The correlation between hs C-reactive protein and left ventricular mass in the obese women

Idrus Alwi*, S Harun*, Satrio Sukmoko/, Pradana Soewondo§, Sarwono Waspadji§, Sidartawan Soegondo§

Abstrak

Kadar C-reactive protein (CRP) dalam plasma dilaporkan meningkat pada individu obes. Pada penelitian ini, akan dievaluasi korelasi antara hsCRP dan massa ventrikel kiri. Empat puluh lima wanita obes sehat dan empat puluh lima wanita non obes sehat sebagai kontrol dilakukan evaluasi ekokardiografi dan pengukuran kadar hsCRP. Tidak terdapat korelasi antara hsCRP dan massa ventrikel kiri pada wanita obes (r=0,29, p 0,06). Terdapat korelasi bermakna antara hsCRP dan indeks massa tubuh= 0.46, p 0,002), dan juga hsCRP dan ketebalan lemak viseral (r= 0.33, p 0.03). (Med J Indones 2006; 15:100-4)

Abstracts

Plasma C-reactive protein (CRP) concentrations are increased in obese individuals. In this study, we examined the correlation between hsCRP and left ventricular mass (LV mass). Fourty five healthy obese women and fourty five healthy non obese women as the controls group were studied by echocardiography and hsCRP. There was no significant correlation between hsCRP and left ventricular mass in obese women (r=0,29, p 0,06). There was a significant correlation between hs CRP and body mass index (r= 0.46, p 0,002), and also hsCRP and visceral fat (r= 0.33, p 0.03). (Med J Indones 2006; 15:100-4)

Keywords: hs C-reactive protein, LV mass, obese women

Several studies showed that obesity influences cardiovascular morbidity and mortality.[1-5] Clinical and necropsy studies on morbid obesity corfirmed the the entity of obese cardiomyopathy, characterised by volume overload and hyperdynamism,[6] frequently leading to congestive heart failure.[7]

Studies using echocardiography, cardiac catheterisation, and necropsy examination have shown relations between morbid obesity, structural alterations of the heart, and systolic function.[7] These associations appear to be present even in cases of slight or mild obesity.[8]

Sukmoko et al,[9] showed that left ventricular mass was higher in the obese patients compare to normal and there was a correlation between visceral fat and left ventricular mass. Body mass index is a strong determinant of left ventricular hypertrophy[10] and that adiopose tissue is a recognized site of cytokine production, in particular interleukin-6 and tumor necrosis factor α, therefore influencing hsCRP level.[10] Obesity is also associated with markers of inflammation[11] and prothrombotic risk.[12,13]

Palmieri et al,[14] in the Strong Heart Study reported a relation of left ventricular hypertrophy to inflammation and albuminuria in adults with type 2 diabetes. However, the correlation between hsCRP and left ventricular mass in obese patients has not been reported.

Our aim in this study was to determine the correlation between hsCRP and left ventricular mass in the obese women.

METHODS

We studied 45 obese women and 45 non-obese control women. Obesity was defined as a body mass index

* *Division of Cardiology Department of Internal Medicine, Faculty of Medicine University of Indonesia / Dr. Cipto Mangunkusumo General Hospital, Jakarta, Indonesia*
/ *Department of Internal Medicine, Faculty of Medicine University of Indonesia / Dr. Cipto Mangunkusumo General Hospital, Jakarta, Indonesia*
§ *Division of Metabolic, Endocrinology and Diabetes, Department of Internal Medicine, Faculty of Medicine University of Indonesia / Dr. Cipto Mangunkusumo General Hospital, Jakarta, Indonesia*

(BMI) of > 25 kg/m2, with clear evidence on physical examination of excessive subcutaneous adipose tissue.

Inclusion criteria : no previous history or clinical evidence of coronary artery disease, heart failure, or cardiac valve disease; normal ECG; no connective tissue disease; not suffering from any chronic or acute infection; not taking any drugs that could affect the heart and inflammation. Echocardiographic images had to be of sufficient quality to allow reproducible cross sectional, M-mode and 2-D studies.

All subjects provided fully informed written consent for their participation in the study, and the protocol was approved by the ethics committee of our hospital.

All participants provided information on age, family history, personal habits (alcohol intake, tobacco consumption, type and level of physical exercise, drug ingestion, known pathological conditions) and the duration of the obesity.

Physical examination was conducted to exclude cardiac comorbidities. Height and weight were measured and the BMI was calculated as the weight (kg)/height2 (m2). A 12 lead ECG was obtained. Haematological and biochemical variables were determined from fasting blood samples and included glucose, total cholesterol, triglycerides, high density lipoprotein cholesterol, urea and full blood count. hsCRP was measured using an enzyme-linked immunosorbent assay.

A cross sectional echocardiogram was obtained on all participants (Philips). Echocardiograms were undertaken in our echocardiographic laboratory following standard methods. They included cross sectional, M mode, and Doppler studies. Measurements of LV internal dimensions and wall thicknesses were obtained from two-dimensionally guided M-mode tracings or parasternal long-axis 2-D images according to the American Society of Echocardiography recommendations.[15,16,17] Measurements of all variables were made by one observer who was blinded to the patients' clinical details.

Statistical Analysis

Descriptive statistics were done on each of the variables to obtain the frequency distributions. Quantitative variables were described as mean (SD). Comparisons between the obese group and the normal weight group were analysed by *t* tests. Correlations between clinical variables and left ventricular mass were determined by Spearman correlation. Probability values of $p < 0.05$ were considered significant.

RESULTS

Baseline Characteristics

No significant differences in age and height between obese and normal groups. Obese subjects had higher weight, body mass index, waist, hip, waist hip ratio, visceral fat, systolic and diastolic blood pressure than normal subjects.

Table 1. Baseline Characteristics

Variable	Obese	Normal	P
Age (years)	36.70 (6.92)	36.44 (6.27)	0.84
Height (cm)	154.01 (3.40)	155.33 (4.28)	0.11
Weight (kg)	77.00 (17.00)	53.49 (5.14)	0.00
Body mass index (kg/m2)	32.07 (6.48)	22.15 (1.62)	0.00
Waist	93.82 (11.25)	71.88 (4.76)	0.00
Hip	109.08 (10.28)	94.64 (4.99)	0.00
Waist hip ratio	0.86 (0.05)	0.76 (0.05)	0.00
Visceral fat	362.29 (75.82)	276.20 (38.17)	0.00
Sistolic blood pressure	113.05 (10.77)	106.93 (9.03)	0.00
Diastolic blood pressure	70.64 (8.99)	65.4 (8.14)	0.00

Values are mean (SD)

Table 2. Indices of Left Ventricular Structure

Variable	Obese	Normal	P
LVEDD	45.65 (4.50)	44.30 (7.14)	0.29
LVESD	26.70 (4.43)	26.64 (4.14)	0.94
IVS	1.01 (0.19)	0.79 (0.15)	0.00
LVPWD	0.96 (0.26)	0.69 (0.14)	0.00
LV mass	156.01 (44.45)	105.09 (27.42)	0.00

LVEDD, left ventricular end diastolic dimension; LVESD, left ventricular end systolic dimension; IVS, interventricular septum; LVPWD, left ventricular posterior wall; LV, left ventricular mass.

There were no significant differences in LVEDD and LVESD between obese and normal group. Obese subjects had higher intraventricular septum, left posterior wall and LV mass than normal subjects.

Correlates of hsCRP

In univariate analysis performed in all obese subjects, hsCRP was significantly correlated with body mass

index (r= 0.46, p 0,002; figure 1) and visceral fats (r= 0.33, p 0.03; figure 2). The correlation between hsCRP and body mass index still significant even in non obese group. Also the correlation between hsCRP and visceral fats in non obese group. hsCRP was not related to LV mass (r=0,29, p 0,06; figure 3A), but there was a tendency correlate. In the normal group (non obese), the correlation between hsCRP and LV mass was not significant (r= 0,17, p 0,26; figure 3B).

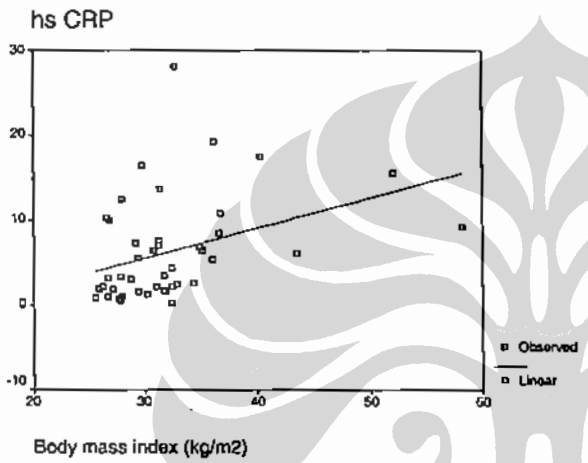

Figure 1. The Correlation Between hsCRP and Body Mass Index

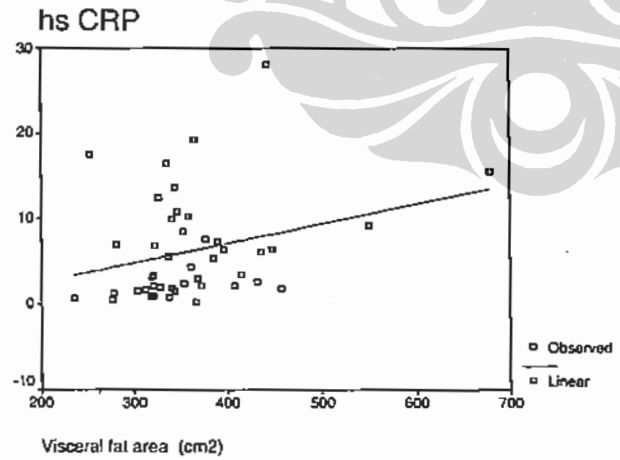

Figure 2. The Correlation Between hsCRP and Visceral fat

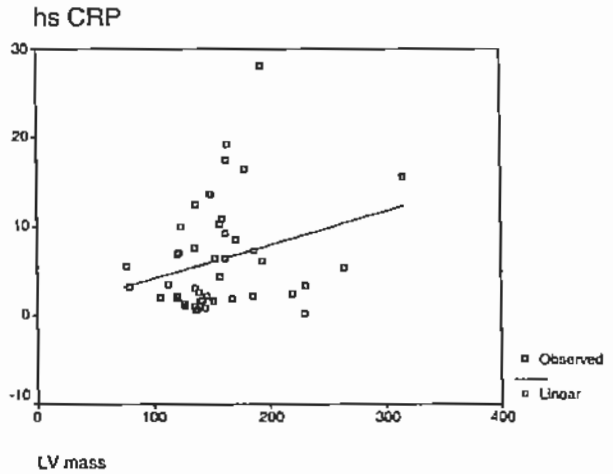

Figure 3A. The Correlation Between hsCRP and LV Mass in Obese Women

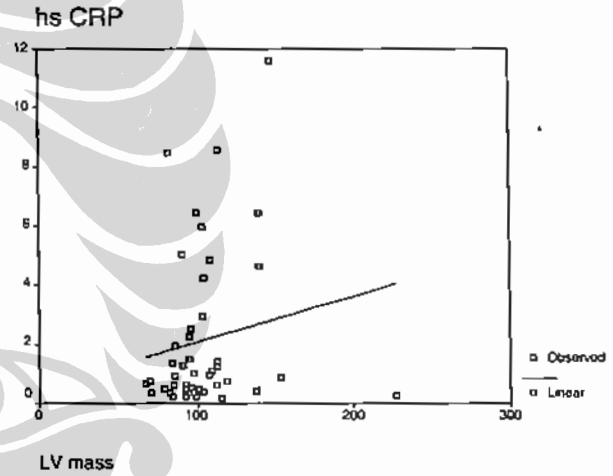

Figure 3B. The Correlation Between hsCRP and LV Mass in Non Obese Women

DISCUSSION

Sukmoko et al,[9] showed changes in LV structure (LV mass) in obese women who have no other clinically cause of heart disease; left ventricular mass was higher in the obese women than non obese and there was a correlation between visceral fat and left ventricular mass. Wong et al,[18] showed changes in the LV structure and function in healthy subjects with exess weight who have no other clinically appreciable cause of heart disease. These changes appear to

related to degree of obesity and some are even present with less severe obesity. These finding differ in a study reported by Iacobellis G,[19] that showed obesity per se, in absence of glucose intolerance, hypertension and dyslipidemia, seem to be not associated with true LV hypertrophy, but severely uncomplicated obese subjects showed greater LV mass and indexed LV mass than normal weight subjects.[20] Another study by Iacobellis et al,[21] showed that insulin resistance in uncomplicated obesity, is associated with an increased LV mass and precocious changes of left ventricular geometry, whereas preserved insulin sensitivity is not associated with increased LV mass.

Inflammation, is associated with the development of atherosclerosis and consequent vascular events.[22] LVH is associated with atherosclerosis.[23] Our data showed that hsCRP is related to body mass index and visceral fat in obese women. The correlation still exist even in non obese women. The correlation between hsCRP and LV mass was not significant in the normal (non obese) women, but there was a tendency correlate in the obese women. Palmieri et al,[14] reported that LVH was associated with higher hsCRP and albuminuria independent of cardiovascular risk factors, including BMI in adults with type 2 diabetes. The hypothesis is that LVH may interact with endothelial dysfunction, cytokines, insulin resistance, and hemodynamics to increased markers of inflammation and albuminuria. Experimental evidence suggests that strechted myocardium is a site of cytokine production.[24] In addition there is evidence in humans that LV hemodynamic overload is associated with increased circulating tumor necrosis factor-α.[25] Hak et al,[26] reported adiposity is strongly associated with CRP in healthy middle aged women and BMI accounted for the relationship between CRP and other variables of the insulin resistance syndrome.

In this study adiposity (BMI and visceral fat) also correlate with hsCRP, but LV mass was not correlate with hsCRP. This result may be influence by obesity per se not LV mass. The discrepancy results from study by Palmieri et al,[14] may be because the populations was difference (diabetes mellitus vs obese). Another reason was the sample in this study was small.

CONCLUSIONS

There was a tendency correlation between hsCRP and LV mass in obese women. This correlations between hsCRP and body mass index/visceral fat were significant. This correlation may be influence by insulin resistance.

REFERENCES

1. Freedman DS, Williamson DF, Croft JB, et al. Relation of body fat distribution to ischemic heart disease. The National Health and Nutrition Examination survey I (NHANES I) epidemiologic follow-up study. Am J Epidemiol 1995; 142:53–63.
2. Kannel WB, d'Agostino RB, Cobb J. Effect of weight on cardiovascular disease. Am J Clin Nutr 1996; 63(suppl): 419–22.
3. Jover Sanz E. Waist/hip ratio: obesity and cardiovascular risk. Ann Intern Med 1997;14:3–8.
4. Kortelainen ML, Sarkioja T. Extent and composition of coronary lesions and degree of cardiac hypertrophy in relation to abdominal fatness in men under 40 years of age. Arterioscler Thromb Vasc Biol 1997; 17:574–9.
5. Smith HL, Willius FA. Adiposity of the heart. Arch Intern Med 1933; 52:929–31.
6. Kasler EK, Hruban RH, Baughman KL. Cardiomyopathy of obesity: a clinicopathologic evaluation of 43 obese patients with heart failure. Am J Cardiol 1992; 70:921–4.
7. Katz AM. Cardiomyopathy of overload: a major determinant of prognosis in congestive heart failure. N Engl J Med 1990; 322:100–10.
8. Larsson B, Björntorp P, Tibblin G. The health consequences of moderate obesity. Int J Obes 1981; 5:97–106.
9. Sukmoko S, Waspadji S, Alwi I, et al. The Correlation between left ventricular mass and visceral fat of obese women. In Publish.
10. de Simone G, Devereux RB, Kimball TR, Mureddu GF, Roman MJ, Contaldo F, Daniels SR: Interaction between body size and cardiac workload: influence on left ventricular mass during body growth and adulthood. Hypertension 1998; 31:1077–82
11. Festa A, D'Agostino R Jr, Howard G, Mykkanen L, Tracy RP, Haffner SM: Chronic subclinical inflammation as part of the insulin resistance syndrome: the Insulin Resistance Atherosclerosis Study (IRAS). Circulation 102:42–47, 2000
12. Weyer C, Yudkin JS, Stehouwer CD, Schalkwijk CG, Pratley RE, Tataranni PA: Humoral markers of inflammation and endothelial dysfunction in relation to adiposity and in vivo insulin action in Pima Indians. Atherosclerosis 2002;161:233–42.
13. Campos SP, Baumann H: Insulin is a prominent modulator of the cytokine-stimulated expression of acute-phase plasma protein genes. Mol Cell Biol 1992; 12:1789–97.
14. Palmieri V, Tracy PT, Roman MJ et al. Relation of left ventricular hypertrophy to inflammation and albuminuria in adults with type 2 diabetes. The Strong Heart Study. Diabetes Care 2003; 26:2764-9.
15. Sahn DJ, DeMaria A, Kisslo J, Weyman A: Recommendations regarding quantitation in M-mode echocardiography: results of a survey of echocardiographic measurements. Circulation 1978; 58:1072–83.

16. Schiller NB, Shah PM, Crawford M, De- Maria A, Devereux R, Feigenbaum H, Gutgesell H, Reichek N, Sahn D, Schnittger I: Recommendations for quantitation of the left ventricle by two-dimensional echocardiography. American Society of Echocardiography Committee on Standards, Subcommittee on Quantitation of Two-Dimensional Echocardiograms. J Am Soc Echocardiogr 1989;2:358–67.
17. Devereux RB, Alonso DR, Lutas EM, Gottlieb GJ, Campo E, Sachs I, Reichek N: Echocardiographic assessment of left ventricular hypertrophy: comparison to necropsy findings. Am J Cardiol 1986;57:450–8.
18. Wong CY, O,Moore-Sullivan T, Leano R, et al. Alterations of left ventricular myocardial characteristics associated with obesity. Circulation 2004;110:3081-7.
19. Iacobellis G, Ribaudo MC, Leto G, et al. Influence of excess fat on cardiac morphology and function: study in uncomplicated obesity. Obes Res. 2002;10:767–73.
20. Iacobelis, G, Ribaudo MC, Terreno AZ, Iannuci CV, Di Mario U, Leonetti F. Adapted changes in left ventricular structure and function in severe uncomplicated obesity. Obes Res. 2004;12:1616 –1621.
21. Iacobellis G, Ribaudo MC, Zappaterreno A, et al. Relationship of insulin sensitivity and left ventricular mass in uncomplicated obesity. Obes Res. 2003;11:518 –24.
22. Ross R: Atherosclerosis: an inflammatory disease. N Engl J Med 1999;340:115–126.
23. Roman MJ, Pickering TG, Schwartz JE, Pini R, Devereux RB: Association of carotid atherosclerosis and left ventricular hypertrophy. J Am Coll Cardiol 1995;25:83–90.
24. Kapadia SR, Oral H, Lee J, Nakano M, Taffer GE, Mann DL: Hemodynamic regulation of tumor necrosis factor-alpha gene and protein expression in adult feline myocardium. Circ Res *1997*;81:187–95.
25. Kapadia SR, Yakoob K, Nader S, Thomas JD, Mann DL, Griffin BP: Elevated circulating levels of serum tumor necrosis factor-alpha in patients with hemodynamically significant pressure and volume overload. J Am Coll Cardiol 2000;36:208– 12.
26. Hak AE, Stehouwer CDA, Bots ML, et al. Associations of C-reactive protein with measures of obesity, insulin resintance, and subclinical atherosclerosis in healthy, middle aged women. Arterioscler Thromb Vasc Biol. 1999;19:1986-91.