High sensitivity C-reactive protein, left ventricular mass, and systolic function in obese adolescents

Erling David Kaunang1, Suryani As’ad2, Sarah M. Warouw1, Peter Kabo2

Abstract

Background Obesity has been associated with structural and functional cardiac muscle defects. High sensitivity C-reactive protein (hs-CRP) has been utilized as an independent predictor of future cardiovascular disease.

Objective To assess for correlations between hs-CRP, left ventricular mass, and systolic function in obese adolescents.

Methods This cross-sectional study was conducted from August 2013 to February 2014. Subjects were obese adolescents aged 13-18 years with a body mass index (BMI) >95th percentile, according to the 2000 Centers for Disease Control and Prevention Growth Chart. Subjects underwent laboratory testing of serum hs-CRP levels, as well as left ventricular mass and function measurements by echocardiography. Descriptive analysis was performed on patients’ characteristics and correlation analysis was done by Pearson’s test with a significance level of P<0.05.

Results Subjects were 40 obese adolescents. There was no statistically significant correlation between hs-CRP and left ventricular mass (r=0.083; P=0.305). There was a moderate correlation between hs-CRP with ejection fraction (EF) (r=0.372 and P=0.009) and fractional shortening (FS) of the left ventricle (r=0.420 and P=0.003).

Conclusion In obese adolescents, we find no correlation between hs-CRP and left ventricular mass. However, hs-CRP is moderately correlated with left ventricular EF and FS. [Paediatr Indones. 2016;56:124-8].

Keywords: hs-CRP, left ventricular mass, left ventricular function, obesity

Obesity has been associated with abnormalities in the structure and function of cardiac muscle. Previous studies have shown that obese children have larger left ventricular mass, thicker wall, and wider ventricular space compared to non-obese children. Increases in left ventricular mass can lead to left ventricle hypertrophy, which is a cause of morbidity and mortality in cardiovascular disease.1-3 Obesity has also been associated with left ventricular systolic and diastolic dysfunction, which may eventually lead to cardiomyopathy.4,5 M-mode echocardiography is considered to be essential to approximate left ventricular mass in obese children. Echocardiography can be a trustworthy, non-invasive indicator of left ventricular hypertrophy.6,7

C-reactive protein is an acute phase, serum protein. Increases in hs-CRP indicate the presence of inflammation. The relationships between inflammation, obesity, and insulin resistance has been previously described.8 C-reactive protein has been utilized as a predictor of cardiovascular disease, as it can be

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detected in the initial phase of the atherosclerosis development. The hs-CRP can be used to evaluate cardiovascular disease, as increased hs-CRP without any infection may independently predict future metabolic disease. This study was conducted to assess for the correlations between hs-CRP and left ventricular mass and systolic function in obese adolescents.

**Methods**

We conducted a cross-sectional study in obese adolescents aged 13-18 years from junior high and high schools in Manado, from August 2013 to February 2014. Study subjects were obese adolescents who were enrolled consecutively. We excluded children with congenital heart disease, acquired heart disease, or metabolic disorders. Parental informed consent was obtained for every subject. Subjects underwent physical examinations and data collection comprising of identity, measurement of body weight (BW) and height, and calculation of BMI. Body mass index (kg/m$^2$) was calculated as body weight (kg) divided by body height squared (m$^2$) and categorized as obese for BMI >95th percentile, based on the CDC 2000 Growth Chart for age and sex. Serum hs-CRP levels were measured on all subjects. Left ventricular mass and systolic function (ejection fraction/EF and fractional shortening/FS) was measured by echocardiography (E. SaoteMylab 4.0).

Data were reported in the form of distributive tables. Parametric data was analyzed by mean, standard deviation (SD) and 95% confidence interval (CI), while non-parametric data was analyzed by median, minimum and maximum values. Correlations between hs-CRP levels and left ventricular mass and function were done by Pearson’s test and simple linear regression, with a P value of <0.05 was considered statistically significant. Data analysis were done by using the Statistical Product and Service Solutions (SPSS) for Windows version 22 software. The study was approved by Ethics Committees of the Sam Ratulangi University Medical School, Manado.

**Results**

Of the 40 obese adolescent subjects, 15 (38%) were boys and 25 (63%) were girls. Subjects’ characteristics are shown in Table 1. Mean body weight was 83.11 kg, ranging from 58 kg to 131 kg. Mean body height was 158.3 cm, ranging from 135.0 to 179.0 cm. Subjects’ mean BMI was 32.99 kg/m$^2$, ranging from 25.80 to 43.00 kg/m$^2$.

The lowest levels of hs-CRP was 0.40 mg/dL and the highest was 19.80 mg/dL with a mean of 3.60 mg/dL. Mean and range of cardiac parameters can be seen in Table 1. There was no statistically significant correlation between hs-CRP with left ventricular mass ($r=0.083, P=0.305$). However, hs-CRP was moderately correlated with left ventricular EF ($r=0.372, P=0.009$, Figure 1) and FS ($r=0.420$ and $P=0.003$, Figure 2).

**Discussion**

Obesity is known to be a major risk factor for high rates of morbidity and mortality in cardiovascular disease. In obese children, ventricular wall thickening may occur, accompanied by large ventricular chambers, compared to those of normal weight children. The ratio between the ventricular wall width and the radius of the chamber, which identifies relative wall thickening, is greater in obese than in normal weight children.2

<table>
<thead>
<tr>
<th>Table 1. Subjects’ characteristics</th>
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<tr>
<td>Characteristics</td>
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<tr>
<td>Mean height (SD), cm</td>
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<tr>
<td>Mean weight (SD), kg</td>
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<tr>
<td>Mean BMI (SD), kg/m$^2$</td>
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<td>Mean hs-CRP (SD), mg/dL</td>
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<td>Mean left ventricular mass (SD), g</td>
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<td>Mean EF (SD), %</td>
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<td>Mean FS (SD), %</td>
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EF=ejection fraction; FS=fractional shortening
This study was carried out in obese adolescents aged 13-18 years in junior high and high schools in Manado. A total of 40 adolescents each underwent history-taking, physical examination, hs-CRP measurement, and echocardiography. We chose adolescents aged 13-18 years as our sample population, because previous study found that the prevalence of obesity was increased in that age group. A study in Saudi Arabia reported one obese child in every 6 children aged 6-18 years. In Indonesia, the results of a survey on favorites elementary school children and junior high schools in large cities found that the prevalence of obesity ranged from 15-30%. A Jakarta study reported that the highest prevalence of obesity was at the age of 17-18 years (11.4%), followed by 12-18 years (6.2%), and 6-12 years (4%). Of the 40 obese adolescents in our study, there were fewer boys (15 or 37.5%) than girls (25 or 62.5%). However, Simsek et al. reported more boys than girls (52% vs. 36%, respectively) among 75 obese children with a mean age of 10.79 years. Another study also found more obese boys than girls, but neither of these
had a mean left ventricular mass of 98.5 (36.4) g. A previous study reported that the left ventricular mass in obese adolescents was 126 (SD 27) g, while that of non-obese subjects was 90 (SD 20) g (P<0.001). Another study found that obese children aged 11.2 (SD 2.9) years had a mean left ventricular mass of 98.5 (36.4) g. Left ventricular hypertrophy detected by echocardiography is a risk factor for morbidity and mortality in cardiovascular disease. Obesity in children and adolescents is the main factor that determines left ventricular mass. In obese children, increased plasma volume also increases cardiac output, which enhances the work of the left ventricle, causing an increase in left ventricular mass.

In our study, the mean hs-CRP of obese adolescents was 3.60 mg/dL. Pearson’s correlation analysis showed that there was no significant correlation between hs-CRP and left ventricular mass (r=0.083;P=0.305). The CRP levels are influenced by several factors, such as smoking, obesity, and level of physical activity. A study from the National Heart, Lung, and Blood Institute (NHLBI) stated that socio-economic factors (age, level of education, and place of residence), obesity, sedentary lifestyle, hormone replacement therapy (HRT), alcohol consumption, and diabetes mellitus had a 30% impact on CRP variability in men and a 22% impact in women. Genetic factors also play an important role. Because of the racial and ethnic variations in CRP levels, the value limit of 3 mg/L, according to the CDC/AHA guidelines, cannot be applied to all individuals.

The relationship between inflammation, obesity, and insulin resistance has been studied. In susceptible individuals, the release of adipokines, such as tumor necrosis factor α and interleukin-6 (IL-6) produced by macrophages and adipocytes, can directly stimulate production of CRP in the liver. A cross-sectional study showed that CRP levels correlated with atherogenic dyslipidemia, obesity, hypertension, and insulin resistance. The continuous production of CRP can aggravate chronic inflammation by means of endothelial cell activation. The importance of measuring CRP was heightened when a more sensitive measurement method for CRP, called high sensitivity-CRP (hs-CRP) was discovered. C-reactive protein is the most sensitive acute phase protein and is, therefore, called the golden marker for inflammation. High sensitivity C-reactive protein is used as a predictor of vascular disease because it has the ability to stimulate the early stages of the formation of atherosclerosis, including increased expression of endothelial cell adhesion molecules, chemokines, and chemoattractants, as well as uptake of low-density lipoprotein (LDL) by macrophages. In addition, CRP can modulate the production of vasoactive endothelial cells, such as lowering the (NOS) mRNA vasoconstriction and increase the production of endothelin-1. The NOS (nagos) itself is subject to translation regulation that is reminiscent of the requirement for localization of mRNA for its translation. Another negative influence of CRP is its stimulation of nuclear factor kappa β (NF-kβ), which activates programmed cell death (apoptosis) of endothelial cells and reduces the formation of blood vessels (angiogenesis).

C-reactive protein can lead to the thickening of the neo-intima through angiotensin as well as inhibiting endothelial progenitor cell differentiation and function. C-reactive protein is not only a marker of inflammation in atherosclerosis, but it is also a mediator of the disease, due to its contribution to the pathogenesis of lesion and plaque formation, as well as thrombosis, through interactions of C-reactive protein with neo-intima and their effects on endothelial cells. Pearson's correlation analysis revealed a statistically significant moderate correlation between hs-CRP and left ventricular EF (r=0.372;P=0.009) or FS (r=0.420;P=0.003) in obese adolescents, indicating that hs-CRP level is associated with systolic function.

The limitations of this study were its cross-sectional research design, as it cannot accurately be used to evaluate other risk factors that may have led to increased left ventricular mass. Also, we did not evaluate the timespan of obesity in our subjects. Long exposure to obesity can effect increases in left ventricular mass. Although we asked subjects from when they first experienced obesity, the answers given were unclear, as they may have been based on the onset of weight gain. As such, we could not distinguish between overweight and obese nutritional status. Further study needs to be done with prospective cohort design to assess the increase in left ventricular mass of obese children.
In conclusion, hs-CRP level is not significantly correlated with left ventricular mass, however it has some moderate correlations with left ventricular systolic function. Further study should be conducted to assess whether long-term childhood obesity is associated with increased left ventricular mass and left ventricular function.

**Conflict of interest**

None declared.

**References**


