Relationship of Body Mass Index with Changes in Cardiac Geometry and Function in 5,898 Patients Evaluated by Transthoracic Echocardiography

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Abstract

Introduction: This study describes the relationship between Body Mass Index (BMI) and the cardiac geometry and heart function assessed by transthoracic echocardiography.

Materials and methods: We analyzed 5,898 echocardiographic studies in an age range between 18.0 and 98.6 years.

Results: The BMI ranged from 15.23 to 49.61 kg/m². The increased BMI had a statistically significant direct association with left ventricular mass initially observing a light concentric hypertrophy, which becomes eccentric as it increases, especially when allometric ratio is normalized (Height$^{2.7}$). An increase in ejection volume and cardiac output was observed, as well as an inverse association between body mass index and the E/A ratio of mitral filling, with a significant reduction of e' velocity of tissue Doppler, showing a relaxation-type diastolic dysfunction in overweight or obese individuals. We observed a slight yet significant increase in the left atrial area and volume indexed to body mass. There were no differences in the right ventricular geometry and function.

Conclusions: The present study demonstrated a significant direct association between the increase in BMI and LV myocardial mass. Indexing LV mass to height 2.7 avoids artifacts related to body mass index, especially in subjects with grade II and III obesity. (Arq Bras Cardiol: Imagem cardiovasc. 2015; 28(1):3-16)

Keywords: Body Mass Index; Heart/Physiology; Echocardiography; Ventricular Function; Obesity; Cardiac Output.

Introduction

The prevalence of overweight and obesity is growing worldwide, constituting an epidemic that affects individuals of all ages and socioeconomic levels. In Latin America, considering both conditions, their prevalence is 40%, and in Colombia in particular, 50%[1-3].

Overweight or obese patients have persistent myocardial wall stress because of an increase in circulatory volume and minute volume, proportional to excess body weight, which occur due to increased blood flow in the adipose tissue, with minimum involvement of the heart rate at rest, but with increased systolic volume. This increase in minute volume invariably generates a compensatory increase in myocardial mass and consequent pre-clinical and clinical ventricular hypertrophy, with an eventual ventricular dilatation, with systolic and diastolic dysfunction, making up a spectrum described as cardiomyopathy of obese patients, which occur in the absence of hypertension or coronary disease[4,5].

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On the other hand, abnormal left ventricular filling has been described in asymptomatic obese individuals that are healthy in other aspects, and a prolongation of isovolumic relaxation time. These findings can be observed in the absence of Left Ventricular systolic dysfunction (LV). Weight reduction is better associated with diastolic filling and normalization of left ventricular isovolumic relaxation time[6]. Compared with control individuals of normal weight and blood pressure, obese patients have larger left atrial (LA) and aortic root diameter and greater septal and posterior wall diastolic thickness and LV mass[7].

The normal values of LV mass differ between men and women, even when they adjust to body surface area. The best method to normalize the LV mass measurement in adults is under discussion. Although the body surface is most often used in clinical trials, this method underestimates the prevalence of LV hypertrophy in obese and overweight people. The ability to detect the LV hypertrophy associated with obesity and cardiovascular disorders is improved by indexing the LV mass to the power of its allometric ratio (a term that refers to changes in the relative size of body segments correlated with changes in total size) to height$^{2.7}$ [8]. The normal values for myocardial mass normalized by height$^{2.7}$ in obese patients have been described by the European Society of Echocardiography, and the quantification of cardiac chambers, by the American Society of Ecocardiography[9].

Hence, the objective of this study is to determine the relationship of body mass index (BMI) with cardiac geometry and function assessed by transthoracic echocardiography in a group of adults without any heart disease that would affect the measurements to be performed at Clínica Medellín (Medellin, Colombia).

Methodology

From the echocardiograms performed at the Echocardiography Service from October 2010 and February 2013, reports of patients aged between 18 and 92 years who had not limited acoustic window or any of the following diagnoses or history were taken: atrial fibrillation; presence of intraventricular electrodes; ischemic heart disease; hypertrophic cardiomyopathy; congenital heart disease; valve prostheses; chemotherapy; pericarditis; intracardiac masses or thrombi; moderate or severe stenosis or regurgitation; *cor pulmonale*; pulmonary thromboembolism or heart failure. The study was previously approved by the Ethics and Research Committee of Universidad CES, Medellin, Colombia.

Measurements of different echocardiographic variables were performed according to the recommendations of the American Society of Echocardiography (ASE) for the quantification of cardiac chambers. The measurements were:

- Ejection fraction through the biplane Simpson method and the Teichholz formula.
- Left ventricular mass (LVM) in grams calculated by the Devereux formula: $LVM = 0.8\{1.04[([LVEDD+IVSd+PWd]^3-LVEDD^3)]\}+0.6$, where LVEDD is the left ventricular end-diastolic diameter; IVSd is the interventricular septal dimension during diastole; and PWd is the dimension of the posterior wall during diastole.
- Left ventricular mass index (LVMI) calculated in three ways: 1) LVMI=LVM/m, where m = patient's height in meters; 2) LVMI=LVM/BS, where BS = body surface (kg/m^2); and 3) $LVMI=LVM/height^{2.7}$ where $height^{2.7}$ = height raised to the 2.7 power.
- Relative wall thickness (RWT), calculated as RERP = (IVSd+PWd)/LVDd where IVSd is the interventricular septal dimension during diastole; PWd is the dimension of the posterior wall during diastole; and LVDd is the left ventricular end-diastolic diameter.
- Systolic volume (*SV*) calculated using pulsed Doppler, obtaining the spectrum of flow velocity at the LV outflow tract (LVOT) level using apical five chamber view.
- Cardiac output (CO) as $CO=0.785xD^2xVTIxHR$, where D is the diameter of the LVOT; VTI is velocity time integral in the LVOT; and HR is the heart rate in beats per minute.
- TAPSE (Tricuspid Annular Plane Systolic Excursion) measured on M mode and representing the distance that the tricuspid annulus travels from end-diastole to end-systole.
- Left atrial volume measured using the Simpson method or the ellipsoid model obtained from apical 4 and 2 chamber views; after obtaining this value and considering the differences between men and women, according to the ASE recommendations, atrial volume was indexed to body surface[9].

Data were analyzed using Stata/SE version 12.1 (Stata Corp, College Station, 2013) accepted as significant differences with $\alpha<0.05$. Qualitative variables are described as proportions and continuous variables with mean and standard deviation (SD). The number of patients allowed us to establish six groups of individuals according to BMI: 15.0 to 19.9 kg/m^2; 20.0 to 24.9 kg/m^2; 25.0 to 29.9 kg/m^2; 30.0 to 34.9 kg/m^2; 35.0 to 39.9 kg/m^2; and 40.0 to 49.9 kg/m^2. For each group of sex and BMI, the distribution of age and sex was established, as well as the prevalence of existing comorbidity: high systolic or diastolic blood pressure (BP) (given from blood pressure values at the time of the test), clinical history of chronic kidney failure; chronic obstructive pulmonary disease, diabetes mellitus, pulmonary hypertension and cancer. The odds ratios (OR) were calculated along with their confidence intervals of 95% (95% CI) of BMI with the presence of diabetes mellitus, systolic hypertension or diastolic hypertension.

To establish the association between BMI and echocardiographic measurements, the best multiple linear regression model was estimated, in which the primary data of each measurement correlated with the primary data of BMI and patient age, including sex, the date of the procedure and the existing comorbidity. The coefficient β was calculated and considered significant if 95% CI was positive (direct association) or negative (inverse association). In all measurements, the association between each measurement and the quadratic or cubic terms of BMI (BMI^2 or BMI^3) was explored according to the recommendations of Rabe-Hesketh and Skrodal[10]. The transformed data were not considered since the large number of observations (> 5,000) makes it unnecessary to do so. Finally, the multiple correlation coefficient (σ^2) for each model was established, as well as the graphics predicted and its confidence interval of 95%.

Results

Characteristics of the population

The original database contained 11,202 records, of which 5,304 were eliminated for various reasons (Figure 1). A total of 5,898 tests remained for analysis. Many of the records eliminated had more than one reason for this, and Figure 1 presents only the first reason detected that led to their removal.

The 5,898 patients included accounted for 3,606 (61.1%) women and 2,292 (38.9%) men; age ranged between 18.0 and 98.9 years, averaging 61.7 (SD 17.0) years, without any difference between men (mean 61.7 years, SD 17.2) and women (61, 4 years, SD 16.9, p = 0.395).

The BMI ranged from 15.23 to 49.61 kg/m^2, averaging 26.39 (SD = 4.96) kg/m^2 and median of 25.81 (interquartile range of 23.05 to 29.05) kg/m^2. The average among women was higher than among men: 26.73 (SD = 5.31) kg/m^2 vs. 25.87 (SD = 4.29) kg/m^2 (p < 0.001). Table 2 shows the relationship between age, sex and comorbidity in six groups of BMI. Obesity was associated with the presence of diastolic

or systolic hypertension as well as diabetes mellitus, regardless of gender and age, which is also associated with the three conditions (Table. 3).

In Table 4 and Figures 2 to 8, it is possible to see the average variation in the values of vital signs (blood pressure and heart rate) and echocardiographic measurements according to BMI. Only three measurements required the inclusion of a cubic term of BMI (IMC^3). Figure 2 shows how the two blood pressures are higher as the BMI, rather than heart rate, increases.

Left ventricular diastolic function

The maximum mitral filling E-wave velocity, which shows an ascending ratio that goes from 74 to 81 cm/s; the mitral filling A wave has a similar behavior, although with a sharper curve, presenting a greater speed as the BMI increases (Table 4 and Figure 3).

The finding described above is reflected in the E/A ratio, which maintains an inverse association with BMI, decreasing from 1.05 to 0.95 (β = -0.019, 95% CI -0.035 to -0.004; σ^2 = 0.2974). This decrease in E/A ratio, although minimal in quantitative terms, is statistically significant and implies an association between increased body mass and abnormal relaxation type diastolic dysfunction.

In turn, the tissue Doppler lateral e' speed decreases approximately 10 cm/s, showing a statistically significant inverse association with BMI increase (β = -0.025, 95% CI -0.152 to -0.102; σ^2 = 0.4232); this behavior does not cause any significant increase in the E/e' ration suggesting increased filling pressures, but it corroborates the relaxation disturbance (Table 4 and Figure 3).

Left ventricular systolic function

Left ventricular ejection fraction ranged from 61% to 64% without any significant abnormalities to the extent that BMI increased (β = 0.16, 95% CI -0.080 to 0.408; σ^2 = 0.0371), as shown in Table 4 and Figure 4.

Cardiac output ranged from 3.9 L/min and increased to 5.5 L/min to the extent that BMI increased to 35 kg/m^2, from which point it decreases to 5 L/min when it reaches the maximum BMI of 50 kg/m^2; although this increase shows a statistically significant direct association with BMI (β = 0.16, 95% CI 0.109 to 0.331), this behavior is not explained by this variable only, but also by the male gender. These two covariates explain only 5% of the cardiac output increasing trend (σ^2 = 0.0447).

Ejection volume in turn presents a behavior similar to cardiac output, with an increment proportional to BMI increase, reaching 73 mL for a BMI of 37 kg/m^2, and decreasing to 69 mL with a BMI of 50 kg/m^2, being a statistically significant direct association (β = 2.7, 95% CI 1.23 to 4.18; σ^2 = 0.0215).

Left atrium

Two left atrial measurement variables were analyzed: left atrial volume area and index (Table 4 and Figure 5). The left atrial area increases with BMI, which ranged from 15 cm^2 at a BMI of 15 kg/m^2 to 21 cm^2 at a BMI of 50 kg/m^2. In turn, the assessment of atrial volume indexed by body surface area

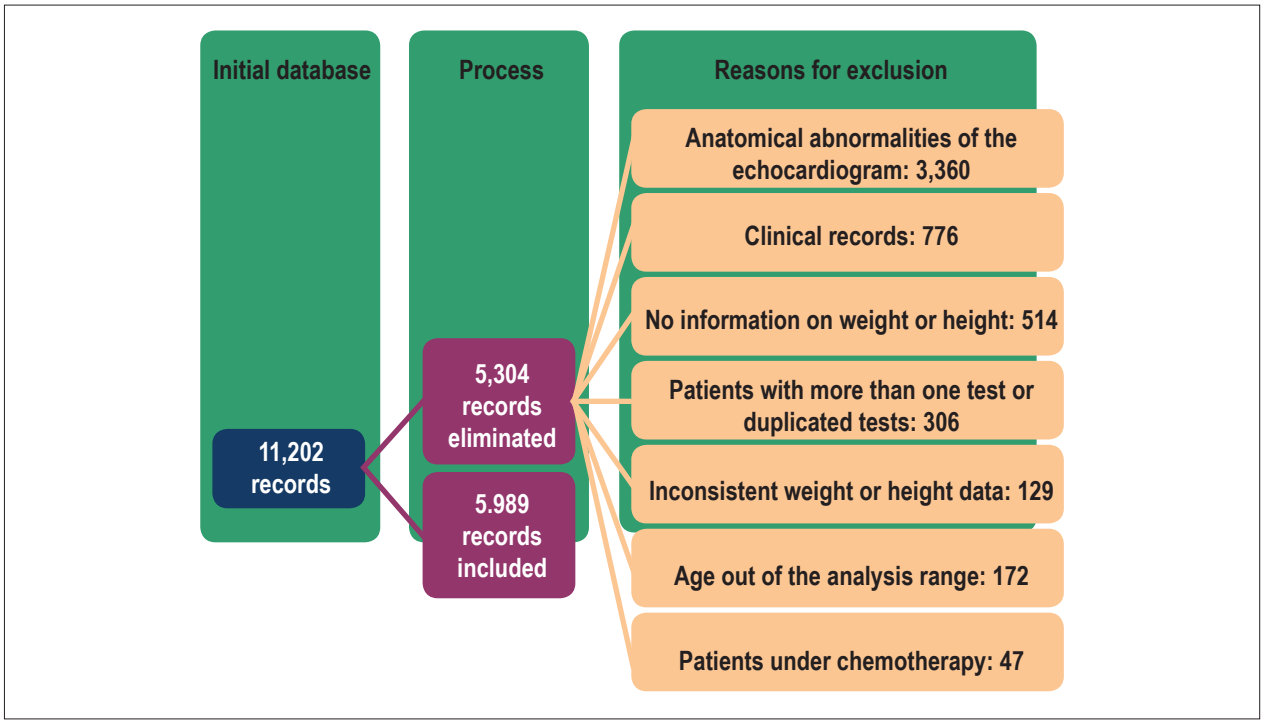

Figure 1 – *Results of the assessment of the database of records to be analyzed.*

Table 1 – Pathological conditions observed among the patients studied

History	Global population (n=5,989)	Gender		p value
		Women (n = 3,606)	*Men (n=2,292)*	
Systolic hypertension	1.564 (26.5%)	957 (26.5%)	607 (26.5%)	0.999
Diastolic hypertension	570 (9.7%)	244 (10.7%)	326 (9.0%)	0.126
Chronic renal failure	65 (1.1%)	29 (0.8%)	36 (1.6%)	0.006
COPD	110 (1.9%)	57 (1.6%)	53 (2.3%)	0.043
Diabetes mellitus	255 (4.3%)	156 (4.3%)	99 (4.3%)	0.990
Pulmonary hypertension	21 (0.4%)	17 (0.5%)	4 (0.2%)	0.062
Cancer	54 (0.9%)	43 (1.2%)	11 (0.5%)	0.005

COPD: chronic obstructive pulmonary disease.

Table 2 – Prevalence of comorbidity recorded by groups of body mass index

Characteristic	BMI Group (kg/m²)						p value
	15.0-19.9	*20.0-24.9*	*25.0-29.9*	*30.0-34.9*	*35.0-39.9*	*40.0-49.9*	
Patients	434	2.120	2.163	848	238	95	
Men	159 (36.6%)	891 (42.0%)	888 (41.1%)	284 (33.5%)	55 (23.1%)	15 (15.8%)	<0.001
Age* (years)	58.0 (56.1-59.9)	60.8 (60.0-61.5)	62.9 (62.3-63.6)	63.0 (62.1-64.0)	60.7 (58.9-62.6)	54.7 (51.3-58.0)	<0.001
Systolic HT	86 (19.8%)	500 (23.6%)	585 (27.1%)	275 (32.4%)	81 (34.0%)	37 (39.0%)	<0.001
Diastolic HT	23 (5.3%)	166 (7.8%)	221 (10.2%)	106 (12.5%)	35 (14.7%)	19 (20.0%)	<0.001
Chronic renal failure	5 (1.2%)	20 (0.9%)	30 (1.4%)	10 (1.2%)	-	-	0.319
COPD	15 (3.5%)	35 (1.7%)	36 (1.7%)	18 (2.1%)	5 (2.1%)	1 (1.1%)	0.172
Diabetes mellitus	7 (1.6%)	55 (2.3%)	112 (5.2%)	51 (6.0%)	23 (9.7%)	7 (7.4%)	<0.001
Pulmonary HT	1 (0.2%)	7 (0.3%)	9 (0.4%)	3 (0.4%)	1(0.4%)	-	0.976
Cancer	4 (0.9%)	18 (0.9%)	20 (0.9%)	6 (0.7%)	4 (1.7%)	2 (2.1%)	0.619

HT: hypertension; COPD: chronic obstructive pulmonary disease.
**Mean and confidence interval of 95%*

shows a statistically significant direct association with BMI ($\beta = 0.456$, 95% CI 0.097 to 0.815; $\sigma^2 = 0.13$).

Left ventricular systolic function

The systolic excursion of the tricuspid annulus (TAPSE) increases from 20.5 mm to 22.5 mm with BMI, being a direct and significant association ($\beta = 0.023$, 95% CI 0.006 to 0.039; $\sigma^2 = 0.0609$). The tissue Doppler S-wave velocity shows an inverse association ($\beta = -0.096$, 95% CI -0.222 to -0.031; $\sigma^2 = 0.0453$). These findings were not relevant to the interpretation of right ventricular systolic function (Table 4 and Figure 6).

Left ventricular geometry

The evaluation of ventricular geometry requires the ratio of relative wall thickness and left ventricular mass index (Table 4 and Figure 7). The relative wall thickness increases from 0.37 to 0.43 to achieve a BMI of 33 kg/m², to further decrease to 0.34 in BMI of 50 kg/m², with a direct and significant association ($\beta = 0.014$, 95% CI 0.007 to 0.021; $\sigma^2 = 0.0061$. However, this relative wall thickness behavior would indicate that the increase in myocardial mass associated with obesity is concentric up to BMI 33 kg/m²; thereafter it starts to decrease.

Myocardial mass ranged from 99 to 170 g, reaching its maximum value at a BMI of 35 kg/m², decreasing to 139 g when the BMI reaches 50 kg/m². This increase in myocardial mass has a statistically significant direct association with BMI ($\beta = 13.41$, 95% CI 8.74 to 18.08; $\sigma^2 = 0.027$). This indicates that although the myocardial mass is influenced by the increase in BMI, this is not the only influencing factor; in fact, only 3% of this behavior can be explained by the male gender. By indexing ventricular mass by body surface area, there is a progressive increase in left ventricular mass index ranging from 30 to 35 kg/m² of BMI, reaching a maximum rate of left ventricular mass of 90 gr/m², from which it decreases. The progressive increase of 75 to 90 gr/m² has a statistically significant direct association with BMI ($\beta = 5.2$, 95% CI 2.49 to 7.89; $\sigma^2 = 0.0123$).

Table 3 – Odds ratios (OR) of body mass index with the presence of diabetes mellitus or systolic or diastolic hypertension

Characteristic	Comorbidity (OR and 95% CI)		
	Systolic HT	*Diastolic HT*	*Diabetes mellitus*
BMI (kg/m^2)			
15.0-19.9	Referent	Referent	Referent
20.0-24.9	1.18 (0.91-1.54)	1.48 (0.94-2.31)	1.54 (0.70-3.41)
25.0-29.9	1.37 (1.05-1.77)	1.96 (1.26-3.05)	3.05 (1.41-6.61)
30.0-34.9	1.80 (1.36-2.39)	2.51 (1.57-4.01)	3.65 (1.64-8.11)
35.0-39.9	2.08 (1.45-2.99)	3.15 (1.81-5.48)	6.57 (2.77-15.61)
40.0-49.9	3.06 (1.88-4.98)	4.82 (2.50-9.29)	5.63 (1.91-16.57)
Female sex	1.05 (0.93-1.19)	1.27 (1.06-1.52)	1.10 (0.85-1.43)
Age (years)	1.028 (1.024-1.032)	1.001 (1.000-1.011)	1.026 (1.017-1.035)
Set precision	0.786	0.456	0.981

HT: hypertension.

Table 4 – β coefficient and 95% CI adjusted between body mass index, age and gender with clinical and echocardiographic measurements*

Characteristic	Covariates				σ^2
	BMI	*BMI^2*	*Age*	*Male*	
Systolic blood pressure (mmHg)	0.969 (0.244 to 1.694)	-0.007 (-0.020 to 0.005)	0.303 (0.273 to 0.333)	0.707 (-0.389 to 1.802)	0.0867
Diastolic blood pressure (mmHg)	0.602 (0.140 to 1.034)	-0.005 (-0.127 to 0.004)	0.034 (0.015 to 0.052)	1.335 (0.694 to 1.978)	0.0255
Heart rate (lpm)	-0.920 (-1.494 to -0.346)	0.018 (0.008 to 0.027)	-0.077 (-0.101 to -0.053)	-2.828 (-3.665 to -2.011)	0.0238
Maximum mitral E velocity (cm/s)	0.208 (-0.561 to 0.977)	0.001 (-0.013 to 0.014)	-0.355 (-0.389 to -0.321)	-6.052 (-7.152 to -4.952)	0.1121
Maximum mitral A velocity (cm/s)	1.277 (0.520 to 2.035)	-0.016 (-0.029 to -0.003)	0.694 (0.662 to 0.726)	-8.598 (-9.712 to -7.484)	0.3657
Mitral E/A ratio	-0.019 (-0.035 to -0.004)	0.0001 (0.0001 to 0.0005)	-0.014 (-0.015 to -0.013)	0.033 (0.009 to 0.057)	0.2974
Lateral mitral S velocity (cm/s)	0.019 (-0.081 to 0.118)	-0.0003 (-0.0020 to 0.0014)	-0.032 (-0.036 to -0.027)	0.271 (0.131 to 0.411)	0.0885
Mitral deceleration time (ms)	0.911 (-1.126 to 2.948)	-0.006 A:	0.831 (0.742 to 0.920)	1.900 (-1.161 to 4.960)	0.1051
Septal e' wave velocity (cm/s)	-0.060 (-0.161 to 0.041)	0.0004 (-0.0013 to 0.0022)	-0.094 (-0.098 to -0.090)	0.005 (-0.121 to 0.131)	0.3702
Septal a' wave velocity (cm/s)	0.471 (0.002 to 0.940)	-0.014 (-0.030 to 0.002)	0.016 (0.012 to 0.020)	0.558 (0.419 to 0.697)	0.0811
Lateral e' wave velocity (cm/s)	-0.025 (-0.152 to 0.102)	0.0000 (-0.0021 to 0.0022)	-0.138 (-0.143 to -0.132)	-0.021 (-0.187 to 0.145)	0.4232
Wave velocity lateral a' cm/seg	0.296 (0.172 to 0.419)	-0.0044 (-0.0065 to -0.0220)	0.043 (0.038 to 0.048)	0.061 (-0.122 to 0.243)	0.1141
Lateral E/e' ratio	-0.154 (-0.453 to 0.145)	0.003 (-0.002 to 0.009)	0.070 (0.061 to 0.078)	-0.771 (-1.055 to -0.488)	0.0890
Septal E/e' ratio	-0.060 (-0.373 to 0.252)	0.002 (-0.003 to 0.008)	0.074 (0.064 to 0.084)	-1.001 (-1.373 to -0.638)	0.0753
left atrial indexed volume (ml/m^2 SC)	0.456 (0.097 to 0.815)	-0.007 (-0.013 to 0.001)	0.155 (0.138 to 0.171)	1.843 (1.272 to 2.415)	0.1332
systolic volume left indexed (ml/m^{2}SC)	3.176 (0.354 to 6.000)	-0.054 (-0.099 to -0.010)	-0.071 (-0.306 to 0.164)	-1.461 (-7.470 to 4.548)	0.0016

Continued

Ejection volume (ml)	2.70 (1.23 to 4.18)	-0.035 (-0.059 to -0.011)	-0.028 (-0.108 to 0.052)	6.98 (4.05 to 9.90)	0.0215
TAPSE (mm)	0.023 (0.006 to 0.039)	-0.0003 (-0.0006 to 0.0001)	-0.004 (-0.005 to -0.003)	0.056 (0.033 to 0.079)	0.0609
RV baseline diastole** (mm)	-0.196 (-0.301 to -0.091)	0.007 (0.003 to 0.010)	0.0008 (0.000 to 0.0016)	0.345 (0.316 to 0.374)	0.1367
Max tricuspid E wave velocity (cm/seg)	0.242 (-0.316 to 0.800)	-0.004 (-0.014 to 0.006)	-0.219 (-0.243 to -0.196)	-1.582 (-2.137 to -0.847)	0.1039
Tricuspid A wave max velocity¶ (cm/seg)	-1.871 (-4.944 to 1.202)	0.076 (-0.030 to 0.183)	0.154 (0.132 to 0.175)	-1.037 (-1.756 to -0.318)	0.2311
Tricuspid E/A ratio (cm/seg)	-0.010 (-0.030 to 0.010)	-0.0000 (-0.0004 to 0.0003)	-0.011 (-0.012 to -0.010)	-0.014 (-0.050 to -0.021)	0.1222
Pulmonary artery systolic pressure (mmHg)	-4.12 (-7.03 to -1.20)	0.126 (0.028 to 0.224)	0.178 (0.157 to 0.198)	0.173 (-0.527 to 0.873)	0.1210
Left ventricular S' wave velocity (cm/seg)	-0.096 (-0.222 to -0.031)	0.0016 (-0.0006 to 0.0038)	-0.019 (-0.024 to -0.014)	0.367 (0.179 to 0.554)	0.0453
Cardiac output (mL/min)	0.220 (0.109 to 0.331)	-0.003 (-0.005 to -0.001)	-0001 (-0.007 to 0.004)	0.512 (0.294 to 0.731)	0.0447
LV diastole index	-0.054 (-0.066 to -0.042)	0.0005 (0.0003 to 0.0007)	0.0010 (0.0005 to 0.0015)	-0.110 (-0.128 to -0.092)	0.1653
Posterior wall during diastole (mm)	0.039 (0.024 to 0.054)	-0.0006 (-0.0008 to -0.0004)	0.0000 (-0.001 to 0.001)	0.072 (0.040 to 1.03)	0.0122
Left ventricle during systole (mm)	0.036 (0.014 to 0.057)	-0.0004 (-0.0008 to -0.0000)	-0.003 (-0.004 to -0.002)	0.274 (0.240 to 0.307)	0.0809
Relative wall thickness	0.014 (0.007 to 0.021)	-0.0002 (-0.0003 to -0.0001)	0.0004 (-0.0010 to 0.0009)	0.003 (-0.012 to 0.018)	0.0061
Left ventricular myocardial mass (g)	13.41 (8.74 to 18.08)	-0.189 (-0.264 to -0.114)	-0.121 (-0.436 to 0.193)	34.72 (25.75 to 73.69)	0.0271
Left ventricular myocardial mass index (gr/m^2 Sc)	5.20 (2.49 to 7.89)	-0.086 (-0.129 to -0.043)	0.052 (-0.120 to 0.224)	9.47 (4.39 to 14.55)	0.0123
Ejection fraction (%)	0.164 (-0.080 to 0.408)	-0.001 (-0.005 to 0.003)	-0.025 (-0.035 to -0.015)	-1.858 (-2.281 to -1.433)	0.0371
LV mass/height (gr/m)	0.082 (0.053 to 0.111)	0.001 (-0.002 to -0.006)	0.001 (-0.002 to -0.006)	0.143 (0.088 to 0.198)	0.0220
LV mass/height$^{2.7}$ (gr/m$^{2.7}$)	3.57 (2.22 to 4.92)	-0.05 (-0.21 to -0.08)	0.05 (-0.03 to 0.14)	0.93 (-0.67 to 3.40)	0.0190

**Adjusted by the study date, values of heart rate, systolic and diastolic blood pressure as well as by the presence of chronic renal failure, chronic obstructive pulmonary disease, diabetes mellitus, pulmonary hypertension and cancer.*
*** Includes IMC^3 with β of -0.00007 (95% CI -0.00011 to -0.00003).*
¶ Includes IMC^3 with β of -0.00008 (95% CI -0.00002 to 0.00004).

To reduce the effect of obesity with an estimated left ventricular mass, its normalization was performed by the height to the power 2.7, also showing a progressive increase in left ventricular mass indexed to the extent that the mass body is increased, reaching a maximum of 1.1 and 50 g/m$^{2.7}$, respectively, with body mass index of 36 kg/m^2. In both cases, there is a direct association (β = 0.082, 95% CI 0.053 to 0.111; σ^2 = 0.0220 for height and β = 3.57, 95% CI 2.22 to 4.92; σ^2 = 0.0190 for height indexation$^{2.7}$). Although in both cases there was a direct association, by indexing to height$^{2.7}$ we obtains a better coefficient β (3.57 vs. 0.082), revealing a significant increase in left ventricular mass index above the values currently accepted as normal (women: 18-44 gr/m$^{2.7}$; and men: 20-48 gr/m$^{2.7}$) to the extent that the BMI increases. This increase is identified from overweight, noting an increased ventricular mass in patients with a BMI of 26 kg/m^2 (Table 4 and Figure 6).

Discussion

Obesity is an important risk factor for the development of cardiovascular diseases. After dividing the population object of study according to the BMI and according to the WHO classification, it was observed that to the extent that body mass increased, the prevalence of hypertension and diabetes mellitus significantly increased (Tables 2 and 3), as previously described in the literature by Guh et al. which, in a review and meta-analysis described the incidence of comorbidities associated with overweight and obesity[1-3].

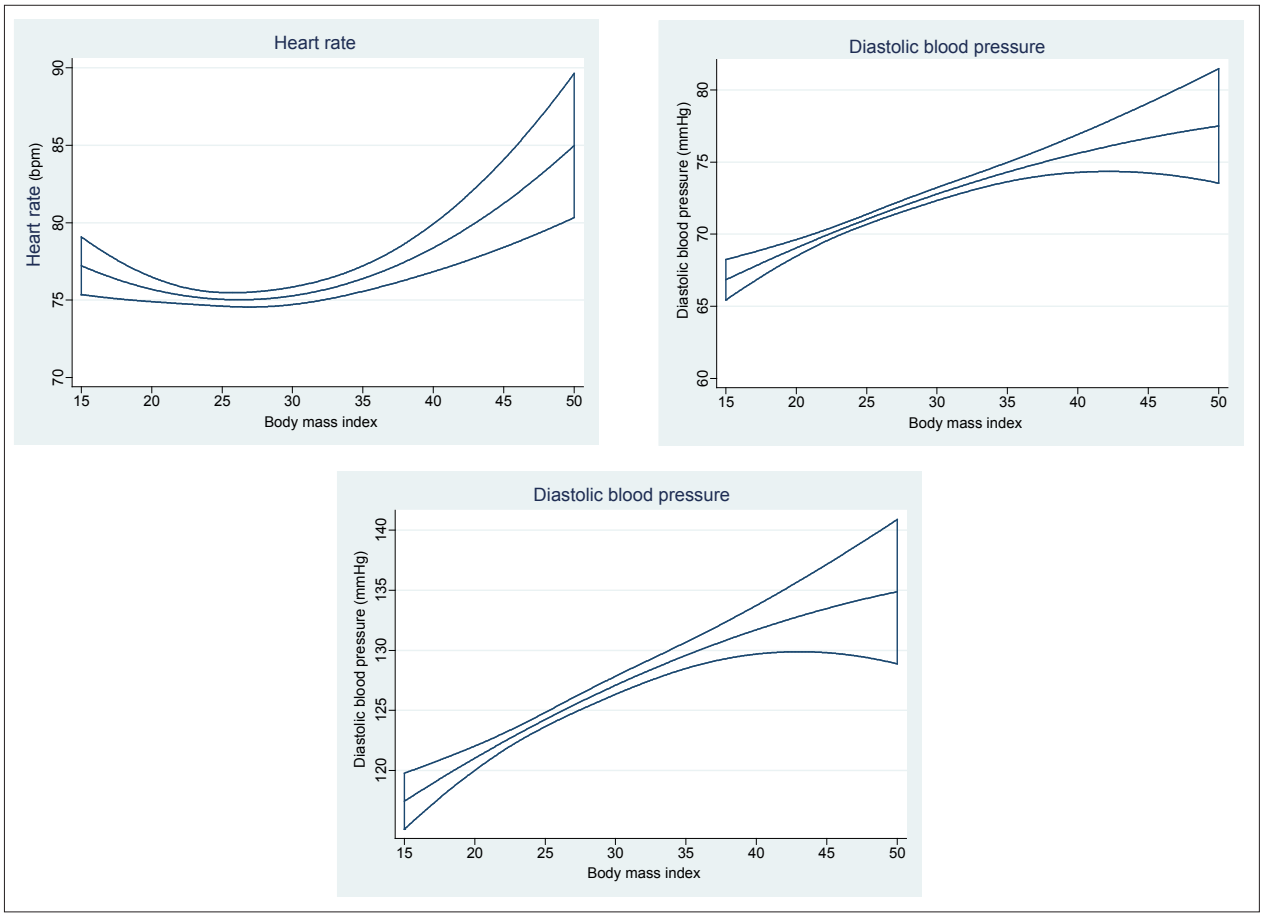

Figure 2 – *Multiple regression and confidence interval of 95% of the effect of body mass index on the vital signs.*

Pascual et al., in a paper dealing with the effects of obesity on systolic and diastolic left ventricular function, reported that obese individuals have an increased circulating blood volume that generates an increase in cardiac output, leading to ventricular dilatation and eccentric left ventricular hypertrophy. It has also been shown that myocardial fat infiltration affects not only the ventricular structure but also the ventricular mechanics [11-14]. This increase in circulating volume was corroborated in this study with a statistically significant direct association between cardiac output, ejection volume and body mass index, identifying a maximum value when mass index reaches 35 and 37 kg/m^2, respectively.

Left ventricular systolic function did not vary in relation to body mass; ejection fraction remained within normal limits in all groups; these findings are similar to those described in other studies in which no significant variations in ejection fraction of obese patients were described [11,15].

In the study of the impact of body mass index on left ventricular diastolic dysfunction, Cil et al.[16] describe an E-wave significantly lower in the groups with BMI > 25 kg/m^2, while A and A' septal waves were significantly higher in these groups. Similarly, the E/e' ratio was significantly higher in groups of patients with overweight and obesity than in those with BMI < 25 kg/m^2 [16]. Regarding the diastolic function in this study, there was an inverse association between the E/A ratio and BMI (β = -0.019, 95% CI -0.035 to -0.004; σ^2 = 0.2974), which is a slight, yet statistically significant decrease from 1.05 to 0.95, and also an inverse association between the tissue Doppler lateral e' velocity and increased BMI (β = -0.025, 95% CI -0.152 to -0.102; σ^2 = 0.4232), showing a diastolic dysfunction predominantly of abnormal relaxation type to the extent that body mass increases. These findings corroborate the findings in the literature, in which increased BMI is a predictor of left ventricular diastolic dysfunction, regardless of age, hypertension and diabetes mellitus[11,16,17]. Neither did the study demonstrate an association between BMI and increased lateral E/e' ratio nor septal E/e' ratio that could be associated with increased filling pressures in overweight or obese patients.

Consistently with the study "Cardiac Remodeling and Obesity" by Ashrafian et al.[7], a slight yet significant increase in the left atrial indexed area and volume was demonstrated to the extent that body mass increased. The variables for the assessment of right ventricular systolic and diastolic function showed no relevant changes related to body mass index, which is consistent with the literature, which describes that the right ventricular function is neither affected by overweight or obesity[12,18].

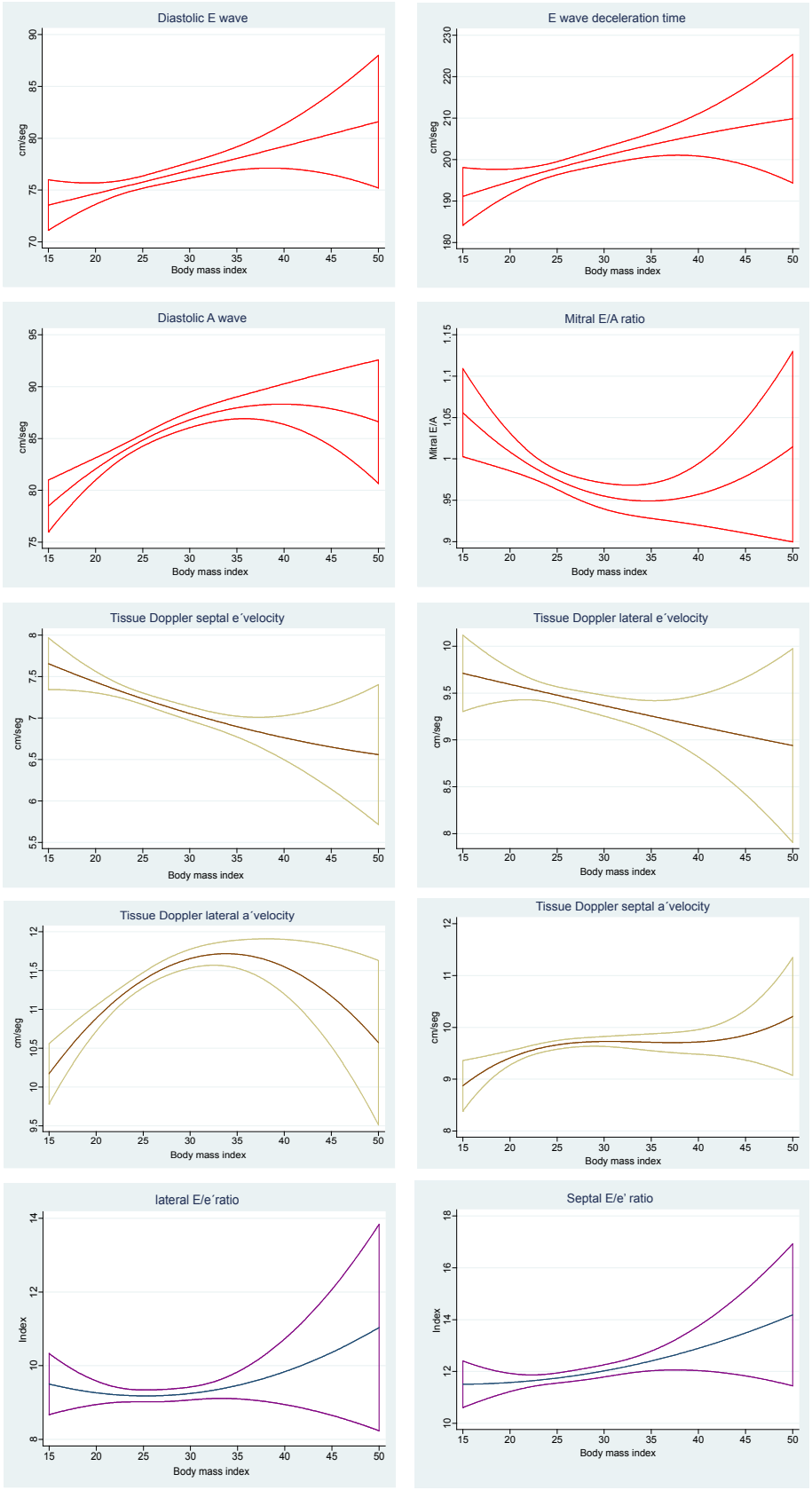

Figure 3 – *Multiple regression and confidence interval of 95% of the effect of body mass index on indicators of left ventricular diastolic function.*

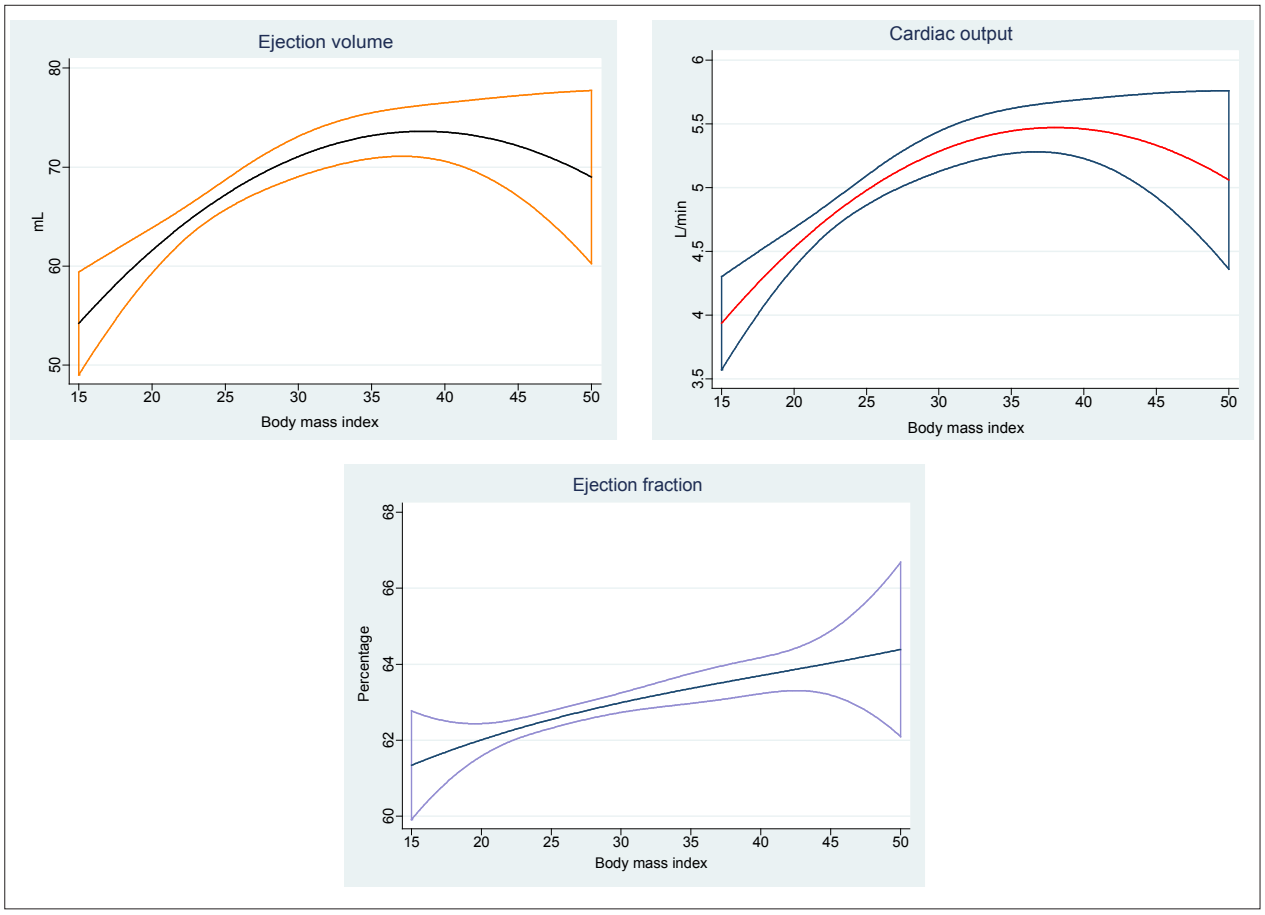

Figure 4 – *Multiple Regression and confidence interval of 95% of the effect of body mass index on left ventricular volumes and function.*

In a study by Movahed et al.[19] on obesity in adolescents, the association between obesity, hypertension and left ventricular hypertrophy was assessed. A total of 2,072 individuals were assessed for the presence of left ventricular hypertrophy and hypertension (defined as systolic blood pressure > 140 mmHg and diastolic blood pressure > 90 mmHg) and obesity as BMI > 30 kg/m^2. Using a multivariate analysis adjusted for age, gender and blood pressure, obesity remains strongly associated with left ventricular hypertrophy (OR 4.51, 95% CI 2.83 to 7.19, p < 0.001).

In this study, 5,898 records were reviewed and through a model of multiple linear regression, raw data of BMI correlated with myocardial mass and myocardial mass indexed to body surface area, finding a statistically significant direct association between overweight (BMI 25-29, 9 kg/m^2), obesity (BMI > 30 kg/m^2) and increased left ventricular mass (β = 13, 41, 95% CI 8, 74 to 18, 08). When the mass was indexed, this direct association persisted, although smaller β[5,2]. In the previous variables, increased myocardial mass has not reached any values that could be correlated with left ventricular hypertrophy, and this phenomenon is accentuated when the mass is adjusted for body surface area. In addition, it is observed that once a BMI ≥ 35 kg/m^2 is reached, myocardial mass and myocardial mass index decreases proportionally. This could indicate that in patients with BMI ≥ 35 kg/m^2, by indexing myocardial mass to body surface area, the true effect of obesity (especially grades II and III) on myocardial mass and ventricular geometry is underestimated. De Simone et al.[8] demonstrated that the normalization of left ventricular mass by body surface area and length introduces artifacts related to the indexation of left ventricular mass to body mass and errors in estimating the impact of overweight. From this analysis, it was decided to index the myocardial mass to height$^{2.7}$. In both cases, there was a direct association between increased myocardial mass and the body mass; however, by indexing ventricular mass to height$^{2.7}$ there was a stronger association (β 3:57 vs. 0.082), revealing a significant increase in left ventricular mass index above the normal currently accepted values[9], to the same extent that the body mass index increases, in which case there is a statistically significant direct association between obesity and left ventricular hypertrophy, once the interference generated by indexing to body mass is eliminated (Figure 8). Also, it was identified that the myocardial mass is affected by body mass from lower values of overweight with BMI of 27 kg/m^2, finding maximum values of myocardial mass indexed to height$^{2.7}$ with a body mass index of 35 kg/m^2.

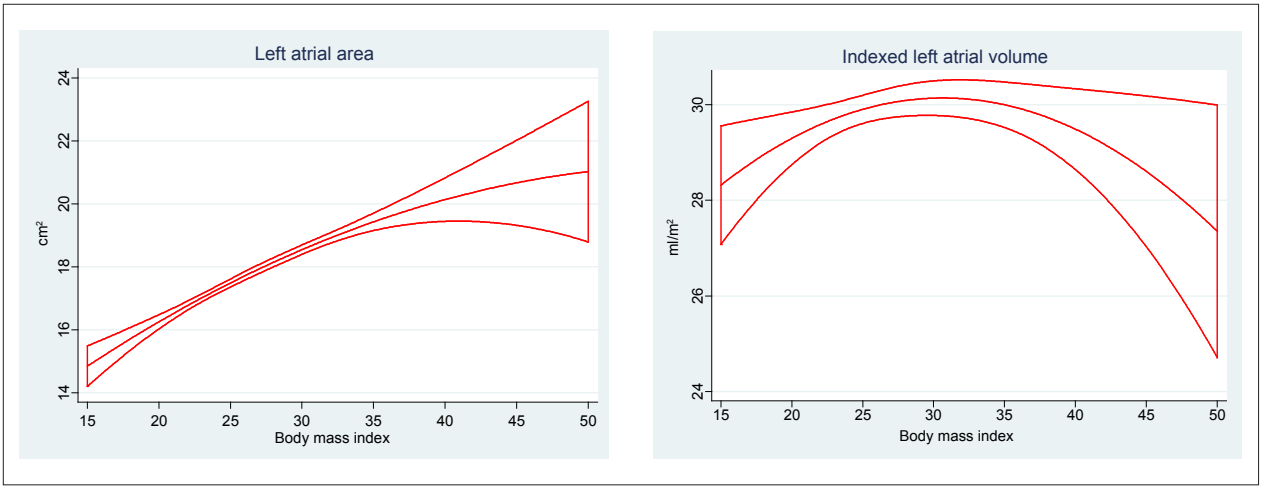

Figure 5 – *Multiple regression and confidence interval of 95% of the effect of body mass index in the area and indexed left atrial volume.*

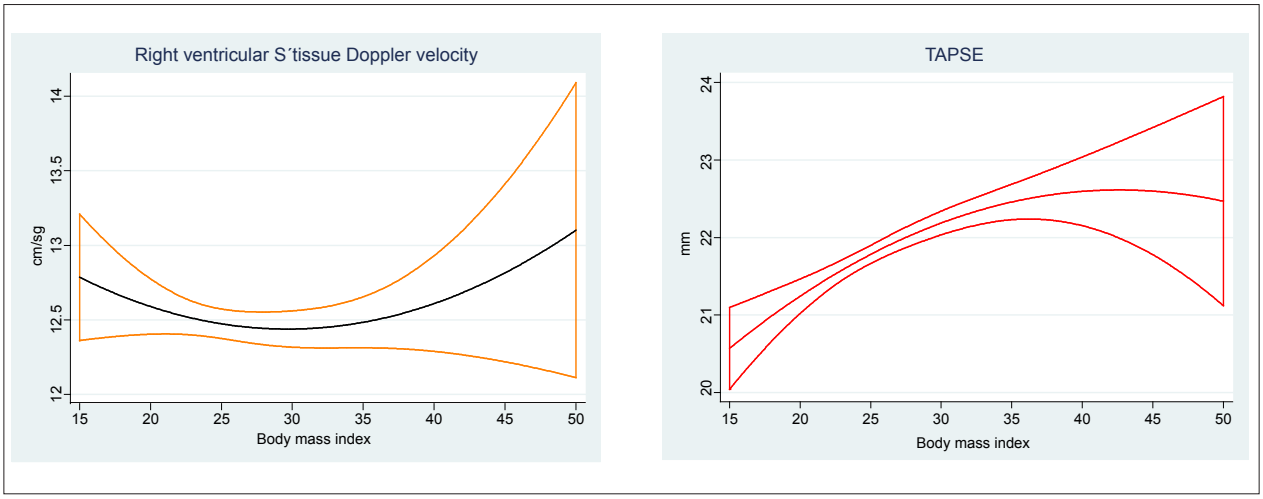

Figure 6 – *Multiple regression and confidence interval of 95% of the effect of body mass index as an indicator of right ventricular systolic function.*

The relative wall thickness also has a direct association with increased body mass, increasing from 0.37 to 0.42, a value that is reached with a BMI of 26 kg/m² and rises to 0.43 when body mass index reaches 30 kg/m², with a subsequent decrease to 0.34 insofar as it continues its increase. Taking into account that there is an association between overweight, obesity and left ventricular hypertrophy, this increase in relative wall thickness could explain an initial concentric increase in myocardial mass in overweight patients, but to the extent that overweight obesity becomes hypertrophy, concentric hypertrophy becomes eccentric hypertrophy (Figures 7 and 8). Rider et al.[20] showed in a study with 88 female individuals, not diabetic or hypertensive, that a slight increase in BMI from normal to overweight results in eccentric myocardial hypertrophy with no expected changes dependent on the volume that lead to myocardial dilatation. The same authors suggest that early hypertrophic abnormalities are secondary to hyperleptinemia, and subsequent left ventricular dilation seen in morbid obesity is probably induced by hypervolemia. This is consistent with the direct association described in this study, increased body mass with increasing ejection volume and cardiac output and decrease of relative wall thickness and myocardial mass index to the extent that BMI ≥ 34 and 38 kg/m², respectively. These findings are similar to the findings of Palmieri and De Simone in the study of various degrees of body mass index in hypertensive patients compared with left ventricular mass, cardiac output and peripheral resistance[21].

This study established the coefficient of multiple correlation for each of the models, demonstrating that although overweight and obesity are factors that determine a significant increase in myocardial mass, when there is a statistically significant direct association, they are not the only factors affecting it.

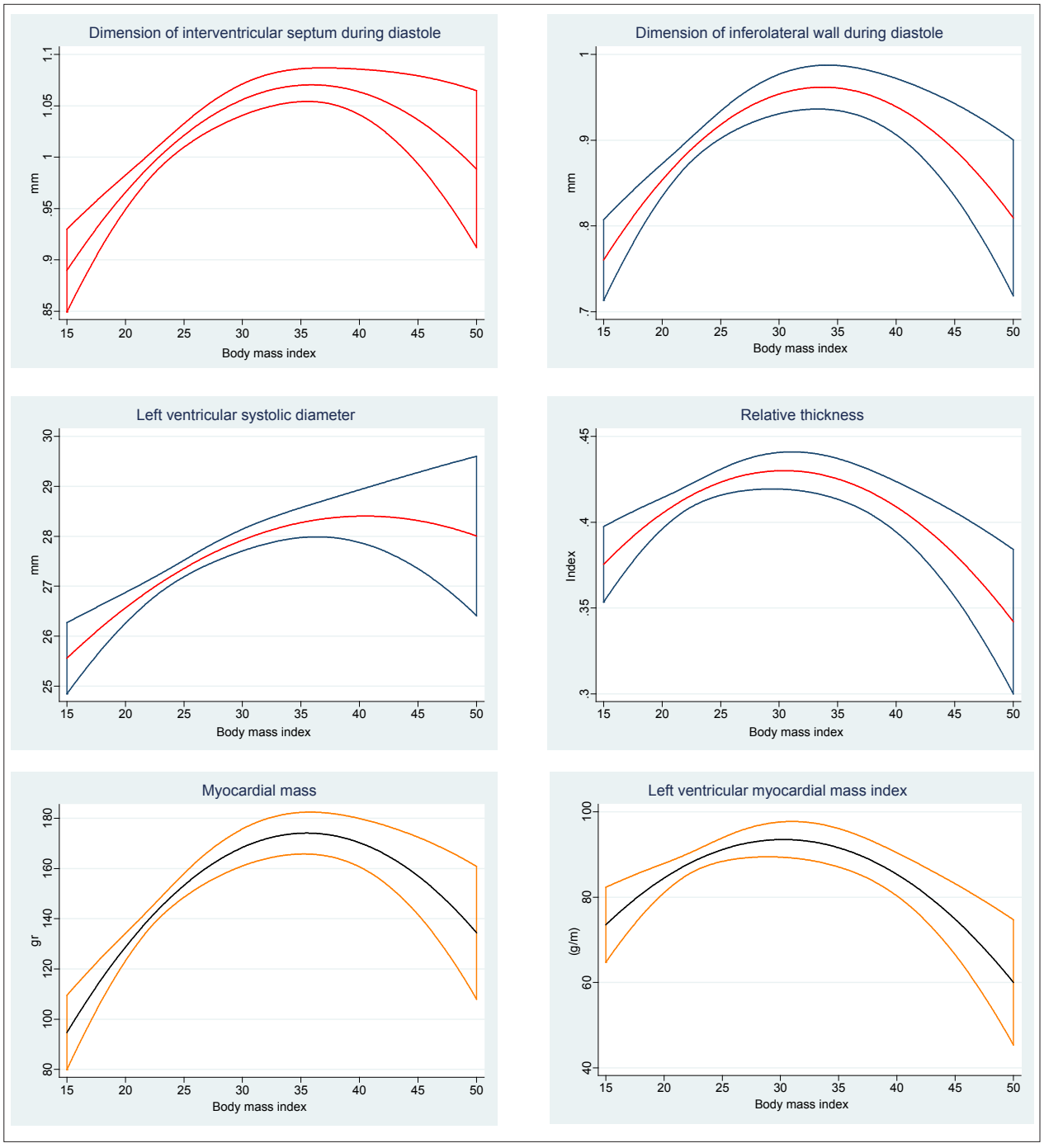

Figure 7 – *Multiple regression and confidence interval of 95% of the effect of body mass index on myocardial mass and left ventricular dimensions.*

The covariate male gender also showed a direct association with increased myocardial mass and comorbidities such as systolic and diastolic hypertension and diabetes mellitus were more prevalent among overweight and obese patients, which in previous studies have been significantly and independently related with left ventricular hypertrophy[22-24].

Conclusions

This study showed a significant direct association between increased BMI and increased myocardial mass. By indexing myocardial mass to height[2.7] we avoid those effects related to normalization for body mass index (ASC) in which the impact of increased body mass on ventricular geometry is underestimated,

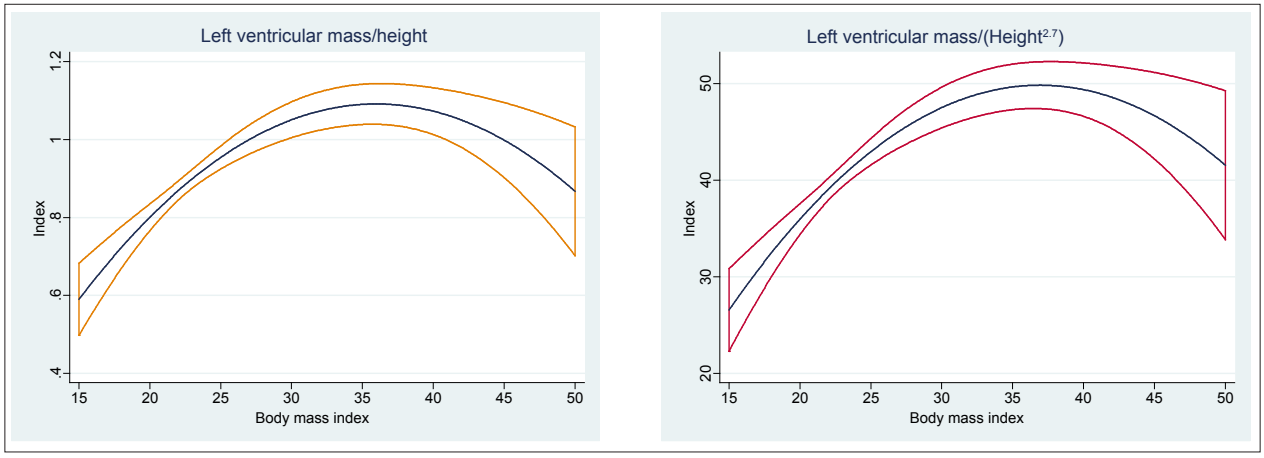

Figure 8 – *Multiple Regression and confidence interval of 95% of the effect of body mass index on myocardial mass normalized by the height and the height raised to the 2.7 power.*

showing a direct relationship between overweight and obesity with left ventricular hypertrophy. Hence, indexing ventricular mass to height$^{2.7}$ is recommended, especially in patients with grade II and III obesity. Considering the behavior of relative wall thickness and myocardial mass, it was confirmed that left ventricular hypertrophy appears from overweight, originally concentric and, to the extent that body mass increases, it becomes eccentric. The description of other authors, who demonstrate a significant increase in cardiac output and ejection volume when body mass is increased, resulting from increased circulating volumes in obese people, is also corroborated.

There was an inverse association between increased body mass and the E/A ratio of mitral filling, with a statistically significant decrease in the tissue Doppler lateral e' speed as BMI increases, showing am abnormal relaxation-type diastolic dysfunction in overweight and obese individuals. There was no increase in the E/e' ratio that could make one assume any increase in filling pressures.

The study also demonstrated a discreet yet significant increase in the left atrial indexed area and volume to the extent that body mass increases.

This study confirms, to a great extent, what has been previously described in the literature and brings new useful knowledge for understanding the effect that overweight and obesity have on cardiac structure and function. Although there are methodological limitations of studies based on records, the important size of the sample analyzed and significant findings demonstrate their relevance.

Authors' contribution

Research creation and design: Silva FC, Rubio LCS, Molina GR, Anaya MLB, Díaz-Martínez LA, Torres JLL, Perilla KE; Acquisition of data: Rubio LCS, Molina GR, Anaya MLB, Díaz-Martínez LA, Torres JLL, Perilla KE; Analysis and interpretation of data: Rubio LCS, Molina GR, Anaya MLB, Díaz-Martínez LA, Torres JLL, Perilla KE; Statistical analysis: Silva FC, Rubio LCS, Molina GR, Anaya MLB, Díaz-Martínez LA, Torres JLL, Perilla KE; Drafting of the manuscript: Rubio LCS, Molina GR, Anaya MLB, Díaz-Martínez LA, Torres JLL, Perilla KE; Critical revision of the manuscript for important intellectual content: Rubio LCS, Molina GR, Anaya MLB, Díaz-Martínez LA, Torres JLL, Perilla KE.

Potential Conflicts of Interest

No relevant potential conflicts of interest.

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Academic Association

This study is not associated with any graduate programs.

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