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

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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 Khoshid 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 40 > BMI ≥ 30, as an obese group (n = 98), and group 3: patients with BMI ≥ 40, 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). 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. 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. Furthermore, it has been proposed that LVDD is a possible physiological link between high body mass index (BMI) and future occurrence of HF, 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. How to cite this article: Shemirani H, Tajmirriahi M, Nikneshan A, Kleidari B. The relation between obesity and left ventricular diastolic function in young people: A cross-sectional study. ARYA Atheroscler 2021; 17: 2251.
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.MUI.MED.REC.1397.203) of Isfahan University of Medical Sciences and was conducted from May 2017 to September 2019 in Khorsid 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 (m²). 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 40 > BMI ≥ 30, 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 ± 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 40 > BMI ≥ 30, as an obese group (n = 98), and group 3: patients with BMI ≥ 40, 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 1 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.15 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 ml/m², E/e′ > 14, e′ lateral < 10 cm/s, e′ septal < 7 cm/s, TRV > 2.8 m/s, and systolic pulmonary artery pressure (sPAP) ≥ 36 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 (Normal weight n = 75) | Group 2 (Obese n = 98) | Group 3 (Morbidly obese n = 100) | P       |
|---------------|-------------------------------|-----------------------|---------------------------------|---------|
| Age (year)    | 26.05 ± 4.05                  | 28.85 ± 5.10          | 27.97 ± 6.82                    | 0.005   |
| Sex           | 40 (53.3)                     | 51 (52.1)             | 56 (56.0)                       | 0.660** |
| Women         | 35 (46.6)                     | 47 (47.9)             | 44 (44.0)                       |         |
| Weight (kg)   | 75.24 ± 8.42                  | 107.69 ± 12.88        | 130.19 ± 20.38                  | < 0.001***|
| Height (cm)   | 169.33 ± 5.93                 | 168.15 ± 7.12         | 168.78 ± 9.27                   | 0.600†  |
| BMI (kg/m²)   | 20.88 ± 1.51                  | 37.27 ± 2.40          | 45.39 ± 4.06                    | < 0.001***|

Data are presented as mean ± 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

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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.
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 L.V.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             | Abnormal function           |                             |         |
|                   | 75 (100)                    | 0 (0)                       | 98 (100)                    | > 0.999 |
|                   | 99 (99.0)                   | 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 accuracy although some investigations have reported that BMI is a stable measurement for assessment of body fat in obese subjects. 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.

**References**

1. Eikendal ALM, Gohar A, Rutten FH, Bots ML, Appelman Y, Hofstra L, et al. Sex-specific relations of cardiovascular risk factors with left ventricular diastolic dysfunction/heart failure with preserved ejection fraction are underreported: A call for action. J Card Fail 2018; 24(6): 412-4.

2. Jadhav S, Valery R, Seliverstov P, Sitkin S. Risk factors for developing diastolic dysfunction in nonalcoholic steatohepatitis. Archiv Euromedica 2019; 9(1): 104-5.

3. van Heerebeek L, Franssen CP, Hamdani N, Verheugt FW, Somsen GA, Paulus WJ. Molecular and cellular basis for diastolic dysfunction. Curr Heart Fail Rep 2012; 9(4): 293-302.

4. Kane GC, Karon BL, Mahoney DW, Redfield MM, Roger VL, Burnett JC, et al. Progression of left ventricular diastolic dysfunction and risk of heart failure. JAMA 2011; 306(8): 856-63.

5. Teo SG, Yang H, Chai P, Yeo TC. Impact of left ventricular diastolic dysfunction on left atrial volume and function: A volumetric analysis. Eur J Echocardiogr 2010; 11(1): 38-43.

6. Russo C, Jin Z, Homma S, Rundek T, Elkind MS, Sacco RL, et al. Effect of obesity and overweight on left ventricular diastolic function: A community-based study in an elderly cohort. J Am Coll Cardiol 2011; 57(12): 1368-74.

7. Choy B, Hansen E, Moss AJ, McNitt S, Zareba W, Goldenberg I. Relation of body mass index to sudden cardiac death and the benefit of implantable cardioverter-defibrillator in patients with left ventricular dysfunction after healing of myocardial infarction. Am J Cardiol 2010; 105(5): 581-6.

8. Saeedi Borujeni MJ, Esfandiary E, Taheripak G, Codoner-Franch P, Alonso-Iglesias E, Mirzaei H. Molecular aspects of diabetes mellitus: Resistin, microRNA, and exosome. J Cell Biochem 2018; 119(2): 1257-72.

9. Saeedi Borujeni MJ, Esfandiary E, Baradaran A, Valiani A, Ghanadian M, Codoner-Franch P, et al. Molecular aspects of pancreatic beta-cell dysfunction: Oxidative stress, microRNA, and long noncoding RNA. J Cell Physiol 2019; 234(6): 8411-25.

10. Gishi O, Gaillard R, Durmus B, Abrahamse M, van der Beek EM, Hofman A, et al. BMI, total and abdominal fat distribution, and cardiovascular risk factors in school-age children. Pediatr Res 2015; 77(5): 710-8.

11. Porter TR, Shillcutt SK, Adams MS, Desjardins G, Glas KE, Olson JJ, et al. Guidelines for the use of echocardiography as a monitor for therapeutic intervention in adults: A report from the American Society of Echocardiography. J Am Soc Echocardiogr 2015; 28(1): 40-56.

12. De Pergola G, Nardecchia A, Giagulli VA,
Triggiani V, Guastamacchia E, Minischetti MC, et al. Obesity and heart failure. Endocr Metab Immune Disord Drug Targets 2013; 13(1): 51-7.
13. Pascual M, Pascual DA, Soria F, Vicente T, Hernandez AM, Tebar FJ, et al. Effects of isolated obesity on systolic and diastolic left ventricular function. Heart 2003; 89(10): 1152-6.
14. Herszkowicz N, Barbato A, Salvi W, Pinheiro D, Pantaleao D, Halpern A, et al. Contribution of Doppler echocardiography to the evaluation of systolic and diastolic function of obese women versus a control group. Arq Bras Cardiol 2001; 76(3): 189-96.
15. Rozenbaum Z, Topilsky Y, Khoury S, Pere D, Laufer-Perl M. Association of body mass index and diastolic function in metabolically healthy obese with preserved ejection fraction. Int J Cardiol 2019; 277: 147-52.
16. van Grootel RWJ, Kauling RM, Menting ME, McGhie J, Roos-Hesselink JW, van den Bosch AE. Influence of age and sex on left ventricular diastolic strain analysis. Int J Cardiovas Imaging 2019; 35(3): 491-8.
17. Sharpe JA, Naylor LH, Jones TW, Davis EA, O'Driscoll G, Ramsay JM, et al. Impact of obesity on diastolic function in subjects < or = 16 years of age. Am J Cardiol 2006; 98(5): 691-3.
18. Harada K, Orino T, Takada G. Body mass index can predict left ventricular diastolic filling in asymptomatic obese children. Pediatr Cardiol 2001; 22(4): 273-8.
19. Mehta SK, Holliday C, Hayduk L, Wiersma L, Richards N, Younoszai A. Comparison of myocardial function in children with body mass indexes >/=25 versus those <25 kg/m2. Am J Cardiol 2004; 93(12): 1567-9.
20. Alpert MA, Lambert CR, Panayiotou H, Terry BE, Cohen MV, Massey CV, et al. Relation of duration of morbid obesity to left ventricular mass, systolic function, and diastolic filling, and effect of weight loss. Am J Cardiol 1995; 76(16): 1194-7.
21. Anstee QM, Targher G, Day CP. Progression of NAFLD to diabetes mellitus, cardiovascular disease or cirrhosis. Nat Rev Gastroenterol Hepatol 2013; 10(6): 330-44.
22. Forlano R, Mullish BH, Nathwani R, Dhar A, Thursz MR, Manousou P. Non-alcoholic fatty liver disease and vascular disease. Curr Vasc Pharmacol 2021; 19(3): 269-79.
23. Pagidipati NJ, Zheng Y, Green JB, McGuire DK, Mentz RJ, Shah S, et al. Association of obesity with cardiovascular outcomes in patients with type 2 diabetes and cardiovascular disease: Insights from TECOS. Am Heart J 2020; 219: 47-57.
24. Lee KS, Moser DK, Lennie TA, Pelter MM, Nesbitt T, Southard JA, et al. Obesity paradox: Comparison of heart failure patients with and without comorbid diabetes. Am J Crit Care 2017; 26(2): 140-8.
25. Cornier MA, Despres JP, Davis N, Grossniklaus DA, Klein S, lamarche B, et al. Assessing adiposity: A scientific statement from the American Heart Association. Circulation 2011; 124(18): 1996-2019.
26. Wang Y, Rimm EB, Stampfer MJ, Willett WC, Hu FB. Comparison of abdominal adiposity and overall obesity in predicting risk of type 2 diabetes among men. Am J Clin Nutr 2005; 81(3): 555-63.