



The relation between obesity and left ventricular diastolic function in young people: A cross-sectional study

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Original Article

Abstract

BACKGROUND: It has been proposed that left ventricular diastolic dysfunction (LVDD) is a possible physiological link between high body mass index (BMI) and future occurrence of heart failure (HF). The present cross-sectional study was aimed to analyze the association between BMI and LVDD by transthoracic echocardiography (TTE).

METHODS: This study was conducted from May 2017 to September 2019 in Khorshid Hospital of Isfahan University of Medical Sciences, Isfahan, Iran. Based on the calculated BMI (kg/m²), patients were divided into three groups: group 1: subjects with BMI < 25, as a normal group (n = 75), group 2: volunteer cases with 25 < BMI ≤ 30, as an obese group (n = 98), and group 3: patients with BMI ≥ 30, as a morbidly obese group (n = 100). TTE was performed by a trained cardiologist and associated variables including left atrium (LA) volume, E, septal e', lateral e', and E/e' were assessed and also subjects were characterized as normal diastolic function, abnormal diastolic function, and inconclusive diagnosis of diastolic dysfunction (DD).

RESULTS: Apart from the ejection fraction (EF) and the tricuspid regurgitation velocity (TRV), there was a significant difference between the other echocardiographic variables including LA volume, E, septal e', lateral e', and E/e' (P < 0.05). One patient with morbid obesity in our study revealed LVDD. There was no significant difference between three groups (P = 0.42).

CONCLUSION: There is no considerable relationship between obesity and LVDD. It seems that the absence of associated comorbidities such as diabetes, coronary disorders, etc. plays a crucial role in preventing LVDD, but for realistic and definitive decision, more cellular and molecular investigations and studies with larger sample size are necessary.

Keywords: Obesity; Body Mass Index; Left Ventricular; Diastolic Heart Failure

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Introduction

One of the most common cardiac complications that is associated with progression of heart failure (HF) is diastolic dysfunction (DD).¹ It has been reported that some parameters such as age, sex, smoking, metabolic syndrome, obesity, high blood pressure, dyslipidemia, and type 2 diabetes mellitus (DM) are related with occurrence of DD.^{2,3} Left ventricular DD (LVDD) is the most common type of DDs that mirrors the deterioration of filling properties of left ventricle (LV) that has been introduced to be a predictor of HF occurrence in community settings.^{4,5} Furthermore, it

has been proposed that LVDD is a possible physiological link between high body mass index (BMI) and future occurrence of HF,⁶ but the issue is open to discussion. As we all know and it is reported in numerous papers, cardiac structural alterations following obesity are crucial determinants of LVDD.⁷

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In the recent years, the prevalence of obesity and associated complications, as a major health issue, is increased in modern communities and it is anticipated that aforementioned condition will become an important player in pathogenesis of DM, metabolic disease, and cardiovascular disease (CVD) in the future years.⁸ Moreover, overweight and obesity is related with other conditions such as hyperlipidemia, DM, and hypertension (HTN), which are recognized as the considerable risk factors of HF. It has been revealed that stress oxidative, as a consequence of obesity, plays a crucial role in the pathogenesis of DD.⁹ Furthermore, an increase in BMI directly affects anatomical and physiological aspects of the heart and these conditions are due to increased peripheral resistance and chronic volume overload.⁶ Additionally, it has been indicated that increased adiposity heightens the effect of blood pressure on LV mass growth and dilation of LV occurs.¹⁰ The present cross-sectional study was aimed to analyze the association between BMI and LVDD by transthoracic echocardiography (TTE).

Materials and Methods

Study design and patients: Present cross-sectional study was approved by Isfahan Cardiovascular Research Center of Isfahan University of Medical Sciences, Isfahan, Iran. Besides, this study obtained the authorization of Ethics Committee (number: IR.MUL.MED.REC.1397.203) of Isfahan University of Medical Sciences and was conducted from May 2017 to September 2019 in Khorshid Hospital of Isfahan University of Medical Sciences. Essential and demographic information (age, gender, weight, and height) of subjects was recorded in special forms. Risk factors and clinical conditions were identified based on self-report of a patient's history and medical records. The inclusion criteria for the participation in the study were normal electrocardiography (ECG), normal LV ejection fraction (LVEF), and normal valve structure and function. Exclusion criteria were positive history or clinical manifestations of coronary artery disease (CAD), HF, cardiomyopathy, respiratory disease, DM, HTN, or cardiac valve anomalies.

In order to define obesity and morbid obesity, we obtained weight and height of subjects, and calculated their BMI as: weight (kg)/height (m)². Based on the calculated BMI (kg/m²), patients were divided into three groups: group 1: subjects with BMI < 25, as a normal weight group (n = 75), group 2: cases with 30 < BMI < 35, as an obese

group (n = 98), and group 3: patients with BMI ≥ 40, as a morbidly obese group (n = 100). Third group subjects were gastric bypass candidates with morbid obesity and age under 45 years old who were referred from Isfahan Clinic of Bariatric Surgery to a cardiac clinic in Isfahan, for their pre-operation cardiovascular evaluation.

Echocardiography: TTE was performed by a trained cardiologist following a standardized protocol. For acquisition of echocardiography measurements, we used GE machine vivid 3 model (General Electrics, Milwaukee, WI, USA). LV linear dimensions were measured according to the guidelines of American Society of Echocardiography (ASE).¹¹ LV relative wall thickness (RWT) was calculated as: (2 × posterior wall thickness)/end-diastolic diameter. We also used the biplane modified Simpson's rule to calculate LVEF. Left atrial volume was also measured by area-length method using apical 4-chamber and apical 2-chamber views at ventricular systole. We used apical four-chamber view with color flow imaging for optimal alignment of pulsed wave (PW) and continuous wave (CW) Doppler with blood flow. PW Doppler sample volume (1-3 mm axial size) between mitral leaflet tips, low wall filter setting (100-200 MHz) and low signal gain, and optimal spectral waveforms did not display spikes or feathering. Early diastolic transmitral inflow velocity was measured at the level of mitral leaflet tips using PW Doppler ultrasound (E). Pulsed tissue Doppler imaging (TDI) sample volume was placed at the level of septal and lateral mitral valve annulus and the early diastolic velocities (E') were measured. Subsequently, E/E' average ratio was measured as an indicator of LV filling pressure. Tricuspid regurgitation velocity (TRV) was measured with CW Doppler ultrasound in peak modal velocity during systole at leading edge of spectral waveform in four-chamber view.

Definition of DD: We characterized individuals as normal diastolic function, abnormal diastolic function, and inconclusive diagnosis of DD based on the four available measures of DD as defined by the latest recommendations of ASE for LVDD. We gave 1 point to the DD scoring parameters if: 1) E/e' > 14, 2) septal e' velocity < 7 or lateral e' velocity < 10 cm/s, 3) TRV > 2.8, and 4) LA volume index > 34 ml/m². Diastolic function of LV is normal if more than 50 percent of the accessible variables do not meet the cutoff values for identifying abnormal function. LVDD is present if more than half of the available parameters meet

these cutoff values. The study is inconclusive if half of the parameters do not meet the cutoff values.

Statistical analysis: For statistical analysis, we used the SPSS software (version 22.0, IBM Corporation, Armonk, NY, USA). Data were shown as mean \pm standard deviation (SD) for continuous variables and frequency (percentage) for categorical variables. Categorical variables were compared using the chi-square test or Fisher's exact test based on Monte Carlo simulations. For continuous variables, the Kolmogorov-Smirnov test was used for the assessment of data normality. For comparison of means between groups, if normality assumptions held, one-way analysis of variance (ANOVA) was done and wherever the test was significant, Scheffe's post-hoc test was performed; otherwise, the non-parametric Kruskal-Wallis test was performed and Mann-Whitney U test with Bonferroni adjustment was used to show the differences. P-value < 0.05 was considered as statistically significant.

Results

A total of 273 patients were evaluated: group 1: subjects with BMI < 25 , as a normal weight ($n = 75$), group 2: cases with $25 < \text{BMI} \leq 30$, as an obese group ($n = 98$), and group 3: patients with BMI ≥ 30 , as a morbidly obese group ($n = 100$). Mean ages in the three groups were 26.05 ± 4.05 , 28.85 ± 5.10 , and 27.97 ± 6.82 , respectively. There was a significant difference between ages in three groups of subjects ($P = 0.005$). The demographic characteristics of patients are summarized in table 1.

Table 2 presents some of the evaluated parameters of echocardiographic assessment. Apart from the EF and the TRV, there was a significant difference between the other echocardiographic variables ($P < 0.050$).

In table 3, we reported distribution of DD of

patients divided into three groups of normal BMI, obese, and morbidly obese. One patient with morbid obesity in our study revealed DD. There was no significant difference between three groups ($P = 0.42$).

Discussion

Present study showed that there was no considerable relationship between obesity and LVDD. As previously mentioned, DD is strongly associated with the occurrence of HF. DD can be considered as a valuable issue in predicting obesity-related cardiac diseases.¹² In some studies, indices of LVDD were impairment of LV diastolic filling or relaxation compared to lean controls.^{13,14} A number of studies have recently focused on the presence and incidence of LVDD in people with morbid obesity, particularly in those who are hypertensive obese individuals. Pascual et al. reported that DD was present in 12% of mildly obese patients, 35% of moderately obese subjects, and 45% of severely obese cases.¹³ In a recent study, Rozenbaum et al. reported that higher BMI accompanied with abnormalities in echocardiographic parameters associated with DD, including left atrial volume index $> 34 \text{ ml/m}^2$, $E/e' > 14$, e' lateral $< 10 \text{ cm/s}$, e' septal $< 7 \text{ cm/s}$, TRV $> 2.8 \text{ m/s}$, and systolic pulmonary artery pressure (sPAP) $\geq 36 \text{ mmHg}$ ($P < 0.01$ for all comparisons).¹⁵ They also declared that morbidly obese patients carried the highest risk compared to those with normal BMI.¹⁵

Age changes have been suggested as an important variable in LV function. Van Grootel et al. in their study demonstrated a strong relationship between LV early diastolic peak strain rate and age changes.¹⁶ In addition, they reported a significant decrease of above parameter of LV with aging, which is especially considerable after the 5th decade of life.¹⁶

Table 1. Demographic information of patients divided into the three groups of normal body mass index (BMI), obese, and morbidly obese

Variable	Group 1	Group 2	Group 3	P
	Normal weight (n = 75)	Obese (n = 98)	Morbidly obese (n = 100)	
Age (year)	26.05 \pm 4.05	28.85 \pm 5.10	27.97 \pm 6.82	0.005*
Sex				0.660**
Women	40 (53.3)	51 (52.1)	56 (56.0)	
Men	35 (46.6)	47 (47.9)	44 (44.0)	
Weight (kg)	75.24 \pm 8.42	107.69 \pm 12.88	130.19 \pm 20.38	< 0.001 ***
Height (cm)	169.33 \pm 5.93	168.15 \pm 7.12	168.78 \pm 9.27	0.600*
BMI (kg/m ²)	20.88 \pm 1.51	37.27 \pm 2.40	45.39 \pm 4.06	< 0.001 ***

Data are presented as mean \pm standard deviation (SD) or number (percentage)

*One-way analysis of variance (ANOVA) was done, Scheffe's post-hoc was used; **Chi-square test was used;

***Kruskal-Wallis test was done, Mann-Whitney U test with Bonferroni adjustment was used to show the statistically different groups.

BMI: Body mass index

Table 2. Echocardiographic measurements of patients divided into three groups of normal body mass index (BMI), obese, and morbidly obese

Variable	Group 1	Group 2	Group 3	P
	Normal weight (n = 75)	Obese (n = 98)	Morbidly obese (n = 100)	
EF	69.01 ± 8.19	67.55 ± 2.71	67.72 ± 3.91	0.140
Left atrial volume	20.76 ± 3.55	23.33 ± 6.00	27.29 ± 6.15	< 0.001
E (cm/sec)	99.24 ± 7.63	94.12 ± 13.64	97.79 ± 13.64	0.017
Septal e' (cm/sec)	11.38 ± 1.53	12.16 ± 1.90	12.19 ± 2.18	0.010
Lateral e' (cm/sec)	14.47 ± 1.52	15.19 ± 1.81	15.14 ± 1.97	0.017
E/e'	8.77 ± 1.14	7.91 ± 1.66	8.13 ± 1.78	0.002
TRV	1.80 ± 0.35	1.80 ± 0.37	1.69 ± 0.41	0.099

Data are presented as mean ± standard deviation (SD)

One-way analysis of variance (ANOVA) was done, Scheffe's post-hoc was used.

EF: Ejection fraction; E: Early diastolic mitral annular tissue velocity; e': Early diastolic annulus velocity;

TRV: Tricuspid regurgitation velocity

So far, some researches have specifically surveyed the impact of overweight on diastolic function of younger people and reported controversial comments about the fact that obesity and weight gain could have an effect on diastolic function. In present cross-sectional study, we reported that there was no significant relation between LVDD and obesity, that was inconsistent with Sharpe et al. study.¹⁷ They showed that the indexes of diastolic function like tissue Doppler measures were considerably impaired in obese young cases.¹⁷ In their study, Harada et al. based on transmitral and pulmonary venous velocities proposed a reduction in early diastolic filling in the young obese subjects.¹⁸ Moreover, Mehta et al. presented anomalies in the early diastolic filling (E') in the young obese cases. They also found that the ratio of E'/A' was inversely associated with BMI.¹⁹ Our result are in agreement with the results of Alpert et al. who reported that obesity was related with eccentric rather than concentric remodeling of the LV.²⁰ Aforementioned paradox in results may be associated with difference in study design, age of participants, duration of obesity, and socioeconomic issues, but the issue is open to discussion.

There are a lot of discussions about the effects of obesity on cardiac anatomical and physiological alterations in healthy obese cases. Our finding that obesity was not associated with LVDD is intriguing.

It has been demonstrated that presence of some conditions such as DM, HTN, and non-alcoholic fatty liver disease (NAFLD) with obesity is considered as a main risk factor for creation of cardiovascular disorders.^{21,22} In our study, we did not see a significant difference between LVDD and obesity. Perhaps one of the most important factors in the current outcome is the absence of comorbidities in patients, but it is not possible to make a definite statement. So far, in many papers, it has been mentioned that type 2 DM is a considerable predictor of occurrence of heart disease in obese people.²³ Lee et al. in their paper reported that obesity was a survival benefit in subjects with HF without DM, as a notable comorbidity.²⁴

In current study, we confronted with some limitations. One of the main limitations was absence of some evaluations in our Doppler flow analysis such as deceleration time of bicuspid valve, isovolumic relaxation time (IVRT), or flow of pulmonary vein. What is certain is that additional evaluation, such as the aforementioned parameters, can be helpful in validating the results. Another limitation was the lack of an overweight group of patients.

The age of bariatric surgery candidates who referred to Khorshid Hospital for pre-operative cardiovascular evaluation was less than 45 years old and because obesity is a chronic disease, its adverse effects occur at older ages.

Table 3. Distribution of diastolic dysfunction (DD) of patients divided into three groups of normal body mass index (BMI), obese, and morbidly obese

Variable	Group 1	Group 2	Group 3	P
	Normal weight (n = 75)	Obese (n = 98)	Morbidly obese (n = 100)	
DD				
Normal function	75 (100)	98 (100)	99 (99.0)	> 0.999
Abnormal function	0 (0)	0 (0)	1 (1.0)	

Data are presented as number (percentage)

Fisher's exact test based on Monte Carlo simulations was used.

DD: Diastolic dysfunction

Our result was confronted with an unwanted bias and may not be extrapolated to older cases with higher cardiovascular risk profiles. This increases the need for further studies at older ages. Due to the absence of obese subjects with comorbidities, the possible correlation between LVDD and obesity has been weakened, and it is recommended that fourth group with comorbidities be considered in future studies. In present study, obesity was characterized on the basis of BMI. As we all know, some other methods to assess obesity such as ratio of waist-to-hip, circumference of waist, and skinfold thickness are available. BMI anthropometric technique is uncomplicated to measure but has limited precise and accuracy²⁵ although some investigations have reported that BMI is a stable measurement for assessment of body fat in obese subjects.²⁶ However, the use of bioelectrical impedance analysis (BIA) is recommended to increase diagnostic accuracy for future studies.

Conclusion

This study showed that there was no considerable relationship between obesity and LVDD independently of vascular risk factors in young people. It seems that the absence of associated co-morbidities such as DM, coronary disorders, etc. plays a crucial role in preventing LVDD, but for realistic and definitive decision, more cellular and molecular investigations and studies with larger sample size are necessary. It seems that if obesity is prevented at a young age, LV dysfunction will be prevented in the future.

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Conflict of Interests

Authors have no conflict of interests.

Authors' Contribution

HS and AN designed the study and wrote the proposal and MT and AN led data collection and analysis. HS conducted data collection and led data collection and AN and MT wrote the final draft of manuscript. All authors have read and approved the manuscript.

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