Original Article

http://dx.doi.org/10.4070/kcj.2012.42.7.471
Print ISSN 1738-5520 • On-line ISSN 1738-5555

kcj
Korean Circulation Journal

Correlation Between Epicardial Fat Thickness by Echocardiography and Other Parameters in Obese Adolescents

Sung Jin Kim, MD[1], Hae Soon Kim, MD[1], Jo Won Jung, MD[2], Nam Su Kim, MD[3], Chung Il Noh, MD[4], and Young Mi Hong, MD[1]

[1]*Department of Pediatrics, School of Medicine, Ewha Womans University, Seoul,* [2]*Department of Pediatrics, School of Medicine, Ajou University, Suwon,* [3]*Department of Pediatrics, College of Medicine, Hanyang University, Seoul,* [4]*Department of Pediatrics, College of Medicine, Seoul National University, Seoul, Korea*

Background and Objectives: Obesity has reached epidemic proportions globally and affects people of all ages. Recent studies have shown that visceral adipose tissue measured by magnetic resonance imaging and/or computed tomography correlates positively with epicardial adipose tissue. Epicardial fat, which is correlated to several metabolic parameters, can be assessed by echocardiography. The aim of this study was to evaluate epicardial fat thickness and other metabolic parameters in obese adolescents and investigate the correlation between epicardial fat thickness and other metabolic parameters in obese adolescents.

Subjects and Methods: We selected 99 subjects, between ages 15-17 years of age, to be enrolled in this study. Sixty five obese adolescents with a body mass index (BMI) >95 percentile and 34 control subjects were included in this study. Echocardiographic measurements including epicardial fat thickness as well as anthropometric and blood pressure (BP) measurements were performed. The following parameters were estimated: blood glucose, total cholesterol, triglyceride, high density lipoprotein-cholesterol, low density lipoprotein-cholesterol, aspartate aminotransferase, alanine aminotransferase, free fatty acid, interleukin-6, tumor necrosis factor-α, leptin, adiponectin and high sensitive C reactive protein.

Results: The obese group showed a statistically significant correlation with echocardiographic epicardial fat thickness and, BMI, waist circumference, obesity index, fat percentage, systolic BP, insulin level, leptin and adiponectin. Multivariate linear regression analysis showed epicardial fat thickness as the most significant independent parameter to correlate with obese adolescents.

Conclusion: These data suggest that epicardial fat thickness measured by echocardiography is a practical and accurate parameter for predicting visceral obesity. **(Korean Circ J 2012;42:471-478)**

KEY WORDS: Epicardial fat; Obesity; Adolescent, Echocardiography.

Introduction

Visceral obesity is correlated with an unfavorable metabolic and cardiovascular risk profile. Epicardial fat is associated with an increased cardiovascular risk.[1)] Childhood, and especially adolescent obesity, is linked to a higher risk of cardiovascular and metabolic diseases, which can continue on into adulthood and promote its earlier development.[2)]

Over the last few decades, many researchers have focused on establishing a link between visceral obesity and the risks of cardiovascular disease. Although obesity is defined in terms of age- and gender-specified body mass index (BMI) by international and population-specific references, BMI alone does not stratify the risks of having cardiovascular disease.[3)] Measurement of BMI, along with waist circumference (WC), obesity index (OI), fat mass,[4)] visceral fat tissue (VFT), subcutaneous fat tissue (SFT), properitoneal fat tissue (PFT), blood pressure (BP), and a set of metabolic variables are all parameters of obesity that play an important part in the development of

Received: November 16, 2011
Revision Received: January 13, 2012
Accepted: January 16, 2012
Correspondence: Young Mi Hong, MD, Department of Pediatrics, School of Medicine, Ewha Womans University, 1071 Anyangcheon-ro, Yangcheon-gu, Seoul 158-710, Korea
Tel: 82-2-2650-2841, Fax: 82-2-2653-3718
E-mail: hongym@chollian.net

• The authors have no financial conflicts of interest.

cardiovascular disease risk factors, such as arterial wall stiffening, left ventricular (LV) hypertrophy, and cardiac diastolic dysfunction.

Adipose tissue surrounds approximately 80% of the surface area of the human heart. It is concentrated on the free wall of the right ventricle (RV), LV apex and atrium, and along the major branches of the coronary arteries and increases in obese patients. Despite this fact, it has been relatively neglected and has not been utilized to its full capacity.[5] Epicardial fat tissue shares its embryological origin with intra-abdominal fat from the splanchnopleuric mesoderm. These adipocytes are smaller in size, but have higher rates of fatty acid uptake and secretion compared to other fat deposits in other visceral tissue.[5] Putatively, its higher basal rates of fatty acid uptake owes to its close proximity to the heart and its capability to take up fatty acids, which ultimately decreases cardiotoxicity.[6-9] Tumor necrosis factor (TNF)-α, leptin, monocyte chemoattractant protein-1, interleukin (IL)-1β, and IL-6 messenger ribonucleic acid expression and secretion, as well as macrophages and other chronic inflammatory cell infiltrations are increased in the epicardial adipose tissue.[10] Anti-inflammatory and antiatherogenic adipokines, such as adiponectin and adrenomedullin, are also produced from epicardial fat.[10]

As visceral fat is typically measured by surrogate markers, such as WC, and often more directly by magnetic resonance imaging and/or CT, the need for a more cost-effective and practical method of identifying and evaluating those with an increased risk for the comorbidities of obesity are warranted.

The aim of this study was to evaluate the parameters of adolescent obesity and correlate these parameters to echocardiographic assessments, with a focus on epicardial fat thickness.

Subjects and Methods

Study population

Sixty five obese adolescents (31 males, 34 females), aged between 15-17 years, were included in this study. Adolescents with a BMI at/or above the 95th percentile for children of the same age and sex and without prior diagnosis of any cardiac disease were included in the obese group. A control group of 34 subjects (15 males, 19 females) was compared to the obese group.

This study was carried out with approval of the ethics committee of Ewha Womans University Hospital Institutional Review Board, and written informed consents were obtained from the parents of all subjects.

Anthropometric measurements

Anthropometric data of weight, height, WC, BMI, and OI were collected from both groups. WC was measured using a metal anthropometric tape at the mid-waist point between the lowest rib and the iliac crest in a standing position at minimal respiration.[11] BMI was calculated by dividing the body weight (measured in kilograms) by height squared (measured in meters). The OI was calculated by the equation below using the standard weight as the value corresponding to the 50th percentile of the weight data chart for Korean children. Obesity was defined as those with a BMI greater than the 95th percentile. Fat mass and fat percentage were estimated by bioelectric impedance analysis (BIA; InBody 720, Biospace Co., Ltd., Seoul, Korea) using the equation in the BIA software.[4] BP was measured using an automatic oscillometric method, Dinamap, Procare-200 (GE Medical System, Milwaukee, WI, USA) in a supine position after 10 minutes of adequate rest.

Blood chemistry testing

Blood was drawn from all 99 adolescents, who had fasted for 14 hours prior to their blood draw to determine blood levels of the following parameters: blood glucose, total cholesterol, high density lipoprotein-cholesterol (HDL-C), low density lipoprotein-cholesterol (LDL-C), triglyceride (TG), free fatty acid (FFA), aspartate aminotransferase (AST), alanine aminotransferase (ALT). Adiocytokines, such as IL-6, TNF-α, adiponectin, leptin and high sensitive C reactive protein (hs-CRP) were also estimated.

Serum IL-6 and TNF-α levels were measured by using a sandwich enzyme immunoassay-based Quantikine Human interleukine and TNF-α kit (R&D system Inc., Minneapolis, MN, USA) according to the manufacturer's instructions.

Serum leptin levels were measured using the Human Leptin 125 tubes radioimmunoassay kit (Linco Resarch Inc., St. Charles, MO, USA) according to the manufacturer's instructions. The plasma concentration of adiponectin was evaluated by radioimmunoassay {Human Adiponectin 125 tubes radioimmunoassay kit (Linco Research, Inc. St. Charles, MO, USA)}. Serum insulin levels were estimated by using human insulin chemiluminescence immunoassay kit (Insulin, Siemens Centaur, Holliston, MA, USA) according to the manufacturer's instructions.

Insulin resistance was measured by the homeostasis model assessment of insulin resistance (HOMA-IR), which was calculated by dividing the multiple of insulin (μU/mL) and serum glucose (mmol/L) by 22.5.[12]

Echocardiographic parameters

Transthoracic echocardiography was performed to estimate the epicardial fat thickness, morphologic, systolic and diastolic parameters of the heart. Echocardiography (Acuson Sequoia-C 512, Siemens, CA, USA) using phased-array echocardiograms in M-mode, 2D, and pulsed and color-flow Doppler settings were used with 3.5 MHz transducers in the left lateral decubitus position.

Epicardial fat thickness was measured on the free wall of the RV from the parasternal long axis and short axis views.[13]

Stroke volume (SV) was calculated by the aortic annular cross-sectional area multiplied by the aortic time-velocity integral. Cardiac output (CO) was calculated by multiplying SV and the heart rate (HR). Ejection fraction (EF) was determined by using the biplane Simpson formula and fractional shortening (FS) was calculated using LV internal dimensions.[13] The diastolic function was assessed with pulsed Doppler mode from the apical window. Early diastolic (E), late atrial (A) peak velocities, E/A ratios, and E-wave deceleration time (ms) were measured.

Abdominal sonography

Abdominal fat thickness including subcutaneous fat thickness, visceral fat thickness and preperitoneal fat thickness were measured by a 3.5 MHz linear array probe using Acuson XP128 (Acuson, Mountain View, CA, USA) sonography above the navel at the end-expiratory phase.

Pulse wave velocity

Brachial-ankle pulse wave velocity (baPWV) and ankle brachial index were measured in a supine position using a volume-plethysmographic apparatus (Colin Co. Ltd., Komaki, Japan).[14][15] The average of the left and right baPWVs in each subject was used as the PWV.

Statistical analysis

We performed all statistical analyses using Statistical Package for the Social Sciences (SPSS) (version 17, SPSS Inc. Chicago, IL, USA). Descriptive statistics were presented as means and standard deviations. The comparison of continuous variables was done using the Student t-test or one-way analysis of variance. A p less than 0.05 was considered as statistically significant.

Univariate and multivariate regression analysis were performed to investigate the correlations between epicardial fat thickness and other metabolic parameters.

Results

Clinical characteristics

The demographics and clinical characteristics of all 99 adolescents are presented in Table 1. Thirty-four adolescents were included in the control group and 65 were designated as the obese group. The ages of all males and females in both groups were similar with a range from 15 to 17 years. The mean weights were 87.2±16.2 kg and 71.2±8.5 kg for obese males and females, respectively, and 58.3±6.3 kg and 51.4±6.3 kg for control males and females, respectively. The obese group had significantly higher weight, BMI, WC, HC, WH-R, OI, fat percentage, fat mass, and systolic BP compared to control group. The obese females had significantly elevated diastolic BP compared with the control group in addition to the aforementioned parameters (Table 1).

Biochemical data

Insulin levels were significantly higher in the obese group (17.6±9.3 mU/L in male vs. 15.0±10.9 mU/L in female) compared to control subjects (7.6±3.9 mU/L in male vs. 8.8±4.8 mU/L in female). HOMA-IR was significantly increased in the male obese group compared to the male control group (3.8±1.7 vs. 1.8±0.8). AST and ALT were significantly increased in the obese male group (Table 2).

Low density lipoprotein-cholesterol, TG and FFA were significantly

Table 1. Anthropometric data from the obese and control groups

	Male (n=46)			Female (n=53)		
	Control group (n=15)	Obese group (n=31)	p	Control group (n=19)	Obese group (n=34)	p
Age (year)	16.4±0.1	16.4±0.9	0.714	16.6±0.4	16.7±0.8	0.687
Height (cm)	170.4±5.2	172.2±5.1	0.274	158.9±6.3	159.4±4.8	0.780
Weight (kg)	58.3±6.3	87.2±16.4	0.001	51.4±6.3	71.2±8.5	0.001
BMI (kg/m^2)	20.0±1.5	29.3±4.5	0.001	20.4±2.2	27.9±2.5	0.001
WC (cm)	69.0±4.9	92.6±10.8	0.001	64.0±4.8	79.8±5.3	0.001
HC (cm)	87.9±3.4	105.3±8.5	0.001	88.1±5.2	100.2±5.8	0.001
WH-R	0.76±0.06	0.87±0.06	0.001	0.73±0.05	0.79±0.04	0.001
OI (%)	91.3±6.8	133.4±19.7	0.001	98.0±11.8	134.6±12.3	0.001
Fat (%)	17.2±4.4	32.1±5.9	0.001	31.6±4.6	41.7±3.9	0.001
Fat mass (kg)	10.1±3.4	28.8±11.3	0.001	16.4±3.9	30.2±5.0	0.001
Sys BP (mm Hg)	116.7±6.9	125.7±14.8	0.001	107.2±6.2	115.6±9.2	0.001
Dias BP (mm Hg)	73.4±7.5	78.0±10.9	0.148	67.8±5.1	72.0±6.7	0.022

BMI: body mass index, WC: waist circumference, HC: hip circumference, OI: obesity index, WH-R: waist hip-ratio, Sys BP: systolic blood pressure, Dias BP: diastolic blood pressure

http://dx.doi.org/10.4070/kcj.2012.42.7.471

increased in male obese group compared with male control group. HDL-C was significantly decreased in both male and female obese groups compared with the control groups (Table 2).

Adipocytokines

The hs-CRP levels were significantly increased in the obese female group compared to female control group. IL-6 and TNF-α levels were not significantly different between the two groups and between

Table 2. Comparison of blood chemistry data between the obese and control groups

	Male			Female		
	Control group	Obese group	p	Control group	Obese group	p
Glucose (mg/dL)	87.1±6.6	89.8±7.6	0.312	87.8±6.3	86.4±5.9	0.044
Insulin (mU/L)	7.6±3.9	17.6±9.3	0.001	8.8±4.8	15.0±10.9	0.033
HOMA-IR	1.8±0.8	3.8±1.7	0.001	1.7±1.2	3.2±2.6	0.064
AST (IU/L)	20.2±5.7	27.2±15.1	0.036	20.2±2.0	23.6±13.7	0.195
ALT (IU/L)	18.2±11.4	36.6±24.6	0.002	13.2±2.0	23.0±29.7	0.067
Chol (mg/dL)	146.2±16.4	159.2±34.3	0.109	178.4±29.5	171.5±32.0	0.467
LDL-C (mg/dL)	73.1±16.2	97.5±27.2	0.001	99.3±20.4	103.0±29.3	0.603
TG (mg/dL)	70.7±34.5	99.9±52.8	0.047	72.8±28.3	78.0±45.1	0.671
HDL-C (mg/dL)	61.8±10.3	49.5±6.5	0.003	66.4±13.7	56.8±10.6	0.009
FFA (uEq/L)	80.0±324.5	591.4±312.1	0.013	834.3±364.7	677.5±396.1	0.189

HOMA-IR: homeostasis model assessment of insulin resistance, AST: aspartate aminotransferase, ALT: alanine aminotransferase, Chol: cholesterol, LDL-C: low density lipoprotein-cholesterol, TG: triglyceride, HDL-C: high density lipoprotein-cholesterol, FFA: free fatty acid

Table 3. Comparison of adipocytokine between the obese and control groups

	Male			Female		
	Control group	Obese group	p	Control group	Obese group	p
hs-CRP (mg/L)	0.4±2.2	1.4±2.1	0.682	0.4±0.6	1.6±1.9	0.003
IL-6 (pg/mL)	4.9±3.3	6.0±3.0	0.340	3.9±2.2	6.9±6.4	0.173
TNF-α (pg/mL)	3.4±8.2	1.5±2.3	0.280	0.2±0.4	1.3±2.6	0.193
Leptin (ug/L)	2.5±1.2	8.8±4.7	0.001	7.3±2.2	17.7±6.0	0.000
Adiponectin (ng/mL)	11108.6±5895.3	7197.6±4258.0	0.039	10025.4±4152.0	7928.7±2929.6	0.107

hs-CRP: high sensitive C reactive protein, IL-6: interleukin-6, TNF: tumor necrosis factor

Table 4. Echocardiographic parameters between the obese and control groups

	Male			Female		
	Control group	Obese group	p	Control group	Obese group	p
SV (mL)	47.9±6.6	65.4±10.0	0.001	42.2±5.1	60.9±18.5	0.001
CO (L)	3.6±0.8	4.6±0.8	0.001	3.0±0.4	4.6±1.5	0.001
IVS (mm)	0.8±0.1	0.9±0.1	0.001	0.7±0.1	0.9±1.1	0.293
PWT (mm)	0.8±0.1	0.9±0.1	0.001	0.8±0.2	0.8±1.1	0.176
LV mass (g)	151.5±36.3	204.4±48.1	0.001	111.9±21.6	144.3±24.5	0.001
LVMI (g/m^2)	69.1±2.3	73.6±0.8	0.001	71.1±0.7	75.2±3.5	0.001
EF (%)	64.1±4.8	59.9±6.2	0.030	60.8±7.2	62.2±5.3	0.447
FS (%)	35.2±3.5	32.5±3.3	0.015	35.1±6.6	33.4±4.6	0.303
E (m/sec)	0.9±10.0	0.9±0.2	0.337	0.9±0.1	1.0±0.2	0.131
A (m/sec)	0.46±0.05	0.50±0.12	0.032	0.50±0.09	0.51±0.08	0.646
E/A	1.8±18.3	1.9±0.4	0.318	1.9±0.4	2.0±0.5	0.565
E-DT (ms)	138.2±19.8	156.0±31.2	0.052	148.1±28.7	147.1±24.4	0.901

SV: stroke volume, CO: cardiac output, IVS: interventricular septal thickness, PWT: posterior wall thickness, LV: left ventricle, LVMI: left ventricle mass index, EF: ejection fraction, FS: fraction shortening, E: early diastolic velocity, A: late atrial peak velocity, DT: deceleration time

both sexes. Leptin levels were significantly increased in the obese group, in both sexes. The female obese group had a relatively higher leptin level compared with female control group (17.7±6.0 μg/L vs. 7.3±2.2 μg/L). Male obese group had also high leptin levels compared to male control group (8.8±4.7 μg/L vs. 2.5±1.2 μg/L). Adiponectin levels were significantly decreased in the male obese group compared with male control group (7197.6±4258.0 ng/mL vs. 11108.6±5895.3 ng/mL, whereas no significant increase was observed in the female obese group (Table 3).

Echocardiographic parameters

Stroke volume, CO, LV mass, and LVMI were significantly increased in the obese group without gender differences. However, interventricular septal thickness (IVS), posterior wall thickness (PWT), LV mass, EF, FS, and A was only significantly increased in the obese male group compared with control group (Table 4). Epicardial fat thickness was significantly increased in the obese group compared with the control group in both sexes. Epicardial fat thickness was measured to be 1.5±0.5 mm in the obese male group compared with the control group (1.1±0.1 mm). Epicardial fat thickness was measured to be 1.5±0.3 mm in the obese female group compared with the control group (1.2±0.2 mm) (Table 5). Incidence of increased epicardial thickness was 70.4% in male obese adolescents and 32.1% in female (data was not shown).

Table 5. Epicardial fat thickness between obese and control group (mm)

Male		Female	
Obese group	Control group	Obese group	Control group
1.5±0.5	1.1±0.1	1.5±0.3	1.2±0.1

p<0.05 obese group vs. control group

Abdominal fat thickness

Abdominal fat tissues were measured in both groups and classified as VFT, SFT, and PFT. A comparison of abdominal fat tissue between the two groups is shown in Table 6. SFT and PFT were significantly increased in the obese group, regardless of sex, and VFT showed a significant increase in only the female obese group. VFT was significantly increased to 33.0±8.1 mm in obese females compared to 16.4±10.6 mm of control females (Table 6).

Pulse wave velocity and ankle brachial index

In our results, a slight increase of left brachial ankle index (LBAI) was observed in the obese female group. However, there was no significant difference of HR, right brachial ankle pulse wave velocity (RbaPWV), left brachial ankle index (LbaPWV) and right brachial ankle index (RBAI) between the control and obese group (Table 7).

Correlations with epicardial fat thickness and other metabolic parameters

In obese males, univariate analysis revealed that epicardial fat thickness was significantly correlated with BMI, WC, fat mass, fat percentage, SFT, and PFT.

In obese females, epicardial fat thickness was positively correlated with weight, BMI, WC, fat mass, fat percentage, leptin, VFT, SFT, and PFT (Table 8). With multivariate linear regression analysis, epicardial fat thickness was a significant parameter that was correlated with fat percentage, adiponectin, and RbaPWV (Table 9).

Discussion

In our study, epicardial fat thickness was significantly increased

Table 6. Abdominal fat tissue between obese and control group

	Male			Female		
	Control group	Obese group	p	Control group	Obese group	p
VFT (mm)	29.4±10.5	37.5±18.2	0.060	16.4±10.6	33.0±8.1	0.001
SFT (mm)	7.6±4.0	20.9±7.1	0.000	7.4±5.0	20.1±5.2	0.001
PFT (mm)	5.6±2.3	11.8±4.7	0.000	6.0±3.2	14.1±3.7	0.001

VFT: visceral fat tissue, SFT: subcutaneous fat tissue, PFT: properitoneal fat tissue

Table 7. Comparison of pulse wave velocity and ankle brachial index between obese and control group

	Male			Female		
	Control group	Obese group	p	Control group	Obese group	p
HR (/min)	73.4±8.4	70.6±9.2	0.344	70.6±9.1	75.2±10.1	0.121
RbaPWV (cm/sec)	1103.1±140.2	1118.9±138.0	0.722	930.8±100.1	957.6±110.8	0.392
LbaPWV (cm/sec)	1131.3±119.3	1122.0±147.2	0.835	920.1±105.1	962.0±105.1	0.178
RABI	103.9±8.9	106.3±8.7	0.399	105.8±7.2	101.9±7.9	0.096
LABI	105.2±7.1	106.4±6.8	0.595	106.1±7.4	100.6±8.1	0.023

HR: heart rate, RbaPWV: right brachial ankle pulse wave velocity, LbaPWV: left brachial ankle pulse wave velocity, RBAI: right brachial ankle index, LBAI: left brachial ankle index

http://dx.doi.org/10.4070/kcj.2012.42.7.471

Table 8. Epicardial fat thickness by univariate analysis

	Male				Female			
	PLAX		PSAX		PLAX		PSAX	
	r	p	r	p	r	p	r	p
Weight	0.276	0.077	0.346	0.025	0.692	0.001	0.717	0.001
BMI	0.338	0.029	0.321	0.038	0.650	0.001	0.694	0.001
WC	0.327	0.034	0.301	0.053	0.623	0.001	0.713	0.001
Fat mass	0.321	0.041	0.254	0.109	0.698	0.001	0.754	0.001
Fat (%)	0.443	0.004	0.279	0.078	0.538	0.001	0.660	0.001
Leptin	0.253	0.142	0.112	0.523	0.425	0.011	0.435	0.009
Adiponectin	-0.213	0.219	-0.152	0.379	-0.124	0.218	-0.344	0.043
VFT	0.107	0.498	0.110	0.486	0.397	0.006	0.550	0.001
SFT	0.316	0.041	0.348	0.024	0.433	0.002	0.573	0.001
PFT	0.315	0.042	0.188	0.232	0.298	0.042	0.373	0.010

PLAX: parasternal long axis, PSAX: parasternal short axis, BMI: body mass index, WC: waist circumference, VFT: visceral fat tissue, SFT: subcutaneous fat tissue, PFT: properitoneal fat tissue

Table 9. Epicardial fat thickness by multivariate analysis

	Beta	p
Fat (%)	0.002	0.001
Adiponectin	0.001	0.044
RbaPWV	0.001	0.001

RbaPWV: right brachial ankle pulse wave velocity

in the obese group compared with the control group. In obese males, univariate analysis revealed that epicardial fat thickness was significantly correlated with BMI, WC, fat mass, fat percentage, SFT, and PFT. In obese females, epicardial fat thickness was positively correlated with weight, BMI, WC, fat mass, fat percentage, leptin, VFT, SFT, and PFT. With multivariate linear regression analysis, epicardial fat thickness was a significant parameter that was positively correlated with fat percentage, adiponectin, and RbaPWV.

Waist circumference is widely used as a parameter to evaluate visceral obesity. It has been associated with adverse cardiovascular risks,[16] but could be confounded by increased subcutaneous fat. It is speculated to be less reliable in older populations,[17] and in severely obese patients.

Epicardial fat is a metabolically active organ that could serve as a reliable marker of visceral obesity.[6] Also, epicardial fat thickness has been associated with obesity and cardiovascular risk parameters in adult studies, but there have been few studies that included adolescents.[18]

Transthoracic echocardiography is a non-invasive, easy, and reliable method of measuring epicardial fat thickness. However, the association between epicardial fat thickness with obesity is not fully understood and its mechanisms remain to be revealed.

The findings of our study suggest that epicardial fat thickness can be used as an independent parameter of evaluating adolescent obesity. In accordance with previous studies, epicardial fat thickness is shown to be positively correlated with indirect measures of obesity, such as BMI, WC, systolic and diastolic BP, blood insulin, and lipid concentrations, although gender differences exist.

Also, our results showed that obese adolescents had distinctive features that distinguished them from the non-obese group. In obese female adolescents, anthropometric parameters such as weight, BMI, WC, HC, WH-R, OI, fat percentage, fat mass, systolic BP and diastolic BP were significantly increased. In our assessment of metabolic risks and lipid profiles, increased serum insulin and decreased HDL-C was observed in obese patients of both sexes. In obese males, significant increases of HOMA-IR, AST, ALT, LDL-C, and FFA was observed. In addition, blood chemistry data also revealed that serum leptin was significantly increased in the obese group of both sexes. Adiponectin was significantly decreased in obese adult studies that revealed increased levels of IL-6 and TNF-α,[10] however no significant increase was observed in our obese adolescent group.

Many recent studies have delved into revealing the endocrine and paracrine functions of visceral and epicardial fat and have revealed the protective effects of adipocytokines, including leptin, adiponectin, TNF-α, resistin, IL-6, and fatty acid binding proteins.[10][19] Leptin, an adipocyte-derived hormone that regulates food intake and energy expenditure, is speculated to be a link between obesity and increased cardiovascular sympathetic activity. [8] Mazurek et al.[8] studied obese adult patients with coronary artery disease (CAD) and revealed that serum TNF-α, IL-6, and IL-1 were increased more in the epicardial fat when comparing epicardial fat to subcutaneous fat. Additional studies have shown that adiponectin levels were decreased and leptin was increased in epicardial fat in patients with obesity and CAD.[20][21] This result was similar to our data. Gormez et al.[10] compared epicardial fat to paracardial and subcutaneous fat

and revealed that TNF-α and leptin gene expressions were significantly increased in the epicardial fat tissue, while adiponectin was significantly decreased. Such novelties revealed by these studies indicate that epicardial fat may be an entity that is distinctive of subcutaneous and visceral fat. However, an insignificant difference in TNF-α and IL-6 levels in obese adolescents in our study raises the question as to whether differences in adipocytokines levels exist between the adolescent and the adult population. Therefore, the need for more studies of adipocytokine activity in the adolescent population is warranted.

Echocardiographic measurements in our study revealed SV, CO, LV mass, and LVMI were significantly increased in the obese group of both sexes. In addition to these parameters obese males showed significant increases of IVS, PWT, FS, and A on echocardiography. Epicardial fat thickness was significantly increased in all obese adolescents enrolled in our study, regardless of sex.

Pulse wave velocity is a surrogate marker for arterial stiffness, which has been validated in adult[6)15)] and adolescent[22)23)] studies. It is considered a non-invasive technique that can estimate vascular pressures. Studies of healthy adolescents have reported that baPWV is significantly correlated with the known risk factors of cardiovascular disease.[23)] Niboshi et al.[23)] reported a correlation between baPWV and the parameters of cardiovascular risks, such as BMI, WC, waist-hip ratio, systolic and diastolic BP, serum insulin, TG, CRP, and homocysteine levels. However, in our study, no significant increase of baPWV was observed in the obese group. LABI was slightly increased in the obese female group. This may be due to a shorter period of obesity.

However, there are several limitations to this study. One limitation may be the accuracy and the abilities to reproduce epicardial fat measurements due to the subjective choices of where to measure fat thickness by the sonographer. This may explain why data was different at different centers. Iacobellis et al.[24)] measured epicardial fat thickness perpendicularly on the free wall of the RV at end-systole in 3 cardiac cycles. The aortic annulus was used as an anatomical landmark and maximum thickness was measured at the point on the free wall of the RV along the midline. Bettencourt et al.[25)] quantified epicardial fat thickness at the right atrioventricular groove at the free wall of the RV and in the middle on third of the anterior interventricular groove. Studies evaluating the validity and differences of the landmarks used to quantify epicardial fat thickness remains as a future project.

Another limitation of this study includes the population size. The population size consisted of a small, selected population to avoid other confounding variables. Future prospective studies including those with multi-centers and larger population groups are warranted.

In conclusion, epicardial fat thickness is a significant parameter that was positively correlated with obese parameters, such as fat percentage, adiponectin, and RbaPWV, in adolescents. Therefore, echocardiography could be utilized as a cost-effective, easy way of evaluating obese adolescents.

Acknowledgments

This research was supported by a grant from the Korean Heart Research Foundation (2009).

References

1. Poirier P, Giles TD, Bray GA, et al. Obesity and cardiovascular disease: pathophysiology, evaluation, and effect of weight loss: an update of the 1997 American Heart Association Scientific Statement on Obesity and Heart Disease from the Obesity Committee of the Council on Nutrition, Physical Activity, and Metabolism. *Circulation* 2006;113:898-918.
2. Mookadam F, Goel R, Alharthi MS, Jiamsripong P, Cha S. Epicardial fat and its association with cardiovascular risk: a cross-sectional observational study. *Heart Views* 2010;11:103-8.
3. Poirier P. Adiposity and cardiovascular disease: are we using the right definition of obesity? *Eur Heart J* 2007;28:2047-8.
4. Cha K, Chertow GM, Gonzalez J, Lazarus JM, Wilmore DW. Multifrequency bioelectrical impedance estimates the distribution of body water. *J Appl Physiol* 1995;79:1316-9.
5. Shirani J, Berezowski K, Roberts WC. Quantitative measurement of normal and excessive (cor adiposum) subepicardial adipose tissue, its clinical significance, and its effect on electrocardiographic QRS voltage. *Am J Cardiol* 1995;76:414-8.
6. Iacobellis G, Corradi D, Sharma AM. Epicardial adipose tissue: anatomic, biomolecular and clinical relationships with the heart. *Nat Clin Pract Cardiovasc Med* 2005;2:536-43.
7. Marchington JM, Mattacks CA, Pond CM. Adipose tissue in the mammalian heart and pericardium: structure, foetal development and biochemical properties. *Comp Biochem Physiol B* 1989;94:225-32.
8. Mazurek T, Zhang L, Zalewski A, et al. Human epicardial adipose tissue is a source of inflammatory mediators. *Circulation* 2003;108:2460-6.
9. Iacobellis G, Willens HJ. Echocardiographic epicardial fat: a review of research and clinical applications. *J Am Soc Echocardiogr* 2009;22:1311-9.
10. Gormez S, Demirkan A, Atalar F, et al. Adipose tissue gene expression of adiponectin, tumor necrosis factor-α and leptin in metabolic syndrome patients with coronary artery disease. *Intern Med* 2011;50:805-10.
11. Lee S, Bacha F, Gungor N, Arslanian SA. Waist circumference is an independent predictor of insulin resistance in black and white youths. *J Pediatr* 2006;148:188-94.
12. Wallace TM, Levy JC, Matthews DR. Use and abuse of HOMA modeling. *Diabetes Care* 2004;27:1487-95.
13. Mercier JC, DiSessa TG, Jarmakani JM, et al. Two-dimensional echocardiographic assessment of left ventricular volumes and ejection

 http://dx.doi.org/10.4070/kcj.2012.42.7.471

fraction in children. *Circulation* 1982;65:962-9.
14. Gil TY, Sung CY, Shim SS, Hong YM. Intima-media thickness and pulse wave velocity in hypertensive adolescents. *J Korean Med Sci* 2008;23:35-40.
15. Alpert BS, Collins RT. Assessment of vascular function: pulse wave velocity. *J Pediatr* 2007;150:219-20.
16. Wei M, Gaskill SP, Haffner SM, Stern MP. Waist circumference as the best predictor of noninsulin dependent diabetes mellitus (NIDDM) compared to body mass index, waist/hip ratio and other anthropometric measurements in Mexican Americans: a 7-year prospective study. *Obes Res* 1997;5:16-23.
17. Iwao S, Iwao N, Muller DC, Elahi D, Shimokata H, Andres R. Does waist circumference add to the predictive power of the body mass index for coronary risk? *Obes Res* 2001;9:685-95.
18. Bonora E, Micciolo R, Ghiatas AA, et al. Is it possible to derive a reliable estimate of human visceral and subcutaneous abdominal adipose tissue from simple anthropometric measurements? *Metabolism* 1995;44:1617-25.
19. Sacks HS, Fain JN. Human epicardial adipose tissue: a review. *Am Heart J* 2007;153:907-17.
20. Baker AR, Silva NF, Quinn DW, et al. Human epicardial adipose tissue expresses a pathogenic profile of adipocytokines in patients with cardiovascular disease. *Cardiovasc Diabetol* 2006;5:1.
21. Iacobellis G, Pistilli D, Gucciardo M, et al. Adiponectin expression in human epicardial adipose tissue in vivo is lower in patients with coronary artery disease. *Cytokine* 2005;29:251-5.
22. Im JA, Lee JW, Shim JY, Lee HR, Lee DC. Association between brachial-ankle pulse wave velocity and cardiovascular risk factors in healthy adolescents. *J Pediatr* 2007;150:247-51.
23. Niboshi A, Hamaoka K, Sakata K, Inoue F. Characteristics of brachial-ankle pulse wave velocity in Japanese children. *Eur J Pediatr* 2006;165:625-9.
24. Iacobellis G, Lonn E, Lamy A, Singh N, Sharma AM. Epicardial fat thickness and coronary artery disease correlate independently of obesity. *Int J Cardiol* 2011;146:452-4.
25. Bettencourt N, Toschke AM, Leite D, et al. Epicardial adipose tissue is an independent predictor of coronary atherosclerotic burden. *Int J Cardiol* 2012;158:26-32.