



Clinical Research

# Clinical Importance of Epicardial Fat Thickness Defining in Obese Patients

Galina A. Chumakova, PhD, ScD<sup>1,3\*</sup>, Nadezhda G. Veselovskaya, PhD<sup>2,3</sup>

<sup>1</sup>Altai State Medical University, Barnaul, Russia

<sup>2</sup>Research Institute for Complex Issues of Cardiovascular Diseases,  
Siberian Branch of the Russian Academy of Medical Sciences, Kemerovo, Russia

<sup>3</sup>Altai State Cardiological Dispensary, Barnaul, Russia

## Abstract

Obesity is a global epidemic characteristic of the 21st century; therefore, studying the subclinical markers of coronary atherosclerosis in overweight patients is current and relevant. With weight increase, hypertrophy and hyperplasia of adipocytes occur not only in the abdominal area, but also in the ectopic local fat depots, including the epicardial ones. As the myocardium and coronary arteries are anatomically related, hormonally active epicardial fat seems to be a pathologic link between obesity and coronary heart disease (CHD). The objective of this research is to study the relationship between epicardial adiposity and abdominal obesity with metabolic risk factors and visceral fat adipokines. The influence of epicardial fat thickness (EFT) and waist circumference (WC) on the risk of development of significant coronary atherosclerosis in obese patients with CHD was studied (138 men, 55.47±9.07 years and BMI 35.2±5.2 kg/m<sup>2</sup>). The ROC analysis reveals that EFT is more informative in diagnosing significant stenoses (≥70 %): sensitivity of the given marker constituted 80.4 %, specificity – 67.6 % (cut-off value=6 mm). On comparison of the epicardial and abdominal adiposity as predictors of coronary atherosclerosis, EFT was found to be more significant than WC. In patients with CHD, the increase in EFT is associated with the more serious involvement of the coronary arteries, whereas the WC analysis did not establish similar regularities. Evaluation of EFT in obese patients can be used as a noninvasive marker indicative of the presence of subclinical stenoses of the coronary arteries. IJBM 2012; 2(3):161-168. © 2012 International Medical Research and Development Corporation. All rights reserved.

**Key words:** epicardial fat, abdominal obesity, cardiovascular risk factors, coronary atherosclerosis.

## Introduction

Obesity has reached epidemic proportions in the 21st century. Over the last 10 years, a tendency for an increase in the number of obese people has been observed [1, 3]. Obesity is one of the major risk factors of the cardiovascular system pathology, a leading cause of morbidity and mortality in the adult population of the developed world [4-6].

The number of obese patients with CHD who

undergo myocardial revascularization is on the increase. Such obese patients have several associated pathologies, like multiple coronary atherosclerosis and often the involvement of the left coronary arterial trunk. Young people form a large percentage [7].

In modern cardiology, particular attention is being paid to the topical studies of pre-clinical markers of coronary artery stenoses and the development of risk stratification of cardiovascular complications in obese patients with CHD prior to myocardial revascularization. From among the major factors of cardiovascular risk, abdominal obesity (AO) ranks as an important noninvasive marker of insulin resistance, which causes the development of metabolic syndrome (MS) - the CHD predictor. Abdominal obesity leads to the accumulation of visceral fat in the mesentery, loop space, greater omentum and lesser omentum. Unlike

\*Corresponding author: Prof. Galina A. Chumakova, PhD, ScD, Department of Hospital and Polyclinical Therapy, Altai State Medical University, 40, Lenin ave., Barnaul, 656038, Altai Krai, Russian Federation.  
E-mail: g.a.chumakova@mail.ru

the brown adipose tissue characteristic of subcutaneous fat (SCF), visceral fat is white adipose tissue (WAT), hormonally active and capable of producing a large number of bioactive substances (adipokines, chemokines, cytokines, hormone-active proteins) involved in metabolic disorders, inflammation, thrombo- and atherogenesis processes [8,9].

In clinical practice, waist circumference is used to identify AO. However, this method includes both the available visceral fat and SCF thickness in the lumbar region, anterior abdominal wall and fat in the retroperitoneal space. As the WC method has not yet been standardized, and the WC value is dependent upon the patient position at the time of measurement, food intake, respiration and constitution, it leads to misdiagnosis of visceral obesity and MS.

Being overweight leads to hypertrophy and hyperplasia of the adipocytes in the visceral fat, not only in the typical (abdominal) areas, but also in the ectopic local fat depots, including epicardial ones. Evidence was found to prove that visceral fat is responsible for the major factors of inflammation, chemotaxis and angiogenesis which participate in CHD pathogenesis and its progress [8]. Being anatomically and functionally related to the myocardium, epicardial fat directly impacts the morphology of the coronary artery via the paracrine mechanisms [10].

The objective of this research was to study the influence of epicardial adiposity and abdominal obesity on the risk of development and severity of coronary atherosclerosis.

## Material and Methods

In all, 138 men with the diagnosis of CHD and angina II-III functional class,  $55.7 \pm 9.1$  years, with class I-III obesity, body mass index (BMI)  $35.2 \pm 5.2$  kg/m<sup>2</sup> were included in the research. For the diagnosis of stenoses, all the patients had undergone coronary angiography during the first six months from the time of specification of the diagnosis. However, patients with type II diabetes, who had suffered acute myocardial infarction less than three months prior, with heavy concomitant pathology, were excluded from the research.

Prior to blood sampling, all the patients were subjected to over 12 hours of fasting and blood analysis was performed in a clinical laboratory. Total serum cholesterol and triglycerides (TG) were measured using the enzymatic calorimetric test. High-density lipoprotein (HDL) cholesterol was measured using the selective inhibition method, whereas low-density lipoprotein (LDL) cholesterol was calculated employing the Friedewald formula. Following the blood sampling, a sodium fluoride tube was used to store and transfer the fasting glucose sample which was measured using the hexokinase method. The leptin and resistin levels were assessed by ELISA (Sweden). The basic apolipoproteins (apolipoprotein A1 (ApoA1) and apolipoprotein B (ApoB)) were defined based on Konelab PRIME 60 Chemical Chemistry Analyzer (Finland) by the immunoprecipitation method. All laboratory research were performed after diagnosing CHD and prior to statin therapy, then at three-month intervals, within 12-18 months of supervision.

An automatic blood pressure monitor (HEM712C

automatic digital device with a cuff adjusted to the brachial circumference; Omron Health Care, USA) was used to measure the systolic (sBP) and diastolic blood pressure (dBP). After resting for 10 minutes, three sBP and dBP measurements were taken, and the final value was defined as the mean of the latter two. Hypertension was defined as sBP > 140 mm Hg or dBP > 90 mm Hg or the regular use of medication for hypertension.

### Anthropometry

Anthropometric characteristics, including height and weight in patients with CHD were used to calculate BMI (kg/m<sup>2</sup>). Abdominal obesity was assessed by waist circumference.

### Measurement of echocardiographic epicardial fat thickness

Two-dimensional transthoracic echocardiography (GE Vivid 7 with 4.0 MHz transducer) was used to calculate the epicardial fat thickness (EFT). We registered three cycles of the two-dimensional parasternal long-axis view and the parasternal short-axis view at the basal left ventricular level. The EFT was calculated in millimeters (mm) on the free wall of the right ventricle (RV) in the still images obtained at the end of systole on both parasternal long-axis and short-axis views. The anterior echolucent space between the RV outer wall and the linear echodense parietal pericardium was considered to be epicardial fat.

### Coronary angiography

To prove the stenoses of the coronary arteries and to recommend myocardial revascularization, coronary angiography was performed on all the patients, using the Philips (USA) equipment.

### Statistical analysis

We used STATISTICA 6.1, MedCalc 5.4 software for statistical analysis. Data in the text and Tables are expressed as mean  $\pm$  standard deviation and the median (interquartile range). The hypothesis of normal distribution was checked by the Shapiro-Wilks Normality Test. Hypothesis check of equality of the EFT mean values in some groups was performed using the Kruskal-Wallis method. The correlation between the parameters was tested employing the Spearman correlation coefficients. For the estimation of EFT sensitivity and specificity as a prognostic criterion, the ROC-curve (Receiver Operator Characteristic) was constructed. To assess the influence of various predictors on the development of significant coronary atherosclerosis, we used the binary logistic regression method. All statistical analyses were two-sided, and P value < 0.05 was considered to be statistical significance.

## Results

Based on the analysis of metabolic and hormone disorders, the patients examined were segregated into three groups: two groups with AO (WC=94-101 cm) and (WC $\geq$ 102 cm) and one without AO (WC<94 cm). The results of the analysis of the basic metabolic risk factors are given in Table 1.

**Table 1**  
Peculiarities of risk factors and adipokines in patients with different WC

WC, cm Risk factor	<94 (n=51)	94-101 (n=37)	≥102 (n=50)	P
WC, cm (mean±SD)	88.51±7.32	97.06±8.63	110.22±9.51	$p_1 < 0.001$ $p_2 < 0.001$
HDL, mmol/L (median(interquartile range))	1.02 (0.8;1.23)	0.98 (0.88;1.28)	0.88 (0.73;1.09)	$p_1 = 0.627$ $p_2 = 0.029$
sBP, mm Hg (mean±SD)	152.91±22.82	149.78±18.23	156.76±21.08	$p_1 = 0.356$ $p_2 = 0.069$
dBp, mm Hg (mean±SD)	93.25±9.70	92.65±8.67	94.07±7.67	$p_1 = 0.576$ $p_2 = 0.154$
TG, mmol/L (median (interquartile range))	1.51 (1.3;2.0)	1.32 (1.0;2.0)	2.05 (1.5;2.5)	$p_1 = 0.138$ $p_2 = 0.019$
glucose, mmol/L (median (interquartile range))	5.20 (4.7;5.6)	4.82 (4.5;5.6)	5.54 (5.0;6.8)	$p_1 = 0.669$ $p_2 = 0.006$
leptin, ng/mL (median (interquartile range))	6.3 (2.3;8.2)	7.25 (6.4;12.5)	28.84 (23.4;34.8)	$p_1 = 0.045$ $p_2 < 0.001$
resistin, ng/mL (median (interquartile range))	10.34 (6.4;11.6)	9.81 (6.8;12.1)	11.54 (8.6;14.6)	$p_1 = 0.345$ $p_2 = 0.129$

**Note:** WC - waist circumference; HDL - high-density lipoprotein cholesterol; sBP - systolic blood pressure; dBp - diastolic blood pressure; TG - triglyceride.

$p_1$  - statistical significance between groups with WC<94cm and WC 95-101 cm;

$p_2$  - statistical significance between groups with WC≤94cm and WC ≥102 cm.

Meaningful distinctions in the major metabolic risk factors and adipokines in both groups [with AO (WC 94-101 cm) and without AO] were not registered. The obese patients (WC≥102 cm) showed increased TG, glucose, leptin and decreased HDL values, compared with patients from the group without AO. Moreover, in the group with AO (WC≥102 cm) abnormal tolerance to glucose was evident in 8

persons (16%). Mean indices of sBP and dBp were practically the same in all the groups. A resistin mean value tended to increase, although in groups it differed insignificantly.

The outcomes of the analysis of metabolic disorders and adipokines in groups with different EFT are presented in Table 2.

It follows from Table 1 that, metabolic disorders

**Table 2**  
Peculiarities of risk factors and adipokines in patients with different EFT

Risk factor	EFT, mm ≥3 (n=37)	4-6 (n=51)	7-10 (n=29)	>11 (n=21)	P
EFT, mm	1.0 (1.0;2.0)	5.0 (4.0;6.0)	9.0 (7.5;10)	12.0 (11;13)	<0.001
HDL, mmol/L	1.02±0.18	1.22 (1.0;1.3)	1.0 (0.95;1.2)	0.98 (0.95;1.11)	0.035
sBP, mm Hg	140 (130;150)	137 (130;140)	145 (130;160)	140 (130;150)	0.056
dBp, mm Hg	80 (70;95)	80 (80;85)	80 (70;90)	80 (80;90)	0.054
TG, mmol/mL	1.37 (1.1;1.6)	1.42 (1.2;1.7)	2.0 (1.45;2.5)	2.15 (1.9;2.5)	<0.001
Glucose, mmol/L	5.21±0.58	4.90±0.56	5.33±0.65	5.80±0.96	0.036
Leptin, ng/mL (median (interquartile range))	5.83 (3.2;8.4)	7.25 (6.4;12.5)	17.9 (13.1;22.8)	32.64 (26.3;34.6)	<0.001
Resistin, ng/mL (median (interquartile range))	4.62 (2.3;9.7)	9.2 (8.2;12.4)	12.53 (10.3;16.1)	13.22 (10.1;14.2)	<0.001

**Note:** EFT- epicardial fat thickness; HDL- high-density lipoprotein cholesterol; sBP- systolic blood pressure; dBp- diastolic blood pressure; TG- triglyceride

become stronger with the increase in EFT. For instance, in patients with EFT>11 mm, the mean values of TG were the highest, whereas the HDL values were the lowest. Moreover, patients with EFT>11 mm showed the highest values of hormones (leptin and resistin) in the visceral fat. High and mean glucose content in the group of patients with epicardial adiposity is explained by their intolerance to glucose and fasting hyperglycemia in 5 patients. No significant difference in sBP and dBP indices was found, probably, because most patients had hypotensive drug therapy.

The amount of epicardial fat is correlated with the level of abdominal obesity [11]. Earlier studies revealed the relationship of EFT with metabolic risk factors, indices of insulin resistance, and the proinflammatory markers in patients with metabolic syndrome [12-13]. Using correlation analysis, we assessed the EFT association with basic and additional metabolic risk factors, age and BMI. It appears that EFT is correlated with plasma lipids: positively with TG ( $r=0.398$ ;  $p<0.001$ ) and negatively with HDL ( $r=-0.295$ ;  $p=0.004$ ). Also, EFT is correlated with additional markers of cardiovascular risk (ApoA ( $r=-0.309$ ;  $p=0.002$ ) and ApoB ( $r=0.351$ ;  $p<0.001$ )). Also, a positive correlation between EFT and visceral fat hormones (leptin ( $r=0.586$ ;  $p<0.001$ ) and resistin ( $r=0.241$ ;  $p=0.023$ )) was established (Fig.1).

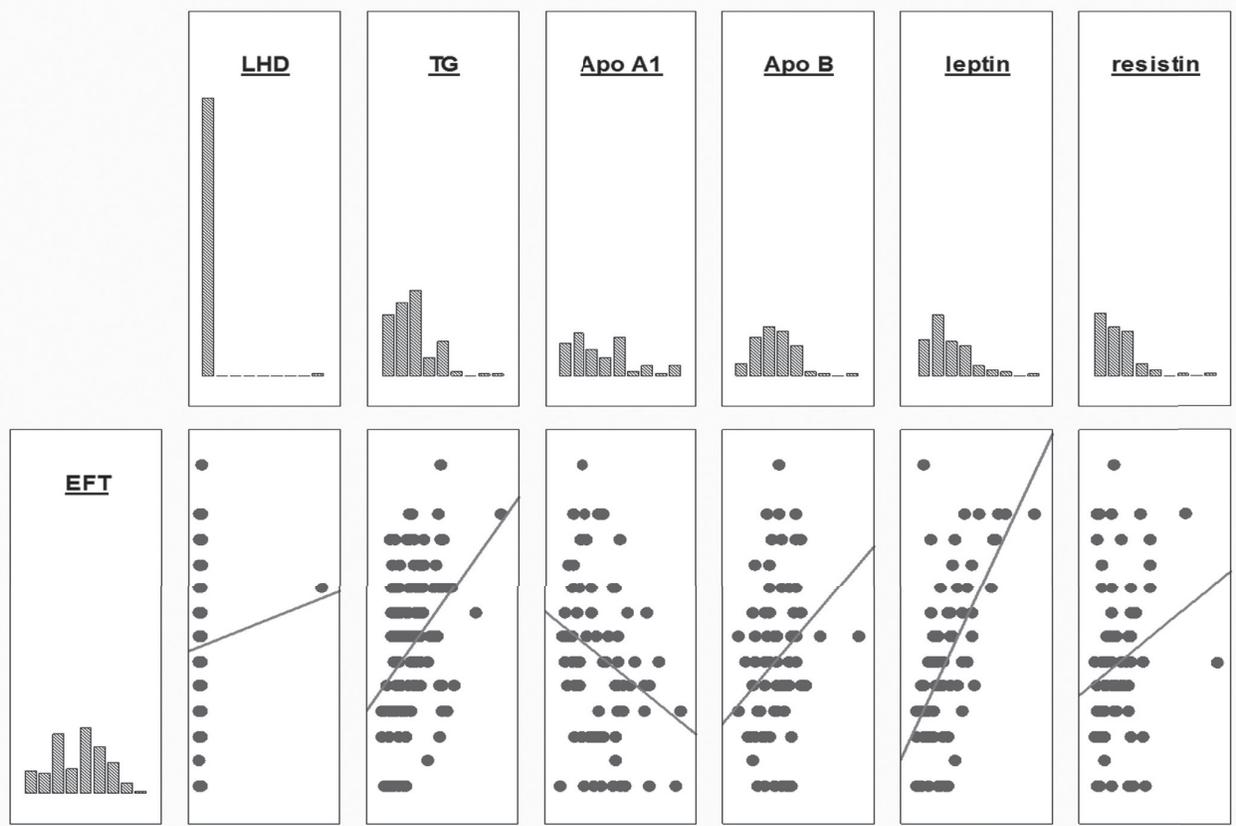
We failed to trace the EFT association with sBP ( $r=0.148$ ;  $p=0.107$ ) and dBP ( $r=0.136$ ;  $p=0.109$ ), as 92% of hypertensive patients reported the use of the antihypertensive drug treatment. Moreover, the patients with imbalanced

carbohydrate metabolism were excluded from the research. Therefore, we could not obtain valid data on the glucose and EFT relationship ( $r=0.145$ ;  $p=0.090$ ). We also did not establish any association between EFT and IBM ( $r=0.135$ ;  $p=0.114$ ) because it is not necessary that weight gain occurs solely due to atherogenic visceral fat accumulation (expressed by EFT index); it could also happen due to inert hormonally inactive subcutaneous fat as well. Perhaps, it is one of the reasons why some investigations do not associate IBM with cardiovascular risk [14, 15].

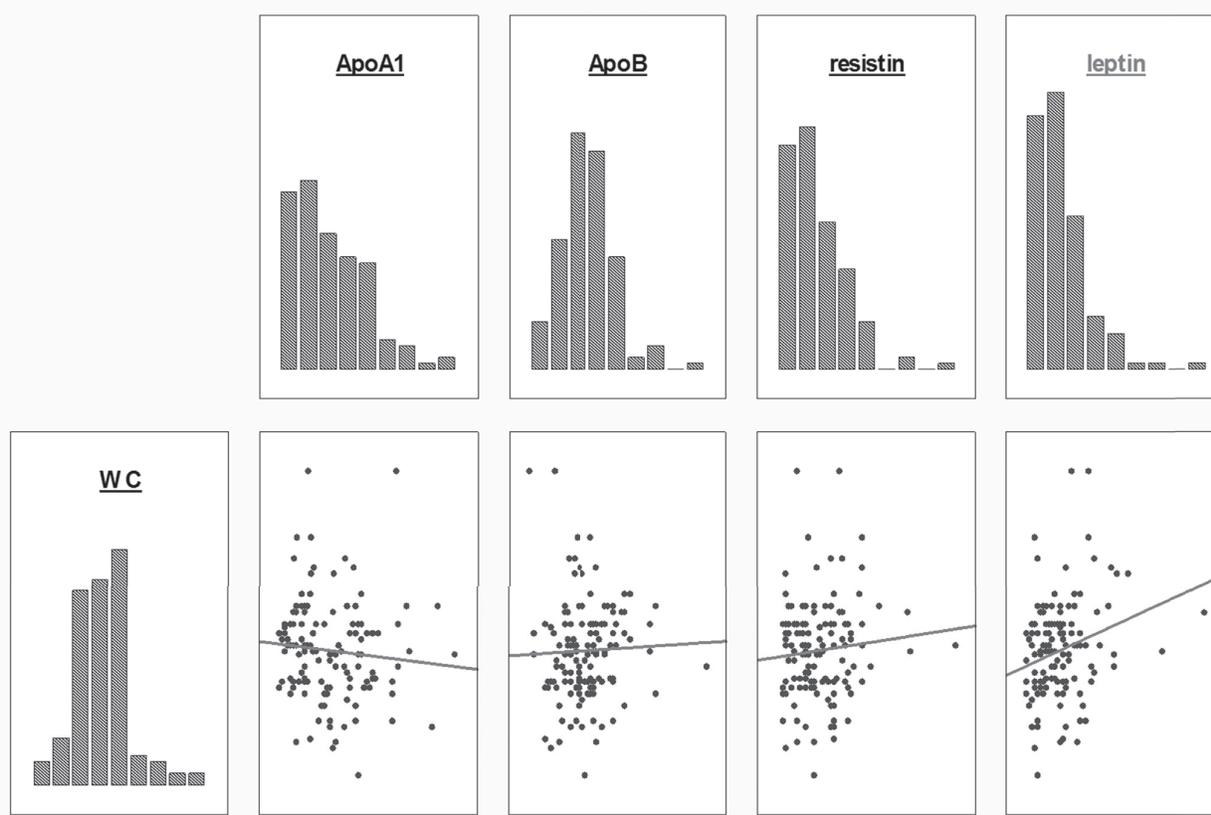
On analyzing WC and the additional markers of cardiovascular risk, we found a strong positive correlation of WC only with plasma leptin, and no correlation with apolipoproteins and resistin (Fig. 2).

Epicardial fat appears to be the source of proinflammatory and prothrombotic cytokines, like the tumor necrosis factor (TNF $\alpha$ ), monocyte chemoattractant protein (MCP-1), interleukins 1 and 6 (IL-1, IL-6), resistin, omentin, leptin, visfatin, inhibitor of plasminogen tissue activator (PAI-1) and angiotensinogen [16]. We studied the hormone activity of the epicardial adipose tissue in 42 patients who underwent the myocardial revascularization surgery. It was then found that epicardial fat produces proinflammatory cytokines (TNF $\alpha$ , IL-1, IL-6) and chemokines MCP-1), thus strongly affecting the coronary arteries [16]. In women, the increase in EFT by 7 mm and more was associated with subclinical atherosclerosis of the coronary arteries [17]. In another clinical study ( $n=998$ ), the EFT increase detected by

**Figure 1**  
EFT correlation analysis



**Figure 2**  
WC correlation analysis



computed tomography (CT) was associated with high risk of CHD during the 5-year supervision, regardless of sex [18].

In our analysis of the relationship of epicardial adiposity and severity of coronary arteries involvement, and based on the results of the coronary angiography, the patients were grouped by the number of affected arteries. The first group included patients with single-vessel involvement of coronary arteries ( $n=27$ ), the second group: 2-vessel involvement ( $n=39$ ), the third one: 3-vessel affection ( $n=54$ ), and the fourth group consisted of patients with multiple stenoses and diffuse lesion of coronary arteries ( $n=18$ ). Analysis of the mean indices of EFT showed that the patients with multiple stenoses had the highest mean EFT - 10 (8;10) mm, while the lowest ones - 3 (2;5) mm and 4 (2;8) mm were registered in patients with single- and two-vessel involvement, respectively. In the groups, a significant difference ( $p=0.004$ ) was observed.

Figure 3 presents the coronary angiography and echocardiography results of patients with multiple stenoses of the coronary arteries and epicardial adiposity of 13 mm.

We analyzed the WC of patients affected with different coronary artery conditions and found that the mean value in patients with single-vessel involvement was  $97.12 \pm 10.17$  cm; two-vessel -  $95.23 \pm 10.68$  cm; three- vessel -  $100.8 \pm 9.9$  cm and diffuse lesion -  $101.38 \pm 15.19$  cm. Although the mean values of WC ( $p=0.231$ ) were increased, the difference among the groups was insignificant.

Following this, the patients were divided into two

groups based on the severity of the coronary artery stenosis. The first group consisted of seriously ill patients (with significant lumen stenoses ( $\geq 70\%$ ) of one or several coronary arteries) who were in need of myocardial revascularization ( $n=82$ ). The patients with insignificant stenoses ( $<70\%$ ) of one or several coronary arteries fell into the second group ( $n=56$ ). To diagnose significant stenosis of the coronary arteries ( $\geq 70\%$ ), the information value of EFT and WC was assessed using the ROC-analysis (Fig. 4).

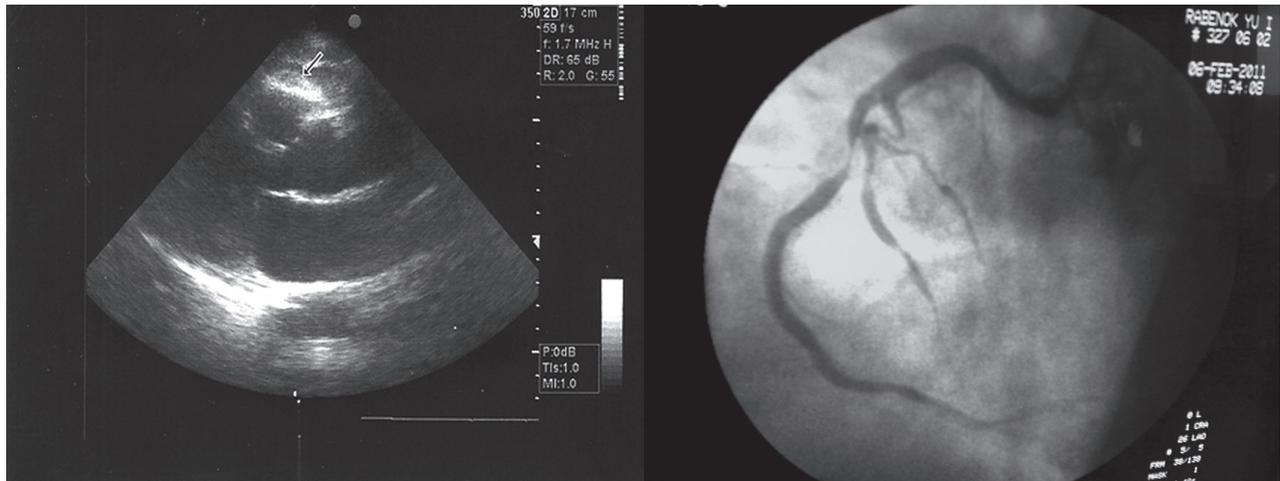
The area under the ROC-curve (AUC) was estimated as a diagnostic efficiency criterion (Fig. 4). It was 0.740 which is evidence of EFT as a classifier ( $p=0.0001$ ). Statistically, the value obtained (AUC) differs from the area above the diagonal curve (0.5) with  $p=0.0001$ . The ROC-model sensitivity (a share of true-positive results—the presence of significant stenosis) is 80.4%; specificity (share of true-negative results – the absence of significant stenosis) is 67.6%. The cut-off value for EFT makes up 6 mm (Fig. 5) that is an optimal threshold for revealing significant stenoses of the coronary arteries ( $\geq 70\%$ ) in obese patients.

The data obtained are corroborated by the Korean research ( $n=557$ ), which reports that a value above 3 mm in EFT indicates an independent risk factor for coronary atherosclerosis associated with stenoses of more than 50% arteries [19].

We also performed the ROC-analysis to assess WC sensitivity and specificity for diagnosing significant coronary atherosclerosis. The area included in the ROC-curve (AUC)

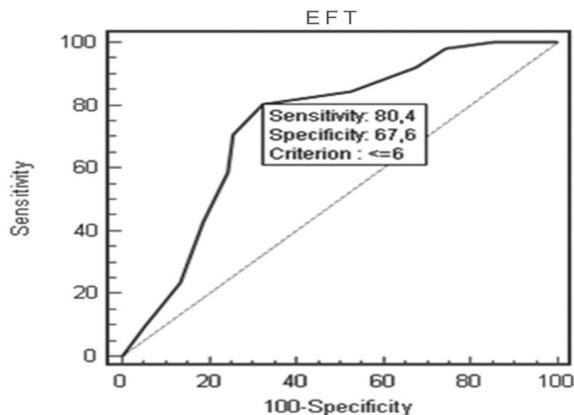
**Figure 3**

Coronary angiography and echocardiography of patients with multiple stenoses of coronary arteries and epicardial adiposity



**Figure 4**

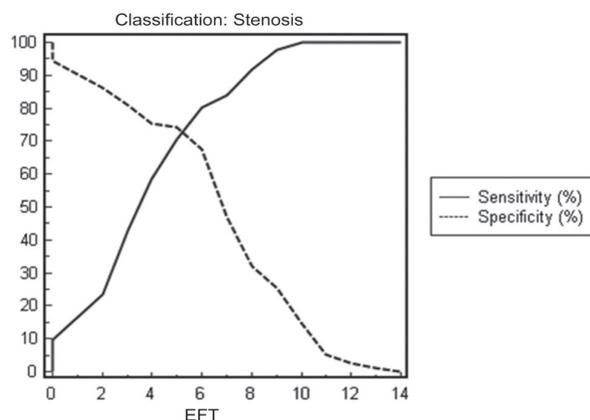
ROC-curve estimations of EFT for revealing significant coronary atherosclerosis



**Notes:** Area under the ROC curve (AUC)=0.740;  
Standard error=0.0437;  
95% Confidence interval 0.653 to 0.814;  
z statistic=5.487;  
Significance level P (Area=0.5)=0.0001

**Figure 5**

Cut-off value for EFT indicator



was 0.505, which is proof of the poor quality of the given classifier because it is less than 0.60. The standard error of AUC made up 0.044. The confidence interval of AUC at 95% probability ranged between 0.430 and 0.580 (0.505±0.044; p=0.95). The AUC obtained did not statistically differ from the area above the diagonal curve (0.5) with p=0.9107. The ROC-model sensitivity for WC (a share of true-positive results, indicating the presence of significant stenosis) is 65.7%, which is satisfactory, as it exceeds 60%. Specificity (a share of true-negative results, indicating the absence of significant stenosis) is 39.5%, which is a poor result, because it is less than 60%. Therefore, if we compare abdominal obesity and epicardial adiposity, EFT appears to be more informative than WC to diagnose significant coronary atherosclerosis.

Based on the univariate binary logistic analysis, we studied the influence of various factors (predictors) on the development of significant atherosclerosis. Along with EFT, age, basic (WC, TG, HDL, glucose, sBP, dBP) and additional (ApoA1, ApoB, leptin, resistin) metabolic risk factors were considered as predictors.

The analysis clearly demonstrates that EFT and age are significant predictors of stenosing coronary atherosclerosis in obese patients (Table 3).

Besides, the relationship existing between leptin, resistin, WC and stenosing coronary atherosclerosis was established. It was noted, that on comparison of abdominal obesity and epicardial adiposity as predictors of coronary atherosclerosis, EFT (OR 4.44; 95% CI: 2.06-9.59; p<0.001) appeared to be more informative than WC (OR 1.65; 95% CI: 0.72-3.80; p=0.018). Values of lipidic metabolism (TG, HDL, ApoA1, ApoB), sBP and dBP were not informative, as prior to the coronary angiography, more than 80% of the patients examined from a risk group underwent hypolipidemic and hypotensive treatment during one to six months.

## Discussion

Thus, in both groups: with AO, WC>94 cm and without AO, no significant metabolic and hormone disorders

**Table 3***Data on the binary logistic regression: predictors of the presence of significant coronary atherosclerosis ( $\geq 70\%$ )*

Predictors	OR	95%CI	$\chi^2$	P
Age	6.56	2.59-16.60	10.12	0.001
EFT	4.44	2.06-9.59	22.36	<0.001
Leptin	3.50	1.46-8.37	11.65	<0.001
Resistin	3.13	1.32-7.42	10.89	<0.001
WC	1.65	0.72-3.80	5.55	0.018

**Notes:** OR – Odds Ratio; 95% CI - 95% Confidence Interval.

were found. Perhaps, it may be explained that the group with AO consisted of patients with visceral obesity, which directly induces metabolic and hormone disorders, as the ones with the larger WC due to SCF and its characteristic constitution. Moreover, the WC index did not show any positive correlation with markers of cardiovascular risk, i.e. ApoA1, ApoB and resistin - a visceral fat hormone, which plays an important role in insulin resistance and atherogenesis. The increased mean values of TG, glucose, leptin and lower HDL were registered in patients with  $WC \geq 102$  cm and evident AO. In clinical practice, such obesity is associated with severe pathology that impedes pre- and postexposure prevention of cardiovascular diseases.

It was quite clear that EF accumulation is associated with progressive visceral obesity [11]. For instance, our studies of patients with CHD show that the increase in EFT causes more severe metabolic disorders. Moreover, we also established the relationship between EFT and plasma lipids (HDL, TG), apolipoproteins (ApoA1, ApoB), visceral fat hormones (leptin, resistin). The results obtained are supported by research conducted earlier reporting on the positive correlation between EFT and blood pressure, glucose in the blood, proinflammatory markers [20] and the relation between EF and dBP, C-reactive protein, fibrinogen, insulin resistance index HOMA – IR and plasma lipids [12].

Patients with badly affected coronary arteries, showed increased EFT mean values. In obese patients,  $EFT = 6$  mm is informative for the ROC-curve-based diagnostics of stenosing coronary atherosclerosis. We used the univariate binary logistic analysis to confirm the data obtained. Interestingly, the analysis established no relationship between WC and coronary atherosclerosis.

## Conclusion

Our findings showed that the EFT increase in patients with CHD is associated with more severe involvement of the coronary arteries, whereas the WC analysis did not reveal a similar relationship. It clearly follows from the results of the echocardiography that EFT is a factor influencing the development of coronary atherosclerosis. Hence, EFT in obese patients can be used as a noninvasive marker to indicate the presence of subclinical stenoses of the coronary arteries, and the obtained  $EFT > 6$  mm may serve as a reference point

for further investigations that could include other groups of patients without established CHD.

## References

1. Eckel RH, York DA, Rossner S, et al. American Heart Association. Prevention Conference VII: obesity, a worldwide epidemic related to heart disease and stroke: executive summary *Circulation* 2004; 110:2968-2975.
2. Enwald HP, Huotari ML. Preventing the Obesity Epidemic by Second Generation Tailored Health Communication: An Interdisciplinary Review *J Med Internet Res* 2010; 12:24-30.
3. Kaidar-Person O, Bar-Sela G, Person B. The Two Major Epidemics of the Twenty-First Century: Obesity and Cancer *Obes Surg* 2011; Aug 13 [Epub ahead of print].
4. Douketis JD, Sharma AM. Obesity and cardiovascular disease: pathogenic mechanisms and potential benefits of weight reduction *Semin Vasc Med* 2005; 2325:25-33.
5. Pérez PA, Muñoz YJ, Cortés BV. Obesity and cardiovascular disease *Public Health Nutr* 2007; 10:1156-63.
6. Padwal RS, Sharma AM. Prevention of cardiovascular disease: Obesity, diabetes and the metabolic syndrome *Can J Cardiol* 2010; 26:18-20.
7. Gruberg L, Weissman NJ, Waksman R, et al. The impact of obesity on the short-term and long-term outcomes after percutaneous coronary intervention: the obesity paradox? *J Am Coll Cardiol* 2002; 39:578-584.
8. Juge-Aubry CE, Henrichot E, Meier CA. Adipose tissue: a regulator of inflammation *Best Pract Res Clin Endocrinol Metab* 2005; 19:547-566.
9. Brook RD. Obesity, weight loss, and vascular function. *Endocrine*. 2006; 29 (1):21-25.
10. Iacobellis G, Willens HJ. Echocardiographic Epicardial Fat: A Review of Research and Clinical Applications *JASE* 2009; 22:1311-1319.
11. Iacobellis G, Assael F, Ribaldo MC, et al. Epicardial fat from echocardiography: a new method for visceral adipose tissue prediction *Obes Res* 2003; 11:304-310.

12. Aydın H, Toprak A, Deyneli O, et al. Epicardial Fat Tissue Thickness Correlates With Endothelial Dysfunction and Other Cardiovascular Risk Factors in Patients With Metabolic Syndrome *Metab Syndr Relat Disord* 2010; 8:229-234.
13. Pierdomenico SD, Pierdomenico A.M, Neri M, et al. Epicardial Adipose Tissue and Metabolic Syndrome in Hypertensive Patients With Normal Body Weight and Waist Circumference *Am J Hypertens* 2011 Aug 4 [Epub ahead of print].
14. Lofgren I, Herron K, Zern T. Waist Circumference Is a Better Predictor than Body Mass Index of Coronary Heart Disease Risk in Overweight Premenopausal Women *J Nutr* 2004; 134:1071-1076.
15. Kahn HS. The «lipid accumulation product» performs better than the body mass index for recognizing cardiovascular risk: a population-based comparison *BMC Cardiovasc Disord* 2006; 6:5-26.
16. Mazurek T, Zhang L, Zalewski A, et al. Human epicardial adipose tissue is a source of inflammatory mediators *Circulation* 2003; 108:2460–2466.
17. Eroglu S, Sade LE, Yildirim 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; 19:211–217.
18. Ding J, Hsu FC, Harris TB. The association of pericardial fat with incident coronary heart disease: the Multi-Ethnic Study of Atherosclerosis (MESA) 1,2,3 *Am J Clin Nutr* 2009; 90:499-504.
19. Ahn SG, Lim HS, Joe DY. Relationship of epicardial adipose tissue by echocardiography to coronary artery disease *Heart* 2008; 94:7-13.
20. Malavazos AE, Ermetici F, Cereda E, et al. Epicardial fat thickness: relationship with plasma visfatin and plasminogen activator inhibitor-1 levels in visceral obesity. *Nutr Metab Cardiovasc Dis*. 2008; 18(8):523-530.