MAR Cardiology & Heart Diseases (2024) 3:11

Research Article

The Assessment of Left Ventricular Function in Patients with and without Left Ventricular Systolic Dysfunction by the Resting Versus Peak Exercise Left Ventricular Ejection Fraction-An Observational Study

Dr Ayesha Mohammed Abdul Raoof [1]*, Dr Abdullah Ansari [2]

1. *Department of Internal Medicine, Adam hospital, Ministry of Health, Sultanate of Oman.*
2. *Department of Internal Medicine (Cardiology Unit), Nizwa hospital, Ministry of Health, Sultanate of Oman.*

*__Correspondence to:__ Dr Ayesha Mohammed Abdul Raoof, Department of Internal Medicine, Adam hospital, Ministry of Health, Sultanate of Oman.

Copyright

© 2024 **Dr Ayesha Mohammed Abdul Raoof.** This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Received: 10 September 2024

Published: 01 October 2024

Abstract

Background: *Ejection fraction (EF) is widely used as a measure of systolic function. However, it doesn't correlate well with exercise tolerance and other measures of peak cardiac output. Present study was conducted to compare resting ejection fraction and peak exercise left ventricular ejection fraction as a measure of left ventricular function and correlate it with peak exercise capacity, symptom class and morbidity index in patients with and without left ventricular systolic dysfunction.*

Material and Methods: *Baseline and peak exercise LV dimensions, stroke volume and cardiac output were measured in patients who were referred for stress echocardiography (treadmill or dobutamine stress testing). We analysed the relationship between exercise capacity, symptom class, morbidity index and LVH with change in LV dimensions during rest and exercise. In addition, we also analysed the change in LV dimensions in young adults, elderly hypertensives and patients of ischemic or dilated cardiomyopathy with exercise.*

Results: *Exercise time and the maximal achieved workload were similar between elderly hypertensives and low resting EF patients (total exercise time ≈ 6 and half minutes and MWL≈ 8 METS in both the groups) but were significantly impaired in patient groups compared with young adults (total exercise time ≈ 10 minutes and MWL≈ 11 METS). At peak exercise, young adults and patients with HFrEF (Low EF) showed no change in LVedD, but there was a significant decrease in peak exercise LVedD (43.33 mm to 39.04 mm) in patients with HFpEF. Stroke volume increased in healthy adults (from 60.95 ml to 74.11 ml) and patients with HFrEF (from 53.55 ml to 60.20 ml) but showed no change in patients with HFpEF (52.25 ml at rest, 51.75 ml at peak exercise). Increase in peak exercise cardiac output was 2.9-fold in healthy adults, 2.5-fold in HFrEF, and 2.1-fold in elderly hypertensives.*

Conclusion: *Resting ejection fraction in young patients with past infarctions reflects increased end-diastolic volume with normal resting stroke volume; it is not due to systolic dysfunction. Elderly hypertensive patients fail to grow their ventricle by eccentric hypertrophy and they have systolic dysfunction, with impaired contractile reserve and little augmentation of systolic ejection during stress and severe worsening of abnormalities of relaxation during stress, with decrease in ventricular end-diastolic dimension, unlike healthy individuals and young patients with low EF. Therefore, normal resting echocardiography does not preclude the presence of significant functional abnormalities on exercise that can contribute to symptoms in patients with HFpEF. LVEF is a flawed measure of contractility and normal resting LVEF does not imply normal LV systolic function.*

Introduction

Ejection fraction (EF) is widely used as a measure of systolic function. However, it doesn't correlate well with exercise tolerance and other measures of peak cardiac output.

Ejection fraction is the LV stroke volume expressed as a percentage of the end-diastolic volume. There is no ideal measure of myocardial contractility despite extensive investigation. By default, because it is relatively easy to measure and to understand, the LV ejection fraction has maintained its position as the most commonly used index. In patients with HFpEF, ejection fraction can be preserved or even be supranormal if the end-diastolic volume is significantly reduced. Thus, accurate measurement and reporting of global LV systolic function should include not just ejection fraction but also the volumes, LV end-diastolic or end-systolic, which reflect the remodeling process. Similar findings are seen with normal ageing and the typical precursors of heart failure with a normal ejection fraction such as hypertension, diabetes, and ischemia. There appears to be a spectrum of abnormalities of systolic function from the truly normal to systolic heart failure with heart failure with a normal ejection fraction occupying an intermediate position [1].

LVEF is recognized to be a poor measure of contractility because of its sensitivity to load and chamber remodeling1. Cardiac output may be adequate at rest in heart disease. Abnormalities may be present only during stress. Stroke volume, cardiac output, and their augmentation during stress or exercise are biologically relevant measures of systolic function, whereas ejection fraction is a mathematical calculation and correlate with prognosis but is not a measure of LV function. A normal LVEF does not imply normal LV function [2].

In order for the left ventricle to function as an effective pump, it must not only be able to empty but also to fill without requiring an elevated left atrial pressure. Furthermore, the stroke volume must be able to increase in response to stress, such as exercise, without much increase in left atrial pressure [3].

In response to external demands the myocardium undergoes adaptive changes. This process has been termed cardiac plasticity and changes at the cellular and macroscopic levels have been documented under various environmental conditions[4]. The most common and best understood cardiac adaptation is concentric left ventricular remodelling, which most commonly develops in response to pressure overload due to hypertension and aortic stenosis [5,6].

The adaptive changes that occur with endurance exercise and deconditioning are not as well understood but have been described in the exercise physiology literature [7-9]. Adaptive eccentric remodelling with left ventricular chamber enlargement is well documented in endurance athletes such as long-distance cyclists [7]. Extreme physical inactivity induced by bed rest or zero-gravity conditions in healthy subjects has been demonstrated to rapidly reduce left ventricular chamber volumes and mass [8,9].

Although population or disease-based studies provide interesting structural insights into the remodelling of the left ventricle they typically do not directly relate left ventricular dimensions and cardiac output to exercise capacity. Moreover, patients with markedly reduced myocardial contractility at rest (ischemic or dilated cardiomyopathy), but with good residual contractile reserve, have a favourable exercise capacity. On the other hand, patients with mildly abnormal myocardial contractility at rest, but reduced contractile reserve have a poor exercise capacity [10].

Therefore, I proposed to study comparison of resting ejection fraction and peak exercise left ventricular ejection fraction as a measure of left ventricular function and correlate it with peak exercise capacity, symptom class and morbidity index in patients with and without left ventricular systolic dysfunction.

Aim and Objective:

- Resting ejection fraction versus peak exercise ejection fraction as a measure of left ventricular function as assessed by peak exercise capacity, symptom class and morbidity index.

Materials and Methods

Study Area

The study was carried out in the Cardiology Department of Batra Hospital and Medical Research Centre, New Delhi, India.

Study Population

All patients with age more than 18 years who fulfilled the inclusion and exclusion criteria and presented to the echocardiographic laboratory for physical or dobutamine echocardiography were enrolled as cases.

Sample Size

As there were no previous studies on this subject, so we had proposed to do a pilot study with a minimum of 50 patients, including at least half in symptom class 2 or 3, and also a minimum of 10 patients with resting ejection fraction below 50%.

Study Design

It was a prospective, observational study. The present study compared resting ejection fraction and peak exercise ejection fraction as a measure of left ventricular function and correlated it with peak exercise capacity, symptom class and morbidity index.

Time Frame

May 2016 to April 2017

Inclusion Criteria

- All patients aged 18 years and above referred for stress echocardiography to our laboratory were screened for inclusion.

Exclusion Criteria

- Patients with stress induced ischemia, or those who were already known to have significant coronary obstructions.
- Patients with atrial fibrillation or other persistent arrhythmia.
- Patients with significant mitral or aortic valvular disease.
- When echo visualization was suboptimal due to poor echo window.

Methodology

Data on age, sex, BMI, co-morbidities, clinical diagnosis, and NYHA class was collected. An informed consent was obtained from all patients enrolled for study for their will to undergo stress echocardiography using GE vivid E-9 and Philips CX50 echocardiography machines. Patients were kept fasting for at least 4 hours prior to stress test and they were advised to avoid tea, coffee and smoking 4 hours prior to stress echocardiography.

Patients were subjected to treadmill stress test using standardized Bruce protocol. Images were obtained both at rest and at peak exercise following recommended guidelines. Patients who were unable to exercise underwent pharmacological stress echocardiography using intravenous dobutamine which was delivered using an infusion pump starting at 5mcg/kg/min which was stepwise increased to 10, 20 & 40 mcg/kg/min every 3 minutes. If even after this dose, 85% of age-predicted maximum heart rate was not achieved then atropine in divided doses of 0.25-0.5mg to a maximum of 1 mg was given to achieve target heart rate. Images were obtained at baseline, low dose and peak dose of dobutamine [20,21].

Resting heart rate and resting LV dimensions by M-mode echocardiography were measured. Resting ejection fraction and resting stroke volume was calculated using Teichholz formula [22]. Resting Cardiac output was calculated by multiplying resting stroke volume by the resting heart rate. Peak heart rate and peak exercise LV dimensions were measured. From these measurements, LV ejection fraction, stroke volume and cardiac output at peak exercise were calculated.

Change in LV end-diastolic dimension (ΔLVedD), change in LV end-systolic dimension (ΔLVesD), change in left ventricular ejection fraction (ΔLVEF) and change in stroke volume (ΔStroke volume) at peak stress (i.e. peak stress value minus resting value) was also calculated.

Peak exercise capacity was calculated from total exercise time (measured in minutes) and maximum workload (measured as METS). One "metabolic equivalent" (MET) is equated with the resting metabolic rate (≈ 3.5ml of O2/kg/min) [23].

Morbidity index was calculated by modified Cardiac index which was derived by modifying the CAD specific index 24 and included 10 risk factors-

a) a)Current smoking which was divided into mild and moderate to severe depending upon whether the number of pack-years smoked (pack-year is calculated by multiplying the number of packs of cigarettes smoked per day by the number of years the person has smoked) was less than or more than 5 and was given a score of 1 & 2 respectively.

b) Hypertension was divided into mild (mild LVH), moderate (moderate LVH) and severe (severe LVH) and was given a score of 1, 2 and 3 respectively.

c) Diabetes mellitus was divided into mild (less than 5 years), moderate (more than 5 years) and severe (more than 5 years with sequelae) and was given a score of 1, 2 and 3 respectively.

d) Clinical atherosclerotic event included old CVA, old CAD, post PCI and post CABG and was given a score of 2.

e) Peripheral vascular disease was given a score of 2 as it is associated with severe atherosclerosis.

f) Chronic obstructive pulmonary disease was given a score of 2.

g) Chronic kidney disease was divided into mild to moderate (those without dialysis) and severe (those on dialysis) and was given a score of 2 and 5 respectively.

h) Malignancy was divided into non-metastatic and metastatic and was given a score of 2 and 4 respectively.

i) Miscellaneous morbidities (those not included in above like rheumatoid arthritis, osteoarthritis, hypothyroidism, peptic ulcer disease) were divided into mild to moderate (without complications) and severe (with complications) and were given a score of 1 and 2 respectively.

j) In addition for each decade more than 40 years of age, a score of 1 was added to the above score.

- Symptom class was defined according to NYHA classification which places patients in one of four categories based on how much they are limited during physical activity [25].

NYHA Class	Patient Symptoms
I	Patients with cardiac disease but without resulting limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea, or anginal pain.
II	Patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea, or anginal pain.
III	Patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity causes fatigue, palpitation, dyspnea, or anginal pain.
IV	Patients with cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of heart failure or the anginal syndrome may be present even at rest. If any physical activity is undertaken, discomfort is increased.

Ordinary effort is that of the person himself as regard his previous effort tolerance and usual life style.

To see the relationship between exercise capacity, symptom class, morbidity index and LVH with LV dimensions, we selected patients from the study group on the basis of-

- Poor exercise capacity versus excellent exercise capacity - poor exercise capacity was defined as the inability to exercise more than 6 minutes as compared to excellent exercise capacity which was defined as the ability to exercise more than or equal to 9 minutes according to standard Bruce treadmill protocol.
- NYHA Class 0-I versus NYHA Class II-III.
- Low morbidity index versus high morbidity index- low morbidity index was defined as morbidity index less than 6 and high morbidity index was defined as morbidity index more than equal to 6.
- LVH versus without LVH - inclusion criteria for LVH patients was an increase in wall thickness (>12mm regardless of gender)[22].

In order to gain insight into the relationship of young adults, elderly hypertensives and patients of ischemic or dilated cardiomyopathy with the LV dimensions, we divided the study group into-

A) Young-those with age <60 years with normal resting LVEF (LVEF>50%) along with a total exercise time more than or equal to 9 minutes when subjected to standard Bruce treadmill stress testing or a morbidity index less than or equal to 3 in case of Dobutamine stress testing.

B) Old-those with age >60 years with normal resting LVEF (LVEF>50%) and a morbidity index more than or equal to 6 or presence of LVH.

C) Low EF-those with resting LVEF<50% irrespective of age.

Statistical Methods

- Statistical correlation of resting measurements and peak exercise measurements was done with peak exercise time and with NYHA symptom class in patients who underwent exercise echocardiography. In patients who underwent dobutamine stress echocardiography, we correlated resting and peak stress measurements with morbidity index. In addition, statistical correlation of resting and peak stress measurements was done between young adults (Young), elderly hypertensives (Old) and ischemic or dilated cardiomyopathy (Low EF) patients.

- Data contained both continuous and categorical variables. Therefore, mean with SD for continuous and frequency with proportions was used for their presentation. Student‘t’ or Mann-Whitney ‘U’ test was used for the quantitative variables with two independent groups and Chi-square/Fisher’s test was used for statistical significance between qualitative variables. The oneway analysis of variance (ANOVA) was used for the three group comparisons and the Dunnett’s (2-sided) t test and Tukey’s HSD (honest significant difference) were performed to explore the significant pair(s) in the multiple comparison tests. The two sided p value less than 0.05 considered as statistical significant. Data was entered and coded in MS Excel (version 7). The statistical software IBM PASW (Version 22.0) was used for entire data analysis.

Ethical Considerations

The Research Ethics Committee of the Hospital reviewed and approved the study protocol.

Observation:

A total of 93 patients, with or without heart muscle disease were enrolled for stress testing in our study over a one year study period.

58 patients underwent treadmill stress testing using Bruce protocol and 35 patients underwent Dobutamine stress testing.

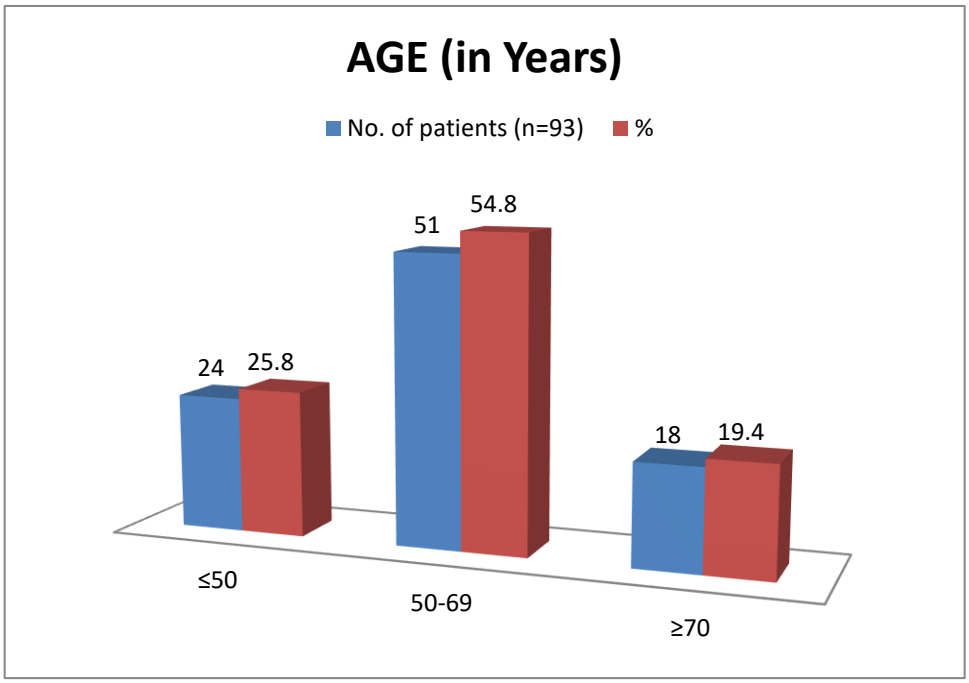
The results of the study are tabulated as follows:

Age (years)	No. of patients (n=93)	%
≤50	24	25.8
50-69	51	54.8
≥70	18	19.4

MEAN ± SD AGE = 57 ± 14

Table 1: Age Distribution of study group (n=93)

74.2% (n=69) of the patients in our study were aged 50 years or above with 19.4% (n=18) aged more than 70 years of age. The mean age of study population was 57 years (Table 1, Figure 1).



Gender	No. of Patients (n=93)	%
Male	62	66.7
Female	31	33.3

Male: Female ratio- 2: 1

Table 2: Sex Distribution of study group (n=93)

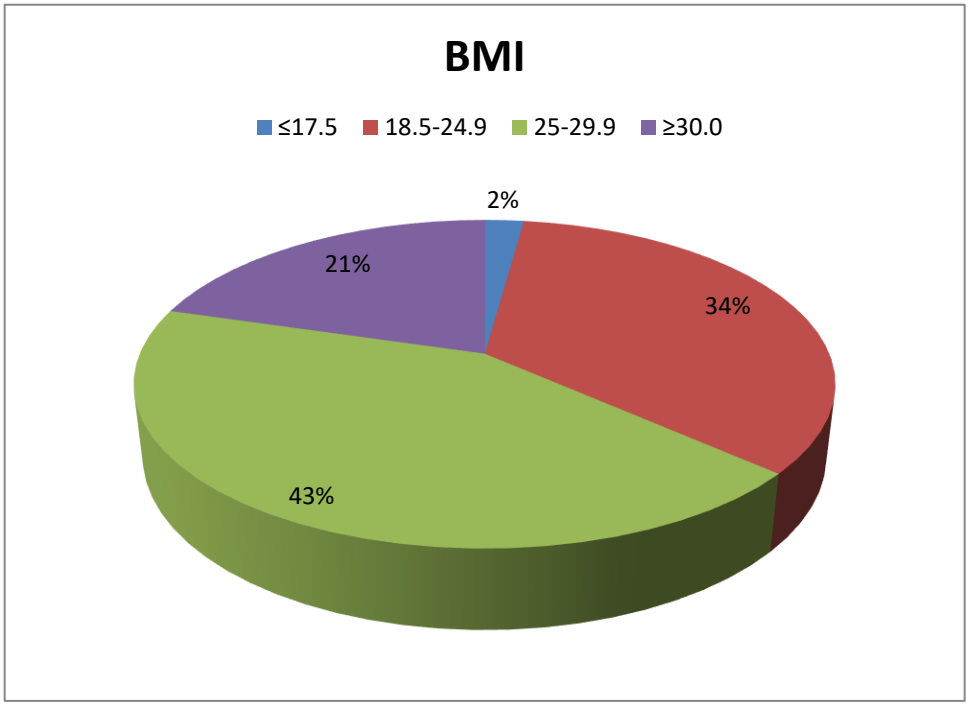
62 patients were male (66.7%) and 31 patients were females (33.3%) with male: female ratio of 2: 1 (Table 2).

BMI	No. of Patients (N=93)	%
≤18.5	2	2.2
18.5-24.9	32	34.4
25-29.9	40	43.0
≥30.0	19	20.4

MEAN ± SD BMI = 26.75 ± 4.48

Table 3: Distribution of study group (n=93) on the Basis of BMI

Patients were divided on basis of BMI into four groups- underweight [BMI (≤18.5)], normal [BMI (18.5-24.9)], overweight [BMI (25-29.9)] and obese [BMI (≥30)]. 63.4% (n=59) patients in our study were either overweight or obese (43.0% and 20.4% respectively). (Table 3, Figure 2).

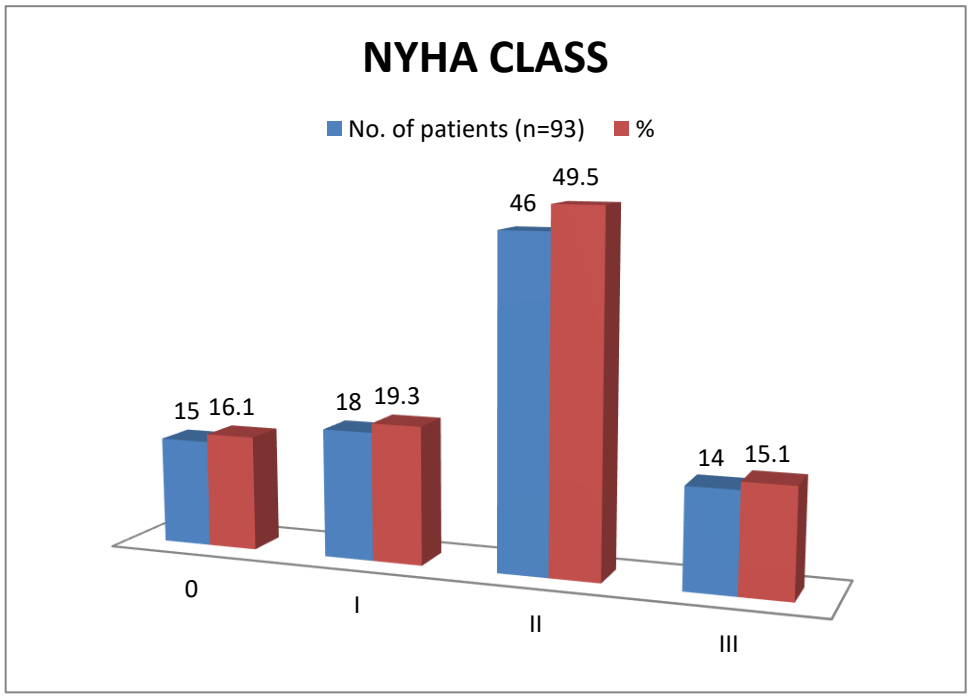


NYHA Class	No. of Patients (N=93)	%
0	15	16.1
I	18	19.3
II	46	49.5
III	14	15.1

Table 4: Distribution of study group (n=93) on the Basis of NYHA Class

Patients were divided on basis of NYHA Class into five groups- 0, I, II, III and IV.

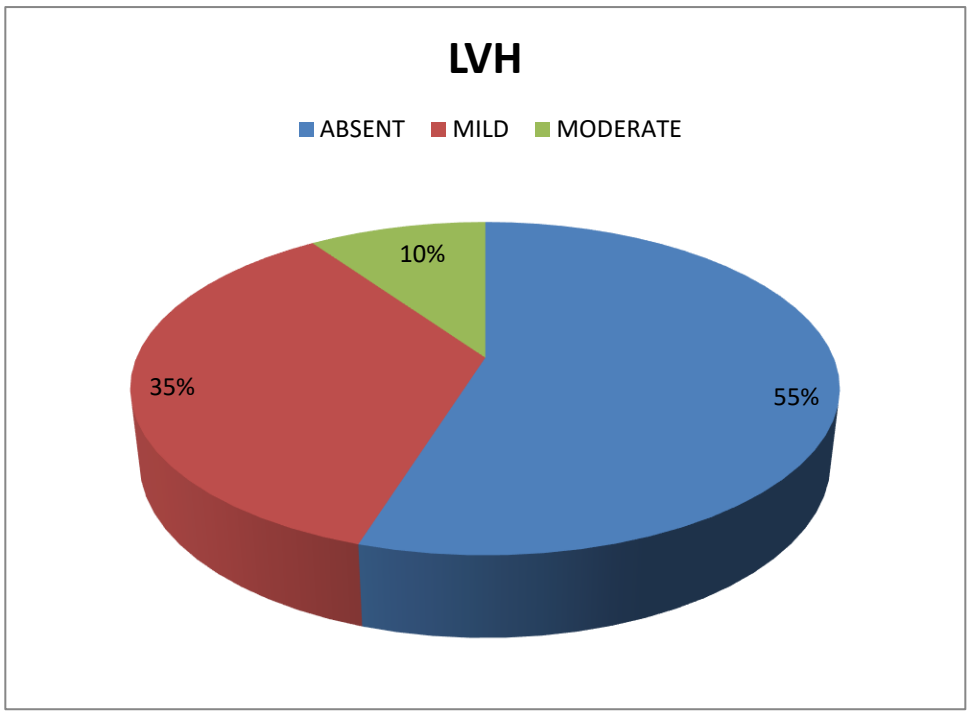
In our study, 64.6% (n=60) patients were in NYHA Class II or more. There was no patient in NYHA Class IV in our study (Table 4, Figure 3).



LVH	No. of patients (n=93)	%
Absent	51	54.8
Mild	33	35.5
Moderate	9	9.7

Table 5: Distribution of study group (n=93) on the Basis of LVH

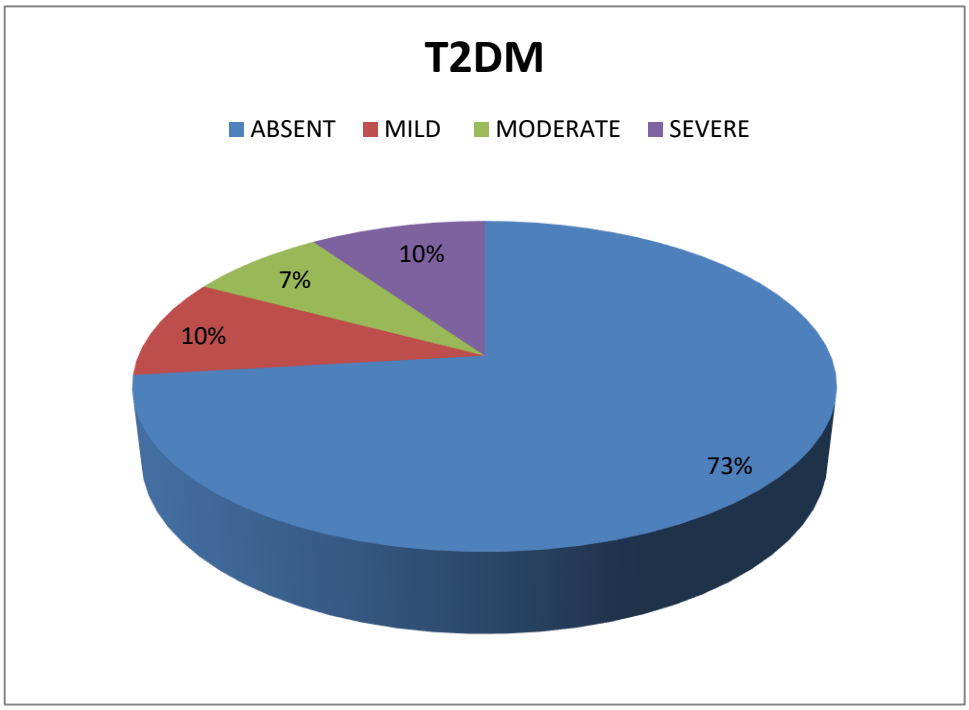
Patients were divided on basis of LVH into three groups- mild, moderate and severe. In our study, 45.2% (n=42) of patients had LVH, out of which 35.5% (n=33) had mild LVH and 9.7% (n=9) had moderate LVH. There was no patient of severe LVH in our study (Table 5, Figure 4).



T_2DM	**No. of Patients (N=93)**	**%**
Absent	68	73.1
Mild	9	9.7
Moderate	7	7.5
Severe	9	9.7

Table 6: Distribution of study group (n=93) on the Basis of T_2DM

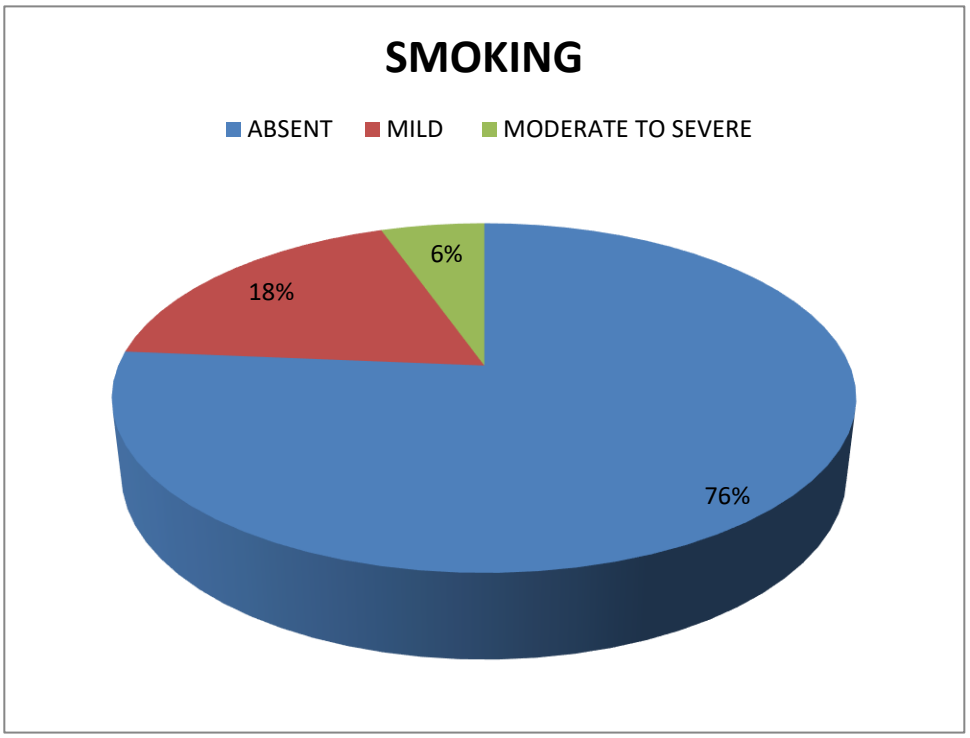
26.9% (n=25) patients who underwent stress echocardiography in our study had diabetes mellitus. Out of which 9.7% (n=9) had mild (less than 5 years of diabetes), 7.5% (n=7) had moderate (more than 5 years of diabetes) and 9.7% (n=9) had severe (more than 5 years of diabetes with sequelae) diabetes mellitus (Table 6, Figure 5).



Current Smoking	No. of patients (n=93)	%
Absent	71	76.3
Mild	17	18.3
Moderate To Severe	5	5.4

Table 7: Distribution of study group (n=93) on the Basis of Current Smoking

In our study, 23.7% (n=22) of the patients were current smokers with 18.3% (n=17) in the Mild group and 5.4% (n=5) patients in the moderate to severe group depending upon whether the number of pack-years smoked (pack-year is calculated by multiplying the number of packs of cigarettes smoked per day by the number of years the person has smoked) is less than or more than 5 (Table 7, Figure 6).



CAD	No. of patients (n=93)	%
Absent	58	62.4
Present	35	37.6

Table 8: Distribution of study group (n=93) on the Basis of CAD

Procedure	No. of patients (n=93)	%
Post PCI	23	24.7
Post CABG	5	5.4

Table 9: Distribution of study group (n=93) on the Basis of Post PCI/ Post CABG Status

Number of patients who had CAD in our study was 35 (37.6%). Out of those who had CAD, 23 patients (24.7%) had undergone PCI and 5 patients (5.4%) had undergone CABG (Table 8, 9).

Resting LVEF	No. of patients (n=93)	%
<50%	20	21.5
≥50%	73	78.5

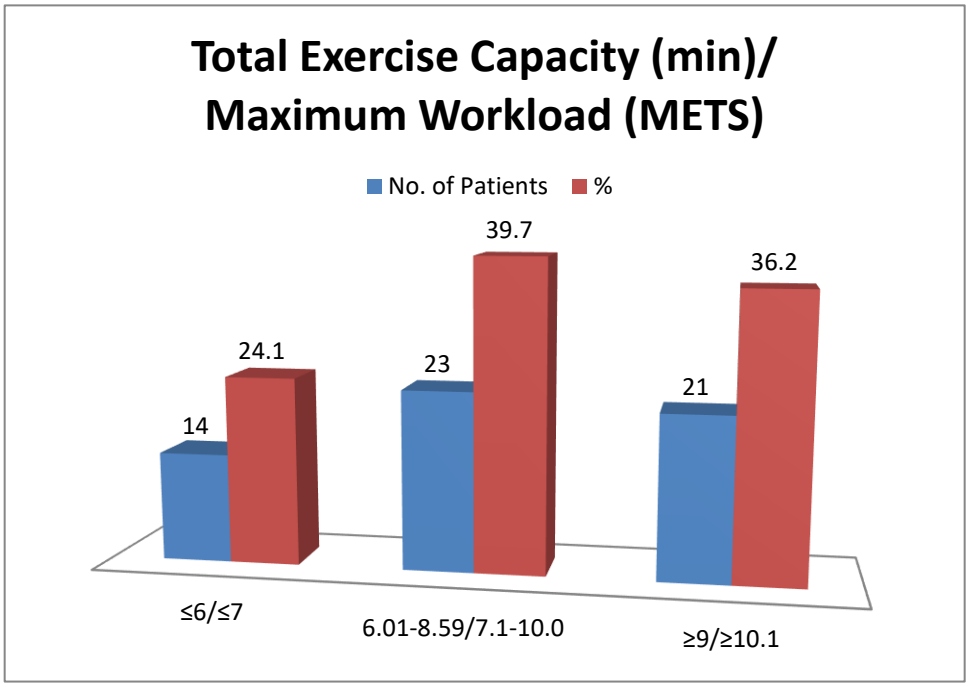
Table 10: Distribution of study group (n=93) on the Basis of Resting LVEF

21.5% (n=20) of the patients in our study had resting LVEF less than 50% while rest 78.5% (n=73) of the patients had resting LVEF more than or equal to 50% (Table 10).

TEC (min)/MWL (METS)	No. of Patients (n=58)	%
≤6/≤7	14	24.1
6:01-8:59/7.1-10.0	23	39.7
≥9/≥10.1	21	36.2

Table 11: Distribution of study group (n=58) subjected to Treadmill Stress testing on the Basis of Total Exercise Capacity (TEC) & Maximum Workload (MWL)

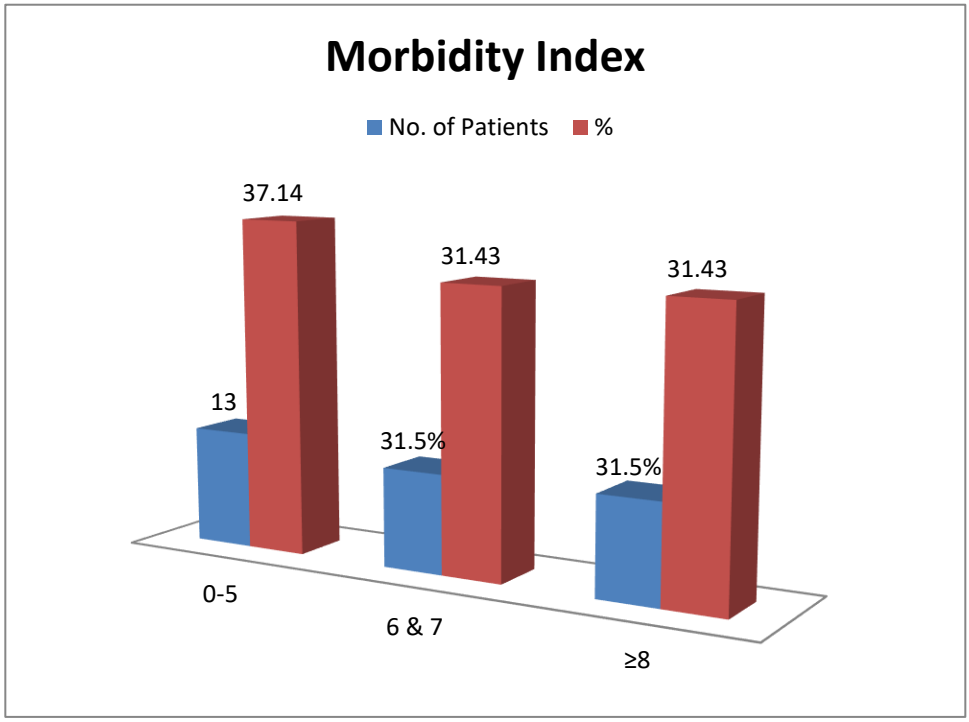
Out of the 58 patients who were subjected to treadmill stress testing in our study, 36.2% (n=21) patients had excellent exercise capacity (TEC ≥9minutes and MWL ≥10.1METS) while 24.1% (n=14) patients had poor exercise capacity (TEC ≤6 minutes and MWL ≤7.0 METS). 39.7% (n=23) of the patients had good exercise capacity (TEC 6:01-8:59 minutes and MWL 7.1-10.1 METS) [Table 11, Figure 7].



Morbidity Index	No. of Patients (n=35)	%
0-5	13	37.14
6 & 7	11	31.43
≥8	11	31.43

Table 12: Distribution of study group (n=35) subjected to Pharmacological (Dobutamine) Stress testing on the Basis of Morbidity Index

35 patients in our study were subjected to dobutamine stress testing; out of which 37.14% (n=13) patients had morbidity index less than 6 while 31.43% (n=11) patients had morbidity index more than or equal to 8. Equal number of patients i.e. 31.34% (n=11) had morbidity index 6 & 7 (Table 12, Figure 8)



Baseline Character	Value/No. of Patients
Age	57±14
Gender (M/F)	62/31
BMI	26.75 ± 4.48
NYHA (0,I,II,III)	15/18/46/14
Hypertension	52
Diabetes mellitus	25
Current Smoking	22
CAD	35
POST PCI/POST CABG	23/5

Table 13: Baseline Characteristics of study group subjected to Stress testing (n=93)

Parameter	Resting	Post Stress
LVedD (mm)	45.63 ± 6.56	43.72 ± 8.02
ΔLVedD	-1.9 ± 5.53	
LVesD (mm)	31.47 ± 7.03	25.82 ± 8.39
ΔLVesD	-5.71 ± 4.74	
LVEF %	58.37 ± 10.53	71.26 ± 11.97
ΔLVEF	12.84 ± 5.62	
Stroke Volume (ml)	56.22 ± 15.32	62.83 ± 19.29
ΔStroke Volume	6.83 ± 14.50	
Heart Rate (b/min)	72 ± 13	161 ± 18
Cardiac Output (L/min)	4029.13 ± 1308.37	10164.8 ± 3534.33

Table 14: Echocardiographic Characteristics of study group subjected to Stress testing (n=93) at Rest and Post Stress

Parameter	Stress Testing	Resting	Post Stress
Age	Treadmill	53.74±12.59	
	Dobutamine	62.20±12.83	
BMI	Treadmill	26.62±3.60	
	Dobutamine	26.95±5.10	
LVedD (mm)	Treadmill	45.97±6.25	44.93±8.10
	Dobutamine	45.09±6.17	41.71±6.46
ΔLVedD	Treadmill	-1.03±5.01	
	Dobutamine	-3.37±5.45	
LVesD (mm)	Treadmill	31.71±6.51	26.64±8.67
	Dobutamine	31.09±6.88	24.46±6.54
ΔLVesD	Treadmill	-5.07±4.77	
	Dobutamine	-6.77±3.73	
LVEF %	Treadmill	58.71±9.60	71.34±11.80
	Dobutamine	57.80±10.84	71.11±11.11
ΔLVEF	Treadmill	12.55±5.65	
	Dobutamine	13.31±4.74	
Stroke Volume (ml)	Treadmill	57.21±14.65	66.19±18.74
	Dobutamine	54.57±14.46	57.26±17.84
ΔStroke Volume	Treadmill	9.33±12.97	
	Dobutamine	2.68±14.33	
Heart Rate (b/min)	Treadmill	71±13	168±18
	Dobutamine	73±10	149±10
Cardiac Output (L/min)	Treadmill	4.06±1.26	11.15±3.44
	Dobutamine	3.98±1.19	8.53±2.73

Table 15: Difference in Baseline and Echocardiographic Characteristics of study group subjected to Treadmill (n=58) and Dobutamine Stress testing (n=35) at Rest and Post Stress:

Dependent Variable	NYHA Class	N	Mean	Standard Deviation	p -value**
Total exercise time	0 - I	30	8.683	2.0363	**.000***
	II - III	28	6.528	1.6643	
Resting EF	0 - I	30	62.033	7.5039	**.006***
	II - III	28	55.143	10.5750	
ΔLVedD	0 - I	30	-2.500	4.6219	**.021***
	II - III	28	.536	5.1098	
ΔLVesD	0 - I	30	-12.513	5.4683	**.001***
	II - III	28	-7.329	5.5845	
Maximum Workload	0 - I	30	10.013	2.2413	**.000***
	II - III	28	7.864	1.5073	
ΔStroke Volume	0 - I	30	8.333	11.5470	.554
	II - III	28	10.393	14.6928	

** p -value is significant at the 0.05 level.*

*** p -value was calculated using t -test 58 Patients who were subjected to treadmill stress testing were compared on the basis of NYHA Class (NYHA Class 0-I vs. NYHA Class II-III) using t-test.*

Table 16: Correlation between NYHA Class with Total Exercise Time, Maximum Workload, Resting LVEF, ΔLVedD, ΔLVesD and ΔStroke Volume in the study group subjected to Treadmill Stress testing

Statistical significance ($p<0.05$) was noted for NYHA Class with Total Exercise Time ($p=0.000$), Maximum Workload ($p=0.000$), Resting LVEF ($p=0.006$), ΔLVedD ($p=0.021$) and ΔLVesD ($p=0.001$), i.e. patients with NYHA class 0-I had higher exercise capacity, higher resting LVEF, higher change in LVedD and LVesD with exercise as compared to NYHA class II-III, but no statistically significant difference in the change in Stroke Volume with exercise ($p=0.554$).

Dependent Variable	Total Exercise Time	N	Mean	Standard Deviation	p –value**
Resting EF	≤6 mins	14	54.14	10.92	**.028***
	≥9 mins	21	61.95	6.09	
ΔLVedD	≤6 mins	14	0.64	5.64	.200*
	≥9 mins	21	-1.95	5.40	
ΔLVesD	≤6 mins	14	-5.79	6.00	**.003***
	≥9 mins	21	-13.21	6.08	
ΔLVEF	≤6 mins	14	9.07	4.55	**.003***
	≥9 mins	21	14.67	4.88	
ΔStroke volume	≤6 mins	14	7.93	14.89	.973
	≥9 mins	21	10.00	15.42	

* p -value is significant at the 0.05 level.

** p -value was calculated using Mann Whitney 'U' test 58 Patients who were subjected to treadmill stress testing were compared on the basis of Total Exercise Capacity (poor exercise capacity vs. excellent exercise capacity) using Mann-Whitney's 'U' test.

Table 17: Correlation between Total exercise time with Resting LVEF, ΔLVedD, ΔLVesD, ΔLVEF and ΔStroke Volume in the study group subjected to Treadmill Stress testing

Statistical significance ($p<0.05$) was noted for Total Exercise Time with Resting LVEF ($p=0.028$), ΔLVesD ($p=0.003$) and ΔLVEF (0.003), i.e. patients with poor exercise capacity had a lower resting LVEF and a lower change in LVesD and LVEF with exercise as compared to patients with excellent exercise capacity but no statistically significant difference was seen in ΔStroke Volume ($p=0.973$) and ΔLVedD ($p=0.200$) with exercise.

Dependent Variable	**Morbidity Index**	**N**	**Mean**	**Standard Deviation**	**p -value****
Resting EF	<6	13	64.23	6.35	.630
	≥6	12	63.08	5.30	
ΔLVedD	<6	13	-0.62	6.12	**.045***
	≥6	12	-5.50	5.32	
ΔLVesD	<6	13	-5.08	3.77	**.038***
	≥6	12	-8.33	3.63	
ΔLVEF	<6	13	11.85	3.85	.238
	≥6	12	14.08	5.32	
ΔStroke volume	<6	13	5.85	19.45	.351
	≥6	12	-0.58	13.49	

** p -value is significant at the 0.05 level.*

*** p -value was calculated using t -test*

Out of the patients who were subjected to pharmacological stress testing (n=35) with Dobutamine, 25 patients (10 patients had low EF) were compared on the basis of Morbidity Index (Morbidity Index <6 vs. Morbidity Index ≥6) using t-test.

Table 18: Correlation between Morbidity Index with Resting LVEF, ΔLVedD, ΔLVesD, ΔLVEF and ΔStroke Volume in the study group subjected to Pharmacological Stress testing with Dobutamine.

Statistical significance ($p<0.05$) was noted for Morbidity Index with ΔLVedD ($p=0.045$), ΔLVesD ($p=0.038$), i.e. patients with Morbidity Index ≥6 had significant decrease in LVedD and LVesD after dobutamine stress testing as compared to patients with Morbidity Index<6. In addition, patients with Morbidity Index ≥6 were unable to increase their stroke volume with peak dobutamine stress as compared to patients with Morbidity index <6 but it wasn't statistically significant ($p=0.351$).

Dependent Variable	LVH	N	Mean	Standard Deviation	p-value**
LVedD (mm) resting	Absent	51	45.76	6.17	.839
	Mild	33	45.76	7.01	
	Moderate	9	44.44	3.97	
LVedD (mm) Peak stress	Absent	51	44.71	7.72	**.044***
	Mild	33	43.82	7.72	
	Moderate	9	37.78	5.52	
LVesD (mm) resting	Absent	51	31.31	6.57	.746
	Mild	33	32.06	7.15	
	Moderate	9	30.22	6.20	
LVesD (mm) Peak stress	Absent	51	26.18	8.36	.150
	Mild	33	26.61	8.07	
	Moderate	9	20.89	4.14	
Stroke Volume (ml) resting	Absent	51	57.27	15.0	.688
	Mild	33	55.42	15.69	
	Moderate	9	53.11	9.05	
Stroke Volume (ml) Peak stress	Absent	51	65.96	19.13	**.050***
	Mild	33	61.61	18.14	
	Moderate	9	49.56	16.92	
Cardiac Output (L/min) resting	Absent	51	4033.14	1283.42	.996
	Mild	33	4032.00	1288.76	
	Moderate	9	3995.89	852.31	
Cardiac Output (L/min) Peak stress	Absent	51	11005.35	3635.98	**.008***
	Mild	33	9591.88	2939.29	
	Moderate	9	7502.22	2423.94	

** p -value is significant at the 0.05 level.*

*** p -value was calculated using oneway ANOVA test*

In our study, 42 patients had LVH, out of which 33 patients had mild LVH and 9 had moderate LVH. There was no patient with severe LVH in our study.

Table 19: Correlation between LVH with Resting and Peak Stress LVedD, LVesD, LVEF, Stroke Volume and Cardiac Output

Statistical significance ($p<0.05$) was noted for LVH with Peak stress LVedD ($p=0.044$), Peak stress Stroke Volume ($p=0.050$) and peak stress Cardiac Output ($p=0.008$) i.e. significant decrease in peak stress LVedD was seen in patients with LVH while there was no significant change in the peak stress LVedD in patients without LVH and the amount of decrease in Peak stress LVedD increased with the severity of LVH. In addition, patients with LVH were unable to increase their stroke volume as compared to patients without LVH. In fact there was a fall in stroke volume at peak stress in patients with moderate LVH (from 53.11ml to 49.56ml). Peak stress cardiac output increase was 2.7 fold in patients without LVH, 2.4 fold in patients with Mild LVH, and 1.9 fold in patients with Moderate LVH.

Measurement	Group	N	Mean	Standard Deviation	p-value**
LVedD (mm)-Resting	Young	19	44.95	5.55	**.001***
	Old	24	43.33	4.06	
	Low EF	20	50.35	8.22	
LVedD (mm) - Peak stress	Young	19	44.79	5.46	**.000***
	Old	24	39.04	4.72	
	Low EF	20	49.20	10.07	
LVesD (mm)-Resting	Young	19	29.37	4.17	**.000***
	Old	24	28.96	4.05	
	Low EF	20	39.85	7.75	
LVesD (mm) - Peak stress	Young	19	23.37	4.37	**.000***
	Old	24	21.96	3.28	
	Low EF	20	35.85	9.73	
LVEF % - Resting	Young	19	63.84	4.23	**.000***
	Old	24	61.33	7.66	
	Low EF	20	41.85	5.41	
LVEF % - Peak stress	Young	19	78.26	5.92	**.000***
	Old	24	74.25	6.05	
	Low EF	20	53.55	9.07	
Stroke Volume (ml) - Resting	Young	19	60.95	16.13	.098
	Old	24	52.25	11.61	
	Low EF	20	53.00	14.13	
Stroke Volume (ml) - Peak stress	Young	19	74.11	17.04	**.000***
	Old	24	51.75	12.53	
	Low EF	20	60.20	20.83	

Cardiac output(L/min) - Resting	Young	19	4512.74	1417.92	.102
	Old	24	3747.63	923.61	
	Low EF	20	3858.25	1287.42	
Cardiac output(L/min)- Peak stress	Young	19	13094.42	3171.94	**.000***
	Old	24	7825.04	2263.08	
	Low EF	20	9487.55	3475.83	
ΔLVedD	Young	19	-0.16	4.79	**.013***
	Old	24	-4.29	4.02	
	Low EF	20	-1.15	5.23	
ΔLVesD	Young	19	-6.00	4.40	.077
	Old	24	-7.00	2.90	
	Low EF	20	-4.00	5.52	
ΔLVEF	Young	19	14.42	4.93	.262
	Old	24	12.92	5.22	
	Low EF	20	11.70	5.24	
ΔStroke volume	Young	19	13.16	13.09	**.001***
	Old	24	-0.50	11.29	
	Low EF	20	7.20	10.98	

** p -value is significant at the 0.05 level.*

*** p-value was calculated using oneway ANOVA test*

19 Young adults, 24 Old hypertensives, and 20 patients of ischemic or dilated cardiomyopathy were evaluated by 2D echocardiograms (n=63) at rest and after peak exercise on treadmill (n=39), or dobutamine stress (n=24).

Table 20: Comparison between Young, Old and Low EF patients with respect to Resting and Peak stress LVedD, LVesD, LVEF, Stroke Volume, Cardiac Output, as well as with ΔLVedD, ΔLVesD, ΔLVEF, ΔStroke Volume

Statistical significance ($p<0.05$) was noted between these three groups with respect to Resting LVedD ($p=0.001$), Resting LVesD ($p=0.000$), Resting LVEF ($p=0.000$), Peak stress LVedD ($p=0.000$), Peak stress LVesD ($p=0.000$), Peak stress LVEF ($p=0.000$), Peak stress Stroke Volume ($p=0.000$), Peak stress Cardiac Output ($p=0.000$), ΔLVedD ($p=0.013$) and ΔStroke Volume($p=0.001$).

Low EF patients were having large cavities while Old patients had the smallest cavities amongst the three groups. Old patients were unable to increase their Stroke Volume with peak stress (from 52.15 ml at rest to 51.75 ml Peak stress) in contrast to young adults and Low EF patients who were able to increase their Stroke Volume with peak stress (from 60.95 ml to 74.11 ml in Young adults and from 53 ml to 60.20 ml in Low EF group). Peak stress cardiac output increase was 2.9 fold in Young, 2.5 fold in Low EF, and 2.1 fold in Old patients.

Dependent Variable	**(I) Group**	**(J) Group**	**Mean Difference (I-J)**	**Standard Error**	**p - value**
LVedD (mm)-Resting	Old	Young	-1.61	1.87	.591
	Low EF	Young	5.40*	1.95	**.014**
LVedD (mm) - Peak stress	Old	Young	-5.75*	2.16	**.019**
	Low EF	Young	4.41	2.26	.098
LVesD (mm)-Resting	Old	Young	-.41	1.70	.957
	Low EF	Young	10.48*	1.77	**.000**
LVesD (mm)- Peak stress	Old	Young	-1.41	1.94	.684
	Low EF	Young	12.48*	2.02	**.000**
LVEF % - Resting	Old	Young	-2.501	1.87	.306
	Low EF	Young	-21.99*	1.95	**.000**
LVEF % - Peak stress	Old	Young	-4.01	2.18	.125
	Low EF	Young	-24.71*	2.28	**.000**
Stroke Volume (ml) - resting	Old	Young	-8.70	4.27	.082
	Low EF	Young	-7.95	4.45	.138
Stroke Volume (ml)-Peak stress	Old	Young	-22.36*	5.18	**.000**
	Low EF	Young	-13.91*	5.41	**.023**
Cardiac Output (L/min)-resting	Old	Young	-765.11	370.41	.078
	Low EF	Young	-654.49	386.43	.165
Cardiac Output (L/min)-Peak stress	Old	Young	-5269.38*	911.33	**.000**
	Low EF	Young	-3606.87*	950.75	**.001**

** The mean difference is significant at the 0.05 level.*

Table 21A: Post Hoc Analysis

Post hoc analysis was done using Dunnett's test (2-sided) [J was the reference group (Young) that compared with Old and low EF group in all dependent variables] to explore the significant pair(s) in the three groups with respect to LV dimensions.

Statistical significance ($p<0.05$) was noted between Young vs. Low EF with respect to Resting LVedD ($p=0.014$), Resting LVesD ($p=0.000$), Resting LVEF ($p=0.000$) and Peak stress LVesD ($p=0.000$), Peak stress LVEF ($p=0.000$), Peak stress Stroke Volume ($p=0.023$), Peak stress Cardiac Output ($p=0.001$).

Similarly, statistical significance ($p<0.05$) was noted between Young vs. Old with respect to Peak stress LVedD ($p=0.019$) and Peak stress Cardiac Output ($p=0.000$).

Dependent Variable	(I) Patient's subgroups	(J) Patient's subgroups	Mean Difference(I-J)	Standard Error	p-value
ΔLVedD	Young	Old	4.13*	1.43	**.015**
	Old	Low EF	-3.14	1.41	.075
	Low EF	Young	-.99	1.49	.785
ΔLVesD	Young	Old	1.00	1.33	.733
	Old	Low EF	-3.00	1.31	.064
	Low EF	Young	2.00	1.38	.325
ΔLVEF	Young	Old	1.50	1.58	.609
	Old	Low EF	1.22	1.56	.715
	Low EF	Young	-2.72	1.65	.232
ΔStroke volume	Young	Old	13.66*	3.61	**.001**
	Old	Low EF	-7.70	3.56	.086
	Low EF	Young	-5.96	3.77	.262

** The mean difference is significant at the 0.05 level.*

Table 21B: Post Hoc Analysis

Post hoc analysis was done using Tukey's HSD (honest significant difference) test, to find out the significant pair (s) in the three groups with respect to change in LV dimensions.

Statistical significance ($p<0.05$) was noted only between Young adults vs. Old patients with respect to ΔLVedD ($p=0.015$) and ΔStroke Volume ($p=0.001$) but no statistical significance was seen between Young adults vs. Low EF patients i.e. at peak stress, young adults and patients with Low EF showed no change in LVeDD, but there was a significant decrease in peak stress LVeDD in Old patients. Stroke volume increased in Young and patients with Low EF, and showed no change in Old patients at peak stress.

Discussion

Resting LV ejection fraction (LVEF) is widely used as a measure of systolic function. However, LVEF is a flawed measure of contractility because it depends upon loading conditions (systolic pressure), chamber remodeling (ventricular enlargement by eccentric hypertrophy), etc. More importantly resting measurements can be normal as resting cardiac output is normal, approximately 5L/min, except in advance stage (NYHA class IV) heart disease or acute decompensated heart failure. So measures which suggest normal function at rest don't guarantee contractile reserve or normal exercise systolic performance.

Our present concept is that the ratio of resting stroke volume divided by chamber size (ejection fraction) is a good predictor of exercise systolic performance, but this is fallacious in many conditions with excess eccentric growth (athletes heart) or deficient growth (Hypertrophic cardiomyopathy). We therefore have studied exercise parameters to assess LV function in ambulatory population including young adults, those with eccentric growth (i.e. low EF group) and in patients predisposed to HFpEF (elderly hypertensives).

The present concept is normal resting LVEF guarantees normal contractility and normal LV systolic function. When resting EF is used for assessment of LV systolic function, patients with normal resting LVEF and heart failure are assumed to have failure due to diastolic dysfunction. However both these assumptions are not based directly on heart function during stress or exertion.

In our study, maximum number of patients who were advised to undergo stress echocardiography were above 50 years of age (74.2%) with male preponderance. Mean BMI of our study group was 26.7±4.48 kg/m2 with 63.4% patients in our study group being either overweight or obese. 60 patients (64.6%) in our study group were in NYHA Class II or III (46 in NYHA class II and 14 in NYHA class III). In our study, 55.9% (n=52) patients were hypertensives, 26.9% (n=25) patients were diabetic, 37.6% (n=35) patients had CAD and 23.7% (n=22) patients were still smoking. Similar patient group characteristics were seen in the previous studies15,18,26,27 in which patients with HFpEF or hypertension were compared with controls. Comparison of various baseline parameters between our study and few of the previous studies is tabulated below.

Baseline Parameters	**Group**	**Study**				
		Tan (2010)[15] Hypertensive (30) Vs. Controls (22)	**Kesri (2012)[27] HFPEF (23)Vs. Controls (15)**	**Donel (2012)[26] HFPEF (21) Vs. Control (15)**	**Kasner (2015)[18] HFPEF (52) Vs. Control (26)**	**This Study Old (24) Vs. Young (19)**
Gender (m/f), n	HFPEF	18/12	11/12	12/9	27/25	16/8
	Controls	16/6	10/5	8/7	13/13	17/2
Age (years)	HFPEF	71±8	66±10	76±6	55±12	69±6
	Controls	70±6	67±7	75±5	48±11	43±12
BMI (kg/m2)	HFPEF	30±5	27±4	29±6	27±5	26±5
	Controls	25±4	25±4	30±4	25±4	24±2
NYHA II/III, n	HFPEF	19/11	17/2	-----	39/9	15/4
	Controls	0/0	0/0	-----	0/0	4/0
HTN	HFPEF	6.6±5.2	18	19/21	28	19/24
	Controls	0	7	9/15	0	4/19
Diabetes mellitus	HFPEF	6/30	13	5/21	10	7/24
	Controls	0/22	3	2/15	0	2/19
Coronary artery disease	HFPEF	-----	10	5/21	-----	13/24

	Controls	-----	0	0/10	-----	0/19
Obesity (BMI>30 kg/m2)	HFPEF	-----	-----	-----	15	5
	Controls	-----	-----	-----	4	0
Smoking	HFPEF	-----	9	-----	17	9
	Controls	-----	3	-----	5	2

Table 22: Comparison of various baseline parameters between our study and previous studies

21.5% (n=20) patients in our study had resting LVEF less than 50% (ischemic or dilated cardiomyopathy) while rest of the patients had resting LVEF more than or equal to 50%. Ischemic or dilated cardiomyopathy patients were included to see the change in LV parameters with stress in this group in comparison to young healthy and elderly hypertensives. The study of Wang et al, 2014 [2] included 27.7% patients with LVEF less than 50%.

In our study, out of the 93 patients who underwent stress echocardiography, 58 patients underwent physical stress testing using Bruce protocol and 35 patients underwent Dobutamine stress testing. A similar group of patients were studied in the study of Meyer et al, 2015 [19].

Baseline and echocardiographic parameters of patients who were subjected to treadmill stress testing when compared with patients who were subjected to dobutamine stress testing in our study group showed that dobutamine group had older patients with greater decrease in LV dimensions with exercise but similar resting LVEF and ΔLVEF. In addition, dobutamine group patients were unable to increase their stroke volume with exercise and were able to increase their cardiac output with exercise only by 2.1 fold in comparison to patients subjected to treadmill stress testing who were able to increase their cardiac output with exercise by 2.7 fold which was in accordance with the previous study of Meyer et al, 2015 [19].

Exercise time and the maximal achieved workload were similar between elderly hypertensives and low resting EF patients (total exercise time ≈ 6 and half minutes and MWL≈ 8 METS in both the groups) but were significantly impaired in patient groups compared with young adults (total exercise time ≈ 10 minutes and MWL≈ 11 METS). In the study of Wang et al, 2014 [2] similar results were seen.

We looked at systolic and diastolic LV size to determine systolic and diastolic performance. Significant exercise-induced increase in diastolic chamber volume (which conceivably could be accomplished by a shape change from an ellipsoidal to a spherical LV geometry) could improve stroke volumes since the normal pericardium precludes significant LV expansion [28]. In normal adults, augmentation of contractility and increase in stroke volume with exercise was similar as with previous studies using bicycle ergometer [11,29,30] and treadmill testing [31,32].

Low EF group - Our study showed that reason for low ejection fraction in this group was due to enlargement of LV cavity (increase in denominator). This growth of ventricle by eccentric hypertrophy in our data suggests is to improve LV systolic function after myocardium is being injured by infarction or cellular dysfunction (dilated cardiomyopathy). There was augmentation of contractility and increase in stroke volume with activity but since the eccentric growth was secondary to myocardial damage, change in stroke volume with exercise and peak cardiac output was less than young healthy adults.

Elderly hypertensives - Our data showed that these patients had normal resting LVEF because of deficient eccentric hypertrophy. This may be due to lack of contractile reserve or due to aged ventricle or lack of adaptability after concentric LVH. Loss of remodeling or growth potential occurs after concentric LVH. Elderly hypertensives in our study showed no increase in stroke volume with exercise similar to previous studies [12,13,33,34,35]. Although this strongly implicates fibrosis, ageing, myocardial infarction and lack of contractile reserve as a cause of heart failure in the elderly; we also surprisingly found stress induced aggravation of relaxation in diastole.

Healthy individuals had no change in LV filling during tachycardia or stress or a minimal increase. Patients with low EF group had similar ventricular behavior during stress. The response in elderly hypertensives was strikingly different (mean ventricular size decreased from 43.33 mm to 39.09 mm). The elderly fibrotic ventricle fails to increase LV dimension which also shows major deterioration of diastolic relaxation with decrease in LV cavity size with stress (21.4% decrease in LV end-diastolic volume with stress). Diastolic relaxation abnormality in elderly hypertensives (with pacing) was also shown in the study of Selby et al, 2011 [36].

To put this into perspective, if we draw the pressure-volume curves in patients with HFpEF compared to young adults we see the steeper diastolic pressure rise, decreased end-diastolic and end-systolic volumes and decreased stroke volume in patients with HFpEF as compared to adults.

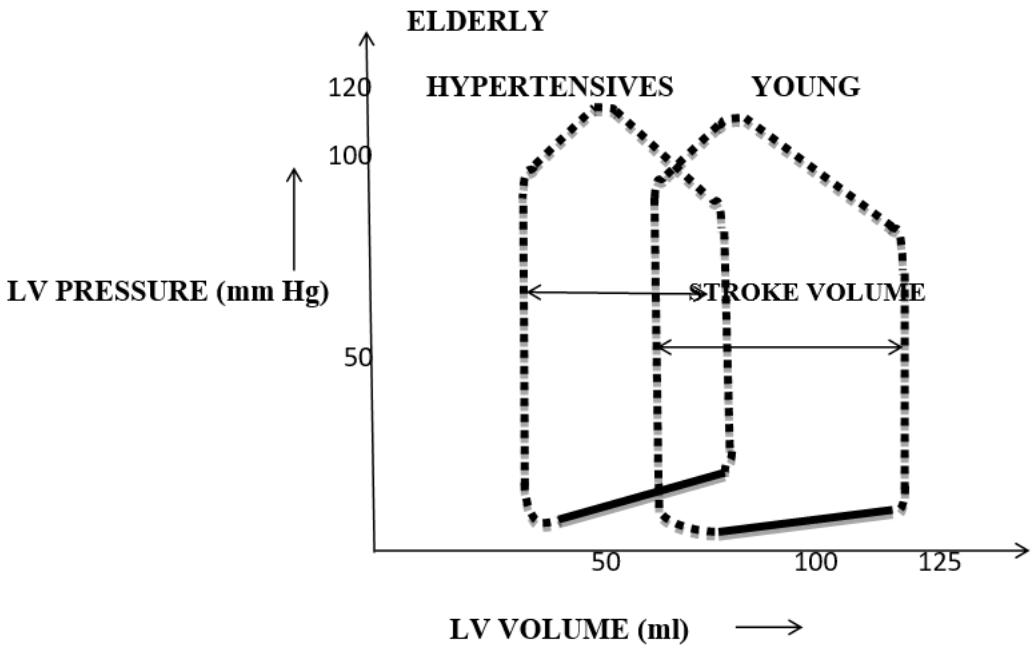


Figure 9: Pressure-volume curves in elderly hypertensives and young adults [Solid line showing the diastolic pressure rises in both groups (not measured in our study) and is definitely steeper in elderly hypertensives]

Various studies have been done in the past which have looked at the diastolic echocardiographic parameters at rest and exercise in patients with HFpEF or elderly hypertensives and compared them with controls. In our study, we have compared young adults, elderly hypertensives and patients with ischemic or dilated cardiomyopathy on the basis of change in LV dimensions, stroke volume and cardiac output with rest and peak stress. However, when I analysed few of the previous studies closely, I found that they have also taken various echocardiographic LV dimensions both at rest and peak exercise and have calculated resting and exercise LVEF, stroke volume and cardiac output in their studies, which I have tried to put in a tabular form and compare their findings with our study.

Echo Derived Parameter	Group	Studies				
		Tan (2010)[15]	Kesri (2012)[27]	Donel (2012)[26]	Kasner (2015)[18]	This Study
LVEDD (mm)	HFPEF	46.7±5.7	------	51.5±7.1	47±5.2	43.3±4.1
	Controls	46.1±5.8	------	45.6±4.1	49±5.1	44.9±5.5
LVESD (mm)	HFPEF	29.0±4.6	------	------	------	29.0±4.0
	Controls	28.7±4.6	------	------	------	29.4±4.2
SV(mL) Baseline	HFPEF	71±17	40 ± 2	62±19	64±19 63±23	52±12
	Controls	62±14	43 ± 2	53±14	68±18	61±16
SV(mL) Exercise	HFPEF	74±23	39 ± 2	66±24	73±31 54±24	52±12
	Controls	75±15	46 ± 2	62±16	92±36	74±17
△Stroke volume	HFPEF	------	------	6±18	------	4±13
	Controls	------	------	4±17	------	8±16
CO(L/min) Baseline	HFPEF	4.9±1.6	------	5.0±1.4	5.0±1.9 5.2±1.7	3.7±0.9
	Controls	4.2±1.1	------	5.2±1.5	5.3±1.1	4.5±1.5
CO(L/min) Exercise	HFPEF	6.4±2.1	------	6.6±1.7	8.5±3.5 6.9±3.0	7.8±2.3
	Controls	6.8±1.8	------	8.0±1.7	12.9±4.4	13.1±3.2
EF % Baseline	HFPEF	62±6	------	56±11	60±8 63±6	61±8
	Controls	62±8	------	66±6	62±5	64±4
EF % Exercise	HFPEF	67±9	------	59±14	62±11 64±8	74±6
	Controls	65±8	------	69±8	75±9	78±6
△LVEF	HFPEF	------	------	2±9	------	12±5
	Controls	------	------	3±10	------	14±5

Table 23: Summary of Echocardiographic parameters in our study in comparison to previous studies

Summary & Conclusion

- A total of 93 patients, with or without heart muscle disease were enrolled for stress testing in our study over a one year study period.

- 58 patients underwent physical stress testing using Bruce protocol and 35 patients underwent Dobutamine stress testing.

- The mean age of study population was 57±14 years with nearly 20% of the patients above 70 years. 62 patients were males and 31 patients were females with male: female ratio of 2: 1.

- Mean BMI of the study population was 26.7 ± 4.48 kg/m2. 63.4% (n=59) patients were either overweight or obese. 60 patients (64.6%) were in NYHA class II or more with no patient in NYHA class IV. 52 patients (55.9%) were hypertensives with 42 (45.2%) patients having LVH on echocardiography. 26.9% (n=25) patients were diabetic and 22 patients (23.7%) were still smoking. 35 patients (37.6%) had CAD out of which 23 patients (24.7%) had undergone PCI while 5 (5.4%) had undergone CABG.

- 21.5% (n=20) of the patients in our study had resting LVEF less than 50% while rest 78.5% (n=73) of the patients had resting LVEF more than or equal to 50%

- Out of the 58 patients who were subjected to physical stress testing in our study, 36.2% (n=21) patients had excellent exercise capacity (TEC ≥9minutes and MWL ≥10.1METS) while 24.1% (n=14) patients had poor exercise capacity (TEC ≤6minutes and MWL ≤7.0 METS). 39.7% (n=23) of the patients had good exercise capacity (TEC 6:01-8:59 minutes and MWL 7.1-10.1 METS).

- 35 patients in our study were subjected to dobutamine stress testing; out of which 37.14% (n=13) patients had morbidity index less than 6 while 31.43% (n=11) patients had morbidity index more than or equal to 8. Equal number of patients i.e. 31.34% (n=11) had morbidity index 6 & 7.

- Baseline and echocardiographic parameters of patients who were subjected to treadmill stress

testing when compared with patients who were subjected to dobutamine stress testing in our study group showed that dobutamine group had older patients with higher decrease in LV dimensions with exercise but similar resting LVEF and ΔLVEF. In addition, dobutamine group patients were unable to increase their stroke volume with exercise and were able to increase their cardiac output with exercise only by 2.1 fold in comparison to patients subjected to treadmill stress testing who were able to increase their cardiac output with exercise by 2.7 fold.

- NYHA Class showed statistical significance with Total Exercise Capacity, Maximum Workload, Resting LVEF, ΔLVedD and ΔLVesD, i.e. patients with NYHA class 0-I had higher exercise capacity, higher resting LVEF, higher change in LVedD and LVesD with exercise as compared to NYHA class II-III.

- Total Exercise Time showed Statistical significance with Resting LVEF ΔLVesD and ΔLVEF, i.e. patients with poor exercise capacity had a lower resting LVEF and a lower change in LVesD and LVEF with exercise as compared to patients with excellent exercise capacity; this relation was due to more number of patients of ischemic or dilated cardiomyopathy in the poor exercise capacity group. No statistical significance was seen with ΔStroke Volume and ΔLVedD with exercise.

- Exercise time and the maximal achieved workload were similar between elderly hypertensives and low resting EF patients (total exercise time ≈ 6 and half minutes and MWL≈ 8 METS in both the groups) but were significantly impaired in patient groups compared with young adults (total exercise time ≈ 10 minutes and MWL≈ 11 METS).

- Morbidity Index showed statistical significance with ΔLVedD, ΔLVesD, i.e. patients with Morbidity Index ≥6 had significant decrease in LVedD and LVesD after dobutamine stress testing as compared to patients with Morbidity Index<6. In addition, patients with Morbidity Index ≥6 were unable to increase their stroke volume with peak dobutamine stress as compared to patients with Morbidity index <6 but it wasn't statistically significant.

- Statistical significance was noted for LVH with Peak stress LVedD, Peak stress Stroke Volume

and peak stress Cardiac Output i.e. significant decrease in peak stress LVedD was seen in patients with LVH while there was no significant change in the peak stress LVedD in patients without LVH and the amount of decrease in Peak stress LVedD increased with the severity of LVH. In addition, patients with LVH were unable to increase their stroke volume as compared to patients without LVH. In fact there was a fall in stroke volume at peak stress in patients with moderate LVH (from 53.11 ml to 49.56 ml). Increase in peak stress cardiac output was 2.7 fold in patients without LVH, 2.4 fold in patients with Mild LVH, and 1.9 fold in patients with Moderate LVH.

- 19 healthy adults (Young), 24 elderly hypertensives (Old), and 20 patients of ischemic or dilated cardiomyopathy (Low EF) were evaluated by 2D echocardiograms (n=63) at rest and after peak exercise on treadmill (n=39), or dobutamine stress (n=24). Echocardiograms at rest showed no difference in heart rate, LV dimensions, LVEF, stroke volume and cardiac output between elderly hypertensives (Old) and healthy adults (Young). At peak exercise, healthy adults and patients with HFrEF (Low EF) showed no change in LVedD, but there was a significant decrease in peak exercise LVedD from 43.33 mm to 39.04 mm in HFpEF (Old). Stroke volume increased from 60.95 ml to 74.11 ml in normal (Young), from 53.55 ml to 60.20 ml in HFrEF (Low EF), and showed no change in HFpEF [Old] (52.25 ml at rest, 51.75 ml at peak exercise). Increase in peak exercise cardiac output was 2.9 fold in healthy adults (Young), 2.5 fold in HFrEF (Low EF), and 2.1 fold in elderly hypertensives (Old).

Conclusion

LVEF is a flawed measure of contractility and normal resting LVEF does not imply normal LV systolic function. Our study shows that resting ejection fraction in young patients with past infarctions reflects increased end diastolic volume with normal resting stroke volume; it is not due to systolic dysfunction. The results of our study also suggest that elderly hypertensive patients have failure to grow their ventricle by eccentric hypertrophy. They have systolic dysfunction, with impaired contractile reserve and little augmentation of systolic ejection during stress.

Our study also demonstrated severe worsening of abnormalities of relaxation during stress, with decrease in ventricular end diastolic dimension, unlike healthy individuals and young patients with low

EF (eccentric hypertrophy).

Reference

1.Sanderson JE, Fraser AG. Systolic dysfunction in heart failure with a normal ejection fraction: echo-Doppler measurements. Prog Cardiovasc Dis. 2006;49:196-206.

2.Wang J, Fang F, Yip GK, Sanderson JE, Lee PW, Feng W, et al. Changes of ventricular and peripheral performance in patients with heart failure and normal ejection fraction: insights from ergometry stress echocardiography. Eur J Heart Fail. 2014;16:888-897.

3.Little WC. Diastolic dysfunction beyond distensibility: adverse effects of ventricular dilation. Circulation. 2005;112:2888-2890.

4. Hill JA, Olson EN. Cardiac Plasticity. N Engl J Med. 2008;358:1370-1380.

5. Linzbach AJ. Heart failure from the point of view of quantitative anatomy. J Am Coll Cardiol. 1960;5:370-382.

6. Gaasch WH, Zile MR. Left Ventricular Structural Remodeling in Health and Disease with Special Emphasis on Volume, Mass, and Geometry. J Am Coll Cardiol. 2011;58:1733-1740.

7. Abergel E, Chatellier G, Hagege AA, Oblak A, Linhart A, Ducardonnet A, et al. Serial left ventricular adaptations in world-class professional cyclists: implications for disease screening and follow-up. J Am Coll Cardiol. 2004;44:144-149.

8. Levine BD, Zuckerman JH, Pawelczyk JA. Cardiac atrophy after bed-rest deconditioning: a nonneural mechanism for orthostatic intolerance. Circulation. 1997;96:517-525.

9. Perhonen MA, Franco F, Lane LD, Buckey JC, Blomqvist CG, Zerwekh JE, et al. Cardiac atrophy after bed rest and spaceflight. J Appl Physiol. 2001;91:645-653.

10. Nagaoka H, Isobe N, Kubota S, Lizuka T, Imai S, Suzuki T, et al. Myocardial contractile reserve as

prognostic determinant in patients with idiopathic dilated cardiomyopathy without overt heart failure. Chest. 1997;111:344-350.

11. Higginbotham MB, Morris KG, Williams RS, McHale PA, Coleman RD, Cobb FR. Regulation of stroke volume during submaximal and maximal upright exercise in normal man. Circ Res. 1986;58:281-291.

12. Cuocolo A, Sax FL, Brush JE, Maron BJ, Bacharach SL, Bonow RO. Left ventricular hypertrophy and impaired diastolic filling in essential hypertension: Diastolic mechanisms for systolic dysfunction during exercise. Circulation. 1990;81:978-986.

13. Ennezat PV, Lefetz Y, Mare´chaux S, Carpentier MS, Deklunder G, Montaigne D et al. Left ventricular abnormal response during dynamic exercise in patients with heart failure and preserved left ventricular ejection fraction at rest. J Card Fail. 2008;14:475-480.

14. Grewal J, McCully RB, Kane GC, Lam C, Pellikka PA. Left ventricular function and exercise capacity. JAMA. 2009;301:286-294.

15. Tan YT, Wenzelburger F, Lee E, Heatlie G, Frenneaux M, Sanderson JE. Abnormal left ventricular function occurs on exercise in well-treated hypertensive subjects with normal resting echocardiography. Heart. 2010;96:948-955.

16. Kitzman DW, Brubaker PH, Morgan TM, Stewart KP, Little WC. Exercise training in older patients with heart failure and preserved ejection fraction: a randomized, controlled, single-blind trial. Circ Heart Fail. 2010;3:659-667.

17. Andersen MJ, Olson TP, Melenovsky V, Kane GC, Borlaug BA. Differential Hemodynamic Effects of Exercise and Volume Expansion in People With and Without Heart Failure. Circ Heart Fail. 2015;8:41-48.

18. Kasner M, Sinning D, Lober J, Post H, Fraser AG, Pieske B, et al. Heterogeneous responses of systolic and diastolic left ventricular function to exercise in patients with heart failure and preserved ejection fraction. ESC Heart Fail. 2015;2:121-132.

19. Meyer M, McEntee RK, Nyotowidjojo I, Chu G, LeWinter MM. Relationship of Exercise Capacity

and Left Ventricular Dimensions in Patients with a Normal Ejection Fraction. An Exploratory Study. PLoS ONE. 2015;10:e0119432.

20.Fletcher GF, Ades PA, Kligfield P, Arena R, Balady GJ, Bittner VA, et al. AHA Scientific Statement. Exercise Standards for Testing and Training. A Scientific Statement from the American Heart Association. Circulation. 2013;128:873-934.

21.Pellikka PA, Nagueh SF, Elhendy AA, Kuehl CA, Sawada SG. American Society of Echocardiography recommendations for performance, interpretation, and application of stress echocardiography. J Am Soc Echocardiogr. 2007;20:1021-1041.

22. Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA, et al. Chamber Quantification Writing Group; American Society of Echocardiography's Guidelines and Standards Committee; European Association of Echocardiography. J Am Soc Echocardiogr. 2005;18:1440-1463.

23. American College of Sports Medicine. Guidelines for Exercise Testing and Prescription. 6th ed. Baltimore, MD: Lippincott, Williams & Wilkins; 2000.

24. Sachdev M, Sun JL, Tsiatis AA, Nelson CL, Mark DB, Jollis JG. The prognostic importance of comorbidity for mortality in patients with stable coronary artery disease. J Am Coll Cardiol. 2004;43:576-582.

25. The Criteria Committee of the New York Heart Association. Nomenclature and Criteria for Diagnosis of Diseases of the Heart and Great Vessels. 9th ed. Boston, Mass: Little, Brown & Co; 1994:253-256.

26. Donal E, Thebault C, Lund LH, Kervio G, Reynaud A, Simon T, et al. Heart failure with a preserved ejection fraction additive value of an exercise stress echocardiography. Eur Heart J Cardiovasc Imaging. 2012;13:656-665.

27. Tartie`re-Kesri L, Tartie`re JM, Logeart D, Beauvais F, Solal AC, et al. Increased proximal arterial stiffness and cardiac response with moderate exercise in patients with heart failure and preserved ejection fraction. J Am Coll Cardiol. 2012;59:455-461.

28. LeWinter MM, Tischler MD. Pericardial Diseases. In: Bonow RO et al editors. Braunwald's Heart

Disease: A textbook of cardiovascular medicine. 9th ed. Philadelphia; Elsevier Saunders; 2011;1651-1671.

29. Astrand P, Cuddy TE, Saltin B, Stenberg J. Cardiac output during submaximal and maximal work. J Appl Physiol. 1964;19:268-274.

30. Gledhill N, Cox D, Jamnik R. Endurance athletes' stroke volume does not plateau: Major advantage is diastolic function. Med Sci Sports Exerc. 1994;26:1116-1121.

31. Chapman CB, Fisher JN, Sproule BJ. Behavior of stroke volume at rest and during exercise in human beings. J Clin Investigation. 1960;30:1208-1213.

32. Ekblom B, Hermansen L. Cardiac output in athletes. J Appl Physiol. 1968;25:619-625.

33. Liu CP, Ting CT, LawrenceW, Maughan WL, Chang MS, Kass DA. Diminished contractile response to increased heart rate in intact human left ventricular hypertrophy. Systolic versus diastolic determinants. Circulation. 1993;88:1893-1906.

34. Kasner M, Westermann D, Steendijk P, Dröse S, Poller W, Schultheiss HP, et al. Role of left ventricular stiffness in heart failure with normal ejection fraction. Circulation. 2008;117:2051-2060.

35. Wachter R, Schmidt-Schweda S, Westermann D, Post H, Edelmann F, Kasner M, et al. Blunted frequency: dependent upregulation of cardiac output is related to impaired relaxation in diastolic heart failure. Eur Heart J. 2009;30:3027-3036.

36. Selby DE, Palmer BM, LeWinter MM, Meyer M. Tachycardia-induced diastolic dysfunction and resting tone in myocardium from patients with a normal ejection fraction. J Am Coll Cardiol. 2011;58:147-154.

37. Komajda M, Lam CS. Heart failure with preserved ejection fraction: a clinical dilemma. Eur Heart J 2014;35:1022-1032

Medtronic