- 2224.
- 17. Tirosh A, Shai I, Bitzur R, et al. (2008). Changes in triglyceride levels over time and risk of type 2 diabetes in young men. *Diabetes Care*. 31:2032- 2037.
- 18. Walter M. (2009). Interrelationships among HDL metabolism, aging, and atherosclerosis. *Arterioscler Thromb Vasc Biol.* 29:1244- 1250.
- 19. Mika M, Kanzaki H, Hasegawa T, et al. (2020). Arterial stiffening is a crucial factor for left ventricular diastolic dysfunction in a community- based normotensive population. *Int J Cardiol Hypertens*. 6: 100038.
- 20. Pavlopoulos H, Grapsa J, Stefanadi E, et al. (2008). The evolution of diastolic dysfunction in the hypertensive disease. *Eur J Echocardiogr*. 9:772-778.
- 21. Kenchaiah S, Pfeffer MA. (2004). Cardiac remodeling in systemic hyper -tension. Med Clin North Am. 88:115-130.