The Effect of Visceral Fat Area and Adipocytokines on Acute Myocardial Infarction: A Case-Control Study in Adult Korean Population
급성심근경색에서 내장지방면적과 Adipocytokines의 영향: 환자 대조군 연구

Kang-Kon Lee, Young-Sung Suh[(1)], Keun-Sang Yum*

Department of Family Medicine, Uijeongbu St. Mary's Hospital, College of Medicine, The Catholic University of Korea; and Department of Family Medicine, Keimyung University Dongsan Medical Center[(1)]

이강건 · 서영성[(1)] · 염근상*

가톨릭대학교 의정부성모병원 가정의학과, 계명대학교 동산의료원 가정의학과[(1)]

ABSTRACT

Background: This study aimed to analyze visceral fat area (VFA) and the pattern of secretion of adiponectin, leptin, TNF-α, IL-6, and IL-10. It also studies the effect of VFA and adipocytokines on the risk of Acute myocardial infarction (AMI) in adult Korean population.

Methods: A patient group (PG) consisting of 121 patients, who were hospitalized for AMI from 2008 to 2009, and a control group (CG) consisting of 115 healthy adults, who visited the same hospital for health examination within the same period, were included in this study. Physical measurements were performed and VFA was measured using computed tomography. Lipid, metabolic index, adipocytokine levels were also measured after 12 hours of fasting.

Results: BMI, waist circumference, levels of leptin, TNF-α, and IL-6 were significantly higher in the PG, while adiponectin level was significantly higher in the CG. According to the comparison study analyzed by gender, VFA level was significantly higher in the PG, and IL-10 level was significantly higher in the CG. After adjusting for the conventional risk factors (CRF) of AMI, regression analysis showed that adiponectin and IL-10 levels reduced the risk of AMI; whereas VFA, TNF-α, leptin, and IL-6 increased the same risk.

Conclusion: It is postulated that adipocytokines and VFA

요 약

연구배경: 급성심근경색증은 복합적인 원인에 의해 발생하지만 염증반응이 필수적인 역할을 하고 있다. 지방조직이 adipocytokine이라 불리는 염증성 cytokine을 분비한다고 알려져 있어 급성심근경색 환자와 대조군을 대상으로 내장지방면적, 아디포넥틴, 렙틴, TNF-α, IL-6, IL-10의 분비 양상을 분석하고, 급성심근경색 위험도를 얼마나 높이는지 동시에 살펴보고자 한다.

방법: 2008년부터 2009년까지 의정부성모병원과 동산의료원을 내원하여 급성심근경색을 진단받은 환자군과 동병원 건강검진을 목적으로 내원한 자를 대조군으로 체질량지수, 체지방률, CT를 이용한 복부 내장지방면적을 측정하고 12시간 공복상태에서 지질, 대사지표 및 아디포넥틴, 렙틴, IL-6, IL-10 농도를 측정하였다.

결과: 대상자는 총 236명으로 환자군이 121명, 대조군이 115명이었다. 환자군에서 BMI, 허리둘레, 렙틴, TNF-a, IL-6가 유의하게 높았고, 대조군에서, 아디포넥틴 수치가 유의하게 높았다. VFA, IL-10은 양 군 간의 차이는 있었으나, 통계적 유의성은 없었다. 그러나, 환자를 성별로 나눠서 비교했을 때는 환자군에서 VFA가 유의하게 높았고, 대조군에서 IL-10이 유의하게 높았다. 급성심근경색의 고전적인 위험요소를 보정한 후 분석한 결과 아디포넥틴, IL-10은 수치가 낮을 수록 급성심근경색 위험도를 높였고, 내장지방면적, TNF-a, 렙틴, IL-6는 수치가 높을수록 급성심근경색 위험도를 높였다.

결론: 내장지방과 adipocytokine들은 급성심근경색의 고전적인 관상동맥질환의 위험인자의 영향에서 벗어나서 독립적인

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Corresponding author: Keun-Sang Yum, Department of Family medicine, Uijeongbu St. Mary's Hospital, The Catholic University of Korea, 65-1 Geumo-dong, Uijeongbu-si, Geyonggi-do, 480-717, Korea
Tel: +82-31-820-3179, Fax: +82-31-848-3179, E-mail: yks6303@catholic.ac.kr, mobile: 010-6326-3790

* All the authors have contributed equally to this work.

will act as independent risk factors of AMI regardless of CRF of coronary artery disease.

Key words: Myocardial infarction, Visceral fat, Adipocytokines

위험인자로 작용할 것으로 추정된다. 향후 adipocytokine 이외의 위험인자를 통제한 대규모의 환자-대조군 연구가 필요할 것으로 생각된다.

중심단어: 심근경색, 내장지방, Adipocytokines

Introduction

Mortality of acute myocardial infarction (AMI) is about 30%, and half or more of the mortality occur before the patient's arrival at the hospital. Although survival rate after hospitalization has improved over the past 20 years, 5~10% of survivors of AMI die in the first year after AMI.[1)]

Inflammatory reaction is known to play a key role in the development of coronary artery disease, although complex causes contribute to the development of coronary artery disease.[2,3)] However, the cause of inflammatory reaction, and the relation between inflammation and coronary artery disease remain unclear.

So far, adipose tissue has received attention in studies as an inflammatory burden of coronary artery disease, and adipose tissue is known to synthesize and secrete adipocytokines, a pro-inflammatory agent.

The relation between visceral fat as a risk factor and coronary artery disease has become clearer since adipose tissues, particularly visceral fat, as endocrine organs have been known to secrete cytokines which influence various metabolic processes.[4-7)] Adiponectin is a protein that is expressed specifically in the adipose tissue. It improves insulin sensitivity by promoting oxidation of fatty acid in muscles.[8)] In addition, it exerts anti-inflammatory effect by inhibiting the expression of adhesion molecule and the secretion of cytokine in macrophage.[8)] Blood adiponectin level is also known to decrease in the case of AMI.[5)]

Vascular smooth muscle cells are known to have anti-arteriosclerosis effect by inhibiting cell proliferation and migration caused by platelet-derived growth factor.[9)]

Leptin is a hormone secreted by adipocyte, which controls appetite and energy metabolism, and is directly related with body fat volume.[10)] It has been reported that leptin level is significantly related to insulin resistance after adjustment of BMI.[11)] Numerous studies have shown that leptin could play an important role in the development of cardiovascular diseases.[12,13)]

Interleukin-6 (IL-6) is a cytokine that is involved in acute phase reaction, immune reaction, and hematopoiesis. Studies have shown that blood IL-6 level increases in proportion to the increase in postprandial blood insulin and glucose level in patients with type II diabetes, particularly in type II diabetes patients with insulin resistance.[14-16)]

IL-10, a cytokine that has strong anti-inflammatory effect, is secreted by macrophages in response to stimulation of infectious agents, and reduces tissue damage caused by the secretion of inflammatory cytokines.[18,19)] Decrease in IL-10 may be a factor in inducing the rupture of arteriosclerotic thromobotic plaque, and it has been reported that IL-10 level is low in patients with unstable angina.[20)]

The secretion and function of adipocytokines and the imbalance in such secretion and function are believed to be linked to abdominal visceral obesity and cardiovascular disease and is thought to act as independent risk factors of coronary artery disease.

Thus, this study aimed to investigate how much visceral fat area (VFA) and various adiopocytokines increase the risk of AMI at the same time by examining patients with AMI and a control group in Adult Korean Population.

Methods

1. Subjects

Patients aged 19 and above who were hospitalized after being initially diagnosed with AMI at the Department of Cardiology at two university hospitals, from December 2008 to June 2009, were included in the patient group. Healthy people aged 19 and above who visited the Department of Family Medicine for health examination within the same period, who did not have risk factors for cardiovascular disease, were included in the control group.

Patients with chronic diseases or cardiovascular diseases other than AMI, and drug history of cardiovascular disease were excluded from the patient group.

This study was approved by the Institutional Review Board of Catholic University Uijeongbu St. Mary's Hospital (UCMC07BR046).

2. Methods

1) Clinical Trial Methods

Subjects who agreed to participate in this study, after being briefed on its objectives, underwent physical examination including measurement of blood pressure, height, weight and waist circumference. Blood test was done after 12 hours of fasting. In the patient group, the specimens were collected on the second day of hospitalization after fasting (7 o'clock AM).

2) Diagnosis of AMI

Diagnosis was based on collective findings such as non-Q-wave myocardial infarction, Q-wave myocardial infarction (presence or absence of typical chest pain), continuous ECG change (ST-segment elevation in two or more leads, presence or absence of Q-wave), cardiac-enzyme changes (CK, CK-MD, LDH, Troponin-I, and Troponin-T increase), regional-wall movement abnormality in echocardiography, and coronary artery stenosis in angiography.

3) Survey

Family history of coronary artery diseases including hypertension, diabetes, hyperlipidemia, and myocardial infarction (MI), stroke and obesity, the subject's medical history, and drug abuse were examined. Given that drinking history is a lifestyle-related risk factor, the frequency of drinking alcohol per week, amount and type of alcohol per drinking session were examined. For smoking history, the number of packs, and smoking duration were examined (for ex-smokers, smoking-free duration was examined). For exercise history, the number of days per week of exercise and the number of hours per exercise session were examined.

4) Physical Measurement

Subject's body mass index (BMI, kg/cm^2) was obtained by measuring height (cm) and weight (kg). Waist circumference (cm) was measured using a tape measure at the umbilical level after expiration while the subject stood with feet 30 cm apart. BP was measured twice at 5-minute intervals using a mercury sphygmomanometer after the subject was rested in a seated position for at least 10 minutes after 12-hr fasting. The average of the two measurements was used.

5) Measurement of Visceral Fat Area using Abdominal Computed Tomography

Computed tomography (High Speed Advantage, General Electric Co., USA) was performed at the umbilical level, and the regions that belong to Hounsfield unit area -250 to -50 were measured. Using the peritoneum as the boundary line, VFA and subcutaneous fat area were measured.

6) Blood Test

Total cholesterol, triglyceride, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, fasting blood glucose, and blood insulin were measured using venous blood collected after 12-hr fasting.

In a portion of isolated serum that had been stored at -80℃, antigen-antibody reaction was induced using anti-human antibody. Adiponectin, leptin, TNF-*α*, IL-6 and IL-10 levels were then measured using ELISA (Enzyme linked immunosorbent assay) kit (Quantikine®, R&D Systems, Inc. USA).

For the patient group, given the time variations, the blood test specimens were taken after fasting on the second day of hospitalization.

3. Statistics and Analysis

The general features of both groups were expressed as mean ± SD, and the mean of each group was compared using t-test.

Multiple logistic regression analysis was performed to correlate the levels of various adipocytokines and VFA with the risk of AMI. Stepwise logistic regression analysis was performed to compare the existing risk factor of MI as an independent risk factor with adipocytokines and VFA.

SPSS for Windows (version 12.0) was used for statistical analysis and $P < 0.05$ was considered statistically significant.

Results

1. Clinical Features of Subjects

A total of 236 subjects participated in the study (patient group, n = 121; control group, n = 115). There were no significant differences between the two groups in age, gender, blood pressure, smoking history and alcohol consumption. In the patient group, fasting glucose, blood insulin, total cholesterol, triglyceride, and LDL-cholesterol levels were significantly higher. In the control group, HDL-cholesterol level was significantly higher (Table 1).

In the patient group, 61 cases (50%) of diabetes mellitus, 44 cases (36%) of hypertension, and 30 cases (25%) of dyslipidemia were noted. In the control group, 23 cases (20%) of hypertension were found but no cases of diabetes mellitus or dyslipidemia were noted.

2. Body Size, Visceral Fat, and Adipocytokines by Gender

Comparison was made between patient and control groups for BMI, waist circumference-related indicators, and adipocytokines.

In a comparison analysis between the two groups where gender was not considered, significant difference in all indicators except for VFA and IL-10 were found. When gender was taken into consideration, significant

Table 1. Clinical characteristics of study subjects

Variables	Cases (n = 121)	Controls (n = 115)	*P*-value
Age (years)	61.4 ± 11.5	63.4 ± 11.0	NS
Male	88 (72.7)	42 (36.5)	-
Female	33 (27.3)	73 (63.5)	-
SBP (mmHg)	131.7 ± 20.0	127.2 ± 15.4	NS
DBP (mmHg)	78.3 ± 11.7	77.2 ± 12.3	NS
FBS (mg/dL)	147.9 ± 64.6	86.8 ± 14.8	< 0.001
Fasting insulin (μIU/mL)*	9.9 (6.2-15.6)	5.6 (4.3-8.0)	< 0.001
TC (mg/dL)	196.4 ± 41.6	172.4 ± 39.3	< 0.001
TG (mg/dL)*	116.0 (75.2-174.0)	96.0 (65.0-147.5)	0.023
HDL (mg/dL)	39.6 ± 10.2	51.6 ± 13.8	< 0.001
LDL (mg/dL)	119.0 ± 37.5	105.4 ± 33.3	0.004
Smoker	43 (35.5)	56 (48.7)	NS
Non-smoker	78 (64.5)	59 (51.3)	NS
Alcohol consumption (g/week)	190.08 ± 10.5	253.44 ± 13.7	NS

Data are n (%) or means ± SD.

* median (25~75%); SBP, Systolic Blood Pressure; DBP, Diastolic Blood Pressure; FBS, Fasting Blood Sugar; TC, Total Cholesterol; TG, Triglyceride; HDL, High Density Lipoprotein; LDL, Low Density Lipoprotein.

Table 2. Distribution of fat measures and adipocytokines for women and men

Variables	Total			Women			Men		
	Cases n = 121	Controls n = 115	*P*-value	Cases n = 33	Controls n = 73	*P*-value	Cases n = 88	Controls n = 42	*P*-value
BMI (kg/m^2)	26.2 ± 4.7	24.6 ± 2.7	0.003	25.2 ± 5.4	24.5 ± 3.1	NS	27.8 ± 2.6	24.7 ± 2.6	< 0.001
WC (cm)	90.1 ± 8.3	86.9 ± 12.5	0.021	90.0 ± 9.7	81.7 ± 12.2	0.001	95.8 ± 6.6	90.1 ± 7.7	< 0.001
VFA (cm^2)	124.1 ± 42.1	107.1 ± 52.7	NS	113.7 ± 37.2	91.3 ± 56.6	0.041	134.5 ± 29.6	115.9 ± 44.0	0.014
SFA (cm^2)	188.7 ± 86.8	113.7 ± 49.6	< 0.001	198.3 ± 97.8	143.7 ± 55.7	0.004	171.9 ± 60.0	102.5 ± 42.2	< 0.001
Adipocytokines*									
Adiponectin (ng/mL)	31.8 (18.8~46.9)	38.4 (15.4~106.2)	0.011	33.2 (21.7~48.0)	99.6 (27.9~113.2)	< 0.001	14.8 (9.9~19.3)	30.2 (17.4~47.2)	< 0.001
Leptin (pg/mL)	47.8 (23.1~95.4)	5.4 (2.1~11.5)	< 0.001	69.0 (29.6~124.3)	7.8 (4.0~12.1)	< 0.001	42.7 (21.9~78.2)	2.0 (1.6~5.0)	< 0.001
TNF-*α* (pg/mL)	2.1 (0.9~2.9)	0.8 (0.5~1.0)	< 0.001	2.0 (0.8~2.8)	0.8 (0.5~1.0)	< 0.001	2.1 (0.9~2.9)	0.7 (0.5~1.2)	< 0.001
IL-6 (pg/mL)	9.3 (5.1~18.2)	2.8 (1.3~4.2)	< 0.001	7.7 (4.9~12.5)	2.8 (1.5~4.2)	< 0.001	10.2 (5.2~25.1)	1.8 (0.9~4.7)	< 0.001
IL-10 (pg/mL)	5.9 (1.2~54.2)	9.0 (5.2~13.9)	NS	7.5 (5.2~13.6)	48.8 (3.9~58.7)	0.005	1.3 (1.0~3.2)	9.3 (5.0~14.1)	< 0.001

Data are means ± SD.

* median (25~75%); BMI, Body Mass Index; WC, Waist Circumstance; VFA, Visceral Fat Area; SFA, Subcutaneous Fat Area; TNF-*α*, Tumor Necrotic Factor-alpha; IL, Interleukin.

Table 3. Logistic regression analyses for baseline adipocytokines and risk of myocardial infraction

Variables	Total		Women		Men	
	n = 236 OR (95% CI)	Nagelkerke R^2	n = 106 OR (95% CI)	Nagelkerke R^2	n = 130 OR (95% CI)	Nagelkerke R^2
VFA (cm^2)	3.18 (2.14-4.56)	0.514	3.23 (1.34-5.14)	0.472	4.01 (1.98-6.13)	0.634
Adiponectin (ng/mL)	1.06 (0.67-1.69)	0.531	0.29 (0.12-0.65)	0.702	1.10 (0.51-4.34)	0.519
Leptin (pg/mL)	2.83 (2.05-3.90)	0.714	2.23 (1.42-3.48)	0.739	3.43 (2.14-5.50)	0.744
TNF-α (pg/mL)	4.18 (2.30-7.60)	0.629	7.84 (2.30-10.01)	0.741	3.20 (1.63-6.28)	0.540
IL-6 (pg/mL)	3.14 (2.01-4.89)	0.645	2.37 (1.20-4.49)	0.679	3.61 (2.05-6.34)	0.633
IL-10 (pg/mL)	0.70 (0.32-1.25)	0.516	0.88 (0.33-1.68)	0.632	0.16 (0.07-0.83)	0.638

Adipocytokin measures have been log transformed.

* adjusted for age; adjusted age, sex, VFA and adipocytokines VFA, Visceral Fat Area; TNF-α, Tumor Necrotic Factor-alpha; IL, Interleukin.

difference was noted in all indicators in male subjects while in female subjects all indicators except for BMI showed significant difference (Table 2).

3. Correlation of Risk of AMI with Visceral Fat and Adipocytokines

To correlate the risk of AMI with VFA and various adipocytokines, odds ratio was obtained using multiple logistic regression analysis after adjusting for age and gender. The analysis showed that the higher the VFA, leptin, TNF-α and IL-6 levels, the higher the risk of AMI. The higher the IL-10 level, the lower the risk of AMI (OR = 0.70), and a strong association was found particularly in men (OR = 0.16). In contrast, adiponectin level showed a decrease in the risk of AMI in women (OR = 0.29) whereas it showed nearly no change in the risk of AMI in entire subjects and men (Table 3).

4. Correlation of Risk of AMI with Conventional Risk Factors of Cardiovascular Disease, VFA and Adipocytokines

This study tried to correlate the risk of AMI with conventional risk factors of cardiovascular disease, VFA and adipocytokines by using stepwise logistic regression analysis after adjusting for age, gender, BMI, BP and VFA, and fasting glucose, total cholesterol, triglyceride, HDL-cholesterol, and LDL-cholesterol levels.

The analysis showed that the higher the VFA, IL-6, TNF-α, leptin, and triglyceride levels, the higher the risk of AMI; and the higher the adiponectin, IL-10 and HDL cholesterol levels, the lower the risk of AMI (Table 4).

Table 4. Independent predictors of MI; stepwise logistic regression analyses including traditional cardiovascular risk factors and VFA, adipocytokines

Variables	OR (95% CI)	Nagelkerke R^2
VFA	2.10 (0.87-5.45)	0.941
Adiponectin	0.12 (0.04-0.45)	0.948
TNF-α	3.63 (1.03-4.24)	0.928
Leptin	2.01 (0.92-3.39)	0.714
IL-10	0.15 (0.12-0.35)	0.874
IL-6	2.71 (1.01-3.25)	0.919
FBS	1.14 (1.05-1.24)	0.849
TG	2.06 (1.01-3.49)	0.908
HDL	0.88 (0.79-0.97)	0.890

Adjusted for age, sex, BMI, SBP, FBS, TC, TG, HDL, LDL, VFA, Adipocytokines;

VFA, Visceral Fat Area; IL, Interleukin; FBS, Fasting Blood Sugar; TG, Triglyceride; HDL, High Density Lipoprotein (No significant variables were not shown).

Discussion

In this study, the difference in VFA and the pattern of secretion of such hormones as adiponectin, TNF-α, leptin, IL-6 and IL-10, which are known to be important in human energy metabolism, were compared and investigated to determine how much these differences increase the risk of AMI in patients with AMI and in a control group.

Majority of the previous studies were based on the correlation of AMI with adipocytokine levels and insulin resistance, obesity and metabolic syndrome. Only a few studies compared adipocytokine levels in patients with AMI and in a control group. To the authors' best knowledge, this is the first study to investigate various adipocytokines and VFA in relation to the risk of AMI.

Studies reported that severe obesity and stronger insulin resistance led to a decreased level of adiponectin, a hormone specifically secreted in adipocytes; and that when insulin sensitivity improved after weight loss or glitazone treatment, adiponectin level increased.[21)]

Accordingly, our study showed that adiponectin level was lower in the patient group than in the control group, and the lower the adiponectin level, the higher the risk of AMI.

Leptin controls appetite and energy metabolism, and is directly related with body fat volume. Leptin is assumed to play an important role in the development of cardiovascular disease by stimulating the proliferation and migration of vascular smooth muscle cells, accelerating vascular calcification, increasing blood pressure through activation of sympathetic nerve, inducing oxidative stress in epithelial cells, and promoting platelet aggregation.[12)]

It is also known that higher leptin levels increase levels of small and concentrated LDL cholesterol, thereby resulting in increased cardiovascular diseases.[10)] Similar to the results of other studies, our study showed that leptin level was significantly higher in the patient group, and the higher the leptin level, the higher the risk of AMI.

IL-6, a cytokine involved in acute phase reaction, immune reaction, and hematopoiesis, is known to increase in proportion to postprandial blood insulin and glucose levels in patients with type II diabetes, particularly in type II diabetes patients with insulin resistance.[14-16)]

It is known that about 1/3 of total serum IL-6 is secreted in the adipose tissue, and IL-6 is related with BMI. As such, in obesity cases, IL-6 is secreted three times more in the visceral adipocyte than in the subcutaneous adipocyte, and the amount of secretion is greater when the waist circumference-to-hip ratio is high.[15)]

Consistent with this, in our study, the secretion of IL-6 was higher in both male and female patients with high VFA. Particularly, it is known that the higher the VFA, the higher the level of IL-6 in the hepatic portal vein, inducing the secretion of triglyceride in the liver, and consequently leading to hypertriglyceridemia that is related with visceral obesity.[17)]

IL-10, a cytokine that has strong anti-inflammatory effect is secreted by histiocyte, monocyte and lymphocyte in response to stimulation by infectious agents, and reduces tissue damages caused by the formation and secretion of inflammatory cytokines such as TNF-α and IL-6.[18)] When inflammatory cytokine is secreted by monocyte in response to stimulation from various endotoxins in the body, it induces the secretion of IL-10, and the resulting increase in IL-10 levels reduces the secretion and activity of inflammatory cytokine in the monocyte.[19)] Recent studies have reported that IL-10 is involved in maintaining the stability of thrombotic plaque by reducing the cellular damage and controlling the expression of iNOS on the surface of artherosclerotic plaque.[20)] The decrease in IL-10 level may become a factor in inducing the rupture of arteriosclerotic thrombotic plaque, and it has been reported that IL-10 level is low in patients with unstable angina.[20)] Similar to the results of other studies, our study showed that IL-10 level is associated with the risk of AMI as is adipocytokines.

According to a study, in an obese person, increase in body fat resulted in inconsistent changes in adipocytokines (e.g., decrease in adiponectin level, and increase in leptin, IL-6 and TNF-α levels or increase or decrease in resistin level).[21)] Studies on interactions between these adiocytokines showed that treatment of rat or human adipocytes with TNF-α or IL-6 activated the expression of their mRNA, and reduced the expression of mRNA of adiponectin; whereas treatment with adiponectin inhibited the expression of TNF-α.[22,23)] As such, adiponectin and leptin secreted in adipocytes are expected to perform opposite functions. Recent studies have shown that in obese patients, decrease in adiponectin level and increase in leptin level were observed, and that leptin-to-adioponectin ratio could be used as indicator for pediatric obesity and arteriosclerosis in patients with type II diabetes.[24)]

Consistent with the results of other studies, our study showed that adipocytokines could be a risk factor of AMI. The significant difference in the VFA and IL-10 levels between the patient and control groups, when gender was considered (but not when gender was disregarded), is attributable to the difference in the number of female subjects (ratio 27.3% vs 63.5%). Thus, VFA and IL-10 levels were found to be associated with the risk of myocardial infarction after adjustment of age and gender.

This study has several limitations. First, the control group does not represent the general population because the control group consisted only of patients who visited the hospital. Second, in the patient group, blood tests

were collected during the acute stage of the disease. Third, the number of subjects in both the patient and control groups was small. Despite these limitations, this study is meaningful in that it investigated the several risks and multiple adipocytokines of AMI at the same time through a study of a case-control group in adult Korean population. Prospective large-scale case-control studies are required to investigate the independent effects of visceral fat and adipocytokines on AMI by comparing the data on pre- and post-AMI.

References

1. Baker AR, Silva NF, Quinn DW, Harte AL, Pagano D, Bonser RS, et al. Human epicardial adipose tissue expresses a pathogenic profile of adipocytokines in patients with cardiovascular disease. Cardiovasc Diabetol 2006;5:1.
2. Fox CS, Massaro JM, Hoffmann U, Pou KM, Maurovich -Horvat P, Liu CY, et al. Abdominal visceral and subcutaneous adipose tissue compartments: association with metabolic risk factors in the Framingham Heart Study. Circulation 2007;116:39-48.
3. Steffes MW, Gross MD, Lee DH, Schreiner PJ, Jacobs DR Jr. Adiponectin, visceral fat, oxidative stress, and early macrovascular disease: the Coronary Artery Risk Development in Young Adults Study. Obesity (Silver Spring) 2006;14:319-26.
4. Kim DG, Lee KM, Jung SP. Clinical Significance of Abdominal Deep Subcutaneous Adipose Tissue in the Obese: Associations with Cardiovascular and Risk Factors. J Korean Acad Fam Med 2007;28:100-5.
5. Kopff B, Jegier A. Adipokines: adiponectin, leptin, resistin and coronary heart disease risk. Przegl Lek 2005;62 Suppl 3:69-72.
6. Kim JY, Shin HW, Jeong IK, Cho SW, Min SJ, Lee SJ, et al. The relationship of adiponectin, leptin and ghrelin to insulin resistance and cardiovascular risk factors in human obesity. Korean J Med 2005;69:631-41.
7. Hwang JS, Kim YP, Park HK, Hwang HS. The association of visceral fat area with anthropometric variables and its risk for metabolic syndrome. J Korean Acad Fam Med 2005;26:766-73.
8. Lim S, Jang HC. Clinical implication of adiponectin. Korean Diabetes J 2008;32:85-97.
9. Jung CH, Rhee EJ, Kim SY, Shin HS, Kim BJ, Sung KC, et al. Association between two SNPs (+45T>G and +276G>T) of the adiponectin gene and coronary artery diseases. Korean J Med 2006;70:393-401.
10. Shim WS, Kim HJ, Kang ES, Rhee YM, Ahn CW, Lim SK, et al. The Relationship between the Leptin Concentration and the Small Dense Low Density Lipoprotein Cholesterol Concentration in Korean Type 2 Diabetic Patients. J Korean Soc Endocrinol 2006;21:319-27.
11. Haffner SM, Mykkänen L, Rainwater DL, Karhapää P, Laakso M. Is leptin concentration associated with the insulin resistance syndrome in nondiabetic men? Obes Res1999;7:164-9.
12. Soderberg S, Ahren B, Jansson JH, Johnson O, Hallmans G, Asplund K, et al. Leptin is associated with increased risk of myocardial infarction. J Intern Med 1999;246:409-18.
13. Wallace AM, McMahon AD, Packard CJ, Kelly A, Shepherd J, Gaw A, et al. Plasma leptin and the risk of cardiovascular disease in the west of Scotland coronary prevention study (WOSCOPS). Circulation 2001;104:3052-6.
14. Cha BS, Kim SK. Role of Interleukin-6 in Human Obesity and Insulin Resistance. J Korean Diabetes Assoc 2001;25:332-6.
15. Mohamed-Ali V, Goodrick S, Rawesh A, Katz DR, Miles JM, Yudkin JS, et al. Subcutaneous adipose tissue releases interleukin-6, but not tumor necrosis factor-alpha, in vivo. J Clin Endocrinol Metab 1997;82:4196-200.
16. Pickup JC, Mattock MB, Chusney GD, Burt D. NIDDM as a disease of the innate immune system: association of acute-phase reactants and interleukin-6 with metabolic syndrome X. Diabetologia 1997; 40:1286-92.
17. Ko GJ, Kim JY, Kim MK, Suh SY, Choi HM, Hyun YY, et al. Association of IL-10 genotypes with cardiovascular risk factors in patients with hemodialysis. Korean J Med 2005;68:528-36.
18. Moore KW, O'Garra A, de Waal Malefyt R, Vieira P, Mosmann TR. Interleukin-10. Annu Rev Immunol 1993;11:165-90.
19. Smith DA, Irving SD, Sheldon J, Cole D, Kaski JC. Serum levels of the anti-inflammatory cytokine interleukin-10 are decreased in patients with unstable

angina. Circulation 2001;104:746-9.
20. Fasshauer M, Paschke R. Regulation of adipokines and insulin resistance. Diabetologia 2003;46:1594-603.
21. Kappes A, Loffler G. Influences of ionomycin, dibutyrylcyclo-AMP and tumor necrosis factor-alpha on intracellular amount and secretion of apM1 in differentiating primary human preadipocytes. HormMetab Res 2000;32:548-54.
22. Diez JJ, Iglesias P. The role of the novel adipocyte derived hormone adiponectin in human disease. Eur J Endocrinol 2003;148:293-300.
23. Diamond FB Jr, Cuthbertson D, Hanna S, Eichler D. Correlates of adiponectin and the leptin/adiponectin ratio in obese and non-obese children. J Pediatr Endocrinol Metab 2004;17:1069-75.
24. Satoh N, Naruse M, Usui T, Tagami T, Suganami T, Yamada K, et al. Leptin-to-adiponectin ratio as a potential atherogenic index in obese type 2 diabetic patients. Diabetes Care 2004;27:2488-90.