INTERRELATIONS BETWEEN SERUM N-TERMINAL PRO B-TYPE NATRIURETIC PEPTIDE (NT-PROBNP) LEVELS AND EARLY CARDIOVASCULAR RISK FACTORS AND ECHOCARDIOGRAPHIC PARAMETERS IN OBESE ADOLESCENTS

OBEZ ADOLESANLARDA SERUM N-TERMİNAL PRO B-TİPİ NATRİÜRETİK PEPTİT (NT-PROBNP) DÜZEYLERİ, ERKEN KARDİYOVASKÜLER RİSK FAKTÖRLERİ VE EKOKARDİYOGRAFİK PARAMETRELER ARASINDAKİ İLİŞKİLER

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ABSTRACT

INTRODUCTION: This study aimed to evaluate the associations between the N-terminal pro-B-type natriuretic peptide (NT-proBNP) levels and the metabolic, echocardiographic parameters, carotid intima-media thickness (IMT) and epicardial adipose tissue thickness (EATT) in adolescent obesity.

MATERIAL AND METHOD: The study participants consisted of 138 obese adolescents in the study group and 63 non-obese adolescents as control subjects. All the subjects underwent transthoracic echocardiographic examination for determination of left ventricular (LV) systolic function and mass index, myocardial tissue rates, and myocardial performance index (MPI). Epicardial adipose tissue thickness and carotid IMT were also measured during echocardiography. Serum NT-proBNP levels were measured at the time of the evaluation.

RESULTS: The NT-proBNP values averaged 67.20 ± 64.40 pg/ml in mildly-moderately obese, 76.00 ± 49.70 pg/ml in the severely obese group and 44.30 ± 23.30 pg/ml in the control group (p = 0.007, p = 0.002, respectively). The average carotid IMT was 0.91 ± 0.23 and 0.88 ± 0.18 mm in the obesity groups and 0.52 ± 0.08 mm in the control group (p= 0.0001), but differences were not observed between obesity groups and the EATT which averaged 7.38 ± 1.76 and 7.42 ± 1.55 mm in the obesity groups and 4.28 ± 0.79 mm in the control group (p = 0.0001). The NT-proBNP levels showed statistically significant positive correlations with left ventricular systolic and diastolic functions, carotid IMT, or EATT values, especially in severe obesity.

CONCLUSION: The study showed higher measurements of serum NT-proBNP levels in mildly-moderately and severely obese adolescents than control and NT-proBNP might be a useful marker for predicting atherosclerosis and cardiac dysfunction in the obese adolescent.

Keywords: *Adolescent obesity, echocardiography, N-terminal pro-B-type natriuretic peptide, atherosclerosis, early cardiovascular risk*

ÖZET

AMAÇ: Bu çalışmada; adolesan obezitesinde N-terminal pro B- tipi natriüretik peptit (NT-proBNP) düzeyleri ile metabolik, ekokardiyografik parametreler, karotis intima media ölçümü (IMT) ve epikardiyal yağ dokusu (EATT) düzeyleri arasındaki ilişki incelenmiştir.

GEREÇ VE YÖNTEMLER: Çalışma grubuna 138 obez ergen ve kontrol grubuna ise 63 obez olmayan ergen kabul edildi. VKİ'ye göre; 33,90± 9,30 olan hastaların 95'i hafif-orta obez, 39,40± 4,00 olan hastaların 43'ü ise şiddetli obez olacak şekilde alt gruplara ayrıldı. Tüm hastalara sol ventrikül (SV) sistolik fonksiyonu ve kitle indeksi, miyokardiyal duvar kalınlığı ve miyokardiyal performans indeksi (MPI) saptanması için transtorasik ekokardiyografik inceleme yapıldı. Ekokardiyografide epikardiyal yağ dokusu ve karotis IMT ölçüldü. Eş zamanlı serum NT-proBNP değerleri ölçüldü.

BULGULAR: NT-proBNP değerleri; şiddetli obez grupta 76,00 ± 49,70 pg / ml, hafif-orta derece obez grupta 67,20 ± 64,40 pg / ml(p=0,007) ve kontrol grubunda ise 44,30 ± 23,30 pg / ml (p= 0,002) olarak bulundu (p= 0,007, p= 0,002).Ortalama karotis IMT ölçümleri sırasıyla obez gruplarda 0,91± 0,23 ve 0,88 ± 0,18 mm kontrol grubunda ise 0,52 ± 0.08 mm idi (p= 0;0001). Obez alt gruplar arasında istatistiksel anlamlı farklılık yoktu. EATT ölçümleri obez alt grupları ortalaması, 7,42 ± 1.55 mm ve 7.38± 1,76, kontrol grubunda ise 4,28 ± 0,79 mm olarak ölçüldü (p= 0,0001). NT-proBNP seviyesi, şiddetli obezitede sol ventrikül sistolik ve diyastolik fonksiyonları ile karotis IMT veya EATT oranları fonksiyonel olarak belirgin pozitif korelasyon göstermiştir.

SONUÇLAR: Çalışmamızda, hafif-orta ve şiddetli obez ergenlerde serum NT- proBNP düzeylerinin kontrol grubuna göre daha yüksek olduğunu ve NT- proBNP'nin obez ergenlerde ateroskleroz ve kardiyak disfonksiyonu öngörmede yararlı bir belirteç olabileceğini gösterdi.

Anahtar Kelimeler: *Adolesan obezitesi, ekokardiyografi, N-terminal pro-B tipi natriüretik peptid, aterosklerozis, erken kardiyovasküler risk*

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INTRODUCTION

Childhood obesity is accompanied by increased cardiovascular disease (CVD) risk profile in adulthood (1). Hypertension, hypercholesterolemia, dyslipidemia, cardiomyopathy, and coronary heart disease are known as cardiovascular complications of obesity, together with insulin resistance (IR), diabetes mellitus, and sleep apnea, which often accompany with obesity (2,3). Epidemiological, echocardiographic, and autopsy studies have identified obesity cardiomyopathy as an isolated clinical entity (4-6). In these studies, elevated body mass index (BMI) is described as a risk factor for left ventricular (LV) remodeling and overt heart failure. Left ventricular enlargement and eccentric hypertrophy are the most common morphological cardiac abnormalities in obese individuals (5).

Cardiac remodeling depends on the intensity and duration of obesity and the influence of adverse loading conditions (7,8).

N-terminal-pro-brain natriuretic peptide (NT-proBNP) and brain natriuretic peptide (BNP) are useful for the diagnosis of heart failure, and their high levels in serum and plasma, respectively, are related to wall stress, which is often increased in severe obesity. High BNP as well as high NT-proBNP are new promising cardiovascular risk markers and have been associated with high blood pressure, and LV hypertrophy (9,10). These are sensitive markers of cardiac dysfunction and may be useful in the early diagnosis of cardiac loading.

NT-proBNP is extremely reliable due to the high negative predictive value so it is used more frequently than from BNP (11,12). Recent findings on the relationship between NT-proBNP and metabolic parameters, morphologic and dynamic cardiac abnormalities in adolescent obesity are still inconsistent and controversial. Therefore, the aim of the present study was to evaluate the association of NT-proBNP to cardiovascular risk factors, echocardiographic and metabolic parameters in obese adolescents.

MATERIALS and METHODS

Patients

In this study, 138 pubertal obese adolescents aged between 116-210 month (mean age for n=66 girls is 160.90 ± 20.30 mo and for n=72 boys is 164.90 ± 21.20 mo) and 63 healthy control adolescent (mean age 170.30 ± 27.00 mo, range 102–216 mo) were enrolled and evaluated according to their sex and age between September 2011 to November 2012. During this period, the cases admitted to the Pediatric Endocrinology Department of Istanbul Sisli Etfal Education and Research Hospitals with the complaint of obesity were enrolled in the study. The 63 healthy age-and sex-matched adolescents selected to be control subjects were referred for cardiac murmurs detected by auscultation but later proved to be innocent murmurs by clinical and laboratory methods.

The adolescent with anemia, chronic conditions, psychiatric illnesses, or administration of medications for any reason was excluded from the study. During the pubertal evaluation, Tanner staging was used. Testis size ≥ 4 ml in males and the Tanner stage of breast development ≥ stage II in females were assumed as puberty.

The adolescents receiving treatment for any reason, syndromic ones and patients having either an endocrinological disease or familial dyslipidemia were dismissed from the study. Patients were excluded if they had any systemic disease, including type 1 or type 2 diabetes mellitus, taking medications, or had a condition is known to affect insulin action, or insulin secretion (e.g. glucocorticoid therapy, hypothyroidism, Cushing's disease). This study was conducted in accordance with the guidelines proposed in the Helsinki Declaration and was received the approval of Istanbul Sisli Etfal Education and Research Hospitals Ethics Committee on 19 July 2011. The informed consent form was obtained from the patients or the legal guardians.

Anthropometric Variables

Anthropometric measurements were performed in all patients. Height and weight were measured with an empty bladder in post absorptive conditions. For height measurement, Harpenden stadiometer (sensitive to 0.1 cm) was used, and weight was determined to the nearest 0.1 kg on a standard physician's beam scale with the subject dressed only in light underwear without shoes. BMI was calculated by the weight (kg)/height (m2) formula. To compare BMI for different ages and for both boys and girls, BMI SDS was considered. Body mass index SDS was calculated with the Lambda, Mu and Sigma (LMS) method. The Z-score represents the number of SD above or below the considered population mean value based on standardized tables for children (13). Obesity was defined as a BMI above 2 SD which corresponds to the 97th adjusted for age and gender. The degree of obesity was determined using BMI SDS and the cases were divided into two groups according to their SDS. BMI SDS between 1.65–2.49 and 2.50–2.99 represented mildly-moderately and severe obesity, respectively (14). Waist circumference was measured with a non-elastic tape measure. The waist circumference was recorded at the end of expiration and between the midpoint of the last rib and superior iliac crest (15).

Blood Pressure

Blood pressure was measured by a mercury sphygmomanometer with an appropriate sleeve according to different ages after at least ten-minute rest. We used the National High Blood Pressure Education Program Working Group normal values for children as a reference to evaluate blood pressure measurements (16). Blood pressure ≥ 95th percentile for age, sex and height were accepted as hypertension.

Laboratory Analyses
Indices of all patients, including glucose, insulin, lipid profiles [(triglyceride (TG), total cholesterol (T. CHO), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein-cholesterol (LDL-C), and very-low-density lipoprotein-cholesterol (VLDL-C)] and high-sensitivity C-reactive protein (hs-CRP) were recorded in the morning after an overnight hunger. The glucose oxidase method was used in the determination of blood glucose levels. Insulin levels were measured using a radioimmunoassay kit (Immunotech kit). Serum lipid profiles were measured using a modular analytical system (Roche/Hitachi). Serum hs-CRP was determined by using particle-enhanced immunoturbidimetry with the latex micro particles sensitized in the duck anti-CRP Immunoglobulin Y (Missouri).

N-Terminal Pro B-Type Natriuretic Peptide Measurement
In both groups, blood samples of 0.5 ml were obtained from the antecubital vein using a heparinized syringe, and serum NT-pro BNP was measured by a solid-phase, enzyme-labeled chemiluminescent immunometric assay. Immulite 1000 was supplied by Siemens Medical Solutions Diagnostic (Los Angeles, CA, USA).

Insulin Sensitivity Measurement
Insulin resistance was analyzed using the homeostasis model assessment of insulin resistance (HOMA-IR) based on the following formula: (fasting insulin mIU/Lx fasting glucose mmol/L)/22.5. A HOMA-IR value greater than 3.16 was used to determine IR in pubertal patients (17).

Echocardiographic Evaluation
Transthoracic echocardiographic examinations were performed by a single experienced pediatric cardiologist. Echocardiographic measurements were performed with a Vivid 7 Pro (GE Vingmed Ultrasound, Horten Norway). An electrocardiogram was taken from all subjects. The patients were studied without sedation while they were lying in the left lateral positions. 3 MHz transducers were used in all echocardiographic studies. All possible echocardiographic windows obtained from the different Doppler devices such as two-dimensional, colored, pulsed-wave, continuous-wave, and pulsed-wave tissue was analyzed for the subjects lying supine or in the left lateral semi recumbent position. Left ventricular systolic functions and LV mass index was assessed using M-mode and 2 D, whereas myocardial tissue rates and myocardial performance indices (MPI) were studied using tissue Doppler methods.

Conventional echocardiography measurements were performed by using recommendation of the American Society of Echocardiography (18). The LV mass and the LV mass index were calculated by using the method of Woythaler and his colleagues, which is also a modification of the method of Devereux and Reichek (1). According to this calculation, LV mass is 1.04 ([left ventricular diameter at end diastole + end-diastolic interventricular septum thickness -left ventricular posterior wall thickness at end-diastole] x 3 - [left ventricular diameter at end diastole] x 3 - 13.6]), and LV mass index is the LV mass/body surface area.

Pulsed-wave Tissue Doppler Imaging
A pulsed Doppler and tissue Doppler were performed using a 3-MHz transducer. We measured early (E) and atrial (A) transmitral maximal flow velocities by pulsed-wave Doppler. Then we calculated the ratio E/A. Tissue Doppler sample volume of 2–5 mm, a Nyquist limit adjusted to a velocity rate of 15 to 20 cm/s and monitor velocity to 100 mm/s. The gain was minimized to allow for a clear tissue signal with minimal background noise. Using the apical four-chamber view, the sample volume was placed at the mitral valve annuli at the LV free wall. Early (E') and late (A') diastolic peak velocities were measured. The ratio of early and late diastolic annular velocities was calculated. Cardiac time intervals; isovolumic contraction time, isovolumic relaxation time and systolic ejection time were measured. Tissue Doppler-derived by MPI was calculated as (isovolumic contraction time + isovolumic relaxation time)/ systolic ejection time. And we also measured E' wave acceleration and deceleration time.

The thickness of the epicardial adipose tissue was measured from the right ventricular free wall in the parasternal long axis view. The epicardial adipose tissue was identified as an echo-free space in the pericardial layers on the two-dimensional echocardiography, and its thickness was measured perpendicularly on the free wall of the right ventricle at end diastole (19,20).

To standardize the set point of measurement between different observers, the aortic annulus was used as the anatomic reference. The measurement was performed at a point on the free wall of the right ventricle along the midline of the ultrasound beam perpendicular to the aortic annulus. The average value from three cardiac cycles was used for the statistical analyses.

Carotid Intima-Media Thickness Measurements
Carotid IMT measured by 7 MHz probs. In three groups, the carotid IMT was measured from the common carotid artery at a point 5 mm proximal to its bifurcation, as often preferred in the literature (21). The transducer was placed perpendicular to the common carotid artery, and its long axis was adjusted parallel to the flow direction. Images obtained from the anterior wall were magnified threefold, and measurements were made with an electronic caliper. The measurements from three consecutive beats were averaged and recorded as the carotid IMT (22).

Statistical Analysis
Differences among the study groups were analyzed using Student's t-test. Correlations were analyzed

using Pearson's correlation coefficient. Using multiple regression analyses, correlations were adjusted for age and gender, body composition (body mass index and waist circumference), metabolic cardiovascular risk factors (glucose, insulin, and lipid levels), hemodynamic cardiovascular risk factors (heart rate, blood pressure), and subclinical cardiovascular damage (LV mass index, LV ejection fraction, MPI, carotid IMT and EATT), calculating the standardized regression quotient (B). Only variables with P values <0.10 entered the final multiple regression models, in which we performed by stepwise, backward selection. All p values less than 0.05 were considered statistically significant.

RESULTS

The characteristics of the study population were shown in Table 1. This study investigated 138 obese adolescents and 63 healthy age-and sex-matched control. The obese adolescents were divided into two groups based on BMI-SDS. The three groups did not differ significantly in terms of age (170. 30 ± 27. 00, 169. 60 ± 20. 10 , 162.10 ± 23.20 mo, respectively) (p>0.05). However, the groups differed significantly in terms of BMI (20. 10 ± 1. 30, 33.90 ± 9.30, 39.40 ± 4.00 kg/m2, respectively) (p=0.001). The obesity and the control groups did not differ significantly according to the heart rate (79 ± 5 vs. 78 ± 7 beats/min; p>0.05) or average hemoglobin value (13.10 ± 1.04 vs. 12.90 ± 1.10 g/dl, p>0.05). However, the average systolic and diastolic blood pressure values differed significantly between the obesity and the control groups (p= 0.001) **(Table 1).**

The average LV mass index was greater in the mildly-moderately and severely obese group than in the control group (88.50 ± 2.00, 87. 50 ± 34.80 and 62.40 ± 18.20 g/m2 respectively= 0.012), but there was no difference between the groups in obesity (p>0.05).

The average carotid IMT was 0.88 ± 0.18 and 0.91 ± 0.23 mm respectively in the mildly-moderately and severely obese group and 0.52 ± 0.08 mm in the control group (p=0.002). However, significant differences were not observed between obesity groups (p>0.05). The average EATT was 7.38 ± 1.76 and 7.42 ± 1.55 mm respectively in the mildly-moderately and severely obese and 4.28 ± 0.79 mm in the control group (p= 0.0032).

In the all obese group, there were statistically significant correlations between BMI and LV mass index (p= 0.03 and r=0.38), MPI (p= 0.003 and r= 0. 72) carotid IMT (p= 0.033 and r=0.34) and EATT (p=0.023 and r=0.45). Moreover; a statistically significant positive correlation was found between EATT and the carotid IMT (p= 0.002 and r= 0. 60)

NT-proBNP In Relation To Obesity, Metabolic And Hemodynamic Risk Factor

The NT-proBNP values averaged 76.00 ± 49.70 pg/ml pg/ml in the severe obese group and 44.30 ± 23.30 pg/ml in the control group (p = 0.001). However, NT-proBNP levels were not different between the obesity groups.

NT-proBNP was positively correlated with BMI (r= 0.667, p < 0.001), waist circumference (r = 0.545, p < 0.001), hip circumference (r =0.516, p < 0.001), diastolic blood pressure (r = 0.598, p < 0.001) in the severely obese group **(Table 2).**

After adjusting for age and gender using multiple regression analyses, higher NT-proBNP was associated with higher BMI (B= 0.13; P<0.05), higher waist circumference (B= 0.12; P<0.05), lower serum triglycerides (B=-0.16; P<0.001), higher serum insulin (B= 0.15; P< 0.001), and higher diastolic blood pressure (B= 0.07; P<0.01).

Nt-proBNP In Relation Subclinical Cardiovascular Damage

The variables correlated to NT-proBNP were left ventricular posterior wall diastolic thickness (r= 0.424, p < 0.001), interventricular septum diastolic thickness (r =0.495, p < 0.001), left ventricular posterior wall systolic thickness (r =0.456, p <0.001), left ventricular posterior wall thickness (r =0.544, p<0.001), ejection fraction (r =0.297, p =0.021), acceleration time (r = 0.279, p =0.045), LV mass index (r =0.649, p <0.001), MPI (r =0.288, p = 0.042), EATT (r =0.339, p=0.022) and the carotid IMT (r =0.325, p =0.003) in severe obesity **(Table 2).**

After adjusting for age, gender, and metabolic and hemodynamic cardiovascular risk factors, NT-proBNP was correlated to LV ejection fraction (B= 0.08; P<0.001), LV mass index (B= 0.04; P < 0.05) and MPI (B= 0.06; P<0.01) in multiple regression analyses.

NT-proBNP In Relation To Hypertension

Obese adolescents with normal and elevated systolic and diastolic blood pressures (109.10 ± 9.40 mmHg systolic and 67.30 ± 4.30 mmHg diastolic vs. 120.10 ± 11.90 mmHg systolic and 80.50 ± 7.50 mmHg diastolic) were further compared for serum NT-proBNP, LVMI and carotid IMT significant correlations were noted (p<0.05) **(Table 3).**

DISCUSSION

This cross-sectional study provides evidence that obese adolescents exhibit increased carotid IMT, increased EATT and abnormalities of LV structure related with NT-proBNP levels. This study showed a positive significant association between increased NT-proBNP levels and increased carotid IMT and EATT. To our knowledge, we are the first to demonstrate that between serum NT-proBNP is higher in patients with the obesity attributable to straight relationships between serum NT-proBNP and LV mass index, LV ejection fraction and myocardial performance index independently of age, gender, and metabolic and hemodynamic cardiovascular risk factors in the obese adolescent.

Childhood obesity caused changes in the heart's structure and function and it is associated with cardiovascular risk factors (23). Starting from childhood, myocardial mass parallels the increase in BMI. It is shown that left ventricular hypertrophy occurs in obesity and that this hypertrophy is associated with an increased risk of CVD, mortality, and morbidity (24,25).

In the current study, the LV mass index was higher in the obese group than in the control group. This difference was statistically significant because it is known that LV hypertrophy affects diastolic function negatively. On the other hand, in obese patients with no ventricle hypertrophy, cardiac functions may deteriorate. Moreover, this deterioration may be seen in each ventricle (26-28).

Obesity is an important risk factor for atherosclerotic cardiovascular disease. In an adulthood study, the EATT was significantly correlated with the severity of coronary artery stenosis for patients with the known coronary artery disease (29). Obesity seems to be a predisposing factor for the accumulation of excessive epicardial fat (30), but with our data, there was no correlation between EATT and BMI in obese cases.

Carotid IMT measurement is a widely used method in the early diagnosis of atherosclerosis (31). Di Salvo et al. (32) showed that carotid IMT was not greater in obese children than in nonobese control children. Iannuzzi et al. (33) reported that carotid IMT was increased in children with metabolic syndrome, but that this increase was not statistically significant. Numerous studies have shown that carotid IMT was increased in obese children and it is widely agreed that this increase in childhood is related to atherosclerosis in adulthood (34-35). In our study, too, the carotid IMT was significantly increased in the obese group compared to the control group. In addition to the study, a statistically significant correlation was found between EATT and carotid IMT. It is shown that the thickness of epicardial adipose tissue is associated with atherosclerosis. According to this result, the thickness of epicardial adipose tissue in obese patients may be associated with atherosclerosis.

We found significant differences in NT-proBNP levels among the groups. In children, there are a few studies examining the relations between NT-proBNP and obesity. In one study NT-proBNP concentrations were found to be higher in obese children than in the control group (40). In this study, the average serum NT-proBNP levels were found to be significantly higher in obese children than in the control group.

Natriuretic peptide hormones are very important for the maintenance of extracellular fluid volume within a narrow range despite wide variations in dietary sodium intake. The primary stimulus for natriuretic peptide release is myocyte stretching. Plasma levels of BNP and NT-proBNP are elevated in adult patients with a wide range of heart diseases including LV systolic and diastolic dysfunction. Thus, they serve as markers for heart disease 36. Increased NT-proBNP was found to be closely related to cardiac structure and function and to be a strong independent indicator for long-term outcome in obese patients. Serum NT-proBNP levels are found to be increased in cases with left ventricular systolic and diastolic dysfunction (37-38). Kim et al. (39) studied adults with hypertrophic cardiomyopathy and found a positive correlation between the serum NT-proBNP levels with the end-diastolic thickness of the interventricular septum and LV mass index. The serum NT-proBNP levels were higher in cases with diastolic dysfunction than in normal control subjects.

Other adult studies have found the reliability of the NT-proBNP to be comparable with tissue Doppler echocardiography and even higher than that of conventional echocardiography because this method had the best negative predictive value among the three methods and also exhibited a strong correlation with the left ventricular filling index measured invasively. Consequently, it was reported that this method was reliable for detecting patients with isolated diastolic dysfunction (37-39).

In this study, NT-proBNP levels were found to be significantly higher in obese adolescent than healthy controls and it levels the serum NT-proBNP levels were higher in obese cases with asymptomatic cardiac dysfunction than in normal control subjects. To the best of our knowledge, serum NT-proBNP levels in obese children have been previously reported in two different studies to date regardless of the presence of systolic and/or diastolic dysfunction. Sarıtaş et al. (40) showed that NT-proBNP was greater in obese children than in nonobese control children but they did not find a correlation between the serum NT-proBNP levels and the body weight, carotid intima-media thickness, EATT, systolic and diastolic blood pressures, LV mass index and MPI values. Contrary to this study performed with children, in our study statistically significant correlations were detected between the serum NT-proBNP and BMI, blood pressure, LV mass index, carotid IMT and EATT in severely obese adolescent compared with non-obese control adolescent. Other pediatric studies, NT-proBNP levels in obese children were not different from healthy controls (41). Moreover; in this study, NT-proBNP was not associated with cardiac function.

Similar to the studies performed with adults, statistically significant correlations were detected between the mitral annular myocardial performance index values and serum N-terminal pro-B-type natriuretic peptide levels in obese adolescent compared with nonobese control (42).

In the hypertensive adult, statistically significant positive correlations have been reported between the serum NT- proBNP and blood pressure and/or LV hypertrophy (9). In male children, NT-proBNP concentrations were found to be lower in the obese than the normal BMI group but higher in the obese hypertensive than the obese normotensive group (43). In another pediatric study, NT-proBNP levels in hypertensive obese children were not different from non-hypertensive (40). In this study, the average serum N-terminal pro-B-type natriuretic peptide levels, average LVMI, and carotid IMT were found to be significantly higher in the hypertensive obese adolescent than the non-hypertensive obese group.

CONCLUSIONS

Consequently, cardiac structural and functional changes affect systolic and diastolic functions in obese patients and increase the serum NT-proBNP values positive correlated with the LV mass index, MPI, EATT, and carotid IMT. The LV mass index computed with the Doppler and tissue Doppler methods can be an important parameter for the early detection of cardiac dysfunction in the obese adolescent. Measurements of the serum NT-proBNP levels might be related to elevation of, especially diastolic dysfunction. Carotid IMT and EATT measurements in an obese adolescent may be useful in predicting atherosclerosis in adulthood. In our study, a significant positive correlation was found between NT-proBNP and carotid IMT and EATT in severely obese cases. A thus high NT-proBNP level may be a risk factor in predicting atherosclerosis in adulthood.

Summary Points

- Childhood obesity is accompanied by an increased cardiovascular disease risk profile in adulthood
- N-terminal-pro-brain natriuretic peptide (NT-proBNP) and brain natriuretic peptide are useful for the diagnosis of heart failure, and their high levels in serum and plasma, respectively, are related to wall stress, which is often increased in severe obesity.
- In this study, serum NT-proBNP levels were found to be significantly higher in obese children than in the control group.
- In this study; we determined statistically significant correlations between the serum NT-proBNP and BMI, blood pressure, LV mass index, carotid IMT, and EATT in severely obese adolescent compared with non-obese control adolescent.

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MB and OP wrote the manuscript and analyzed the data. BD, FC, BA, and NE contributed to the discussion and reviewed and edited the manuscript. MP and OP had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. No potential conflicts of interest relevant to this article are reported.

Table 1: Characteristics of Leans and Obese Adolescents

	Leans	**Obese**	
		Mild-moderate	**Severe**
n	**63**	**95**	**43**
Age (mo)	170.30 ± 27.00	169.60 ± 20.10	162.10 ± 23.20
BMI (kg/m2)	20.10± 1.30	33.90± 9.30‡	39.40± 4.00†.*
BMI-SDS	1.20± 0.20	2.20± 0.20‡	2.70± 0.20*
Waist circumference (cm)	67.00± 5.80	102.70± 8.70‡	112.30± 11.10†.*
Hip circumference (cm)	91.00± 7.60	114.40± 8.50‡	124.30± 10.00†.*
Glucose (mg/dl)	84.50± 10.30	90.10± 9.30‡	91.60± 9.20†
Insulin (mIU/ml)	10.90± 2.50	26.60± 15.20‡	27.00± 11.50†
HOMA-IR	2.20± 0.60	5.90± 3.90‡	5.70± 2.70†
HDL-C (mg/dl)	48.20± 16.80	46.10± 10.20	45.30± 11.30
LDL-C (mg/dl)	80.40± 29.20	110.10± 142.50‡	100.80± 25.30†
Triglycerides (mg/dl)	144.50± 37.30	122.80± 62.00‡	131.70± 59.90†
Total cholesterol (mg/dl)	164.10± 36.20	168.90± 35.70	174.40± 35.00†
NT- proBNP (pg/ml)	44.30± 23.30	67.20± 64.40‡	76.00± 49.70†
Hs- CRP (mg/L)	1.70± 0.80	1.90± 1.10‡	2.70± 1.00†.*
Systolic blood pressure (mm Hg)	105.20± 11.70	128.00± 14.30‡	127.70± 23.30†
Diastolic blood pressure (mm Hg)	71.80± 7.00	83.00± 10.30‡	86.70± 10.80†
Left ventricular mass index (LVMI) (gr/m2)	62.40 ± 18.20	88.50 ± 23.00‡	87.50 ± 34.80†
Myocardial performance index (MPI)	0.40± 0.10	0.40± 0.10	0.50± 0.10†.*
Carotid intima-media thickness (CIMT (mm)	0.52 ± 0.08	0.88 ± 0.18‡	0.91 ± 0.23†
Epicardial adipose tissue thickness (mm)	4.28 ± 0.79	7.38 ± 1.76‡	7.42 ± 1.55†

Values are mean ±SD. BMI: Body Mass Index; HOMA-IR: Homeostasis Model Assessment of Insulin Resistance; HDL-C: High Density Lipoprotein Cholesterol; LDL-C: Low Density Lipoprotein Cholesterol; NT- proBNP: N-Terminal Pro B-Type Natriuretic Peptide
* $p < 0.05$ Mild-moderate obese vs. severe obese
‡ $p < 0.05$ Leans vs. mild-moderate obese
† $p < 0.05$ Leans vs. severe obese

Table 2: Relationships between NT-pro BNP and Cardiovascular Factors and Echocardiographic Findings in Obese Adolescents

	Obese			
	Mild-moderate		Severe	
	r	p	r	p
Body composition				
BMI (kg/m2)	0.484	0.001	0.667	<0.001
BMI-SDS	0.384	0.004	0.667	<0.001
Waist circumference (cm)	0.226	0.04	0.545	<0.001
Hip circumference (cm)	0.315	0.01	0.516	<0.001
Metabolic factors				
Fasting glucose (mg/dl)	0.122	NS	0.135	NS
Fasting insulin (mIU/L)	0.133	NS	0.123	NS
HOMA-IR	0.116	NS	0.084	NS
HDL-Cholesterol (mg/dl)	0.020	NS	0.023	NS
LDL-Cholesterol (mg/dl)	0.114	NS	0.119	NS
Triglyceride (mg/dl)	-0.183	NS	-0.112	NS
Total Cholesterol (mg/dl)	0.056	NS	0.077	NS
High sensitive CRP (mg/dl)	0.063	NS	0.067	NS
Hemodynamic factors				
Systolic Blood Pressure (mm Hg)	0.128	NS	0.289	0.04
Diastolic Blood Pressure (mm Hg)	0.319	0.004	0.598	<0.001
Heart rate	0.088	NS	0.022	NS
Left ventricular thickness				
LVPWd(cm)	0.155	NS	0.424	<0.001
IVSs (cm)	0.134	NS	0.114	NS
IVSd (cm)	0.394	<0.001	0.495	<0.001
LVPWs (cm)	0.451	<0.001	0.456	<0.001
LVPWt (cm)	0.435	<0.001	0.544	<0.001
LV mass index (gr/m2)	0.383	0.0019	0.649	<0.001
Left ventricular systolic function				
Ejection fraction (%)	0.043	NS	0.297	0.021
Fractional shortening (%)	0.015	NS	0.025	NS
Left ventricular diastolic function				
Diastolic early wave peak velocity (cm/sn)	0.021	NS	0.040	NS
Diastolic late wave peak velocity (cm/sn)	0.028	NS	0.024	NS
E'/A'	0.012	NS	0.021	NS
Acseleration time (ms)	0.305	0.034	0.279	0.045
Deceleration time (ms)	0.059	NS	0.044	NS
Left ventricular systolic and diastolic function				
Myocardial performance index	0.033	NS	0.288	0.042
Indicators of early atherosclerosis				
Carotid IMT (mm)	0.299	0.029	0.325	0.003
EATT (mm)	0.233	NS	0.339	0.022

BMI: Body Mass Index; HOMA-IR: Homeostasis Model Assessment of Insulin Resistance; HDL-C: High Density Lipoprotein Cholesterol; LDL-C: Low Density Lipoprotein Cholesterol; LV: Left ventricular; IV: İnterventricular; IVSs: Interventricular septum systolic thickness; IVSd: Interventricular septum diastolic thickness; LVPWs: Left ventricular posterior wall systolic thickness; LVPWd: Left ventricular posterior wall diastolic thickness; LVPWt: Left ventricular posterior wall thickness; EATT: Epicardial adipose tissue thickness NS:Non significant

Table 3: Comparison of the Plasma N-terminal pro B-type Natriuretic Peptide Levels, Left Ventricular Mass Index Values, Myocardial Performance Index, Carotid Intima-Media, and Epicardial Adipose Tissue Thicknesses in Obese Subjects with Normal and Elevated Blood Pressures

	Obese		
	Hypertensive	Normotensive	p
n	**34**	**104**	
NT-proBNP (pg/ml)	86.50±39.70	63.20±44.40	0.023
Left Ventricular Mass Index (gr/m2)	78.50 ± 27.00	68.40±16.80	0.042
Myocardial Performance Index	0.42±0.10	0.40±0.10	0.860
Carotid Intima-media Thicknesses (mm)	0.88 ± 0.20	0.71 ± 0.13	0.012
Epicardial Adipose Tissue Thicknesses (mm)	7.12 ± 1.45	7.28 ± 1.56	0.980

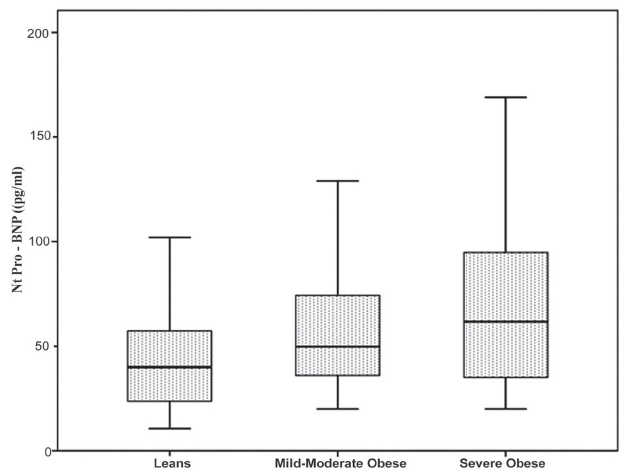

Figure: Comparisons of the plasma N-terminal pro B-type natriuretic peptide levels in leans,mild-moderate and severe obese groups.

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