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Original Article

Left ventricular diastolic dysfunction without left ventricular hypertrophy in obese children and adolescents: a Tissue Doppler Imaging and Cardiac Troponin I Study

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Abstract *Background:* Obesity increases the risk for various cardiovascular problems. Increase in body mass index is often an independent risk factor for the development of elevated blood pressure and clustering of various cardiovascular risk factors. *Objective:* To determine early markers of left ventricular affection in obese patients before the appearance of left ventricular hypertrophy. *Methods:* In this cross-sectional study, we evaluated 42 obese patients and 30 healthy controls. Their ages ranged from 6 to 19 years. Studied children were subjected to anthropometric, lipid profile, and serum Troponin I level measurements. Echocardiographic evaluation performed to assess the left ventricle included left ventricular dimension measurement using motion-mode echocardiography, based on which patients with left ventricular hypertrophy (10 patients) were eliminated, as well as conventional and tissue Doppler imaging. *Results:* Tissue Doppler findings in the study groups showed that the ratio of transmitral early diastolic filling velocity to septal peak early diastolic myocardial velocity (E/e′) was significantly higher in cases compared with controls [6.9 ± 1.4 versus 9.0 ± 1.6, p (Pearson's coefficient) = 0.001, respectively]. The level of cardiac troponin I was significantly higher in cases compared with controls [0.14 ± 0.39 ng/ml versus 0.01 ± 0.01 ng/ml, p (Pearson's coefficient) = 0.047, respectively] and there was a significant correlation between troponin I and transmitral early diastolic filling velocity to septal peak early diastolic myocardial velocity ratio (E/e′) [R (correlation coefficient) = 0.6]. *Conclusion:* Tissue Doppler Imaging and Troponin I evaluation proved useful tools to detect early affection of the left ventricle in obese patients even in the absence of left ventricular hypertrophy.

Keywords: Diastolic dysfunction; obesity cardiomyopathy in children; tissue Doppler imaging; cardiac troponin I; left ventricular hypertrophy

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Obesity, a New World Syndrome, in childhood is a growing public health issue since the last few decades that requires proper global attention. In 2015, the number of overweight children under the age of 5 years was estimated to be over 42 million.[1] Obesity has major health consequences for youngsters. Those who have a high body mass index are at more risk for developing cardiovascular disorders such as obesity cardiomyopathy, hypertension, and hyperinsulinaemia with resultant atherogenesis. Mechanisms of obesity-induced cardiomyopathy are multifactorial, involving the right and left ventricles, as well as their diastolic and systolic functions. The high metabolic activity of adipose tissue and increased muscle mass lead to increased preload and after load, leading to left ventricular remodelling and dilatation and increase in wall stress,

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which would increase myocardial oxygen consumption with eventual left ventricular dysfunction. Myocyte contractile dysfunction will activate a cardiac adrenergic drive, which would compensate for but contribute to remodelling and progressive dysfunction. Once myocardial dysfunction occurs, various neurohormonal compensatory systems kick in, preserving cardiac output and blood pressure. Their activation will lead to progressive loss of cardiac myocytes due to accelerated apoptosis and necrosis, which would lead to further myocardial dysfunction. At the cellular level, activation of the Renin–Angiotensin–Aldosterone system and the sympathetic nervous system creates defects in adrenergic-receptor signal transduction and induction of the cardiac fetal gene programme, which characterises failing hearts.[2] Obstructive sleep apnoea also plays an important role in induction of subclinical myocardial injury.[3] Some endocrinal and metabolic disturbances may also contribute, such as oversecretion of leptin and decreased secretion of adinopectin. Leptin acts by attenuating contraction of isolated ventricular myocytes.[4] Adiponectin, which is an adipose-derived cytokine, inhibits adrenergic-receptor-stimulated hypertrophy of cardiac myocytes. The reduction in its secretion in obesity states gives room for fatty infiltration of the myocardium.[5] Last but not least lipotoxicity adds to the aforementioned factors by inducing cardiac myocyte apoptosis.[6] Several diagnostic challenges exist as regards the early detection of obesity cardiomyopathy, especially that the routine tools for detection of systolic dysfunction of the left ventricle such as fractional shortening and ejection fraction are usually affected late in the disease course.[7] Also most of the previous studies have linked the occurrence of left ventricular diastolic dysfunction in obese patients to left ventricular hypertrophy.[8] Also few studies have highlighted the importance of biomarkers such as Troponin in detection of subclinical myocardial injury in obese patients.[3]

The aims of this study are as follows: to evaluate the reliability of different conventional and tissue Doppler-derived indices of systolic and diastolic dysfunction of the left ventricle in early detection of obesity cardiomyopathy; to check the solidity of the previous studies relating left ventricular diastolic dysfunction with the occurrence of left ventricular hypertrophy; and to test the possibility of using a biomarker such as troponin I in detection of subclinical myocardial injury in obese patients.

Patients and methods

Study population

This study was designed as a case–control cross-sectional study.

It included two groups:

Group A. Initially, 42 obese children of both sexes – 22 male and 20 female – aged 6–19 years, were enrolled in this study. This study was performed in Diabetes, Endocrine & Metabolic Pediatric Unit, Cairo University Children Hospital, during the period from April, 2013 to June, 2013; 10 patients were then excluded based on the presence of left ventricular hypertrophy as mentioned below.

Obesity was defined on the basis of the standardised percentile curves of body mass index suggested for Egyptian children and adolescents as >95th percentile of body mass index for age and sex. Overweight is defined as being in the 85th to 95th percentile of body mass index for age and sex. Normal weight is defined as being <85th percentile of body mass index for age and sex. These centile curves were constructed by researchers from Diabetes, Endocrine & Metabolic Pediatric Unit of Cairo University, and those at the National Research Center in Cairo, in collaboration with Department of Community Health Life Span, Health Research Center, School of Medicine, Wright State University. These charts were conducted from a total sample size of 33,189 girls and boys for the period from birth to the age of 21 years.[9]

Any obese child who had any impaired mentality, associated with genetic syndrome and endocrinal causes of obesity such as diabetes mellitus, Cushing syndrome, and hypothyroidism were excluded.

Group B. A total of 30 healthy children matched for age and sex were set as the control group.

Both groups were enrolled in the study after obtaining consent from the patients or their legal guardians and the approval of the ethical committee of Cairo University.

Methods

Patients were subjected to:

Full clinical assessment

Complete medical history was obtained from all included patients; patients were subjected to clinical examination: complete general and systemic examination was performed for each subject in order to exclude chronic diseases that affect growth; for all patients, anthropometric measurements were taken, including measurements of body weight (kg), height (cm), and body mass index, which was calculated as weight (kg)/height (m) and plotted on Egyptian centile curves of body mass index according to age and sex. Pubertal staging was carried out using the Tanner staging method.[10a]

[a]It is to be noted that only two of the 32 (6%) patients demonstrated habitual snoring as evidence of obstructive sleep apnoea syndrome.

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Echocardiography

This was performed using a General Electric Vivid 7-dimension medical system, model N-3190 Horten, Norway, with probe frequencies appropriate for patient size according to the guidelines for carrying out echocardiography given by American Society of Echocardiography.[11]

Motion-mode echocardiographies. These were initially performed to exclude patients and controls with left ventricular hypertrophy using the traditional cut-off point for left ventricular mass index of >38.5 g/m$^{2.7}$.[12] Motion-mode parameters included left ventricular end diastolic dimensions, left ventricular end systolic dimensions, left ventricular fractional shortening, ejection fraction according to Teichholz method,[13] interventricular septal dimension at diastole, left ventricular posterior wall dimension at diastole, and left ventricular mass (g) calculated by the following equation:

$$0.8\{1.04([\text{left ventricular end diastolic dimensions} + \text{interventricular septal dimensions at diastole} + \text{posterior wall dimension at diastole}]^3 - \text{left ventricular end diastolic dimensions}^3)\} + 0.6$$

And the left ventricular mass index was calculated by dividing the left ventricular mass (g) by the height in metres$^{2.7}$ to correct the left ventricular mass for body size.

10 patients and no controls were excluded

The remaining 32 patients – 16 male and 16 female – and 30 controls were subjected to the rest of the echocardiographic examination and to the laboratory investigations mentioned below.

Tricuspid annular plane systolic excursion. It is a well-known established tool to assess right ventricular systolic function. Tricuspid annular plane systolic excursion was measured using the transapical four-chamber view on two-dimensional echocardiography. The end systolic distance between the tricuspid annulus and a fixed point of reference was subtracted from the end diastolic distance – in millimetres. Measurements were performed according to the American Society of Echocardiography guidelines.[11]

Systolic pulmonary artery pressure. The normal tricuspid regurgitation jet has a maximum velocity of <2.5 m/second. The normal estimated systolic pulmonary artery pressure (SPAP) is ⩽35 mmHg. Systolic pulmonary artery pressure can be estimated from peak tricuspid regurgitation velocity though continuous-wave Doppler using the modified Bernoulli equation in the absence of right ventricular outflow tract obstruction. This is the most useful non-invasive method to predict systolic pulmonary artery pressure. The mean right atrial pressure must be added to the result from the Bernoulli equation to determine the right ventricular systolic pressure. In the absence of right ventricular outflow obstruction, the systolic pulmonary artery pressure equals the right ventricular systolic pressure. The equation is given below:

$$\begin{aligned}&\text{Right ventricular systolic pressure}\\ &= \text{systolic pulmonary artery pressure}\\ &= 4(\text{maximum tricuspid regurgitation velocity})^2\\ &+ \text{mean right atrial pressure}\end{aligned}$$[14]

Pulsed Doppler method. This method was used for blood flow measurements from mitral and tricuspid valves: transmitral and transtricuspid early diastolic filling velocity (E), transmitral late diastolic filling velocity (A), and ejection time (ET) were measured and then E/A – that is, the ratio of transmitral early diastolic filling velocity to transmitral late diastolic filling velocity – was calculated. The global myocardial performance index (or Tei index) was calculated through conventional pulsed-wave Doppler using the following equation: Tei index = a – b/b, where "a" is the sum of isovolumetric contraction time and isovolumetric relaxation time and "b" is ejection time. The sum "a" of isovolumetric and isovolumetric relaxation time was determined by measuring the time from the end of transmitral or transtricuspid late diastolic filling – end of A-wave – to the onset of transmitral or transtricuspid early diastolic filling – onset of E-wave – minus "b", the ejection time. Ejection time was determined by measuring the left ventricular and right ventricular outflow velocity using pulsed Doppler in the parasternal long-and short-axis views, respectively, just below the aortic and pulmonary annulae.[15]

Pulsed tissue velocity. The following parameters were measured at the septum, mitral and tricuspid annulae: peak systolic myocardial tissue velocity (s′), peak early-diastolic myocardial tissue velocity (e′), and peak late-diastolic myocardial tissue velocity (a′).

For tissue Doppler imaging, Tei index was calculated using the same equation previously mentioned; isovolumetric contraction time, isovolumetric relaxation time, and ejection time were measured from tissue Doppler myocardial velocity images. Isovolumetric contraction time was defined as the duration of the bidirectional spike between a′ (peak late-diastolic myocardial tissue velocity) and s′ (peak systolic myocardial tissue velocity) in the tissue Doppler tracing. isovolumetric relaxation time was defined as the duration of the bidirectional spike between s′ (peak systolic myocardial tissue velocity) and e′ (peak early-diastolic myocardial tissue velocity). Ejection time was defined as the duration of

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s′ (peak systolic myocardial tissue velocity). The tissue Doppler imaging Tei index was calculated from the same equation used for the conventional Tei index.

Laboratory investigations

Fasting lipid profile. This was obtained using the Synchron Backman CX5 system and included the following measurements: total cholesterol, high-density lipoproteins, low-density lipoproteins, and triglycerides.

Troponin I measurement. Monoclonal antibody-based immunoassays specific for cardiac troponin I (9) were provided by SIEMENS in Egypt (Dimension Clinical Chemistry).

Statistical analysis

Data were statistically described in terms of mean ± standard deviation (± SD), median and range, or frequencies – that is, the number of cases – and percentages, as appropriate. Comparison of numerical variables between the study groups was performed using Student's t test for independent samples for comparing two groups when normally distributed, and using Mann–Whitney U test for independent samples when samples were not normally distributed. Comparison of numerical variables between more than two groups was performed using the one-way analysis of variance test with post hoc multiple two-group comparisons. For comparing categorical data, χ^2 test was performed. The exact test was used, instead, when the expected frequency was <5. Correlation between various variables was analysed using the Pearson moment correlation equation. p (Pearson coefficient) values <0.05 were considered statistically significant. All statistical calculations were carried out in SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, Illinois, United Sates of America) version 15 for Microsoft Windows.

Results

Demographic and anthropometric characteristics of the studied population

As shown in Table 1, there was a statistically significant difference between obese patients (group A) and controls (group B) as regards weight, height, systolic blood pressure (118.4 ± 7.3 versus 104.4 ± 6.7; p [Pearson coefficient] value <0.001) and diastolic blood pressure (81.1 ± 11.1 versus 66.6 ± 4.8; p [Pearson coefficient] value <0.001); the aforementioned parameters were all significantly higher in obese patients.

Table 1. Demographic and anthropometric characteristics of the groups

	Group A (n = 32)	Group B (n = 30)	p value
Age	10.8 ± 3.1	10.4 ± 3.0	0.6
Sex			
Male	16 (50.0%)	14 (46.7%)	0.8
Female	16 (50.0%)	16 (53.3%)	0.9
Weight (kg)	59.2 ± 17.8	35.9 ± 11.7	<0.001
Weight (SD)	4.5 ± 1.9	0.04 ± 0.8	<0.001
Height (cm)	138.2 ± 15.0	134.7 ± 15.7	0.4
Height (SD)	−0.16 ± 1.26	−0.79 ± 0.43	0.01
BMI (kg/m^2)	30.6 ± 4.2	19.1 ± 2.3	<0.001
BMI (SD)	3.3 ± 0.7	0.79 ± 0.82	<0.001
SBP	118.4 ± 7.3	104.4 ± 6.7	<0.001
DBP	81.1 ± 11.1	66.6 ± 4.8	<0.001
HR	92.1 ± 15.2	88.1 ± 14.1	0.3
Obstructive sleep apnoea symptoms	6%	0%	–

BMI = body mass index; DBP = diastolic blood pressure; HR = heart rate; p value = Pearson's correlation coefficient; SPB = systolic blood pressure.
Data are presented as mean value ± SD.

Table 2. Comparison between obese cases and controls as regards cardiac troponin I and lipid profile.

	Group A (n = 32)	Group B (n = 30)	p value
cTnI	0.14 ± 0.039	0.01 ± 0.01	**0.047**
LDL	101.8 ± 36.0	92.4 ± 20.3	0.2
HDL	40.7 ± 11.8	43.2 ± 11.1	0.4
TC	162.6 ± 29.4	146.9 ± 25.8	0.03
TGs	90.5 ± 38.5	57.2 ± 15.3	<0.001

cTnI = cardiac troponin I; HDL = high-density lipoprotein; LDL = low-density lipoprotein; p value = Pearson's correlation coefficient; TC = total cholesterol; TGs = triglycerides; .
Data are presented as mean value ± SD.

Laboratory data of the studied population

As shown in Table 2, there was a statistically significant elevation in levels of cardiac troponin I (0.14 ± 0.039 versus 0.01 ± 0.01; p [Pearson coefficient] value = 0.047), triglycerides (90.5 ± 38.5 versus 57.2 ± 15.3; p [Pearson coefficient] value <0.001), and cholesterol (162.6 ± 29.4 versus 146.9 ± 25.8; p [Pearson coefficient] value = 0.02) in obese Patients versus controls; obese patients had lower levels of the protective high-density lipoproteins, which did not reach statistical significance compared with controls.

Conventional echocardiographic parameters

These were shown in Table 3.

Parameters of left ventricular function. These values were calculated after exclusion of cases with left ventricular hypertrophy, which, as mentioned before,

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Table 3. Comparison between obese and controls regarding conventional echocardiographic parameters for systolic and diastolic functions.

	Group A (n = 32)	Group B (n = 30)	p value
IVSd (cm)	0.60 ± 0.12	0.58 ± 0.11	**0.8**
LVEDD (cm)	4.0 ± 0.6	3.9 ± 0.5	**0.7**
LVESD (cm)	2.6 ± 0.6	2.5 ± 0.3	**0.25**
LVPWd (cm)	0.71 ± 0.25	0.69 ± 0.16	**0.3**
LVMI ($g/m^{2.7}$)	37.4 ± 8.4	36.7 ± .8	**0.29**
FS%	38.4 ± 5.3	38.2 ± 4.6	0.9
EF%	68.6 ± 6.5	69.2 ± 5.7	0.7
TAPSE	17 ± 2.3	18 ± 2.6	0.8
Mitral valve (E/A ratio)	1.92 ± 0.37	1.93 ± 0.38	0.8
Mitral E (cm/second)	110.2 ± 14.3	114.3 ± 20.3	0.004
Mitral A (cm/second)	57.2 ± 10.3	59.3 ± 13.1	0.4
Conventional LV Tei index (mm/second)	0.37 ± 0.09	0.38 ± 0.12	0.6
SPAP (mmHg)	23 ± 3.2	22 ± 2.3	0.6
Tricuspid valve (E/A ratio)	1.49 ± 0.32	1.50 ± 0.33	0.32
Tricuspid E (cm/second)	76.7 ± 10.3	78.4 ± 11.1	0.28
Tricuspid A (cm/second)	51.8 ± 7.8	52.2 ± 8.4	0.34
Conventional RV Tei index (mm/second)	0.31 ± 0.08	0.30 ± 0.06	0.6

A = late-diastolic filling velocity; E = early-diastolic filling velocity; EF = ejection fraction; FS = fractional shortening; IVSd = interventricular septum dimension at diastole; LV = left ventricle; LVEDD = left ventricular end diastole dimension; LVESD = left ventricular end systole dimension; LVPWd = left ventricular posterior wall dimension at diastole; LVMI = left ventricular mass index; p value = Pearson's coefficient value; SPAP = systolic pulmonary artery pressure; TAPSE = tricuspid annular plane systolic excursion.
Data are presented as mean value ± SD.

Table 4. Comparison between obese cases and controls regarding tissue Doppler findings

TDI	Group A (n = 32)	Group B (n = 30)	p value
Mitral annular a′ (cm/second)	8.2 ± 2.0	7.0 ± 2.0	0.02
Mitral annular e′ (cm/second)	18.7 ± 3.4	17.3 ± 3.8	0.2
Mitral annular s′ (cm/second)	8.5 ± 1.5	7.4 ± 1.9	0.009
Septal a′ (cm/second)	8.9 ± 1.8	7.4 ± 1.8	0.001
Septal e′ (cm/second)	12.1 ± 3.0	16.4 ± 2.5	0.001
TDI derived LV Tei index (mm/second)	0.38 ± 0.11	0.38 ± 0.7	0.9
LV E/e′ ratio	9.0 ± 1.6	6.9 ± 1.4	0.001
Tricuspid annular a′ (cm/second)	7.8 ± 1.8	7.6 ± 1.7	0.4
Tricuspid annular e′ (cm/second)	16.5 ± 3.5	16.9 ± 4.2	0.4
Tricuspid annular s′ (cm/second)	8.2 ± 1.8	8.4 ± 1.4	0.5
TDI derived RV Tei index (mm/second)	0.30 ± 0.12	0.29 ± 0.11	0.5
RV E/e′ ratio	4.65 ± 0.98	4.63 ± 0.97	0.7

a′ = peak late-diastolic myocardial tissue velocity; e′ = peak early-diastolic myocardial tissue velocity; LV = left ventricle; LV E/e′ ratio = transmitral early-diastolic filling velocity to septal peak early-diastolic myocardial velocity ratio; RV E/e′ ratio = transtricuspid early-diastolic filling velocity to tricuspid annular peak early-diastolic myocardial velocity ratio; p value = Pearson's coefficient value; s′ = peak systolic myocardial tissue velocity; TDI = tissue Doppler imaging.
Data are presented as mean value ± SD.

have failed to show any statistically significant increase in left ventricular end diastolic and end systolic dimensions as well as in interventricular septal dimensions and posterior wall dimensions, between obese patients and controls.

There was, however, a statistically significant reduction in transmitral early-diastolic filling velocity in cases compared with controls (110.2 ± 14.3 versus 114.3 ± 20.3; p [Pearson coefficient] value = 0.004).

Parameters of right ventricular function. Including systolic pulmonary artery pressure, tricuspid annular plane systolic excursion, and transtricuspid early- and late-diastolic filling velocities failed to show any statistical difference between cases and controls.

Tissue Doppler parameters

These parameters are shown in Table 4.

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Parameters of left ventricular function. There was a statistically significant increase in septal a′ (8.9 ± 1.8 versus 7.4 ± 1.8; p value = 0.001) in obese patients compared with controls as well as a significant increase in transmitral early-diastolic filling velocity to septal peak early diastolic myocardial velocity ratio (E/e′ ratio) (9.0 ± 1.6 versus 6.9 ± 1.4; p [Pearson coefficient] value = 0.001), which is a potential index of left ventricular filling pressure in obese patients when compared with controls.

Parameters of right ventricular function. Including tricuspid annular peak systolic myocardial velocity, peak early- and late-diastolic myocardial velocities as well as transtricuspid early diastolic filling velocity to tricuspid annular peak early-diastolic myocardial velocity ratio failed to show any statistically significant difference in cases compared with controls.

Correlations

Figure 1 shows a statistically significant correlation between body mass index and transmitral early-diastolic filling velocity to septal peak early-diastolic myocardial velocity ratio (E/e′ ratio) with a correlation coefficient of 0.79 and a p (Pearson coefficient) value <0.000, whereas Figure 2 shows that cardiac troponin I is a good predictor of left ventricular diastolic dysfunction, being well correlated with transmitral early-diastolic filling velocity to septal peak early diastolic myocardial velocity ratio (E/e′ ratio) (R [Correlation coefficient] = 0.61 and p [Pearson Coefficient] = 0.000); finally, Figure 3 shows poor correlation between systolic blood pressure and troponin I with a correlation coefficient of 0.11 and a p (Pearson coefficient) value of 0.31.

Multivariate analysis of predictors of troponin I as shown in Table 5.

It has been shown that the best predictor of troponin I is the diastolic function of left ventricle, represented by the transmitral early-diastolic filling velocity to septal peak early-diastolic myocardial velocity ratio (E/e′ ratio) with a Pearson predictive value of <0.001 compared with right ventricular diastolic function and systolic blood pressure, which failed to show a statistically significant predictive value for Troponin I.

Discussion

To our knowledge, this study is the first study on left ventricular diastolic dysfunction in obese patients who do not display left ventricular remodelling in the form of left ventricular hypertrophy or dilatation. Also, this is the first study to combine tissue Doppler imaging indices together with a biomarker of myocardial injury such as troponin I. Last but not least this is the first study to involve troponin I as a marker of myocardial injury in obese patients as all previous studies were conducted on troponin T, especially as a marker of obstructive sleep apnoea-induced myocardial injury in obese patients.

In the current study, systolic blood pressure and diastolic blood pressure showed a statistically significant elevation in obese patients compared with controls. Similarly, Schiel et al studied 86 obese children and 86 controls, and found that obese children had significantly higher blood pressure values – systolic 117.9 ± 9.7 mmHg, diastolic 75.6 ± 8.8 mmHg – than control subjects – systolic

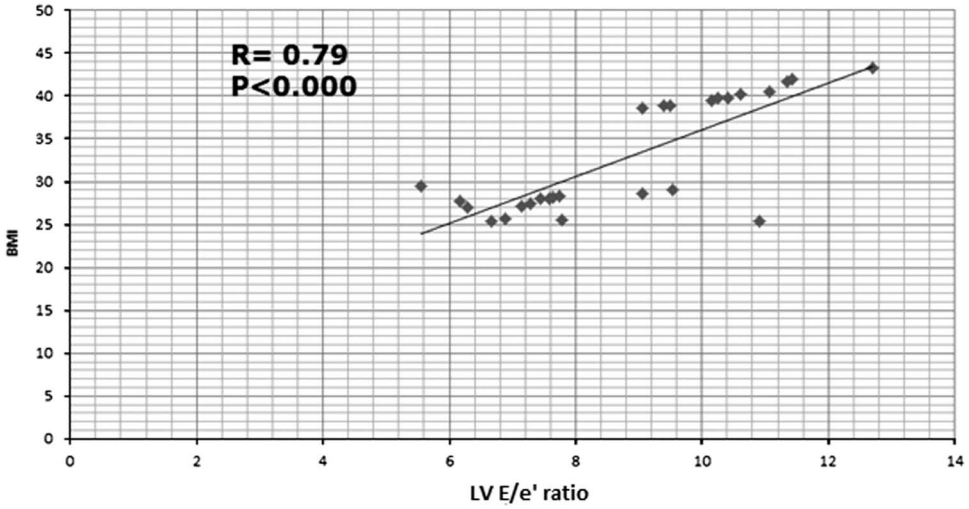

Figure 1.
Correlation between body mass index (BMI) (kg/m^2) and transmitral early-diastolic filling velocity to septal peak early-diastolic myocardial velocity ratio (LV E/e ratio) in obese patients. Note that there is a direct relationship between BMI and LV E/e ratio. The higher the BMI the higher the LV E/e ratio.

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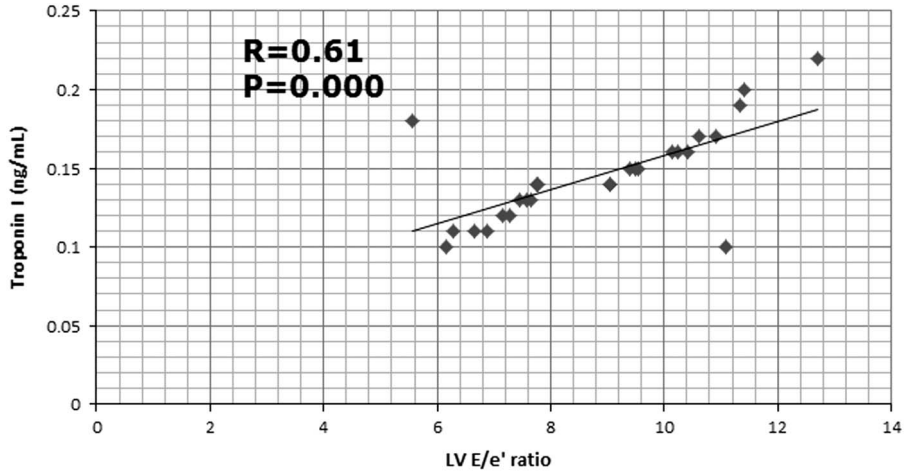

Figure 2.
Correlation between troponin I (cTnI) (ng/ml) and transmitral early-diastolic filling velocity to septal peak early-diastolic myocardial velocity ratio (LV E/e ratio) in obese patients. Note that there is a direct relationship between cTnI and LV E/e ratio; the higher the LV E/e ratio the higher the cTnI levels.

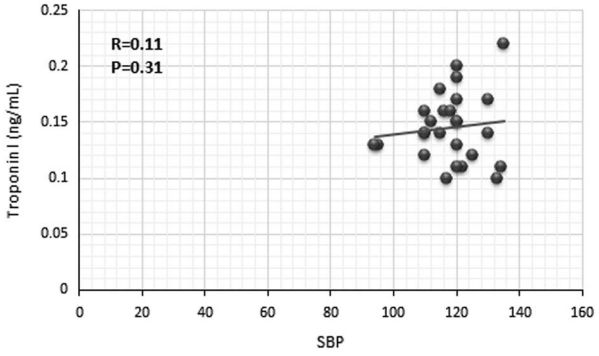

Figure 3.
Correlation between troponin I (ng/ml) and systolic blood pressure (SBP) in obese patients: there is no statistically significant correlation, with a correlation coefficient (R) = 0.11 and a Pearson coefficient value (p value) = 0.31.

111.4 ± 11.0 mmHg, diastolic 69.5 ± 8.8 mmHg, $p < 0.001/0.001$.[15] A logical explanation was presented by Palmieri and Bella,[16] who stated that obesity predisposes to hypertension because of concomitant metabolic and haemodynamic abnormalities, leading to inadequate lowering of systemic resistance and, therefore, to a more severe cardiovascular burden.

Despite the elevation in systolic and diastolic blood pressures, the findings from this study failed to demonstrate a positive correlation with either troponin I or left ventricular diastolic function represented by transmitral early-diastolic filling velocity to septal peak early-diastolic myocardial velocity ratio (E/e′ ratio). This was in agreement with findings from a study previously conducted by Di Salvo et al,[17] which demonstrated abnormal myocardial deformation in obese non-hypertensive patients.

Table 5. Multivariate analysis for predictors of Troponin I

	Unstandardised Coefficients			
	Coefficient value	SE	Test statistics	p value
LV E/e′	0.01	0.001	9.3	<0.001
RV E/e′	0.0002	0.003	0.77	0.44
SBP	0.0006	0.003	0.19	0.84

LV E/e′ ratio = early-diastolic filling velocity to septal peak early diastolic myocardial velocity ratio; RV E/e′ ratio = early-diastolic filling velocity to tricuspid annular peak early-diastolic myocardial velocity ratio; SBP = systolic blood pressure, p value: Pearson's coefficient.

Obesity induces several modifications in cardiac structure and function, dependent on haemodynamic overload, and is in itself a risk factor for heart failure. Several previous studies have shown the preservation of ejection fraction and fractional shortening in obese subjects compared with controls,[7] and the subsequent unreliability of these indices for the detection of subclinical affection of myocytes in obese patients. Our study just confirmed those findings, highlighting the importance of the use of other parameters of diastolic function for early detection of myocardial affection in obese patients.

Studies exploring the relationship between severity of obesity and increase in left ventricular mass have consistently shown a positive correlation. Several factors may lead to eccentric left ventricular hypertrophy; one of them is myocyte infiltration with fat and alteration in loading conditions of the myocardium. Those studies have also pointed to a causative relationship between left ventricular hypertrophy and left ventricular diastolic dysfunction.[8] In the current study parameters of left

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ventricular diastolic dysfunction such as septal peak late-diastolic myocardial tissue velocity (a′) and transmitral early-diastolic filling velocity to septal peak early-diastolic myocardial velocity ratio (E/e′ ratio) were affected in obese patients without statistically significant left ventricular hypertrophy compared with controls. This denotes the usefulness of utility of tissue Doppler imaging-derived parameters of diastolic dysfunction for screening of myocardial affection in patients with frank obesity or even in those with borderline body mass index.

The hallmark of dyslipidaemia in obesity is elevation of triglycerides. Triglyceride elevation may be the underlying cause of other lipid abnormalities encountered in obese patients such as low levels of high-density lipoproteins.[18] As mentioned before, adiponectin, a cytokine released from the adipose tissue, plays a role in one of the most important mechanisms underlying obesity cardiomyopathy.[5] This points towards the role of dyslipidaemia in induction of myocardial injury in obese patients. In the current study, statistically significant elevation of triglycerides has been depicted in obese patients, which is in concordance with the aforementioned studies.

The cardiac troponin complex is immobilised on the thin filament of the contractile apparatus of the cardiac myocytes and plays a critical role in the regulation of excitation–contraction coupling in the heart. With myocardial injury, cardiac troponin I and cardiac troponin T are both released from necrotic myocardium as intact proteins. Several studies have shown that cardiac troponin I can be detected earlier in the bloodstream than can cardiac troponin T, which makes it a better marker of subtle myocardial injury.[19]

All previous studies have focussed on the use of cardiac troponin T as a maker of obstructive sleep apnoea-induced myocardial injury. Sou et al[20] showed no statistically significant correlation between parameters of systolic and diastolic dysfunction and cardiac Troponin T. This is probably due to delayed release of cardiac troponin T into the bloodstream following myocardial injury; this fact points to the need for a biomarker for earlier detection of subtle myocardial injury in obese patients.

In the current study, not only did troponin I show a marked elevation in obese patients compared with controls but it also showed a statistically significant correlation with transmitral early-diastolic filling velocity to septal peak early-diastolic myocardial velocity ratio(E/e′ ratio); this may point to the possible utility of cardiac troponin I as a potential early marker of obesity cardiomyopathy even in the absence of left ventricular hypertrophy or left ventricular dilatation.

Troponin I, however, failed to be correlated with any of the parameters of right ventricular function, whether using conventional or tissue Doppler. This may be attributed to the low prevalence (6%) of obstructive sleep apnoea symptoms, as previously mentioned, in the studied subjects. The low prevalence of obstructive sleep apnoea symptoms may also explain the absence of pulmonary hypertension in cases and the absence of any statistical difference between cases and controls as regards parameters of right ventricular function.

Study limitations

There were several limitations in the current analysis. First, the sample size was limited, thus calling for other analyses with a larger number of patients. Another limitation is the cross-sectional nature of the study, which overlooks the effect of weight reduction measures on the possible normalisation of affected parameters. Added to the limitations is ignoring the effect of hyperinsulinaemia as a potential cause for myocardial injury. The correlation of insulin levels with troponin I and transmitral early-diastolic filling velocity to septal peak early-diastolic myocardial velocity ratio (E/e′ ratio) may offer new insights into the mechanisms of obesity cardiomyopathy. Finally, screening for obstructive sleep apnoea in patients should be carried out as mentioned by Di Salvo et al using polysomnography rather than on the basis of presence or absence of habitual snoring.[17]

Conclusion

The current study points to the potential use of transmitral early-diastolic filling velocity to septal peak early diastolic myocardial velocity ratio (E/e′ ratio) and cardiac troponin I as early markers of obesity cardiomyopathy even in the absence of left ventricular hypertrophy and dilatation. This contradicts the previous assumption about the mandatory linkage between left ventricular diastolic dysfunction and left ventricular hypertrophy.

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Conflicts of Interest

None.

Ethical Standards

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national guides and have been approved by the ethical committee of Cairo University.

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