

Effect of Obesity on Left Ventricular Mass and Diastolic Function

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ABSTRACT

Background: obesity, a common problem, is possibly associated with left ventricular (LV) structural and functional abnormalities such as left ventricular hypertrophy (LVH) and diastolic dysfunction, even in the absence of comorbidities as hypertension, diabetes.

Aim of the study: to assess LV structure and diastolic function in healthy obese participants (individuals with non-complicated obesity).

Methods: 90 individuals (female :60, male:30) were enrolled in this case-control study, using body mass index (BMI) participants were divided into two groups; lean (BMI cut off values of (18.5-25) kg/m²) and obese (≥ 30 kg/m²) each group include 30 female and 15 male. LVM was indexed to the height using the allometric signal of (1.7), LVH was defined using cut off values of 80 g/m^{1.7} (for male) and 60 g/m^{1.7} (for female). Diastolic dysfunction was defined according to the ASE/EACVI guidelines for the evaluation of left ventricular diastolic dysfunction.

Results: Obese participants have a significantly higher LVMI (P-value < 0.001), while RWT didn't show a significant difference between the two groups (P-value: 0.14). Non-complicated obesity had a significant association with LVH which was of eccentric type (P-value < 0.001). Diastolic dysfunction wasn't encountered in the study (neither in the healthy obese nor in the lean control), but obese participants had exhibit a statistically significant differences in parameters of LV relaxation (P-value < 0.002 for Lateral e' velocity and < 0.001 for E-velocity DT, IVRT,VP) and filling pressures (P- value: 0.014 for PASP, < 0.001 for LAVI) that indicate a subclinical lower diastolic function in obese individuals.

Conclusions: Non-complicated obesity has a significant association with Eccentric type of LVH with a subclinical deterioration in parameters of LV relaxation and filling pressures.

Keywords:

Obesity, Left ventricular mass, Left ventricular hypertrophy, Diastolic function, Echocardiography

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INTRODUCTION

Obesity is a growing public health problem that had reached epidemic level, with a continuously increasing prevalence among all age groups¹, traditionally obesity was considered as a problem of the high income countries, but its prevalence now is rising even in the low and middle income communities, currently most of the world's population live in countries where overweight and obesity kills more people than underweight². World health organization (WHO) noted that the global prevalence of obesity has tripled since 1975, and that in 2016, more than 1.9 billion adults (39%), were overweight from which over 650 million (13%) were obese³.

Traditionally obesity was looked at as a condition of excess body weight relative to body height using the body mass index (BMI)⁴. While body weight has many determinants (or components) such as muscle mass, fat mass, weight of the skeleton supporting the muscles⁵, health risks in obesity are related to a specific component that is fat mass⁶. That's why many clinicians now prefer to define obesity as a condition of excess body fat stores (excess adipose tissue mass) rather than excess body weight⁷.

Accurate measurement of adipose tissue mass needs a sophisticated techniques⁸ that cannot be applied in the large epidemiological studies, consequently calculating

BMI is still the most widely used method to assess adiposity status (although it is not a direct measure of adiposity)^{9,10}.

Using weight based methods that cannot differentiate between body weight components such as BMI to detect obesity, people with large muscle mass (lean but very muscular individuals) may be classified as an overweight without having an adipose tissue excess⁷, based on that when using BMI obesity should be defined using cut off values that are adopted based on its significant correlation with morbidity and mortality¹⁰. Accordingly in both men and women a BMI of 30 is the commonly used threshold for obesity based on data of substantial morbidity, lower BMI cut off points Should be used for some ethnic groups (eg: south east Asians), a BMI of 30 to 34.9 is considered as class I obesity, 35 to 39.9 is a class II obesity and 40 or higher is a Class III obesity (severe or morbid obesity)⁹.

linking obesity with its associated cardiac and metabolic complications body fat distribution is more relevant than the degree of adiposity or BMI alone¹¹. it's well recognized that central obesity (excessive fat deposition intra-abdominally and in the abdominal wall subcutaneous tissue) is associated with a higher risk of metabolic and cardiovascular disease as many of the most important obesity-related complications such as insulin resistance, diabetes, hypertension and dyslipidemia are

more strongly linked to central rather than peripheral obesity¹².

Clinically a crude assessment of abdominal adiposity can be obtained by measuring the waist circumference (WC) which correlates highly with abdominal and intra-abdominal fat content¹³ and can be used for cardiometabolic risk stratification¹⁴ (WC >94cm for overweight and obese men and WC >80 cm for overweight and obese women is associated with increased cardiometabolic risk¹⁵, or by measuring the relative size of the waist and hip „the waist: hip ratio (WHR)¹³ „, for which a (WHR ≥ 0.90 cm men and ≥ 0.85 cm for women confer increased cardiometabolic risk)¹⁵.

In the literature obesity was reported to be associated with left ventricular (LV) structural and functional abnormalities such as left ventricular hypertrophy (LVH) and impairment of diastolic function^{16,17}, however given the fact that obese individuals commonly present with obesity-related complications such as hypertension and type II diabetes and that such conditions can independently affect LV structure and function¹⁸, only few studies had accounted for such potential confounders. Furthermore, to compare the left ventricular mass (LVM) of obese individuals with that of lean it should be corrected for or (indexed to) a measure that represent body size such as body surface area (BSA), height¹⁹. many different indexing methods had been adopted by the previous studies such as ratiometric normalization of LVM to body height or BSA²⁰, various allometric signals of height^{19,21}. Considering its central role in determining whether an obese individual have a normal LVM or LVH , it is important to adopt an optimum indexing method - a point that remained questionarry in all the previous studies - for example: ratiometric normalization of LVM to measures of body size was proposed based on an assumption that the relationship between LVM and body size is linear¹⁹, while in fact it is an allometric²¹, also the commonly used allometric signal of height (i.e. height²⁷) was found to have a negative residual relationship with height²¹ (i.e. overcorrect for height).

This study aims to investigate the effects of obesity per se on LV structure and diastolic function by enrolling healthy obese participants (i.e. individuals with non-complicated obesity) and utilizing the ultimate indexing method -that was proposed based on data from two large population-based studies -which account for the potential limitations in the previous methods²¹.

PARTICIPANTS AND METHODS

1-The study participants and the study groups

Participants selection

Ninety persons (aged 18- 45 year) were included in this study. Their verbal and written agreements were taken. The subjects involved in the study were chosen from the consultation clinic of the Middle Euphrates teaching hospital. The study was approved by the local ethical committee and conducted from June 2019 to January 2020.

Anthropometric measurements

Height (cm) and weight (kg) were obtained, by means of portable stadiometer and digital weight scale respectively. BMI was calculated by applying the following equation²²: [BMI = Weight (kg) / Height (m)²] for each one. Waist circumference was measured in the horizontal plane midway between the lower margin of the last rib and the iliac crest (WC-mid) according to the world health organization guidelines²³. Regarding waist-to-hip ratio, the hip circumference measurement was taken around

the widest portion of the buttocks according to WHO guidelines²³.

Accordingly, the study participants were divided into two groups, the obese persons (BMI>30), and lean persons (BMI 18.5 – 25 kg/m²).

Exclusion criteria

In order to exclude conditions that might affect our outcomes, subjects with any of the following were excluded from the study:

1- Any metabolic disorder like type II diabetes mellitus, dyslipidemia, hypertension. metabolic normality was defined using Wildman criterion²⁴ for the identification of those who are obese without cardiometabolic risk factor if they had one or none of the following components: blood pressure $\geq 130/85$ mmHg or use of antihypertensive drugs, triglycerides ≥ 150 mg/dL or use of lipid-lowering drugs, HDL-c <50 mg/dL, CRP above the 90th percentile among all participants, fasting glucose ≥ 101 mg/dL or use of medications for diabetes, HOMA-IR above the 90th percentile among all participants. (As HOMA-IR was not done in this study, all persons included had non-of the first five exclusion criteria).

Casual BP was manually measured in the sitting position using a mercury sphygmomanometer and an appropriately sized cuff (a cuff bladder at least 80% of the patient's arm circumference). In the incidence of an elevated BP reading (i.e. more than 140/90 mmHg) the measurement will be repeated up to three times (With 10-min intervening intervals) and the lower of the second and the third measurement was recorded as clinic blood pressure²⁵.

2- Those with pre-existing cardiac disease, respiratory disease, renal or liver disease.

3- Subjects with polycythaemia.

4- Athletics.

5- Those who are found to have abnormal ejection fraction, valvular disease, regional hypokinesia on 2D and M-mode echocardiography.

The study groups

According to the inclusion and exclusion criteria 45 persons (female:30, male:15) constitute the first group (obese subjects) and 45 persons (female:30, male:15) constitute the second group (the lean subjects).

2-Methods

Echocardiography

Transthoracic echocardiography study (included M-mode, two-dimensional, spectral and colour Doppler and TDI technique) were performed on each participant by the same professional echo-operator with a commercially available Doppler echocardiograph (Vivid E9, 2015, GE Healthcare, United States), using a M5sc probe, with the patients in the left lateral position.

Calculation of the LVM and LVMI:

2D-guided M-mode measurements of the left ventricular (LV) wall thicknesses, internal diameter, were done for each participant from the parasternal long axis view, at end-diastole according to the American Society of Echocardiography (ASE) recommendations²⁶(Figure 1), LVM was calculated using devereux formula that was validated with necropsy²⁷.

$$LVM=0.8[1.04(IVSd+ PWTd+ LVIDd) ^3-(LVIDd)^3] +0.6.$$

After Echocardiographic determination of LV-mass in grams, and to minimize LV mass differences between participants that are related to differences in body size LVM was indexed to the height using the allometric signal of (1.7)²¹.

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Defining left ventricular hypertrophy and its Geometric pattern

Left ventricular hypertrophy is defined as left ventricular mass index (LVMI) > 80 g/m^{1.7} in male and LVMI > 60 g/m^{1.7} in female²¹, the relative wall thickness is calculated

according to the following formula: [RWT = (IVSd + LVPWd)/LVEDd], and a cut off value of (0.45) was used²⁸. LVH with increased RWT is defined concentric; LVH with normal RWT is defined as eccentric²⁹.

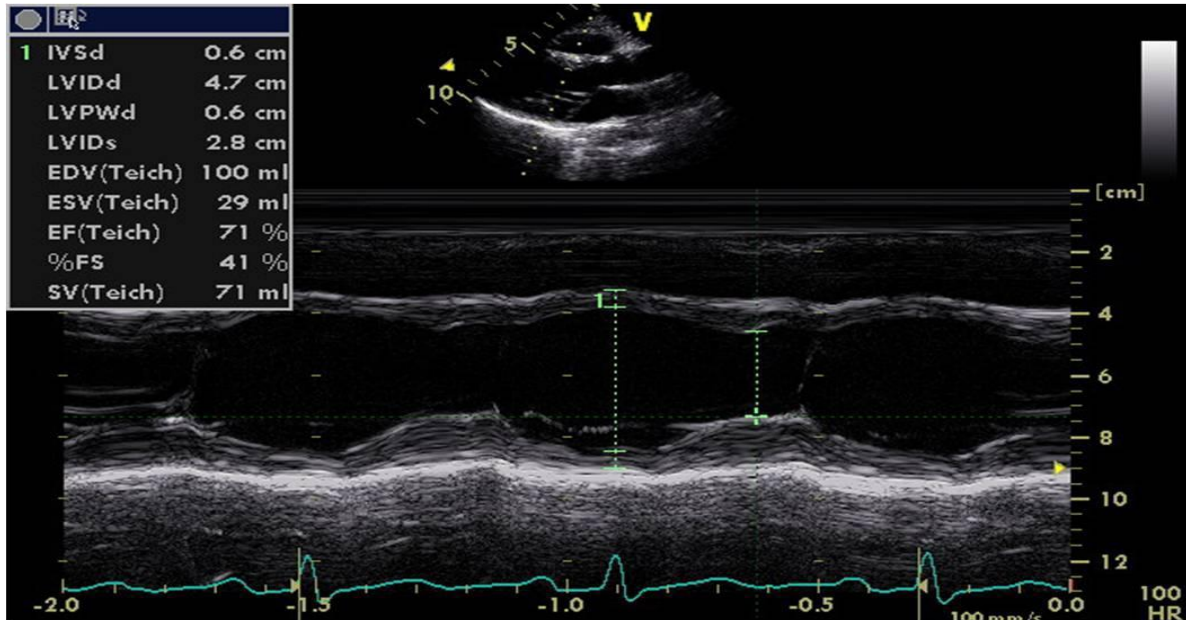


Figure 1 Measurement of LV wall thicknesses and internal diastolic diameter.

Assessment of transmitral flow

From an apical four chamber view using conventional pulsed wave Doppler with a sample volume of (3 ml) measurement of transmitral flow parameters were done including the early (E) wave and late (A) wave diastolic

filling velocities, the resultant E/A ratio, the E-wave velocity deceleration time (DT) and the isovolumic relaxation time (IVRT), all measurements are the average of three consecutive cardiac cycles. Figure 2

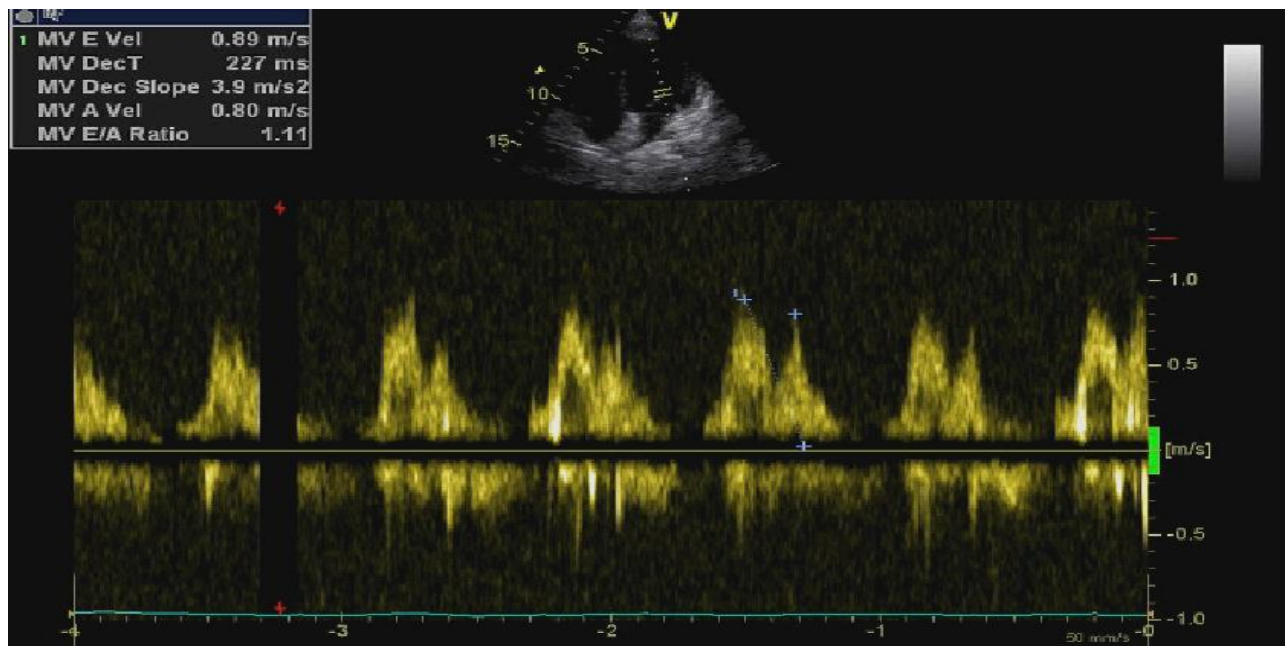


Figure 2 measurements of transmitral flow velocities and mitral valve deceleration time.

Tissue Doppler imaging:

Using tissue Doppler in the 4-chamber view, the peak early diastolic velocity of the lateral mitral annulus (e')

was measured. The average E/e' was obtained by dividing the early transmitral (E) wave velocity by the lateral mitral annulus (e') velocity. Figure 3

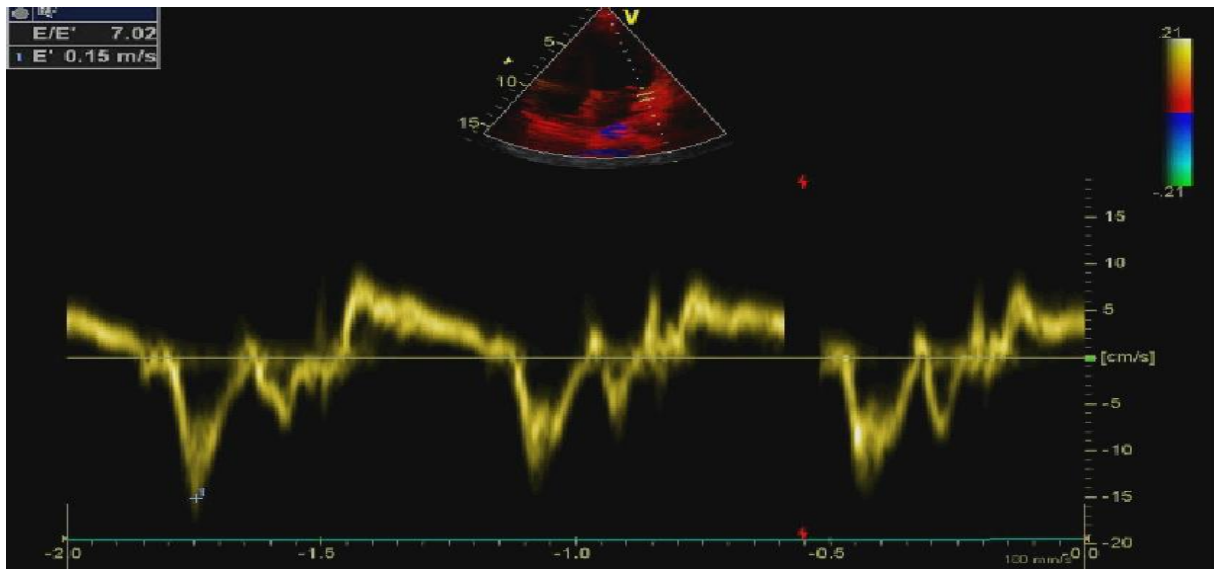


Figure 3 measurement of lateral e' velocity and calculation of E/e' ratio

Flow propagation velocity:

In the apical four chamber view, colour Doppler M-mode imaging was applied to provide a two-dimensional representation of the velocity of early diastolic filling as

the bolus of blood propagates through the mitral valve towards the LV apex (flow propagation velocity or VP). Figure 4

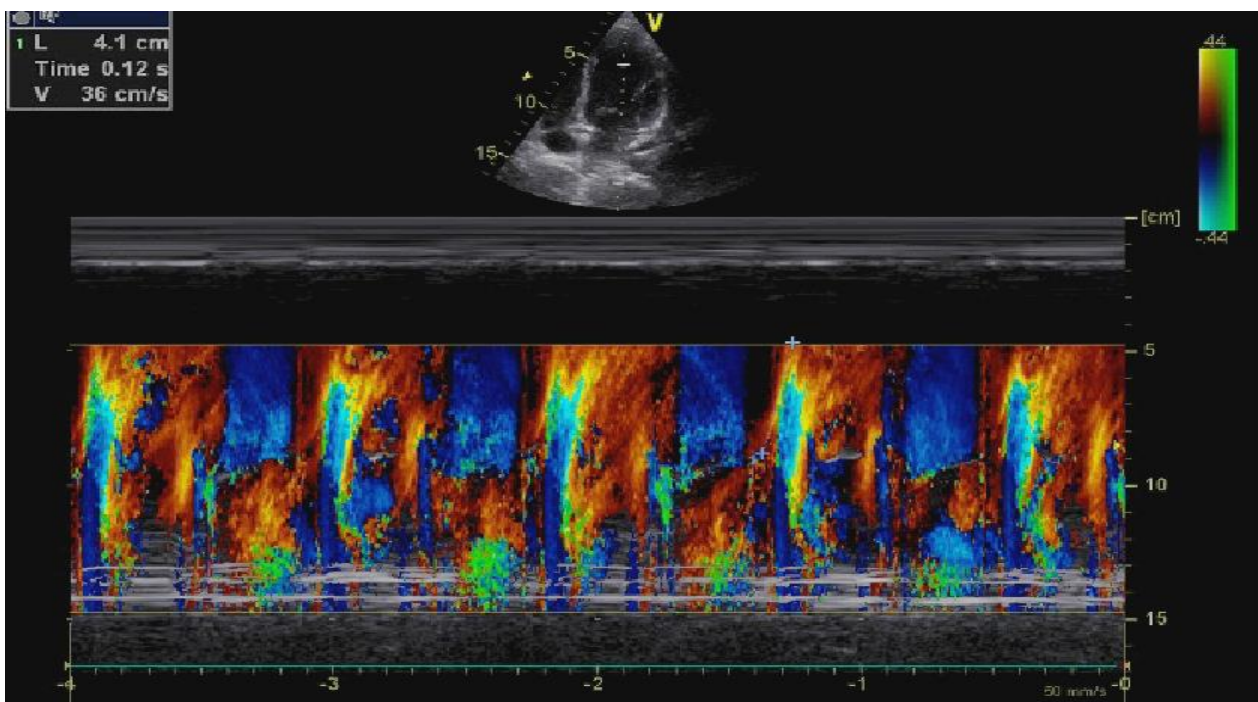


Figure 4 measurement of flow propagation velocity.

Tricuspid regurgitation velocity for pulmonary artery pressure estimation:

The tricuspid regurgitation (TR) jet was identified in the apical 4-chamber view with the help of colour Doppler, and continuous wave (CW) Doppler of the tricuspid regurgitation (TR) trace was used to measure the pressures gradient between the right ventricle and right atrium. The simplified Bernoulli equation ($\Delta P = 4[TR\ max]^2$) was used to calculate the pressure difference using peak TR velocity. Then the pressure contribution coming from the right atrium (RAP) is estimated [by assessing the inferior vena cava (IVC) size

and response to respiration] and added to obtain the pulmonary artery systolic pressure (PASP) according to the equation ($PASP = 4[TR\ max]^2 + RAP$)³⁰.

Left atrial volume:

Using the biplane approach, from the apical four- and two-chamber views the left atrial area was measured at end-systole (just prior to mitral valve opening, when volume is greatest) and the left atrial volume is calculated using modified Simpson's method according to the (ASE) guidelines for cardiac chamber quantification²⁶. Because of the relationship between atrial size and body size, it is

recommended that the volume be corrected for body surface area³¹ and reported in mL/m². Figure 5

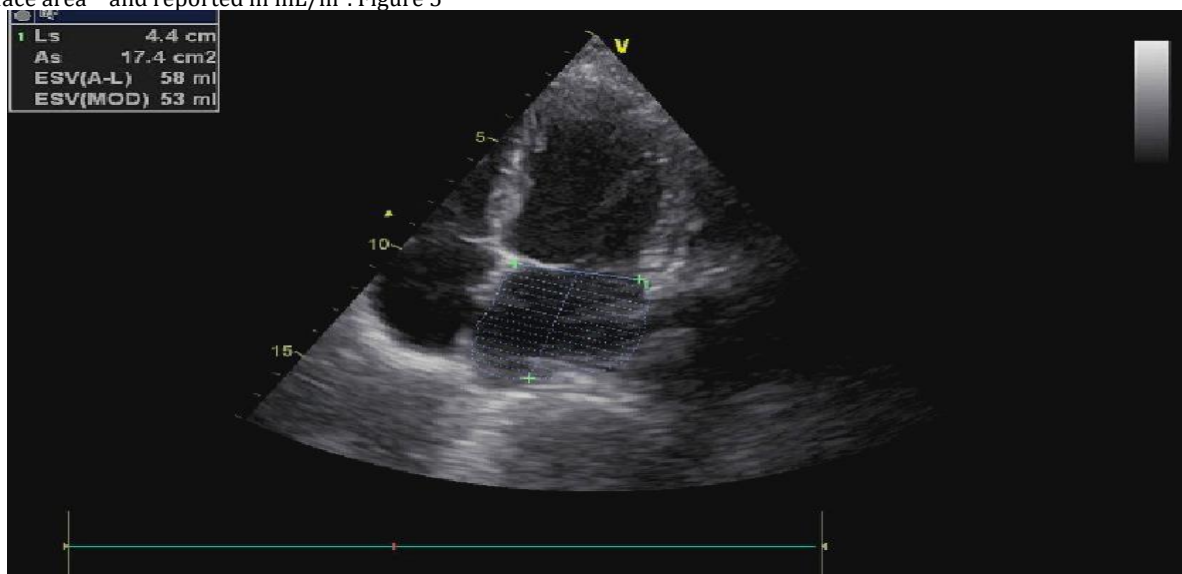


Figure 5 measurement of left atrial volume.

Defining diastolic function

Diastolic dysfunction was defined according to the American society of echocardiography/European association of cardiovascular imaging (ASE/EACVI) guidelines for the diagnosis of left ventricular diastolic dysfunction³²

Grade I DD was recognized as (1) an E/A ratio of (0.8) or less with a peak mitral E-velocity of 50 cm/second or less or (2) an [E/A ratio of (0.8) or less with a peak E velocity of more than 50 cm/second, or an E/A of 0.8 - <2] with at least two of the following criteria are negative (a) lateral E/é >13 (b) TR velocity >2.8 m/second (c) left atrial volume index (LAVI) >34 ml/m².

Grade II DD was recognized as an [E/A ratio of (0.8) or less with peak mitral E-velocity of more than 50 cm/second or E/A 0.8 - <2] with at least two of the above-mentioned criteria are positive. an E/A ratio ≥ 2 indicates grade III diastolic dysfunction.

Statistical analysis:

Data were expressed as mean ± standard deviation (SD) for continuous variables and as a percentage for categorical variables, comparisons between the study groups

regarding continuous variables were done using the independent-sample T test, the associations between categorical variables were assessed using Chi-square test. Relations between the different echocardiographic variables or with anthropometric measurements were done using simple regression analysis. The differences between the study groups regarding the diastolic function parameters after adjusting for covariates were assessed using analysis of covariance (ANCOVA).

A 2-tailed p < 0.05 was considered significant, Statistical analyses were performed using SPSS 23.00 (SPSS Inc., Chicago, Illinois) software.

RESULTS

1- Characteristics of the groups in the study:

The characteristics of the participants studied are presented in (table 1). There were significant differences between the two groups (obese, lean) regarding the weight, BMI, BSA, waist circumference, hip circumference, waist/hip ratio. Age and height were not significantly different between the study groups.

Table 1. Characteristics of the study participants

character	Obese Mean ± SD	Lean Mean ± SD	Mean difference	P-value
Age	29 ± 5.58	28.3 ± 4.75	0.688	0.69
Weight	102.6 ± 17.6	58.3 ± 5.9	44.3	< 0.001
Height	1.61 ± 0.78	1.61 ± 0.93	0.0007	0.96
BMI	38.96 ± 4.88	22.27 ± 1.98	16.69	< 0.001
BSA	2.14 ± 0.22	1.61 ± 0.11	0.52	< 0.001
Waist circumference (male)	121.9 ± 10.88	75.5 ± 6.75	46.4	< 0.001
Waist	111.4 ± 12.26	75.5 ± 7.86	35.88	< 0.001

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circumference (female)				
Hip circumference (male)	115.76 ± 7.36	88 ± 3.55	27.76	< 0.001
Hip circumference (female)	118.5 ± 14.24	90.45 ± 8	28	< 0.001
Waist/hip ratio (male)	1.05 ± 0.73	0.85 ± 0.45	0.19	< 0.001
Waist/hip ratio (female)	0.93 ± 0.1	0.83 ± 0.06	0.098	< 0.001

BMI: Body Mass Index, BSA: body Surface Area.

2- Echocardiographic variables

The left ventricular dimensions, LVMI, the percentage of LVH and association with obesity

This study demonstrates statistically significant differences between the two groups regarding the mean of left ventricular wall thickness (P-value< 0.05 for IVST in both male and female, P-value< 0.001 for PWT in both

male and female), internal diastolic diameter (P-value< 0.05 in both male and female) and left ventricular mass index (P-value< 0.001 in both male and female), obese participants have significantly higher IVST, PWT, LVIDd, LVMI, while the mean of the RWT is not significantly different between the two groups (P-value: 0.14). Table 2

Table 2. The left ventricular mass index, wall thickness and internal diastolic diameter of the study groups

	Obese Mean ± SD	Lean Mean ± SD	Mean difference	P-value
IVST (cm) male	1 ± 0.13	.76 ± .074	0.24	< 0.001
IVST (cm) female	0.8 ± 0.16	0.7 ± 0.08	0.1	0.004
LVID (cm) male	4.94 ± 0.65	4.38 ± 0.39	0.56	0.008
LVID (cm) female	4.56 ± 0.44	4.08 ± 0.43	0.48	< 0.001
PWT (cm) male	0.91 ± 0.09	0.73 ± 0.06	0.18	< 0.001
PWT (cm) female	.83 ± 0.084	0.7 ± 0.069	0.13	< 0.001
RWT	0.365 ± 0.066	0.347 ± 0.047	0.018	0.14
LVMI (g/m ^{1.7}) male	69.11 ± 14.3	40.23 ± 7.32	28.88	< 0.001
LVMI (g/m ^{1.7}) female	54.39 ± 10.45	38.18 ± 7.6	16.2	< 0.001

IVST: Interventricular Septal Thickness, LVID: Left Ventricular Internal Diameter, PWT: Posterior Wall Thickness, RWT: Relative Wall Thickness, LVMI: Left Ventricular Mass Index.

LVH was encountered in (28.88%) of obese participants only, and demonstrates a significant association with obesity (chi-square test: 15.2), figure 6

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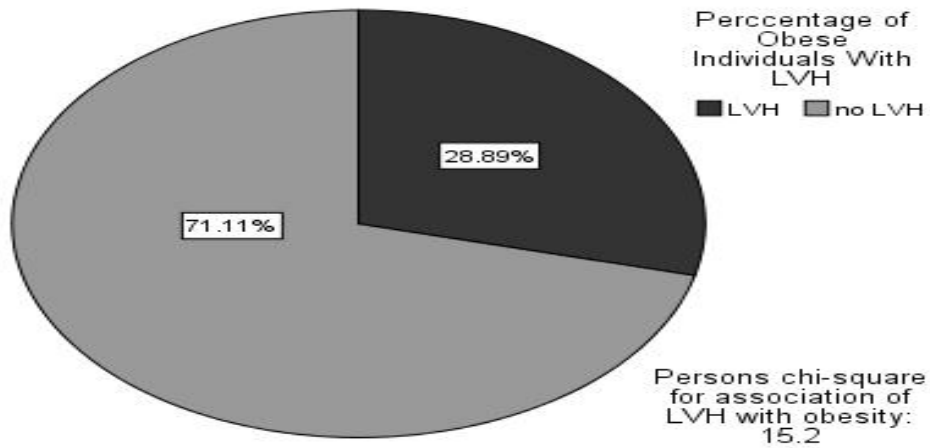


Figure 6 Percentage of LVH in the Study Participants and its Association with Obesity (All lean participants have normal LVMI, i.e. no LVH).

Correlation of LVMI with anthropometric measurements

LVMI demonstrated a significant positive correlation with BMI, i.e. LVMI increases with increasing BMI (R: 0.658,

P -value < 0.001), it also had a significant positive correlation with measures of central adiposity, i.e. WC, WHR, (R: 0.644, 0.550 respectively, P-values< 0.001). Figure 7,8,9.

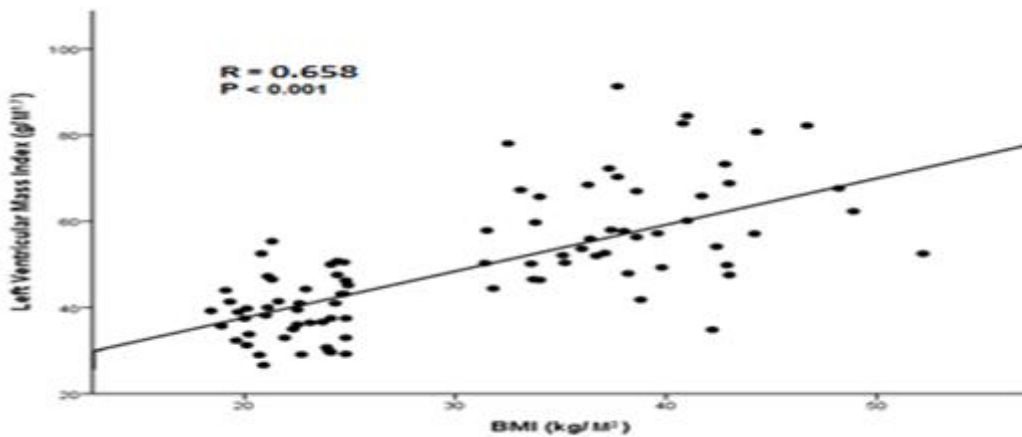


Figure 7 Relations between left ventricular mass index and body mass index

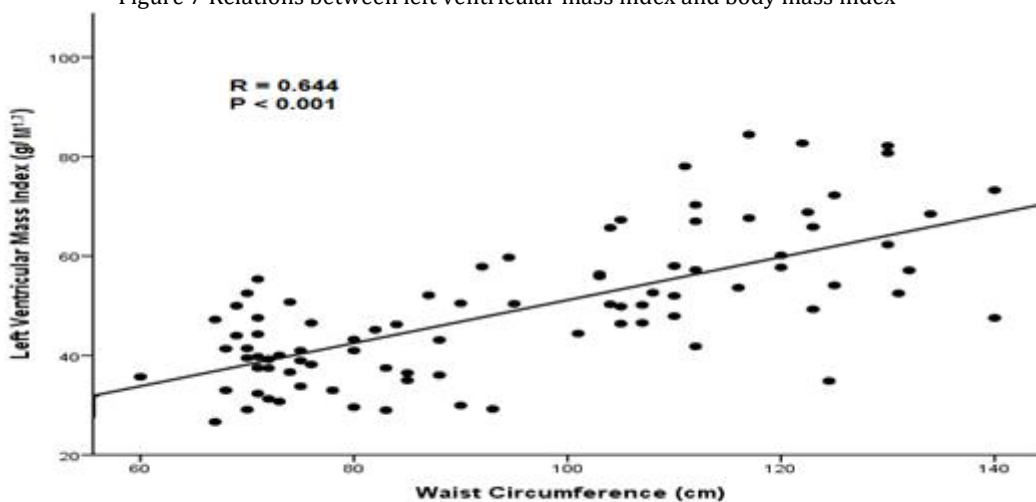


Figure 8 Relations between left ventricular mass index and waist circumference

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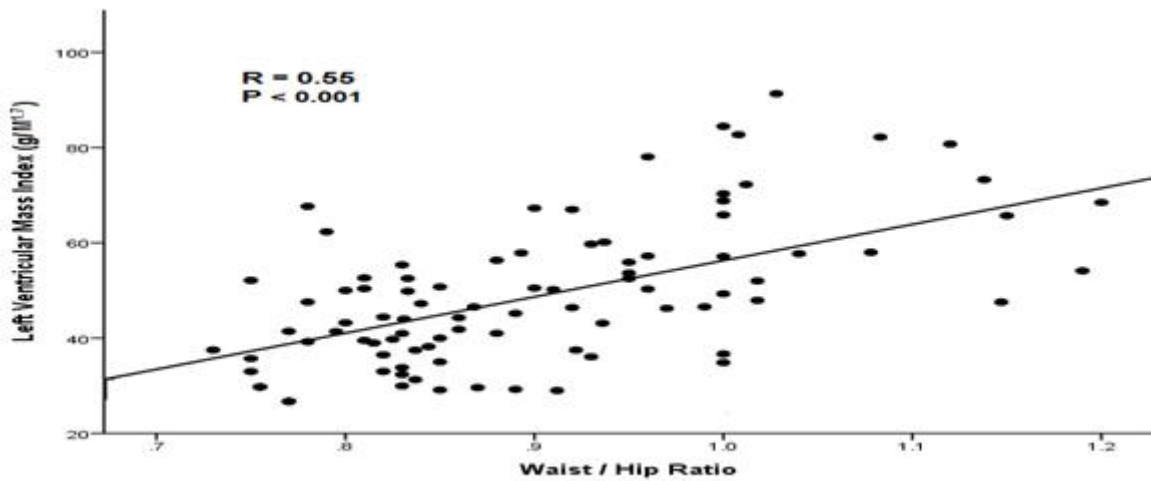


Figure 9 Relations between left ventricular mass index and waist/hip ratio

Left ventricular internal diameter in diastole (as a surrogate of preload)

LVEDd exhibited a positive correlation with BMI (R: 0.434, p-value <0.001) on the other hand LVMI was found

to have a positive correlation with LVEDd (R: 0.747, P-value <0.001). Figure 10.11

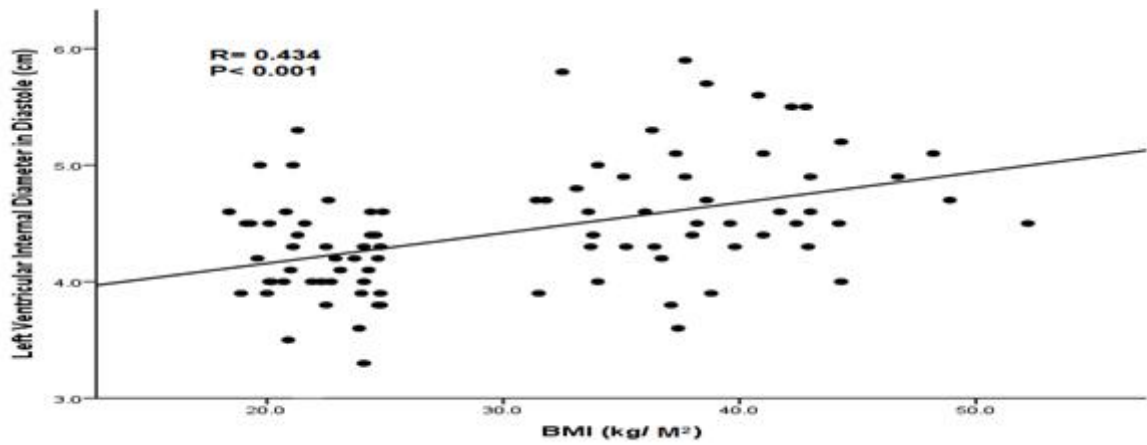


Figure 10 Relations between body mass index (BMI), left ventricular internal diameter in diastole (LVEDd)

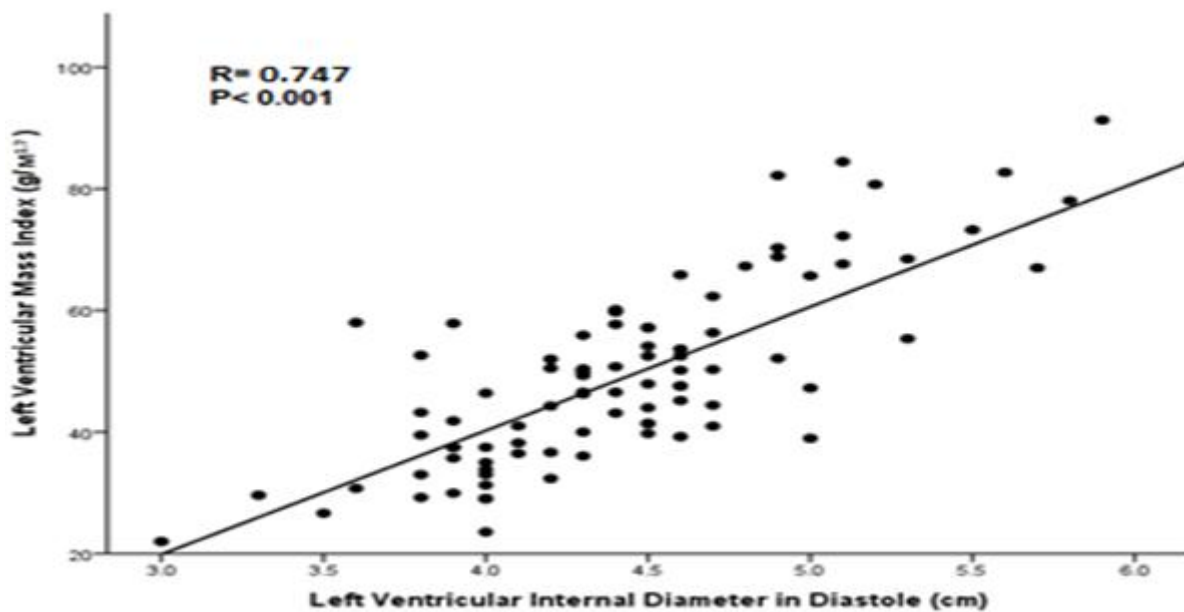


Figure 11 Relations between Left ventricular internal diameter in diastole (LVEDd) and left ventricular mass index (LVMI).

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Parameters of diastolic function

No diastolic dysfunction was encountered in this study (neither in obese nor in lean control) according to the ASE/EACVI guidelines for the diagnosis of left ventricular diastolic dysfunction³².

Transmitral flow parameters

No statistically significant differences between the two groups regarding the mean of the early (E) and the late (A) peak transmitral flow velocities (P-values are 0.49, 0.44) respectively and the E/A ratio (P-value: 0.51), the transmitral E-velocity Deceleration Time is significantly longer in obese (P-value: 0.001). table 3

Table 3. Diastolic function parameters of the study participants

Diastolic parameter	Obese Mean ± SD	Lean Mean ± SD	Mean difference	P-value
Peak E-wave velocity (cm/s)	84 ± 23	87 ± 15.9	3	0.49
Peak A-wave velocity (cm/s)	63.6 ± 21.7	60.6 ± 16.3	3	0.44
E/A ratio	1.32 ± 0.37	1.37 ± 0.23	0.044	0.512
Mitral E-velocity Deceleration Time (msec)	222.5 ± 43.9	194.4 ± 30.58	28.06	0.001
Lateral e' velocity (cm/s)	13.16 ± 3.91	15.4 ± 2.78	2.23	0.002
Mitral E/e' ratio	6.11 ± 1.96	5.5 ± 1.64	0.6	0.118
IVRT (msec)	81.78 ± 15.52	63.97 ± 10.5	17.81	< 0.001
VP (cm/sec)	40.66 ± 10.35	58.4 ± 8.7	17.7	< 0.001
LAVI (ml/m ²)	27.84 ± 6.29	20.9 ± 3.53	6.94	< 0.001
PASP (mmHg)	23.62 ± 6.32	20.73 ± 4.46	2.88	0.014

IVRT: Isovolumic Relaxation Time, VP: Flow Propagation Velocity, LAVI: Left Atrial Volume Index, PASP: Pulmonary Artery Systolic Pressure.

Indicis of LV Relaxation

Apart from the transmitral flow parameters the other indicis of LV relaxation exhibit significant difference between the two groups, in this regard, the Lateral (e') velocity is significantly lower in obese participants (P-value: 0.002), the isovolumic relaxation time is significantly longer in obese subjects (P-value < 0.001) and the early diastolic flow propagation velocity (VP) is significantly lower in obese participants (P-value < 0.001). Table 3

Diastolic indexes that correlate with LV filling pressures

The mean Mitral E/e' ratio was not significantly different between the two groups (P-value: 0.11), but obese subjects have significantly higher PASP (P-value: 0.01), LAVI (P-value < 0.001). Table 3

Left Atrial Volume (as a marker of volume overload)

Interestingly the higher left atrial volume index (LAVI) in obese had maintained its statistical significance even when other variables that can cause left atrial (LA) enlargement in obesity (such as increased LVM and diastolic dysfunction) were controlled for, adjusted means were (27.3, 21.4) for obese and lean respectively, (p-value < 0.001), Figure 12

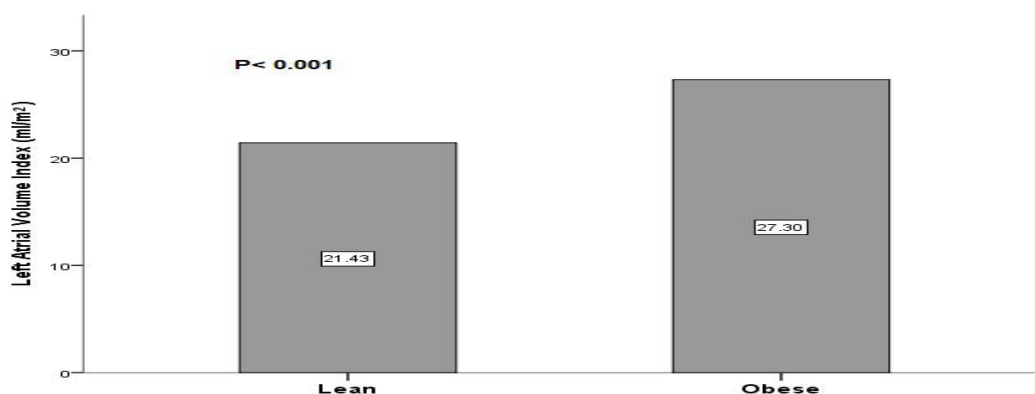


Figure 12. Left atrial volume index in obese versus lean after controlling for left ventricular mass and diastolic function.

LAVI had exhibit a positive correlation with BMI (R: 0.476, p-value <0.001) on the other hand LVMI was found to

have a positive correlation with LAVI (R: 0.469, P-value <0.001). Figure 13, 14.

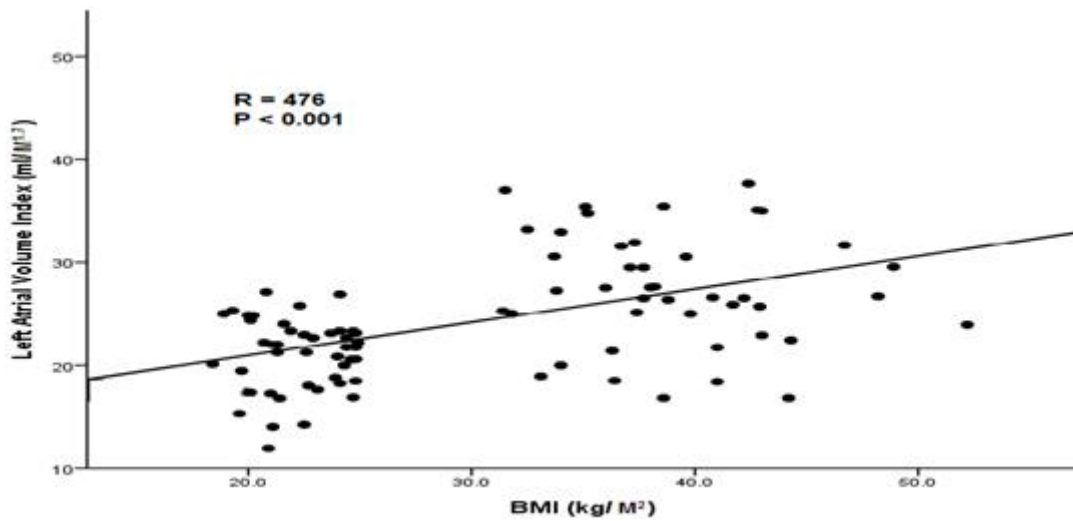


Figure 13. Relation of left atrial volume index (LAVI) with body mass index (BMI)

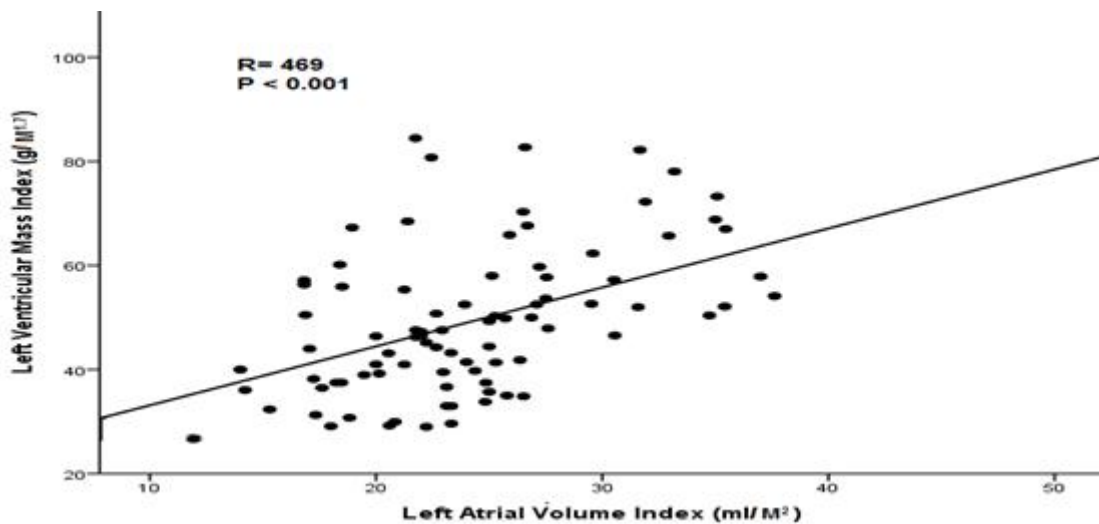


Figure 14 Relation of left atrial volume index (LAVI) with left ventricular mass index (LVMI).

DISCUSSION

Left ventricular mass and Geometry in obesity

The effects of obesity on LVM reported in the literature was variable. Most studies found that obesity is associated with increased LVM^{16,33} while others did not³⁴. This controversy may be due to (1) the different methods used to normalize LVM for body size which is either based on an inaccurate assumption about body size-LVM relationship²⁰, or have a limited ability to describe it³⁴ (2) the presence or absence of obesity associated complications such as hypertension, diabetes...etc¹⁸.

We sought to evaluate the effects of obesity on LVM in obese individuals who are healthy (i.e. without obesity-related complications), utilizing the ultimate normalization method (LVM normalized for height using the allometric signal of 1.7)²¹ that was proposed after analysing data from two large population-based studies and account for the potential limitations in the previous methods.

This study demonstrates that LVM and LVMI are significantly greater in obese subjects and that non complicated obesity is significantly associated with LVH. This finding is concordant with that of Alpert MA, et al¹⁶, Iacobellis G, et al³⁵ and Okpura IC, et al³⁶ and in contrast to that of Zhang N, et al³⁴ which reported that non-complicated obesity was not associated with LVH, but it should be kept in mind that their indexing method (LVM indexed to the height using an allometric signal of 2.7) is known to overcorrect for height^{37,21} and consequently it may underestimate the prevalence of LVH.

Although the traditional measure of general obesity (i.e. BMI) cannot differentiate between body weight components^{4,38} such as lean body mass (fat-free mass) and the total fat mass (adipose tissue mass), but from the other hand LVM was indexed to the allometric signal of height (height is a surrogate of what should be the normal fat-free muscle mass in each individual)^{39,40}. Consequently if there is a relationship between these two variables (i.e. BMI and LVMI) then it is mainly due to the

effects of adipose tissue mass. In this regard our study demonstrated a highly significant positive correlation between BMI and LVMI (figure 7). And this finding indicates that the left ventricular mass increases with increasing adipose tissue mass and it is concordant with that of Rocha IE⁴¹, et al (that reported a similar correlation) and Alpert MA, et al⁴² (that reported a positive correlation between the percentage of overweight and LVMI). In this study WC and WHR were also found to positively correlate with LVMI (figure 8,9) and this finding is concordant with that of Panchal H, et al⁴³ and it further support the hypothesis that adiposity is associated with increased left ventricular mass (since WC, WHR are the surrogate markers of abdominal fat contents)⁴⁴.

Traditionally LVH in context of obesity was attributed to the associated hemodynamic changes which typically would result in an eccentric type of LVH⁴⁵. Subsequent studies reported that obesity can also be associated with concentric LVH or remodelling (i.e. concentric LV morphology)⁴⁶. It is obvious that such variable geometric pattern that reported to occur with obesity cannot be explained by obesity-related hemodynamic profile only. Several studies reported that obesity-related metabolic and neurohormonal abnormalities are implicated in the development of concentric LVH⁴⁶. Consequently, the controversy regarding LV morphological changes associated with obesity can be explained by the differences in the methodology (and in particular: the exclusion criteria) between these studies, for example all studies that had reported a high incidence of concentric LV morphology did not exclude those with hypertension^{33,46}.

In this study there was no significant difference in RWT between the study groups, and all the obese subjects with LVH have a normal RWT, i.e. have eccentric type of LVH (that traditionally reported to occur with obesity)⁴⁵.

Obese subjects exhibited a difference in their hemodynamic profile (compared to that of their lean counterparts). The LV internal diastolic dimension (a surrogate of preload)⁴⁷ was significantly larger in the obese group and this finding is concordant with that of Merlino G, et al⁴⁸ and Karason K, et al⁴⁹. LAVI (marker of volume overload)⁴⁵ was also found to be significantly larger in the obese group and interestingly, it had maintained its statistical significance even when factors (other than volume overload) that can cause LA enlargement in obesity⁴⁶ were adjusted for. (Figure 12)

LVEDd and LAVI were found to positively correlate with BMI (figure 10, figure 13), this finding is concordant with that of Sun T, et al⁵⁰ and Patil S, et al⁵¹, and it indicates that increasing adiposity is associated with increased blood volume and preload, from the other hand left ventricular mass was found to positively correlate with LVEDd - a surrogate of preload⁴⁷- (figure 11), this finding is concordant with that reported by Alpert MA, et al⁴².

Left ventricular diastolic function in obesity

Diastolic dysfunction is the leading cause of heart failure in obesity (heart failure with preserved ejection fraction or systolic function)⁵² and it is independent predictor of mortality⁵³ even in those with normal systolic function⁵⁴. Unfortunately, obesity commonly presents with conditions that are independently implicated in the development of diastolic dysfunction⁵⁵ (eg: hypertension, diabetes mellitus). Furthermore, echocardiography parameters of diastolic function are known to deteriorate with aging⁵⁶. So, it is worthy to evaluate diastolic function in a study that involve obese subjects who are healthy (i.e.

have no cardiometabolic or other complications of obesity) and young.

This study demonstrated no significant differences between the study groups regarding the left ventricular passive and active filling velocities (E, A) and their ratio (E/A ratio), and these results are concordant with that of Pascual and colleagues¹⁷, wala F and colleagues⁵⁷ (both studies were conducted on a sample of young age, healthy obese subjects).

Studies that describe the transmitral filling velocities in context of obesity provide variable and inconsistent results, for example: Di Bello and colleagues⁵⁸ found that obesity is associated with an increase in A-wave velocity, no significant changes in E-wave velocity and a decrease in E/A ratio, Mureddu GF and coworkers⁵⁹ reported similar results but with a decrease in E-wave velocity, Stoddard MF and associates⁶⁰ found that both E and A wave velocities are significantly increased in obesity while the E/A ratio was not altered.

An important point that should be kept in mind is that conventional Doppler imaging modality that used to assess the transmitral filling velocities is load dependant⁶¹. and that obesity is associated with increased plasma volume (i.e. increased preload)^{20,17}. consequently; (1) the variable association (between the transmitral flow velocities and obesity) reported in the literature can be explained in part by differences in loading conditions²⁰, (2) when using such load dependant indices to evaluate diastolic function in context of volume overload-as in obesity-normal values may result (the alterations in the transmitral flow that occur in the early phases of abnormal LV relaxation can be obscured by augmented preload)¹⁷.

In this study the E-wave velocity deceleration time was found to be significantly prolonged in the obese subjects, a result consistent with that reported by Mureddu GF and coworkers⁵⁹ in a study that involve obese subjects without hypertension or other metabolic complications. Such finding indicates that the LV relaxation process is slower in obese⁶² (when LV relaxation is slow then it will continue throughout the early diastolic filling phase and this will maintain a low pressure gradient between the LA and LV, consequently the early diastolic filling will be distributed throughout a longer time, i.e. prolonged deceleration time)^{62,59}.

The isovolumic relaxation time was found to be significantly prolonged in obese and this is the diastolic abnormality that most of the echocardiography studies in obese subjects agreed on^{59,63,64}, it indicates abnormal LV relaxation^{59,65} and correlates with the time of calcium ion energy dependant uptake by the sarcoplasmic reticulum^{59,66} and it is hypothesized to be one of the primary changes in left ventricular diastolic properties⁵⁹. And taking in consideration the load dependence of conventional Doppler-derived diastolic parameters⁶¹, it is interesting to find that DT and IVRT are significantly prolonged in obese despite that the hemodynamic profile in obesity is unfavourable to such detection.

The flow propagation velocity was significantly lower in obese, this finding is concordant with that of (Schuster I et al.)⁶⁷ and it indicates slower LV relaxation⁶⁸.

TDI-derived, load independent peak early diastolic LV myocardial velocity was significantly lower in obese subjects, this finding indicates that their LV relaxation is slower^{68,62}. On the other hand, the resultant E/e' ratio which is the most widely used correlate of LV filling pressure didn't show a significant difference between the two groups.

To our knowledge, few studies had adopted the (the lateral e') to represent the peak early diastolic LV myocardial velocity^{69,70}. they reported a lower peak e' velocity (in concordance with our finding) and higher E/ e' ratio in obese (we assumed that this is due to the confounding effects of the hypertensive and diabetic subjects included in the studies sample).

Other studies that adopted (septal e') or (average e') are also confounded by diabetes and hypertension^{71,72, 73}. it is interesting to find that in a study conducted on young, healthy obese individuals²⁰ adopting (the average e' velocity), the early diastolic LV myocardial velocity was lower in obese while E/ e' ratio was not significantly different from that of control, this is concordant with our finding despite the difference in the site from which the peak e' velocity was obtained.

In this study the E/ e' ratio and PASP was adopted as non-invasive correlates of LV filling pressures. It was found that the difference between the two groups did not reach the level of statistical significance regarding the E/ e' ratio while it did so for PASP and this is logical as the E/ e' index has a lower sensitivity to elevation in filling pressures⁶⁴. This is supported by our finding that the indexed left atrial volume (which reflects the cumulative effects of filling pressures over time)⁶⁸ is significantly higher in obese.

CONCLUSION

Non-complicated obesity has a significant association with eccentric type of LVH, although it is not associated with diastolic dysfunction, but obese individuals had exhibited a subclinical deterioration in parameters of LV relaxation and filling pressures.

RECOMMENDATIONS

Prolonged follow up study of obese persons to ascertain the effects of obesity duration and the effects of weight reduction on LV structure and function

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