

Obesity as an Independent Risk Predictor of Mild to Moderate Diastolic Dysfunction

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- BACKGROUND** Increased adiposity is associated with an increase risk in heart failure¹. Diastolic dysfunction is prevalent among obese individuals hence, is associated with increased cardiovascular morbidity and mortality risk. As to how severe in terms of diastolic dysfunction and which parameter among of the diastolic function indices is affected as the level of body mass index increases remains elusive.
- OBJECTIVE** To determine risk and degree of developing diastolic dysfunction based on the levels of body mass index (BMI) with the use of different echocardiographic indices of LV diastolic function.
- METHODS** Patients admitted for executive check up at St. Luke's Medical Center, Philippines from January 2006 to July 2007 with 2 Dimensional Echocardiogram were included in the study. Risk profiles of subjects and measurement of BMI were reviewed as well as in the subgroup analysis with uncomplicated obesity.
- RESULTS** There are 2711 Filipinos with different grades of obesity with subgroup composed of 531 uncomplicated obese patient composed of 276 females and 255 males. Age, gender, diabetes, hypertension, dyslipidemia, coronary artery disease (CAD), prior angina, presence of atrial fibrillation, smoking history and cardio-respiratory fitness are significantly associated with diastolic dysfunction. Consequently, the presence of CAD, arrhythmia, and prior angina were the only clinical risk factors not associated with the different grades of obesity. After adjustment of clinical risk factors, the risk of diastolic dysfunction was strongly correlated independent with the different grades of obesity. The risk was doubled (Adjusted OR- 2.02, CI: 0.99 - 4.1, p-value 0.05) among overweight patients as compared to the normal population. There was a 4-fold increased (Adjusted OR - 4.00, CI: 1.94 - 8.21, p-value <0.001) in the risk of developing diastolic dysfunction independent among grades 2 and 3 obese patients. Adjusted means of the diastolic function indices showed that Mitral A inflow velocity (positive correlation, p-value 0.0008), Mitral E/A ratio (negative correlation, p-value <0.0001), Pulmonary vein diastolic velocity (negative correlation, p-value <0.0001) and Pulmonary vein diastolic/systolic velocity ratio (positive correlation, p-value 0.0012) were significantly associated with the different levels of BMI.
- CONCLUSION** As the level of BMI increases, there is an independent risk of developing mild to moderate diastolic dysfunction with as much as 2 times the risk among overweight and 4 times the risk among grades 2 and 3 obese individuals as compared to the normal population. The adverse hypervolemic state of obesity was consistent with the diastolic load indices imposed on the heart brought about by the increase in adiposity.

Whether obesity is accompanied with other risk factors or as with uncomplicated obesity, it portends a poor prognosis as compared to those with normal weight counterpart. There are a lot of studies elucidating the alteration in cardiac function and structure brought about by obesity. Environmental, behavioral, and genetic factors have been shown to contribute to the development of obesity. Body mass index, BMI, has been utilized by various studies as a measure of obesity. Elevated body mass index, particularly abdominal or upper body obesity

has been associated with the development of a number of other diseases and metabolic disorders. It greatly contributes to the prognosis of this particular subset of patients. Although BMI is limited by the fact that it does not translate to a specific information regarding the type of regional fat distribution, it is clinically relevant in terms of risk assessment. It remains to be an independent, applicable, and valid measure of adverse cardiovascular outcomes that warrants close monitoring and treatment.

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Weight loss among obese subjects decreases the risk of cardiovascular complications. In the study of Burjonrappa, et. al., the elevated risk of coronary artery disease in the obese is well appreciated. Evidence from several studies indicates that obesity and weight gain are also associated with an increasing risk of diabetes mellitus and hypertension. Kenchaiah, et. al., investigated the role of obesity and being overweight in heart failure. It suggested that obesity is an important risk factor for heart failure in both genders. In the Framingham Heart Study, the 26-year incidence of coronary artery disease in women and men was related proportionately to excess weight. It also showed that the incidence of coronary artery disease increased by a factor of 2.4 in obese women and by a factor of 2.0 in obese men under the age of 50 years old¹

The underlying mechanism linking obesity to cardiovascular disease requires further investigation. Obesity is associated with neuroendocrine activation, renal sodium retention, and heightened systemic oxidative stress.² It is the confounding factors associated with obesity that makes it difficult to fully understand its effect on overall cardiac performance; its mechanism and structural implications. Each component may independently contribute to adverse consequences such that uncomplicated obesity. It was aimed in this study to isolate the effect of obesity and was able to conclude that excess weight has an independent risk of developing diastolic dysfunction.

METHODS

Study population

A total of 2711 Patients admitted for executive check up at St. Luke's Medical Center, Philippines from January 2006 to July 2007 with 2 Dimensional Echocardiogram were included in the study. Excluded patients are those with abnormal, equivocal, uninterpretable stress test results, those with recent admission of acute coronary syndromes or current infection, heart failure, current illness, any indication reason that necessitates hospital admission. Retrospective review was utilized with the assistance of the CVRU (Cardiovascular Research Unit) of gathering all patients with 2 Dimensional Echocardiogram and Treadmill Exercise Test. Risk profiles of subjects and measurement of BMI were reviewed. Obesity was defined as a body mass index (BMI) of $> 23 \text{ kg/m}^2$. The

participants in the study were classified according to WHO Asian Classification based on BMI: normal weight had BMI of $18.5 - 22.99 \text{ kg/m}^2$; overweight was classified as a BMI between $23 - 27.49 \text{ kg/m}^2$; grade 1 obesity, as a BMI between $27.5 - 34.99 \text{ kg/m}^2$; grade 2 obesity, as a BMI between $35 - 39.99 \text{ kg/m}^2$, and morbid obesity, as a BMI $> 40 \text{ kg/m}^2$.

Uncomplicated obesity

A subgroup analysis was done among uncomplicated subjects or those without other co-morbidities. None had any history of coronary artery disease, hypertension, diabetes, prior angina, dyslipidemia, arrhythmias, nor cerebrovascular disease. None of them was taking any medications during the time of inclusion.

Echocardiography

Each subject underwent trans-thoracic two-dimensional (2D) guided M-mode, Doppler echocardiogram. Echocardiograms were performed with a Siemens instrument by standard techniques with subjects in the left lateral decubitus position. Echocardiograms were recorded on videotape. Full LV and Doppler measurements were obtained with recordings of > 10 cycles of parasternal long- and short- axis LV views as well as on M-mode with optimal cursor beam orientation in each view. Echocardiograms were initially read by research fellow and/or cardiology fellows-in-training and subsequently finalized by a highly trained experienced echocardiographer.

Left ventricular diastolic function—Pulsed Doppler measurements were obtained in the apical four chamber view: the Doppler beam was aligned as perpendicularly as possible to the plane of the mitral annulus and a 5 mm pulsed wave Doppler sample volume was placed between the tips of the mitral leaflets during diastole. The following variables were calculated: maximum velocity of passive mitral filling (E); maximum velocity of active mitral filling (A); ratio of passive to active velocity (E/A); area under the curve of the velocity range corresponding to passive mitral filling (AE); area under the curve of the velocity range corresponding to active mitral filling (AA); ratio of AE/AA; area under the curve of the velocity of the pulmonary valve systole (Ps) and diastole (Pd) and ratio (Ps/Pd ratio); deceleration time (DT), and isovolumic relaxation time (IVRT). Echocardiographic evidence of left ventricular diastolic dysfunction of at least two indices

with normal ejection fraction (>50%) were categorized as those patient with diastolic dysfunction.

Cardio respiratory fitness was quantified as the duration of a maximal treadmill exercise test consisting of 2-minute stages graded by 1 MET (1 MET=3.5 ml O₂/kg/min) per stage. The American Heart Association has developed a cardio respiratory fitness classification to determine the relationship between oxygen uptake and heart rate during exercise utilized in this study. Classification of fitness ranges from "low" - "average" - "high" (appendix I)

Data Analysis

Chi-square test was used to determine association of obesity grade with gender, diabetes, hypertension, CVD, CAD, dyslipidemia, smoking, history of heart disease, prior angina, arrhythmia and cardiorespiratory fitness. Pearson's *r* was used to determine the correlation of the actual BMI measure and age with LV diastolic function indices while Spearman's rank was used to determine the correlation of cardio fitness level with LV diastolic function indices. Multiple linear regression was used to control for the effects of probable confounder.

RESULTS

Using all the 2711 patient information, age($P=0.004$), gender($P<0.001$), diabetes($P<0.001$), hypertension($P<0.001$), dyslipidemia($P<0.001$), smoking($P<0.001$), and cardio-fitness($P<0.001$), were significantly associated with levels of BMI (Table 1). Gender, smoking and cardio-fitness were significantly associated with diastolic function indices (Table 2). Diabetes, hypertension, CAD, dyslipidemia, prior angina and arrhythmia were also associated with diastolic function indices (Table 3).

Although CAD, prior angina and arrhythmia were associated with diastolic function indices, they were not associated with levels of BMI therefore probable confounders in the relationship of BMI with diastolic functions were age, gender, diabetes, hypertension, dyslipidemia, smoking and cardio-fitness (Tables 1-3). In estimating the association of BMI with diastolic functions, patients with diabetes, hypertension, dyslipidemia and

smokers were excluded from the analysis. Effects age, gender and cardio-fitness were adjusted for in the multiple linear regression. The subgroup was composed of 531 patients with 276 females and 255 males.

With 2711 patients, average measures of E($P=0.0013$), A($P=0.0001$), E/A ratio($P=0.0001$), Pd($P=0.0001$) and IVRT($P=0.0016$) had differences among the levels of BMI (Table 4).

In the subgroup crude mean of E($P=0.0060$), A($P=0.0116$), E/A ratio($P<0.0001$), Pd($P<0.0001$) and Ps/Pd ratio($P=0.0040$) had differences among levels of BMI (Table 5). Adjusted means of the diastolic function indices showed that A($P=0.0008$), E/A ratio($P<0.0001$), Pd($P<0.0001$) and Ps/Pd ratio($P=0.0012$) were the indices with differences among levels of BMI (Table 6).

Adjusted for the effects of Age, Gender, and Cardiorespiratory Fitness, the risk of developing diastolic dysfunction was observed from the Overweight (OR, 2.02; 95%CI, 0.99-4.1; $P=0.052$) and Obese grade 2 and 3 (OR, 4.00; 95%CI, 1.94-8.21; $P<0.001$).

(Footnotes)

¹ Hubert HB, Forler WR, Hirsh J and Van Itallie TB "Health Implications of Obesity: An NIH Consensus Development Conference: Int. J Obese (1985), 9:155-170.

² Keaney JF, Jr, Larson MG, Vasan RS, et. al.

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study. *Atheroscler Thromb Vasc Biol* 2003;23:434-439.

CONCLUSION

After adjusting to the different risk factors that significantly affect the development of diastolic dysfunction, there is a continuous risk associated with excess weight (Table 6). As the level of BMI increases, there is an independent risk of developing mild to moderate diastolic dysfunction with as much as 2 times the risk among overweight and 4 times the risk among grades 2 and 3 obese individuals as compared to the normal population (Table 7).

The increasing value mitral A velocity coupled with the decreasing pulmonary vein diastolic flow; the reversal of mitral E/A ratio; and increasing trend of Ps/Pd ratio are all consisted with the adverse hemodynamic load on the heart brought about by the increase in adiposity (Graph I).

Table 1. Baseline Characteristics of Subjects by Different Grades of Obesity

Variable	Normal n = 591	Obese 1 n = 1183	Obese 2 n = 787	Obese 3 & up n = 150	p-value
Age; Years (mean $\pm$ sd)	50.37 $\pm$ 13.13	51.76 $\pm$ 11.23	51.01 $\pm$ 10.63	48.67 $\pm$ 10.20	.004*
Gender, no (%)					
Males n = 1621	219 (13.51)	735 (45.34)	568 (35.04)	99 (6.11)	
Females n = 1090	372 (34.13)	448 (41.10)	219 (20.09)	51 (4.68)	<.001
Diabetics	102 (17.26)	260 (21.98)	223 (28.34)	46 (30.67)	<.001
Hypertensives	301 (50.93)	722 (61.03)	519 (65.95)	99 (66.00)	<.001
CVD	10 (1.69)	24 (2.03)	18 (2.29)	1 (0.67)	.573
CAD	14 (2.37)	32 (2.70)	23 (2.92)	4 (2.67)	.941
Dyslipidemic	210 (35.53)	514 (43.45)	371 (47.14)	67 (44.67)	<.001
Smokers	129 (21.80)	337 (28.49)	283 (35.96)	53 (35.33)	<.001
History of Heart Disease	246 (41.62)	467 (39.48)	322 (40.91)	66 (44.00)	.653
Prior Angina	67 (11.34)	171 (14.45)	104 (13.21)	21 (14.00)	.337
Arrhythmia	32 (5.41)	46 (3.89)	23 (2.92)	5 (3.33)	.125
Cardio-fitness					
Very Low	31 (5.25)	50 (4.25)	34 (4.34)	8 (5.33)	
Low	7 (1.18)	14 (1.19)	12 (1.53)	3 (2.00)	
Average	234 (39.59)	492 (41.80)	354 (45.15)	64 (42.67)	<.001
Fair	79 (13.37)	160 (13.59)	129 (16.45)	47 (31.33)	
Good/High	240 (40.61)	461 (39.17)	255 (32.53)	28 (18.67)	

*obese 1 and obese 3 were significantly different ($p=0.011$), using Bonferroni multiple comparisons test

* $P < 0.05$; ** $P < 0.001$; *** $P < 0.0001$

DISCUSSION

This study was designed to evaluate the influence of obesity alone in the development of diastolic dysfunction with the different indices of diastolic function. To do this we used the different grades of BMI against the different parameters of LV diastolic function indices using multiple regression analysis. Moreover we also selected subjects with uncomplicated obesity (without risk factors) and correlated it with the same parameters in order to come up with a conclusion.

In agreement with data from the literature, we found that obesity significantly influence the development of diastolic dysfunction. In our study, gender, diabetes, hypertension, dyslipidemia, smoking and cardio-respiratory fitness in the total population were all significantly associated with different grades of BMI. This can be explained by the fact that obesity is almost always accompanied by other co-morbidities which greatly contributed to the development of diastolic dysfunction or at the least have an effect of the different diastolic parameters. In terms of gender, there are more obese males than females in all grades of obesity. This is in contrary to foreign studies where the obese female usually is the majority. It might be due to the genetic make-up, heredo-

familial predisposition and even culture among Asians that make us more different among our Caucasian counterparts. It was also logical to think that there is an increasing trend in the proportion of diabetics, hypertensives, dyslipidemics and smokers was seen as obesity grade increases. Those with grade 2 obesity and above had the lowest proportion of good/high cardio-fitness which could be explained that aside from the fact that more obese you are, the more oxygen requirement during exercise on top of a pre-existing hyperdynamic heart.

Obesity is associated with hemodynamic overload.¹ The increase in metabolic demand due to expanded adipose tissue results in hyperdynamic circulation associated with increased blood volume. This translates to increased preload and also afterload coupled with arterial stiffness and increased peripheral resistance. Sometimes this is confounded by other cardiovascular risk like hypertension and diabetes mellitus. The duration of obesity in an obese individual has a great additive effect in the overall ventricular remodeling and particularly systolic and diastolic function. Ventricular systolic function as assessed by ejection fraction or with load independent measures is usually normal in obesity. This is supported in the study of Iacobellis G., et. al., where he

Table 2. Correlation of Risk Factors with Left Ventricular Diastolic Function Indices

Variable	MV1M	MV2M	EA Ratio	PSV	PDV	PSV / PDV	ARD	DT	IVRT
Age; Years (correlation)	-.1541***	.4453***	-.4485***	.0735**	-.1942***	.2484***	.0861***	.1282***	.1774***
Gender, no (%)									
Males	0.78 ± 0.21	0.70 ± 0.19	1.19 ± 0.48	0.54 ± 0.12	0.44 ± 0.11	1.30 ± 0.33	91.86 ± 22.2	195.64 ± 39.1	80.10 ± 14.5
Females	0.84 ± 0.23	0.75 ± 0.21	1.19 ± 0.39	0.57 ± 0.12	0.43 ± 0.11	1.37 ± 0.32	93.03 ± 20.8	200.26 ± 63.8	77.40 ± 14.1
p-value	<.0001	<.0001	0.6605	<.0001	0.3631	<.0001	0.1673	0.0341	<.0001
Smoking Status									
Smoker	0.79 ± 0.22	0.71 ± 0.18	1.19 ± 0.52	0.55 ± 0.13	0.43 ± 0.11	1.31 ± 0.34	91.92 ± 22.9	197.34 ± 36.8	79.70 ± 14.54
Non-smoker	0.81 ± 0.22	0.72 ± 0.21	1.19 ± 0.41	0.56 ± 0.12	0.43 ± 0.11	1.33 ± 0.33	92.50 ± 21.1	197.56 ± 55.3	78.73 ± 14.34
p-value	0.0168	0.1132	0.8047	0.0982	0.8477	0.1420	0.5415	0.9027	0.1130
Cardio-fitness									
Very Low	0.94 ± 0.47	0.84 ± 0.31	1.15 ± 0.57	0.53 ± 0.13	0.44 ± 0.15	1.30 ± 0.42	93.84 ± 23.3	225.58 ± 133.0	78.17 ± 16.1
Low	0.84 ± 0.13	0.82 ± 0.19	1.08 ± 0.28	0.55 ± 0.14	0.43 ± 0.14	1.33 ± 0.40	91.64 ± 24.4	183.81 ± 54.1	74.54 ± 13.7
Average	0.80 ± 0.18	0.71 ± 0.20	1.21 ± 0.47	0.56 ± 0.12	0.43 ± 0.11	1.32 ± 0.33	92.00 ± 20.6	197.35 ± 45.7	78.68 ± 15.5
Fair	0.81 ± 0.21	0.73 ± 0.19	1.17 ± 0.42	0.55 ± 0.12	0.43 ± 0.11	1.31 ± 0.31	90.64 ± 22.7	192.09 ± 43.3	78.98 ± 13.0
Good/High	0.79 ± 0.21	0.70 ± 0.19	1.19 ± 0.71	0.56 ± 0.12	0.43 ± 0.10	1.34 ± 0.33	93.27 ± 22.2	196.98 ± 34.8	79.70 ± 13.4
p-value	<.0001	<.0001	0.1930	0.0693	0.9725	0.6080	0.2824	0.0152	0.0119

Table 3. Correlation of Risk Factor with Left Ventricular Diastolic Function Indices

Co-morbidity	MV1M	MV2M	EA Ratio	PSV	PDV	PSV / PDV	ARD	DTI	VRT
Diabetic Status									
Diabetic	0.79 ± 0.21	0.80 ± 0.20	1.04 ± 0.36	0.56 ± 0.12	0.42 ± 0.11	1.38 ± 0.32	91.98 ± 22.1	200.57 ± 44.3	79.83 ± 14.1
Non-diabetic	0.81 ± 0.22	0.69 ± 0.20	1.24 ± 0.46	0.55 ± 0.12	0.44 ± 0.11	1.31 ± 0.33	92.44 ± 21.5	196.56 ± 52.3	78.77 ± 14.5
p-value	0.0434	<.0001	<.0001	0.1118	0.0020	<.0001	0.6461	0.0016	0.1081
Hypertensives									
Hypertensive	0.80 ± 0.20	0.75 ± 0.20	1.12 ± 0.42	0.56 ± 0.13	0.43 ± 0.11	1.35 ± 0.33	93.09 ± 21.8	198.73 ± 41.1	80.13 ± 14.0
Normotensive	0.82 ± 0.25	0.67 ± 0.20	1.30 ± 0.46	0.55 ± 0.12	0.45 ± 0.11	1.29 ± 0.32	91.16 ± 21.4	195.59 ± 62.3	77.29 ± 14.8
p-value	0.0032	<.0001	<.0001	0.4806	<.0001	<.0001	0.0259	0.0002	<.0001
CVD									
With	0.83 ± 0.22	0.77 ± 0.22	1.15 ± 0.55	0.54 ± 0.11	0.45 ± 0.12	1.26 ± 0.32	97.58 ± 26.7	194.76 ± 44.1	80.67 ± 12.0
Without	0.81 ± 0.22	0.72 ± 0.20	1.19 ± 0.44	0.55 ± 0.12	0.43 ± 0.11	1.33 ± 0.33	92.23 ± 21.5	197.55 ± 50.7	78.98 ± 14.4
p-value	0.4861	0.0526	0.5818	0.5133	0.3704	0.1825	0.1617	0.6993	0.4082
CAD									
With	0.83 ± 0.41	0.76 ± 0.19	1.18 ± 0.69	0.54 ± 0.16	0.46 ± 0.15	1.22 ± 0.31	95.89 ± 28.0	195.53 ± 41.1	79.79 ± 12.3
Without	0.81 ± 0.21	0.72 ± 0.20	1.19 ± 0.43	0.55 ± 0.12	0.43 ± 0.11	1.33 ± 0.33	92.23 ± 21.5	197.55 ± 50.8	78.99 ± 14.5
p-value	0.6660	0.0839	0.8536	0.4127	0.1521	0.0047	0.2833	0.6832	0.6389
Dyslipidemia									
With	0.80 ± 0.22	0.74 ± 0.20	1.13 ± 0.40	0.55 ± 0.13	0.43 ± 0.11	1.34 ± 0.35	92.71 ± 21.8	197.61 ± 42.5	79.87 ± 14.03
Without	0.81 ± 0.21	0.70 ± 0.20	1.23 ± 0.47	0.55 ± 0.12	0.44 ± 0.11	1.31 ± 0.32	92.04 ± 21.5	197.41 ± 55.8	78.37 ± 14.65
p-value	0.6124	<.0001	<.0001	0.7886	0.0237	0.0433	0.4338	0.9171	0.0079
History of Heart Disease									
With	0.81 ± 0.21	0.72 ± 0.21	1.19 ± 0.40	0.55 ± 0.12	0.43 ± 0.10	1.33 ± 0.32	91.85 ± 21.7	198.71 ± 52.5	79.18 ± 15.9
Without	0.80 ± 0.23	0.71 ± 0.20	1.19 ± 0.47	0.55 ± 0.12	0.43 ± 0.11	1.32 ± 0.34	92.66 ± 21.7	196.66 ± 49.2	78.90 ± 13.3
p-value	0.3617	0.3968	0.9431	0.9489	0.3800	0.7417	0.3455	0.3078	.62.91
Prior Angina									
With	0.82 ± 0.28	0.74 ± 0.19	1.15 ± 0.47	0.54 ± 0.13	0.43 ± 0.12	1.33 ± 0.34	92.92 ± 23.4	198.03 ± 53.4	78.72 ± 13.4
Without	0.80 ± 0.21	0.71 ± 0.20	1.20 ± 0.44	0.56 ± 0.12	0.43 ± 0.11	1.33 ± 0.33	92.24 ± 21.4	197.41 ± 50.1	79.06 ± 14.6
p-value	0.4171	0.0079	0.0532	0.0897	0.1912	0.9901	0.6024	0.8269	0.6586
Arrhythmia									
With	0.84 ± 0.29	0.69 ± 0.25	1.28 ± 0.46	0.55 ± 0.14	0.46 ± 0.12	1.28 ± 0.37	89.80 ± 23.0	194.36 ± 41.0	79.72 ± 17.1
Without	0.80 ± 0.22	0.72 ± 0.20	1.19 ± 0.44	0.55 ± 0.12	0.43 ± 0.11	1.33 ± 0.33	92.43 ± 21.6	197.62 ± 50.9	78.99 ± 14.3
p-value	0.1587	0.2055	0.0384	0.9423	0.0365	0.1247	0.2395	0.4391	0.6718

Table 4. Correlation of Diastolic Function Indices of the Study Population

Parameter	Normal n = 590	Obese 1 n = 1182	Obese 2 n = 786	Obese 3 & up n = 150	p-value
Mitral Inflow					
E, m/s	0.83 (0.26)	0.79 (0.22)	0.80 (0.19)	0.84 (0.18)	.0013 ^a
A, m/s	0.68 (0.20)	0.72 (0.21)	0.74 (0.19)	0.74 (0.19)	<.0001 ^b
E/A ratio	1.28 (0.44)	1.18 (0.44)	1.15 (0.46)	1.18 (0.35)	<.0001 ^c
Pulmonary vein flow					
Ps, m/s	0.56 (0.12)	0.55 (0.12)	0.55 (0.12)	0.54 (0.12)	.1636
Pd, m/s	0.45 (0.12)	0.43 (0.11)	0.43 (0.11)	0.41 (0.09)	<.0001 ^d
Ps/Pd ratio	1.30 (0.36)	1.33 (0.34)	1.34 (0.31)	1.34 (0.30)	.1313
PVARdur, ms	92.04 (22.10)	93.47 (21.99)	90.98 (21.08)	91.54 (20.10)	.0897
DT	200.15 (69.25)	198.46 (49.09)	194.14 (37.25)	197.17 (32.41)	.1393
IVRT	77.36 (13.81)	79.97 (15.87)	79.29 (12.72)	76.61 (11.95)	.0006 ^e

Note. Values presented are mean (sd). Analysis of variance was used.

^aNormal vs obese1 (p=.005), normal vs obese 2 (p=.021), Bonferroni multiple comparisons test

^bNormal vs obese 1 (p=.005), normal vs obese 2 (p<.001), normal vs obese 3 (p=.011)

^cNormal vs obese 1 (p<.001), normal vs obese 2 (p<.001)

^dNormal vs obese 1 (p=.002), obese 1 vs obese 3 (p=0.042)

* P < 0.05; ** P < 0.001; ***P < 0.0001

Table 5. Correlation of Diastolic Function Indices among Uncomplicated Obese Subjects

Parameter	Normal n = 110	Obese 1 n = 146	Obese 2 n = 86	Obese 3 & up n = 12	p-value
Mitral Inflow					
E, m/s	0.90 (0.35)	0.84 (0.22)	0.79 (0.17)	0.84 (0.16)	0.0060 ^a
A, m/s	0.62 (0.21)	0.65 (0.25)	0.70 (0.18)	0.69 (0.16)	0.0116 ^a
E/A ratio	1.47 (0.45)	1.39 (0.46)	1.19 (0.36)	1.28 (0.42)	<.0001 ^a
Pulmonary vein flow					
Ps, m/s	0.56 (0.12)	0.55 (0.12)	0.55 (0.12)	0.52 (0.12)	0.4141
Pd, m/s	0.50 (0.13)	0.45 (0.10)	0.43 (0.11)	0.39 (0.05)	<.0001 ^b
Ps/Pd ratio	1.19 (0.34)	1.25 (0.32)	1.33 (0.33)	1.36 (0.30)	0.0040 ^a
PVARdur, ms	91.10 (19.7)	93.04 (23.7)	91.97 (21.2)	80.65 (12.5)	0.0731
DT	202.90 (109.7)	196.55 (66.9)	191.56 (39.5)	187.88 (44.1)	0.5967
IVRT	73.70 (11.88)	77.64 (20.55)	77.82 (12.36)	74.58 (13.13)	0.0665

Note. Values presented are mean (sd). Analysis of variance was used.

^aNormal vs obese2 (p<.01)

^bNormal vs obese 1 (p=.002), obese 2 & obese 3 (p<.001)

Table 6. Correlation of Diastolic Function Indices among Uncomplicated Obese Subjects Adjusted for Age, Gender and Cardiorespiratory Fitness

Parameter	Normal n = 110	Obese 1 n = 146	Obese 2 n = 86	Obese 3 n = 12	p-value ^d
Mitral Inflow					
E, m/s	0.96 (0.02)	0.95 (0.02)	0.93 (0.02)	0.92 (0.05)	0.6041
A, m/s	0.71 (0.02)	0.77 (0.02)	0.80 (0.02)	0.84 (0.04)	0.0008 ^a
E/A ratio	1.31 (0.04)	1.23 (0.04)	1.10 (0.04)	1.04 (0.08)	<.0001 ^b
Pulmonary vein flow					
Ps, m/s	0.56 (0.12)	0.55 (0.01)	0.55 (0.01)	0.53 (0.03)	0.7821
Pd, m/s	0.48 (0.01)	0.44 (0.01)	0.42 (0.01)	0.35 (0.02)	<.0001 ^c
Ps/Pd ratio	1.23 (0.03)	1.30 (0.03)	1.35 (0.03)	1.46 (0.07)	0.0012 ^b
PVAR dur, ms	90.61 (2.30)	92.34 (2.17)	90.60 (2.39)	82.35 (4.69)	0.2035
DT	223.58 (7.50)	226.39 (6.98)	221.99 (8.01)	218.99 (15.84)	0.9364
IVRT	75.53 (1.61)	77.78 (1.50)	76.99 (1.72)	76.63 (3.37)	0.6196

Note. Values presented are mean (SE). Multiple linear regression was used.

^aNormal vs obese 1 to 3 ($p < .01$)

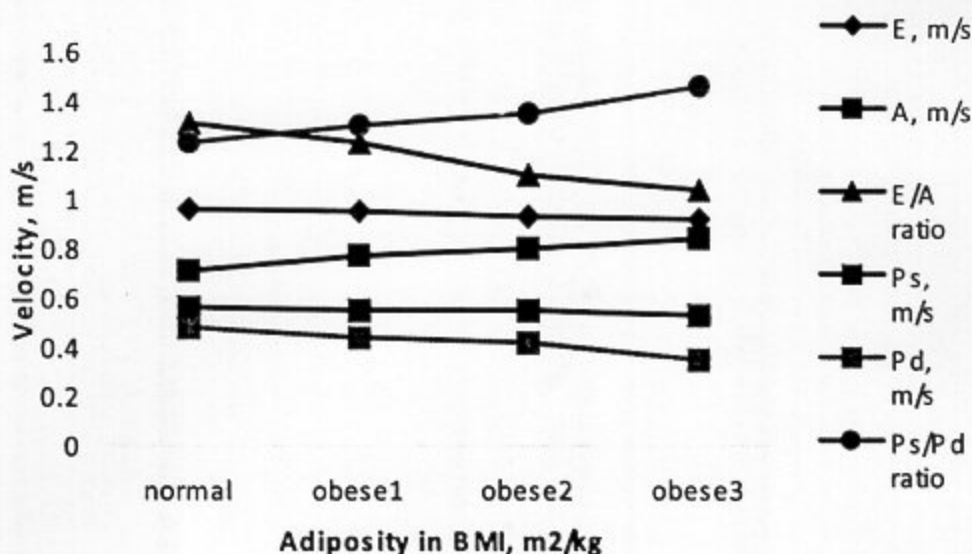
^bNormal vs obese 2 & 3 ($p < .01$)

^cNormal vs obese 1 to 3 ($p < .001$)

Table 7. Association of Uncomplicated Obesity and Risk of Isolated Diastolic Dysfunction

BMI Group	Crude OR	C. I.	p - value	Adjusted OR*	C.I.	p - value
Normal	—	—	—	—	—	—
Obese 1	1.83	0.97 - 3.45	0.062	2.02	0.99 - 4.1	0.052
Obese 2 and 3	3.86	2.06 - 7.23	<0.001	4.00	1.94 - 8.21	< 0.001

* Adjusted for the effects of Age, Gender, and Cardiorespiratory Fitness

Diastolic Function Indices Among Patients with Isolated Obesity**Graph I.** Diagrammatic Representation of the Significant Correlation of the Diastolic Function Indices of Uncomplicated Obesity Subgroup Adjusted for Age, Gender and Fitness.

investigated the influence of only excess fat on cardiac morphology and function. In his paper, he showed that obesity per se is associated only with an impairment of diastolic function and that no left ventricular hypertrophy occurs uncomplicated obese subjects. Obese people, however, may fail to increase their ejection fraction during exercise. Obesity can alter the LV filling indexes which can adversely affect the passive filling properties of the ventricle. In a recent study, body mass index (BMI) emerged as a key correlate of impaired diastolic filling indexes. However, there are at present a lot of new measures of measuring filling indexes in interpreting the diastolic function of the left ventricle, particularly with the use of Tissue Doppler Imaging (TDI). However, here in our country, the new modality has just been introduced and that it needs skill and consistency of results in order to maximize its full benefits. It may obviate the use of other Doppler parameters in measuring diastolic function particularly its load-independent quality results. Nevertheless, doppler parameters i.e., mitral (E, A, E/A ratio) and pulmonary vein flow (Ps, Pd, Ps/Pd ratio, PVAR duration) patterns, DT, and IVRT are masterfully being utilized to classify different levels of diastolic dysfunction.

Our study was consistent with the prospective case-control study of Pascual, Pascual, Soria, et. al., found out that BMI correlated positively with MV $\frac{1}{2}$ T and left atrial diameter, and inversely with deceleration slope with the conclusion that subclinical diastolic dysfunction is present in all grades of uncomplicated obesity. There was also a significant association of diastolic dysfunction with the different levels of BMI particularly in uncomplicated obesity subgroup in our study (Table 6). Although the results were similar, the subjects in the Pascual Study were purely obese females as compared to our study were majority are males and that BMI classification was different. Contemporary studies have demonstrated a more continuous risk of diastolic dysfunction and even heart failure associated with increasing excess weight. Thus, promotion of optimal body weight is imperative with lifestyle modification, adequate exercise and proper nutrition may be the best preventive measure.

Limitations

The duration of obesity and its pattern as this can influence diastolic dysfunction and that a definite effect

will yield better correlation of results. The sample was purely taken in the hospital setting, hence, the findings may not be generalizable to the average obese person in the community. Lastly, independent loading parameters will greatly give more consistent results as to the different diastolic function parameters in this study.

Recommendation

A prospective study aside from good history and physical exam with detailed follow-up on the duration, measurement of actual extent of fat deposition, and even biomarkers for adiposity among these patients' particularly uncomplicated obese patients with age-matched controls is warranted to better measure the alteration in the cardiac structure and function. "Stable" or independent measure of filling pressure or diastolic function like the use of TDI, measures of left atrial volume/remodeling should be utilized to correlate more directly with levels of BMI is also recommended for future studies.

(Footnotes)

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