Factors associated with left atrial size in obese children: an observational study

Obez çocuklarda sol atriyumun boyutu ile ilişkili etmenler: Gözlemsel bir çalışma

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ABSTRACT

Objective: Left atrial size can be considered an independent risk factor for cardiovascular diseases. The measurements of left atrium may be used to assess obesity, which is an important risk factor of cardiovascular diseases. It is aimed to determine the factors that effect to the left atrial size, which is an indicator of cardiac risk in obese children without hypertension.

Methods: The cross-sectional observational study was performed between April 2008 and September 2009 at the clinic of Pediatric Cardiology. Eighty obese and 82 lean children were studied. Diagnosis of obesity was defined according to the World Health Organization classification as the standard deviation score of body mass index being over + 2 standard deviation of the same gender and age. All subjects underwent two-dimensional, M-mode, and Doppler echocardiographic studies. Student's t-test, Chi-square test, Pearson correlation analysis, and multiple stepwise regression analyses were used to compare the subjects, differences in group proportions, evaluate the relation of variables with the left atrial size, and examine the effects of significant independent variables, respectively.

Results: The mean age of obese patients was 11.7±2.2 years and it of lean subjects was 11.7±2.2 years. Body weight, body mass index, standard deviation score of body mass index, waist circumference, systolic and diastolic blood pressure, fasting insulin, and insulin resistance statistically increased in obese children ($p<0.05$). The left atrial size statistically correlated ($p<0.05$) with age ($r=0.523$), body mass index ($r=0.394$), waist circumference ($r=0.421$), diastolic blood pressure ($r=0.230$), insulin resistance ($r=0.350$), and left ventricular mass ($r=0.535$). It was determined that age (beta=0.491; 95% CI=0.091-0.892; $p=0.001$) and left ventricular mass (beta=0.055; 95% CI=0.026-0.085; $p=0.017$) were the most effective independent factors associated with left atrial size among other independent factors in multiple regression analysis.

Conclusion: We found that left atrial size was mostly influenced by age and left ventricular mass in obese children. Therefore, it is important that left atrial size is follow up in childhood obesity. *(Anadolu Kardiyol Derg 2011 Nov 1; 11(7): 633-7)*

Key words: Children, echocardiography, insulin resistance, left atrial size, obesity, regression models

ÖZET

Amaç: Sol atriyal boyutun kalp-damar hastalıkları için bağımsız bir risk faktörü olduğu kabul edilmektedir. Sol atriyum ölçümleri kalp-damar hastalıklarının önemli bir risk faktörü olan obeziteyi değerlendirmede kullanılabilir. Bu çalışmada, hipertansiyonu olmayan obez çocuklarda, kardiyak risk belirteci olan sol atriyal boyutu etkileyen faktörlerin belirlenmesi amaçlanmıştır.

Yöntemler: Bu enine-kesitsel gözlemsel çalışma Çocuk Kardiyolojisi Kliniğinde Nisan 2008 ile Eylül 2009 arasında yapılmıştır. Seksen obez çocuk ve 82 normal vücut ağırlıklı çocuk çalışmaya alınmıştır. Obezite tanısı, Dünya Sağlık Örgütü sınıflamasında tanımlanan, vücut kitle indeksi standart sapma skorunun aynı cinsiyet ve yaş için olanının + 2 standart sapma üzerinde olması şeklinde tanımlanmıştır. Bütün çocuklara iki-boyutlu, M-mod ve Doppler ekokardiyografi çalışmaları yapılmıştır. Olguların karşılaştırılmasında, grup oran farklılıklarında, sol atriyal boyut ile ilişkili değişkenlerin değerlendirilmesinde ve bağımsız değişkenlerin etkilerinin araştırılmasında sırasıyla Student's t-testi, Ki-kare testi, Pearson korelasyon analizi ve çoklu regresyon analizi kullanılmıştır.

Bulgular: Obez hastaların ortalama yaşı 11.7±2.2 yıl ve normal çocukların ortalama yaşı 11.7±2.2 yıl olarak belirlendi. Obez çocuklarda, vücut ağırlığı, vücut kitle indeksi, vücut kitle indeksi standart sapma skoru, bel çevresi, sistolik ve diyastolik kan basıncı, açlık insülini ile insülin direnci istatistiksel olarak artmış bulundu ($p<0.05$). Sol atriyal boyutun, yaş ($r=0.523$), vücut kitle indeksi ($r=0.394$), bel çevresi ($r=0.421$), diyastolik kan basıncı ($r=0.230$), insülin direnci ($r=0.350$) ve sol ventrikül kütlesi ($r=0.535$) ile istatistiksel olarak ilişkisi de saptandı ($p<0.05$). Çoklu regresyon

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analizinde sol atriyal boyut üzerinde en etkili bağımsız faktörlerin yaş (beta=0.491; %95 GA=0.091-0.892; p=0.001) ve sol ventrikül kütlesi (beta=0.055; %95 GA=0.026-0.085; p=0.017) olduğu bulundu.
Sonuç: Obez çocuklarda sol atriyal boyutun en fazla yaş ve sol ventrikül kütlesinden etkilendiği bulundu. Bu sonuç sol atriyal boyutun çocukluk çağı obezite izleminde önemli olabileceğini göstermektedir. *(Anadolu Kardiyol Derg 2011 Nov 1; 11(7): 633-7)*
Anahtar kelimeler: Çocuk, ekokardiyografi, insülin direnci, sol atriyal boyut, obezite, regresyon modelleri

Introduction

Obesity is a disease with excess storage of fats in the body when energy intake with foods exceeds the energy requirement for basal metabolism and body activities. Obesity prevalence has increased three folds between 1980s and 2002 (1). Obesity prevalence among children of 6- to 11-year-olds and 12- to 19-year-olds of age has been reported to be 15.3 and 15.5, respectively (2). Children and adolescents today are less physically active as a group than were previous generations, and less active children are more likely to be overweight and to have higher cardiovascular disease risk factors such as high blood pressure, dyslipidemia, and insulin resistance (3).

Left atrial size in adults has been shown to be related with hypertension, obesity, insulin resistance, and early stage cardiovascular diseases and be associated with increased risk for stroke and death in adults (4). Similarly, it is related with hypertension and obesity in adolescents (5, 6). Therefore, left atrial size can be considered an independent risk factor for cardiovascular diseases. However, relation between insulin resistance and left atrial size in obese children has been shown in one study only (7). The factors associated with left atrial size in obese children have not been clearly defined.

In our study, we aimed to determine any potential relation between obesity and left atrial size, which has been suggested as an early cardiac risk factor predictor in non-hypertensive obese children (6, 7).

Methods

Study design and population

This cross-sectional observational study was performed between April 2008 and September 2009 at the Pediatric Cardiology Department of Keçiören Training and Research Hospital in Ankara, Turkey. We studied 80 obese children (34 female and 46 male; mean age, 11.2±2.2 years) consequently recruited among patients evaluated for overweight or obesity from the clinic for outpatients of the department of pediatrics. Eighty- two healthy lean subjects (36 female and 46 male; mean age, 11.7±2.2 years) who were referred to our hospital for innocent murmur comprised the control group. Children having initial pathologic physical examination, or chronic drug use, or cardiovascular, respiratory, hormonal, metabolic, and liver disease were excluded from the study. The study was designed in agreement with Declaration of Helsinki. Informed consent was obtained from the parents of the children. The study was also approved by the local Ethics Committee.

Assessment of obesity and associated clinical and laboratory variables

Definition of obesity was made according to World Health Organization classification, as 2 points greater standard deviation score of body mass index (SDS BMI) in the same age and gender (8). Healthy lean subjects were defined as having SDS BMI <+1.

The heights of children were measured with Harpenden Stadiometer while standing up; body weights were measured with SECA balance scala when suited only with underwear. Body mass index (BMI) of subjects was calculated as the individual's body weight divided by the square of his or her height (9). Waist circumference was measured in centimeters at the end of the expirium, from the middle point of the line between the lowest costa and spina iliaca anterior spine (10). Standard clinic sphygmomanometer (ERKA, Germany) was used to measure blood pressure, as the lower side of the cuff placed 2 centimeter above the cubital fossa, and stethoscope placed on the brachial artery pulse. Appropriate cuffs were selected according to the right arm circumferences of the children. Systolic and diastolic blood pressure measurements were repeated three times at 5-minute resting intervals while the children were sitting and supported from the back and right arm, and the cubital fossa and the heart were at the same level (11).

Blood samples from the antecubital vein were obtained after at least 12-hour fasting. Fasting glucose was measured enzymatically with automatic analyzer (Konelab 60I, Thermo Scientific, Finland - Lot no. D426, Konelab). Fasting insulin was measured with Liaison immunoluminometric assay (ILMA, DiaSorin, Saluggia, Vercelli, Italy). Insulin resistance was estimated using the homeostasis model assessment [Fasting insulin (μU/L) x fasting glucose (mmol/L) / 22.5] (12).

Echocardiography

Two-dimensional, M-mode, and Doppler echocardiography was performed by using 3- and 7-MHz probes on Vivid 3 Expert device (General Electric Medical Systems, USA), and simultaneous electrocardiography was recorded. The children were evaluated while in supine position and were awake. All the variables were measured three times according to the recommendations of American Society of Echocardiography by investigators unaware of the clinical status of the children (13). Left ventricular mass (LVM) was measured as described previously (14, 15). With parasternal long-axis view, the widest left atrial size was measured between the posterior aortic wall and the left atrial posterior wall at the end of the systole. With apical 4 -chamber view, Doppler indicator was replaced on the tip of mitral leaflets and peak E (early) flow, peak A (atrial=late) flow, and ratio of E/A were recorded.

Statistical analyses

The statistical packages for the social sciences (SPSS, version 16.01 for windows; SPSS Inc., Chicago, IL, USA) were used for statistical analyses. The results are expressed as mean values±standard deviation. Normal distribution of the data was evaluated with Kolmogorov-Smirnov test. Student's t-test was used to compare the groups. Differences in group' proportions were evaluated by using Chi-square test. Pearson correlation analysis was used to evaluate the relation of variables with the left atrial size. To examine the effects of significant independent variables on the left atrial size, multiple analyses with stepwise regression was used. The p values less than 0.05 were considered statistically significant.

Results

Clinical characteristics of studied groups

Weight, BMI, SDS BMI, waist circumference, systolic and diastolic blood pressure, fasting insulin, and homeostasis model assessment-insulin resistance (HOMA-IR) values were statistically significantly higher in the obese children ($p<0.05$) (Table 1).

The measurements of echocardiography such as the left atrial size and LVM in the obese subjects were statistically higher than in the lean subjects ($p<0.05$). There was no statistical difference between the two groups for mitral valve E/A velocity ratio ($p>0.05$)

Association of clinical variables and left atrial size in obese children

Statistically significant correlation was determined between the left atrial size and BMI (Fig. 1), age, waist circumference, diastolic blood pressure, HOMA-IR value (Fig. 2), and LVM in the analysis ($p<.05$) (Table 2).

Age, BMI, waist circumference, diastolic blood pressure, and HOMA-IR were added as independent variables to a multiple stepwise regression model including all obese subjects and left atrial size as dependent variable. It was determined that age and LVM were the most effective independent factors associated with increase of left atrial size among other independent factors in multiple regression analysis (Table 3). According to multiple stepwise regression model, one year increase in age is associated with an increase in the left atrial size by 0.491 mm (beta=0.491, 95% CI 0.091-0.892, p=0.001). One gram increase in LVM is associated with an increase in the left atrial size by 0.055 mm (beta=0.055, 95% CI 0.026-0.085, p=0.017).

Discussion

In obese children, endothelial dysfunction due to insulin resistance, free fatty acids, nitric oxide, and inflammatory cytokines are suggested to cause cardiovascular diseases (16). In a study investigating these underlying mechanisms, children with insulin resistance due to obesity were found to have left atrial size enlargement independent from blood pressure (6). However,

Table 1. Comparison of the baseline characteristics and echocardiographic findings

Variables	Obese subjects (n=80)	Lean subjects (n=82)	p*
Age, years	11.2±2.2	11.7±2.2	0.145
Gender, female/male, n	34/46	26/36	0.946
Standing height, cm	147.9±12.5	146.1±13.4	0.394
Body weight, kg	64.9±16.7	39.4±9.7	0.001
BMI, kg/m^2	29.1±3.5	18.1±1.9	0.001
SDS BMI	3.1±0.57	0.04±0.63	0.001
WC, cm	94.1±11.0	65.0±8.9	0.001
SBP, mm Hg	107.8±13.0	98.1±11.8	0.001
DBP, mm Hg	70.3±9.4	64.3±10.4	0.001
Fasting glucose, mg/dl	91.2±7.0	92.9±8.5	0.190
Fasting insulin, µU/L	16.9±9.6	8.43±4.85	0.001
HOMA-IR	3.87±2.39	1.97±1.17	0.001
Left atrial size, mm	32.2±4.0	28.0±3.7	0.001
LVM, g	110.8±32.8	84.6±28.7	0.001
Mitral E/A ratio	1.58±0.27	1.53±0.26	0.269

Data are presented as the mean±SD and proportions
*unpaired Student's t-test and Chi-square test
BMI - body mass index, DBP - diastolic blood pressure, HOMA-IR - homeostasis model assessment-insulin resistance, LVM - left ventricular mass, Mitral E/A - early (E) and late (A) mitral velocities ratio, SBP - systolic blood pressure, SDS BMI - standard deviation score of body mass index, WC - waist circumference

Table 2. The correlation between left atrial size and clinical variables in obese children

Variables	Left atrial size, mm	
	r	p*
Age, years	0.523	0.001
BMI, kg/m^2	0.394	0.001
WC, cm	0.421	0.001
SBP, mm Hg	0.110	0.333
DBP, mm Hg	0.230	0.040
HOMA-IR	0.350	0.001
LVM, g	0.535	0.001
Mitral E/A ratio	0.108	0.339

*: Pearson correlation analyses
BMI - body mass index, DBP - diastolic blood pressure, HOMA-IR - homeostasis model assessment-insulin resistance, LVM - left ventricular mass, Mitral E/A - early (E) and late (A) mitral velocities ratio, SBP - systolic blood pressure, WC - waist circumference

Table 3. Factors associated with increased left atrial size in obese children

Independent variables	Beta (95% CI)	p*
Age, years	0.491 (0.091-0.892)	0.001
Left ventricular mass, g	0.055 (0.026-0.085)	0.017

*Stepwise multiple regression analysis
Beta - regression coefficient, CI - confidence interval
Dependent variable - left atrial size, independent variables included in this model are: age, body mass index, waist circumference, homeostasis model assessment-insulin resistance index, diastolic blood pressure, and left ventricular mass

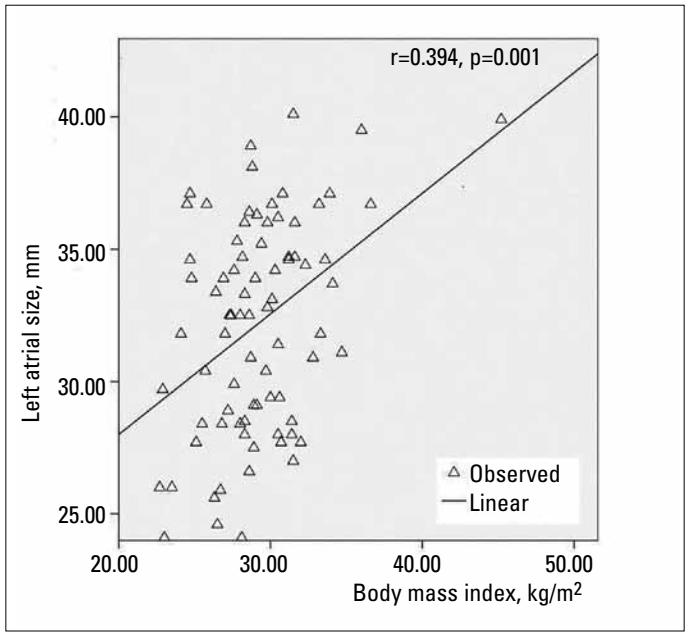

Figure 1. The relation of left atrial size and body mass index

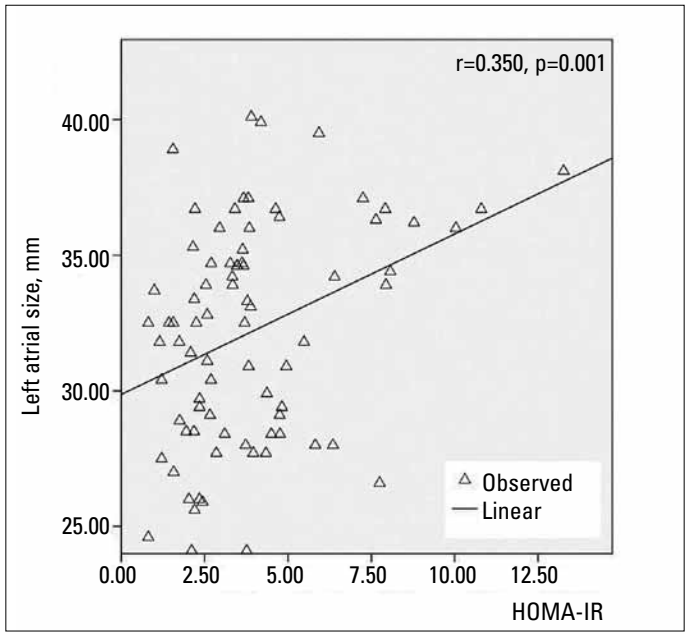

Figure 2. The relation of left atrial size and insulin resistance

in that study, Hirschler and et al. (6) assumed that blood pressure of the obese group was statistically higher although they were in normal ranges. Therefore, it is not clear whether left atrial size is a consequence of insulin resistance or high blood pressure even when it is in normal ranges in obese individuals.

Left atrial size is important in detecting diseases that affect the heart. There have been reports of left atrial size in adolescents with essential hypertension (5). Consequently, it has been shown that left atrial size also exists in non-hypertensive obese children (6). There is a positive correlation between weight gain and circulating blood volume; thereby, the cause of increased preload in obese individuals may be explained as increasing left atrial size with BMI (17). However, no definitive factor that causes left atrial size in obese children has been determined to date.

In our study, we found that left atrial size was higher in obese children, which is compatible with the findings of earlier studies (6, 7). However, it is not clear whether left atrial size in children is an independent risk factor for cardiovascular diseases as in adults. As shown in Table 2, left atrial size was statistically correlated with BMI, waist circumference, diastolic blood pressure, HOMA-IR value, and LVM. However, which factors in obesity associate cardiac alterations could not be explained. To determine the factors responsible for cardiac alterations, in this study, multiple regression analysis was used. In multiple regression analyses, age and LVM were the most effective independent associations of left atrial size among other independent factors. Increasing one gram in LVM and one year in age are associated with a growing in the left atrial size by 0.055 mm and 0.491 mm, respectively.

Furthermore, we observed in Doppler measurements that diastolic functions remained the same although the LVM had increased in size, which is compatible with the findings of earlier studies (18). The increase in the LVM is considered an early finding. Therefore, it has also been shown that systolic functions of these patients are maintained. Conventional Doppler studies may fail to show diastolic dysfunctions. Thereby, tissue Doppler imaging may detect early diastolic dysfunctions even when conventional Doppler findings are normal in the patients (19).

Study limitations

There are some limitations to consider in the interpretation of our results. The current study was cross-sectional in design; therefore, longitudinal measurement and comparison of variables over time were impossible. It is not clear at present whether the increase of left atrial size in overweight children is an independent risk factor of cardiovascular disease, as in adults. In the future, extensive long-term studies including larger subject numbers are needed to determine the long-term consequences of this cardiovascular abnormality. Follow-up studies should be helpful in elucidating the cause-and-effect relations and the underlying mechanism in childhood obesity.

Conclusion

We found that left atrial size correlated with age, BMI, waist circumference, diastolic blood pressure, insulin resistance, and LVM. It was also determined that left atrial size was mostly influenced by age and LVM in obese children. Therefore, it is important that left atrial size is follow up in childhood obesity. Considering a potential left atrial size, obese children should be evaluated with echocardiography, and left atrial size should be measured even if they have normal blood pressure ranges.

Conflict of interest: None declared.

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