Original article

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Investigation of the relationship between non-alcoholic fatty liver disease and coronary artery disease

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Abstract

Aims. The purpose of the study was to examine the association between visceral adiposity form of non-alcoholic fatty liver and coronary artery disease severity and also to investigate the relationship between the epicardial adipose tissue thickness and non-alcoholic fatty liver disease with clinical and anthropometric measurements.

Materials and Methods. This study included 105 patients (mean age of patients were 57 ± 11, 82 of them male) who were hospitalized for coronary angiography because of chest pain. Nonalcoholic fatty liver disease was investigated by using ultrasonography. Thickness of the epicardial adipose tissue was measured by transthorasic echocardiography to right ventricular free wall adjacent to the parasternal long and short axis images. Gensini score was used for the severity of coronary artery disease.

Results. In patients with non-alcoholic fatty liver disease, right ventricular free wall epicardial adipose tissue thickness average of parasternal long and short axis were thicker than those who do not have non alcholic fatty liver disease (0,90 ± 0,19 cm; 0.58 ± 0.18 cm, p<0.001). Also, in patients with severe coronary artery disease, right ventricular free wall parasternal long and short axis average thickness of epicardial fat tissue was thicker than those of patients without severe coronary stenosis (0.86± 0.21 cm; 0,66 ±0.26 cm, *p*=0.001). For predictability of coronary artery disease, Receiver Operating Characteristic analysis of the area under the curve was found to be 0.60 (50.2 to 74.7, 95% Confidence Limits)

Conclusions. Not only the fatty tissue which surrounds the heart effects the coronary arteries but also other visceral organs adiposity effects the coronary arteries atherosclerotic process. ***Clin Ter 2014; 165(1):e46-51. doi: 10.7417/CT.2014.1671***

Key words: *coronary artery disease, epicardial adipose tissue, non-alcoholic fatty liver disease*

Introduction

Today, coronary artery diseases has become a serious epidemic reason of morbidity and mortality. Numerous studies are investigating on many parameters as a marker for the coronary artery diseases.

One of the main issues of the cardiology studies are prevent the development of coronary artery disease in the light of some markers and to estimate the risk of the disease before it becomes clinically symptomatic. The numerous studies on this subject put forward some of new parameters and biomarkers. Some of the oxidative stress markers are (paraoxonase-1, CD-40 ligand, such as plasma lipoproteins associated with), C-reactive protein, serum uric acid levels, flow mediated dilation, carotid intima media thickness and coronary artery calcium score as evaluate by computed tomography (CT) .

Fat tissue is producing a wide range of molecules and act like a highly complex endocrine organ that have wide variety of local and systemic effects (1, 2). In recent years several investigations have been the subject of the relationship between the epicardial adipose tissue (EAT) thickness and the coronary artery disease (CAD).

Regional adiposity is now supported by several studies, have a significant impact in the formation adverse metabolic and cardiovascular risk profile. Therefore, visceral adiposity was regarded as one of the features of the metabolic syndrome today (1, 3). Although the qualitative characteristics of the fat stores was found similar quantitative properties, different fat tissues were understood that especially subcutaneous fat and visceral fat stores have a different quantitative characteristics (4, 5). While much of the attention directed to the importance of intra abdominal adipose tissue, there were several new investigations about mediastinal and epicardial regions visceral adiposity (6).

Today, as a result of the studies emphasized that there were some parallelism between visceral adiposity and ischemic heart disease (7, 8). At this point, because of the increasing epicardial adipose tissue mass and the development of non-alcoholic fatty liver disease (NAFLD) have common risk factors, we suggest that these two conditions might be associated with each other.

The aim of this study was considering the existing common risk factors and to examine the relationship between the NAFLD and severity of CAD; and with NAFLD which is the simple criterion used in imaging visceral adiposity, as a marker for additional information and to evaluate useability

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of early diagnosis and prevention of coronary artery disease. In this study, we tried to get additional informations and markers for protection against CAD.

Materials and Methods

Patient population

In this study 105 patients who were hospitalized due to chest pain for coronary angiography to Erciyes University Department of Cardiology Coronary Care Unit between July 2008 and May 2010 was comprised the case group. All patients were underwent the standard treatments as prescribed by international guidelines. Informed consent was obtained from the patient about the research. Study protocol was approved by the Ethics Committee of Erciyes University School of Medicine.

The patient who drank alcohol more than (>20 g/day), and the patients with chronic liver disease due to viral or other conditions were excluded from study after taken detailed history. Cirrhosis were excluded from the absence of hypoalbuminemia, prolonged prothrombin time, hyperbilirubinemia, acid and other signs of portal hypertension.

Patients with poor echogenicity, pericardial effusion above 0.5 cm, calcified pericardium, pericardial thickness above 5 mm, with coronary artery disease undergoing CABG were excluded from the study.

All patients coronary angiography was performed the standard poses Philips Medical Systems Integris H 5000 or Toshiba® Infinix CC-i monoplan cardiac angiography with using standard Judkins approach aids.

Clinical and demographic characteristics of the patients were evaluated. Age and gender were recorded. All patients weight and height were measured and body mass index (BMI) was calculated by the formula: weight (kg)/height (m^2). Waist circumference was measured between the center distance of the last rib and iliac crest as World Health Organization's proposed. Patients fasting blood glucose, cholesterol, triglycerides, LDL and HDL values were measured.

Diagnosis of hypertension was considered, known to be a history of hypertension with taking antihypertensive treatment or measurements of the blood pressure above 130/89 by two times. Diagnosis of diabetes mellitus was considered, known to be on treatment of diabetes mellitus disease or fasting serum glucose level was above the 126 mg/dl. Hypercholesterolemia was defined as; known to be on a treatment of hypercholesterolemia or fasting serum cholesterol level was above the 200 mg/dl. History of coronary artery disease was identified in the presence of angiographically documented 50% and above stenosis of the coronary artery lesions, or as the history of intervention on coronary arteries. Cigarette smoking was defined as a history of cigarette smoking, or in the past twelve months history of active smoking cigarettes.

Ultrasonography

Ultrasonography (USG) was evaluated in 105 patients to determine fatty liver disease. Liver adiposity of USG examination were expressed as Grade I, Grade II and Grade III.

Echocardiography

EAT thickness were acquired by transthoracic echocardiography transthoracic echocardiography in the left lateral decubitus position using the long and short parasternal axis (with using 2.5-3.5 MHz transducer with a GE Vivid 7 device). To view the right ventricular free wall, both ventricular systole were measured simultaneously (9). Epicardial adipose tissue thickness was determined by taking the long and short axis measurements of a maximum three average results.

Coronary angiography: Selective coronary angiography was performed with using 6F or 7F catheters standard Judkins technique by the left or right femoral approach. The coronary artery stenosis above the >50% was named critical lesions, <50% stenosis as non critical.

Gensini score calculation

Gensini score was calculated by taking into consideration regional importance and degree of coronary artery stenosis (10). Lumen diameter by 25%, 50%, 75%, 90%, 99% and 100% percent stenosis was given the narrowing score, respectively 1, 2, 4, 8, 16 and 32. According to the importance of the functional significance of myocardial coefficient identify areas were given significant coefficient of stenosis in the vessel area. This coefficient was x5 for the left main coronary artery, for proximal left anterior descending artery it was x2.5, for the proximal circumflex artery it was x2.5, anterior descending artery to the middle segment it was x1.5, the right coronary artery, anterior descending artery distal to the first diagonal branch, posterolateral branch marginal branches and for it was x1, and for the other side branches it was x0.5. For all the vessels stenosis, strictures separate functional significance scores and the numbers multiplied and the results was collected to create Gensini score.

Statistical analysis

At the end of the study for statistical analysis SPSS statistical software program (version 15.0, SPSS®, USA) was used. Continuous variables are presented as mean ± standard deviation, discrete variables were presented as number or percent (%). All statistical tests were a two way. Suitability of the normal variables distribution were analyzed by Kolmogorov Smirnov Z test. Non parametric tests were applied to non normal distribution, parametric tests were performed in a normal distribution signifiers. X + SD (mean ± standard deviation) was used for who were conform to normal distribution data and these who do not conform the normal distribution data was expressed in the form as median (minimum value- maximum value). In data between the two groups normality analysis, "One Way ANOVA" significance and unpaired *t* test was performed. A non normal distribution of data among groups was used to compare Kruskal Wallis and Man Whitney U test. A p value ≤0.05 was considered as statistically significant

Spearman correlation analysis was used for the relationship between the data. ROC analysis was used for epicardial fat pad thickness cut off value.

Results

The study group was constituded by with the complaint of typical chest pain patients who were scheduled for coronary angiography. Twenty three (22%) of the patients were female, eighty two (78%) were male. Non critical (below the 50% stenosis) coronary artery disease was detected in thirty two patients. The mean age of patients was 57 ± 11 and demographic and the laboratory characteristics of patients were summarized in Table 1.

In the study 46% of patients (49 patients) with the history of hypertension and 46% patients (49 patients) with the history of diabetes mellitus, 20% in the (21 patients) had a history of coronary artery disease before. In addition, 69.5% of the patients with the history of (73 patients) smoking, 7.6% (8 patients) had a previous history of cerebrovascular disease (Table 2).

Non alcoholic fatty liver disease (NAFLD)

All patients were examined by ultrasonography for NAFLD. A total of 71, including one patient with severe NAFLD (Grade 3), was detected of NAFLD. There were 34 (32.4%) patients with no steatosis (Grade 0) (Fig. 1).

In 67 of 71 patients with fatty liver disease, average EAT thickness was examined above the cutt off value. In patients with NAFLD compared with patients had no steatosis in liver, the parasternal long and short axis right ventricular free wall thickness was thicker than the average EAT (0.90 ± 0.19 cm and 0.58 ± 0.18 cm, respectively, p <0.001). In addition, degree of adiposity was associated with epicardial fat thickness. Average of 34 patients diagnosed as mild fatty liver (Grade 1), the average thickness of long and short axes was detected 0.81 ± 0.21 cm, moderate fatty liver (Grade 2) identified 32 patients average was 1.00 ± 0.12 cm. In one patient with severe steatosis (Grade 3) the average thickness of long and short axes was detected 0.95 cm. Average of 34 patients with no steatosis, epicardial fat thickness was 0.58 ± 0.18 cm (Table 3).

When we examined the patients mean Gensini with each other in those with NAFLD, mean Gensini score was 47.6 ± 29.2 and in those without NAFLD, the mean Gensini 22.7 ± 21.6 (Respectively, p <0.001). Increase in the degree of steatosis was significantly parallel with the incresing values of the Gensini scores. Gensini score was 37.9 ± 23.5 in patients with Grade 1, in patients with Grade 2, it was found 57.5 ± 31.4. In a single patient with grade 3 steatosis, Gensini score was found 114 (Respectively, p <0.001). The mean Gensini score of 34 patients who had no NAFLD was found 22.7 ± 21.6 (Table 4).

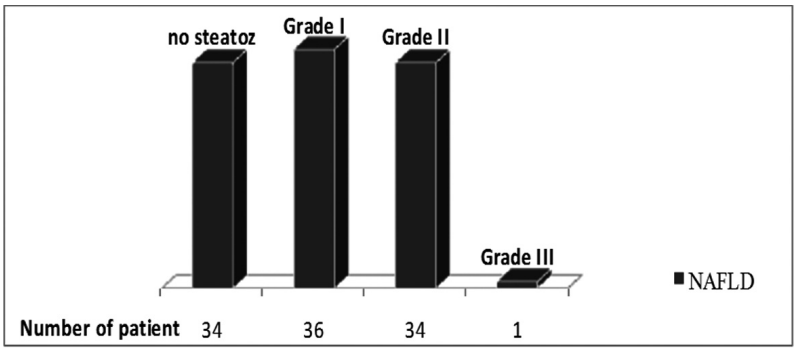

Fig.1. The distributions of NAFLD in patient populations.

Table 1. The distribution of the basic characteristics of the patients

Parameters	X±SS	
Age	57 ± 11	
Gensini score	42,7 ± 29,6	
Starving blood sugar (mg/dl) LDL (mg/dl) HDL (mg/dl) TG (mg/dl) T.cholesterol (mg/dl)	138,1 ± 51,4 111,4 ± 36,5 39,0 ± 10,0 174,7 ± 79,9 180,8 ± 43,1	
	n	%
Female	23	22
Male	82	78

***LDL:** Low density lipoprotein, **HDL:** High density lipoprotein, **TG:** Triglyceride, CAD: Coronary artery disease, **X:** Average, **SD:** Standart deviation*

Table 2. The distribution of comorbidities of the patients

Comorbidities		n	%
DM	Diabetics	49	46
	Nondiabetics	56	54
HT	Hypertension	49	46
	Nonhypertension	56	54
Smoking	yes	73	69.5
	no	32	30.5
CAD history	yes	21	20
	no	84	80
CVD history	yes	8	7.6
	no	97	92.4

HT: Hypertension, **DM:** Diabetes mellitus, **CAD:** Coronary artery disease, **CVD:** Cerebrovascular disease

Table 3. Relationship between degree of liver steatosis and average EAT thickness.

NAFLD	Cut off EAT >06 cm(n)	p values	Mean. EAT thickness(cm)	p values
NS (n:34)	14	<0.001	0.58 ± 0.18	<0.001
Grade 1 (n:36)	32	<0.001	0.81 ± 0.21	<0.001
Grade 2 (n:34)	34	<0.001	1.00 ± 0.12	<0.001
Grade 3 (n:1)	1	<0.001	0.95	<0.001

NAFLD: Non Alcoholic Fatty Liver Disease, EAT: epicardial adipose tissue, NS: no steatosis

Table 4. Relationships between tdegree of NAFLD, average EAT thickness and average Gensini score.

NAFLD	Gensini	p values	Av. EAT thickness (cm)	p values	Cut off EAT >06 cm (n)	p values
NS (n:34)	22.7 ± 21.6	<0.001	0.58 ± 0.18	<0.001	14	<0.001
Grade 1 (n:36)	37.9 ± 23.5	<0.001	0.81 ± 0.21	<0.001	32	<0.001
Grade 2 (n:34)	57.5 ± 31.4	<0.001	1.00 ± 0.12	<0.001	34	<0.001
Grade 3 (n:1)	114	< 0.001	0.95	<0.001	1	<0.001

NAFLD: Non Alcoholic Fatty Liver Disease, EAT: epicardial adipose tissue, NS: no steatosis

Epicardial adipose tissue measurements

TTE measurements showed that EAT's average thickness was 0.80 ± 0.24 cm. ROC analysis for the prediction of severe coronary artery disease EAT cut off thickness was found 0.6 cm, and the test sensitivity was found 77.84% (95% confidence lmits, 71.2 to 83.6), and the specificity was found 63.08% (95% confidence limits: 50.20 to 74.70). In 73 patients EAT average thickness of the cut off value was found 0.86 ± 0.21 cm. In 32 patients average of EAT thickness was measured with a mean of 0.66 ± 0.26 cm which was below the cut off value.

According to the severity of coronary artery disease, epicardial adipose tissue thickness was observed statistically significantly higher in the cases. In patients who do not have significant stenosis, EAT average thickness was found 0.66 ± 0.26 cm measured. In patients with severe stenosis coronary artery disease, this value was measured as 0.86 ± 0.21 cm (Table 5).

Identified 73 patients with severe coronary artery disease, mean waist circumference was measured 97.3 ± 11.6 cm, this value was 92.7 ± 12.5 cm for the patients with non critical stenosis (respectively, p <0.06).

The mean body mass index (BMI) of all patients in the study was 29.5 ± 4.9 kg/m2. This value was measured 30.3 ± 4.8 kg/m2 in patient with severe coronary artery disease and it was measured 27.7 ± 4.8 kg/m^2 in patients without critical coronary artery stenosis (Respectively, p: 0.014) (Table 5).

Discussion

Epicardial adipose tissue is an organ that gives paracrine control and affects the cardiac function by producing many

Table 5. Relationship between Antropometric values and severity of CAD.

Parameters	<50% stenosis group (n:65)	>50/ stenosis group (n:185)	p values
Average EAT thickness	0.66 ± 0.26	0.86 ± 0.21	0.001
Metabolic syndrome	23	104	0.001
Waist circumference(cm)	92.7 ± 12.5	97.3 ± 11.6	0.057
BMI(kg/m2)	27.7 ± 4.8	30.3± 4.8	0.014

CAD: Coronary artery disease, EAT: epicardial adipose tissue, BMI: Body Mass Index

bioactive molecules (11). Clinical studies were showed that morphology and function of the heart is associated with each other. EAT thickness was shown in the development of cardiovascular adverse effects by the agency of inflammatory mediators. Several studies were emphasized that obesity, increased abdominal and subcutaneous adipose tissue and body mass index lead to an increased general inflammation mediators (12).

EAT's relationship between the local and systemic effects on biochemical, cardiovascular and metabolic complications is a subject of the current researchs. However recent studies tries to find the question that does EAT thickness is a evidence of cardiovascular and metabolic complications.

It has been shown that inflammation markers which was produced by adipose tissue were also found in EAT (13). All of the fat tissue in the body tissue, especially abdominal fat tissue increases insulin resistance by elevation the TNF-α serum levels which is known to be a risk factor for coronary artery disease (14). KH Cheng et al. took a total of 58 patients, 46 of them were applied CABG operation and 12 of them were applied external coronary open heart surgery. Fourty six patient with coronary artery disease epicardial tissue Leptin, visfatin, and IL-6 level was high but the adiponectin level was low (15).

Multislice CT was preferred rather than echocardiography to measure the EAT thickness and the average thickness of coronary plaque morphology because of echocardiography have a limited windows for full measurment of fat mass surronding the heart. However, Iacobellis et al. were proposed directly measured by echocardiography for the detection of EAT thickness (16, 17). We also used coronary angiography study for the diagnosis of visceral adiposity which is cheap and easy to use method and it is the gold standard method for detecting the coronary artery disease.

Iacobellis et al. were investigated the 246 patients and 58% of them diagnosed with metabolic syndrome. EAT thickness was found 0.95 cm in men and 0.75 cm in women of these patients (18). In another study, Eroglu and et al. were reported that the thickness of EAT cut off value for CAD was 0.52 cm (8). Likewise in our study, in accordance with ROC analysis for the predictability of CAD, the cut off value of the EAT thickness was found 0.6 cm.

In this study EAT thickness was found statistically significantly higher in the group of high Gensini score. In addition, the patients with the EAT cut off value was above the 0.6 cm, anthropometric measurements were also significantly higher. As a result of these findings we think that, patients with EAT thickness above the 0.6 cm might be a cardiometabolic risk.

Insulin resistance is associated with visceral adiposity. Fatty liver appears the most visceral adiposity model in clinical practice. Clinically, this steatosis is expressed nonalcoholic fatty liver disease (NAFLD) (19-23). In recent years, many studies have been demonstrated that NAFLD was associated with insulin resistance. In Sargin et al. study was showed that, in patients without diabetes mellitus disease, insulin resistance was related to NAFLD. In recent studies have emphasized that, EAT thickness was found to be significantly related in a metabolic syndrome's clinical and anthropometric parameters with the similar way (24). acobellis et al. were studied for visceral adiposity by using magnetic resonans imaging and were found that EAT measurement was easy and right method for visceral adiposity measurment (25).

The question which was not mentioned before is out of EAT regional adiposity and severity of coronary artery disease might be associated with the each other? Various studies were performed in order to answer this question. Assy N and et al were investigated a total of 29 metabolic syndrome patients and found that the presence of NAFLD in particular way might effect the development of CAD. The presence of NAFLD and CAD were evaluated with CT angiography and coronary artery disease is named presence of >50% lesions. Even without the presence of the metabolic syndrome, NAFLD is a strong risk factor for atherosclerosis (26)**.** Alper et al. examined the relationship between nonalcoholic fatty liver disease and coronary artery disease with a diagnosis of the metabolic syndrom in 43 patients presence of NAFLD by using ultrasonography. At the end of the study they found an association between NAFLD, CAD and Gensini score. The presence of NAFLD patients with metabolic syndrome should be investigated for CAD (27). CH Chen et al. found that the relationship between NAFLD and calcium score (CAC> 100) on coronary artery by using CT (28). Also; the patients who have diagnosis of NAFLD, steatohepatitis increase the incidence of cardiovascular events (29). EAT and NAFLD have similar effects due to the metabolic syndrome and insulin resistance, but the clinical association of these two fatty model is not clear. In this study, we aim to investigate the relationship beween the NAFLD which was indicated of abdominal obesity, as a marker of metabolic syndrome and EAT thickness; both the relationship between the presence of CAD.

In this study positive correlation was found between EAT and NAFLD. Sonographic evaluation made by for the presence of both fatty model. USG which is cheap and easy method could be used safely in the measurement of visceral adiposity. Gensini scores and the degree of NAFLD were found in this study to be associated with each other. As a result of this finding we believe that patients with high visceral fatness and risk profile for CAD need to be further examined in clinical progress.

On the basis of 0.6 cm in thickness of İacobellis et al. were showed that; severity of NAFLD was higher in patients with EAT thickness above the cut off value. In addition, when we classified every EAT average thickness according to the degree of adiposity, EAT average thickness was showed an increase in the similar way with the degree of adiposity.

In this study, it was found a statistically significant relationship with the severity of NAFLD and CAD, which was similar relationship between EAT and CAD. Moreover, the average Gensini score was significantly correlated with the degree of hepatic steatosis. In the light of this information in fatty liver disease, which is related to insulin resistance in metabolic syndrome patients, should be considered a risk factor for coronary artery disease.

This study was emphasized that EAT thickness and NAFLD had a positive relationship between the similar way effects on CAD formation. These two adiposity may be an association between the idea of the common risk factors they have been supplied. The presence of NAFLD which was

component of visceral adiposity, have a close relationship between EAT and could be viewed easily during the examination of echocardiographic view. The presence of NAFLD ise closely related to metabolic and cardiovascular markers. All patients with the risk of visceral adiposity, especially diagnosis of NAFLD, proposed to be considered as an additional risk factor for coronary artery diseases.

Some patients with high BMI values, who have epicardial, abdominal and subcutaneous fatness may have normal coronary anatomy. This contradiction was suggested that the other factors might effected the patogenesis of relationship between adiposity models and CAD.

Local fat tissues, likewise EAT and NAFLD, could affected the regional, paracrine, endocrine and also cardiovascular system. We think that, more advanced and expanded studies should be investigated to clarify the patogenesis of the local fat tissues influence on systemic atherosclerosis.

References

1. Carr DB, Utzschneider KM, Hull RL,et al. Intra-abdominal fat is a major determinant of the National Cholesterol Education Program Adult Treatment Panel III criteria for the metabolic syndrome. Diabetes 2004; 53: 2087-94
2. Kershaw EE, Flier JS. Adipose tissue as an endocrine organ. J Clin Endocrinol Metab 2004; 89:2548-56
3. Grundy SM, Hansen B, Smith SC Jr, et al. Clinical management of metabolic syndrome: report of the American Heart Association/National Heart, Lung, and Blood Institute/American Diabetes Association conference on scientific issues related to management. Circulation 2004; 109:551-6
4. Dusserre E, Moulin P, Vidal H. Differences in mRNA expression of the protein secreted by the adipocytes in human subcutaneous and visceral adipose tissues. Biochim Biophys Acta 2000; 1500:88-96
5. Wajchenberg BL. Subcutaneous and visceral adipose tissue: their relation to the metabolic syndrome. Endocr Rev 2000; 21:697-738
6. Sharma AM. Mediastinal fat, insulin resistance, and hypertension. Hypertension 2004; 44:117-8
7. Alexopoulos N, McLean DS, Janik M, et al. Epicardial adipose tissue and coronary artery plaque characteristics. Atherosclerosis 2010; 210:150-4
8. Eroglu S, Sade LE, Yildirir A, et al. Epicardial adipose tissue thickness by echocardiography is a marker for the presence and severity of coronary artery disease. Nutr Metab Cardiovasc Dis 2009; 19:211-7
9. Fried SK, Bunkin DA, Greenberg AS. Omental and subcutaneous adipose tissues of obese subjects release interleukin-6: depot difference and regulation by glucocorticoid. J Clin Endocrinol Metab1998; 83:847-50
10. Gensini GG. Coronary arteriogaphy. Mount Kisco, New York: Futura Publishing Co, 1975
11. Iacobellis G, Corradi D, Sharma AM. Epicardial adipose tissue: anatomic, biomolecular and clinical relationships with heart. Nat Clin Pract Cardiovasc Med 2005; 2:536-43
12. Mazurek T, Zhang L, Zalewski A, et al. Human epicardial adipose tissue is a source of inflammatory mediators. Circulation 2003; 108:2460-6
13. Cancello R, Tordjman J, Poitou C, et al. Increased infiltration of macrophages in omental adipose tissue is associated with marked hepatic lesions in morbid human obesity. Diabetes 2006; 55:1554-61
14. Wellen KE, Hotamisligil GS. Obesity-induced inflammatory changes in adipose tissue. J Clin Invest 2003; 112:1785-8
15. Cheng KH, Chu CS, Lee KT, et al. Adipocytokines and proinflammatory mediators from abdominal and epicardial adi pose tissue in patients with coronary artery disease. Int J Obes (Lond)2008; 32:268-74
16. Iacobellis G, Assael F, Ribaudo MC, et al. Epicardial fat fromechocardiography: a new method for visceral adipose tissue prediction Obes Res 2003; 11:304-10
17. Iacobellis G, Ribaudo MC, Assael F, et al. Echocardiographic epicardial adipose tissue is related to anthropometric and clinical parameters of metabolic syndrome: a new indicator of cardiovascular risk J Clin Endocrinol Metab 2003; 88:5163-8
18. Iacobellis G, Willens HJ, Barbaro G, et al. Threshold values of high-risk echocardiographic epicardial fat thickness. Obesity (Silver Spring) 2008; 16:887-92
19. Pyorala M, Miettinen H, Halonen P, et al. Insulin resistance syndrome predicts the risk of coronary heart disease and stroke in healthy middle-aged men: the 22-year follow-up results of the Helsinki Policemen Study. Arterioscler Thromb Vasc Biol 2000; 20:538-44
20. Kozan O, Oguz A, Abaci A, et al. Prevalence of the metabolic syndrome among Turkish adults. Eur J Clin Nutr 2007; 6:548-53
21. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive summary of the third report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). JAMA 2001; 285:2486-97
22. American Diabetes Association. Diagnosis and Classification of Diabetes Mellitus. Diabetes Care 2004; 27:5-10
23. Onat A, Ceyhan K, Basar O, et al. Metabolic syndrome: major impact on coronary risk in a population with low cholesterol levels a prospective and cross-sectional evaluation. Atherosclerosis 2002; 165:285-92
24. Mazurek T, Zhang L, Zalewski A, et al. Human epicardial adipose tissue is a source of inflammatory mediators.Circulation 2003; 108:2460-6
25. Iacobellis G, Assael F, Ribaudo MC,et al. Epicardial fat from echocardiography: a new method for visceral adipose tissue prediction. Obes Res 2003; 11:304-10
26. Assy N, Djibre A, Farah R, et al. Presence of coronary plaques in patients with nonalcoholic fatty liver disease. Radiology 2010; 254:393-400
27. Alper AT, Hasdemir H, Sahin S.The relationship between nonalcoholic fatty liver disease and the severity of coronary artery disease in patients with metabolic syndrome. Turk Kardiyol Dern Ars 2009; 37:364-400
28. Chen CH, Nien CK, Yang CC, et al. Association between nonalcoholic fatty liver disease and coronary artery calcification. Dig Dis Sci 2010; 55:1752-60
29. Treeprasertsuk S, Lopez Jimenez F, Lindor KD. Nonalcoholic Fatty Liver Disease and the Coronary Artery Disease. Dig Dis Sci 2011; 56:35-45